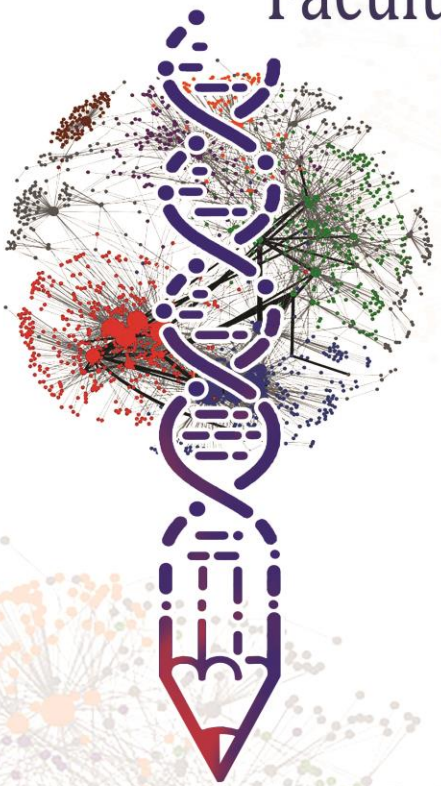
4th International Iranian Conference on

BIOINFORMATICS

Faculty of Engineering, University of Zanjan

February 4-6, 2025



MAIN TOPICS :

- Systems Biology
- AI & Machine Learning
- Structural Bioinformatics
- Biological Sequences Analysis
- Modelling in Computational Biology
- Computational Drug Design and Discovery

دانشگاه زنجان

IBIS Iranian Bioinformatics Society

ISC Islamic World Science Citation Center

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Detailed Schedule

5th February 2025

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Feb 5, 2025

4th International Iranian Conference on Bioinformatics

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07:45-08:15	**Welcome reception**	
08:15-09:00	**Conference opening ceremony**	
09:00-09:45	 **Dr. Fatemeh Zare**	**Computational Innovation in the Design of Biological Molecules**
09:45-10:05	Amir Mahdi Zhalefar	Enhancing Drug-Target Interaction Predictions through the Integration of Self-Organizing Maps and Graph-Based Representation Learning
10:10-10:30	Hassan Alavi	In-silico Drug Generation using Masked Language Modeling
10:30-11:00	Break and Poster Presentations	
11:00-11:45	 **Dr. Chuan Xu**	**CellTypist and CellHint: Towards Automated Annotation and Integration of Single-Cell Data**
11:45-12:05	Seyedeh Fatemeh Sajjadi	Comprehensive Integrated Single-Cell RNA Sequencing Analysis of Brain Metastasis and Glioma Microenvironment: Contrasting Heterogeneity Landscapes
12:10-12:30	Amir Ebrahimi	A Contrastive Learning Framework for Single-Cell Multi-Omics Data Integration
12:30-14:00	Lunch and Poster Presentations	
14:00-14:45	 **Dr. Mahya Mehrmohammadi**	**Classifying Somatic Mutation using Machine Learning-Based Approaches**
14:45-15:05	Hassan Salarabadi	HETLN: A Hybrid Ensemble Model for Precise Localization of Breast Cancer Tumors in Radiotherapy Treatment
15:05-15:25	Donya Afshar Jahanshahi	Comprehensive Gene and Protein Catalog for Antimicrobial Environments: A Metagenomic Approach to Mitigate Antimicrobial Resistance
15:25-15:45	Zahra Bayat	Uncovering Disrupted Cell-Cell Interactions in Alzheimer's Disease Using Variational Graph Autoencoders on Single-Cell Spatial Transcriptomics Data
15:45-16:30	Break and Poster Presentations	
16:30-17:15	 **Prof. Benjamin Raphael**	**Machine learning for Spatial Biology**
17:30-18:15	 **Dr. Mohammad Lotfollahi**	**Generative Machine Learning to Model Cellular Perturbations**

Plan Table

Detailed Schedule

6th February 2025

ICB13 Iranian Conference on Bioinformatics — سیزدهمین همایش ملی بیوانفورماتیک ایران

Plan Table
Feb 6, 2025

4th International Iranian Conference on Bioinformatics

Time	Speaker	Title
09:00-09:45	 **Dr. Leila Safari**	**Leveraging Language Models and Deep Transformer Networks in CRISPR-Based Genome Editing**
09:45-10:05	Roghayyeh Alipanahi	DTMP-Prime: A Deep Transformer-based Model for Predicting Prime Editing Efficiency and PegRNA Activity
10:10-10:30	Marzieh Khodadadi	Predicting Anticancer Drug Repurposing Candidates using Knowledge Graphs
10:30-11:00	Break and Poster Presentations	
11:00-11:45	 **Dr. Sajjad Gharaghani**	**From Traditional Drug Design to Deep Generative Models: Revolutionizing Drug Discovery**
11:45-12:05	Sajede Fadaei	A Knowledge Graph-Based Approach for Drug Repurposing Using Graph Neural Networks and Language Models
12:10-12:30	Sobhan Ahmadian Moghadam	Integrating Biological Networks and Deep Learning for Microbe-Disease Prediction
12:30-14:00	Lunch and Poster Presentations	
14:00-14:45	 **Prof. Sofia Kossida**	**IMGT®, the International ImMunoGeneTics Information System® Current Endeavors and Future Perspecrives**
14:45-15:05	Shahla Sahraei	Bioinformatic Approach to Predict the Regulatory Mechanisms: TF–miRNA–mRNA–lncRNA Network during Cluster Development in Grape
15:05-15:25	Ali Yazdizadeh Kharrazi	Orthology inference at scale with FastOMA
15:25-15:45	Break and Poster Presentations	
15:45-16:30	 **Dr. Alireza Khanteymoori**	**Democratising Bioinformatics: Accessible and Scalable Data Analysis with Galaxy**
16:30-17:00	**Conference closing ceremony**	

Keynote Speaker

Dr. Fatemeh Zare-Mirakabad

Main research areas

Her research focuses on various aspects of computational biology, including drug repositioning, the prediction of adverse drug reactions, bioinformatics sequences, biological networks, and structural bioinformatics.

Affiliations

- Assistant Professor of Computer Science at Amirkabir University of Technology
- Founder of the Computational Biology Research Center (CBRC)

Brief research description

Dr. Zare-Mirakabad's work aims to bridge the gap between computational techniques and biological data to provide innovative solutions for drug development and disease management. Through her research, she contributes to advancing the understanding of drug efficacy and safety while exploring the structural complexities of biological systems.

Computational Innovation in the Design of Biological Molecules

Biological features and embeddings are essential for molecular representation, enabling a structured and informative encoding of molecular properties for computational analysis. Traditional representations, such as SMILES and molecular fingerprints, primarily capture structural patterns, whereas biological features (e.g., physicochemical properties and bioactivity profiles) provide deeper insights into molecular function. Machine learning models, particularly transformer-based architectures like ChemBERTa and ProtALBERT, generate embeddings that capture complex biochemical and biophysical properties. In this study, we analyze these models to assess their ability to encode relevant molecular features. We compare their embeddings with standard biochemical and biophysical descriptors, evaluating their effectiveness in molecular property prediction tasks. Our findings reveal the strengths and limitations of each model in representing molecular complexity, offering insights into optimizing transformer-based embeddings for bioinformatics applications.

Keynote Speaker

Dr. Chuan Xu

Main research areas

His research focuses on understanding the genetic principles behind complex tissue organization and function, leveraging cell-atlasing and cellular genetics to map cells in the human body.

Affiliations

- Senior researcher at the University of Cambridge, Cambridge Stem Cell Institute, in Dr. Sarah Teichmann's group

Brief research description

He earned his Ph.D. in Computational Biology from the CAS-MPG Partner Institute for Computational Biology in 2018 and later conducted postdoctoral research at Yale School of Medicine, investigating how evolution and development shape the molecular organization of the brain. Since joining the Teichmann lab in 2020, he has been a key contributor to CellTypist and CellHint, automated tools for annotating, harmonizing, and integrating single-cell RNA sequencing (scRNA-seq) datasets.

Keynote Speaker

Dr. Mahya Mehrmohamadi

Main research areas

Her research is focused on bioinformatic design of molecular diagnostics, with primary interests in epigenomics, cancer genomics, cell-free DNA-based liquid biopsy, NGS data analysis, machine learning, cancer metabolomics and systems biology.

Affiliations

- Assistant Professor of Biotechnology at University of Tehran

Brief research description

Dr. Mehrmohamadi received her PhD in Genetics and Genomics from Cornell University. Her work involved deciphering the metabolic regulation of cancer cell epigenetics through computational approaches. She completed her postdoctoral training at the Cancer Institute of Stanford University, where she developed a novel liquid biopsy test based on cell-free DNA fragmentation.

In addition to her academic research, Dr. Mehrmohamadi has years of valuable experience in the biotechnology industry, including positions at renowned liquid biopsy companies in the US. Currently, she is collaborating with ReNAP to develop computational pipelines for cancer vaccine design.

Classifying somatic mutation using machine learning based approaches

Next generation genome sequencing technologies have enabled rapid and reliable identification of mutations. Despite years of algorithm development and data analysis standardization, correctly classifying mutations of interest remain challenging across many clinical contexts. As such, distinguishing between pathogenic cancer-associated mutations and other somatic variants present in cell-free DNA (cfDNA) is a difficult task in the field of liquid biopsy. This distinction is critical, since the misclassification of mutations stemming from clonal hematopoiesis (CH) as tumor-derived and vice versa could result in inaccurate diagnoses and inappropriate therapeutic interventions for patients. We applied deep learning to this issue and obtained improved identification of mutation origins. We demonstrate the potential of machine learning and feature prediction to stand as a robust and cost-effective alternative to conventional multi-analyte sequencing methods.

Keynote Speaker

Prof. Benjamin J. Raphael

Main research areas

His work focuses on cancer evolution, tumor heterogeneity, genetic network analysis, and structural variation in human and cancer genomes. His algorithms have played a crucial role in major cancer genomics initiatives, including The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC). He also co-led the TCGA Pancreatic Adenocarcinoma project and the network analysis in the ICGC Pan-Cancer Analysis of Whole Genomes (PCAWG).

Affiliations

- leading researcher in computational biology, specializing in combinatorial and statistical algorithms for interpreting biological data

Brief research description

With a strong mathematical foundation—an B.S. from MIT and a Ph.D. from UCSD—Prof. Raphael has made significant contributions to bioinformatics. Before joining Princeton, he was a faculty member at Brown University, where he also directed the Center for Computational Molecular Biology. His outstanding contributions have earned him prestigious awards, including the Alfred P. Sloan Research Fellowship and the NSF CAREER award. He is also an elected Fellow of the International Society for Computational Biology (ISCB).In addition to her academic research, Dr. Mehrmohamadi has years of valuable experience in the biotechnology industry, including positions at renowned liquid biopsy companies in the US. Currently, she is collaborating with ReNAP to develop computational pipelines for cancer vaccine design.

Keynote Speaker

Dr. Mohammad Lotfollahi

Main research areas

His work primarily focuses on leveraging artificial intelligence and advanced experimental techniques to engineer cells, modulate their responses to disease and perturbations, and apply these innovations in diagnostics, therapeutics, and drug discovery. He has received multiple awards for his research and has been featured in various press outlets and journals.

Affiliations

- Faculty member at the Wellcome Sanger Institute and the Cambridge School of AI in Medicine at the University of Cambridge
- Member of the European Laboratory for Learning and Intelligent Systems (ELLIS)

Brief research description

In addition to his academic work, he has experience in both biotech and tech industries, having worked at Relation Therapeutics and Cellarity, as well as Facebook AI.

Keynote Speaker

Dr. Leila Safari

Main research areas

Her main research interests include Natural Language Processing (NLP), information retrieval, Clinical Information Systems (CIS) and text mining.

Dr. Safari received her PhD in Software Engineering from the University of Sydney, Australia, under the supervision of Professor Jon Patrick. Her thesis focused on developing a Clinical Data Analytics Language (CliniDAL).

Affiliations

- Assistant Professor at the Department of Computer & Electronic Engineering, University of Zanjan

Brief research description

She has also worked with Professor Jon Patrick at Innovative Clinical Information Management Systems (iCIMS), Australia's award-winning cancer informatics solutions, developing software that integrates backend NLP solutions into user-friendly CIS Interfaces, enabling clinical specialists to use them for Data Analytics and Question Answering purposes.

Leveraging Language Models and Deep Transformer Networks in CRISPR-Based Genome Editing

The recent advancements in CRISPR-based genome editing, coupled with the progress in AI technologies sparked the promise of significant breakthroughs in the field of molecular biology. However, the complexity of biological systems and the vast amount of genomic data pose considerable challenges in designing efficient and accurate CRISPR systems. This talk highlightsthe potential of advanced deep transformer networks and large language models (LLMs) to encounter challenges in CRISPR-based genome editing and enhancing the accuracy and efficiency of edits. The capability of these models in capturing intricate patterns and contextual understanding within biological sequences, including DNA, RNA, and protein data, suggest significant advancements in guide RNA (gRNA) design, off-target effect prediction, and on-target activity estimation. This could lead to increased safety and efficacy in genome editing, while also reducing costs, saving time, and maintaining accuracy comparable to experimental observations.

Keynote Speaker

Dr. Sajjad Gharaghani

Main research areas

His research encompasses chemoinformatics, pharmacoinformatics, chemogenomics, biological networks, Computer-Aided Drug Design (CADD), drug-target interactions, and drug discovery.

Affiliations

- Associate Professor and the head of the Department of Bioinformatics at the University of Tehran
- founder of the Laboratory of Bioinformatics and Drug Design (LBD)

Brief research description

His work includes the development of predictive models for drug-target interactions using deep learning approaches, such as TripletMultiDTI, and applying support vector machines for chemoinformatics tasks. He also explores biological networks and integrates computational methods with experimental data to enhance the drug discovery process and deepen the understanding of complex biological systems.

From Traditional Drug Design to Deep Generative Models: Revolutionizing Drug discovery

Drug discovery has undergone a transformative shift from traditional design methodologies to the integration of deep generative models, revolutionizing the field. Conventional drug design, rooted in structure-based and ligand-based approaches, has long depended on structure-activity relationships, empirical screening, and high-throughput experimentation. While effective, these methods are often time-consuming, costly, and constrained by the vast chemical space. Deep generative models, a class of artificial intelligence (AI) techniques powered by deep learning, offer a data-driven approach to generate novel molecular structures with desired pharmacological properties, thereby accelerating the discovery process. This presentation will provide an overview of the transition from traditional drug design techniques to cutting-edge generative models, emphasizing their impact on virtual screening, lead optimization, and de novo drug design. Key advancements such as variational autoencoders (VAEs), generative adversarial networks (GANs), and reinforcement learning frameworks will be discussed in the context of their ability to explore chemical space more efficiently and identify promising drug candidates. Despite their potential, the adoption of deep generative models presents several challenges, including data quality, model interpretability, and regulatory hurdles that must be addressed for widespread implementation. By integrating classical methodologies with modern AI-driven approaches, deep generative models represent a paradigm shift that holds the promise of expediting drug development while reducing costs and improving success rates.

Keynote Speaker

Prof. Sofia Kossida

Main research areas

A leading expert in immunoinformatics, she oversees IMGT®, the international ImMunoGeneTics® information system, which has been a key resource in immunogenetics since 1989. IMGT® integrates high-quality genomic, proteomic, and structural data for immunoglobulins and T-cell receptors across various species.

Affiliations

- Professor at the University of Montpellier, France
- Director of IMGT at CNRS (National Center for Scientific Research)

Brief research description

Prof. Kossida has extensive experience in both the public and private sectors and has made significant contributions to bioinformatics, with over 120 scientific publications and 23 patent publications. She earned her DPhil in Computational Biology and Viral Phylogenetics from Oxford University, UK, and completed her postdoctoral research at Harvard University, contributing to the FlyBase project.

Keynote Speaker

Dr. Alireza Khanteymoori

Main research areas

His work bridges AI and neuroscience, with a strong background in machine learning and bioinformatics.

Affiliations

- Researcher and lecturer in Artificial Intelligence and Cognitive Neuroscience at the Psychology Department, University of Freiburg

Brief research description

Previously, Dr. Khanteymoori was a researcher in Prof. Rolf Backofen's lab and a member of the Galaxy Project team—a widely used biomedical computational workbench supporting tens of thousands of scientists worldwide. His expertise spans supervised machine learning and its applications in biomedicine and neuroscience.

SYSTEMS BIOLOGY

Topics

Systems biology is an interdisciplinary field that seeks to understand complex biological systems by integrating data from molecular, cellular, and organismal levels, focusing on interactions and dynamics rather than isolated components.

The roots of systems biology can be traced back to the early 2000s when advancements in high-throughput technologies, such as genomics and proteomics, allowed scientists to begin studying biology in an integrated way. However, the roots of systems thinking in biology extend much further, with systems theory influencing the development of computational biology since the mid-20th century. Early pioneers, including Ludwig von Bertalanffy, whose work on general system theory laid the groundwork for modeling complex systems, and Alfred J. Lotka and Richard A. Fisher, who contributed to mathematical biology, helped shape the conceptual basis of systems biology.

SYSTEMS BIOLOGY

A major turning point in the evolution of systems biology was the advent of the Human Genome Project in the late 20th century, which provided the genomic data necessary for the systems biology approach. Key figures such as Leroy Hood, one of the pioneers of systems biology, advanced the idea of using quantitative data to model biological systems comprehensively. This foundational work has led to an explosion of research, with systems biology now playing a crucial role in understanding complex diseases, gene regulation, metabolic networks, and cell signaling.

Early research in systems biology primarily focused on the development of computational models to predict the behavior of biological systems, using tools like gene expression profiling and metabolic flux analysis. Today, research has expanded to include the integration of data from diverse sources, including transcriptomics, proteomics, metabolomics, and single-cell sequencing, enabling a more comprehensive understanding of biological processes. Current hot topics include network biology, synthetic biology, multi-omics integration, and personalized medicine.

Systems biology offers broad applications in drug development, complex disease modeling, and environmental biotechnology. Its strength lies in its capacity to deliver an integrated view of biological processes, enabling more accurate predictions of disease mechanisms and therapeutic responses. As the field continues to evolve, systems biology is expected to play a transformative role in advancing biomedical science and precision medicine.

Artificial Intelligence in Bioinformatics

Topics

Artificial Intelligence (AI) refers to the branch of computer science that involves the creation of systems and algorithms capable of performing tasks typically requiring human intelligence, such as learning, reasoning, and decision-making.

In bioinformatics, AI is used to analyze complex biological data, where algorithms identify patterns, predict outcomes, and discover new relationships in biological datasets. This process uses various techniques like machine learning, deep learning, and advanced computational models.

The integration of AI in bioinformatics began in the late 20th century when the need for advanced computational methods to process and interpret vast amounts of biological data became evident. Early AI techniques, such as rule-based systems and

decision trees, were applied to tasks like gene annotation and protein structure prediction. As data collection methods, like high-throughput sequencing and mass spectrometry, became more prevalent, AI methods evolved to handle the increasing complexity and volume of biological data.

A key milestone in the growth of AI in bioinformatics was the reemergence of deep learning techniques in the 2010s, which allowed for significant improvements in predictive accuracy, especially in tasks like protein structure prediction, gene expression analysis, and the identification of biomarkers. Notable breakthroughs, such as AlphaFold for protein structure prediction, highlight the power of AI to solve complex biological challenges that were previously thought to be intractable.

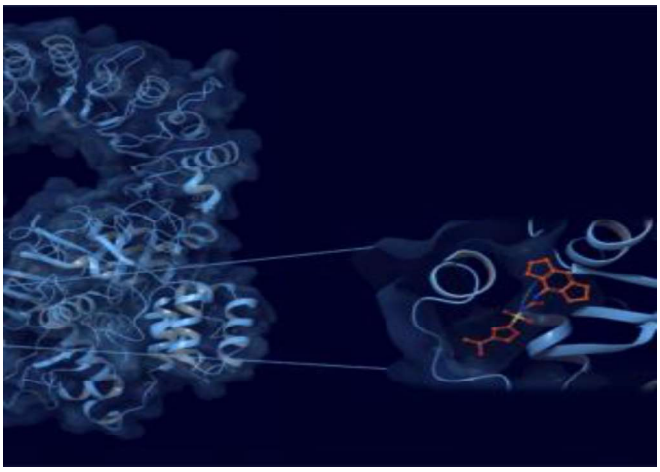
Early research in AI-driven bioinformatics primarily focused on the development of supervised learning models to classify genetic data and identify patterns in gene expression. Today, AI in bioinformatics spans a wide range of applications, including predicting protein-protein interactions, genomic data analysis, drug discovery, and personalized medicine. The use of reinforcement learning, unsupervised learning, and neural networks has expanded the scope of research, allowing for the analysis of increasingly complex datasets, such as single-cell RNA sequencing and multi-omics integration.

Artificial Intelligence in Bioinformatics

Furthermore, AI is being used to develop more accurate predictive models of disease progression, to identify new drug targets, and to design personalized treatment plans based on genetic and clinical data. The importance of AI in bioinformatics lies in its ability to process vast datasets at unprecedented speeds, uncover hidden patterns, and provide insights that drive forward the next generation of biomedical research and healthcare.

Structural Bioinformatics

Topics



Structural bioinformatics is a specialized branch of bioinformatics focused on the analysis and interpretation of the three-dimensional structures of biological macromolecules such as proteins, nucleic acids, and biomolecular complexes. The core objective is to understand how molecular structure governs biological function, using computational techniques to model, compare, and predict spatial conformations.

This field gained momentum alongside advances in experimental structure determination techniques, including X-ray crystallography, NMR spectroscopy, and cryo-electron microscopy. The accumulation of structural data in repositories such as the Protein Data Bank (PDB) highlighted the need for computational methods capable of efficiently handling and analyzing this information, leading to the establishment of structural bioinformatics as a critical domain within computational biology. Pioneers such as John Kendrew, who

contributed to early protein structure determination, and Michael Levitt, a Nobel laureate recognized for molecular modeling, significantly advanced this discipline.

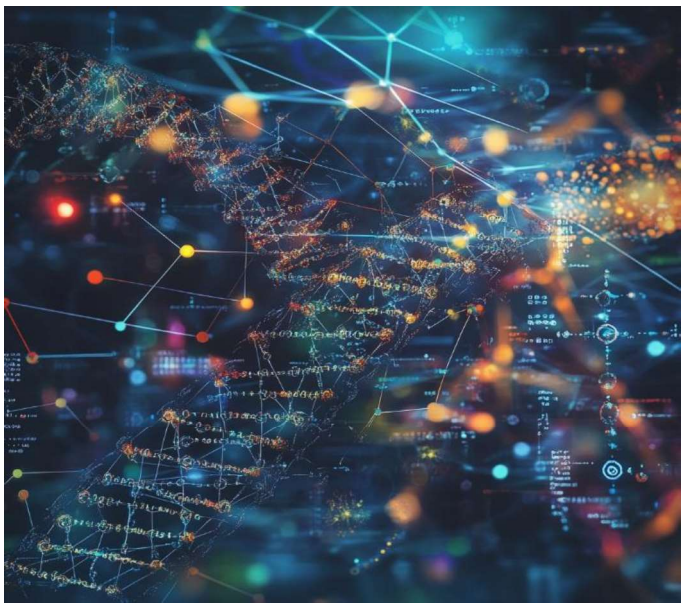
While early research was focused on individual structures, today's studies leverage machine learning, large-scale molecular models, and single-cell data to explore dynamic interactions, functional mechanisms, and therapeutic design with higher precision. Modern research tools, such as Rosetta for protein structure prediction, PyMOL for visualization, and GROMACS for molecular dynamics simulations, are widely used to explore biomolecular structures in greater detail. Current hot topics in structural bioinformatics include structural genomics, drug design, protein-protein interaction networks, and the application of deep learning to predict protein folding.

The applications of structural bioinformatics are crucial for many areas of biological research and medicine. It plays a fundamental role in drug discovery, where understanding the 3D structure of proteins can help identify potential drug targets and design molecules that interact effectively with these targets. Structural bioinformatics is also important in disease understanding, particularly in the study of diseases caused by protein misfolding, such as Alzheimer's and Parkinson's. Additionally, it contributes to synthetic biology, biotechnology, and the design of biomolecular sensors. Structural bioinformatics plays a pivotal

role in modern biomedical research by providing spatial insight into the molecular architecture that underpins life itself.

Mathematical Modeling in Bioinformatics

Topics



Mathematical modeling in bioinformatics involves the use of mathematical structures, equations, and algorithms to describe, analyze, and predict the behavior of biological systems at various levels. It plays a critical role in offering mechanistic insights into complex biological phenomena, from molecular interactions to population-level dynamics.

The foundations of this field trace back to the early 20th century, when mathematical models were first applied to the study of infectious disease spread—most notably, the SIR model developed in the 1920s. These early efforts laid the groundwork for future approaches in biological dynamics and therapeutic strategy design. With the emergence of molecular biology and

high-throughput data, mathematical modeling expanded to include gene regulatory networks, metabolic pathways, and cellular signaling dynamics.

Influential figures such as Alan Turing, who explored morphogenetic pattern formation, and Lionel Penrose, known for early biological modeling, contributed to shaping the theoretical backbone of this discipline. Also, the development of systems biology in the 2000s, which integrates data from multiple sources and uses mathematical models to study the dynamic interactions in biological networks, significantly advanced the field. Today, mathematical modeling combines differential equations, dynamic systems, probabilistic frameworks, and computer simulations to interpret experimental data and guide hypothesis generation. Current hot topics in mathematical modeling include synthetic biology, genomic prediction, machine learning-based modeling, and the modeling of disease dynamics.

The applications of mathematical modeling range from infectious disease modeling and systems stability analysis to drug design, PK/PD modeling, and predicting cellular responses to treatment. The strength of mathematical modeling lies in its ability to provide a reproducible, quantitative structure for biological analysis, which helps to predict the outcomes of interventions, optimize experimental designs, and uncover hidden relationships between biological components.

Biological Sequence Analysis

Topics

Biological sequence analysis is a core area of computational biology focused on the interpretation and comparison of DNA, RNA, and protein sequences. It serves as a foundation for genome annotation, gene identification, mutation detection, and functional prediction.

The field began to take shape with the advent of sequencing technologies in the 1970s, particularly the development of Sanger sequencing. The launch of the Human Genome Project in the 1990s marked a turning point, generating massive datasets that demanded advanced analytical tools. Pioneers like Margaret Dayhoff and Michael Waterman made significant contributions

through the development of sequence alignment algorithms and statistical models.

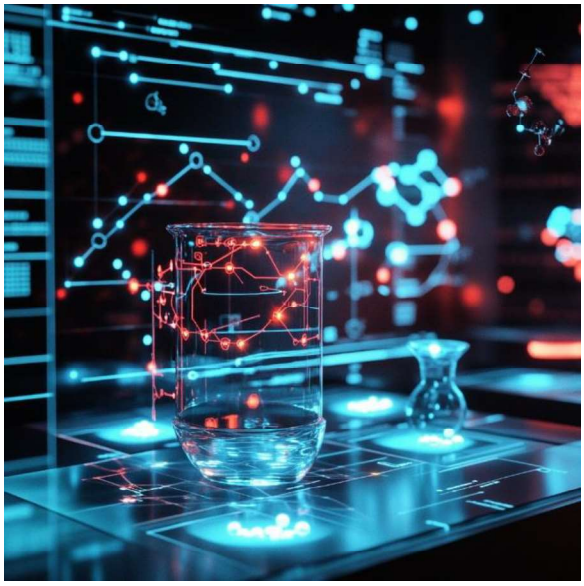
Initially, biological sequence analysis focused on the alignment and comparison of sequences to identify conserved regions and evolutionary patterns. Today, it encompasses a wide range of techniques, including sequence alignment, motif discovery, phylogenetic analysis, and functional annotation of genes and proteins.

With the development of next-generation sequencing technologies, biological sequence analysis has expanded to include large-scale analysis of genomic, transcriptomic, and metagenomic data. Current research is heavily focused on big data integration, machine learning for sequence prediction, and multi-omics data analysis.

The applications of biological sequence analysis include disease gene discovery, genetic variation analysis, vaccine design, and protein structure prediction. The power of sequence analysis lies in its ability to transform raw sequence information into biologically meaningful insights, making it indispensable in personalized medicine, cancer bioinformatics, and evolutionary research.

Computational drug design

Topics



Computational drug design is a field of bioinformatics that leverages algorithmic modeling to accelerate the identification and optimization of therapeutic compounds. Instead of relying on traditional trial-and-error approaches, it uses molecular simulations to anticipate how candidate drugs might interact within biological systems.

The origins of computational drug design date back to the 1960s when the first attempts were made to apply computer simulations to predict the binding of molecules to biological receptors. Over time, advancements in computational power and algorithms, along with the increasing availability of biological data, have transformed drug discovery from a trial-and-error process to a more rational, data-driven approach. Pioneers such as C. R. B. Kauffman and Paul A. Wade in the 1970s laid the early foundations of quantitative structure-activity relationship

(QSAR) models, which became a cornerstone of modern drug design.

A major milestone in computational drug design was the development of molecular docking techniques in the 1980s and 1990s, which allowed researchers to predict how small molecules bind to their target proteins. This was followed by the advent of high-throughput screening and the integration of large-scale databases such as the Protein Data Bank (PDB), enabling the identification of potential drug candidates with greater efficiency. Key figures in this period, like Robert Stroud and Brian Kobilka, have been instrumental in advancing the understanding of protein-ligand interactions, which is at the heart of computational drug design.

Initial efforts primarily focused on optimizing molecular structures using techniques like molecular dynamics and QSAR modeling. Today, the scope has broadened to include machine learning techniques, inverse molecular design, and hybrid modeling strategies. Public databases such as PDB, ChEMBL, and DrugBank now serve as valuable resources in this domain.

Computational drug design has critical applications in accelerating new drug discovery, developing targeted therapies for cancer and infectious diseases, and enabling personalized medicine. By significantly reducing the time and cost of pharmaceutical research, it is shaping the future of data-driven, precision healthcare. By providing a deeper understanding of molecular interactions, computational drug design is

revolutionizing the way new treatments are developed, offering the potential for more effective and tailored therapies for a wide range of diseases.

ICB13 Workshops

February 4, 9:00-17:00


Dr. Kaveh Kavousi — **Dr. Donya Afshar Jahanshahi**

University of Tehran

Metagenomic Data Analysis

Dr. Omid Abbaszadeh

University of Zanjan

Gene Regulatory Network Inference


Dr. Najmeh Salehi — **Ms. Mahshid Heidari**

University of Tehran

Protein Structure Prediction

Dr. Saeed Rahmani

University of Zanjan

Biomedical And Biological Information Retrieval in Action


Dr. Zahra Ghorbanali — **Mr. Hasan Alavi**

Amirkabir University

Making the Most of Less: Deep Learning with Limited Data

Committees

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Keynote Speaker's Abstract

Computational Innovation in the Design of Biological Molecules

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Biological features and embeddings are essential for molecular representation, enabling a structured and informative encoding of molecular properties for computational analysis. Traditional representations, such as SMILES and molecular fingerprints, primarily capture structural patterns, whereas biological features (e.g., physicochemical properties and bioactivity profiles) provide deeper insights into molecular function. Machine learning models, particularly transformer-based architectures like ChemBERTa and ProtALBERT, generate embeddings that capture complex biochemical and biophysical properties. In this study, we analyze these models to assess their ability to encode relevant molecular features. We compare their embeddings with standard biochemical and biophysical descriptors, evaluating their effectiveness in molecular property prediction tasks. Our findings reveal the strengths and limitations of each model in representing molecular complexity, offering insights into optimizing transformer-based embeddings for bioinformatics applications.

Keynote Speaker's Abstract

Classifying somatic mutation using machine learning based approaches

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Next generation genome sequencing technologies have enabled rapid and reliable identification of mutations. Despite years of algorithm development and data analysis standardization, correctly classifying mutations of interest remain challenging across many clinical contexts. As such, distinguishing between pathogenic cancer-associated mutations and other somatic variants present in cell-free DNA (cfDNA) is a difficult task in the field of liquid biopsy. This distinction is critical, since the misclassification of mutations stemming from clonal hematopoiesis (CH) as tumor-derived and vice versa could result in inaccurate diagnoses and inappropriate therapeutic interventions for patients. We applied deep learning to this issue and obtained improved identification of mutation origins. We demonstrate the potential of machine learning and feature prediction to stand as a robust and cost-effective alternative to conventional multi-analyte sequencing methods.

Keynote Speaker's Abstract

Leveraging Language Models and Deep Transformer Networks in CRISPR-Based Genome Editing

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The recent advancements in CRISPR-based genome editing, coupled with the progress in AI technologies sparked the promise of significant breakthroughs in the field of molecular biology. However, the complexity of biological systems and the vast amount of genomic data pose considerable challenges in designing efficient and accurate CRISPR systems. This talk highlights the potential of advanced deep transformer networks and large language models (LLMs) to encounter challenges in CRISPR-based genome editing and enhancing the accuracy and efficiency of edits. The capability of these models in capturing intricate patterns and contextual understanding within biological sequences, including DNA, RNA, and protein data, suggest significant advancements in guide RNA (gRNA) design, off-target effect prediction, and on-target activity estimation. This could lead to increased safety and efficacy in genome editing, while also reducing costs, saving time, and maintaining accuracy comparable to experimental observations.

Keynote Speaker's Abstract

From Traditional Drug Design to Deep Generative Models: Revolutionizing Drug Discovery

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Drug discovery has undergone a transformative shift from traditional design methodologies to the integration of deep generative models, revolutionizing the field. Conventional drug design, rooted in structure-based and ligand-based approaches, has long depended on structure-activity relationships, empirical screening, and high-throughput experimentation. While effective, these methods are often time-consuming, costly, and constrained by the vast chemical space. Deep generative models, a class of artificial intelligence (AI) techniques powered by deep learning, offer a data-driven approach to generate novel molecular structures with desired pharmacological properties, thereby accelerating the discovery process. This presentation will provide an overview of the transition from traditional drug design techniques to cutting-edge generative models, emphasizing their impact on virtual screening, lead optimization, and de novo drug design. Key advancements such as variational autoencoders (VAEs), generative adversarial networks (GANs), and reinforcement learning frameworks will be discussed in the context of their ability to explore chemical space more efficiently and identify promising drug candidates. Despite their potential, the adoption of deep generative models presents several challenges, including data quality, model interpretability, and regulatory hurdles that must be addressed for widespread implementation. By integrating classical methodologies with modern AI-driven approaches, deep generative models represent a paradigm shift that holds the promise of expediting drug development while reducing costs and improving success rates.

ICB13 -1001

New inhibitors of the Toxoplasmosis by in-silico drug repurposing

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The common treatment for toxoplasmosis was pyrimethamine. It has been noticed in recent years that this parasite becomes resistant to this treatment and it thus needs immediate alternative therapies. Materials and Methods: In this study, using drug repurposing and in silico methods we tried to make selective treatment by inhibiting the Calcium-Dependent Protein Kinase 1 from Toxoplasma gondii which does not exist in mammalians. We screened the FDA approved drugs by molecular docking and, after ranking them by their binding energies and inspecting the top scoring ones, we selected Cefpiramide, Ceftriaxone and Cefotiam as the hit compounds. Afterwards, we used molecular dynamic simulations to evaluate the hit compounds in a much more realistic environment. Through analyzing the results, we have found that all of the hit compounds are effective and can be strongly bound to the active site of the protein. They may therefore be potential candidates for the inhibition of Calcium-Dependent Protein Kinase 1 from Toxoplasma gondii. Given that the predicted compounds are FDA approved drugs, their toxicity profiles are established and their potentially predicted use can be evaluated in clinical trials.

Keywords: Toxoplasma Gondii, drug repurposing, docking, molecular dynamic

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ICB13 -1004

Leveraging Machine Learning Models for Virtual Screening of ZINC Database to Identify JAK1 Inhibitors

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JAnus Kinase 1 (JAK1) inhibitors have emerged as promising therapeutic agents, playing crucial roles within the Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway. This pathway is vital for modulating immune responses and regulating inflammation, particularly in autoimmune diseases, inflammatory disorders, and cancers (Lv and Qi, 2024). The current investigation employed various machine learning models such as Support Vector Machine (SVM), XGBoost, and Random Forest (RF) to identify potential JAK1 inhibitors. The model training and validation dataset consisted of 7,374 JAK1 inhibitors, with SMILES (Simplified Molecular Input Line Entry System) strings sourced from ChEMBL (Gaulton and Hersey, 2017), BindingDB (Gilson and Liu, 2016), and PubChem (Kim and Chen, 2019). Each inhibitor was annotated with an activity label 1 for active JAK1 inhibition and 0 for inactive compounds. Input for the machine learning models was generated by processing reference compounds with RDKit, a cheminformatics toolbox, to extract molecular descriptors characterized by MACCS (Molecular ACCess System) fingerprinting (Kong and Huang, 2023). The models' performance was evaluated using several metrics, including precision, F1 score, recall, specificity, and area under the curve (AUC). The achieved AUC-ROC scores were 0.97 for SVM, 0.981 for XGBoost, and 0.986 for the Random Forest model, demonstrating superior performance across all evaluation criteria. Due to its accuracy and robustness, the RF model was selected for virtual screening of the ZINC database (Sterling and Irwin, 2015.), a comprehensive repository of commercially available compounds. According to the predicted activity scores, the screening process identified several promising candidates as effective JAK1 inhibitors. Our findings emphasize the effectiveness of Random Forest combined with MACCS fingerprinting as a powerful method for the virtual screening of the kinase inhibitors. This approach facilitates the identification of potential JAK1 inhibitors for further experimental validation, potentially accelerating the discovery of new therapeutic agents for immunological and inflammatory diseases while providing insights for developing targeted therapies.

Keywords: Janus Kinase 1 Inhibitors, virtual screening, machine learning, MACCS fingerprint, random forest

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ICB13-1006

Machine Learning-Driven Discovery of JAK2 Inhibitors from ChEMBL Databank

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This study aims to identify potent JAnus Kinase 2 (JAK2) inhibitors using machine learning models for virtual screening of the small molecule subset of the ChEMBL databank. JAK2 is a key player in the JAK-STAT signaling pathway, which regulates immune responses and inflammation. Hence, JAK2 inhibitors have significant potential for treating autoimmune disorders, inflammatory diseases, and certain cancers (Lv and Qi, 2024). The machine learning models utilized in this study included Support Vector Machine (SVM), XGBoost, and Random Forest (RF). For training the models, datasets of 6,847 active JAK2 inhibitors were sourced from ChEMBL (Gaulton and Hersey, 2017), BindingDB (Gilson and Liu, 2016), and PubChem (Kim and Chen, 2019), along with 6,500 inactive compounds from the DUD-E database (Mysinger and Carchia, 2012). Each compound was labeled with an activity status (1 for active and 0 for inactive). Molecular characteristics were represented using extended connectivity fingerprints (ECFP4) (Baptista and Correia, 2022), alongside molecular descriptors such as molecular weight, polar surface area (PSA), and logP. The datasets were processed using RDKit to extract ECFP4 fingerprints and additional descriptors.The performance of the models was evaluated using several metrics, including accuracy and area under the curve (AUC). The Random Forest model achieved the highest performance, with a testing set accuracy of 0.9970 and an AUC of 0.9996. The SVM model achieved an accuracy of 99.63% and an AUC of 99.93%, while the XGBoost model had an accuracy of 99.55% and an AUC of 99.85%.Therefore, according to the performance data, the Random Forest model was used for virtual screening on a large-scale compound database containing 1,930,555 molecules. The model identified 99,653 compounds as potential JAK2 inhibitors (active) and classified the remaining 1,830,902 as inactive. These findings demonstrate that combining ECFP4 fingerprints and molecular descriptors with the Random Forest model highlights the effectiveness of machine learning-driven virtual screening in accelerating drug discovery for JAK2 inhibitors.

Keyword: Janus Kinase 2 Inhibitors, virtual screening, machine learning, random forest, ECFP4 fingerprints

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ICB13 -1007

Inhibition of angiogenesis based on the dynamic model of tumor growth using adaptive control method

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The primary objective of high-dose chemotherapy is to eradicate rapidly proliferating cancer cells. While conventional chemotherapy offers numerous benefits, it is often associated with significant adverse effects. Metronomic chemotherapy represents a novel approach that employs continuous and low-dose administration of chemotherapeutic agents for cancer treatment(Basar et al., 2024). This approach specifically targets endothelial cells active in new tumor blood vessels, which play a crucial role in tumor nutrition and growth(Lien et al., 2013). Mathematical and computational modeling, as a powerful tool, has revolutionized our understanding and treatment of diseases, especially cancer. By accurately simulating tumor growth and utilizing engineering principles, researchers seek to find the most effective treatment strategies. Biomedical control engineering, leveraging advanced mathematical models, offers an innovative approach to optimizing cancer treatment processes. By precisely designing treatment protocols and intelligently adjusting chemotherapy drug dosages, this approach significantly improves treatment outcomes and reduces side effects. Using this method, physicians will be able to design personalized treatments for each patient, tailored to the unique characteristics of the tumor and the patient's body(Kuznetsov, Clairambault and Volpert, 2021). This leads to increased treatment efficacy and reduced risk of drug resistance. Additionally, by optimizing drug dosage, it is possible to mitigate severe side effects associated with chemotherapy and significantly improve patients' quality of life. In this Article, a model reference adaptive controller is proposed to determine the optimal dosage of chemotherapy drugs. The controller is based on the well-established Hanfeld mathematical model, which describes the complex interaction between endothelial and tumor cells as a two-dimensional nonlinear dynamical system. This study proposes an efficient method to control tumor growth and reduce the volume of endothelial cells by optimizing drug consumption. Ultimately, the goal is to control tumor growth and increase the effectiveness of treatment. By applying the approach presented in this research, a significant decrease in drug consumption and a significant decrease in the volume of endothelial cells and tumors were observed. Simulation results indicate that within a relatively short period of 84 days, the system's variables decreased to below 1 mm3 and eventually reached a negligible value of 0.007 mm3.

Keywords: dynamic system of cancer, mathematical model of tumor, targeted therapy, adaptive control, optimal medication, metronomic chemotherapy.

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ICB13 -1009

Discovery of effective markers in the severity of the disease in the genome of Iranian patients with covid-19 and introduction of an effective plant in controlling the severity of the disease

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There are various miRNAs in the human body and today it has been confirmed that human miRNAs are effective in regulating the expression of viral genes and can be used to limit the infection caused by the virus. Also, nowadays, the transfer of plant miRNAs to the human body through their oral consumption or other methods is obvious, and therefore, one of the effects of medicinal plants in curing diseases can be the result of the function of this genetic structure of plants in the human body. In this study, the information related to the genetic sequence of viruses belonging to corona patients in the population of 110 Iranian patients, including 55 with high severity of the disease and 55 with low severity, was used. After extracting and storing the information of different human miRNAs, unique miRNAs (hsa-miR-548bb and hsa-miR-548b p, hsa-miR-548ay and hsa-miR-548aq) were present in patients with low severity. In the structure of the virus, a target sequence was identified for them and they were introduced as important markers affecting the severity of the disease. This finding indicates that the presence of the target sequence of these miRNAs in the genome of viruses extracted from patients with low severity indicates the possibility of their effect on the expression of viral genes and ultimately limiting the amount of virus replication of the severity of the disease. Since the use of medicinal plants to control and control the corona virus has less side effects and their availability is more for patients all over the world, in this research, with the aim of introducing an effective plant to control the coronavirus, to investigate the interactions of human target sequences and miRNA The results of ten types of plants along with the miRNAs extracted in the previous step that were related to the severity of the disease were performed using the mintRULS method. The output of the mintRULS model in predicting possible interactions showed that miRNAs of the cinnamon plant had the most interactions with the target sequences in the coronavirus, which were similar to the regions identified in the previous step.

Keywords: miRNAs, interactions, genetic sequence, effective plant, viruses

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ICB13 -1012

A Transformer-based Model for Diagnosis of Multiple Sclerosis using MRI Images

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Multiple Sclerosis (MS) is an autoimmune inflammatory disease that leads to the degradation of myelin in the central nervous system (brain and spinal cord), resulting in issues with movement, sensation, and balance. This disease has significant effects on individuals' quality of life. In this study, a Vision Transformer (ViT)-based model is proposed for diagnosing MS using MRI images. One of the primary challenges in this research is the lack of a standard dataset for implementing the proposed model. To address this issue, the two techniques of transfer learning and fine-tuning have been employed. Two relatively large datasets, including over 21,000 general image samples and 5,000 pneumonia images, were used for pre-training the proposed model. Additionally, a smaller dataset containing 3,427 MRI images associated with MS, labeled with patient classes and healthy classes in both axial and sagittal views (four classes in total), was used to fine-tune the ViT model for MS diagnosis. The results of MRI image classification with pre-trained models show an accuracy of 0.100 for the two-class scenario with both pre-training datasets, 0.96 for the four-class scenario with the pneumonia dataset, and 0.95 for the four-class scenario with the general dataset. These results indicate that dataset selection for fine-tuning the model in ViT implementation is highly significant. Moreover, the high performance of the proposed method confirms the effectiveness of the emerging ViT model and its notable superiority over traditional neural network architectures, such as deep convolutional networks.

Keywords: multiple sclerosis (MS), diagnosis, MRI images, transformer-based models, vision transformer(ViT), overfitting, fine tuning

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ICB13 -1013

Enhancing Drug-Target Interaction Predictions through the Integration of Self-Organizing Maps and Graph-Based Representation Learning

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Accurate prediction of drug-target interactions (DTIs) is crucial for accelerating drug discovery and therapeutic development. This task poses a significant challenge due to the complexity of drug-target relationships and the limitations of traditional experimental methods, which are often time-intensive and resource-demanding. GSRF-DTI (Zhu and Ning, 2024), a recently developed framework, integrates drug-target pair networks with graph representation learning to address these challenges. It constructs drug and target homogeneous networks and employs GraphSAGE for scalable node representation learning, followed by a random forest classifier for interaction prediction. GSRF-DTI has demonstrated robust performance across benchmark datasets, identifying both known and novel DTIs with high accuracy. This study enhances the GSRF-DTI framework by integrating an auxiliary extension that explores the incorporation of Self-Organizing Maps (SOM) (Pasa and Navarin, 2022) to improve predictive accuracy and biological interpretability. In this approach, features are derived from the drug-target pair network (DTPs-NET) using methods adapted from GSRF-DTI. GraphSAGE captures local neighborhood relationships within the network, while SOM provides an additional perspective by preserving global topological patterns and identifying biologically meaningful clusters. This integration of SOM resembles vector quantization techniques, encoding complex network patterns while maintaining computational efficiency. The combined feature representations are processed through dense layers, merged, and utilized by a Random Forest classifier, to make DTI predictions. Evaluations on benchmark datasets reveal that incorporating SOM yields an improvement in predictive performance compared to the baseline GSRF-DTI framework. Moreover, the use of SOM facilitates interpretability by mapping DTI data into biologically coherent clusters, potentially uncovering hidden relationships that may inform drug research. This combined approach underscores the value of integrating topological pattern recognition with graph-based learning for more accurate DTI predictions in computational drug discovery.

Keywords: drug-target interaction prediction, graph representation learning, self-organizing maps, vector quantization, computational drug discovery

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ICB13 -1017

Encoding the gRNA-DNA Pairs with Deep Transformers to Predict off-target Effects of CRISPR

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CRISPR is a revolutionary technology for genome editing, with significant potential in medicine. Improving the accuracy and precision of CRISPR is essential to the further development and widespread application of this novel genome editing technique. The accuracy of CRISPR-based genomic edition depends on two issues: the cutting power of Cas enzyme and the performance of the gRNA sequence. To achieve accurate edits, scientists must select the optimal gRNAs containing high on-target activity and low (no) off-target efficiency. To enhance the accuracy and precision of genome editing with CRISPR and make it practical, it is crucial to concentrate on predicting CRISPR off-target effects and reduce them. Although numerous deep learning-based models have been developed to predict off-target sites, current methods suffer from low precision and overfitting caused by insufficient data. Furthermore, most of these algorithms use only gRNA sequences in on-hot vector form as input. However, recent research illustrated that both gRNA and DNA beside some epigenetic features strongly impact on the prediction precision of off-target sites. To address these challenges, we propose a novel multi-head attention based deep transformer model to encode both the gRNA and DNA sequences, and use them to predict off-target sites. Using multi-head attention–based transformer model, lead to capture any relationship between each nucleotide and k-mer with other nucleotides and K-mers within the gRNA and DNA sequences. This enhancement allows for a more comprehensive analysis of sequence characteristics and significantly improves the model's capacity to predict off-target sites. Furthermore, the utilization of multi-head attention architecture has enabled us to improve the accuracy and generalizability of our model across diverse CRISPR systems and cell lines. Comparison of off-target prediction results using our proposed gRNA-DNA encoding scheme, deployed in multi-head attention architecture with state-of-the-art models highlights the superior performance of our approach over multiple evaluation criteria.

Keywords: CRISPR/Cas, gRNA Design, off-target, encoding, deep transformers

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ICB13 -1019

AI-Driven Discovery of Novel AChE Inhibitors for Alzheimer's Disease Treatment: Model Development, Molecular Docking, and MD Simulation

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Alzheimer's disease (AD) is a progressive neurological disorder that primarily affects memory, thinking, and behavior (Stopschinski and Diamond, 2017). Acetylcholinesterase (AChE) is an essential enzyme in the nervous system responsible for breaking down acetylcholine, a neurotransmitter involved in transmitting signals between nerve cells (Chaves, Calheiro, 2020). In Alzheimer's, reduced levels of acetylcholine are linked to cognitive decline (Aktaş, Taslimi, Gülçin, Gök, 2017). The main goal of this study is to design a chemical language model (CLM) capable of generating novel AChE inhibitors that can effectively bind to AChE. A dataset of 613 known AChE inhibitors was compiled from the PubChem and ChemBL databases. The SMILES strings were tokenized into their constituent atomic and bonding elements. Data augmentation was employed to broaden the dataset, enabling the generation of a more diverse range of potential candidates. Here, 5 stages of data augmentation (0, 1, 3, 9, 19) were used. To convert each token into a dense vector representation, a 100-dimensional embedding layer was employed. The model architecture consisted of two LSTM layers, with 512 and 256 units, respectively. Training was carried out over 100 epochs. Libraries of compounds were then generated from the trained model at five distinct temperatures (0.2, 0.4, 0.6, 0.8, and 1), with each temperature yielding a unique set of compounds. A new library of novel and unique compounds was curated, and the highest-performing output was selected. Molecular docking and MD simulation were used to evaluate the generated compounds. MD simulations help to depict the long-range interactions, conformational changes, and flexibility of the inhibitor and protein. The results obtained from this modeling were as follows: The model was trained using 9-fold data augmentation, resulting in more novel compounds at a temperature of 0.8. Overall, the model performed superbly in terms of considering compound novelty. At lower temperatures (0.2, 0.4), the model acted more conservatively, and generated more similar molecules. On the other hand, at higher temperatures (0.6, 0.8, 1.0), the model generated more diverse and novel molecules, possibly with new scaffolds or unconventional functional groups. The docking analysis demonstrated that the newly designed ligands, established crucial interactions with key tryptophan residues at positions 286 and 86. Additionally, the complex predicted by docking exhibited remarkable stability during a 100 ns molecular dynamics simulation. The artificial intelligence model successfully learned the pharmacophore of AChE inhibitors from SMILES strings. After training, the model was able to generate novel inhibitors that retained the key pharmacophore features of the original compounds. Docking and molecular dynamics (MD) simulations further demonstrated that the predicted inhibitors effectively interact with crucial amino acid residues within the enzyme's active site.

Keywords: AI-assisted drug discovery, LSTM, Acetylcholinesterase inhibitors, Alzheimer's disease, docking, MD simulation

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The Role of Itaconate in the Advancement of Colorectal Cancer: A Mathematical Modeling Perspective

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Colorectal cancer (CRC), ranking as the second most common cancer in women and the third in men, remains a significant global health concern. While the immune system is inherently designed to combat cancer, recent studies have revealed that certain immune components can paradoxically promote tumor growth. One such factor is itaconate, a metabolite produced by macrophages. Itaconate exerts its pro-tumorigenic effects by modulating gene expression within the tumor microenvironment. Specifically, it downregulates the expression of interleukin-10 (IL-10), an anti-inflammatory cytokine. This reduction in IL-10 intensifies inflammation within the tumor, leading to increased blood vessel formation and nutrient supply, thereby fostering tumor progression and metastasis. To delve deeper into the complex interplay between itaconate, the immune system, and tumor cells, we developed a mathematical model using ordinary differential equations. This model simulated the dynamics of key biological processes, including itaconate production, immune cell activation, tumor cell (human colorectal adenocarcinoma cell line HT-29) proliferation, and IL-10 secretion. By incorporating experimental data, we were able to calibrate the model and assess the impact of varying itaconate concentrations on tumor growth. The findings from the model simulation reveal that higher levels of itaconate are associated with lower levels of the anti-inflammatory cytokine interleukin-10 (IL-10), which in turn supports tumor growth. Additionally, the sensitivity analysis of the model pinpointed the rates at which itaconate decreases IL-10 and its influence on tumor reduction as crucial elements impacting the model's results. By targeting itaconate-related pathways, we may be able to develop novel therapeutic strategies to combat CRC. This study provides a mechanistic understanding of itaconate's pro-tumorigenic role in CRC by modulating IL-10 signaling and highlights the utility of mathematical modeling in deciphering complex biological interactions in cancer.

Keywords: colorectal cancer, Interleukin-10, Itaconate, mathematical modeling

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Genetic Insights into Osteosarcoma: Implications for Targeted Drug Therapy

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Osteosarcoma is a type of bone cancer that primarily affects the long bones, such as those in the arms and legs, but it can also occur in other bones. It is most commonly diagnosed in adolescents and young adults, typically between the ages of 10 and 20, although it can occur at any age. By exploring the genetic landscape of Osteosarcoma, this research aimed to compile an extensive list of genes associated with Osteosarcoma, then identify the critical genes that drive this condition and to elucidate their significant roles in its progression. To achieve this, we collected Osteosarcoma-related genes by thoroughly reviewing the literature available on PubMed, specially selecting studies that showed a significant correlation between genes and Osteosarcoma (p-value < 0.05). In addition, we used databases such as My Cancer Genome Database, Cancer Genetics Web Database and osteosarcoma-db.uni-muenster.de. GeneMANIA (http://www.genemania.org) is a flexible, user-friendly web interface for generating hypotheses about gene function, analyzing gene lists and prioritizing genes for functional assays. Utilizing GeneMANIA Cytoscape software along with the CytoHubba plugin, we investigated the biological connections among these genes, visualizing a comprehensive network that highlights their interrelationships. Among all the osteosarcoma related genes collected, 168 genes were linked to drugs. These drugs included VX-702, Minocycline, MP470, Arsenic trioxide, Purvalanol, Flavopiridol, ABT-263, Olomoucine, SB-681323, SCIO-469. Among these drugs, Minocycline can affect *ILB1-CYCS- CASP1- VEGFA-MMP9- CASP3- ALOX5* genes, Arsenic trioxide can affect *MAPK1-MAPK3- JUN-AKT1- CCND1- IKBKB- TXNRD1* genes and VX-702 drug have a significant relationship with *IL6-IL1B-TNF-MAPK14* genes and can affect these genes. This analysis not only allows us to identify crucial genes but also to discover the most important drugs associated with the genes related to Osteosarcoma, providing a better understanding of gene function. As a result, even in the later stages of our work, we can find non-coding RNAs associated with the top genes in Osteosarcoma and study their effects on these genes. This study could lead to the prescription of drugs that target non-coding RNAs, effectively silencing the genes that contribute to cancer progression.

Keywords: osteosarcoma, targeted therapy, GeneMANIA , bioinformatics analysis

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In Silico Design of DNA G-Quadruplex Aptamers Targeting Lipopolysaccharide Core and Capsular Polysaccharide in Multidrug-Resistant Klebsiella pneumoniae

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Klebsiella pneumoniae is linked to serious infections such as pneumonia, urinary tract infections (UTIs), and sepsis, particularly affecting immunocompromised and hospitalized individuals (Paniagua-Contreras and Bautista-Cerón, 2023). The increasing prevalence of multidrug-resistant (MDR) strains, including extended-spectrum beta-lactamase (ESBL) and carbapenemase producers, has significantly elevated mortality rates and posed treatment challenges (Paniagua-Contreras and Bautista-Cerón, 2023). Although traditional detection methods remain effective, they typically require specialized equipment, limiting accessibility in resource-limited environments. Research has identified conserved regions in lipopolysaccharides (LPS) (Kim and Jang, 2022) and capsular polysaccharides (CPS) as promising targets for biosensor development (Kaszowska and Majkowska-Skrobek, 2021). This study used in silico techniques to design a library and potential specific DNA aptamers for cost-effective detection of K. pneumoniae, circumventing the experimental SELEX process. To identify G-quadruplex-forming sequences, six K. pneumoniae gene sequences were obtained from NCBI GenBank (Benson and Cavanaugh, 2013): KPHS_37010, KPHS_20120, KPHS_51230, KPHS_47480, KPHS_51270, and KPHS_20620. These sequences were used to construct an initial nucleotide pool. Molecular models of LPS core oligosaccharides, which link the lipid A component to the O-antigen, and Type 1 CPS, a polysaccharide capsule aiding immune evasion, were generated using CHARMM-GUI (Jo and Kim, 2008). QGRS Mapper (Kikin and D'Antonio, 2006) identified 44 DNA G-quadruplex sequences between 20 and 40 nucleotides in length, each with a G-score above 15, indicating stability and specificity. Aptasuite (Hoinka and Backofen, 2018) clustered these sequences into four structural groups with consensus sequences of 38 nucleotides. The 3D structures of the top five G-quadruplexes with G-scores above 30 were modeled using AlphaFold (Abramson and Adler, 2024), along with the four clusters, and docked to LPS and CPS glycan targets using HADDOCK2.4 (Honorato and Trellet, 2024). Among these, the Optimal G-quadruplex—identical in sequence to the Final Selected Cluster—demonstrated strong binding to both LPS and CPS. Docking analysis revealed that the Optimal G-quadruplex exhibited the highest binding affinity for CPS (HADDOCK score 1.9 ± 5.1; vdW energy -28.3 ± 1.9; electrostatic energy -34.1 ± 3.9), while the Final Selected Cluster showed superior scores for LPS (HADDOCK score 16.4 ± 1.6; vdW energy -20.4 ± 0.7; electrostatic energy -31.7 ± 11.2). Both structures achieved negative binding energies, highlighting their stability and suitability for biosensing applications. This study provides a foundation for developing stable, specific DNA G-quadruplex aptamers for the rapid detection of K. pneumoniae. The structurally conserved LPS core oligosaccharides represent a universal target, making the findings applicable to both clinical and field biosensor development.

Experimental validation is needed to confirm the diagnostic potential and optimize efficacy.

Keywords: SELEX, G-quadruplex, molecular diagnostics, glycans, aptamers, multidrug-resistance

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Molecular Investigation of Periplasmic Sensor Histidine Kinase Interactions in Regulating UV Shield Formation of Cyanobacteria Nostoc Sp.

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Microorganisms utilize predominant signaling systems to monitor environmental changes and modify gene expression. One of the primary adaptive mechanisms in bacteria is the Two-Component Regulatory System (TCRS), which consists of a sensor histidine kinase and a Response Regulator (RR) (Ibrahim et al., 2016). The histidine kinase protein detects external signals and phosphorylates the RR, which then regulates gene expression. In cyanobacteria, including Nostoc species (Janssen and Soule, 2016), histidine kinases are often transmembrane proteins with a sensor domain in the periplasm and a kinase domain in the cytoplasm (Affandi et al., 2016). This enables them to sense and react effectively to variations in the environment. Nostoc punctiforme bacterias are activated by UV stress to produce scytonemin, a protective pigment that absorbs harmful UV-A radiation (Klicki et al., 2022). Genomic analyses suggest that the biosynthesis of scytonemin is regulated by TCRS proteins, through a signaling process likely mediated by histidine kinases (Janssen and Soule, 2016). However, the detailed molecular interaction, between scytonemin and the sensor domain of histidine kinase has not been completely understood This research utilizes molecular docking to explore the binding interactions between scytonemin and the periplasmic sensor domain of histidine kinase in Nostoc species. The 3-dimensional structure of the sensor histidine kinase was obtained from UniProt (ID: A0A1Z4I2R9), while the scytonemin structure was retrieved from PubChem database (CID: 135473381) information source. Using AutoDock Vina via Chimera software (Butt et al., 2020), docking simulations were conducted to generate a total of 10 binding modes. The grid box used in docking was centered at coordinates x = 1.44, y = -3.02, and z = -3.56, with dimensions of 110 Å in each direction to ensure comprehensive coverage of the binding site. The docking analysis shows that the binding energies of the conformations range from -9.7 to -8.3 kcal/mol, indicating a strong binding affinity. The optimal binding mode has an energy of -9.7 kcal/mol with no RMSD deviation (0.000) from the reference conformation. This suggests that specific interactions contribute to the stability of the scytonemin-histidine kinase complex. Important stabilizing connections involve Pi-Pi T-shaped bonds with phenylalanine units (PHE A:39 and PHE A:146) and Pi-Sigma stacking with PHE A:149. Furthermore, Pi-Alkyl interactions with proline (PRO A:134) and leucine (LEU A:138) enhance the complex's hydrophobic stability. A Pi-Cation interaction between arginine (ARG A:89) and an aromatic ring in scytonemin suggests an important electrostatic contribution to binding stability. These findings suggest an enduring binding process that may impact the kinase's structure and function, potentially amplifying its involvement in signal transduction. These observations provide a molecular perspective on how scytonemin contributes to the regulation of the cellular UV shield and interacts with histidine kinase to modulate bacterial stress responses

under UVA radiation. This study highlights the critical role of molecular interactions that could be key to bacterial adaptation to environmental stresses. The findings hold potential for future applications in engineering UV shields at the cellular level.

Keywords: Nostoc bacteria, Periplasmic sensor histidine kinase, scytonemin, two-component system, molecular docking

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ICB13 -1027

Biomechanical Characterization of Realistic Bacterial Membranes Across Different Biofilm Ages: A Molecular Dynamics Study

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The cell membrane plays a crucial role in cellular activities, making understanding its biophysical and biomechanical characteristics essential. Bacterial biofilms, resist antibiotics, posing challenges in clinical settings (Flemming et al., 2016). A comprehensive understanding of mechanical properties can lead to novel treatment methods to overcome antimicrobial resistance. Pseudomonas aeruginosa, an opportunistic pathogen, excels at biofilm formation, causing chronic infections in immunocompromised patients and complicating conditions like cystic fibrosis (Linnane et al., 2015). As biofilm age increases, the biofilm's matrix thickness and the fatty acid profile of the inner membrane significantly change (Pericolini et al., 2018; Wagner and Iglewski, 2008). In this study, membrane constructs representing planktonic, 24-hour (BF1), 48-hour (BF2), and 6-day biofilms (BF6) were modeled using lipidomic analysis from Benmara et al. and the online CHARMM-GUI tool (Benamara et al., 2014; Wu et al., 2014). The lipid bilayers were fully hydrated and neutralized with sodium and chloride ions at a concentration of 0.15 M. Following standard equilibration in CHARMM-GUI, input files for the simulations were created. Energy minimization addressed excessive forces from structural deviations to achieve stability. Simulations were conducted under NPT ensemble conditions (constant pressure of 1 bar) using the Parrinello-Rahman algorithm with a two-femtosecond time step (Parrinello and Rahman, 1981). A fixed temperature of 310.15 K was maintained with a Nosé-Hoover thermostat (Hoover, 1985; Nosé, 1984). Bond constraints were applied using the LINCS algorithm, while non-bonded interactions, including electrostatics and van der Waals forces, were calculated with the PME method and a cutoff of 1.2 nm (Darden et al., 1993; Hess, 2008). The CHARMM36m force field was utilized for 500-nanosecond simulations in Gromacs 2018.1. For each lipid bilayer, the head-to-head thickness (DHH), hydrophobic thickness (DC), area per lipid (APL), bilayers' interdigitation, and compressibility moduli (KA and KC) were calculated over the 500-nanosecond simulation. Order parameters and lateral diffusion coefficients were computed to evaluate the microscopic fluidity of the lipid bilayers. The BF1 showed the lowest APL, indicating tighter molecular packing when transitioning from planktonic to biofilm states, which decreased as the biofilm aged. This change led to a 1.78-fold increase in the lateral diffusion coefficient, linked to reduced packing. Increased interdigitation may also influence lateral diffusion due to higher membrane viscosity (Frewein et al., 2022). The packing variations of lipid bilayers significantly impact microscopic fluidity during the transition from planktonic to biofilm states and biofilm aging. As this transition occurs, lipid bilayers become more ordered, decreasing APL. This increased order is followed by a gradual decline as the biofilm ages from one to six days, approaching a state similar to planktonic. Microscopic fluidity and lipid bilayer interdigitation changes were

noted with biofilm aging. As biofilms mature, lateral diffusion coefficients and lipid interdigitation decrease, gradually resembling planktonic conditions, as Benamara et al. pointed out (Benamara et al., 2014). This suggests that the membrane composition prepares bacteria for potential detachment. Understanding biomechanical features is vital for developing strategies to disrupt biofilm formation and enhance treatment efficacy, paving the way for future research into targeted therapies against biofilm-associated infections.

Keywords: biomechanical properties, biofilm aging, lipid bilayers, membrane, molecular dynamics

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Investigation of the interaction of syringic acid with carbonic anhydrase using molecular docking

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Carbonic anhydrases are a large group of zinc metalloenzymes that catalyze the physiological reaction of carbon dioxide hydration to bicarbonate and protons (1). Inhibition of the carbonic anhydrase enzyme is effective in the treatment of many diseases, including glaucoma and gastric ulcer (2). Recently, it has been found that carbonic anhydrase inhibitors can also be used as anti-obesity, anti-cancer and anti-diabetic drugs. Syringic acid is a phenolic compound that is found in olives, dates, pumpkins, grapes, honey and shows excellent antioxidant, antimicrobial, anti-obesity and anti-cancer activities (3). In this study, the molecular targets of syringic acid were first identified using the Swiss Target Prediction platform, and carbonic anhydrase family proteins were at the top of the list. Then using RCSB and CB-Dock2 websites, the active sites and their amino acids were identified and the interaction of syringic acid with carbonic anhydrases 2, 4, 9 and 12 was investigated by molecular docking method using Autodock software. The grid box was designed to be placed on the active site pocket of the enzyme. The results showed that syringic acid binds to the similar binding site on all these enzymes by hydrogen bonds and hydrophobic interactions. Some of these amino acids were common in all four enzymes, for example, histidine 119, that binds to Zn2+ ion in the native structure of carbonic anhydrase, is one of the amino acids that can form a hydrogen bond with syringic acid in these human carbonic anhydrase isoforms. The binding free energy range for carbonic anhydrases was calculated between -5.2 and -4.2 kcal/mol. The highest and lowest binding energy are related to carbonic anhydrases 2 and 12, respectively. Based on previous experimental studies, phenols, including syringic acid, are anchored in the water molecule bound to (Zn2+) and in the cavity of the active site of the enzyme, then bind to different amino acid residues (4). The results of this study suggest that syringic acid can bind to the active site and inhibit carbonic anhydrase enzyme, therefore as a bioactive compound is a suitable candidate for further studies to design new carbonic inhibitor drugs.

Keywords: carbonic anhydrase inhibitors, Zn2+, Glaucoma, syringic acid, docking

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ICB13 -1034

A Clustering-Based Method for Preserving Manifold Structure in EEG Signals Classification

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Accurate classification of EEG signals is essential for brain-computer interface (BCI) and neuroprosthetic applications, enabling precise interpretation and control. Traditional EEG classification methods often ignore the non-Euclidean manifold structure in EEG data, which distorts relationships between signals and reduces classification accuracy (Lotte et al., 2018). Preserving this manifold information is crucial for capturing the true geometry of EEG signals, which Euclidean-based approaches inadequately address (Fu et al., 2024; Tibermacine et al., 2024). To overcome this limitation, this study introduces Clustering-Based Methods for Preserving Manifold Structure in EEG Signal Classification, a method that maintains Riemannian manifold geometry by preserving curvature-related information, ensuring essential non-Euclidean relationships are retained for accurate classification. The methodology comprises four phases: in feature engineering phase, covariance matrices and radial basis function (RBF) kernels are used to capture linear and non-linear relationships among EEG channels, enriching the data with a comprehensive view of brain activity (Davis and Curriero, 2019; Uehara et al., 2017). In the data clustering phase, the feature-enhanced data is projected into a Riemannian manifold space, where clustering is performed using a novel k-means algorithm. This algorithm employs a metric combining Riemannian distance and tangent plane slope, preserving intrinsic structural relationships through locally sensitive clustering. In the dimensionality reduction phase, clustered data points are projected onto the tangent space of the manifold, reducing dimensionality for simplified representation in subsequent classification. This projection retains essential local structures, reduces noise, and prevents overfitting while preserving manifold-related information (Gao et al., 2021). The tangent space provides a linear approximation of the manifold, facilitating efficient handling of high-dimensional data in a lower-dimensional Euclidean context (Djebra et al., 2022). Finally, in the classification phase, a support vector machine (SVM) classifier is applied to the dimensionally reduced, clustered data. By leveraging preserved geometric features, the SVM enables efficient, accurate classification, suitable for real-time BCI and neuroprosthetic applications. The method's effectiveness is validated on the BCI Competition IV dataset 2a (Tangermann et al., 2012), which includes 25 channels (22 EEG and 3 EOG) sampled at 250 Hz, recorded from nine subjects performing four motor imagery tasks (left hand, right hand, both feet, and tongue). The dataset's label structure necessitates a multi-label classification approach, with four target labels to capture distinct motor imagery tasks. The proposed clustering-based, multi-label classification approach achieves an accuracy of 92% over all subjects, showing substantial improvement over baseline models on the same dataset. These results confirm that preserving manifold structure in EEG data enables more sensitive and precise clustering and classification,

advancing EEG analysis for BCI and neuroprosthetic applications.

Keywords: brain-computer interfaces (BCIs), EEG signal classification, ensemble modeling, clustering-based classification.

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ICB13 -1035

Reconstruction and analysis of lncRNA-miRNA-mRNA ceRNA network to explore the potential biomarkers for colorectal cancer

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Colorectal cancer (CRC) is ranked among the most prevalent and most life-threatening cancers worldwide. Despite progress in treatment methods, CRC is still responsible for a significant percentage of cancer deaths, as it is often diagnosed at advanced stages. Early detection and identifying novel therapeutic targets are crucial for enhancing clinical outcomes, a goal that bioinformatics is making increasingly achievable. Through molecular-level analysis of disease mechanisms and structure, bioinformatics enables researchers to uncover critical biomarkers and regulatory pathways, leading to earlier diagnosis and development of targeted and personalized therapies. In Colorectal cancer, miRNAs have a significant contribution to the genesis, cellular differentiation, and disease progression. The current study proposes four miRNAs as biomarkers through the analysis of the lncRNA-miRNA-mRNA tripartite network for the diagnosis and treatment of colorectal cancer. Furthermore, the biological functions of obtained biomarkers in colorectal cancer were analyzed. Using colorectal cancer-filtered data from the dbDEMC database, cancer-specific differentially expressed miRNAs (DEmiRNAs) were identified. The interactions between lncRNAs and mRNA were identified using lncACTdb and miRTarBase databases, respectively. Using the interactions between the specified molecules a ceRNA network was constructed by integrating lncRNA-miRNA and miRNA-mRNA networks which was visualized using Cytoscape. Then Protein-Protein Interaction (PPI) network was constructed based on the identified target genes using the STRING database and analyzed further using the MCODE algorithm to extract gene modules. Finally, functional enrichment for the identified lncRNAs, miRNAs, and their target genes was conducted using the GeneCodis platform to reveal their biological roles, cellular components, molecular function, and involved pathways. Two bipartite networks linking lncRNAs to miRNAs and miRNAs to mRNAs were constructed and subsequently integrated to create a ceRNA network comprising lncRNAs, miRNAs, and mRNAs. This integration enables us to determine the key biomarkers associated with the CRC. The obtained networks highlighted potential regulatory interactions involved in the pathogenesis and facilitated the identification of candidate biomarkers for further studies. By constructing a tripartite lncRNA–miRNA–mRNA ceRNA network, four miRNAs were identified as potential biomarkers for the studied disease. Among these four miRNAs, three were upregulated and one was downregulated under disease conditions, suggesting their involvement

in regulatory roles.

Keywords: colorectal cancer, ceRNA network, non-coding RNAs, lncRNAs, miRNAs, mRNAs, biomarker, bioinformatics

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ICB13 -1040

Identification of a natural specific inhibitor for Akt1 protein through molecular docking studies and evaluation of DFT calculations and molecular dynamics simulations

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The protein kinase B (Akt1) is a pivotal component in cellular signaling pathways and the regulation of cancer-related processes, establishing it as a vital target for the development of innovative therapeutic agents[1]. This research examines natural inhibitors, including quercetin, resveratrol, and zingiberene, to assess their interactions with Akt1 using molecular docking and free energy calculations density functional theory (DFT)[2]. Molecular docking[3] analysis indicated that all three compounds possess the ability to bind to Akt1's allosteric site, with quercetin displaying the strongest interaction due to its lower binding energy and more stable hydrogen bonding. Detailed evaluation of van der Waals and electrostatic forces through DFT calculations identified these factors as critical to the stability of the complexes. Although resveratrol and zingiberene also demonstrated significant interactions with Akt1, their binding energies and complex stabilities were comparatively weaker than those of quercetin. These findings suggest that quercetin holds substantial promise as a natural inhibitor for Akt1 and could serve as a cornerstone for developing anticancer therapies derived from natural compounds. This study not only emphasizes the therapeutic potential of quercetin but also highlights the indispensable role of molecular modeling and DFT calculations in elucidating protein-ligand interactions. These discoveries provide a foundation for subsequent experimental research and practical innovations in drug design.

Keywords: *AKT1*, quercetin, resveratrol, zingiberene, molecular docking, DFT

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ICB13 -1041

Investigation of the interaction between 2-aminothiazole and bovine serum albumin (BSA), using the methods of molecular docking calculations and density functional theory (DFT)

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Serum albumin, which constitutes a large protein of plasma, plays an essential role in regulating the distribution and bioavailability of biologically active substances, including drugs[1]. Understanding how drugs interact with serum albumins is vital for assessing their pharmacokinetic behavior and therapeutic effectiveness. This study examines the binding interaction between 2-amibothazole, a heterocyclic compound, and bovine serum albumin (BSA) using various computational techniques, including Molecular Docking[2] and density functional theory (DFT) calculations[3]. The research provides in-depth analysis of the binding affinity between 2-aminothiazole and BSA, offering a clear understanding of the binding mechanism through DFT simulations. Additionally, the study evaluates the potential toxicity of the drug by applying quantum theory of atoms in molecules (QTAIM) noncovalent interaction indices (NCI) and reduced density gradient (RDG) analysis. These findings emphasize the critical role of serum albumins in the distribution and stability of drugs, especially active compounds used in cancer, antibacterial and anti-inflammatory treatments. The results also highlight the therapeutic significance of 2-aminothiazole and its derivatives, demonstrating the potential of BSA as a model for studying drug-protein interactions, this research contributes to the development of more effective drug delivery systems and combination therapies, offering valuable insights into the pharmacodynamics, pharmacokinetics and toxicity of biologically active compounds.

Keywords: BSA, 2-amibothiazole, molecular docking, DFT

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Molecular Docking Study of Pyrazole Interaction with Bovine Serum Albumin (BSA): Insights from Drug-Protein Binding

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The interaction of drugs with plasma proteins, especially Bovine Serum Albumin (BSA), affects the half-life and biological activity of the drug (Al-Mehizia, Bakheit 2019). Serum albumins, due to their abundance, flexibility, and ability to bind to both hydrophilic and hydrophobic groups, are responsible for key functions such as maintaining blood pH and osmotic pressure, as well as transporting various substances including fatty acids, steroids, hormones, amino acids, metal ions, carbohydrates, and other molecules throughout the bloodstream, both intracellularly and extracellularly. Bovine Serum Albumin is used as a model to study these type of interactions due to its high structural similarity to Human Serum Albumin (HAS) (Mittal, Gandhi 2022). Pyrazole has been considered as an important active pharmaceutical scaffold with high potential in various pharmaceutical fields (Karrouchi, Radi 2018). This study investigates the interaction of pyrazole with BSA using the molecular docking method. The aim of this study was to better understand the binding of drug to albumin and its effect on the biological activity of the drug, as well as, to investigate the medicinal potential of pyrazole and its derivatives. Three-dimensional (3D) structure of the ligand and BSA(4F5S) were obtained from the PubChem database and Protein Data Bank (PDB), respectively. Finally, the molecular docking was studied using Autodock 4.1 software. Analysis of the molecular docking exhibited that Pyrazole interacts with the B chain of the protein with the binding energy of -3.37 kcal/mol. As results showed, pyrazole binds to BSA protein, and therefore, it may affect the protein interior interactions.

Keywords: Bovine Serum Albumin (BSA), protein, Pyrazole, molecular docking

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ICB13 -1044

Statistical Investigation on the Occurrence of Liquid-Liquid Phase Separation in Proteins Involved in Neurodegenerative Proteins

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A considerable number of people are affected by neurodegenerative diseases worldwide annually. Due to the heterogeneous and complex pathological mechanisms, there is still no standard therapy for these really annoying diseases. A common feature among them is protein aggregation, which varies due to the specific protein and/or peptide. Investigations show there might be relationships between amino acid sequences and the occurrence of aggregation. According to amyloid cascade hypothesis the main pathogenic mechanism that occurs in neurodegenerative diseases is the aggregation (i.e., amyloid formation) of a specific kind of protein or peptide in each disease, during which it converts from the native state to the amyloid state by oligomerization and fibrillation pathway. Another mechanism, proposed recently, is through the establishment of separate phase (liquid-liquid phase separation (LLPS)), containing the amyloidogenic peptide or protein. In this work, we have investigated the effects of occurrence of specific amino acids (content) or specific nearest neighbor (sequence) in neurodegenerative peptides and proteins (e.g., beta-amyloid (Aβ42), tau, alpha-synuclein) that might affect the production of a separate phase, through Data mining approaches. We have analyzed sequence-based statistics investigating the occurrence of LLPS in the LLPSv2 database, and on neurodegenerative peptides and proteins. By making use of LLPSv2 database we calculated amino acid (AAC) and dipeptide compositions (DPC). The calculations were based on linear algebra methods such as PCA, LDA, and PLS, as well as statistical methodologies. Our results indicated that specific AACs such as A, L, F, and Y, and DPCs such as KK, VG, GV, and YY were important in the occurrence of LLPS. We then studied DPC in neurodegenerative peptides and proteins. We concluded that electrostatic, hydrophobic, and hydrophilic interactions were the most important physicochemical properties and were frequently involved in the interactions that play crucial roles in the occurrence of LLPS.

Keywords: bioinformatics, phase separation, aggregation, amino acid content and sequence

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ICB13 -1045

Investigating hsa-miR-146b and Its Targets TRAF6 and IRAK1 In Gastric Cancer Using Bioinformatic Tools

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Gastric cancer is one of the leading causes of cancer-related mortality worldwide, often diagnosed at late stages with poor prognostic outcomes. Gastric cancer development is a multifactorial process with complicated interactions among genetic, environmental, and lifestyle factors (Morgan, Arnold et al. 2022). MicroRNAs (miRNAs) are small non-coding RNAs established as major regulators of gene expression involved in various biological processes, such as cell proliferation, differentiation, and apoptosis (Statello, Guo et al. 2021). Specific miRNAs, like hsa-mir-146b, have been identified in gastric carcinoma as key players in controlling inflammatory pathways and tumor progression (Azari, Nazari et al. 2023). Clinical data and expression levels of hsa-miR-146b in gastric cancer patients were obtained from The Cancer Genome Atlas (TCGA) based on the following selection criteria including basic clinical information of sample types (normal and primary tumor), individual cancer stage, tumor histology and nodal metastasis status. To identify potential target genes of hsa-miR-146b, we utilized TargetScan and miRDB. From the list of predicted target genes, the 10 genes with the highest target scores were selected for further analysis (Target score>95). To investigate the interactions and relationships between hsa-miR-146b target genes, we utilized STRING. Data for TRAF6 and IRAK1 were retrieved from TCGA Stomach Adenocarcinoma (STAD). Cell line data were obtained from the DepMap database. Our results demonstrate that the expression level of hsa-miR-146b is increased in STAD in comparison with normal tissue. This increase was discovered in different nodal metastasis status (N0-N3), different GC stages (1-4) and in seven different histological subtypes. TargetScan and miRDB identified TRAF6 and IRAK1 as high-confidence targets of hsa-miR-146b, with scores of 100 and 99, respectively. STRING network analysis further highlighted a strong functional relationship between TRAF6 and IRAK1. Additionally, analysis of TCGA Stomach Adenocarcinoma (STAD) data revealed altered expression of TRAF6 and IRAK1 in gastric cancer tissues compared to normal gastric tissues. Data from the DepMap database confirmed consistent expression of both genes in gastric cancer cell lines, with variability across lines, highlighting their active roles in gastric cancer biology. Our investigation places significant importance on hsa-miR-146b in the development of gastric cancer and identifies that its potential regulatory role for two high target score genes, TRAF6 and IRAK1, was determined by bioinformatic analyses. The findings suggest that hsa-miR-146b exhibits altered expression levels in gastric cancer, potentially influencing key signaling pathways mediated by TRAF6 and IRAK1, which are critical components of the NF-κB pathway and immune response regulation (Wang, Wu et al. 2020). These findings provide insights into the molecular mechanisms underlying gastric cancer progression and suggest that hsa-miR-146b and its target genes might act as promising biomarkers or therapeutic targets for managing gastric cancer.

Keywords: gastric cancer, hsa-miR-146b, TRAF6, IRAK, TCGA, bioinformatics

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ICB13 -1046

Investigation and comparison of TYDC2 gene expression in different tissues (root, leaf, capsule and petal) of medicinal plant poppy (Papaver somniferum L.) in terms of bioinformatics

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Poppy with the scientific name Papaver somniferum L. belongs to the Papaveraceae family. More than 40 types of alkaloids are known in poppy, the most important of which are morphine, codeine, thebaine, noscapine and papaverine(Hayat, Hameed, & Zia-Ul-Haq, 2023). Alkaloids of the morphine group in poppy are synthesized from two amino acid L-tyrosine molecules through 17 enzymatic steps during several continuous oxidative reactions(Aghaali & Naghavi, 2024). The first key enzyme in this pathway is L-tyrosine decarboxylase (TYDC2). In this research, TYDC2 gene was compared and investigated in four tissues of a poppy plant. The sequence of these tissues (root, leaf, capsule and petal) was identified by NGS method and studied bioinformatically, these sequences were selected from the Gene section of NCBI website and downloaded by SRAtoolkit tool and their quality was determined by the tool. FastQC was evaluated and gene expression graphs and heatmap graphs were drawn by Rstudio. Finally, it was analyzed and evaluated by gprofiler in terms of gene ontology. In this research, the expression level of the production gene was different in the mentioned tissues and the expression level was detected in the leaf tissue more than the other tested tissues, and the lowest expression level was observed in the root tissue. Finally, gene ontology, genes were also examined and it was found that; The molecular function and the extent of the biological process of this gene play a great role in the catalytic activity. It has been observed in various plant species that the biosynthesis of a large number of primary metabolites as well as secondary metabolites are dependent on this gene. Gene expression is a process in which the information contained in a gene is used to produce a functional product(Alharbi & Vakanski, 2023). Therefore, modeling and identifying the expression level of tissues helps significantly in the production of products with high efficiency, especially in the field of medicinal plants that have effective substances(Guo et al., 2024). This study can be useful for the production of important and essential alkaloids of poppy medicinal plants.

Keywords: Alkaloid, gene expression, sequencing, Poppy

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Designing Guide RNAs Considering Essential Genes for Genome Editing of Yarrowia lipolyticaUsing Deep Learning in the CRISPR System

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The CRISPR/Cas system is used to precisely remove and add one or more genes to the genome. In this system, a protein called Cas is combined with a short RNA called sgRNA, which makes a double-strand break precisely at the desired location in the genome. The designed sgRNA should be designed in a way that not only accurately targets the desired location without off-target effects but also avoids affecting vital genes. The yeast *Yarrowia lipolytica* can produce valuable natural and recombinant compounds with commercial, industrial, and therapeutic significance. Given the importance and application of this yeast, designing appropriate sgRNAs can yield optimal efficiency for genome editing and the production of economically valuable products. The cutting score (CS) and fitness score (FS), which indicate changes in gene activity following sgRNA deletion, were obtained in the laboratory for each sgRNA sequence in the Cas12a protein by Ramesh et al. In current study, we used these values and deep learning based on a convolutional neural network (CNN), unsupervised learning was first performed with a convolutional autoencoder (CAE) to extract sgRNA features in the *Y. lipolytica* genome. Then, supervised learning by the CNN yielded the FS value for each sgRNA in the Cas12a dataset, resulting in Spearman values of 0.70% and Pearson values of 0.72%. The FS results for each sgRNA sequence were fed into a neural network to predict the CS, which indicates sgRNA effectiveness. Finally, the model's predictions achieved Spearman values of 0.96% and Pearson values of 0.95% for predicting the sgRNA with the highest efficacy, outperforming existing algorithms for *Y. lipolytica*.

Keywords: guide RNA, deep learning, yeast, genome editing, vital genes

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ICB13 -1050

Reduced PINK1 Expression in Bladder Cancer: Insights into Autophagy Dysregulation and Therapeutic Potential

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Bladder cancer (BC) is one of the most common malignancies worldwide, characterized by high recurrence and progression rates, which pose significant challenges for patient management (Tran, Xiao et al. 2021). Understanding its molecular underpinnings is essential for developing more effective therapies (Mikhaleva, Pechnikova et al. 2021). Autophagy, a vital cellular process that degrades and recycles damaged organelles and proteins, plays a dual role in cancer, supporting cell survival under stress while potentially suppressing tumor initiation (Das, Shukla et al. 2021). The PTEN-induced kinase 1 (PINK1) gene, best known for its role in mitochondrial quality control, has emerged as a key regulator of autophagy. Aberrations in PINK1 expression disrupt autophagic pathways, contributing to cancer progression (Gan, Callegari et al. 2022). Investigating the relationship between PINK1 and autophagy in bladder cancer may reveal promising therapeutic targets. PINK1 expression levels in bladder cancer patients were retrieved from The Cancer Genome Atlas (TCGA) using specific selection criteria. These criteria included basic clinical data such as sample types (normal and primary tumor), histological subtypes, molecular subtypes, patient weight, and cancer stage. The analysis utilized a large sample size (>400), and the datasets were compared to identify statistically significant p-values. Our findings reveal that PINK1 expression levels are reduced in bladder cancer tissues compared to normal tissues. This reduction was consistently observed across various BC stages (1–4), weight categories, histological subtypes, and molecular subtypes. Our study demonstrates a significant reduction in PINK1 expression levels in bladder cancer tissues compared to normal tissues, consistently observed across various clinical and molecular subgroups, including different stages, weight categories, and histological and molecular subtypes. These findings suggest that PINK1 dysregulation may play a crucial role in BC pathogenesis, potentially through its impact on autophagic pathways and mitochondrial quality control. The consistent downregulation of PINK1 across diverse patient subsets highlights its potential as a biomarker for BC progression and a candidate for targeted therapeutic intervention. Further research is warranted to elucidate the precise mechanisms linking PINK1 to bladder cancer biology and to explore its clinical utility in improving diagnosis, prognosis, and treatment strategies.

Keywords: bladder cancer, PINK1, TCGA, bioinformatics, autophagy

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Enhancing the Clustering and Sorting Procedures in the MAGUS Method for Multiple Sequence Alignment

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Multiple sequence alignment (MSA) is a foundational computational technique in bioinformatics, enabling the comparative analysis of sequences to uncover evolutionary, structural, and functional relationships among DNA, RNA, or protein sequences. By aligning homologous sequences, MSA identifies conserved regions, variations, and patterns critical for understanding biological processes and guiding experimental studies. It serves as a cornerstone for applications such as phylogenetic tree construction, protein structure prediction, and gene annotation. Modern MSA methods leverage sophisticated algorithms, including dynamic programming, heuristic approaches, and machine learning, to balance accuracy and computational efficiency for large datasets. This work adopts MAGUS (Multiple Sequence Alignment using Graph Clustering) (Smirnov et al. 2021)and improves the clustering step along with the sorting steps. For improving the clustering step, we use repeated random walk algorithm (RRW)(Macropol et al. 2009) and for sorting step we simply replace A* with quicksort. The result shows that these modifications can efficiently improve performance of the algorithm.

Keywords: multiple sequence alignment, algorithms, phylogenetic trees, dynamic programming, protein sequences

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ICB13 -1054

Homology modeling and molecular docking studies for discovering FlgK protein inhibitors; Helicobacter pylori flagellar subunit.

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The flagella of the pathogens play significant roles in the initial phase of the bacterial infection process. It has been shown that FlgK is important for flagella formation and Helicobacter pylori (H. pylori), therefore deletion of the flgK flagellum, prevents normal flagellar assembly and reduces H. pylori colonization on the gastrointestinal mucosa (Gu, 2017) Two proteins, FlgK and FlgL form the hook-filament junction, therefore, the one of the best point to target Flgk, is interface area of FlgK/FlgL. With this concept, a molecular docking investigation was carried out for natural organic compounds (1000 molecules) with interface area of FlgK/FlgL.The amino acid sequences of the FlgK and FlgL were retrieved from the UniProt database (Apweiler and Bairoch, 2004) and the three-dimentional structure of the proteins were predicted using Modeller 9 & 22 software (Fiser and Sali, 2003).The Verify-3D, PROCHECK program and ProSA II web server were used for evaluation of models. GRAMM-X and ClusPro 2.0 were exploited to predict and assess the interactions between the hook-filament junction proteins FlgK and FlgL and the interaction sites were determined using the PDBePISA and Discovery Studio 4.1. The ligand-binding residues were predicted on FlgK by FTMap and COACH server. The ligand binding sites of FlgK which overlapped with the interface area of FlgK/FlgL, were selected as the target locations (V568, E572, E573, N576, A585, A586, N587, A588, K589, I598, D599 and T600) for Molecular docking study. The molecular docking was down using Autodock Vina (Trott and Olson, 2010) and Autodock 4 in pyRx program (Dallakyan and Olson, 2015) and the output results were evaluated using soft Discovery Studio software. The results of ligand docking assessments against FlgK, revealed that the ligands with best binding affinity scores –i.e., the most negative binding energies are observed for the compounds; Asiatic acid with Binding energy -11.5, S3899 Hederagenin with Binding energy -10.8, S3847 Panaxatriol with Binding energy -10.8, S4754 Betulin with Binding energy -10.5, Betulinic acid with Binding energy -10.5, Oleanolic acid with Binding energy -10.5, Ursolic Acid with Binding energy -10.3, Digoxin with Binding energy -10 and Enoxolone with Binding energy -9.7. Finally, this in silico study suggests that FDA approved natural organic compounds; exhibited powerful potential inhibitory against flagellar biogenesis in H. pylori.

Keywords: helicobacter pylori, molecular docking, natural organic compounds, Flgk

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Molecular Docking Studies of Natural Organic Compounds against Urease of Helicobacter Pylori

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Helicobacter pylori exploited urease to infect the highly acidic human stomach (Graham, and Miftahussurur, 2018). Clinically drug therapies in the treatment of H. pylori are associated with many adverse effects; therefore, there is a need for replacing pharmaceutical compounds with less harmful and preferably natural compounds as novel drugs to treat Helicobacter pylori infection. The purpose of this study was to investigate the molecular docking studies of oxadiazole natural compounds (1000 molecules) as potential urease inhibitors of H. pylori The 3-D of Urease (PDB ID. 1e9y) was retrieved from the Protein Data Bank (Berman and Westbrook, 2000), and cleaned with Discovery Studio 4.1, then minimized and changed using MGLTools to pdbqt format. 1000 approved natural organic compounds were obtained from Selleckchem Inc website. The docking process of all compounds to important residues of the urease enzyme was performed using Autodock Vina (Trott and Olson, 2010) and Autodock 4 in pyRx program (Dallakyan and Olson, 2015) and AutoDock Vina software. Finally, ligand and junction interactions were analyzed and evaluated by Discovery Studio 4.5 Client software. According to this study, the organic natural compounds exhibited powerful inhibitory activity against the human pathogen H.pylori. All affinities of the compounds were calculated, and the best compounds with low ΔG (-ΔG) were obtained as follow; Sclareolide with Binding energy -8.5, Rutaecarpine with Binding energy -8.2, Cryptotanshinone with Binding energy -8.1, Chrysin with Binding energy -8.0, Tanshinone IIA with Binding energy -7.9, Indirubin with Binding energy -7.9, Vitamin K1 Tanshinone I with Binding energy -8.0 and Kinetin with Binding energy -8. That above mentioned ligands have occupied and interacted with the substrate binding site and also active site of the urease i.e: His136, His138, Ala169, KCX219, His221, His248, and Asp362. The present findings revealed the inhibitory effect of the natural organic compounds on the urea enzyme of Helicobacter pylori and can be a very good alternative to chemical drugs

Keywords: helicobacter pylori, urease, natural organic compounds, molecular docking simulation.

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Molecular Docking Study of Natural Compounds from Daucus carota as Inhibitors of VEGFR-2: A Computational Approach for Drug Design

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The utilization of natural compounds from plants for drug design and development has been a prominent area of interest in pharmaceutical research (Smith & Brown, 2020). This study focuses on identifying and evaluating the potential of bioactive compounds from Daucus carota (carrot) for inhibiting the vascular endothelial growth factor receptor-2 (VEGFR-2), a protein critically involved in angiogenesis and cancer progression (Lee & Chang, 2019). The primary objective of this research was to discover natural inhibitors of VEGFR-2 by analyzing compounds derived from carrot through computational methods.Initially,a comprehensive list of natural compounds found in Daucus carota was obtained from reliable databases. These compounds were screened and filtered based on Lipinski's rule of five to assess their drug-likeness properties (Johnson & Nguyen, 2021). A total of 27 compounds were identified, out of which 23 adhered to Lipinski's criteria, suggesting their potential suitability for oral administration and therapeutic application. The subsequent phase involved molecular docking studies to investigate the binding affinity of these compounds to the active site of VEGFR-2. Molecular docking was conducted using advanced computational tools to determine the interaction energies between the selected compounds and VEGFR-2 (Smith & Brown, 2020). The docking results revealed that the average binding energ of the carrot-derived compounds with the VEGFR-2 active site was -5.7 kcal/mol. Among the tested compounds, daucol and germacrene D emerged as the most promising inhibitors, exhibiting binding energies of -7.67 kcal/mol and -7.51 kcal/mol, respectively. These values indicate strong interactions between these compounds and VEGFR-2, suggesting their potential efficacy as inhibitors. The docking analysis further revealed that the compounds formed stable interactions with critical residues in the VEGFR- 2 active site, which are essential for its enzymatic activity (Lee & Chang, 2019). This finding supports the hypothesis that the identified compounds can effectively block the VEGFR-2 pathway, thereby inhibiting angiogenesis. Such inhibition is particularly significant in the context of cancer, where angiogenesis plays a pivotal role in tumor growth and metastasis.In conclusion, this study highlights the potential of natural compounds from Daucus carota as inhibitors of VEGFR-2, paving the way for the development of plant-based therapeutic agents for cancer treatment. The promising results of daucol and germacrene D underscore the importance of further in vitro and in vivo validation to confirm their efficacy and safety. Future research should also focus on exploring the synergistic effects of these compounds with existing chemotherapeutic agents to enhance their therapeutic impact. This study not

only contributes to the growing body of knowledge on plant-derived bioactive compounds but also emphasizes the importance of integrating computational approaches in drug discovery to identify novel therapeutic candidates efficiently (Smith & Brown, 2020; Johnson & Nguyen, 2021).

Keywords: natural compounds from daucus carota, VEGFR-2 Inhibition, molecular docking

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ICB13 -1061

Curcumin's Journey Through Cellulose: Binding Dynamics Across Cellulose-derived Bio-Nanofibers

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Curcumin is a polyphenolic compound extracted from Curcuma longa with promising anti-cancer and anti-inflammatory properties (Karaboga Arslan et al., 2022; Zoi et al., 2021). The bioavailability of curcumin is limited due to its short half-life, low solubility, instability, rapid metabolism, and systemic clearance. Therefore, developing drug delivery systems for the efficient transfer of curcumin would be eminent (Hardwick et al., 2021; Huang et al., 2023; Tabanelli and Brogi, 2021). A way forward would be using cellulosic compounds as it has been proposed as a well-suited candidate for drug-delivery applications. Cellulose, with its hydrophilicity, superior mechanical qualities, biocompatibility, high water retention, surface modification, and slow drug release abilities has been a prominent choice (Liu et al., 2021; Pandey, 2021; Raghav and Sharma, 2021; Wang et al., 2024). Additionally, cellulose can be surface-modified by chemical groups, promising greater possibilities in efficient and targeted drug-delivery applications (Khine and Stenzel, 2020; Lukova and Katsarov, 2023). In this structural study, different forms of cellulose were studied for their potential in drug delivery of curcumin The 3D structures of cellulose fibers I (α and β), II, IIII, IVI, IVII, I triacetate, II triacetate, and II hydrate were obtained from the Polysac3db database (Sarkar and Pérez, 2012). Two common cellulose nanofiber arrangements in natural systems (cylindrical and planar) were obtained from a molecular dynamics study, validated by SEM analysis on electrospun cellulose nanofibers (Azimzadeh Irani et al., 2023). The 2D structures of curcumin (PubChem CID: 969516) and modified units of cellulose, namely methylcellulose, cellulose triacetate, hydroxypropyl methylcellulose, and hydroxyethyl cellulose were extracted from PubChem (PubChem CIDs: 51063134, 230396, 57503849, and 24846132, respectively) (PubChem). Subsequently, the 3D coordinates of these structures were generated using Open Babel (O'Boyle et al., 2011; OPENBABEL). The obtained structures were geometrically optimized using Avogadro with 1000 steps of Steepest Descent (Hanwell et al., 2012; Avogadro). Molecular dockings of curcumin and cellulose nanofibers were performed using AutoDock 4.2 and AutoDockTools (Morris et al., 2009). All dockings included 10 genetic algorithm runs with 25000000 as the maximum energy evaluations. The results were visualized using PyMOL (PyMOL).According to the results, cellulose II and Iβ fibers formed the strongest interactions with curcumin among the oligomeric structures, with binding energies of -5.84 and 5.31 kcal/mol, respectively. The results also demonstrated that the acetylation of cellulose I and II oligomers led to a higher affinity for curcumin. The binding energy of curcumin and cellulose I triacetate was -8.25 kcal/mol, followed by a binding energy of -7.70 kcal/mol in interaction with cellulose II triacetate. Moreover, when comparing the data obtained from cellulose units, hydroxypropyl methylation of cellulose resulted in the lowest binding energy with curcumin, -3.80 kcal/mol. This was compared to hydroxyethylation, acetylation, and methylation on cellulose units, with curcumin binding

energies of -3.74, -3.59, and -2.82 kcal/mol, respectively. This study demonstrates that different cellulose structures and specific surface modifications influence the binding affinity of curcumin. Cellulose fibers Iβ and II interact strongly with curcumin, while acetylation and hydroxypropyl methylation modifications on cellulose create even stronger candidates for curcumin delivery.

Keywords: curcumin, cellulose nanofibers, molecular docking, acetylation, hydroxypropyl methylation

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ICB13 -1064

Phylogenetic and In Silico Analysis of SQUAMOSA PROMOTER BINDING PROTEIN-LIKE (SPL) Gene Family in Crops

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The SQUAMOSA-PROMOTER BINDING PROTEIN-LIKE (SPL) genes represent a crucial transcription factor family in plants. We have developed a systematic bioinformatics pipeline for identification and characterization of SPL gene family in crop plants, using safflower (Carthamus tinctorius L.) as a case study. Our computational workflow combined sequence similarity searches and domain prediction algorithms to identify 44 SBP domain-containing sequences. In silico characterization using machine learning-based approaches revealed diverse protein architectures with sequences ranging from 60 to 7994 amino acids. Motif analysis using MEME identified conserved patterns ranging from 6 to 49 amino acids, while subcellular localization predictions demonstrated nuclear targeting for 60.7% of proteins. Evolutionary relationships were investigated through Maximum Likelihood phylogenetic reconstruction, revealing distinct patterns when compared with model plants like Arabidopsis and rice. Gene Ontology analysis highlighted significant overrepresentation of DNA binding (57.1%) and glycosyltransferase activity (35.7%). This integrative computational framework demonstrates the power of bioinformatics in understanding gene family evolution and can be applied to various crops.

Keywords: phylogenetic analysis, in-silico characterization, transcription factors, computational pipeline

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ICB13 -1066

Exploring the Genes Located on Chromosome Y in Non-obstructive Azoospermia: A Bioinformatic Approach

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Infertility affects an estimated 8–12% of couples worldwide, with male factors being a primary or contributing cause in approximately 50% of these cases. Non-obstructive azoospermia (NOA) is characterized by the absence of spermatozoa in the ejaculate and represents the most severe form of male factor infertility, accounting for 10%–15% of cases. Differentially expressed genes (DEGs) were analyzed using data from the GSE190752 dataset available in the Gene Expression Omnibus (GEO). The DEGs were compared to a list of human chromosome Y genes obtained from literature reviews to identify overlaps (Y-DEGs). The protein-protein interaction (PPI) network, and hub gene identifications were analyzed using the STRING database and cytoHubba plugin of Cytoscape software for Y-DEGs. The top 5 hub genes were then subjected to the ToppGene database to investigate biological processes and human-related phenotypes. The analysis identified 1,327 DEGs, including 928 downregulated and 445 upregulated genes. By comparing the DEGs with human chromosome Y genes, 22 genes were identified as the final list. The top five2 hub genes identified from the PPI network were ZFY, CDY2A, DDX3Y, USP9Y, and BPY2. According to the ToppGene database, the human phenotypes associated with the top five genes were “Y-linked inheritance”, “Male infertility”, “Decreased fertility in males”, “Gonosomal inheritance”, and “Infertility”. The biological processes of the mentioned top five gene include “gamete generation”, “multicellular organismal reproductive process”, “sexual reproduction”, “reproductive process”, and “spermatogenesis”. The results of this study demonstrate that genes on chromosome Y are critical for normal spermatogenesis and play a significant role in male infertility.

Keywords: male infertility, non-obstructive azoospermia, chromosome Y, microarray, gene expression

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ICB13 -1067

A Computational Approach to Identify Potent Inhibitors of Janus Kinase 1 from Natural Products: Structure-Based High-Throughput Virtual Screening and LightGBM Classifier

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Computational approaches play an important role in drug development because they reduce time and costs while boosting the likelihood of generating effective therapeutic candidates. The combination of several approaches, such as virtual screening and quantitative structure-activity relationship (QSAR) models, allows for the investigation of the link between molecular structure and biological activity against specific targets. In recent years, advances in computational tools have revolutionized the drug discovery environment, allowing researchers to effectively navigate enormous chemical landscapes and uncover potential candidates for clinical development. This study aims to find natural compounds from the IMPPAT database that effectively inhibit the JAK1 protein. JAK1 (Janus kinase 1) is a pivotal enzyme in the JAK-STAT signaling pathway, influencing immune responses and hematopoiesis. Its dysregulation is associated with multiple diseases, such as atopic dermatitis, rheumatoid arthritis, and certain cancers. The critical role of JAK1 in mediating signals from various cytokines underscores the importance of developing selective JAK1 inhibitors for therapeutic intervention. By targeting JAK1, it may be possible to modulate inflammatory responses and improve treatment outcomes for patients suffering from these conditions. This study's methodology includes several important phases to ensure a complete evaluation of potential JAK1 inhibitors. Initially, the 3D crystallographic structure of the JAK1 protein was acquired from the PDB database. The structures of known JAK1 inhibitors were collected from the PubChem database, and their structural fingerprints were computed using the RDkit tool in Python. In the next step, a LightGBM (LGBM) classifier was constructed and trained utilizing structure fingerprints to accurately assess the link between chemical structure and biological activity. Next, natural product structures were downloaded from the IMPPAT database, which offers a plethora of information on bioactive substances produced from natural sources, and morgan fingerprints were calculated for them. High-throughput virtual screening (HTVS) has emerged as a pivotal to screen thousands of chemical structures rapidly and efficiently is essential for identifying viable leads. The first step in our HTVS approach was employing molecular docking simulation to evaluate the binding affinities and quickly identifying compounds that exhibit favorable interactions with the JAK1 protein, the next step was to apply Lipinski's Rule of Five as a filtering mechanism. This rule serves as a guideline for assessing the drug-likeness of compounds based on their molecular properties. The filtered compounds were then subjected to predictive modeling using machine learning classifiers. The best-performing structures were then selected for predictive modeling to assess their potential biological activity. Finally, the activity of selected structure against JAK1 were predicted by LGBM classifier and four natural products (IMPHY004857, IMPHY009380, IMPHY000451, and IMPHY008874) were identified as promising

inhibitors. These compounds demonstrate significant potential as effective JAK1 inhibitors based on their predicted interactions and favorable pharmacokinetic properties. The study effectively identified four natural compounds as potential JAK1 inhibitors, highlighting the significant role of computational approaches in drug discovery. However, it is essential to conduct experimental validation to confirm the biological activity and therapeutic efficacy of these identified structures.

Keywords: computational drug discovery, virtual screening, JAK1 inhibitors

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ICB13 -1068

Design and Analysis of siRNA for Silencing the NS3 Gene of Hepatitis C Virus: A Novel Therapeutic Approach

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This study focuses on the design and analysis of siRNA to inhibit the NS3 gene of the Hepatitis C Virus (HCV). The main objective was to identify mRNA sequences of the NS3 gene and design siRNAs to suppress its activity. Using NCBI, the NS3 gene sequence was identified, and the coding sequence of the helicase domain was selected due to its conserved nature for siRNA design. RNAstructure software was employed to simulate siRNA-mRNA interactions for the HCV genome. Additionally, BLAST and RNAhybrid tools were used to evaluate potential off-target effects on the human genome. These methods quantitatively predicted the targeting accuracy and efficacy of siRNAs in inhibiting HCV replication. The results demonstrate that the designed siRNAs exhibit significant potential as an effective therapeutic strategy for treating HCV infection.

Keywords: siRNA design, Hepatitis C Virus (HCV), NS3 helicase inhibition, RNA interference (RNAi), therapeutic RNA silencing

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ICB13 -1069

Expansion and Sequencing of the DNA Code Used in the COVID-19 Vaccine Using Meta-Heuristic Algorithms

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The Spike gene of the SARS-CoV-2 virus is responsible for encoding the spike protein, which plays a key role in the virus's attachment to the ACE2 receptors on the host cell surface and its entry into the cell. This gene and its associated protein have been one of the primary targets for research in vaccine and drug development. The full length of this gene is approximately 3,822 nucleotides. However, in this part, we are using a partial sequence of 350 nucleotides. Using a shorter section (such as the first 500 base pairs) helps in quickly examining fundamental concepts, genetic patterns, or potential variations. Moreover, the initial region of the gene typically includes the start Codon (ATG) and regulatory regions that control the initiation of protein translation. This section is crucial for understanding the mechanism of protein production and for targeting in research. Using metaheuristic algorithms, we investigate the DNA sequence used in the COVID-19 vaccine by applying algorithms designed to solve the Traveling Salesman Problem (TSP) for generating, extending, sequencing, and matching other DNA sequences. The objective of the problem has been compared using four Single-crossover Genetic Algorithm (GA) (Golberg, 1989), Multi-crossover GA, Teaching-Learning Based Optimization (TLBO) (Rao et al., 2011) and New Improved TLBO (NITLBO) (Aliyari Boroujeni et al., 2023) algorithms with identical parameters, including a population size of 100 and a maximum of 300 iterations. The mutation rate for both types of GA implementations has been set to 0.7. Additionally, for the NITLBO algorithm, the weight of elitism and number of teachers are set to 0.9 and 20, respectively. In these experiments, the Single-crossover GA reached a Hamming distance of 212.5, corresponding to 60.7% accuracy. For the Multi-crossover GA, the values were 233.5 and 66.7% accuracy. The TLBO algorithm showed a Hamming distance of 331 with 94.5% accuracy, while NITLBO achieved a distance of 346 and 98.8% accuracy. The results from comparing these algorithms show that the TLBO and NITLBO algorithms perform better than the GAs. This is because in the GAs, the presence of the mutation rate parameter can cause the sequence code matching not to necessarily follow an increasing trend and although Single-crossover GA executes in a shorter time, it does not always guarantee an optimal solution.

Keywords: gene sequence, COVID-19, traveling salesman problem, genetic algorithm, teaching-learning based optimization

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ICB13 -1071

In silico vaccine design for breast cancer

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Breast cancer is one of the most common types of cancer among women worldwide and is also the most common cause of cancer-related death in women. Triple-negative breast cancer (TNBC) is a highly aggressive and metastatic subtype of breast cancer that lacks responsiveness to targeted therapies (Al-Hawary et al., 2023, Hong and Xu, 2022, Hosseini et al., 2023, Obeagu and Obeagu, 2024). Consequently, it is crucial to explore and develop new treatment strategies for this malignancy. Recent progress in immunoinformatics has paved the way for innovative approaches, including the design of vaccines that utilize specific epitopes (Dariushnejad et al., 2022, Parvizpour et al., 2018, Parvizpour et al., 2020). The aim of this study is to develop a multi-epitope subunit vaccine targeting CEA, WT-1, and Survivin using immunoinformatics techniques. Immunodominant epitopes from cytotoxic T lymphocytes (CTLs), helper T lymphocytes (HTLs), and B cells were selected from epitope prediction servers to develop a peptide vaccine against breast cancer. The selected epitopes were linked using proper linkers. The designed construct demonstrated a significant degree of antigenicity as assessed by VaxiJen, along with non-allergenicity and non-toxicity. The physicochemical properties of the designed vaccine were analyzed using the ProtParam server, which indicated its suitability for immunogenic applications. The 3D model of the construct demonstrated that the refined version was of high quality and exhibited significant structural stability. Molecular docking results revealed that the vaccine exhibits a strong binding affinity for both TLR2 and TLR4, while molecular dynamics simulations confirmed the stability of the docked vaccine-TLR complexes. Our results indicate that the designed multi-epitope vaccine may serve as a promising candidate for protection against breast cancer. However, further experimental studies are required to validate these predictions.

Keywords: in-silico, vaccine, cancer, multi-epitope.

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ICB13 -1072

Development of a Multi-Epitope Vaccine Candidate for Brucella: An Immunoinformatics Approach to Achieve Cross-Protection

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Brucellosis is a worldwide bacterial zoonosis disease transmitted from animals to humans. Despite the use of various strategies in the design of vaccines, such as live attenuated vaccines and dead vaccines, there is still no high –performance vaccine. Based on problems with live vaccines, there is a need to introduce new candidates for immune response against Brucella (Avila-Calderon et al., 2013, Corbel, 1997). Epitope-based vaccines as a new type of subunit vaccines that are composed of immunogenic regions, B-cell and T-cell epitopes, induce targeted immune responses (Goumari et al., 2020, Malonis et al., 2019, Sette and Fikes, 2023, Wang et al., 2024). We designed a vaccine candidate that incorporates T-cell and B-cell epitopes from OMP31, BLS, DnaK, Urease, TF, along with HSP70 linked by an EAAK sequence as an adjuvant to enhance the immunogenicity of the vaccine construct. Antigenicity, physicochemical characteristics, allergenicity, tertiary structure, and molecular docking were evaluated. Subsequently, the most optimal construct was selected, and computational immune simulations were evaluated. Our results revealed that the designed construct has appropriate properties, such as high score for antigenicity, good stability, and more. Moreover, it demonstrates a strong binding affinity for the toll-like receptor. This study presents a vaccine candidate that has been evaluated in silico as a potential option against both Brucella melitensis and Brucella abortus. To confirm the effectiveness of the designed vaccine, laboratory validation through in vivo studies is essential.

Keywords: multi-epitope vaccine, brucella, immunoinformatics, vaccine design.

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ICB13 -1073

In silico analysis of Maize WRKY transcription factors in response to drought and salt stress

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After wheat and rice, maize is the most important agricultural product and is very important for human, livestock, pharmaceutical and food industries. Biotic and abiotic stresses are the most important factors limiting the performance of agricultural plants. The response to stress in organisms usually occurs with changes in gene expression due to the intervention of transcription factors. The WRKY gene family encodes a large group of transcription factors that play a very important role in the regulation of genes responsive to biotic and abiotic stresses. In this research, a comprehensive analysis of maize WRKY transcription factors was investigated using a bioinformatics approach. For this purpose, the entire maize proteome was first obtained from the Ensemble Plants database and a total of 129 significant sequences corresponding to the non-repetitive HMM profile was obtained based on the HMM pattern of the WRKY domain. The highest gene density was found to be associated with chromosome numbers 8 and 3, respectively, with 25 and 23 WRKY genes. A total of 39,669 WRKY transcription factor binding sites were identified in the maize genome, of which 7,503 unique genes had at least one WRKY transcription factor binding site. Of the total 47 WRKY profiles introduced in the JASAPAR database for Arabidopsis, 37 profiles were identified in the maize genome that were significantly present in the maize genome. Based on the study of the phylogenetic relationships of the maize WRKY genes, the genes were classified into three groups. Group I genes, structurally, had two WRKY domains. Finally, based on the information available in gene expression databases, 52 WRKY genes were observed to be involved in drought stress and 26 genes in salt stress. Under drought stress, 31 genes were up-regulated and 21 genes were down-regulated in expression, and in the conditions of salt stress all genes have down-regulated.

Keywords: drought stress, salinity stress, WRKY transcription factors

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ICB13 -1074

A Fuzzy Bayesian Network Model for Personalized Diabetes Risk Prediction: Integrating Lifestyle, Genetic, and Environmental Factors

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This study introduces a novel Fuzzy Bayesian Network (FBN) model for predicting diabetes risk by integrating hereditary traits, environmental influences, and personal lifestyle data. Traditional Bayesian networks, which use Boolean logic and set theory, have limitations in handling the complexity and uncertainty of real-world health data. Boolean logic relies on rigid true/false classifications, which oversimplify relationships between variables. Similarly, set theory groups different samples into the same category, failing to capture their differences. These limitations hinder the accurate representation of overlapping and uncertain data. The proposed FBN model overcomes these challenges by assigning unique fuzzy membership degrees to each sample, ensuring distinct representation. The methodology applies the chain rule and Markov Chain Monte Carlo (MCMC) methods to model complex interactions among variables like age, weight, genetic traits, exercise, and sugar intake, addressing both intrinsic and extrinsic diabetes risk factors. Fuzzy membership functions quantify the degree of belonging to fuzzy sets, with these membership degrees acting as weights in the network. By combining these weights with probabilistic values, the model handles uncertainties and improves prediction accuracy. Genetic information is clustered using fuzzy c-means, simplifying the network while preserving essential variability. Compared to traditional binary models, the FBN offers advantages in managing uncertainty and providing probabilistic risk assessments. Boolean models, limited to rigid true/false relationships, fail to capture the complexities of health data, which often exist on a continuum. Results show that FBN delivers more accurate and flexible predictions, making it valuable for early detection, personalized risk assessment, and preventive care strategies. This adaptable model holds potential for application in other chronic disease research and clinical settings.

Keywords: disease risk prediction, gene-environment interactions, fuzzy bayesian networks, fuzzy clustering.

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3D modeling of the spike protein in the Omicron variant of the coronavirus and comparison with the Delta and Wuhan strains

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The spike protein mediates SARS-CoV-2 entry into human cells, stimulates neutralizing immune responses in humans, and is the basis of current COVID-19 mRNA vaccines (Krammer, 2020, Li, 2016). As the coronavirus spreads, mutations occur in its structure, primarily affecting its spike protein, resulting in multiple variants of this virus (Kandeel et al., 2022, Wang and Cheng, 2022). Omicron is the most distinct variant observed in significant numbers during the pandemic, raising concerns that it may be associated with increased transmissibility and reinfection risk and potentially reduce the effectiveness of existing vaccines (Kumar et al., 2022). This study compares the spike proteins of Delta, Omicron BA.5, and the Wuhan-Hu-1 (wild-type) strain, focusing on their binding affinities to ACE2 and furin, using computational tools to analyze their differences. The spike protein FASTA sequences for Wuhan-Hu-1, Delta, and Omicron BA.5 strains were obtained from Uniprot, ViralZone, and NCBI databases. Protein modeling was performed using the Swiss Model server (Schwede et al., 2003) by selecting appropriate templates and building 3D models. The quality of the models was assessed using the PSVS online tool through Ramachandran plot analysis. Protein domains (S1, S2, and RBD) were identified using the Interproscan (Jones et al., 2014) plugin in the Geneious Prime 2021.1.1 (https://www.geneious.com). The modeled structures were visualized using PyMOL software (Schrödinger LLC). Physicochemical parameters were analyzed using ExPASy ProtParam (Gasteiger et al., 2005). Sequence alignments were performed using Clustal Omega (Sievers and Higgins, 2014) to identify conserved amino acids and mutations. Intrinsically disordered regions (IDRs) were predicted using the IUPred3 online tool, which identifies unstructured protein regions by analyzing amino acid interaction energies (Erdős et al., 2021). The analysis revealed that the Omicron BA.5 variant has accumulated 36 mutations compared to the Wuhan-Hu-1 strain and 35 mutations compared to the Delta variant. More than 40% of these mutations are concentrated in the receptor-binding domain (RBD). The Omicron BA.5 variant demonstrates potentially higher stability due to a higher aliphatic index (84.86) and an increased number of charged amino acids, potentially resulting in stronger ionic interactions. The furin cleavage site mutation (P681H) in Omicron BA.5 likely enhances protease recognition and viral entry. Moreover, the RBD of Omicron BA.5 maintains an "open" conformation, allowing it to be consistently ready for binding with the ACE2 receptor, which may contribute to its increased transmissibility. This protein variant also displays fewer disordered regions than other variants, indicating a more stable structure. Collectively, these structural changes may explain the enhanced transmissibility and immune evasion capabilities of Omicron BA.5. This study used bioinformatics tools to compare the spike proteins of the Omicron BA.5 variant with the Wuhan-Hu-1 and Delta strains. An analysis of the protein sequences and

modeled structures revealed that the spike protein of Omicron BA.5 has undergone numerous mutations compared to earlier variants. These mutations can influence the protein's physical and chemical properties. Most of these mutations are located in the receptor-binding domain (RBD), which could enhance binding efficiency to the ACE2 receptor while potentially reducing vaccine effectiveness.

Keywords: Coronavirus, SARS-CoV-2 variants, spike protein, Omicron BA.5, viral transmissibility, bioinformatics analysis

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ICB13 -1076

Herbal Drug Candidate as DNA Gyrase Inhibitor in M. Tuberculosis (Causative Agent of Tuberculosis)

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Tuberculosis (TB) remains a global health emergency according to WHO (Chakaya et al., 2021), with Sistan and Baluchistan province showing concerning rates, probably related to its long border with Pakistan and Afghanistan, where the CAS family of TB bacteria is prevalent (Haeili et al., 2013). TB, caused by Mycobacterium tuberculosis (Shradheya et al., 2020), primarily affects the lungs (Beiranvand et al., 2014). Some recent studies indicate that natural compounds may offer promising treatment options (Shashidhar et al., 2015, Verma et al., 2023). This research aims to use computational tools to 1) analyze drug resistance probability in the most studied CAS strain (CAS/NITR204) and 2) identify a potential herbal drug candidate that inhibits bacterial DNA gyrase, an essential enzyme for DNA replication, comparing it with moxifloxacin, a known synthetic antibiotic against the bacterial DNA gyrase. The study first compared protein sequences from H37Rv and CAS/NITR204 strains, focusing on rpoB, inhA, katG, pncA, gyrA, and gyrB from UniProt and NCBI databases using Clustal Omega alignment (Sievers and Higgins, 2014). The 3D structure of the drug target was prepared using the PDB database (Berman et al., 2000). Further investigations assessed drug resistance probability in the CAS/NITR204 variant. Molecular docking was performed using Maestro software (Schrödinger LLC) with about 450 natural ligands collected from Sistan and Baluchistan medicinal plants. Docking utilized Glide module with extra precision mode, and protein-ligand binding energies were calculated via MM-GBSA, compared to moxifloxacin. Top candidates were visualized in PyMOL (Schrödinger LLC) to analyze their positioning in the enzyme active site. The analyzed proteins showed that GyrA (DNA Gyrase subunit A) had five mutations, including two in the Quinolone Resistance-Determining Regions (QRDR). Although these mutations did not align with known patterns that typically cause resistance, GyrA was identified as the most likely target for further investigation into drug resistance. Additional studies revealed no significant differences in the interaction patterns of moxifloxacin between the CAS/NITR204 and H37Rv strains, suggesting that the CAS/NITR204 strain has likely not developed antibiotic resistance. Two natural compounds derived from the black myrobalan plant (Terminalia chebula) were identified as the most promising potential inhibitors of DNA gyrase. The first compound, Chebulinic Acid (ZINC000169356891), exhibited mean docking and MM-GBSA scores of -48.15 kcal/mol for the H37Rv strain and -42.9 kcal/mol for the CAS/NITR204 strain in chain 1. The second compound, 3,4,6-tri-O-galloyl-beta-D-glucose (PubChem CID: 14188641), demonstrated scores of -38.13 kcal/mol for H37Rv and -39.58 kcal/mol for CAS/NITR204 in chain 2. In comparison, moxifloxacin recorded approximately -25.7 kcal/mol scores for both strains and chains. Both natural compounds showed a stronger binding affinity than moxifloxacin, suggesting that Terminalia chebula could be a viable treatment

option for both strains. This study identified a local medicinal plant from Sistan and Baluchistan as a potential treatment for tuberculosis, a disease prevalent in this region. Two compounds derived from the myrobalan plant (Terminalia chebula) exhibited stronger binding affinities to the bacterial DNA gyrase than moxifloxacin. This suggests potential efficacy against the H37Rv and CAS/NITR204 strains, although further clinical validation is necessary.

Keywords: Tuberculosis (TB), mycobacterium tuberculosis, CAS/NITR204 strain, DNA gyrase, herbal medicine, computational biology

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Bioinformatics investigation of the structure and function of photoprotein mnemiopsin2 following Glutamine 23 substitutions using a site-directed mutagenesis

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Ctenophores are bioluminescent marine organisms that are found all over the world. Light emission in these organisms is carried out by Ca^{2+}-regulated photoproteins. Ca^{2+} is not essential for light emission in these photoproteins(Stepanyuk and Liu, 2013). However, The light-yielding reaction proceeds at a very slow rate in the absence of Ca^{2+}, and the light intensity is increased up to 1 million-fold with the addition of Ca^{2+}(Eremeeva and Vysotski, 2019). One of the main applications of Ca^{2+}-regulated photoproteins, due to their ability to emit light upon binding to calcium, is their use for detecting calcium ions in biological systems(Natashin and Markova, 2014). These photoproteins consist of a single polypeptide chain and are structurally compact and globular(Hematyar and Jafarian, 2022). Mnemiopsin 2 is a Ca^{2+}-regulated photoprotein extracted from Mnemiopsis leidyi. Light emotion in this photoprotein is blue light, by coelenterazine as a substrate in the presence of calcium ions (Hosseinnia and Khalifeh, 2020). Photoprotein mnemiopsin 2 has three active motifs; EF-hand I, III, and IV, which are located in 45–56, 137–148, and 171–182, respectively(Jafarian and Sajedi, 2018). The Q23E mutation was investigated to increase the negative surface charge for enhanced Ca2+ sensitivity in mnemiopsin 2. Therefore, The three-dimensional structure of the mutant was made with the Modeller program V. 10.4, and the best structure was selected and evaluated using ModEval and SAVES. The VADAR and ProtParam servers were used to Evaluate the secondary structure of the protein, structure stability, and physicochemical properties. The Kyte & Doolittle hydropathy plot was obtained using the ProtScale server. Then, the graphical form of the desirable model was drawn using the UCSF Chimera software, and the compactness of the protein's tertiary structure was examined. Finally, the selected mutant model was compared with the native model. The results indicate a

decrease in the folding free energy of the protein with the Q23E mutation, and as a result, it is more stable than the wild-type protein. Also In terms of hydrophobicity, it has not changed. It seems that by reducing the isoelectric point of the mutated protein due to the substitution of an acidic amino acid and an increase in the protein's accessible surface area, binding to Ca^{2+} increases.

Keywords: calcium sensitivity, Mnemiopsin 2, molecular modeling, photoprotein, site-directed mutagenesis.

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ICB13 -1080

Molecular Interactions Between Vitiligo and Thyroid Diseases: Identification of Hub Genes, Pathways and Therapeutic miRNAs

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Vitiligo is a chronic autoimmune disorder characterized by the loss of skin pigmentation due to the destruction of melanocytes (Bhange et al.). Thyroid diseases are prevalent endocrine disorders that can significantly impact health (Cohen et al., 2023). The relationship between vitiligo and thyroid diseases is well-documented, with studies indicating a strong association between vitiligo and autoimmune thyroid disorders such as Hashimoto's thyroiditis and Graves' disease. This association is attributed to shared autoimmune mechanisms, including genetic predispositions and oxidative stress, which contribute to the destruction of both melanocytes and thyrocytes (Chen et al., 2024; Sandru et al., 2021). Understanding the molecular interactions between these diseases can provide insights into their pathogenesis and potential therapeutic targets. Initially, common proteins related to the disorders vitiligo and thyroid were investigated in various gene-disease databases. To discover important hub genes, build a Protein-Protein Interaction (PPI) network for common proteins achieved via Cytoscape software. Enrichment analysis of biological pathways and processes (Gene ontology and KEGG) was performed using Enrichr. Subsequently, we explored the therapeutic potential of microRNAs (miRNAs) targeting critical hub proteins implicated in vitiligo and thyroid disorders, utilizing databases such as miRNet, miRBase, and TargetScan. Key genes were validated through literature mining, and their interactions were confirmed. The analysis identified several hub genes, including TP53, STAT1, IL6, TNF, STAT3, and PTPN22 which exhibited significant interactions within the network. These genes often play critical roles in inflammation, apoptosis and immune response. Pathway enrichment analysis revealed critical pathways such as autoimmune dysregulation, inflammatory pathways, apoptosis, JAK-STAT signaling, and cytokine-cytokine receptor interaction. Target miRNAs for these hub genes were also identified, including miR-125b, miR-146a, and miR-21 that the highest relation with hub

proteins related to two conditions. This study provides a comprehensive computational analysis of the common molecular mechanisms underlying vitiligo and thyroid disorders. The identified hub genes, enriched pathways, and potential miRNA regulators offer valuable targets for further exploration and validation, ultimately contributing to a better understanding of disease pathogenesis and the identification of shared therapeutic avenues.

Keywords: Vitiligo, Thyroid, PPI network, gene ontology, miRNA

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ICB13 -1081

Identification of key genes associated with glioblastoma multiforme using microarray data

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nervous system that develops between the ages of 45 and 70 years.(Farsi and Allahyari Fard, 2023) The aim of this study was to identify key genes associated with glioblastoma multiforme.(Wang and Wai 2015) Microarray gene expression data related to patients with glioblastoma and healthy individuals were analyzed. Differentially expressed genes between patients and healthy individuals were identified.(Zhou and Yang 2019). Cytoscape software was used to analyze the protein-protein interaction network of these genes. Then, 10 key genes associated with this disease were identified based on the network criteria. The results of the analysis identified 737 differentially expressed genes between patients and healthy individuals, of which 464 genes were up-regulated and 273 were down-regulated. Finally, 10 key genes were identified, among which HLADQA2 and HLADRA were determined as the most important genes. These genes can be considered as potential biomarkers associated with glioblastoma disease. The use of these markers can lead to early diagnosis of this disease and the adoption of more effective treatment methods against this disease.(Hu and Wei 2015)

Keywords: Glioblastoma, microarray, key gene, analyze

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ICB13 -1082

A New LDA-based Genetic Algorithm for Feature Selection and Classification in Gene Expression Data Analysis

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Recent advancements in cancer diagnosis have driven the need for more efficient genetic data analysis methods to improve the accuracy and speed of identifying influential genes. Genetic algorithms, inspired by evolutionary processes in nature, have emerged as powerful tools for optimizing and identifying cancer-related genes. However, a significant challenge in these algorithms is the gradual reduction of population diversity, leading to premature convergence on suboptimal solutions, a phenomenon known as genetic drift. This effect causes certain areas of the search space to be overlooked, ultimately reducing the accuracy of results. This study introduces a repair operation as part of the genetic algorithm's process to address these limitations. This repair operation purposefully and intelligently eliminates irrelevant genes while enhancing essential ones, thus improving the quality of feature selection and preventing premature convergence. This approach uses Linear Discriminant Analysis (LDA) as a crucial tool to guide feature selection precisely. LDA coefficients, which reflect each feature's contribution to class discrimination, are used in a repairing mechanism applied to the individuals. This way, the proposed repair mechanism removes noisy and irrelevant features, preserving only those most influential in distinguishing between healthy and cancerous samples. This approach not only enhances diagnostic accuracy but also simplifies the model by finding more sparse candidate subsets, reducing the risk of overfitting. The proposed repair operation was applied to several gene expression benchmark datasets in terms of convergence speed and the performance of the proposed approach compared with the conventional GA-based feature selection. The results show that the proposed approach produces consistently better subsets with few genes and classification accuracies.

Keywords: genetic algorithm, feature selection, linear discriminant analysis, gene expression data

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ICB13 -1083

Investigation of Missense Mutations in the SHBG Gene: Bioinformatic Analysis and Pathogenesis Prediction in binding and regulating the bioavailability of sex hormones

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Sex Hormone-Binding Globulin (SHBG) is a glycoprotein produced by the SHBG gene, which plays an essential role in binding and regulating the availability of sex hormones, such as testosterone and estradiol. Alterations in the SHBG gene can disrupt its function and lead to various health issues. In this study, we identified ten missense single nucleotide polymorphisms (SNPs) in the SHBG gene using the NCBI SNP database: rs1474417796 (Gly230Arg), rs1473824375 (Leu42Pro), rs1471581717 (Gly245Glu), rs1464753722 (Pro171Ala), rs6258 (Pro185Gln), rs142693170 (Thr398Asn), rs146779355 (Gly224Glu), rs1474554985 (Val315Met), rs1448649216 (Ser266Arg), and rs1427555621 (Leu17Met).Several bioinformatics tools, including PolyPhen2, I-Mutant, SIFT, HOPE, Expasy, and NetSurfP 3.0, were employed to assess the structural and functional impacts of the analyzed single nucleotide polymorphisms (SNPs). PolyPhen2 predictions indicated that all ten SNPs are potentially damaging, with scores exceeding 0.95, which suggests a high likelihood of pathogenicity. I-Mutant analyses consistently showed a decrease in protein stability for these variants, reinforcing the hypothesis that they may have deleterious effects. SIFT results confirmed that these SNPs are likely to disrupt the normal function of the SHBG protein. Structural modeling using HOPE and Expasy revealed significant changes in the protein's conformation, interaction patterns, and hydrophobic properties. Furthermore, NetSurfP 3.0 results indicated altered surface accessibility and changes in secondary structural elements, which could impact the protein's interactions with ligands and other biomolecules. While all analyzed SNPs are predicted to be pathogenic and detrimental to the stability and function of SHBG, their specific impacts differ. These variations underscore the complexity of structural and functional disruptions caused by SNPs, highlighting the importance of experimental validation. Laboratory studies are necessary to confirm these computational predictions and to elucidate the molecular mechanisms through which these SNPs affect SHBG and their potential role in

disease. In conclusion, this bioinformatics-based study suggests that these missense SNPs in the SHBG gene may contribute to pathogenic outcomes by disrupting the protein's stability and functionality. However, further experimental validation is required to confirm the accuracy of these predictions and their clinical significance.

Keywords: SHBG, Missense SNPs, bioinformatics analysis , pathogenicity, polycystic ovary

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ICB13 -1084

In Silico Analysis of the R410W Mutation in ZP1: Effects on Protein Stability and Interactions

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The human zona pellucida (ZP) is an extracellular glycoprotein matrix surrounding the oocyte, playing a critical role in oocyte maturation, sperm-egg interactions during fertilization, and early embryonic protection. It comprises four glycoproteins, including ZP1, which contributes to its structural integrity and function. Mutations in ZP1 have been linked to structural and functional abnormalities of the zona pellucida, leading to female infertility associated with zona pellucida deficiency and Empty Follicle Syndrome (EFS). Among these, the R410W point mutation is associated with oocyte degeneration and the absence of a surrounding zona pellucida, underscoring its potential impact on protein stability and interaction dynamics. This study evaluates the effects of the R410W substitution on ZP1 protein stability and non-covalent interactions using bioinformatics tools. The sequence of the ZP1 protein was accessed from the uniprot database (P60852). The impact of the R410W variant on the stability of the ZP1 protein was assessed using MUpro, I-Mutant, and PremPS prediction tools. The findings from these tools were expressed as ΔΔG values, where a negative value indicates a destabilizing effect from a single point mutation, while a positive value in PremPS indicates a destabilizing mutation. Additionally, the PremPS tool was employed to calculate and visualize the non-covalent interactions involving residue 410 with other residues in both the native and mutant forms of the ZP1 protein. The ΔΔG values obtained from the three online tools uniformly indicate a reduction in the stability of the mutant protein, with values of -0.68797423 for MUpro, -0.50 for I-Mutant 2, and 0.71 for PremPS. Furthermore, the results from the PremPS database

highlighted the loss of a hydrophobic bond between W410 and P537 residues, as well as some van der Waals interactions with Y420 residue and two ionic bonds with E439 residue that were present in the wildtype protein. Additionally, the mutant ZP1 protein exhibited one polar and one hydrophobic bond with E408 that were not present in the wildtype. These findings highlight the potential implications of the R410W substitution on the structural integrity and stability properties of the ZP1 protein

Keywords: ZP1, R410W, point mutation, stability prediction, female infertility

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ICB13 -1085

Site-Directed Mutagenesis to Optimize Anti-TIM-3 Antibody Affinity through In-Silico Modeling

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T-cell immunoglobulin and mucin domain 3 (Tim-3) has been identified as a marker for differentiated interferon-gamma (IFN-γ)-producing CD4+ T helper type 1 (Th1) cells and CD8+ T cytotoxic type 1 (Tc1) cells. Tim-3 serves as an inhibitory co-receptor that plays a crucial role in maintaining the balance between normal immune responses and dysfunctional ones. It has a diverse function related to T cell exhaustion and tolerance, particularly noted in various chronic viral infections in humans. Tim-3 acts as a negative regulator of both Th1 and Tc1 cell functions, promoting cell death when it interacts with its ligand, galectin-9 (Gal-9). This interaction triggers apoptosis, and blocking it in vivo has been shown to exacerbate autoimmunity and disrupt tolerance in experimental models, reinforcing Tim-3's role as a negative regulatory molecule. Consequently, Tim-3 has emerged as a potential therapeutic target and is currently being explored in both preclinical and clinical settings. Site-directed mutagenesis is an effective technique for improving the affinity between molecules. Given the significance of monoclonal antibodies in modern cancer and infectious disease therapies, greater attention should be directed towards site-directed mutagenesis methods. The aim of this research is to enhance the affinity of the anti-Tim-3 monoclonal antibody for Tim-3. To begin, the three-dimensional structure of Tim-3 in complex with the anti-Tim-3 antibody was retrieved from the Protein Data Bank (PDB) using the code 7KQL. The SabDab server was utilized to determine the sequencing of the antibody's complementarity-determining regions (CDRs). Using the PyMOL tutorial server, we identified critical areas in the heavy chain CDRs of the antibody and Tim-3. Following this, PyMOL software was employed to examine the interaction between these two structures and to identify a mutation that could enhance the binding affinity of the antibody to Tim-3. The analysis conducted with PyMOL indicated that mutating the amino acid tyrosine (Y) at position 103 in the heavy chain of the anti-Tim-3 antibody to arginine (R) resulted in a reduction of the bond length between the antibody and Tim-3 from 2.6 angstroms to 2.2 angstroms. This suggests an improvement in the interaction between these two structures and enhances the affinity between the antibody and its antigen.

Keywords: Tim-3, site directed mutagenesis, antibody affinity, monoclonal antibody.

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Assessment of TP53 Gene Mutations by Bioinformatic tools and Their Impact on Tumor Suppressor Function

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The TP53 gene encodes a tumor suppressor protein that is essential for maintaining cellular homeostasis. Commonly known as the "guardian of the genome," TP53 plays a crucial role in regulating processes such as cell cycle arrest, apoptosis, senescence, DNA repair, and metabolic reprogramming in response to cellular stress. This protein functions as a tetrameric transcription factor, binding to specific DNA sequences to control the expression of target genes. Despite its critical role in preventing malignant transformation, TP53 is one of the most frequently mutated genes in human cancers. Mutations, particularly those occurring in its DNA-binding domain, impair its tumor-suppressive functions and are linked to various cancers, including breast cancer. These mutations often exhibit dominant-negative or loss-of-function effects, disrupting key regulatory pathways. In this study, five distinct pathogenic mutations in the TP53 gene were analyzed, with a focus on isoform D. The three-dimensional structure of TP53 was modeled using two tools: AlphaFold2, which predicts protein structure de novo without a template, and SWISS-MODEL, which generated a structure based on a template from the TP53 protein of Macaca fascicularis. The resulting structures were visualized and analyzed in PyMOL, providing a detailed view of their conformations. After modeling, the identified mutations were introduced into the TP53 sequence, and the mutated protein structures were generated using AlphaFold2. These mutated models were then aligned with the wild-type structure in PyMOL for direct comparison. Structural differences were captured as images, highlighting the impact of the mutations on protein conformation and potential functional impairment. The comparison revealed alterations in the protein structure that may affect its overall function. Using multiple Bioinformatic tools, including PolyPhen-2, SIFT, ExPASy, HOPE, and I-Mutant, we systematically evaluated how these mutations affect the protein's structure, stability, and function. Our analyses revealed that all five mutations were pathogenic, significantly disrupting TP53's ability to bind to DNA and destabilizing its structural domains .After computational analysis, PolyPhen-2 identified all mutations as pathogenic, with scores of 0.95 or higher, indicating a high likelihood of damaging the protein's function. SIFT analysis further corroborated these findings, assigning a score of 0 to all mutations, signifying maximum pathogenicity.

Using Expasy, we generated a hydrophilicity plot with Hydropath. / Kyte & Doolittle chosen as the amino acid scale , which revealed that the mutations altered the hydrophilicity scores of residues, likely resulting in significant structural changes and destabilization of the protein's domains. Additionally, both HOPE and I-Mutant analyses confirmed the pathogenic nature of these mutations. This study underscores the value of in-silico approaches in elucidating the molecular consequences of TP53 mutations. These findings contribute to the growing body of knowledge necessary for developing targeted therapeutic interventions aimed at restoring TP53 function in cancer treatment. Future research should focus on experimental validation of these results to confirm the structural and functional impacts of these mutations both in vitro and in vivo.

Keywords: TP53, tumor suppressor protein, pathogenic mutations, cancer-associated variants, molecular modeling

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Structural and Biochemical Insights into Single-Stranded DNA-Binding Protein Complexes: A Comparative Study of DnaT, DnaBC, and Pab-RPA

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Single-stranded DNA binding protein complexes play an important role in maintaining genome stability during essential processes such as replication and repair (Madru et al., 2023). These complexes stabilize ssDNA against degradation and facilitate interactions vital for DNA metabolism (Madru et al., 2023). This study investigates three representative ssDNA-binding complexes—DnaT84-153-dT10 (Liu et al., 2014), DnaB-DnaC (Arias-Palomo et al., 2019), and Pyrococcus abyssi Replication Protein A (Madru et al., 2023)—focusing on their structural and functional characteristics. A comparison of the compositions and active site properties will be particularly addressed. Understanding the unique features of these complexes provides valuable information on genome maintenance and evolutionary adaptations. Structural data for DnaT84-153 (PDB ID 4OU6(Liu et al., 2014)), DnaBC (PDB ID 6QEM(Arias-Palomo et al., 2019)), and Pab-RPA (PDB ID 8AAS(Madru et al., 2023)) were retrieved from the Protein Data Bank (Burley et al., 2023). PyMOL was used to study active site residues and visualization of the structural composition comprising helix, sheet, and loop compositions (Schrödinger, LLC, 2023). Physical and chemical parameters, including hydrophobicity, charge, and stability indices, were calculated using ProtParam (Gasteiger et al., 2005). Hydrophobicity analysis and further details on amino acid interactions were confirmed using Biovia Discovery Studio (BIOVIA, Dassault Systèmes, 2023). The analysis unraveled unique structural and biochemical features at the active sites of the studied complexes. Pab-RPA, the active site of RPA2 consists of one helix, eight sheets, and nine loops, while RPA1 contains three helices, seven sheets, and nine loops, which indicate ssDNA stabilization. The DnaBC complex's active site has nine helices, six sheets, and fourteen loops per subunit, consistent with its helicase-loading function for bacterial replication. Each of the five subunits comprising the active site of DnaT contains three helices, two sheets, and four loops per subunit, stabilizing replication intermediates. Additionally, RPA1 is characterized by a lack of polar residues in conjunction with two non-polar residues, whereas RPA2 contains one polar and one non-polar residue. DnaBC contains four polar residues and zero non-polar residues, while DnaT contains neither polar nor

non-polar residues. Hydrophobicity analysis revealed predominantly hydrophobic active sites, with GRAVY values of -0.354 (RPA1), -0.379 (RPA2), -0.286 (DnaBC), and -0.150 (DnaT). Charge calculations demonstrated diverse ssDNA interaction mechanisms: RPA1 and RPA2 carried negative charges (-14 and -1, respectively), DnaT was neutral, and DnaBC carried a positive charge of +3. Stability indices indicated that DnaT (38.6) and RPA2 (1.37) were more stable compared to DnaBC and RPA1, both of which had instability indices exceeding 40. The findings underscore the structural and biochemical variability of ssDNA-binding complexes, elucidating the presence of unique hydrophobic binding pockets. Such information affords a significant understanding of the strategic targeting of these complexes across diverse applications, encompassing therapeutic interventions and mechanistic investigations.

Keywords: single-stranded DNA-binding proteins, protein-DNA interactions, hydrophobicity analysis, active site architecture

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ICB13 -1089

Comprehensive Multi-Omics Analysis Reveals NPC2 and ITGAV Genes as Potential Prognostic Biomarkers in Gastrointestinal Cancers

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Gastrointestinal cancers (GICs) remain among the leading causes of cancer-related morbidity and mortality worldwide. Despite advances in treatment, the prognosis for many GIC patients is still poor, largely due to the lack of reliable and accurate prognostic biomarkers. The identification of robust biomarkers capable of predicting individual clinical outcomes is a critical challenge in oncology. Although several potential biomarkers have been identified over the years, their predictive accuracy remains limited, and their therapeutic applications are still under exploration. In this context, identifying reliable prognostic biomarkers for GICs is crucial for improving patient outcomes and guiding more personalized treatment strategies. In this study, we conducted a systematic bioinformatics analysis to investigate two genes, NPC2 and ITGAV, as potential biomarkers for predicting prognosis in GICs. We analyzed data from multiple publicly available databases, including GEPIA2, cBioPortal, UALCAN, LinkedOmics, STRING, Enrichr, TISDB, TIMER2.0, hTFTarget, miRTarBase, circBank, and DGIdb, to assess gene expression, genetic alterations, and immune associations of NPC2 and ITGAV in various GIC types. Our results revealed that both NPC2 and ITGAV were significantly overexpressed in a wide range of GICs, including liver hepatocellular carcinoma (LIHC) and stomach adenocarcinoma (STAD), and were associated with poorer clinical outcomes. Notably, genetic alterations in these genes included amplification of NPC2 and deep deletion of ITGAV. Additionally, promoter hypermethylation was observed in NPC2 in pancreatic adenocarcinoma (PAAD) and in ITGAV in colon adenocarcinoma (COAD), suggesting epigenetic regulation. Furthermore, both genes showed strong associations with immune cell infiltration, particularly tumor-infiltrating lymphocytes and macrophages, and were correlated with several immune modulators, indicating their potential role in tumor immunity. Importantly, our analysis identified ten small-molecule drugs targeting ITGAV, providing potential therapeutic options. In conclusion, our findings suggest that NPC2 and ITGAV could serve as valuable prognostic biomarkers for GICs, offering insights into both clinical outcomes and immune-related pathways, and may

ultimately guide the development of targeted therapies for GIC patients

Keywords: gastrointestinal cancer, prognostic factors, bioinformatics, multiomics, NPC2, ITGAV

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ICB13 -1090

Dysregulated genes in the fat tissue of children confer a risk of cancer

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Obesity is a chronic complex disease characterized by the extreme accumulation of body fat. The prevalence of obesity has surged in recent years all over the world specifically in children. Obesity increases the risk of cardiovascular diseases, some types of cancer, type 2 diabetes, and mental problems among others (Xiao and Ding, 2024). The pathophysiology of obesity is not fully understood especially from the genetic causes of obesity. The heritability of obesity is between 40-70% and new technologies could overcome the current gap in the mechanisms of obesity (Concepción-Zavaleta and Quiroz-Aldave, 2024). In this study, we aim to explore the pathways and genes that play a role in obesity development in children.Gene Expression Omnibus (GEO) was searched for datasets in which the expression profile of fat tissue in obese children had been evaluated in comparison to lean children. The two selected datasets were analyzed using GEOquery, then two data were merged and the batch effect was removed using the SVA package. limma package was used for finding differentially expressed genes (DEGS), upregulated and downregulated DEGs. Enrichr was used to detect enriched pathways. Protein-protein interaction (PPI) network was drawn through STRING and Cytoscape software. The top 10 percent of hub genes were gained using the cytohubba plugin based on four centrality methods including degree centrality, closeness centrality, betweenness centrality and maximal clique centrality (MCC). We identified 403 DEGs (p-value<0.05) between obese and lean children from which 9 genes were upregulated (logFC>0.5) and 20 genes were downregulated (logFc<-0.5). Pathway enrichment analysis showed Neuroinflammation And Glutamatergic Signaling (WP5083) enriched pathway and Regulation Of DNA-templated Transcription (GO:0006355) was the biological process related to obesity. PPI network included 353 nodes and 879 edges. Hub gene analysis revealed 13 genes including VCP, NFKB1, CXCL1, TCP1, CHEK1, RPS20, IGF1, COL1A1, DNMT1, NFE2L2, REL, H2BC11, PGK1 linked to obesity. Enrichr-KG highlighted the role of these genes in the Transcriptional misregulation in cancer (KEGG_2021_Human) through Ras; p53; PI3K-Akt signaling pathways. It is well-known that the genetic basis of obesity in children is involved in genetic variations of genes that regulate the

leptin-melanocortin pathway in the gut-brain axis so far (Loos and Yeo, 2022). The results of this meta-analysis also show that genes that are expressed differentially in the fat tissue of obese children compared to lean ones are acting through neurological pathways in general. In specific, this study shows the genes that are related to the comorbidity of cancer with obesity, making it harder and more important to manage. More genomic study of these genes for a better understanding of their role in obesity development is warranted.

Keywords: obesity, gene, gene expression, cancer

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ICB13 -1091

Minimum Error Entropy: A Superior Alternative to Mean Square Error for Heavy-Tailed EEG Signal Classification

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The classification of EEG signals presents unique challenges, particularly when dealing with their heavy-tailed distributions (Wang et al., 2014), which deviate significantly from Gaussian assumptions traditionally used in signal processing. This discrepancy has profound implications for the application of traditional metrics such as Mean Square Error (MSE), which assumes Gaussianity and struggles to effectively capture the dynamics of heavy-tailed data (Heravi and Hodtani, 2018). Recognizing this limitation, this study explores Minimum Error Entropy (MEE) as a superior alternative to MSE, leveraging its foundation in information-theoretic learning (Principe, 2010) to better handle the non-Gaussian characteristics of EEG signals. By addressing this critical gap, we aim to significantly enhance the robustness and accuracy of EEG signal classification.Despite prior advancements in EEG signal processing, most studies have inadequately accounted for the statistical properties of heavy-tailed EEG signals, continuing to rely on second-order statistics like MSE. These approaches falter in accurately modeling and analyzing heavy-tailed distributions, limiting their effectiveness in real-world applications, such as brain-computer interfaces (BCIs). This gap underscores the necessity of a paradigm shift toward metrics like MEE, which inherently incorporate higher-order statistics and are robust against the challenges posed by non-Gaussian data (Kruczek et al., 2020). Our methodology is structured in two pivotal phases. First, we rigorously demonstrate that EEG signals exhibit heavy-tailed, non-Gaussian distributions by performing extensive statistical analyses, including kurtosis measures and distribution fitting. This statistical insight confirms the unsuitability of Gaussian-based methods for EEG signal classification (Xu et al., 2008). Second, we validate the efficacy of MEE over MSE in the classification of heavy-tailed EEG signals. Using the theoretical underpinnings of MEE, which prioritize the minimization of error entropy rather than squared error, we demonstrate its robustness in handling outliers and preserving critical signal features, particularly in heavy-tailed environments (Luan et al., 2016). The proposed approach is evaluated on the widely recognized BCI Competition IV dataset 2a (Tangermann et al., 2012). This dataset includes recordings from nine subjects performing four motor imagery tasks (left hand, right hand, both feet, and tongue) captured using 22 EEG and three EOG channels sampled at 250 Hz. The dataset's structure requires multi-label classification to map the signal data onto four target motor imagery tasks. In this study, the proposed model was trained under

two different conditions using MSE and MEE as optimization metrics, and the performance was compared. Using MSE, the model achieved 76% accuracy, while leveraging MEE increased accuracy to 86%. This 10% improvement demonstrates MEE's superior ability to handle non-Gaussian, heavy-tailed EEG signals, highlighting its effectiveness over traditional MSE-based methods for improving classification performance.
In conclusion, this study bridges a critical gap in EEG signal processing by advocating for MEE as a more robust metric over MSE in heavy-tailed environments. Our findings highlight the necessity of rethinking traditional assumptions about EEG signal distributions, offering a robust and theoretically sound pathway to improve classification accuracy in BCIs and related applications (Gritskikh et al., 2024).

Keywords: EEG signal classification, heavy-tailed distributions, information-theoretic learning, minimum error entropy (MEE), brain-computer interfaces (BCIs)

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ICB13 -1092

ATIC as a Theranostic Biomarker in Gastrointestinal Cancers: Insights from Autophagy Pathway Analysis

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Gastrointestinal (GI) cancers are the cause of the over one-third (35.4%) of cancer-related deaths and over one-quarter (26%) of the global cancer incidence. Autophagy, a cellular degradation process, plays dual roles in tumorigenesis, acting as both a tumor suppressor and promoter depending on context[1]. This study aimed to identify Autophagy related genes (ARGs) which were differentially expressed in tumor tissues compared to normal tissues across different types of gastrointestinal cancers. Autophagy-related genes (ARGs) were analyzed across gastrointestinal cancers (Esophageal, Gastric, Pancreatic, Colon, Rectal, and Liver) using GEPIA2 and GEO databases. Differentially expressed genes (DEGs) were identified with thresholds of |log2 Fold Change| > 1 and adjusted P-value < 0.01. Prognostic value and diagnostic accuracy were evaluated. The protein-protein interaction network (PPI) was constructed and Gene set enrichment, Genetic alterations, immune correlations, the competitive endogenous RNA network (ceRNA) and drug-gene interactions were investigated using different databases. Among 232 identified ARGs, ATIC was identified as a common DEG between GI cancer types. Upregulated ATIC expression was significantly correlated with poor overall survival (OS) in patients with LIHC. ATIC gene expression served as a potential diagnostic biomarker in esophageal, gastric, cholangiocarcinoma, colon, rectal, and pancreatic cancers. Furthermore, approximately all immunoinhibitors demonstrated a significant correlation with ATIC expression in GI cancers. By analyzing ATIC-drug interactions, Pemetrexed Disodium had the highest interaction with ATIC gene expression. Finally, ATIC ceRNA network containing 5 miRNAs and 26 lncRNAs that have interaction with identified miRNAs was constructed. This study identifies ATIC as a key autophagy-related gene with significant prognostic, diagnostic, and therapeutic potential across gastrointestinal cancers, highlighting its role in cancer progression and immune regulation

Keywords: gastrointestinal cancer, theranostic biomarker, autophagy-related gene, ATIC, bioinformatics

analysis

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Enhancing NAFLD Diagnosis with AI: Insights from the Persian Fasa Cohort Through Advanced Machine Learning Techniques

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Non-alcoholic fatty liver disease (NAFLD) is a hepatic manifestation of metabolic syndrome, characterized by fat accumulation in the liver among individuals who do not consume excessive alcohol. Over the past three decades, its prevalence has risen globally, posing a significant public health challenge. NAFLD can progress to cirrhosis, liver failure, and an increased risk of cardiovascular disease, ultimately contributing to higher overall mortality. Despite its widespread occurrence, early detection remains a challenge due to limitations in current screening methods. Here, we aimed to develop an AI-driven model for diagnosing NAFLD based on blood parameters and anthropometric indices. This study utilized data from the Persian Fasa cohort, originally comprising 10,138 records and 226 features, categorized into discrete and continuous features. After preprocessing, normalization, and dimensionality reduction, statistical analyses were conducted using Python. Patients were categorized into three groups based on the Fatty Liver Index (FLI), including healthy (<30), borderline (30–60), and NAFLD (>60). The dataset was divided into training (70%) and testing (30%) subsets. Seven feature selection methods, including ANOVA, Mutual Information (MI), Independent Component Analysis (ICA), Non-negative Matrix Factorization (NMF), Principal Component Analysis (PCA), Penalized Support Vector Machine (SVM_L1), and Elastic Net Logistic Regression, were applied to extract common features. The Random Forest algorithm identified the most important extracted features, which were validated through Receiver Operating Characteristic (ROC) curve analysis. A variety of machine learning models, including Random Forest, Support Vector Machine (SVM), Logistic Regression, K-Nearest Neighbors (KNN), Decision Tree, CatBoost, AdaBoost, and XGBoost, were trained to evaluate classification performance using a 5-fold cross-validation approach. Model diversity was assessed using Kappa statistics and error analysis to ensure robustness. To further improve performance,

Optimized Weighted Averaging (OWA) and Sugeno Fuzzy Integral methods were applied for model combination. Finally, a Convolutional Neural Network (CNN) was trained with 5-fold cross-validation to integrate robust models and enhance classification results. The final dataset comprised 70 clinical and lifestyle variables, including hypertension, smoking status, and others, collected from 10,007 patients (45.2% male and 54.8% female). The number of patients in each category was as follows: healthy (4,444), borderline (2,892), and NAFLD (2,671). Five key features, including BMI, waist-to-hip ratio, triglycerides, and GGT, were identified as the most significant predictors using the Random Forest method. The diagnostic value of these features was confirmed through ROC curve analysis, achieving an Area Under the Curve (AUC) greater than 0.7. SVM and CatBoost models demonstrated exceptional performance, with a Kappa score of 0.96 and an error rate of 0.01, indicating high model diversity and minimal error. Combining these two models using Sugeno Fuzzy Integral, OWA, and CNN-based meta-learning produced outstanding results: Accuracy 0.99, Precision 0.99, Recall 0.99, F1 Score 0.99, and an AUC of 1.00. By highlighting factors that could improve the diagnosis of NAFLD, we underscore the potential of AI in improving NAFLD diagnosis and provide valuable insights for early detection and intervention

Keywords: NAFLD; OWA; Sugeno fuzzy integral, CNN, artificial intelligence.

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Computational study on the inhibitory potential of fungal metabolites against HIV-1 RT

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The main target in creating antiviral drugs is viral polymerase, which is the center of viral replication. Research and development strategies for new antiviral drugs due to the increasing cost of drug research and development, random screening strategies of traditional drugs, and blind optimization of lead compounds consume a lot of resources and time. In recent years, new research strategies have been developed, including the use of natural fungal compounds. (Tsai, Lee et al. 2006, Choi 2012, Peng, Wang et al. 2022) Fungi of the order Sordariales belong to the phylum Ascomycota and are well-known producers of diverse secondary metabolites with significant environmental and biomedical importance. Secondary metabolites from this group exhibit various biological activities, including antimicrobial, antiviral, anticancer, and enzyme inhibition properties. Also, taking advantage of the potential of fungal secondary metabolites, it was decided to evaluate the inhibitory potency of 174 secondary metabolites from species of the order Sordariales against aspartyl viral polymerases, including HIV-1 reverse transcriptase (RT).(Hu and Hughes 2012, Charria-Girón, Surup et al. 2022, Nzimande, Makhwitine et al. 2023, Zhao, Wang et al. 2023) According to two-step virtual screening, ten of the 56 ligands that bind to the active center of the polymerase under investigation with autodock vina had an energy of -7 kcal/mol or less. In the next step, which was performed using autodock 4.2.6, only three ligands, 1 to 3, had the highest binding energy compared to ribavirin (reference drug).(Tarasova, Poroikov et al. 2018) The most significant interaction between hydrogen bonds and basic catalytic motifs, mediated by hydrophobic contacts, has been shown by ligands 1,2 and specifically ligand 3. This implies that inhibiting the action of this enzyme can prevent viral multiplication, highlighting the potential applications of our findings and paving the way for the creation of novel antiviral medications. It is hoped that by utilizing these results, reliable findings can also be obtained in both in vitro and in vivo studies, leading to the necessary scientific validations.

Keywords: HIV-1 RT, fungal metabolites, protein structure, polymerase inhibitors

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Investigation of antiviral potency of fungal metabolites against Hepatitis C NS5B

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Viral polymerases are essential for viral replication and, thus, important targets for developing antiviral therapies. These enzymatic proteins facilitate the assembly of novel viral entities within the compromised host cells by catalyzing the synthesis of either viral RNA or DNA. These enzymes' unique mechanisms of action enable selective inhibition, which markedly contrasts with the functionalities of host polymerases. (Choi 2012, Peng, Wang et al. 2022)This investigation evaluated one hundred seventy-four secondary metabolites derived from the order Sordariales, which belongs to the phylum Ascomycota (Charria-Girón, Surup et al. 2022, Zhao, Wang et al. 2023), encompasses an extensive and diverse fungal group that produces secondary metabolites like terpenes, alkaloids, and polyketides and conducted screening against aspartyl polymerases, including Hepatitis C (HCV) NS5B.(Mosley, Edwards et al. 2012, Manns, Buti et al. 2017) by using a comprehensive two-step virtual screening approach, ten of the 56 identified ligands that demonstrated binding within the active sites of the polymerases under examination exhibited binding energies that were less than -7 kcal/mol. The reference compound, ribavirin, showed lower binding affinity than ligands 1-3. Ligand 3 demonstrated the most important interaction provided by hydrophobic and hydrogen bonds with key residues inside the catalytic active center. The results showed that this enzyme can block virus replication by inhibiting its function.(Ansari, Zarei et al. 2023) A 100 nanosecond (ns) molecular dynamics simulation was used to further study the effect of these ligands on the structural integrity and dynamic properties of the polymerase. (Lindahl, Hess et al. 2001, Schüttelkopf and Van Aalten 2004)The binding of ligands 2 and 3 led to significant structural changes that led to an increase in polymerase activity. The flexibility and operability of hepatitis C virus NS5B polymerase have been significantly reduced. Ligand 3 had the most significant effect on polymerase and exceeded the effectiveness of ribavirin in inhibiting viral replication. In addition, ligand 3 provides a good ADME/T profile, which confirms its potential as a promising candidate for activity against HCV NS5B and justifies further preclinical studies.

Keywords: HCV NS5B polymerase, secondary metabolites, protein structure, molecular simulation

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Identification of potent antiviral from the fungal metabolites against SARS COV-2 RdRp: An in silico study

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Antiviral drugs target viral polymerases and are responsible for regulating viral replication. It is their selectivity that also allows the development of selective inhibitors, which, for example, may as much interfere with viral replication while causing minimum derogation to host cellular functions.(Choi 2012, Peng, Wang et al. 2022)This study investigated the antiviral potential of 174 fungal secondary metabolites from the order Sordariales (Charria-Girón, Surup et al. 2022), specifically on their ability to inhibit the SARS-CoV-2 RNA-dependent RNA polymerase (RdRp), an aspartyl polymerase.(Gao, Yan et al. 2020, Malone, Urakova et al. 2022) Following the blind docking step, which found 56 ligands attached to the active site, the target docking revealed that 10 ligands had binding energy <-7 kcal/mol. This was the first step in the two-part virtual screening process. In the Second step, ligands 1-3 showed the highest binding energy to the active site. The reference ligand (ribavirin) has lower binding affinities than ligands 1–3. In Lig-3, the strongest interaction was seen. These are connected with important catalytic motifs through hydrophobic and hydrogen bonding interactions, which may prevent polymerase activity and hinder viral propagation.(Ansari, Zarei et al. 2023) The impact of these ligands on polymerase dynamics and structure was then examined using 100 nanosecond (ns) Molecular dynamic(MD) simulations.(Van Gunsteren and Berendsen 1988, Lindahl, Hess et al. 2001, Schüttelkopf and Van Aalten 2004, Genheden and Ryde 2015) Lig-1 and Lig-3 caused further structural compressions in SARS-CoV-2 that might destabilize the enzyme. Overall, Lig-3 exerted the most conspicuous impact on polymerase, holding a higher potential for viral replication inhibition than Ribavirin.Lig-3 is a promising antiviral candidate against SARS-CoV-2 RdRp and merits more preclinical investigation due to its favorable ADME/T profile. The enhancement of the pharmacological properties of these candidates will require a combination of in silico modeling with experimental validation. Lig-3 will be going from bench to bedside, with deep understanding fostered by continuous studies in structural biology, to become a great candidate against SARS-CoV-2 and other viral menaces.

Keywords: COVID-19, fungal secondary metabolite, protein structure, molecular modeling

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Modeling and Predicting the Use of Medications Antiplatelets and ARBs Using Logistic Regression

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Cardiovascular diseases account for 40% of mortality in Iran, and heart failure is one of the primary causes. Approximately 1% of individuals in their 50s and 10% in their 80s experience heart failure. One of the methods to manage or treat these diseases is through specific medications. Among these drugs are Antiplatelets, a group of cardiovascular medications that disrupt the process of platelet aggregation, which leads to blood clot formation. By inhibiting this process, Antiplatelets prevent the formation of blood clots, which are the main cause of heart attacks and strokes. Additionally, this medication is used for the prevention and treatment of vascular diseases, such as coronary artery disease. Another class of medications is Angiotensin II Receptor Blockers (ARBs), used to treat high blood pressure and certain other heart and kidney conditions. ARBs work by blocking the angiotensin II receptors in the body. By doing so, they help relax blood vessels and lower blood pressure. In patients with heart failure, ARBs can also improve heart function. Heart failure is usually a lifelong condition requiring ongoing treatment and management, which can significantly impact daily life. In this study, the Minnesota Living with Heart Failure Questionnaire (MLHFQ) (Bilbao et al., 2016) was utilized to assess the impact of heart failure on patients' lives. The questionnaire consists of 21 questions, each rated on a scale from 0 (no problem) to 5 (severe problem), covering three main domains: physical, emotional, and overall quality of life. It was distributed to 100 patients aged 46 to 96. Information related to marital status, income level, hospitalization history, and whether the patients had taken Antiplatelet or ARB medications was collected and evaluated. The overall process aimed to predict the necessity of taking the selected medications, both with and without considering personal information, hospitalization data, and other medications the patient may have been using. To predict the usage of these medications, Logistic Regression (Hosmer et al., 2013) was applied as a binary classification algorithm for the target feature. After performing Principal Component Analysis (PCA) (Jolliffe, 2002) for dimensionality reduction followed by Logistic Regression, the accuracy for Antiplatelet medication prediction was 90%, and for ARBs, it was 85%. Additionally, the results were evaluated in terms of classification metrics such as precision, recall and f1-score, which confirmed the efficacy of this study in predicting the use of these medications for heart patients.

Keywords: cardiovascular diseases, antiplatelets, angiotensin receptor blockers, classification, logistic regression

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BIRC5: The silent architect of tumor persistence and senescence in Hepatocellular carcinoma

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The most common and malignant type of liver cancer is hepatocellular carcinoma (HCC). Due to the lack of early diagnosis methods, people with HCC usually face limited treatment options and poor prognosis [Hajilou and Solhi,2024]. Cellular senescence is a permanent state where cells irreversibly exit the cell cycle and lose their ability to proliferate due to continuous stress-induced damage. Aging and stressors like oxidative stress or oncogene activation cause several liver changes, including reduced size and number of normal hepatocytes, decreased regenerative and metabolic capacity, and an increased proportion of polyploid and multinucleated hepatocytes [Zhang and Zheng,2023]. Initially, the present study aimed to identify differentially expressed genes (DEGs) between tumor and normal tissues from HCC samples and compare with senescence-associated genes to find hub genes that have been involved in both hepatocarcinogenesis and senescence. Raw microarray data of GSE60502, GSE112790 and GSE14520 were obtained from the GEO database. DEGs were obtained using R packages and screened out according to adjusted P-value < 0.05 and -logFC- ≥1. Senescence-associated genes file was taken from the CELLAGE database. First, common genes between the senescence-associated genes and DEGs were collected. Then, the hub genes were identified; these genes have function in cancer and also in senescence. The expression patterns were obtained from GEPIA and UALCAN databases and the expression patterns of normal tissue were obtained from HUMAN PROTEIN ATLAS (HPA) and Gtex databases. Among these genes, we focused on BIRC5 because of its expression pattern and level of expression in normal liver. BIRC5 (Survivin), the smallest member of the inhibitor of apoptosis proteins (IAPs), is highly expressed in precancerous liver lesions and malignant HCC cells. Senescence triggers HCC regression by inducing the inflammatory cytokine TNFα. Depleting BIRC5 or blocking the antiapoptotic pathway significantly increases cell death in response to TNFα [Li and Fu,2016]. One active compound that targets the BIRC5 is Tiliroside, a natural flavonoid glycoside, which is a promising candidate compound [Grochowski and Locatelli,2018]. Several pharmacological activities have been reported regarding its antithrombotic activity, antioxidant, hepatoprotective, and anti-inflammatory action. It has also been investigated to understand its anti-cancer potential [Yang and Lu,2023]. Finally, we performed a molecular docking analysis to investigate the binding affinity between this compound and

BIRC5 protein; After preparing the ligand and receptor molecules, AutoDock Vina was used to conduct molecular docking. The web-based server of Protein-Ligand Interaction Profiler (https://plip-tool.biotec.tu-dresden.de/plip-web/plip/index) was used to analyze hydrogen bonds and hydrophobic interactions. The molecular docking studies confirmed the strong interaction between Tiliroside and BIRC5 and presented evidence for its therapeutic potential as a new agent targeting BIRC5 for HCC. In conclusion, targeting BIRC5 by Tiliroside could be a potential therapeutic approach for HCC treatment

Keywords: liver cancer, molecular targeted therapy, structural bioinformatics, aging, BIRC5

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Analysis of enrichment pathways and ontology of genes related to Feed efficiency in sheep

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Feed efficiency is a very important economic feature in animal husbandry. In other words, improving feed efficiency increases profitability for producers (Lin et al., 2023). The purpose of this study was to investigate protein-protein interactions, identify sub-clusters with high density and analyze signaling pathways and gene ontology. For this purpose, a list of 20 genes, which are significantly involved in biological processes related to feed efficiency in sheep, was extracted from different studies. The program String 1.5.1 was used to draw the network of protein-protein interactions (PPI). After, through the more option in the String 1.5.1 program, the created interactive network was expanded to 59 nodes and 394 edges. MCODE 1.6.1 plugin of Cytoscape 3.7.1 software was used to identify high density regions in sub-clusters (Saberi Anvar et al., 2018). MCODE parameters including degree cutoff: 2, node cutoff: 0.2, K-core: 5 and maximum depth: 100 were considered. This calculation led to the creation of five sub-clusters. In the subcluster with the highest score: 14/421, nodes: 20, edges: 137 and a seed protein named ACACA was identified. Acetyl-CoA carboxylase alpha is considered as the rate-limiting enzyme in the biosynthesis of various fatty acids in lipid metabolism (Ntambi et al., 2002). Also, LEP protein with a member score of 38 in the main network and sub-cluster as the main protein (hub) had the highest degree in the PPI network. The hormone leptin secreted in adipose tissue plays an important role in regulating appetite and energy metabolism. In addition, leptin is associated with fat deposition. After leptin protein binds to the receptor, it creates a series of chemical signals (JAK/STAT signaling pathway) that activates the receptor and trans phosphorylates the associated JAK molecules. This pathway participates in energy homeostasis. The LEP gene is a component of several biological processes, especially those related to fat metabolism, such as the lipid metabolic process and beta-oxidation of fatty acids (Stern et al., 2016). The leptin also plays a vital role in biological processes that are related to the negative regulation of appetite, feeding behavior, intestinal absorption, and bone growth in sheep (Upadhyay et al., 2015). ClueGO 2.5.10 and CluePedia 1.5.10 plugins were used to draw the gene ontology network (Bindea et al., 2013). After analysis, significant ($P<0.05$) gene ontology terms including molecular functions of insulin-like growth factor I binding, insulin-like growth factor II binding, insulin-like growth factor binding, hormonal activity, triglyceride lipase activity and biological processes such as insulin-like growth factor receptor signaling pathway, positive regulation of MAPK cascade, positive regulation of receptor signaling pathway via JAK-STAT, brown fat cell differentiation, muscle organ development, skeletal muscle cell differentiation, glucose homeostasis and response to insulin were identified. It was also found that these genes are significantly related to KEGG enrichment pathways such as AMPK signaling pathway, PPAR signaling pathway, Regulation of lipolysis in adipocytes, Growth hormone synthesis, secretion and action, PI3K-Akt signaling pathway and Insulin signaling pathway.

Keywords: feed efficiency, protein-protein interaction network, gene ontology, sheep, signaling pathway

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Targeting Protein in Neurodegenerative Diseases: A Computational Approach

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Neurodegenerative diseases, including Alzheimer's, Parkinson's, Huntington's, and amyotrophic lateral sclerosis (ALS), pose significant challenges to global healthcare due to their complexity and severe impact on patients. A shared pathogenic feature of these diseases is protein misfolding and aggregation, which leads to neuronal death. Traditional experimental methods for identifying disease-associated proteins are limited by the nervous system's complexity and the difficulty of obtaining biological samples. This study introduces a novel computational model, ITPND, which combines features of single proteins with protein-protein interaction (PPI) networks to identify proteins linked to neurodegenerative diseases. By leveraging Graph Attention Networks (GAT) and the ProtBERT model, our approach effectively classifies proteins by extracting significant features from sequences and PPI graphs. The model outperforms existing methods, achieving an accuracy of 80%, a precision of 85%, and a recall of 90%. Biological validation through pathway enrichment analysis confirms the involvement of predicted proteins in critical neurodegenerative pathways. Furthermore, drug-protein interaction analysis reveals potential therapeutic candidates, underscoring the model's utility in drug target discovery. This approach provides new insights into the molecular mechanisms of neurodegenerative diseases and potential therapeutic interventions

Keywords: neurodegenerative diseases, drug target discovery, graph attention networks, PPI

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Identification of Driver Genes in Glioblastoma Based on Single-Cell Gene Expression Data Using Integrated Pseudotime and Phylogenetic Analysis

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Cancer encompasses a group of diverse diseases characterized by uncontrolled cell growth that can invade nearby tissues. Despite extensive advancements in medicine, treating cancer remains a significant challenge, therefore humankind is still searching for a simpler method of treating cancer. One critical question in this pursuit is identifying the origin of cancer and also understanding the pathways of cancer growth, particularly in mitotic processes. Glioblastoma (GBM), the most aggressive primary brain tumor, exemplifies this challenge, exhibits notable intratumoral heterogeneity and genetic complexity, which make effective treatment highly obscure. Recent researches have approached this subject from two distinct perspectives: gene expression profiles and genetic mutations. While each has provided valuable insights, integrating these viewpoints may offer a more comprehensive understanding of GBM progression. In this study, we combine two models: phylogenetic trees using the neighbor-joining algorithm to map mutation propagation, and the Monocle algorithm to generate pseudo-time paths. Our findings reveal that these two approaches are interconnected, demonstrating that mutations not only drive cancer progression but also provide deeper insights into the pathways underlying GBM evolution.

Keywords: Glioblastoma, phylogenetic trees, pseudo-time analysis, monocle algorithm

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Bioinformatics and computational Studies on Highly Conserved Neurocalcin Protein

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Neuronal Calcium Sensors are a class of calcium-binding proteins that play important roles in various neural functions, including calcium signaling processes. Neurocalcin, a member of this protein family, contains 193 residues (Ivings et al., 2002). Its 3D structure has been determined for the Bos taurus (Bovine) variant. The aim of this study is to conduct a bioinformatics analysis on the sequence and structure of Neurocalcin to develop a biological model for its evolution. The protein sequence and its corresponding information were obtained from the UniProt database (ID: P61601). (Bateman et al., 2021). A similarity search using the local pairwise alignment algorithm implemented in the BLAST program (McWilliam et al., 2013) revealed that the protein is present in 250 different species, of which eight variants are experimentally reviewed proteins. Multiple sequence alignment of the reviewed sequences using the Clustal Omega program (Sievers et al., 2011) surprisingly showed that only two positions have been permitted to accept the random mutations during the evolutionary timescale. The high conservation of the sequence among different organisms suggests that it has been evolutionarily optimized to recognize various targets, limiting its ability to tolerate sequence changes. In other words, any change in the sequence could be deleterious for the organism due to the loss of its ability to interact with some targets. This hypothesis is consistent with the current activity data, which indicates that the protein functions through interactions with other neural system proteins. Dot Plot analysis revealed that Neurocalcin contains four repeating regions, which are the calcium-binding EF-hand motifs.(Burgoyne, 2007) Structurally, it has been reported that among the four calcium-binding loops, only loops II, III, and IV are capable of coordinating calcium ions, while loop I has lost its calcium-binding function. Our computational study suggests that the first loop, which is distinguished from the others by a unique Cys-Pro dipeptide, is involved in dimerization of the protein. We conclude that the dimeric form of the protein, containing six calcium ions and a larger surface area compared to the monomeric form, may be the functional unit. The increased surface area of the dimer could enable simultaneous interactions with two or more targets, allowing the protein to function more effectively. According to our model, the evolution of the Neurocalcin involves multitarget and simultaneous binding to various targets. The first one limits its tolerance against random mutations leading to a high level of identity between its sequence in various organisms, and the second parameter needs more surface area which is obtained by dimerization of the protein due to losing calcium binding affinity at the first EF-hand loop.

Keywords: Neurocalcin, bioinformatics analysis, EF-hand motif

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Morphine pathway analysis with bioinformatics

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Morphine was the initial alkaloid extracted from the opium poppy in the year 1803(Aghaali & Naghavi, 2024). Morphine is the most important alkaloid in terms of abundance and therapeutic use, accounting for 42% of the total alkaloids in opium poppy(Allen et al., 2008). In this research has been conducted on the morphine biosynthesis pathway using bioinformatics tools. A collection of nine genes associated with the morphine biosynthesis pathway was compiled from a comprehensive survey and validated using the NCBI BLAST tool. We used STRING to examine the interactions among genes and used Cytoscape to illustrate the molecular interaction network. Hub proteins were determined through CytoHubba. The enrichment of hub genes was evaluated using the Kyoto Encyclopedia of Genes and Genomes (KEGG) within STRING, as well as Gene Ontology (GO) through gprofiler. The promoter regions of important genes were examined using MEME. Essential genes involved in morphine synthesis were recognized, and they play vital roles in basic cellular activities such as growth, development, and signal transduction. Metabolic processes play an essential role in the production of morphine, suggesting that the gene network associated with the morphine pathway has broader functions beyond merely generating primary metabolites. Investigating the KEGG pathway highlighted the importance of metabolic pathways and the synthesis of secondary metabolites. An examination of the promoter suggested that signal transduction might be involved in morphine synthesis. Regarding the main genes that contribute to morphine production, the pathway for morphine as a secondary metabolite appears to be linked with numerous significant plant pathways. The objective of this research is to investigate and examine the biosynthetic pathway of morphine in the opium poppy through the application of sophisticated bioinformatics tools. This study employs various bioinformatics tools in tandem to pinpoint and evaluate gene interactions and metabolic pathways, resulting in a more comprehensive understanding of the biosynthesis of morphine alkaloids. This approach could help develop novel methods for morphine production and extraction, as well as improve agricultural processes related to medicinal plants.

Keywords: analysis, bioinformatics, hub genes, morphine, Poppy

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Multi-Target Drug Discovery for Rheumatoid Arthritis: A Comprehensive Computational Approach Using Bioactive Compounds

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Rheumatoid arthritis (RA) is one of the most common autoimmune inflammatory diseases in the world. Due to this importance, several drugs have been designed and produced against effective targets in the pathogenesis of the disease. Considering various inflammatory pathways involved in RA, targeting each of these pathways alone cannot achieve sufficient improvement of the patients. Therefore, this study aimed to introduce safe natural product drug candidates screened in silico against several important protein targets (multi-targets) in the pathogenesis of RA. Tyrosine kinase 2 is a member of the Janus Kinase family, and due to its role in the signaling of numerous cytokines, its inhibition is considered an effective treatment option in inflammatory diseases. IL-6 is one of the most important innate immune cytokines that is secreted from activated macrophages in RA, and its level is directly related to the severity of joint destruction. Therefore, its inhibition plays an important role in improving the pathological symptoms of RA. In addition to the level of IL-6, the severity of the disease is directly related to the level of ACPA in the serum and synovial fluid of patients. Therefore, inhibiting its production by precluding the differentiation of B lymphocytes into plasma cells can effectively improve the disease. In this study, after Virtual Screening, Molecular Docking, and Molecular Dynamics, our results introduced 4 compounds including Rutaecarpine, Hecogenin, Angustine, and Vomicine as new drug candidates for the treatment of RA. Rutaecarpine, Hecogenin, and Angustine inhibit all three targets with high affinity and stability, while Vomicine inhibits both TYK2 and IL-6 but not CD20. Future experimental studies can verify these findings.

Keywords: rheumatoid arthritis, MD Simulation, bioactive compounds, anti-inflammation, multi-target drugs

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HLA Class I Alleles as prognostic marker in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is one of the most common and lethal cancers worldwide, accounting for a significant portion of cancer-related deaths. Its aggressive nature, late diagnosis, and resistance to conventional therapies contribute to poor clinical outcomes. Immune evasion, a hallmark of cancer progression, plays a pivotal role in HCC, allowing tumor cells to escape immune surveillance and establish a favorable microenvironment for growth and metastasis. Human Leukocyte Antigen (HLA) Class I molecules are critical components of the immune system that mediate tumor-immune interactions by presenting tumor-derived antigens to cytotoxic T lymphocytes (CTLs). Disruptions in HLA expression or allele-specific variations can impair antigen presentation, reducing immune recognition and facilitating tumor immune escape. Despite this central role, the specific impact of HLA Class I alleles on HCC progression, prognosis, and therapeutic response remains underexplored. A deeper understanding of the relationship between HLA-I alleles and HCC could reveal novel immunogenomic biomarkers for both prognosis and therapeutic intervention. To address this knowledge gap, we conducted a comprehensive analysis of HLA Class I alleles in HCC patients using data from The Cancer Genome Atlas (TCGA). Our dataset comprised 8,998 samples, including patients with HCC and a pan-cancer cohort. We investigated allele frequency disparities across these groups to identify HLA-I alleles with potential prognostic significance. Statistical analyses were performed using Fisher's exact test to determine the significance of allele frequency differences, providing insights into their association with HCC development and clinical outcomes. Several HLA Class I alleles were identified as significantly associated with an increased risk of HCC, including A11:01, A33:03, B46:01, C01:02, C07:06, and C08:01. These alleles demonstrated higher frequencies in HCC patients compared to the pan-cancer cohort, suggesting their role in disease susceptibility. Notably, HLA-B*51:01 exhibited a significant correlation with improved survival outcomes (Log HR -0.769, p-value 0.035), highlighting its potential as a prognostic biomarker. However, the prognostic relevance of other identified alleles remains unclear and requires further validation through detailed survival analyses. This study highlights the importance of HLA Class I alleles in HCC, revealing their association with disease risk and survival outcomes. These findings suggest that specific HLA-I alleles may serve as valuable immunogenomic biomarkers for prognosis, paving the way for tailored therapeutic strategies, including personalized immunotherapy approaches. Future studies are warranted to further elucidate the functional mechanisms underlying these associations and their clinical utility

Keywords: hepatocellular carcinoma, human leukocyte antigen, prognostic factors, bioinformatics

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Fluidity of normal and cancer cell membranes: A molecular dynamics investigation

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Plasma membranes are necessary for physiological functions and regulate intracellular signaling, redox balance and cell death (Preta, 2020). The membrane consists of lipids and proteins (Szlasa et al., 2020). Chemical or functional changes in membranes are central to the pathogenesis of the disease (Goldberg and Riordan, 1986). Cancer is one of these diseases. Cancerous cells show alterations in their membrane's lipid profile and biophysical properties (Alves et al., 2016). The interactions of anticancer drugs with cell membranes are of primary importance for drug transport, accumulation, and activity. Membranes can act as barriers, preventing or allowing drugs to diffuse freely. Additionally, anticancer drugs can change lipid membrane structure and properties. The insights gained from such studies can provide helpful information about the role of membranes in cancer-related mechanisms and drug interactions (Bourgaux and Couvreur, 2014). Structurally Normal cell membranes have an asymmetric lipid composition compared to symmetrical cancerous cell membranes. Additionally, in normal cells, the extracellular leaflet mainly consists of phosphatidylcholine (PC) and sphingolipids, and the intracellular leaflet is composed of phosphatidylethanolamine (PE) and phosphatidylserine (PS) lipids. The concentration of negatively charged PS lipids increases 5–9 times in the outer leaflet when normal cells are transformed into cancer cells, which is usually considered a biological signal. Consequently, cancer membranes have a less negative membrane potential than normal membranes (Sharma and Shah, 2021). The biophysical properties of the cell membrane are essential for understanding the interaction between small molecules and cancer cells. Therefore, studying the biophysical properties of membranes is a key role in developing strategies to overcome cancer (Peetla et al., 2013). Biophysical parameters such as fluidity, permeability, the force and energy in drug-membrane interactions, and the elasticity of the membrane impact drug effectiveness mechanisms (Li et al., 2018, Lee et al., 2008, Kim, 2023). Membrane fluidity is critical in determining the permeability of molecules to pass through the membrane (Zalba and Ten Hagen, 2017). This property is significant because reduced drug absorption in resistant cancer cells is associated with decreased membrane fluidity (Ramalho et al., 2022). Molecular dynamics (MD) simulations can provide valuable insights into membrane properties and the differences between lipid bilayers in normal and cancerous cells (Róg et al., 2021). This study aims to investigate the fluidity of normal and cancer cell membranes using MD simulations. First, we constructed normal and cancer membrane models. Each model contains five lipid types:DOPC(1,2-dioleoyl-sn-glycero-3-phosphocholine),DOPE(1,2-dioleoyl-sn-glycero-3-phosphoethanolamine),DOPG(1,2-dioleoyl-sn-glycero-3-[phospho-rac-(1-glycerol)]),DOPS(1,2-dioleoyl-sn-glycero-3-phospho-L-serine), and CHL (cholesterol) (Almeida et al., 2021). We used the CHARMM-GUI to build the membranes and simulated them with GROMACS. Simulations were carried out 200 ns with the

CHARMM36 force field and TIP3 water model. Lipid membrane fluidity could be related to lipid parameters such as order parameters and lateral diffusion coefficient. The lateral diffusion analysis is based on the mean square displacement (MSD) (Reddy et al., 2012). In the present study, we computed order and MSD parameters to investigate the changes in the bilayer's fluidity. Our results show decreased fluidity in cancer membranes.

Keywords: molecular dynamics simulation, biomembrane, cancer, fluidity

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Identifying mRNAs and miRNAs in extracellular vesicles through comparative transcriptome analyses of healthy and mastitic bovine milk

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Mammary gland inflammation (mastitis) is mainly caused by bacteria in dairy cows (Cheng et al., 2020; Naserkheil et al., 2022) with huge economic losses worldwide, exceeding $2B annually in the USA alone due to reduced milk production and treatment costs (De Oliveira et al., 2000). To elucidate molecular mechanisms associated with subclinical mastitis, comparative transcriptome studies can prioritize candidate mRNAs and miRNAs (Sun et al., 2015; Saenz-de-Juano et al., 2022). Our objective was to compare transcriptomic analyses and mRNA-miRNA regulatory network analyses to identify key mRNAs, miRNAs and potential pathways involved in molecular regulation of extracellular vesicles in milk of healthy cows and cows with mastitis. Twenty-three miRNAs and 48 mRNAs were identified through integrated Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses. We constructed an mRNA-miRNA regulatory network that included 8 miRNAs and 22 mRNAs and based on interactions, identified 6 hub mRNAs (HSPA5, CSN1S1, CSN2, LALBA, SPP1, and FASN) and 1 hub miRNA (miR-29-3p) associated with subclinical mastitis. Analyses of these RNAs revealed 6, 5, and 6 significantly enriched GO terms related to subclinical mastitis in biological process, molecular function, and cellular component categories, respectively. The main metabolic-signaling pathways associated with bovine milk extracellular vesicles in subclinical mastitis were also enriched, including responses to 11-deoxycorticosterone, progesterone, ketones, and estradiol. Other enriched terms involved potassium channel regulator activity, ubiquitin protein ligase binding, structural constituents of post-synapse, as well as components of extracellular space and region, Golgi lumen, and focal adhesion signaling pathway. Identifying these RNAs, potential pathways and their respective functions provided insights into mechanisms regulating subclinical mastitis and are a foundation for future studies assessing key mRNAs and miRNAs associated with bovine mastitis.

Keywords: dairy cattle, hub RNAs, mastitis, milk extracellular vesicles, transcriptome analysis

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ICB13 -1113

Comprehensive Analysis of DCLK Family Kinases in Gastrointestinal Cancers and Neoplastic Progression

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The doublecortin-like kinase (DCLK) family genes encode protein kinases that are critical for cell development, signaling pathways, and tumor progression across various cancers. Understanding the diagnostic and prognostic relevance of DCLK family genes in gastric cancers (GCs) is therefore essential. This study utilized data from The Cancer Genome Atlas (TCGA) and public databases such as GEPIA2, UALCAN, OncoDB, and cBioPortal to analyze the expression, methylation, and genetic alterations of DCLK family genes, along with their association with overall survival (OS). Gene regulatory networks, including transcription factors and competing endogenous RNAs, were explored using tools like htfTarget, mirTarbase, circBank, and TISIDB, while correlations with immune cell infiltration were also assessed. Additionally, DCLK gene expression was validated via quantitative realtime PCR (qRT-PCR) in 120 colon lesions (60 precancerous samples with adjacent normal tissues and 60 cancerous/non-cancerous samples) and 30 pancreatic ductal adenocarcinoma (PDAC) lesions with 30 corresponding non-cancerous tissues from surgical patients. ROC curve analyses were performed to assess the biomarker potential of DCLK genes. Our findings indicate that DCLK genes exhibit frequent mutations across multiple gastric cancer subtypes. Aberrant DCLK gene expression was notably linked to the progression of colon adenocarcinoma (COAD), rectal adenocarcinoma (READ), and pancreatic adenocarcinoma (PAAD). Elevated DCLK1 expression correlated with poorer prognosis in stomachadenocarcinoma (STAD), while reduced expression was associated with worse outcomes in cholangiocarcinoma (CHOL). Similarly, DCLK2 upregulation predicted poor prognosis in STAD, whereas downregulation correlated with unfavorable OS in PAAD. Importantly, DCLK genes influenced the tumor immune microenvironment, with DCLK1 and DCLK2 linked to immune cell infiltration, including CD8, CD4, Th1, NK cells, and macrophages in GCs. Experimental results further confirmed significant upregulation of DCLK1 and DCLK3 in precancerous and cancerous colon lesions compared to normal tissues. In PDAC samples, DCLK2 showed notable upregulation compared to noncancerous tissues. ROC analyses highlighted the DCLK family's potential as prognostic biomarkers, particularly in PDAC.These results underscore the significant prognostic value of DCLK family genes, highlighting their potential as biomarkers for improving patient outcomes through individualized and

targeted treatment approaches

Keywords: DCLK family kinases, gastrointestinal cancers, neoplasia, bioinformatics, biomarkers

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An efficient method based on transformers for antimicrobial peptide prediction

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Antimicrobial peptides (AMPs) are recognized as a diverse group of membrane-penetrating peptides that play a crucial role in the host's innate defense. (Lee EY and Lee MW, 2017) Due to their unique properties in combating various microbes, including bacteria, fungi, and viruses, AMPs have garnered significant attention. (Söylemez ÜG and Yousef M, 2022) However, identifying and designing effective AMPs remains challenging due to their structural and functional complexities. Furthermore, laboratory methods for identifying AMPs are often limited by high costs and time-consuming processes. In this context, computational prediction approaches, particularly machine learning-based models, have gained increasing importance. These models enable the identification of AMPs and the prediction of their functions before conducting laboratory experiments. Nevertheless, a major challenge in these methods lies in their low accuracy in identifying and classifying different types of AMPs, especially regarding the complex and nonlinear features of proteins. Existing methods often face issues such as low accuracy in precisely identifying AMPs and categorizing their functions, and they require large and diverse datasets for more accurate training. Moreover, the use of both local and global features in these models has not been fully explored. In this study, we introduce a novel computational approach based on deep learning and transformer networks, called Tra-AMP, for the identification of AMPs and the prediction of their functional types. In this method, amino acid sequences are first tokenized, and an embedding vector is generated for each token. To account for the position of each amino acid, a positional embedding is also added to the token embeddings. A specific type of positional embedding, known as rotary embedding (Su J and Ahmed M, 2024), is employed in this paper. The resulting vectors are then input into an enhanced transformer model, where local and global attention mechanisms are used to improve the model's focus on diverse features. Following the feature extraction by the transformer network, classification is performed using fully connected layers. This approach is particularly effective in AMP identification as the model can focus on the complex structural and functional features of proteins. The results of this study demonstrate that the proposed model achieves high performance in identifying AMPs and predicting their functional types, with evaluation metrics such as accuracy (96.74) and F1-score (95.48). These findings indicate that the Tra-AMP method not only accurately identifies AMPs but also excels in classifying their functional types. This method has the potential to significantly aid in the prediction and design of novel AMPs for therapeutic applications.

Keywords: antimicrobial peptides, deep learning, transformer network, positional embedding, local attention, global attention, rotary embedding

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Bioinformatics analysis of the binding of various ligands to the acyl homoserine lactonase derived from Bacillus

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Quorum sensing is a fundamental communication system in bacteria, regulating key processes including biofilm formation, virulence factor production, and antibiotic resistance (Paluch and Rewak, 2020). This study aimed to investigate the genetic diversity of the aiiA gene in Bacillus species obtained from soils and assess whether this diversity affects the enzyme's binding affinity to different substrates and instability index. 130 Bacillus isolates were collected from various cities in Iran. PCR screening revealed that eight isolates contained the aiiA gene (Noor and Almasri, 2022). Sequence alignment with reference sequences from the NCBI database and motif analysis using the MEME Suite tool confirmed the presence of conserved catalytic motifs, including HXHXDH, and critical active site residues (Y194-D191-H169-H235). (Liu and Momb, 2008). The preservation of these residues emphasizes their structural and functional importance. Despite minor changes observed in non-catalytic regions, the integrity of the active site was not disrupted. Estimation of the instability index using the ProtParam tool showed that genetic diversity in the aiiA gene does not significantly affect enzyme stability, with the index ranging between 46.35 and 51.88. Molecular docking studies were performed to evaluate the potential impact of the observed genetic diversity on enzyme-substrate interactions. Four isolates (AK3A, ELM21B, H8A, and NB3C) with the most distinct sequences were selected for further analysis. Homology models of these isolates were generated using the Swiss-Model platform, employing the 3DHB structure as a template. Docking simulations using Autodock Vina were carried out with N-acyl homoserine lactones (AHLs) ligands of varying chain lengths, including C4-HSL, C6-HSL, C8-HSL, C10-HSL, and C12-HSL, to assess binding affinity and enzyme-ligand interactions. The docking results revealed no significant changes in the binding free energy (ΔG) for shorter chain AHLs such as C4-HSL, where all isolates, including the reference 3DHB, maintained identical ΔG values (-5.8 kcal/mol). For longer chain ligands like C6-HSL, C8-HSL, and C10-HSL, minor differences in ΔG values were observed. For instance, with C10-HSL, the ΔG values ranged from -6.1 to -6.4 kcal/mol, showing a slight deviation from the reference value of -7.0 kcal/mol. Importantly, these differences did not disrupt the enzyme's substrate binding efficiency or functionality. Furthermore, the results demonstrated that the ligand chain length did not significantly affect the enzyme's binding affinity. Results obtained emphasize that despite genetic variation in the aiiA gene in Bacillus isolates, catalytic motifs, and active site residues remain conserved, ensuring the robustness of the enzyme's quorum-quenching activity. Minor amino acid variations outside the active site had no functional impact on enzyme activity, consistent with prior studies (Noor and Almasri, 2022). This study investigates aiiA gene diversity in Bacillus soil isolates,

marking the first analysis on these samples, and confirms that variations outside the active site do not affect the enzyme's binding affinity. These findings contribute valuable insights into the structural and functional stability of the lactonase in Bacillus isolates and its potential applications in disrupting bacterial quorum sensing for controlling biofilm formation and bacterial infections.

Keywords: Bacillus, aiiA gene, molecular docking, homology modeling, quorum sensing

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ICB13 -1116

Designing Anti-Cancer Peptides Using Bioinformatics to Inhibit Survivin, Disrupt Cell Division, and Trigger Apoptosis in Cancer Cells

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Cancer is a prevalent disease that, despite ongoing research and advancements in treatment and early diagnosis, continues to cause significant mortality worldwide. Research into the characteristics of cancer cells and their differences from normal cells, particularly through proteomic studies, plays a crucial role in cancer prevention, early diagnosis, and treatment. Recently, the Survivin protein has been studied as a key diagnostic marker in autoimmune diseases such as rheumatoid arthritis, as well as in various types of cancer (Wang and Greene, 2024, Zafari et al., 2019). Survivin is highly expressed in multiple human cancers and belongs to the inhibitors of apoptosis proteins (IAPs) family (Fang et al., 2024). As the smallest member of the inhibitors of apoptosis proteins (IAP) family, it plays a vital role in inhibiting apoptosis and regulating the cell cycle in cancer cells. Survivin is a key component of the chromosomal passenger complex (CPC) in the nucleus, playing a multifaceted role in the cell cycle by regulating mitosis and cytokinesis. In the cytoplasm, Survivin binds to an X-linked inhibitor of apoptosis protein (XIAP), leading to increased stability of XIAP, and interactively inhibits apoptosis by inhibiting caspase-9 activity (Singh et al., 2019). Another mechanism by which Survivin inhibits apoptosis is inactivation of the Smac/DIABLO factor (Fang et al., 2020). In this study, anti-cancer peptides were designed to target the functional region of Survivin, aiming to disrupt its interactions with other proteins, induce apoptosis, and arrest the cell cycle in cancer cells (Martínez-García et al., 2019). Anti-cancer peptides were designed based on the chromosomal passenger complex proteins (CPC). The anti-cancer peptides and their efficacy were evaluated using bioinformatics methods, including molecular docking (Alekseenko et al., 2020) and molecular dynamics (MD) simulations. Molecular dynamics simulations were performed for the complex of Survivin and the anti-cancer peptides using GROMACS software (version 2023) with the CHARMM36 force field (Ghavamipour et al., 2014, Kumar and Yaduvanshi, 2023), allowing atoms and molecules to interact over a 100 ns timeframe. Subsequently, GROMACS analyses, including root mean square deviation (RMSD) and radius of gyration (Rg), as well as GROMACS protein-ligand interaction energy (Hollingsworth and Dror, 2018) and gmx_MMPBSA (Valdés-Tresanco et al., 2021) analyses, were conducted to assess the stability and binding affinity of the systems. Among the anti-cancer peptides analyzed for efficiency, the anti-cancer peptide (P2) exhibited the highest binding affinity compared to the native peptide, as determined by interaction energy analysis using GROMACS and gmx_MMPBSA software. Furthermore, root mean square deviation

(RMSD) and radius of gyration (Rg) analyses demonstrated the stability of the systems throughout the molecular dynamics simulations. The anti-cancer peptide (P2), demonstrating a high binding affinity for Survivin, effectively reduces cell proliferation and induces apoptosis in cancer cells. These findings highlight P2 as a promising therapeutic candidate for treating human cancers. (Vadevoo et al., 2023).

Keywords: survivin, anti-cancer peptide, molecular dynamics (MD) simulations, molecular docking

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ICB13 -1117

Investigating the Role of EMT genes in Multiple Myeloma: A Bioinformatic Approach

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Multiple myeloma (MM) is a hematologic malignancy characterized by abnormal clonal plasma cells in the bone marrow. A critical factor in tumor invasion and metastasis is the epithelial-mesenchymal transition (EMT), which allows tumor cells to gain traits like increased motility and invasiveness. Although hematopoietic cells have a mesenchymal origin, they display various intermediate stages associated with specific EMT programs, resulting in a more invasive phenotype. This EMT-like signatures have been noted in MM. This study aims to identify differentially expressed genes (DEGs) between MM and healthy samples and explore how EMT genes affect gene expression and cancer progression. The analysis of differentially expressed genes (DEGs) was conducted using data from the GSE72213 microarray dataset available in the Gene Expression Omnibus (GEO). These DEGs were compared with a list of known human EMT genes obtained from the dbEMT database to identify overlaps, referred to as EMT-DEGs. Furthermore, the protein-protein interaction (PPI) network and co-expression modules for the EMT-DEGs were analyzed using the STRING database and Cytoscape software to clarify the regulatory mechanisms involved. Pathway enrichment analysis related to the top co-expression module was carried out using the Enricher dataset. The analysis of the GSE72213 dataset compared 19 samples from the MM group to 3 samples from the control group, leading to the identification of 790 DEGs (fold change ≥ 1.0; $P < 0.01$). These DEGs were then cross-referenced with a list of 1,184 EMT genes, resulting in the identification of 46 EMT-related DEGs (EMT-DEGs). After constructing the PPI network, one co-expression cluster was identified with a score of 10.545, comprising 12 nodes, including EZH2, UHRF1, CCNA2, MMP9, GAPDH, MYBL2, BIRC5, ERBB2, JUN, E2F1, FOXM1, and LMNB1, along with 58 edges, as determined using MCODE. The Enricher database was used to identify enriched KEGG pathways associated with the EMT-DEGs, applying a p-adjusted value threshold of less than 0.01 for statistical significance. Two of the top pathways identified were "Pathways in Cancer" and "CellularSenescence". This expression study emphasized the important role of EMT-related factors in the progression of MM.

Keywords: multiple myeloma, epithelial-mesenchymal transition, protein-protein interaction, gene expression

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ICB13 -1118

Identification of Essential Genes and Suitable Drug Combinations for Colorectal Cancer Treatment Based on Systems Biology Approaches

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Colorectal cancer is the third most prevalent cancer globally, predominantly affecting the elderly population, with an estimated 2 million new cases and 1 million deaths annually. This incidence is projected to rise in the forthcoming years. Early diagnosis of the disease not only mitigates mortality rates but also reduces treatment costs. Given that colorectal cancer, like other malignancies, is a complex disease influenced by various factors, systems biology approaches that provide a holistic perspective on these factors and their interrelations are more effective and exhibit fewer side effects compared to traditional diagnostic and therapeutic approaches. In this article, we present a comprehensive analysis of diverse omics data to identify essential genes and optimal drug combinations for colorectal cancer treatment. Initially, we selected the expression dataset GSE21510, which encompasses gene expression levels from 148 samples, including 104 cancer patients and 44 healthy individuals (Tsukamoto and Ishikawa, 2011).To identify genes with significantly altered expression, we applied two criteria: p-value < 0.05 and |logFC| > 2, resulting in the identification of 451 significant genes. Additionally, to account for all genes associated with colorectal cancer, we utilized the COREMINE database, which is literature-based. From a total of 11,442 genes related to colorectal cancer, we selected 3,729 genes based on the p-value threshold. Subsequently, we identified 178 common genes between these two sets. These genes are statistically associated with colorectal cancer based on literature and are significant according to our expression data analysis. Using the STRING database, we constructed a protein-protein interaction (PPI) network among the 178 selected genes, incorporating physical and functional relationships with a confidence score of 0.4. In this network, centrality analysis revealed five hub proteins: GAPDH, CDK1, CCNB1, CD44, and HMMR. Furthermore, employing the DGIdb database, we identified drugs that target these hub genes. Three drugs—HISTAMINE, SELICICLIB, and HYALURONIC ACID—were identified as effective drug combinations affecting the five hub proteins. Among these, HISTAMINE plays a role in regulating intestinal physiological functions (Middleton and Sarno, 2002); SELICICLIB is utilized in treating lung cancer and leukemia (Iurisci and Filipski, 2006); while HYALURONIC ACID, known for its applications in pain relief and wound healing (Gupta and Lall, 2019), is proposed as a novel therapeutic agent for colorectal cancer due to its influence on two of the five essential genes associated with colorectal cancer development and progression.

Keywords: colorectal cancer, essential genes, drug combinations, systems biology, PPI network

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Exploring the interaction between hsa-miR-122-5p and CDC25A gene in Breast carcinoma progression via computational analysis

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The most prevalent type of cancer among women is breast carcinoma. An estimated 2.3 million new breast carcinoma cases are diagnosed annually around the world. Numerous risk factors, such as age, genetic predisposition, hormonal factors, and lifestyle, have been identified, although the precise cause is still unknown. Depending on the unique features of the tumor and the patient, treatment strategies usually combine hormone therapy, chemotherapy, radiation therapy, surgery, and, more recently, immunotherapy. Therefore, in order to find potential therapeutic targets and BC biomarkers, it is essential to clarify the molecular pathways underlying the onset and spread of breast carcinoma. The cell cycle can be regulated by members of the CDC25 family. By preventing the phosphorylation of cyclin-dependent kinases (CDKs), CDC25 regulates the progression of the cell cycle and activates the CDK complexes. Several cancer types have been shown to express CDC25A at high levels, and overexpression of CDC25A is associated with a poor prognosis in about 50% of BC cases. By targeting CDC25A, we anticipate that hsa-miR-122-5p may be able to increase the radiosensitivity of breast cancer cells and impede the spread of the disease. CDC25A's regulatory mechanism in BC hasn't been thoroughly investigated, though. Advances in high-throughput profiling methods and the availability of public data sets such as The Cancer Genome Atlas Program (TCGA) have allowed for the profiling of a large number of coding transcripts and the mapping of their underlying mechanisms of action. Many different processes in cell biology are regulated by miRNAs. In addition to helping to suppress these pathways, obtaining the miRNA target genes can advance knowledge of gene therapy and cancer regulation. Using the mirwalk database, we predicted gene expression patterns and assessed TCGA RNA-seq data following miRNA target gene prediction in this endeavor. Hsa-miR-122-5p targets CDC25A, which has a high score, according to the results. Additionally, the TCGA data analysis showed that the tissue from breast carcinomas had a markedly elevated expression of this gene. It is predicted that in breast cancer, downregulating hsa-miR-122-5p expression leads to upregulating CDC25A expression. Furthermore, in addition to acting as a biomarker for breast carcinoma, upregulation of CDC25A expression is anticipated to aid in the disease's progression.

Keywords: CDC25A, breast cancer, hsa-miR-122-5p

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Tissue-Specific Gene Co-Expression Analysis in Pediatric Ependymomas Across Different Anatomical Regions

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Ependymomas are central nervous system tumors that arise from ependymal cells lining the ventricles of the brain and the central canal of the spinal cord. These tumors predominantly affect pediatric populations and exhibit significant heterogeneity in location, histological features, and genetic characteristics. This study aimed to identify tissue-specific gene co-expression modules in pediatric ependymomas located in the posterior fossa, spinal cord, and cerebrum using Weighted Gene Co-Expression Network Analysis (WGCNA). By exploring these modules, we sought to uncover the molecular mechanisms underlying tumor development and heterogeneity across anatomical regions. Gene expression profiles were retrieved from the Gene Expression Omnibus (GEO) database, specifically focusing on dataset GSE27279 related to pediatric ependymomas. Following rigorous normalization and quality control procedures, WGCNA was employed to construct gene co-expression networks, enabling the identification of gene modules associated with specific tissue types (posterior fossa, spinal cord, and cerebrum). Hub genes within significant modules were identified based on intramodular connectivity, and functional enrichment analyses (GO and KEGG pathways) were conducted to elucidate their biological roles. The analysis revealed 31 modules in the supratentorial region, 54 modules in the posterior fossa, and 15 modules in the spinal cord. Among these, the blue and red gene modules exhibited significant correlation with the posterior fossa region while showing a strong negative correlation with the supratentorial and spinal cord regions. Conversely, the yellow, turquoise, and brown modules displayed significant correlation with the supratentorial region. Notably, while the yellow and turquoise modules were also significant in the posterior fossa, they demonstrated negative correlation with this region. Hub genes were identified for each module, showcasing their critical roles in tumorigenesis and tissue-specific processes. For example, in the blue module, MYO15A emerged as a key hub gene, potentially linked to cellular structural dynamics. In the brown module, MDH1B suggested a role in metabolic pathways within the tumor microenvironment. The green module's hub gene, DTL, pointed to its involvement in DNA repair and replication processes crucial for tumor proliferation. These findings highlight the molecular complexity and functional significance of tissue-specific gene networks in pediatric ependymomas. These results provide valuable insights into the tissue-specific molecular landscapes of pediatric ependymomas, highlighting key gene modules and pathways that may drive tumorigenesis and regional heterogeneity. This work lays the groundwork for future studies aimed at understanding the molecular underpinnings of ependymomas and developing targeted therapeutic strategies.

Keywords: Pediatric ependymoma, WGCNA, gene co-expression modules, hub genes, molecular heterogeneity

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Exploring the Regulatory Landscape of LncRNAs in Alzheimer's Disease: Insights into Inflammation

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Alzheimer's disease (AD) is a multifactorial neurodegenerative disorder characterized by progressive cognitive decline, synaptic dysfunction, and widespread gene expression changes (Zhang et al., 2024a). Among regulatory elements, long non-coding RNAs (LncRNAs) have emerged as pivotal modulators of biological processes, influencing pathways associated with inflammation (Statello et al., 2021; Zhang et al., 2024b; Lan et al., 2022). This study applies a bioinformatics approach to explore the regulatory role of LncRNAs in AD pathogenesis, with a focus on their contributions to neuroinflammation. RNA-Seq datasets from multiple brain regions, including hippocampus, frontal lobe, parietal lobe, occipital lobe and temporal lobe, were obtained from public repository, Gene Expression Omnibus (GEO) database. After preprocessing, differential expression analysis (DEG) identified key LncRNAs with significant dysregulation in AD patients compared to controls (Koch et al., 2018; Corchete et al., 2020). Functional enrichment analysis was performed using tools such as Enrichr and GSEA to map these LncRNAs to specific biological pathways. Furthermore, gene regulatory networks were constructed to identify interactions between LncRNAs and genes involved in inflammation. The analysis revealed multiple differentially expressed LncRNAs with significant roles in modulating key pathways. For instance, LncRNAs associated with the NF-κB pathway were found to amplify neuroinflammatory responses by upregulating cytokines like TNFα and IL-6. Expression patterns of these LncRNAs were strongly correlated with disease severity, indicating their potential as biomarkers (Garofalo et al., 2021) for disease progression. In addition to their impact on protein-coding genes, several LncRNAs were identified as regulators of microglial and astrocytic activity, linking cellular neuroinflammation to systemic metabolic dysregulation. This integrative approach underscores the complex interplay between LncRNAs and AD-related pathways. This study highlights the multifaceted regulatory role of LncRNAs in Alzheimer's disease, offering novel insights into their contributions to inflammation. The findings suggest that targeting specific LncRNAs could provide therapeutic opportunities to mitigate AD progression. Future work will focus on experimental validation and exploring the translational potential of these findings.

Keywords: Alzheimer's disease (AD), LncRNA, neuroinflammation, RNA-Seq, biomarkers

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High throughput screening of Plant-Derived Antimicrobial Peptides: A Peptide-Protein Docking Study Against Pathogenic Bacteria

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Antimicrobial resistance poses a significant threat to global health, leading to high morbidity and mortality. The misuse of antibiotics has accelerated the emergence of multidrug-resistant bacterial strains, which have developed resistance through mechanisms such as protein alteration, enzymatic degradation, and changes in membrane permeability. This situation has created an urgent need for new, effective, and less toxic antimicrobial agents. Antimicrobial peptides (AMPs) have grabbed attention due to their broad-spectrum activity and fewer side effects. These peptides are a crucial component of plant innate immunity, protecting against microbial infections. AMPs exhibit structural and functional diversity, enhancing their antimicrobial activity, microbial cell selectivity, and immunomodulatory properties. This makes them promising candidates for developing new therapies (Mustafa and Mehmood, 2022). The study analyzed the binding interactions and binding patterns of selected 35 plant-drived AMPs which obtained from Literature review and PlantPepDB web server, with 3 multidrug-resistant bacterial strains: Mycobacterium tuberculosis, Helicobacter pylori and methicillin-resistant Staphylococcus. The binding interactions were validated by ClusPro (protein-protein docking) and HADDOCK 2.4 web servers, confirming the specific docking and results have analyzed with PDBsum Generate server (Yating and Huang,2021, Patil and Goswami, 2020, Görgüç and Gençdağ, 2020). Among 35 selected AMPs in this study, Cysteine-rich antifungal protein 2 (Bn-AFP2), Antibacterial napin and So-D6 (Defensin), exhibited the ten best scores and binding patterns for all 3 bacterial strains targets. So-D6 (Defensin) exhibited the strongest interactions with penicillin-binding protein 2a of methicillinresistant Staphylococcus aureus (with a docking score of -1042), with glucose-1-phosphate thymidylyltransferase of Mycobacterium tuberculosis H37Rv (with a docking score of -1211), and with oxygen-insensitive NADPH nitroreductase of Helicobacter pylori (with a docking score of -1234). The findings suggest that plant-derived AMPs could serve as natural alternatives to synthetic antibiotics, offering a promising solution to combat multidrug-resistant bacterial infections. Molecular dynamics simulations are needed to validate docking results and further studies are required to fully evaluate the efficacy of these peptides in vivo and to explore their mechanisms of action in more detail.

Keywords: antimicrobial peptides, plant-derived AMPs, protein-protein docking

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Novel Anti-ageing Strategy Via Targeting CST With Vitamin B1

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Biological aging is a complex and inevitable process (López-Otín et al., 2013). Cellular and tissue functionality declines progressively, and diseases associated with aging are developed. One of the hallmarks of aging at the molecular dimension is telomere shortening (Blackburn et al., 2006), which contributes to the promotion of cellular senescence and genomic instability. The CST (Ctc1-Stn1-Ten1) complex is essential for the accurate replication and protection of the telomere (Gu et al., 2012), serving as a promising target for anti-aging therapies. Although the catalytic function of telomerase has been thoroughly investigated concerning telomere upkeep (Greider & Blackburn, 1989), recent research indicates the potential for targeting the CST complex (Gu et al., 2012). Furthermore, there is an increasing interest in the influence of micronutrients, including vitamin B1, on the regulation of cellular mechanisms associated with telomere activity and senescence (Selhub et al., 2010). The potential of vitamin B1 as a modulator of the CST complex activity in aging and telomere maintenance was examined in this work. MODELLER (Sali & Blundell, 1993) was used to model the missing residues and complete the crystal structure of the CST complex (PDB ID: 8D0B). Molecular docking simulations were used to examine the optimized structure's binding affinity with vitamin B1, which was obtained from PubChem (2023). Docking was carried out using AutoDock MGL tools (Trott & Olson, 2010), and a grid box was established around the anticipated active site of the CST complex. The binding energy and important molecular interactions of the resultant binding poses were then examined. The binding energy of the best-ranked docking pose of vitamin B1 was -4.8 kcal/mol, showing that this compound interacts favorably with the CST complex. Key interactions involve amino acid residues important for the functionality of the complex; thus, it suggests that vitamin B1 may affect CST-mediated telomere processes. These findings support the potential of vitamin B1 as a modulator of the CST complex and offer a foundation for the development of anti-aging therapeutic strategies. High-throughput screening of large chemical libraries using sophisticated computational methods like molecular docking, virtual screening, and machine learning algorithms will be essential to find strong and specific CST modulators. The development of innovative therapeutic strategies to modulate telomere maintenance and potentially lessen the effects of aging will be made possible by these approaches, which will make it possible to identify compounds with high binding affinity, selectivity for the CST complex, and favorable drug-like properties.

Keywords: aging, CST complex, telomere maintenance, vitamin B1, molecular docking

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Computational Analysis of the D92V Mutation in the EF-hand II Loop of the Mnemiopsin 2 Photoprotein

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Mnemiopsin 2 is a calcium-regulated photoprotein that has bioluminescent properties. This photoprotein has 207 amino acids with a molecular weight of 24 kDa (Hosseinnia and Khalifeh, 2020). The structure of Mnemiopsin 2 has 4 EF-hand motifs. It's worth noting that EF-hand motifs I-III-IV have calcium binding function, but EF-hand II has lost its activity during evolution (Ghanbarlou and Shirdel, 2018). Three functional motifs are located in positions (I: 45-56), (III: 137-148), (IV: 171-182), respectively. Each EF-hand has a helix-loop-helix structure. In the structure of the loops, the conserved residues in positions 1, 6, and 12 have the ability bind to calcium, and residues 3, 5, 7, and in some cases 9 also have the potential to bind to calcium (Jafarian and Sajedi, 2018). The conserved residues in all the photoproteins include aspartic acid (D) at position 1, glycine (G) at position 6 and glutamic acid (E) at position 12. (Toma and Chong, 2005). In this study, the amino acid aspartic acid (polar) at position 92 in the EF-hand II loop was replaced with valine (non-polar). It should be noted that this amino acid is the eighth residue of the EF-hand II loop. Based on homology modeling, three-dimensional structural models of protein variants were constructed with Modeller v.10.4 software. The PDB input files in this software include files Berovin (PDB code: 5bpj), Mnemiopsin 1 (PDB code: 5vP3) for the structural model, Berovin (PDB code: 4mn0) for the calcium binding model and Aecuorin (PDB code: 1ej3) for coelenterazine binding pattern. The sequence-based parameters, including hydrophobicity, instability index, and PI, were obtained by ProtScale and ProtParam servers. Then, the best model was selected based on RMSD, Zdope, ERRAT, and Verify3D parameters, using Chimera x.1.8 software and ModEval, SAVES servers, respectively. Also, the evaluation of models in this study was done based on the parameters of the second structure on a VADAR server. Our aim in this study is to investigate the effects of replacing hydrophobic residue with hydrophilic ones in the EF-hand II loop. The increase in the isoelectric point in the mutant compared to the wild-type model can cause changes in the function of the loop and its calcium binding affinity. Evaluation of the secondary structure of the mutant shows increases in the coil structure. The results of bioinformatics studies indicate a decrease in the free energy of folding, which indicates the stabilization of the structure of the D92V mutant.

Keywords: bioinformatics, bioluminescence, EF-hand loop, homology modeling, mutation

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ICB13 -1131

In-silico Drug Generation using Masked Language Modeling

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De novo drug discovery is a complex, costly, and time-intensive process involving several phases, such as target discovery, screening, lead optimization, and clinical trials (Paul et al., 2010). Lead optimization is crucial for refining compounds to become viable drug candidates by enhancing their bioactivity and optimizing pharmacological properties. Given the vast chemical space, estimated to contain over 10^60 possible molecular structures, traditional methods are insufficient by themselves (Polishchuk et al., 2013). Consequently, machine learning (ML) techniques, especially deep generative models, have been adopted to efficiently explore this space (Elton et al., 2019). Inspired by advancements in natural language processing (NLP), transformer-based models like ChemBERTa-2 have been developed for molecular machine learning. ChemBERTa-2 leverages the SMILES representation of chemical compounds using a transformer-based architecture to learn intricate chemical features such as functional groups, chirality, and atomic connectivity (Ahmad et al., 2022). It is trained on two tasks: masked language modeling (MLM) and multi-task regression (MTR). The MLM task is particularly beneficial for lead optimization. This study leverages ChemBERTa-2 for generating new chemical compounds from existing leads. Using the BACE dataset, containing data on beta-secretase inhibitors, the model generates novel SMILES sequences by sequentially masking atoms in a compound's SMILES representation and predicting replacements. Only high-likelihood predictions are used to modify the original structure, producing a tree of molecular variations. The generation process is guided by constraints, such as a maximum depth of 10 and 200 variations per compound. Our approach generated 28,911 novel SMILES structures from 303 compounds in the BACE dataset's test set. These were evaluated based on synthetic accessibility and pIC50 improvement. The Synthetic Accessibility Score (SAS) assessed the feasibility of synthesizing new compounds, with scores below 5 considered experimentally feasible. Most generated compounds had SAS scores under this threshold. Moreover, we evaluate the pIC50 values of the generated compounds using a computational model. Notably, for 76 compounds, the pIC50 increased by 1 unit, while for 12 compounds, it increased by 2 units. A 1-unit increase in pIC50 corresponds to a tenfold reduction in the effective inhibitory concentration, representing a significant enhancement in drug efficacy. Our findings demonstrate that ChemBERTa-2, even with self-supervised training on SMILES sequences, effectively captures crucial chemical features that influence molecular properties. By leveraging ChemBERTa-2 for lead optimization, we successfully improved the efficacy of several drug candidates. This approach underscores the potential of transformer-based models in revolutionizing the drug discovery pipeline, offering a scalable and efficient method for exploring vast chemical spaces.

Keywords: de novo drug discovery, lead optimization, chemical language modeling, IC50 Improvement

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Exploring the Anticancer Potential of Flavonoids from Morus alba Against Breast Cancer: An In Silico Approach

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Morus alba, commonly known as white mulberry, is a Moraceae family plant widely used in traditional Chinese medicine. The leaves, bark, and fruit of this plant have been valued for their various medicinal properties, including antibacterial, anti-inflammatory, anti-cancer, anti-obesity, antidiabetic, and antioxidant effects (Batiha and Teibo, 2023). Morus alba contains a variety of compounds, such as tannins, saponins, triterpenes, phenolics, flavonoids, benzofuran, anthocyanins, anthraquinones, aromatic compounds, and minerals (Gryn-Rynko and Bazylak, 2016). Previous studies have shown that the fruit of Morus alba possesses anti-cancer properties, largely attributed to its high concentration of bioactive compounds, particularly flavonoids (Zhumabayev and Zhakipbekov, 2024). Flavonoids exhibit a range of biological activities, including the inhibition of proliferation, cell cycle arrest, induction of apoptosis, antioxidant effects, and anti-metastatic properties (Wen and Fang, 2021). They play a significant role in regulating cell proliferation, invasion, angiogenesis, and oxidative stress. Consequently, flavonoids have become subjects of considerable interest in drug discovery research. Recent studies indicate that natural compounds, such as flavonoids, show promising outcomes with fewer side effects compared to conventional treatments (Slika and Mansour, 2022). Breast cancer is one of the most prevalent types of cancer affecting women worldwide (Ke and Wang, 2021). Caspase-3 is a crucial target in the development of anticancer drugs, as its cleavage and activation lead to the apoptosis of cancer cells (Eskandari and Eaves, 2022). In this study, we evaluate the binding affinities of the main flavonoids found in Morus alba—specifically rutin, morin, quercetin, and myricetin—against the caspase-3 protein. The 3D structure of the caspase-3 protein (PDB ID: 2XYP) was obtained from the RCSB Protein Data Bank, while the 3D structures of rutin, morin, quercetin, and myricetin were downloaded from the PubChem database (PubChem CID: 5280805, 5281670, 5280343, and 5281672, respectively). We employed iGEMDOCK (version 2.1) to conduct molecular docking, utilizing the following docking accuracy parameters: a population size of 300, 70 generations, and 3 solutions. Docking scores (DOS) represent the estimated interaction energy between the ligands and the protein, with more negative scores indicating higher binding affinity (Bhowmik and Nandi, 2021). The interaction between the caspase-3 protein and four selected ligands was investigated. The calculated energy levels for the ligands were as follows: Rutin (-104.15), Morin (-101.85), Quercetin (-97.96), and Myricetin (-99.31). These energy values indicate that the ligand with the highest negative energy affinity will exhibit a stronger binding affinity to the protein. Based on our results, rutin is the most effective ligand for the caspase-3 protein among the flavonoids studied, showing great potential as a candidate for developing caspase-3-targeted anticancer agents. Future studies should focus on validating these findings and exploring the mechanisms underlying the interactions between the ligands and the protein.

Keywords: breast cancer, morus alba, Flavonoids, molecular docking, in-silico

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A Contrastive Learning Framework for Single-Cell Multi-Omics Data Integration

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The advancement of single-cell omics technologies has changed our understanding of biological systems' functionalities and heterogeneities. Methods such as SHARE-seq and SNARE-seq capture gene expression and chromatin accessibility, while CITE-seq measures gene expression and cell surface protein abundance. However, analyzing each modality independently can lead to partial insights. Integrating these modalities offers a solution but is challenging due to differences in their distributions and feature spaces. There has been a lot of effort to develop efficient computational frameworks to address this problem. The majority of these approaches learn low-dimensional joint embeddings of the omics modalities. Some of these methods such as Principal Component Analysis (PCA) and Canonical Correlation Analysis (CCA) use linear transformations of input data, with tools such as Seurat combining PCA, CCA, and Mutual Nearest Neighbors for alignment. MOFA uses matrix factorization to derive shared and modality-specific representations. More recent multi-modal deep learning approaches, such as scglue, employ variational autoencoders to capture hierarchical, non-linear patterns and align multi-omics representations end-to-end. While these methods demonstrate promising results and strong performances, they often suffer from low signal-to-noise ratios (Wang et al., 2023) and over-complicated architectures. Here, we present a neural network architecture inspired by the CLIP model developed by OpenAI (Radford et al., 2021) for paired single-cell multi-omics integration. This framework consists of two encoders, each learning a low-dimensional representation of the input modality. Then, these representations are aligned using a contrastive loss function. We benchmarked this model with two baselines (PCA and an Auto Encoder with reconstruction loss) and three state-of-the-art models (MOFA (Argelaguet et al., 2018), Harmony (Korsunsky et al., 2019), and Con-AAE (Wang et al., 2023)) on three real-world datasets including SHARE-seq (Ma et al., 2020), PBMC (10x Genomics, 2020), and CITE-seq (Stoeckius et al., 2017). All evaluations were performed on unseen test datasets with 10 replications. Benchmarks were based on four measures: Average Silhouette Width (ASW) for clustering quality of latent representations based on cell types, Recall at k, Cell type accuracy, and Median Rank for the quality of integration. Results show that our framework outperforms other models in most of the metrics. Moreover, it achieved high ASW values compared to original datasets which reflect the ability of the model to denoise single-cell data and extract biological signals. In addition, we assess the model's ability to handle unpaired multi-omics data which shows high values for most metrics compared to other frameworks. These findings position our framework as a high-potential platform capable of extending to downstream applications such as cell-type annotation and disease subtyping.

Keywords: single-cell, omics integration, representation learning, contrastive learning, neural networks

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ICB13 -1135

In Silico Design of a Chimeric Protein-Based Vaccine Against Salmonella Typhi: A Bioinformatics and Immunoinformatics Approach

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Salmonella is a Gram-negative, rod-shaped bacterium from the family Enterobacteriaceae. This bacterium is a facultative anaerobe and an intracellular pathogen (Chong et al., 2021). Serovar Typhi causes human typhoid fever that leads to systemic infection in the host. This disease occurs exclusively in humans, whereas other strains like Salmonella Typhimurium are zoonotic and cause human gastroenteritis (Crump and Mintz, 2010). According to reports, approximately 200,000 deaths occur annually out of nearly 20 million typhoid fever cases worldwide. Contaminated water and food are the main factors contributing to the spread of this disease. Generally, underdeveloped regions experience a higher prevalence due to a lack of access to clean drinking water compared to developed areas (Dougan and Baker, 2014). This disease is treated using broad-spectrum antibiotics such as fluoroquinolones, cephalosporins, and ampicillin. However, the emergence of multidrug-resistant (MDR) bacteria has highlighted the urgent need for developing antibiotic-independent therapeutic approaches and prevention strategies through vaccines (Dyson et al., 2019). Since S. Typhi is an intracellular pathogen, the designed vaccine must effectively activate cell-mediated immunity in the host. Due to their peptide nature, Chimeric proteins are well-suited for eliciting cell-mediated immunity, resulting in adequate immunogenicity against S. Typhi (Chauhan and Khasa, 2023). Two antigens, T2942 and FliC, were selected as candidates for the design of a vaccine with these characteristics, among other antigens present in S. Typhi (Bumann, 2014). T2942 or StiV belongs to the outer membrane proteins (OMPs) category, which plays an independent role from the Type 3 Secretion System (T3SS) in the bacterium's attachment to intestinal epithelial cells and subsequent entry (Chowdhury et al., 2015). FliC is an acidic protein that encodes the flagellar protein in S. Typhi and is a mediator of epithelial activation. The protein sequences of these proteins were connected using a rigid linker and subjected to detailed bioinformatics and immunoinformatic analyses (Ghorbani et al., 2021). Phyre2 predicted the three-dimensional structure, and SAVES evaluated biophysical and biochemical parameters. According to the Ramachandran plot, 91.1% of residues are in the most favored region residues, and IUPred2A showed structural abnormalities. After confirming the bioinformatics parameters of the chimeric protein, immunoinformatic evaluations were performed. The protein's immunogenicity and non-allergenic properties were assessed. Bcepred and CBTOPE identified Linear and conformational B-cell epitopes, and T-cell epitope predictions indicated suitable binding to MHC molecules. The results from these analyses demonstrate the stability of the chimeric protein and its ability to elicit an immune response in the host. Detailed documentation for each will be presented in separate tables and charts. The designed chimeric

protein, combining T2942 and FliC antigens, demonstrates promising immunogenic potential and structural stability, making it a viable candidate for a vaccine against Salmonella Typhi, with the capacity to effectively activate cell-mediated immunity in hosts.

Keywords: Salmonella Typhi, multi-epitope vaccine, reverse vaccinology, chimeric protein, immune system simulation, immunoinformatics, infectious disease

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Bioinformatics studies on S35K mutation on Mnemiopsin 2 photoprotein

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Bioluminescence is the process where certain living organisms emit light. This phenomenon occurs in photoproteins when Ca^{2+} binds to their EF-hand loops. Mnemiopsin 2 is a Ca^{2+}-regulated photoprotein that contains three EF-hand motifs capable of binding Ca^{2+}. The coelenterazine-bound form is called a photoprotein, while the protein without coelenterazine is referred to as an apophotoprotein. The S35K mutation is analyzed using professional bioinformatics servers and resources. A BLAST search in the NCBI database identifies S35K as an optimal choice due to direct evolution. Multiple 3D models of the S35K-mutated Mnemiopsin 2 photoprotein are modeled using Modeller v10.4, and these structures are evaluated with parameters such as ERRAT, Verify3D, and Ramachandran score, all accessible via the SAVES website. The Chimera software calculates the RMSD score, which allows the identification of the most accurate and reliable structural model. The selected model undergoes further assessment with the VADAR server. The Expasy server calculates the hydropathy index (based on the Kyte & Doolittle protocol), molecular weight, and instability index. The results show no significant differences in hydrogen bond distances or folding patterns, including alpha helices, beta sheets, and coil percentages, compared to the wild-type Mnemiopsin 2 photoprotein. A detailed comparison performed using Chimera indicates no observable structural changes between the mutated and wild-type photoproteins. This comprehensive analysis suggests that the S35K mutation is non-destructive, and the protein likely retains functionality similar to the wild type, with no significant reduction in stability. Additionally, this mutation decreases the hydropathy of the protein, making it an intriguing candidate for further functional studies and potential biotechnological applications.

Keywords: bioinformatics, bioluminescence, homology modeling, Mnemiopsin 2

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ICB13 -1137

Graphene Oxide Nanosheets as Drug Carriers for Erdafitinib in a Targeted Drug Delivery System: A Cutting-Edge Approach to Cancer Therapy

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This study investigates the interaction of the anticancer drug Erdafitinib with graphene oxide (GO) nanosheets. Quantum mechanics calculations using density functional theory (DFT) at the B3LYP/6-31**G level reveal that oxygen-containing functional groups in graphene oxide, including carboxyl, epoxy, and hydroxyl groups, facilitate the formation of strong hydrogen bonds and π-π interactions with the aromatic structure of Erdafitinib. These interactions contribute to the stabilization of the Erdafitinib-GO complex, enhancing the stability of the drug delivery system. Electronic structure analysis using HOMO-LUMO calculations indicates that the reduction in the energy gap in the presence of graphene oxide improves electronic stability and increases the system's reactivity. Additionally, the density of states (DOS) diagrams reveal fewer absorbed vibrations for the Erdafitinib-GO system, signifying continuous and stable electronic transitions at the molecular level. Furthermore, molecular electrostatic potential analysis shows that the appropriate surface charge distribution in graphene oxide enhances electrostatic interactions, thereby improving the nanocarrier's efficiency. Molecular docking simulations demonstrate that graphene oxide nanosheets, owing to their high surface area and amphiphilic nature, exhibit significant potential for adsorbing Erdafitinib molecules. Both hydrophobic and hydrophilic interactions between the drug and the nanocarrier contribute to greater system stability in biological environments. These findings suggest that graphene oxide nanosheets act as stable and efficient nanocarriers for Erdafitinib, offering significant potential to improve the performance of advanced drug delivery systems.

Keywords: Erdafitinib anticancer nano drug, graphene oxide nanosheets (GO), density functional theory (DFT),density of states(DOS),molecular electrostatic potential (MEP), molecular docking simulations(MDs)

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ICB13 -1138

Molecular docking study of some herbal compounds as potential inhibitors of SARS-CoV-2 spike receptor

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In 2019, the SARS-CoV-2 virus spread throughout the world, and many communities are still affected by this disease. Due to the severe complications and widespread mortality of this pandemic, the discussion of treatment and production of effective drugs and vaccines for this virus quickly became important. Among the various treatment methods, scientists and researchers paid special attention to treatment using substances of natural and plant origin. Flavones are a group of flavonoids that are present in many plants and have attracted attention for the treatment of various diseases due to their biological activities, such as antioxidant and antiviral properties. The aim of this study is to investigate the inhibitory effect of a number of flavone compounds on SARS-CoV disease through the interaction of these compounds with the second receptor binding domain (RBD) of the SARS-COV-2 virus spike protein, using molecular docking. For this purpose, the structures of the studied compounds (Quercetin, Asagin, Tetrandrine, Dehydromyristin) and the Covid protein were extracted from the PDB and PubChem databases. Then, the chemical and physical properties of the mentioned compounds were predicted by i-Tasser and Ligplot+ software. Autodock4, VMD, Discovery Studio software were used to perform molecular docking. The compounds were examined in terms of Lipinski's law and physicochemical conditions using the SweesADME.ch database. Then, using molecular docking software, the docking score of the interaction of the compounds with the receptor on the virus surface was examined. The results obtained showed that among the four compounds, the flavone compound of Asajin had better binding and interaction conditions than the other compounds due to following Lipinski's laws and appropriate physicochemical factors. As a result, after in vitro and in vivo studies on this compound, they can be proposed as a viral inhibitor.

Keywords: SARS-CoV-2 virus, receptor binding domain (RBD), Flavones, molecular docking

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ICB13 -1140

Diagnosis of Diabetic Retinopathy with Fuzzy Technique and Deep Learning

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Diabetic retinopathy is a growing eye disease and one of the most common complications of diabetes worldwide. If not diagnosed in time, it can lead to significant vision problems and eventually blindness. Early detection, before specific symptoms occur, is crucial for preserving vision. However, manual detection of retinal fundus images by ophthalmologists is both time-consuming and costly. This paper introduces a hybrid approach that uses deep learning and fuzzy techniques to classify retinal fundus images into five categories: healthy, mild retinopathy, moderate retinopathy, severe retinopathy, and proliferative retinopathy. Deep learning methods are known for their high accuracy, speed, and ability to automatically extract features from images. However, their performance is highly dependent on the quality and balance of the dataset. The dataset used in this study is Aptos2019 from Kaggle, which contains 5590 images divided into training and test sets, which shows significant imbalance among disease categories. In this study, fundus images are first processed using deep learning techniques to extract image features. The accuracy and extracted features are compared in a simple manual architecture and several popular deep learning frameworks. Then, the most effective features are fed to a fuzzy system to classify the disease into five categories. Fuzzy techniques, with their flexibility and similarity to human reasoning, allow us to calculate the probability percentage for each stage of the disease based on the extracted features. The rules governing the fuzzy system are interpretable by physicians and can be modified using their diagnosis, resulting in outputs that accurately reflect human decision-making. In this research, we attempt to develop a robust and comprehensive system that can be applied to any medical data and achieve desired results. The aim of this study is to combine the strengths of deep learning and fuzzy logic to inspire the development of innovative methods in the field of medical diagnosis and data analysis.

Keywords: diabetic retinopathy, deep learning (DL), fuzzy logic, fundus, classification, image processing.

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ICB13 -1142

Using structural controllability to analyze signaling pathways and PPI networks for the identification of therapeutic targets in colorectal cancer

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Colorectal cancer is the third most common cancer and the second most common cause of cancer deaths worldwide. In 2022, there were an estimated 1.93 million new cases and 904,000 deaths reported worldwide. According to the International Agency for Research on Cancer (IARC), projects an increase in new cases annually to reach 3.2 million, coupled with 1.6 million related deaths by the year 2040 (Bray, F., et al., 2023). Early diagnosis and timely intervention in this malignancy go a long way in securing better survival and improvement in quality of life. Colorectal cancer is a complex disease that results from extensive interactions of genetic, epigenetic, and environmental factors. For that reason, systems biology approaches may provide more profound insights into such processes and thus more effective treatments than traditional methods using complex network-based molecular interaction modeling. This project adopted a comprehensive analysis using omics data for the identification of effective treatment strategies. Gene expression data, GSE261888, were obtained from the GEO database (Escrich, V., et al., 2024). The study first made a comparison between healthy samples and early-stage disease samples. Significant genes were identified by applying two statistical criteria: p-value < 0.05 and |log FC|> 2. These genes were then mapped to the colorectal cancer signaling pathway in the KEGG database and considered as target control genes. Subsequently, a control algorithm was applied to the signaling pathway network, which led to the identification of three driver genes. Additionally, to investigate disease progression, a comparison was made between early-stage and advanced-stage disease samples. Significant genes from this comparison were also identified using the aforementioned criteria. To perform network analysis, a protein-protein interaction (PPI) network was constructed for the identified genes using the STRING database. Hub centrality analysis of this network led to the identification of three hub proteins. Finally, drug-gene interaction analysis was performed for the six identified proteins — three driver proteins and three hub proteins — to identify potential therapeutic targets. These analyses can be utilized in the design of effective drugs for colorectal cancer. In the drug-gene interaction analysis, it was found that the drug Tetradecanoylphorbol Acetate targets the genes CXCL8, MYC, and FOS; the drug Cetuximab targets the genes AREG and CXCL8; the drug Tretinoin targets the genes SHH and CXCL8; and the drug Methotrexate targets the IL1RN gene.

Keywords: colorectal cancer, network analysis, controllability, PPI network, drug target, expression data

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ICB13 -1143

Solving Diffusion Equations Using Physics-Informed Neural Networks: A Biological Application

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A large percentage of processes in the fields of physics, chemistry, biology, economics, and sociology are expressed mathematically by partial differential equations (PDEs). Solving PDEs is often computationally expensive and challenging, particularly for equations with unknown parameters. Traditional methods, such as finite difference or finite element methods, rely on discretization techniques that can become computationally intensive for high-dimensional problems or require detailed knowledge of the unknown parameters (Evans, 2022). Recently, there has been an increasing interest in the study of deep learning techniques and has recently attracted more attention for solving PDEs. Physics-informed neural networks (PINNs) have become a strong framework among them. An efficient machine learning framework which includes the physical rules controlling a system into neural network training is known as PINNs. Due to this framework, PINNs can solve PDEs effectively without require for traditional discretization methods (Raissi et al 2019) .The Fisher–Kolmogorov–Petrovsky–Piscounov (Fisher–KPP) equation is the main subject of this investigation.It was first put up as a model for the transmission of a beneficial gene in a population in the 1930s. In terms of mathematics, it belongs to the broad category of reaction-diffusion equations (Simpson and McCue,2024) . (Wang et al., 2009). We solve Fisher–KPP using PINNs using deep learning. The neural network design is defined by three hidden layers, each of which has 20 neurons and the ReLU activation function. The model is trained using the Adam optimization technique, and the optimal model is obtained at step 10,000: 1.11e-01 for train loss and 1.19e-01 for test loss. This study serves as a first step toward a deeper understanding of the topic under study and establishes the foundation for future research in this field.

Keywords: partial differential equations,biology, deep learning, physics-informed neural network, Fisher–Kolmogorov–Petrovsky–Piscounov

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Molecular Docking Analysis of Eugenol and Paclitaxel Targeting MRAS in Breast Cancer Therapy

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Breast cancer is the leading cause of cancer-related deaths among women globally, with its incidence rising worldwide (Smolarz, Nowak, 2022). MRAS, which has unique functions related to classical RAS oncoproteins, is significantly more expressed in estrogen receptor-negative than in estrogen receptor-positive breast carcinomas and is crucial for cell migration and differentiation, influencing cell polarity and prompting research into potential treatments (Chin, DeVries, 2006; Hess, Anderson, 2006; Young, Rodriguez, 2018). Eugenol has antioxidant and anti-inflammatory effects, and it can induce apoptosis in cancer cells while inhibiting their migration and viability through specific pathways (Ulanowska, Olas, 2022). Additionally, paclitaxel, a taxane chemotherapy agent, is a vital treatment for breast cancer, disrupting microtubule dynamics to stop cell division and induce apoptosis, significantly improving survival rates and reducing cancer recurrence risk (Jivani, Shinde, 2024). The aim of this study is to investigate the molecular interactions of eugenol and paclitaxel with the MRAS protein through protein docking, assessing their binding energies. This study will evaluate how these two compounds bind to and block the MRAS protein, which subsequently has inhibitory effects on downstream pathways. In this study, at first the three-dimensional structure of the MRAS protein and the ligand eugenol was obtained from the Protein Data Bank database and converted to Protein Data Bank format using Open Babel software. The two-dimensional structure of paclitaxel was also retrieved from the PubChem database and converted to three-dimensional format using Avogadro and Open Babel. Then, the protein docking with eugenol was initially conducted, followed using Chimera and AutoDock software to purify and remove excess molecules from the protein, repair amino acids, decreased protein energy level and adjust charges and hydrogen bonds. The PDBQT format was also generated. By using PyMOL, the active site of the protein was identified, which includes 14 amino acids such as Glycine 23, Aspartate 21, Lysine 127, and Asparagine 126 etc. A grid box specific to the active site was defined with dimensions of 36, 40, and 44 along the axes, corresponding to X = 4.874, Y = 10.022, and Z = 11.152. For the ligands, eugenol was docked first, followed by paclitaxel using AutoDock 4. The best binding energy for eugenol was -5.54 kcal/mol, exhibiting two hydrogen bonds. In contrast, the best binding energy for the paclitaxel conformer was -6.36 kcal/mol, with one hydrogen bond. The bond structures were visualized using PyRx, revealing that eugenol primarily interacted with amino acids Phenylalanine 38, Alanine 27, and Lysine 158 through hydrogen bonds with Serine 126 and Aspartate 129. Additionally, paclitaxel showed strong interactions with MRAS through amino acids Phenylalanine 38 and Lysine 127, predominantly forming hydrogen bonds with Glycine 23. In summary, both eugenol and paclitaxel can bind to MRAS with favorable ΔG values, which may induce cell cycle alterations and apoptosis while modulating key cellular proteins involved in migration and cell proliferation.

This mechanism positions them as promising therapeutic agents for breast cancer.

Keywords: molecular docking, MRAS protein, eugenol, paclitaxel, binding energy

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ICB13 -1146

Validation of Prognostic Biomarkers in Pancreatic Cancer Through Multi-Dataset Analysis and Pathway Enrichment

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Pancreatic cancer remains one of the lethal forms of gastrointestinal cancer, characterized by a low five-year survival rate and challenges in early detection. The disease is often diagnosed at an advanced stage due to the pancreas's anatomical position, making it crucial to understand its risk factors for effective prevention (Hu, J.X, 2021). This study aims to identify sets of prognostic biomarkers from pancreatic cancer genomic data by applying to multiple independent datasets to find sets of genes related to the malignant stage of pancreatic cancer. The research will also involve pathway enrichment analysis to elucidate the biological significance of these biomarkers and their potential roles in tumor progression and therapeutic response. Data set GSE32688 with GPL570 was received from the Gene Expression Omnibus, and then the differentially expressed genes (DEGs) between pancreatic cancer and non-malignant pancreas samples were identified using the R package including GEOquery, limma, BiocGenerics, affy, and oligo. Gene ontology and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis were performed to identify the biological function of DEGs by Enrichr (Ma'ayan Laboratory, 2024). String database was used to investigate protein-protein interactions (STRING, 2024). A protein-protein Interaction network was constructed to display key target genes by using CytoHubba plugin in Cytoscape software. For hub genes validation, Gene Expression Profiling Interactive Analysis (GEPIA) databases were used and survival curve plotted by Kaplan-Meier plotter (Gene Expression Profiling Interactive Analysis, 2024; Kaplan-Meier Plotter, 2024). In total 570 DEGs were selected, comprising 444 upregulated (logFC<1, adj.p value <0.01) and 126 downregulated genes (logFC>-1, adj.p value <0.01). The KEGG pathways were significantly enriched including Adherens junctions, Tight junctions, Extracellular matrix receptor interaction, and PI3K-Akt signaling pathway. Also, DEGs were enriched in biological processes associated with Establishment of skin barrier, Skin epidermis development, Cell-Matrix adhesion and Positive regulation of protein Serin-Threonine kinase activity. Molecular functions also were associated with Cadherin binding, Cadherin binding involved in cell-cell adhesion and Myosin Binding. The 10 hub genes include: CDH1, MYC, IL6, ERBB2, KRAS, MET, CCND1, MUC1, IL1B, and TJP1 with CDH1 ranking highest. Among these genes CDH1, KRAS, CCND1, MET and TJP1 were considered by survival analysis. All these hub genes were upregulated in tumor cells based on analysis with GEPIA. These findings contribute to understanding gene regulation in pancreatic cancer and identifying new therapeutic targets and biomarkers in association.

Keywords: pancreatic cancer, hub genes, DEGs, pathway enrichment analysis

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ICB13 -1148

Simultaneous overexpression of CD70 and downregulation of CD84 as a prognostic marker for glucocorticoid resistance in B cell Acute lymphoblastic leukemia

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Acute lymphoblastic leukemia (ALL) is a type of blood cancer originating from lymphocytes of the immune system that spreads rapidly (Gokbuget and Boissel, 2024). ALL is one of the most common cancers in children with an increasing annual rate, although it also occurs in adults (Katebi and Rahgozar, 2023). Based on origin, this cancer is classified into B and T-ALL, with the B type being more common (Brown and Shah, 2021). Glucocorticoids, particularly Prednisolone and Dexamethasone, are highly valuable in the treatment of ALL (Pourhassan and Murphy, 2024). This importance is primarily due to their ability to induce apoptosis in cancer cells through glucocorticoid receptor activation (Inaba and Pui, 2010). However, cancer cell resistance often disrupts their effectiveness (Bergeron and Barnett, 2023). Studying the causes and patterns of drug resistance can aid in accelerating the replacement of treatment protocols and combating this phenomenon (Abdoul-Azize and Hami, 2024). In this study, transcriptomics data were used to compare gene expression levels in glucocorticoid-resistant and sensitive cell lines. Microarray and RNAseq transcriptome data related to glucocorticoid-resistant and sensitive B-ALL cell lines were extracted from the GEO database with accession numbers GSE94302, GSE217428, and GSE214319 (Sarno and Domizi, 2023; Sbirkov and Vergov, 2023). Data analysis was performed using the R and Galaxy (Galaxy, 2024) platforms for microarray and RNAseq data, respectively. DEG analysis was conducted between resistant and sensitive groups for each dataset (Law and Chen, 2014; Phipson and Lee., 2016). Genes with significant expression level changes (Adj.P.Val<0.05, |logFC|>1) in each dataset were extracted and ultimately intersected among all three datasets. Among the final genes, CD70 and CD84 showed significant increases and decreases in expression in resistant cells, respectively. Gene ontology enrichment analysis related to CD70 and CD84 was performed using the String database (Szklarczyk and Kirsch, 2023) and Cytoscape application (Shannon and Markiel, 2003). Although both CD70 and CD84 have a role in activating immune cells, the reason why resistant cancer cells overexpress CD70 is a controversial issue. Based on literature reviews exceeded expression of CD70 can exhaust T cells instead of activating them (Nie and Ren, 2022). In this study, simultaneous overexpression of CD70 and downregulation of CD84 in B-ALL was introduced as a prognostic marker for drug resistance to glucocorticoids. This study can help identify more effective treatment options for B-ALL patients who are resistant to glucocorticoids.

Keywords: drug resistance, glucocorticoids, acute lymphoblastic leukemia, transcriptomics, prognostic

marker

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ICB13 -1150

Single-Cell Transcriptomic Analysis Reveals Cellular Heterogeneity and Molecular Markers in Acute Leukemia Subtypes

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Single-cell transcriptomic profiling has provided new insights into understanding the cellular and molecular diversity of acute leukemias. These malignancies, including T-ALL, B-ALL, and AML, exhibit significant heterogeneity in their cellular composition and gene expression profiles. However, the specific cell populations contributing to leukemia progression and the molecular markers distinguishing subtypes remain poorly understood (García-Sanz and Jiménez, 2021). We characterized the heterogeneous cell populations of leukemia and healthy controls using single-cell RNA sequencing (scRNA-seq) and identified key molecular markers associated with these malignancies. scRNA-seq data were analyzed using the Seurat package for clustering, cell-type identification, and differential gene expression. Cellular frequencies across Blast, T-cell, B-cell, Monocyte, NK, Erythrocyte, and Dendritic Cells were compared, and subtype-specific markers were identified. Blast cells were highly enriched in T-ALL (59.35%) compared to AML, B-ALL, and healthy controls, where healthy cells showed only a small proportion of blast cells (4.93%). B-ALL had higher proportions of NK cells (36.08%) and B cells (35.34%), while monocytes were most abundant in AML (58.96%). CD2AP and RPN1 were identified as distinguishing markers for Blast cells in T-ALL and B-ALL. This study highlights acute leukemia subtypes' cellular heterogeneity and distinct gene expression profiles, providing insights into their classification. The findings contribute to the development of targeted diagnostic and therapeutic strategies.

Keywords: Acute leukemia,single-cell RNA sequencing, cellular heterogeneity,molecular markers, Leukemia subtypes

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ICB13 -1153

Bioinformatics Analysis of Prostate Cancer by the Construction of circRNA-miRNA-mRNA Regulatory Network

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Prostate cancer is the most common cancer by incidence in men in 112 countries (as of 2020), and accounts for one in every 14 cancers diagnosed globally, and 15% of all male cancers (Sung and Ferlay,2020). Among men, the disease ranks second only to lung cancer in terms of cancer mortality (Bray and Colombet, 2023). CircRNAs are proven essential elements in the initiation and progression of human disease, especially cancers, and recent studies indicated that they function as potential biomarkers for cancer diagnosis and treatment (Wilusz and Sharp, 2013). In depth study revealed that some circRNAs might regulate microRNA (miRNA) function as microRNA sponges the and circRNA-miRNA-mRNA axis axes may play a crucial role in cancer-related or non-cancer pathways (Li and Pei, 2020). To conduct this study, circRNA expression data were retrieved from the GEO database. Differentially expressed circRNAs (DECs) were identified using the Limma package in the R programming environment. Subsequently, miRNAs associated with these circRNAs were predicted using a specialized database focused on cancer-related circRNAs. In the next step, target genes of the identified miRNAs were predicted using the miRWalk web tool. To identify key genes, the overlap between these predicted target genes and differentially expressed genes obtained from the TCGA database was analyzed. Functional enrichment analyses were performed to explore the biological pathways associated with these genes. A protein-protein interaction (PPI) network was constructed using Cytoscape software to investigate molecular interactions. Hub genes were identified within this network. Finally, a regulatory network comprising circRNA/miRNA/mRNA interactions was developed and analyzed. In a regulatory genetic study, 32 circRNAs were found to be unregulated, accompanied by the downregulation of 20 miRNAs and the upregulation of 245 genes. These findings suggest a potential role for circRNAs in influencing gene expression by modulating miRNA activity. Studies show that circRNAs influence the expression of key genes by regulating the circRNA-miRNA-mRNA axis, thereby activating pathways related to cell division and chromosomal segregation. These processes play a crucial role in the proliferation of cancer cells and provide new insights into the molecular mechanisms underlying prostate cancer progression.

Keywords: prostate cancer, circular RNA, biomarkers, regulatory network

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ICB13 -1154

Uncovering Disrupted Cell-Cell Interactions in Alzheimer's Disease Using Variational Graph Autoencoders on Single-Cell Spatial Transcriptomics Data from the Human Middle Temporal Gyrus

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The human middle temporal gyrus (MTG) is a susceptible brain region in the early stages of Alzheimer's disease (AD), yet the molecular mechanisms driving this regional vulnerability remain poorly understood. Understanding the intricate cell-cell interactions (CCIs) in this region is crucial for elucidating the pathophysiology of AD. Recent advances in single-cell spatial transcriptomics and deep learning have created new opportunities to explore CCIs in unprecedented detail. Variational graph autoencoders (VGAEs), a state-of-the-art deep generative model for graph-structured data, enable the encoding of complex interactions between cells while preserving their spatial and molecular context. Chen and colleagues (Chen et al. 2020) have used the 10x Visium platform to measure spatial transcriptomics in AD and control MTG samples. The dataset was obtained from GEO (GSE220442) and analyzed with Seurat. Data were log-normalized, scaled, and integrated using reciprocal principal component analysis (RPCA) and the Louvain algorithm was used for dimensionality reduction and clustering. To employ the VGAE model for inferring cell-cell interactions, we used the DeepLinc pipline (Li & Yang 2022) with two graph convolutional layers, which requires two input files: the adjacency matrix of a cell-cell interaction graph (A) and a gene expression matrix (X) as features of the nodes in A. The adjacency matrix was created by using the K-nearest neighbors (KNN) algorithm to find the three closest neighbors for each cell based on geometric closeness, with a distance threshold applied to consider only nearby cells as direct contacts. The latent representations learned by DeepLinc were used to infer known and novel CCIs. Cell-type specific differentially expressed genes (DEGs) were identified using Seurat's FindMarkers function. Next, key cell type pairs were predicted by DeepLinc, and Ligand-Receptor (LR) analysis of the DEGs in these cell types was performed using the NicheNet (Browaeys et al. 2020). Subsequently, we utilized ClusterProfiler to perform Gene Ontology (GO) enrichment and KEGG pathway analysis for the dysregulated LR-associated genes. Our analysis reveals significant disruptions in CCIs in the MTG region of AD. We identified decreased astrocyte and microglial signaling to neurons, downregulated communication between excitatory and inhibitory neurons, and upregulated microglia-to-astrocyte and oligodendrocyte interactions. Additionally, abnormal interactions between endothelial cells and other brain cells were observed. Our integrative analysis identified key dysregulated LR interactions in a cell type-specific manner and key biological functions and pathways associated with them. This study highlights the utility of VGAEs for analyzing spatially resolved single-cell transcriptomic data to restore disrupted cellular communication in AD by unsupervised integration of both the entire transcriptomic landscape and graph topology.

Keywords: middle temporal gyrus (MTG), Alzheimer's disease (AD), cell cell interaction, single-cell spatial transcriptome, variational graph autoencoder (VGAE)

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ICB13 -1155

Comprehensive Analysis of EEG Signals for Machine Learning-Based Depression Detection

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Major Depressive Disorder (MDD) is a prevalent mental illness that is typically diagnosed using questionnaire-based methods. However, these approaches often lack precision. As a result, recent research has increasingly focused on leveraging machine learning techniques for depression diagnosis. This study proposes a novel machine learning-based approach for detecting depression. The method was evaluated using electroencephalogram (EEG) data involving 59 depressed individuals and 49 healthy controls. The resting-state EEG signals were recorded in the eye-closed (EC) condition and sampled at 250 Hz. The EEG signals were recorded using a 19-channel cap, with the electrodes precisely arranged according to the internationally standardized 10-20 placement system. (Jasper, 1958). Initially, the data were preprocessed using a customized version of the Harvard Automated Processing Pipeline (HAPPE) (Gabard-Durnam et al., 2018) , adapted for EEGLAB functions (Delorme and Makeig, 2004) running on MATLAB 2020b. Artifacts caused by power-line noise, eye blinks, and muscle activity were removed during preprocessing. Subsequently, a combination of statistical, spectral, wavelet, and nonlinear features was extracted across three domains—time, frequency, and time-frequency—constructing the feature matrix. Each feature was scaled to a standardized range using the min-max normalization technique. Finally, the classification process was conducted utilizing Support Vector Machine (SVM), k-Nearest Neighbors (KNN), and Random Forest (RF) algorithms. The best accuracies achieved were (SVM = 96.45%, KNN = 91.67%, RF = 99.23%) in the time domain, (SVM = 92.16%, KNN = 93.62%, RF = 94%) in the frequency domain, and (SVM = 98.73%, KNN = 98.32%, RF = 99%) in the time-frequency domain. Additionally, the Sequential Forward Floating Selection (SFFS) method was employed for optimal feature selection, and the Sequential Backward Selection (SBS) method was applied for channel selection, resulting in accuracy improvements of 2.37% in the time domain and 6.18% in the frequency domain. These findings indicate that the proposed method is a promising approach for detecting depression using EEG signals. It has the potential to serve as a reliable supplementary tool for supporting the clinical diagnosis of depression.

Keywords: depression, major depressive disorder (MDD), machine learning, electroencephalogram (EEG), computer-aided diagnosis (CAD)

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ICB13 -1158

Epitope-Based Design of a Dual-Purpose Recombinant Protein Targeting Dengue NS1 for Vaccine and Diagnostic Development

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Dengue fever is a mosquito-borne viral disease caused by four dengue virus serotypes of the Flaviviridae family. It is a major global health concern, with a wide spectrum of symptoms, ranging from mild febrile illness to severe forms like dengue hemorrhagic fever and dengue shock syndrome (Kularatne and Dalugama, 2022). Among the components of the dengue virus, the nonstructural protein 1 (NS1), secreted during infection, plays a pivotal role in immune evasion and pathogenesis. NS1 is a highly immunogenic protein, making it an ideal target for both diagnostic and vaccine development (Munasinghe et al., 2022). This study aims to design a dual-purpose recombinant protein, serving as both an ELISA kit component and a vaccine candidate, by identifying NS1-derived epitopes through in silico analysis. Since there is an overlap in the design principles of vaccines and diagnostic kits, this study emphasizes the selection of epitopes that are conserved (across DENV serotypes), immunogenic, non-pathogenic, non-toxic, safe, non-allergenic, and of wide applicability in the Iranian population. The NS1 protein was first screened using BLASTp to confirm no cross-reactivity with human proteins (Altschul et al., 1997). No similar eukaryotic proteins found. Membrane topology of NS1 protein regions predicted using DeepTMHMM to identify secretable regions (Hallgren et al., 2022). Immunogenicity was assessed with VaxiJen 3.0 (Doneva and Dimitrov, 2024). conserved regions were identified using EMBL-EBI ClustalW (Madeira et al., 2024). T-cell epitopes for MHC I and MHC II were predicted using IEDB tools (Reynisson et al., 2020, Nilsson et al., 2023). For MHC I epitopes, criteria included percentile rank (<0.5) and repeat frequency (>4), yielding 40 epitopes with 97.6% population coverage in Iran. For MHC II, epitopes with similar criteria achieved 97% population coverage (Bui et al., 2006, Abedini et al., 2021). Linear and non-linear B-cell epitopes were predicted using BepiPred3, DiscoTope-3.0 and ElliPro (Clifford et al., 2022, Høie et al., 2024, Ponomarenko et al., 2008) and filtered by length ≥ 10 amino acids and immunogenicity scores. Further, the MHC II epitopes were analyzed for their induction capabilities of IFN-gamma, IL4, and IL10 by using IFNepitope, IL4 Pred, and IL10 Pred (Dhanda et al., 2013b, Dhanda et al., 2013a, Nagpal et al., 2017). Epitopes inducing all three cytokines were selected, totaling four. We also searched literature to find experimentally and clinically validated epitopes. Toxicity, allergenicity and antigenicity validations for 23 experimental and 19 predicted epitopes using ToxinPred3.0, AllerTop2.1 and VaxiJen3.0 online web servers ensured the safety of selected epitopes (Dimitrov et al., 2014, Rathore et al., 2024). Conservancy of epitopes across four DENV serotypes measured by IEDB tools (Bui et al., 2007). The final recombinant protein included five computationally predicted and seven experimentally and computationally validated epitopes, linked with standard linker peptides and HisTag for recombinant protein expression and purification. This work presents a tight epitope selection

process for ensuring immunogenicity and safety, supporting broad Iranian population coverage for both vaccine and diagnostic kits. The integrated approach addresses global health challenges presented by dengue and thus opens up further structural and experimental validation.

Keywords: dengue virus, NS1 protein,precision medicine, vaccine design, immunoinformatics, recombinant protein

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Integrated bioinformatic analysis for the screening of hub genes & therapeutic drugs in high-grade serous ovarian cancer

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High-grade serous ovarian cancer (HGSOC) accounts for nearly 60% of total cases of epithelial ovarian cancer, the highest frequent malignant gynecologic tumor. It is the most aggressive subtype which shows poor prognosis and low patient survival (Topno and Singh, 2021). This study aims to identify hub genes and therapeutic drugs involved in HGSOC. The gene expression profile (GSE235525) was obtained from the Gene Expression Omnibus (GEO), which included miRNA expression data from 70 serum samples, comprising 36 HGSOC cases and 34 normal ovarian samples. Differentially expressed (DE) miRNAs between ovarian cancer tissues and normal tissues were identified using GEO2R analysis, with a P-value < 0.05 and -1 < |log fold change (FC)| < 1. A total of 76 hsa-miRNAs were identified and subsequently analyzed in the DIANA-miRPath database to validate miRNA interactions. Four hsa-miRNAs were highlighted for their extensive interactions: hsa-miR-125b-5p, hsa-miR-145-5p, hsa-miR-21-5p, and hsa-miR-155-5p. The MultiMiR package in R software was employed to determine gene targets, while the Interactive Venn Diagram was utilized to assess gene sharing among these miRNAs (Interactive Venn, 2024). Functional enrichment analysis of these genes was conducted through gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichments using the Enrichr online tool (Ma'ayan Laboratory, 2024). Then, the hub genes were identified by the cytoHubba plugin and the other bioinformatics approaches including protein-protein interaction (PPI) network analysis via STRING and survival analysis (STRING Database, 2024; Kaplan-Meier Plotter, 2024). Finally, the GEPIA (Gene Expression Profiling Analysis) and DGIdb (Drug-Gene Interaction database) databases were utilized to verify the expression levels of hub genes and to select the candidate drugs for HGSOC, respectively (Gene Expression Profiling Interactive Analysis, 2024; The Drug–Gene Interaction Database, 2024). A total of 49 differentially expressed genes (DEGs) were identified. The GO analysis indicated that the molecular functions of these DEGs predominantly pertained to the negative regulation of cell population proliferation. As for the KEGG pathways, the DEGs were primarily linked to human cytomegalovirus infection, pancreatic cancer, and the role of proteoglycans in cancer. Furthermore, ten hub genes (CTNNB1, STAT3, CDKN1A, EGFR, CD44, CDK6, THBS1, SP1, NF2, and MUC1) were identified, and survival analysis revealed that high expression levels of CDK6, EGFR, STAT3, and THBS1 in patients with HGSOC were statistically associated with poorer survival outcomes. Lastly, DGIdb database was used to identify 126 small molecules as the potentially targeted drugs for HGSOC treatment. In summary, the Hub genes and candidate drugs may improve individualized diagnosis and therapy for HGSOC in future.

Keywords: HGSOC, differential expression miRNAs, survival analysis, functional enrichment analysis, protein-protein interaction

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Drug repurposing using bulk RNA-seq based on key genes involved in inflammatory bowel disease

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Inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis, is a chronic inflammatory disorder of the digestive tract characterized by alternating periods of inflammation and remission. The exact cause of IBD is unknown, but it is generally believed that factors such as bacterial infection, changes in the immune system, and genetic changes can lead to the development of the disease (Collij et al,2016). IBD is usually accompanied by symptoms such as persistent diarrhea, abdominal pain, rectal bleeding or bloody stools, weight loss, and fatigue. Approximately 1.6 million people in the United States are affected by this disease, with a higher prevalence in developed European countries, reaching 2 million. Interestingly, the incidence of IBD is increasing in developing countries such as South America, Asia, Africa, and Eastern Europe (Wehkamp et al, 2016). In other words, epidemiological trends of IBD in developing countries due to industrialization suggest that environmental factors may play an important role in the development of IBD, especially in genetically susceptible individuals (Ramos and Papadakis, 2019). Using the scRNA-seq technique, the expression signature of the disease is identified, and therefore this expression pattern can be used for drug retargeting (Garrido-Trigo et al, 2023). This study used a computational drug repurposing pipeline to discover candidate drugs based on IBD differential gene expression signatures derived from RNA sequencing data. The transcriptional sample of whole mucosa was compared with accession code GSE245764 from the GEO database (https://www.ncbi.nlm.nih.gov/geo/). 12 whole mucosa samples of people with IBD and 10 whole mucosa samples of healthy people were analyzed. Differentially expressed genes (DEGs) between whole mucosa samples of IBD subjects and whole mucosa samples of healthy subjects were obtained using GEO2R. Then, the integrated library of network-based signatures (LINCS) was used to identify potential drugs that can reverse the expression of DEGs. Then, by reviewing the significant literature and drug bank studies (https://go.drugbank.com), the top-ranked drugs with the highest p-value were selected. The study identified 250 genes commonly affected by the disease. Among them, genes with $|\log2FC| > 1$ and a P-value of < 0.05 were identified as DEGs. And a network of the main genes involved in the disease was drawn through string(https://cytoscape.org/), and then the selected small molecule was also selected based on its effect on the genes involved in the disease. The results of the data analysis in this study showed that the PIK-75 small molecule can have a positive effect in the treatment of IBD. PIK-75 is a small molecule is a preferential p110 alpha/gamma PI3K inhibitor. And it targets the PIK3CA gene, and by targeting it, it could help improve the symptoms of IBD.

Keywords: drug repurposing, bulk RNA-seq, inflammatory bowel disease

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The key role of genes involved in proline biosynthesis and photosynthesis in drought response during Soybean flowering stage

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Soybean (Glycine Max) is one of the five most important crops in the worldwide that requires significantly more water than cereals (Niwinska et al. 2020). The phonological stage of plant exposed to drought stress is important for choosing the best strategy for agronomic management. The experiments indicate that the flowering stage is the most sensitive stage of the plant's life to drought stress (Farah et al, 1988; Moloi and Merwe, 2021). Therefore, the aim of this study was to identify the functional pathways and effective and key genes in Soybean plants under drought stress during flowering stage. Microarray data of Soybean under drought stress conditions during flowering stage were analyzed. Then, the functional pathways and hub genes identified by in silico tools. The result showed that in total 1368 genes had significant expression, of which 758 genes were upregulated and 610 genes were downregulated. The identified key genes were I1K1F9 (Laspartate oxidase), I1JLN5 (Delta-1-pyrroline-5-carboxylate synthase), Q8W1A1 (Adenosine 5′-phosphosulfate reductase), I1KP26 (Mg-por_mtran_C domain-containing protein) and Q9SYR0 (Nitrate reductase). The results demonstrated that the drought stress during the flowering stage of Soybean plants increased the expression of genes involved in biological processes responsive to abscisic acid and stress response such as genes involved in proline biosynthesis. Drought stress also reduced the expression of genes involved in photosynthesis and flower development, resulting in reduced yield. The identified genes in this study could be considered in Soybean breeding programs.

Keywords: cytoscape, gene ontology, I1JLN5, microarray

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Predicting drug response using omics data and artificial intelligence approach in cancer

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Cancer treatments often yield varied responses among patients, highlighting the urgent need for personalized therapeutic approaches. Leveraging recent advances in artificial intelligence (AI) and systems biology, this study introduces a novel AI-driven framework designed to predict how different cancer cell lines respond to specific drugs. Using a robust dataset comprising approximately 5,627,072 data points—including cell line, genomic, transcriptomic, proteomic, and mutation variations sourced from COSMIC, GDSC, and Ensembl databases—we focused on the comprehensive analysis of 3,008 crucial genes across 933 unique cancer cell lines. Our approach employs a fuzzy vector-based method to construct a gene embedding of dimensions (1, 3008) for each cell line, where each element represents a fuzzy value calculated based on the extensive dataset. This fuzzy value indicates the relative importance of gene mutations, providing a more nuanced representation of mutation impacts on drug sensitivity than traditional binary embeddings. To model drug data, we utilized Morgan fingerprints, enabling detailed molecular characterization. By integrating multi-omics (genomic, transcriptomic, and proteomic) data, we accurately modeled each gene's contribution, reflecting the complexity of molecular interactions and their biological significance. These refined representations were fed into artificial neural networks (ANNs) to predict therapeutic responses to targeted treatments. The results demonstrate that this gene importance-based method, combined with deep learning techniques, achieves a Pearson correlation of 81.12%, which is slightly better than recent work in the field. This work marks a significant step forward in precision oncology, offering a robust, data-driven strategy that not only achieves high predictive accuracy but also elucidates the underlying biological factors influencing drug effectiveness. Ultimately, our framework advances the promise of personalized medicine, tailoring cancer treatments to each patient's unique molecular profile, thereby improving therapeutic efficacy and minimizing adverse effects.

Keywords: precision oncology, personalized medicine, neural networks, drug response prediction

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Development of Novel Cellulose Crystal-Hyaluronic Acid Anti-Cancer Carriers for Targeting

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Breast cancer is responsible for a higher death rate than any other kind of cancer. A significant marker of tumor-initiating cells is the cell surface glycoprotein CD44 receptor, which is noticeably overexpressed in breast cancer. Because of its critical involvement in cancer development, this receptor is an attractive target for drug delivery (Xu, Wu et al. 2016). The first step in creating a targeted medication delivery system that targets the CD44 receptor is choosing an identifier for this protein. Hyaluronic Acid (HA), a well-known ligand for this receptor, is the best option in this instance. Following that, a nano-carrier should be chosen to transport breast cancer medications; in this case, Cellulose NanoCrystals (CNCs) were used. CNCs are rod-shaped nanoparticles derived from cellulose. Their unique physicochemical features make them a suitable platform for drug delivery and therapeutic uses. Furthermore, the vast surface area improves their capacity to load medications and gives them better control over the release of therapeutic drugs (Seo, Lee et al. 2020) (Cirillo 2023). It is crucial to understand how this system interacts with other overexpressed membrane proteins. In particular, the current investigation looked at how HA-CNC interacts with CD44, its main target, as well as other membrane proteins, including CD133 and CD47, which are also overexpressed in breast cancer (Chen, Wang et al. 2022) (Brugnoli, Grassilli et al. 2019). The structures of CNC, HA, CD44, CD47, and CD133 were obtained from Polysac3DB (Nishiyama, Langan et al. 2002), PubChem (CID: 155618327) (Kim, Chen et al. 2023), the Protein Data Bank (PDB IDs: 4PZ4 and 2VSC) (Liu and Finzel 2014) (Hatherley, Graham et al. 2008), and UniProt (ID: O43490) (Varadi, Bertoni et al. 2024), respectively. Docking simulations were conducted using AutoDock 4.2 to investigate the interactions between membrane proteins and HA, and additionally between HA and CNC (Morris, Huey et al. 2009). Following docking, PyMOL 3.0 was employed to superimpose the HA-CNC complex with each membrane protein (Schrodinger 2015). Among the selected proteins, CD44 showed the highest binding affinity with HA (-5.6 kcal/mol), followed by CD47 (-4.2 kcal/mol) and CD133 (-2.9 kcal/mol). According to the docking studies, CD133 and HA have a binding energy of -2.9 kcal/mol, which is lower than that of CD44 but still suggests a significant interaction that may be useful for drug delivery applications. Stronger interactions with CD44 (-5.6 kcal/mol) and CD47 (-4.2 kcal/mol) are further evidence that HA-CNC complexes have the potential to be a multipurpose platform for combination or multi-target anti-cancer approaches. This potential is expected to attract the interest of researchers working on specific therapies for illnesses like breast cancer.

Keywords: drug delivery, breast cancer, hyaluronic acid, cellulose nano crystals

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Potential of Lavender extract to inhibit efflux pump AdeB in multidrug resistant of Acinetobacter baumannii

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Acinetobacter baumannii is one of the six most dangerous multidrug-resistant pathogens in hospitals across the globe which estimated 10% of hospital-acquired infections are thought to be caused by this bacterium. Currently, up to 43% of clinical isolates of A. baumannii have become resistant to at least three different antibiotic classes (CastanheiraMendes and Gales, 2023)Efflux pumps, particularly those belonging to the resistance-nodulation-division (RND) superfamily, significantly contribute to MDR in Gram-negative bacteria. The AdeABC efflux pump is a key player in A. baumannii antibiotic resistance, comprising AdeB (an RND transporter), AdeA (a periplasmic membrane fusion protein), and AdeC (an outer membrane factor protein)(Leus and Roberts, 2024, Goyal and Citu., 2018). Given the reported antimicrobial activity of lavender's chemical constituents(Denkova and Goranvo, 2023). This study investigated the potential of lavender compounds to inhibit the AdeABC pump in A. baumannii. Lavender's chemical composition was identified through a literature review. Compound structures were obtained from PubChem (https://pubchem.ncbi.nlm.nih.gov/). The AdeABC pump structure was retrieved from the Protein Data Bank (PDB ID: 7KGF). Molecular docking was performed using Autodock Vina (https://vina.scripps.edu/). Compounds exhibiting the highest binding affinity to the AdeABC binding site were selected for further analysis using Ligplot package. The Pain Remover web server was applied to exclude compounds with poor properties that could'nt be used as drug candidates(https://www.cbligand.org/PAINS/). Lipinski's rule of five and safety assessment were applied using DataWarrior software to evaluate the physicochemical properties of the top-scoring compounds (https://openmolecules.org/datawarrior/). Docking analysis revealed three distinct potential binding sites on the AdeABC pump. Carvone, caryophyllene, cumin aldehyde, γ-terpinene, and terpinene-4-ol demonstrated strong binding affinities (approximately -6 kcal/mol) to all three sites. LigPlot analysis confirmed effective interactions with key residues within the binding sites of AdeABC pump. PainRemover indicated that all five compounds possessed favorable drug-like properties. According to Lipinski's rule of five, two compounds met the criteria. Finally, a safety assessment indicated that one of these two compounds showed low potential for mutagenesis, tumorigenicity, irritation, and reproductive toxicity.This aligns with Leus et al. (2024), who demonstrated that compounds interacting with key AdeABC residues can effectively inhibit efflux pump activity in Acinetobacter baumannii. Our findings suggest that among Lavender compounds, terpinene-4-ol possesses significant potential as an antimicrobial agent against MDR A. baumannii through AdeABC pump inhibition. Further investigation is

warranted to validate these in silico findings through experimental studies.

Keywords: AdeABC pump, acinetobacter baumannii, lavender, molecular docking

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Dissecting the genetic causes of inflammatory bowel disease based on whole exome sequencing

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IBD refers to the chronic inflammatory diseases of the gastrointestinal tract and mainly encompasses Crohn's disease (CD) and ulcerative colitis (UC). While genetic susceptibility is a major factor in the pathogenesis of IBD, the identification of causal gene variants remains challenging because the disease is heterogeneous. Whole-exome sequencing is an effective approach for identifying rare and novel variants in coding regions ,providing critical insights into the genetic architecture of complex diseases like IBD. This study aimed to identify new genetic variants associated with IBD using WES in one family with familial IBD. We analyzed five individuals, three were affected and two persons were healthy, using high-throughput WES technology, Data processing involved quality control and trimming , alignment to the reference genome (GRCh37) using hisat2 , and for variant calling using GATK toolkit. We identified a novel frameshift variant in FCGBP Gene (NM_003890.2:chr19-40399459 TG>T, p.His2079Ilefs*20) . gene implicated May be involved in the maintenance of the mucosal structure as a gel-like component of the mucosa. This variant exhibited in one patient in a family of under study that showed strong connection with IBD and was absent in healthy controls. These findings demonstrate the use of WES in identifying the genetic causes of IBD and emphasize the role of GeneFCGBP in the development of IBD. This discovery opens up new possibilities for the identification of the mechanisms of disease, the development of new therapies and the advancement of precision medicine in the treatment of IBD patients.

Keywords:inflammatory bowel disease (IBD), whole-exome sequencing (WES), gene variant, novel mutation

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Iron, Oxidative Stress, and Skin Aging: The Therapeutic Potential of TGF-β1 Modulation

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Aging is a biological process causing a gradual, irreversible decline in physical function across all organ systems. It is believed that the aging process begins at different times in different systems, and the skin is one of the first organs to age [Shinde and Deore, 2022], which is not only a cosmetic issue, as it can lead to various dermatological disorders that significantly affect the quality of life of older individuals. These disorders range from pruritus to more serious conditions like melanomas [Kühnel and Pasztorek, 2024]. Iron accumulates in various organs, including the skin, with age, and excess iron can induce oxidative stress through the generation of ROS by the Fenton reaction, which also Iron chelators treatment suppresses the UV radiation-induced upregulation of MMPs and delays skin photodamage. [Liu and Chen, 2022], investigated the effect of blood donation on skin aging by analyzing histological and clinical changes in old mice and found that blood donation reduces the signs of skin aging by increasing collagen synthesis and decreasing collagen degradation. The improvement in skin aging due to blood donation is associated with a reduction in iron deposits and an increase in TGF-β1 in the elderly skin. This study aimed to investigate the role of TGFB1 in humans and to compare it with that in a mouse model to predict the role of blood donation and its effects on skin rejuvenation. We performed a protein BLAST search using NCBI to retrieve the protein sequences of TGFB1 in both Mus musculus and Homo sapiens. Next, we identified the TGF-β signaling pathway using KEGG, focusing on key components, such as TGFBR1, TGFBR2, SMAD proteins, and collagen-related genes (COL1A1 and COL3A1). Protein-protein interaction networks were analyzed using STRING to explore the functional similarities between the species. For structural analysis, the 3D structure of TGFB1 was modeled and aligned for both species using PyMOL. Functional sites of the proteins were extracted using UniProt and compared using PyMOL. Based on the comprehensive bioinformatics analyses conducted in this study, a high degree of similarity between mouse and human systems was confirmed at both the sequence and structural levels. Alignment of the key proteins involved in the TGF-β and PI3K/Akt signaling pathways revealed significant conservation in their sequences, functional domains, and three-dimensional structures. Pathway enrichment analysis indicated that the core components and interactions within these signaling cascades were highly conserved between the two species, suggesting a functional similarity. Additionally, gene expression data supported parallel patterns of expression for genes associated with collagen synthesis (COL1A1 and COL3A1) and tissue remodeling. Our results align with

the findings of a study by [Kühnel and Pasztorek, 2024], which demonstrated that Platelet-Rich Plasma derived from human blood promotes skin rejuvenation by upregulating COL1 and COL3 expression through activation of TGF-β signaling. These findings, combined with the structural and pathway-level similarities observed in this study, support the potential translational application of mouse models in human clinical studies focused on skin rejuvenation and anti-aging therapies.

Keywords: skin rejuvenation, iron deposition, TGF-β1 signaling pathway, intrinsic aging, extrinsic aging

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ICB13 -1167

Dissecting the impact of smoking on epigenetic mechanisms that influence Lung cancer susceptibility

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Epigenetic mechanisms play a crucial role in mediating the effects of environmental factors on cell fate and disease. One such environmental factor is smoking which is a major risk factor in lung cancer. To assess how smoking affect lung cancer susceptibility, we used a publicly available dataset (GSE241468), which examines the epigenetic landscapes and gene regulation in human lung cells by using multiome (transcriptome and chromatin accessibility) maps from 117,911 lung cells derived from 4 males and 4 females in each group of smokers and never-smokers (Long et al. 2024). Here, we reanalyzed this dataset, to identify differentially accessible regions (DARs) and differentially expressed genes (DEGs) between smokers and never-smokers. Seurat and Signac were used for preprocessing of the dataset. We then used a correlation-based approach for identifying candidate CREs in DARs and showed enrichment of binding motifs of transcription factors that are activated in these regions in response to smoking. By characterizing cell-type-specific CREs, our analysis showed that smoking-responsive genes predominantly exhibit cell-type-specific differential expression which contribute to lung cancer susceptibility. Results suggests that DARs contribute to augmented transcriptional responses under smoking conditions and affect lung cancer susceptibility. By linking these epigenetic alterations directly to smoking and identifying key target genes and cell types, our findings provide a map of the epigenetic landscape shaping lung cancer risk and open avenues for targeted interventions in these epigenetically altered pathways.

Keywords: gene regulation, lung cancer susceptibility, differentially accessible regions

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ICB13 -1168

The Regulatory Role of DNA Methylation in Age-Related Macular Degeneration (AMD)

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Age-related macular degeneration (AMD) is a leading cause of vision loss in the elderly, and understanding its molecular underpinnings is crucial for developing targeted therapies. Recent studies have focused on investigating how epigenetic changes such as DNA methylation affect this disease. Advani and colleagues have used a methylation array to measure DNA methylation in 160 postmortem AMD and normal retina samples (Advani et al. 2024). Of these samples, 90 are included in a study by Ratnapriya and colleageus where RNA-seq was used to measure gene expression data in 523 AMD and normal postmortem samples (Ratnapriya et al. 2019). The methylation and RNA-seq datasets were retrieved from the GEO database (GSE231536 and GSE115828 respectively). Differentially expressed genes (DEGs) and Differentially methylated probes (DMPs) were identified using DESeq2 and ChAMP packages. Next, we used the MethReg package to identify distal DMPs that can affect the expression of DEGs. MethReg was designed to identify combinatorial effects of DNA methylation and transcription factor binding on gene expression (Silva et al. 2022). Using this package, we can identify transcription factors where changes in the DNA methylation of their binding site affects the expression of their target genes. The resulting regulatory network will improve our understanding of the underlying regulatory mechanisms in age-related macular degeneration.

Keywords: age-related macular degeneration (AMD), epigenetics, DNA methylation, gene expression, MethReg

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Discovering Moonlighting Proteins with AI and Explainabilit

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Moonlighting proteins perform multiple, distinct biological functions beyond their primary role, posing challenges in traditional protein function annotation. In this study, we present an artificial intelligence-based framework to identify moonlighting proteins, employing advanced machine learning models integrated with Local Interpretable Model-agnostic Explanations. Local Interpretable Model-agnostic Explanations provides interpretability by highlighting the features driving the model's predictions, bridging the gap between performance and explainability.Our results demonstrate 92% accuracy in distinguishing moonlighting proteins from non-moonlighting proteins and 97.6% area under the curve, validated against benchmark datasets. Furthermore, Local Interpretable Model-agnostic Explanations (LIME) explanations reveal biologically plausible insights, such as domain-level correlations and structural motifs associated with multifunctionality. This interpretability not only enhances trust in artificial intelligence predictions but also offers novel hypotheses for experimental validation. This work signifies a step toward transparent and reliable artificial intelligence applications in computational biology.

Keywords: moonlighting proteins, artificial intelligence, machine learning, orotein function annotation, computational biology

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ICB13 -1170

Enhancing Predictive Accuracy of CRISPR- Cas9 on-target efficiency using Deep Learning and Active Learning Optimization for Small Datasets

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The CRISPR-Cas9 gene editing system has revolutionized genetics, but predicting sgRNA cleavage efficiency remains a challenge, particularly with small datasets. We present a deep learning framework optimized for small datasets by integrating active learning, which iteratively prioritizes the most informative data points for labeling. Our model outperforms previous methods on benchmark datasets, capturing complex sequence features through domain-specific properties. Active learning reduces the required dataset size enabling high predictive accuracy even with limited data. This approach provides a scalable and robust solution for improving CRISPR-Cas9 design and precise gene editing across diverse genomic contexts, demonstrating the potential of active learning to enhance deep learning model performance in data-scarce scenarios.

Keywords: CRISPR-Cas9, gene editing, deep learning, active learning

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Accelerating Diffusion-Based Graph Generative Models for De Novo Drug Design via Hessian Trace Approximation

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Diffusion-based models have recently gained prominence in various domains, including graph-structured data and de novo drug design, where they enable the generation of novel molecular structures and optimization of pharmaceutical candidates. In particular, methods such as “Digress” (Vignac et al. 2023) effectively incorporate diffusion processes to model complex interactions within graph data, while Graph Diffusion Policy Optimization (GDPO) (Liu et al. 2024) extends this idea by integrating policy optimization strategies to achieve higher-quality solutions. Compared to Digress, GDPO typically demonstrates higher convergence rate and more robust performance which makes it potentially better solution for advancing graph-based drug design problem and related applications. However, both Digress and GDPO rely heavily on gradient-based optimization, which is not as fast as necessary. On the other hand, computing the Hessian matrix directly to make use of second order methods and follow the curvature characteristics is computationally expensive. To address these issues, we introduce a novel idea to approximate the Hessian matrix with relatively low cost to better guide the optimization process, providing a more accurate and efficient estimation of curvature that leads to improved directions and lower number of iterations. We trained our model on the ZINC-250k dataset, a widely used collection of small molecules, and compared its performance with Digress and GDPO. Our approach demonstrates enhanced efficiency and superior performance over the existing diffusion-based generative models in de novo drug discovery.

Keywords: diffusion-based models, drug discovery, policy optimization, hessian approximation, generative models.

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Evaluation of Penetration Efficiency of BR2 Peptide in Breast Cancer cell Lines Using computational Methods

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Cancer remains one of the most significant health challenges of the 21st century, impacting millions of individuals globally each year. BR2 is a penetration peptide derived from the antimicrobial peptide Buforin II. Experimental evidence indicates that BR2 exhibits approximately four times greater transfer efficiency to cancer cell lines compared to non-malignant cell lines. While the selective permeability of cell-penetrating peptides (CPPs) has been established, the precise mechanisms of internalization remain unclear. Notably, the lipid composition of cancer cell membranes differs significantly from that of non-malignant cells, with further variations observed among different types of malignant cells. Plasma membrane asymmetry is an important feature of normal cells, where phosphatidylserine is located almost exclusively in the inner leaflet of the cell membrane. In many malignant cells, this asymmetry of the plasma membrane is lost, and as a result phosphatidylserine is located in the outer leaflet of the membrane. In this study, we aim to investigate the effects of BR2 on three distinct cell lines derived from both malignant and non-malignant breast tissues, while also exploring the mechanisms underlying its permeation. To achieve this, we employed molecular dynamics simulations using GROMACS, CHARMM GUI, and Grace software. The three-dimensional structure of BR2 was modeled using the I-TASSER server. In this study, we utilized analysis of hydrogen binding, average peptide and membrane distance, density, radius of gyration, RMSF, RMSD, mean square deviation and order parameter. By comparing the graphs obtained from the analysis conducted, including hydrogen binding and distance measurements in selected membranes, significant results were achieved regarding the mechanism of peptide penetration. Our results demonstrate that the interaction and penetration of BR2 in cancer cell lines are significantly more pronounced than in normal cell lines. Furthermore, our analysis suggests that the mechanism of penetration is closely related to the abundance of phosphatidylserine (PS) in the lipidome of cellular membranes. This research contributes to a deeper understanding of the selective permeability of BR2 in varying cellular environments, which may have important implications for the development of targeted therapeutic strategies.

Keywords: BCell penetration peptides(CPP), Lipodome, molecular dynamics simulation ,breast cancer, Bufforin

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ICB13 -1176

Diabetes nephropathy indicators for early diagnosis

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Introduction: Diabetes Mellitus (DM) is marked by excessive blood glucose levels. Diabetes nephropathy is usually first manifested as an increase in urinary albumin excretion. Diabetic nephropathy (DN) is the most common diabetes complication, and renal failure is one important the morbidity and mortality of affected patients (Tooke, 1995). Clinically significant morbidity may often develop before diagnosis, and early diagnosis provides the opportunity for more precise medical care and disease management. Unraveling the mainstay events could support the early diagnosis. Method: To achieve this, we followed the approach of RNAseq data analysis using the Geo dataset, GSE154881. We compared the healthy control, diabetes, and nephropathy groups. Differentially expressed genes were determined, and a Venn diagram of the DEGs was made between the two groups. Gene set enrichment analysis was performed using EnrichR to reveal the related pathways. Results: As it is inferred from the Shared gene between nephropathy and diabetes, the immune system and its components, including the innate and adaptive immune system, JAK/STAT Signaling, interferon signaling, neutrophil degranulation, complement activation, and also metabolic dysregulations interplay both diabetes and nephropathy manifestations. Nephropathy-specific DEGs are involved in the pathway, such as erythrocytes taking up oxygen and releasing carbon dioxide, iron uptake and transport, heme biosynthesis, cell cycle checkpoint and gene expression events, and pentose phosphate pathway. Conclusion: The most important underlying event in diabetes is immune system mediation, which is highlighted in nephropathy, as well (Li et al., 2019; Lindenkamp et al., 2023). The more specific pathways for nephropathy are related to the erythrocytes' function and heme biosynthesis. It indicates the potential role of erythrocytes in the pathological development of diabetic complications (Wang et al., 2021) (Matteucci & Giampietro, 2007). So detecting corresponding indicators of erythrocytes and the molecular driver events can explain the occurrence and progression of nephropathy.

Keywords: Diabetes, nephropathy, complication, RNAseq data

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Predicting Adverse Drug Reactions with Advanced Machine Learning Techniques

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Drug design is a complex and resource-intensive process, partly due to the challenge of adverse drug reactions (ADRs)[(Yang and Kar 2023)], which impacts drug safety and only becomes evident after clinical trials on a drug has already began. In this study, we developed machine learning (ML) methodologies aimed at predicting ADRs by leveraging data from SIDER database [(Kuhn, Letunic et al. 2016)], which contain ADR information for approved drugs. ADR data was collected from 1,430 approved drugs. Molecular descriptors, such as polar surface area and molecular weight, were extracted from drug SMILES strings which were obtained from Chembl [(Nowotka, Gaulton et al. 2017)], and RdKit [(Bento, Hersey et al. 2020)] was used for molecular fingerprinting. We employed several machine learning algorithms, including Support Vector Machine (SVM), Random Forest (RF), and Gradient Boosted Trees (GBT), for ADR classification tasks. To ensure robust evaluation and optimization of these ML methods, we utilized metrics such as accuracy, precision, recall, and F1-score, after addressing class imbalance using synthetic minority over-sampling technique-nominal continuous (SMOTE-NC)[(Gök and Olgun 2021)]. Our results demonstrated that no single algorithm outperformed others in all cases; for example, the best balance between precision and recall for predicting common ADRs might be different from those algorithms for rare ADRs, or some algorithms perform better for some tissues and worse for the others. We suggest the use of ensemble learning to combine the strengths of different algorithms for improved ADR prediction in drug discovery. Future work should focus on optimizing ensemble models and extending the approach to other drug classes.

Keywords: adverse drug reactions, support vector machine, random forest, gradient boosted trees, ensemble leaning

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Elucidating Inflammatory Pathways in Polycystic Ovary Syndrome: A Transcriptomic Investigation of Granulosa Cell Gene Expression

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Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder affecting a significant proportion of women, leading to diverse symptoms such as irregular menstrual cycles, hyperandrogenism, and ovarian cyst formation. While the exact cause remains unclear, increasing evidence suggests a critical role of inflammation in the pathophysiology of PCOS (Singh and Pal, 2023). Granulosa cells (GCs), which are essential for follicular development and hormone production, are often dysregulated in PCOS, contributing to ovarian dysfunction (Dompe and Kulus, 2021). This study aims to investigate the inflammatory mechanisms underlying PCOS, with a focus on gene expression changes in granulosa cells, using a transcriptomic approach. To better understand the molecular underpinnings of this disorder, we performed transcriptomic profiling of GCs from PCOS patients compared to healthy controls using RNA sequencing(GSE138518). Differential gene expression analysis, conducted using DESeq2, revealed 68 genes with significantly increased expression and 119 genes with decreased expression in PCOS GCs. Functional enrichment analysis of these genes highlighted the involvement of inflammatory pathways, immune responses, and cell signaling. Notably, pathway enrichment analysis using Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) revealed that the upregulated genes were primarily linked to inflammation and immune system regulation, suggesting that inflammation may be central to the pathophysiology of PCOS. In a more detailed examination, network analysis identified several hub genes that are critical to inflammatory responses in PCOS. These include ITGB2, PTPRC, SPI1, FCGR3B, HCK, FCGR2A, ITGAX, CSF3R, S100A9, STAT1, and CSF2RB. These genes are involved in immune cell signaling, phagocytosis, leukocyte activation, and cytokine production. For example, ITGB2 and ITGAX are integral to immune cell adhesion and activation, while PTPRC (also known as CD45) regulates T-cell receptor signaling. SPI1 plays a key role in the differentiation of macrophages and dendritic cells, and HCK is involved in immune cell signaling and inflammation. Furthermore, S100A9 and CSF3R are crucial for neutrophil recruitment and activation, amplifying the inflammatory response. STAT1 and CSF2RB are critical transcription factors and cytokine receptors that regulate immune responses and hematopoiesis. The upregulation of these genes suggests a persistent inflammatory environment in the ovaries of PCOS patients, with implications for ovarian dysfunction and the systemic metabolic abnormalities often observed in PCOS. These findings support the hypothesis that chronic inflammation plays a central role in the disease process and highlights potential therapeutic targets. In conclusion, our study provides valuable insights into the inflammatory network in PCOS, identifying key hub genes that could serve as biomarkers or targets for therapeutic intervention.

Future research should focus on further elucidating the role of these genes in ovarian pathophysiology and exploring potential anti-inflammatory treatments to improve clinical outcomes for PCOS patients.

Keywords: polycystic ovary syndrome, RNA-seq, granulosa cells, inflammatory response, bioinformatics

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Investigating the role of ursolic acid in EGFR L858R mutant inhibition in non-small cell lung cancer: Molecular docking and ADMET prediction

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One of the leading causes of cancer deaths worldwide is lung cancer. Human epidermal growth factor (EGFR), a target protein for the treatment of non-small cell lung cancer (NSCLC), plays a critical role in signaling pathways such as cell proliferation and migration (Saini and Grewal, 2022). Mutations such as L858R, T790M, G719S, T790M/L858R or G719S/T790M can alter its structure and consequently the drug responses of lung cancer patients. Therefore, in silico studies are essential to understand how these mutations affect the ligand binding site (Gao and Chen, 2024; García-Godoy and López-Camacho, 2016). In this study, in silico molecular docking was performed using AutoDock Vina by PyRx software for ursolic acid as a triterpenoide and erlotinib as a reference against EGFR. The crystal structure of EGFR L858R mutant kinase domain (PDB ID; 2EB3) was retrieved from the RCSB PDB database and Ursolic acid and erlotinib were obtained Pubchem and converted into PDB format by Chem 3D software. Also, Physicochemical properties and pharmacokinetics parameters were assessed by Lipinski rule of five and ADMET-based analysis. The docking results obtained showed the strong binding affinity of ursolic acid with EGFR and the most important hydrogen interactions are Lys745 and Cys797 and van der Waals interactions with Ala722, Leu718, and Leu844 amino acids. The drug-likeness and pharmacokinetic properties of ursolic acid also displayed drug-like characteristics. Ursolic acid could be a potential source of natural products that have inhibitory effects on lung cancer by blocking the EGFR mutated protein. Further, the experimental investigation of the ursolic acid is a must before any prescription.

Keywords: EGFR L858R mutant, ursolic acid, molecular docking, ADMET

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Exploring the anti-inflammatory potential of the silymarin against IL-17A: in silico molecular docking

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Inflammation plays a major role in maintaining overall health and is caused by pathogens, damaged cells, and toxic compounds, lead to a variety of illnesses, including atherosclerosis, diabetes, rheumatoid arthritis, and several other fatal conditions (Jabbar and Irfan, 2024). IL-17 as an important pathogenic pathway in inflammation, therefore, promising therapeutic strategies focus on targeting IL-17A, which has led to the identification of effective inhibitors (Alvarez-Coiradas and Munteanu, 2020). The present study aimed to evaluate silymarin as a potential anti-inflammatory agent using in silico methods. Docking studies were performed with Auto Dock Vina in PyRX software and IL-17A protein with PDBID: 5HI4 and silymarin ligand were used for docking studies. The crystal structure of IL-17 (PDB ID: 5HI4) was obtained from the RCSB PDB database and silymarin retrieved by Pubchem and converted into PDB format by Chem 3D software. The Docking results showed that silymarin had a strong binding affinity within the same pocket as the co-crystallized ligand for inhibiting IL-17A. Silymarin interacted with Try67 and Gln94 amino acid residues in IL-17A by creating hydrogen bonds and hydrophobic interactions with Ile66, Val65, Leu97, Pro63, and Leu112 amino acids. Therefore, silymarin can interact with IL-17A to reduce inflammation, making it a potential therapeutic strategy to improve inflammation after more studies.

Keywords: inflammation, Silymarin, IL-17A, molecular docking

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Innovative Biomarkers for Lung Cancer Classification and Prediction Using High-Dimensional Machine Learning: A Novel Approach to Targeted Therapies

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Lung adenocarcinoma (LUAD) represents the most prevalent pathological subtype of lung cancer. Unfortunately, a significant proportion of LUAD cases are detected at advanced stages, where the prognosis remains unfavorable. Therefore, our objective was to discover innovative biomarkers to enhance the diagnosis and treatment of early-stage LUAD and to develop targeted therapeutic strategies. In this study, two microarray datasets, GSE75037 and GSE32863, were sourced from the Gene Expression Omnibus (GEO) database for analysis. Data preprocessing and meta-analysis were conducted using the R statistical programming language. Feature selection was carried out through analysis of variance (ANOVA). To predict cancer stages, ordinal regression, ordinal tree, and ordinal forest models were developed, and their predictive performance was evaluated. Differentially expressed genes (DEGs) were identified and subjected to gene set enrichment analysis to uncover significant biological pathways. The validation and diagnostic accuracy of the DEGs were further examined using UALCAN and ROC curve analysis. Additionally, the selected genes were validated using an independent, comprehensive LUAD RNA-Seq dataset from The Cancer Genome Atlas (TCGA). To identify cell types associated with these genes, scRNA-Seq data from the GEO database (dataset GSE131907) including lung cancer and normal samples were analyzed. Differential gene expression was examined using the FindMarkers function from the Seurat package. Finally, potential therapeutic agents were identified through the DGIdb database, followed by molecular docking and molecular dynamics simulations to evaluate their potential efficacy as treatments. Analysis revealed that the top 40 differentially expressed genes (DEGs) were primarily associated with pathways involving drug metabolism via cytochrome P450, xenobiotic metabolism by cytochrome P450, and retinol metabolism. Among these, genes ADH1A, ADH1B, and F10 stood out due to their significant interactions within these pathways. Notably, a negative

correlation was observed between the expression levels of these genes and patient survival rates. Additionally, their expression was significantly reduced in lung adenocarcinoma (LUAD) tissues compared to adjacent non-tumor tissues. The diagnostic potential of these genes was validated through ROC analysis, highlighting their ability to distinguish between cancerous and non-cancerous tissues. TCGA analysis showed that the selected genes were statistically significant across all stages, from I to IV .Based on the single-cell analysis, the ADH1B gene shows a significant differential expression in the Mesothelial cell type, an average log2 fold change of -6.1985, and an adjusted P-value of 0.0043. Moreover, drugs such as abacavir, rivaroxaban, and edoxaban tosylate demonstrated a strong binding affinity to these genes, suggesting their therapeutic relevance. These findings emphasize the value of leveraging bioinformatics and machine learning approaches to uncover new pathways for LUAD diagnosis and treatment, paving the way for more targeted and effective interventions.

Keywords: lung adenocarcinoma, machine learning, precision medicine drug repositioning.

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Molecular docking and bioinformatics study of active compounds of thyme) Thymus vulgaris(in inhibiting COX-2 enzyme related to inflammatory diseases

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Inflammation is a natural response of the body to injury or infection that, if chronic, can lead to diseases such as rheumatoid arthritis, cancer, and heart disease. The cyclooxygenase-2 enzyme plays a key role in the production of prostaglandins and inflammatory processes, and its inhibition is recognized as a therapeutic target. Molecular docking is a method often used in drug design because it can predict how small molecule ligands will bind to target binding sites. Molecular docking can be used to identify potential compounds that inhibit the COX-2 enzyme. thyme)Thymus vulgaris(has proven anti-inflammatory effects with its bioactive compounds such as thymol, carvacrol, and linalool. In this study, bioinformatics methods including molecular docking and molecular dynamics simulations were used to investigate the interaction of these compounds with COX-2. Initially, information related to thymol and carvacrol was extracted from the PubChem database (PubChem Database, 2024). The crystal structure of the COX-2 enzyme was obtained from the Protein Data Bank (Protein Data Bank, 2024). AutoDock Vina software was used for docking simulation (Trott and Olson, 2010). The compounds were placed in the active site of COX-2 and their binding energies were calculated. GROMACS software was used for dynamic simulation. The stability of the complexes was evaluated by indices such as the difference between the crystal structure of the ligand compound and the predicted binding (RMSD) and kinetic energy. The pharmacokinetic properties and toxicity of the compounds were predicted using the SwissADME tool. The docking results showed that carvacrol has a lower binding energy than thymol, indicating its stronger interaction with the COX-2 active site. The hydrogen bond binding energy of thymol with the active site of the COX-2 enzyme was negative 8.6 kcal/mol, while the binding energy of carvacrol was negative 1.7 kcal/mol, making this compound a better option than thymol for pharmaceutical use. The RMSD of the thymol-COX-2 and carvacrol-COX-2 complexes were about 1.2 and 1.8 Å, respectively, indicating the high stability of these interactions during the 50 ns simulation. Kinetic energy changes of the compounds also showed that the carvacrol complex is more stable. Drug absorption, distribution, metabolism and excretion (ADMET) analysis (Dhanaraj and Asok, 2017) showed that carvacrol has high permeability through the blood-brain barrier (BBB) and thymol has lower permeability, making carvacrol a potential candidate for the treatment of nervous system inflammation. This study showed that the carvacrol compound from Shiraz thyme plant interacts strongly with the COX-2 enzyme and can be investigated as a drug candidate for inhibiting this enzyme. Molecular

dynamics simulation and ADMET analysis showed low hepatotoxicity for both compounds, confirming the stability and safety of these compounds. It is suggested that further experimental tests be performed to confirm these results.

Keywords: thyme, molecular binding, bioinformatics, prostaglandin

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Novel lncRNA-miRNA-mRNA competing endogenous RNA regulatory networks in glioma

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Gliomas the most frequent type among primary brain tumors are highly heterogeneous. Understanding molecular mechanisms of glioma is crucial for developing effective therapies. Several altered signaling pathways and cross-linked relationships of ncRNAs and coding RNAs remain to be investigated. Identifying unknown interconnections between these genes may provide valuable clues for developing strategies for cancer therapy. The regulatory mechanisms of the ceRNA network in the pathogenesis of Gliomas remain to be investigated. In this study, we aimed to identify potential regulatory networks involved in glioma tumorigenesis, based on the ceRNA hypothesis. We obtained Four datasets (SRP434123, SRP233221, SRP328814, SRP114556) Which contain mRNA and lncRNA expression RNA-seq from 32 glioma tissues and 32 normal ones. Also, 2 and 12 samples contain miRNA-seq of glioma and 12 normal tissues, respectively. Following a series of analyses such as Survival and co-expression analysis, GO and KEGG enrichment analysis, using online tools including Targetscan, miRwalk, and mirDB the interactions between lncRNA, miRNA, and targeted mRNA were predicted and visualized using Cytoscape software. We constructed a regulatory network associated with glioma tumorigenesis we acquired five axes, "CRNDE/has-mir-223/STAB1", "CRNDE1/has-mir-150/TOP2", "NEAT1/has-mir-150/TOP2", "GRM3-AS1/has-mir-128/TOP2" and "GRM3-AS1/has-mir-128/STAB1" which were found to be related with the prognosis of glioma and present as potential ceRNA regulatory networks in glioma patients. Our results provided a potential regulatory network underlying glioma genesis and displayed that CRNDE can competitively bind to miR-223, and miR-150 also NEAT1 can competitively bind to miR-150 and miR-128. GRM3-AS1 acts as a ceRNA and binds to miR-128. Therefore, based on Functional Enrichment Analysis, modulating STAB1 and TOP2 expression levels in glioma, affects systemic lupus erythematosus (SLA), alcoholism, and Neutrophil extracellular trap pathways in glioma.

Keywords: ceRNA, glioma, lncRNA, miRNA, mRNA interactions, prognosis

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Vaccine design for outer membrane protein C(Shigella Flexneri)

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Shigella flexneri is a highly contagious Gram-negative bacterium that causes severe diarrhea, especially in children under ten years old. Various serotypes in S.flexneri are reported from different regions of the world. The precise approximations of illness and death owing to shigellosis are missing in low socioeconomic countries, although it is widespread in different regions. Outer membrane protein C (OmpC) is located in the outer membrane of Shigella flexneri 3a and other Gram-negative bacteria of the Enterobacteriaceae family. Recent research and clinical trials report multiple approaches used in Shigella-vaccine development. However, despite the efforts of researchers, pharmaceutical companies and health care organizations, there is no licensed vaccine against shigellosis available to the community. Biodata or bioinformatics is the knowledge of using computer science and statistics and probabilities in the branch of molecular biology. The aim of this research is to design Shigella Flexneri vaccine via in silico approach. The present study unveils OmpC 3D structure via in silico approaches. Apart from ab initio, other rational methods such as homology modeling and threading were invoked to achieve the purpose. For homology modeling, BLAST was run on the sequence in order to find the best template. The template was then served to model the 3D structure. In order to vaccine development, attempts should be made to discover peptides that could mimic protein epitopes and possess the same immunogenicity as the whole protein. Subsequently, theoretical methods for epitope prediction exploited to better understanding and characterizing topology, localization, signal peptide sequence, Physical and chemical parameters , single scale amino acid properties and linear and conformational epitopes. In this regard TMHMM, TMBBpred, CELLO, PSLpred, SignalP, Protparam, IEDB, LBtope, SVMtrip and Ellipro servers were applied respectively. In conclusion, amino acids 215-225 were selected as vaccine candidates. This region contains functional exposed amino acids with higher properties score of B cell epitopes. In these regions, the majority of amino acids are hydrophile, flexible, accessible, and favorable for B cells with a view to the point of secondary structure.

Keywords: Shigella Flexneri,epitope, immunogenicity, vaccine

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ICB13 -1190

Designing self-assembled peptide nanovaccine (SAPN) against Respiratory syncytial virus (RSV): An Immunoinformatic approach

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Respiratory Syncytial Virus (RSV) is a highly contagious virus primarily affecting the respiratory tract and posing significant health risks to infants, young children, older adults, and immunocompromised individuals. Nearly all children contract RSV by age two, with some requiring hospitalization for severe respiratory illness. The development of effective RSV vaccines is a major advancement, and as of mid-2023, two vaccines approved for older adults show moderate to high efficacy in preventing symptomatic RSV-related lower respiratory tract disease (LRTD). Clinical trials indicate that these vaccines can substantially reduce severe RSV infections over multiple seasons, potentially easing the burden of the virus among vulnerable groups (Britton, A, 2024). Self-assembled peptide nanoparticles (SAPNs) are promising tools in vaccine design due to their ability to form stable nanostructures that enhance immune responses. These peptides can self-organize into various forms like nanofibers and hydrogels, providing robust antigen presentation and improved stability. SAPNs can also incorporate adjuvants and target specific immune cells, boosting the vaccine's efficacy and safety. This innovative approach offers a versatile platform for developing next-generation vaccines (Abdullah, T and et al, 2020). First, genomic sequences from RSV subtypes A and B were analyzed, and membrane proteins were selected for further study. Gene sequences were examined using IEDB to identify MHCI, MHCII, and B-cell epitopes. The toxigenic, allergenic, and antigenic properties were assessed using Toxinpred, Allertop, and Vaxijen, respectively. Identical epitopes with optimal conditions from both subtypes were chosen for vaccine design, and the final epitopes were derived from the RSV F and G proteins. The vaccine sequence includes HisTag, MHCI epitopes, MHCII epitopes, pentamer and trimer oligomeric domains, B-cell epitopes, and a soluble tag. The vaccine amino acid sequence was assessed using Vaxijen, Toxinpred, Allertop, and Protparam. The secondary and tertiary structures were then defined using Psipred and AlphaFold2 Colab, respectively. Following structure energy minimization, homomer structures were predicted using the GalaxyHomomer server to model RSV-SAPN. Docking of the vaccine with TLRs (TLR1-4 and TLR9) was performed using the Cluspro server. The vaccine construct, containing MHCI, MHCII, B cell epitopes, trimer, and pentamer domains, was developed using proteins F and G from RSV subtypes A and B.The theoretical physicochemical properties are: pI = 9.09, number of amino acids = 392, GRAVY = -0.521, and stability = 45.58.The homo-oligomer of our protein was predicted using GalaxyHomomer. Based on docking results, the 3-mer structure of the protein had the best score (docking score = 769.093).The vaccine construct was docked with TLR receptors using Cluspro, and the lowest energy interactions with TLR1 (-1451.7), TLR2 (-1515.0), TLR3 (-1558.7), TLR4 (-1549.4), and TLR9 (-1971.5) were selected and analyzed using LigPlot-plus and PyMOL software. The antigenicity of the

vaccine was estimated 0.4524 by VaxiJen, exceeding the 0.4 threshold. Based on Allertop result, the vaccine is likely a non-allergen, and Toxinpred also indicated the protein is a non-toxin.

Keywords: respiratory syncytial virus, vaccine design, immunoinformatics, self-assembly peptide

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The inquiry of possible new candidates of inhibitors for Type IV pili of Neisseria gonorrhoeae using Molecular Docking analysis

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There are several complications in women associated with the Neisseria gonorrhoeae infection, such as infertility, cervicitis, ectopic pregnancy, and urethritis, which is a common sexually transmitted infection worldwide (Vaezzadeh et al., 2023). One of the main virulence factors of Neisseria gonorrhoeae is type IV pili, which is responsible for the adhesion, mobility, and pathogenesis of this bacterium (Jacobsen et al., 2020). The rising prevalence of multi-drug resistant Neisseria strains necessitates the exploration of alternative strategies, such as inhibiting this virulence factor and the bacterium's ability to adhere to host cells. This approach presents a promising avenue for the prevention of diseases associated with this pathogen. Therefore, in this study, we aimed to identify the most potent inhibitory ligand for the pili as a potential drug candidate through molecular docking analysis. The 3D structure of the type IV pilin of Neisseria gonorrhoeae was extracted from the RCSB PDB database (PDB ID: 2HI2). The inhibitory ligand of pilin, methyl (2S)-2-amino-3-phenylpropanoate (methyl L-phenylalaninate) with PubchemCID 736234, and a total of its 20 analogs was retrieved from the PubChem database in SDF format. After preparing the protein and its ligands by eliminating the ligand and water from the protein, lowering the energy level, and adding electric charges and hydrogen atoms, molecular docking was conducted using Virtual Docker Molegro v. 6. Subsequently, the best interaction with the lowest energy binding was analyzed using Molegro Molecular Viewer software. Finally, the pharmacokinetic properties of the ligand were investigated using the Admetlab server. Among all the inhibitory ligands of pilin, the best ligand was (2S)-N-(3-fluorophenyl)-2-(3-phenoxyphenyl)-1,3-thiazolidine-3-carboxamide with the molecular weight of 394.12 g/mol, and binding energy of -71.2257 kcal/mol. This ligand formed one Hydrogen bond with Arg152, along with 2 steric interactions involving Arg 152 and Gln 123 residues. The ADME results demonstrated a water solubility score (LogS) of -4.965, the hydrophilic score (LogP) of 4.029, the polarity score (TPSA) of 41.57, and in conclusion the hydrogen bond donors of 4 and hydrogen bond acceptor of 1. Based on the obtained results, (2S)-N-(3-fluorophenyl)-2-(3-phenoxyphenyl)-1,3-thiazolidine-3-carboxamide (PubChem CID: 1025301) demonstrated the best interaction with the lowest energy binding with type IV pilin, and good Druglikeness properties which it may serve as an inhibitor candidate for type IV pilin of Neisseria gonorrhoeae, although further in vivo and in vitro analysis are necessary.

Keywords: molecular docking, Neisseria gonorrhoeae, Type IV pilin, ADME.

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Identification of circRNA-miRNA-mRNA Interaction in Myocardial Infarction

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Myocardial infarction (MI) is a severe cardiovascular condition resulting from sudden blood flow blockage to a heart muscle, causing tissue damage and severe patient outcomes, prompting researchers to explore molecular mechanisms [1,2]. non-coding RNAs, such as miRNAs and circRNAs have recently gained attention due to their regulatory roles in gene expression [3]. Emerging evidence suggests that non-coding RNAs play crucial roles in cardiovascular diseases, including MI. Gene expression profiles (GSE24519 and GSE24548) were downloaded from the Gene Expression Omnibus. Differentially express genes and miRNA were identified using the GEO2R. Enrichr was used to obtain the pathway and biological process. miRTarbase and CircBank databases were used to receive miRNAs and circRNAs. The circRNA-miRNA-mRNA interaction was reconstructed with Cytoscape software. Functional enrichment analysis revealed that several pathways and biological processes associated synthesis of PIPs at early endosome membrane, PI metabolism, adherens junctions interactions, protein deglutamylation, receptor catabolic process and cellular response to potassium ion. The results of this study showed that ZNF701, HOXA10, TSR1, miR-485-5p, miR-142-3p, miR-142-5p, circ_0087424, circ_0087425, circ_0087427 and circ_0087428 have most important regulatory role. This study identifies a circRNA-miRNA-mRNA interaction, offering insights into MI pathophysiology and potential biomarkers for managing this serious cardiac condition.

Keywords: circRNA, miRNA, myocardial infarction, regulatory network

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Machine-learning based biomarker discovery for Striga resistance in sorghum

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Sorghum bicolor is the fifth most important cereal crop in the world, cultivated across the globe in almost 110 countries, predominantly in Asia and Africa but also in Europe, America, and Oceania. Despite its outstanding resilience to abiotic stresses, approximately 20% of sorghum yield is annually lost due to infestation with the parasitic weed *Striga hermonthica*. Identifying sources of Striga resistance gene within sorghum is imperative to developing resistant sorghum cultivars. Feature selection algorithms are frequently employed in preprocessing machine learning pipelines applied to biological data to identify relevant features. The objective of this study is about selecting the important features along with improving the prediction accuracy. Therefore, we propose to use an integrated strategy including Information gain, Gain Ratio, and ReliefF to filter important genes involved in striga resistance in sorghum. For this, were searched in the public database, National Center for Biotechnology Information Gene Expression Omnibus (NCBI GEO) and found a study with accession number GSE216351. The DESeq2 package (v 1.34.0) was employed and the genes less than 10 counts across all samples were filtered out. The resulting matrix including 25037 genes and 31 samples were submitted to the feature selection algorithms and the top 50 genes ranked by Information gain, Gain Ratio, and ReliefF were selected as input for venn diagram. Seven genes including Sobic.001G429700, Sobic.002G087200, Sobic.010G134900, Sobic.005G063800, Sobic.005G192400, Sobic.006G053500, and Sobic.002G307700 were found to be common identified by the three methods. To validate the accuracy of our feature selection methods, we tested different algorithms from classifiers bayes, functions, lazy, meta, rules, and trees and the best performance algorithm from each classifier was selected. Modeling was performed using 10-fold cross-validation. NaiveBayes, SGD, IBK, AdaBoostM1, PART (rules), and j48 prediction models were the best algorithms from each classifier to discriminate control and infected crops. The highest performance was obtained by NaiveBayes with 96.7742% accuracy. Therefore, considering the high efficiency of these seven genes to classify control and infected crops, they could be suggested as biomarkers for striga resistant in sorghum.

Keywords: *Striga hermonthica*, information gain, gain ratio, ReliefF

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ICB13 -1195

Attention based Graph Neural Network for Identifying Coding and Non-coding Breast Cancer Drivers

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Breast cancer remains one of the foremost causes of cancer-related mortality among women worldwide (Heer et al., 2020, Sung et al., 2021), driven by a complex interplay of genetic and epigenetic alterations. Identifying both coding and non-coding cancer driver genes is crucial for understanding tumorigenic mechanisms, developing targeted therapies, and improving patient prognostics (Byler et al., 2014, Dumitrescu, 2018). Traditional methodologies predominantly focus on coding regions, often overlooking the regulatory roles of non-coding regions in cancer progression. To address this gap, we propose an innovative attention-based graph neural network framework designed to identify both coding and non-coding breast cancer driver genes by leveraging multi-omics data integration and sophisticated attention mechanisms. Our proposed model integrates diverse genomic datasets from The Cancer Genome Atlas (TCGA) (Weinstein et al., 2013), including gene expression profiles, mutation data, copy number variations, methylation patterns, and protein–protein interaction networks. We used these datasets to construct a comprehensive heterogeneous gene network containing various types of nodes and edges. To process this network, we utilized a graph convolutional network (GCN) architecture called the heterogeneous graph transformer (HGT) (Hu et al., 2020). The model captures the intricate relationships and dependencies among genes within the network. Incorporating a self-attention mechanism enables the model to assign different weights to various nodes and interactions, allowing it to focus on the most influential features and effectively filter out noise and irrelevant data, thereby enhancing the identification of critical driver genes that play pivotal roles in cancer development and progression amidst the vast genomic landscape. The framework operates through a two-stage process: (1) constructing a condition-specific breast cancer network that encompasses both coding genes and non-coding RNAs, and (2) applying hierarchical attention layers to prioritize nodes based on their significance within the network. This dual approach not only improves the detection of known coding drivers but also uncovers novel non-coding drivers that regulate key oncogenic pathways. Furthermore, the integration of multi-omics data provides a holistic view of the molecular landscape, facilitating the discovery of driver genes with increased accuracy and biological relevance. Comparative analyses show that our proposed model outperforms state-of-the-art methods like CBNA (Pham et al., 2019), and NIBNA (Chaudhary et al., 2021), achieving superior performance in identifying both coding and non-coding drivers. Notably, it predicted a significant number of novel miRNA and coding drivers, many of which have been validated in recent literature. In conclusion, the attention-based graph neural network offers a robust and scalable solution for the comprehensive identification of coding and non-coding breast cancer driver genes. By leveraging multi-omics data integration and advanced attention

mechanisms within a GCN architecture, our proposed model enhances the accuracy of driver gene detection and provides critical insights into the molecular underpinnings of breast cancer. This framework is poised to contribute significantly to the fields of cancer genomics and precision medicine, ultimately aiding in the development of targeted interventions and more effective diagnostic and therapeutic strategies for breast cancer patients.

Keywords: graph neural network, attention mechanism, breast cancer driver genes, coding and non-coding genes, precision medicines

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ICB13 -1196

Structural and Hydrogen Bonding Characteristics of Natural Deep Eutectic Solvent Choline Chloride/Citric Acid: A Molecular Dynamics Simulation Study

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Deep eutectic solvents (DES) were first introduced in 2001 as sustainable alternatives to ionic liquids and volatile organic compounds (Abbott and Capper, 2001). These solvents consist of hydrogen bond donors and acceptors mixed in specific molar ratios, offering unique properties such as non-volatility, low toxicity, high biodegradability, cost-effectiveness, and antifreeze capabilities (Rozas and Zamora, 2023). Their versatility has garnered significant attention in scientific and industrial applications, particularly in the pharmaceutical industry, where they enhance drug solubility, permeability, and absorption. Moreover, their biological activities, including antioxidant, anticancer, and antimicrobial properties, make them promising candidates for diverse biomedical applications (Trombino and Siciliano, 2022). In this study, the structural and physical properties of a natural deep eutectic solvent (NADES) composed of choline chloride and citric acid were investigated through molecular dynamics simulations. Simulations were conducted using GROMACS software and the OPLS force field, (Albertini and Bertoni, 2023) with a 1:1 molar ratio comprising 1500 ion pairs of choline chloride and 1500 molecules of citric acid. The simulation spanned 50 nanoseconds, and the calculated density of the solvent closely matched experimental data, validating the reliability of the computational model. (Savjani and Gajjar, 2012) To understand the structural stability and role of hydrogen bonds in this solvent, combined radial and angular distribution functions (CDF) were employed. This analysis revealed that strong hydrogen bonds are predominantly formed between electron-donor hydrogen atoms and electron-acceptor oxygen atoms, particularly those associated with oxygen atoms 1 and 3 in citric acid. These hydrogen bonds, characterized by distances of 2–3 angstroms and bond angles of 150–180 degrees, play a critical role in stabilizing the solvent's structure. Further analysis using the TRAVIS tool allowed precise characterization of hydrogen bond positions and angles, reinforcing the simulation's findings. The results confirm that the hydrogen bonding network significantly contributes to the unique properties of the choline chloride/citric acid NADES. This structural stability makes the solvent suitable for applications in drug delivery and other industrial processes. In conclusion, this research demonstrates the effectiveness of molecular dynamics simulations in accurately modeling the physical properties and hydrogen bonding characteristics of natural deep eutectic solvents. The findings highlight the pivotal role of citric acid's oxygen atoms in forming stable hydrogen bonds, which enhance the solvent's structural integrity and functional properties. These insights pave the way for the design and optimization of DESs tailored for pharmaceutical and industrial applications.

Keywords: molecular dynamicss imulation, deep eutectic solvents, Choline Chloride, Citric Acid, hydrogen bonding, pharmaceutical applications

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ICB13 -1197

In Silico Design and Evaluation of a Multi-Epitope Vaccine Candidate Against Escherichia coli and Staphylococcus aureus Involved in Bovine Clinical Mastitis

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Bovine mastitis caused by Escherichia coli and Staphylococcus aureus is a significant economic and health burden in the dairy industry[Hoogeveen et al., 2019; Heikkilä et al., 2018]. This study aimed to design and evaluate a computationally optimized multi-epitope vaccine using in silico approaches to combat these pathogens. The Vaxign database screened 79 E. coli and 38 S. aureus proteins based on transmembrane helices, antigenicity, and non-homology to host proteins. Antigenicity analysis shortlisted 10 proteins, from which two highly antigenic candidates—PhoE and ferric enterobactin outer membrane transporter (FEOMT) for E. coli and MS7_2175 and SasA for S. aureus—were selected. CTL, HTL, and linear B-cell epitopes were predicted using IEDB tools with strict selection criteria, resulting in 37 CTL, 31 HTL, and multiple B-cell epitopes. The multi-epitope vaccine construct was designed using GGGS and HEYGAEALERAG linkers to ensure flexibility and immunogenicity. Physicochemical analysis revealed favorable characteristics, including a molecular weight of 40.64 kDa, an instability index of 41.11, and hydrophilic properties (GRAVY score: -0.921). Structural validation using Ramachandran plot showed 93.33% of residues in the favored region, indicating a stable 3D conformation. Molecular docking against TLR11 receptor demonstrated strong binding affinity (-1028.2 kcal/mol), suggesting efficient immune activation. Codon optimization for E. coli expression achieved a CAI of 0.98 and GC content of 71%, enabling successful in silico cloning into the pcDNA3.1(+) vector. This study introduces a novel and promising multi-epitope vaccine candidate designed through integrated immunoinformatics approaches. The vaccine's strong immunogenic potential and stability highlight its suitability for further experimental validation, paving the way for effective control of bovine mastitis caused by E. coli and S. aureus.

Keywords: multi-epitope vaccine, E. coli, S. aureus, bovine mastitis, immunoinformatics, TLR11, in silico cloning

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ICB13 -1198

Molecular Docking Study of Tromethamine and Its Analogues as Streptococcus mutans's Enolase Inhibitors: A Novel Therapeutic Strategy

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Streptococcus mutans is a gram-positive bacterium known to be a causative agent of dental caries and bacterial endocarditis. This bacterium proficiently converts sugars into substantial quantities of lactic acid and exhibits the capability to develop strong biofilms in the presence of sucrose (Zhang et al., 2020). Enolase, a surface-associated protein found in this bacterium, plays a crucial role in the glycolytic pathway and its pathogenesis. Although fluoride inhibits bacterial activity and plaque acid production, recent studies have demonstrated that fluoride-resistant S. mutans mutants are widespread. Nevertheless, it has been proposed that the inhibition of Enolase is attributed to the antibacterial capacity of fluoride (Mitsuhata et al., 2014, Zhang et al., 2020). Therefore, in this study, we investigated the drug repurposing of tromethamine as an inhibitor of Streptococcus pneumoniae Enolase for inhibiting Enolase of Streptococcus mutans using molecular docking analysis. For this purpose, the sequence of Streptococcus mutans's Enolase enzyme was obtained from the UniProt (Q8DTS9). The 3D structure of Enolase was predicted by the ITASSER server and refined using the GalaxyRefine server. The 3D structure of tromethamine (DrugBank ID: DB03754) and its 20 analogs were obtained from the PubChem database in SDF format. After preparing protein and ligands, molecular docking was performed using the Molegro Virtual Docker v. 6. Only the top 1 pose of each ligand was selected in Molegro Virtual Viewer v. 7, and the best ligand with the lowest energy binding was evaluated. Finally, the pharmacokinetic properties of ligands were estimated using the SwissADME database. The best ligand for Enolase was [1-Hydroxy-2-(hydroxymethyl)butan-2-yl]azanium (PubChem CID: 7058177), with a molecular weight of 120.17 g/mol and the most negative ΔGbind (-54/6212 kcal/mol). This ligand formed five hydrogen bonds with the Enolase residues, Glu375, Glu375, Ser377, Gln407, and Arg120, one electrostatic interaction with Glu375, and five steric interactions involving the Enolase residues of Arg120, Glu375, Glu375, Ser377, and Gln407. Moreover, the ADME results indicated that this ligand had a water solubility score of (LogS) 0.43, two hydrogen bond acceptors, three hydrogen bond donors, a lipophilicity score of (XLOGP3) -1.30, and a polarity score (TPSA) of 68.10. Based on the obtained results, [1-Hydroxy-2-(hydroxymethyl)butan-2-yl]azanium (PubChem CID: 7058177) demonstrated the best interaction with the lowest energy binding with Enolase, and good Druglikeness properties which it may serve as an inhibitor candidate for Enolase of Streptococcus mutans, although further in vivo and in vitro analysis are necessary.

Keywords: Streptococcus mutans, Tromethamine, Enolase, [1-Hydroxy-2-(hydroxymethyl) butan-2-yl]

azanium, molecular docking.

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ICB13 -1199

Enzybiotic Activity in Marine Bacteria: Unveiling Cooperative and Competitive Dynamics for Antimicrobial Potential

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Enzybiotics, enzymes with antimicrobial activities, have emerged as promising alternatives to traditional antibiotics because of their high specificity and efficacy against resistant bacteria(Danis-Wlodarczyk et al., 2021; Thallinger et al., 2013; Wang et al., 2023). This study emphasizes the pivotal role of marine bacteria in the production of enzybiotics and addresses the urgent need for novel antimicrobial agents to combat antibiotic resistance. Marine ecosystems, particularly those with extreme conditions, harbor bacteria that have evolved robust enzybiotic production mechanisms along with potent resistance strategies. This study investigated metagenomic datasets from polluted and non-polluted environments across six distinct habitats using computational approaches to explore the co-abundance patterns of enzybiotic-producing bacteria. BLAST analyses with NCBI-BLAST+ identified sequences using 100% identity, and organismal frequency was used as an indicator of co-abundance. Correlations between bacterial species were calculated using the Himsc package, and a co-abundance network was visualized in Cytoscape, revealing critical interactions among key marine bacteria such as Marinomonas mediterranea, Pseudoalteromonas tunicata, and Pseudoalteromonas luteoviolacea. The findings showed a strong positive correlation between M. mediterranea and P. tunicata (correlation coefficient = 0.9902, p = 0.0001), suggesting cooperative interactions driven by shared enzybiotic activities, including antifouling compound production and oxidative enzymes, such as laccases and tyrosinases. These enzymes are crucial for biofilm formation, cell death regulation, and ecological synergy, thereby enhancing their coexistence and functional output in marine ecosystems. In contrast, significant negative correlations, such as between P. tunicata and P. luteoviolacea (correlation coefficient = -0.9266, p = 0.0079), highlighting competitive exclusion mechanisms. The inhibitory effects of broad-spectrum enzybiotics produced by P. tunicata likely suppress the growth of competing species, while M. mediterranea employs marinocine, a hydrogen peroxide-generating protein, to inhibit competitors like P. luteoviolacea thereby gaining a competitive advantage. These results underscore the dual roles of enzybiotic activity in fostering cooperative interactions and driving competitive exclusion within microbial communities. Such dynamics not only shape microbial ecosystem structures but also reveal potential applications for harnessing enzybiotics in combating antibiotic resistance. Cooperative activities, as seen between M. mediterranea and P. tunicata, demonstrated the potential of enzybiotics to enhance ecological functionality, while competitive dynamics provided insights into microbial strategies for dominance in shared environments. Further experimental validation is essential to confirm these findings

and explore how environmental factors influence enzybiotic activity and microbial interactions. These insights are critical for leveraging microbial ecosystems to develop advanced antimicrobial strategies and better understand the ecological role of enzybiotics in managing antibiotic resistance.

Keywords: Enzybiotics, microbial interactions, Co-abundance network, Metagenome, Co-abundance patterns

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ICB13 -1200

Comprehensive Gene and Protein Catalog for Antimicrobial Environments: A Metagenomic Approach to Mitigate Antimicrobial Resistance

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Currently, the rise of antibiotic-resistant microorganisms presents substantial challenges to critical sectors such as healthcare, agriculture, and poultry production (Danis-Wlodarczyk et al., 2021; Thallinger et al., 2013; Wang et al., 2023). Tackling this issue requires the discovery of new antimicrobial agents, such as enzybiotics, that are capable of bypassing resistance mechanisms. A promising approach to identify such agents involves exploring biomolecules found in extreme microbiome environments, where microbial communities compete for survival and develop powerful antimicrobial properties. The role of antimicrobial-exposed environment microbiomes is pivotal for identifying microbes and enzymes to enhance antimicrobial resistance mitigation. Integrating computational methods and metagenomic approaches is essential to improve current strategies for combating antimicrobial resistance. Catalogs of genes, proteins, and metagenome-assembled genomes facilitate taxonomic and functional analysis of antimicrobial metagenome samples. To the best of our knowledge, no integrated gene and protein catalogs exist for environments containing antimicrobial agents. In this study, 15 whole-metagenome samples (including soil, seawater, groundwater, and plastic-contaminated metagenome samples) were combined. A total of 550 Gb of high-quality data were obtained with an average library fragment size. A comprehensive gene and protein catalog was generated by expanding a computational workflow comprising the quality control of reads, trimming, assembly, and binning of contigs from 15 source environments for antimicrobial agents. This catalog comprises 46.8 million nonredundant genes and proteins. Among the carbohydrate-active enzymes (CAZymes), glycoside hydrolases (GHs) were the most abundant, as determined using the dbCAN2 (Zhang et al., 2018) software. The dbCAN2 analysis identified 465,325 CAZyme-encoding genes in the catalog. Our workflow and the catalog generated from 15 source environment samples provide an efficient resource for identifying antimicrobial enzymes and microorganisms, enabling researchers to enhance their understanding of genes and proteins in this metagenomic environment with minimal time and cost.

Keywords: Enzybiotics, gene catalog, genome, metagenomic analysis, environments for antimicrobial agents

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Predicting Anticancer Drug Repurposing Candidates using Knowledge Graphs

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Drug repurposing (DR) offers a promising and efficient alternative to traditional drug discovery by identifying new therapeutic applications for existing drugs, reducing the time and costs associated with development. This study introduces a novel framework that leverages a new hybrid knowledge graph integrating drug, disease, and protein interactions, combined with a dual-channel Convolutional Neural Network for drug-disease association prediction. The knowledge graph captures complex biological relationships through diverse biomedical data, while the neural network architecture enhances the model's ability to extract meaningful patterns. The framework demonstrates superior performance, achieving an AUC of 0.9836 and AUPRC of 0.9686, significantly outperforming state-of-the-art methods. To enhance the reliability of these predictions, molecular docking simulations were conducted, providing crucial biological validation. Integrating advanced machine learning with robust biological validation offers a promising avenue for accelerating drug discovery efforts and addressing critical unmet medical needs.

Keywords: Drug repurposing, Dual_Channel Neural network, Knowledge Graph, Anticancer

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ICB13 -1202

AcrB Inhibition: A Molecular Docking Approach to Combat Escherichia coli Infections

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Urinary tract infections caused by multi-drug resistant Escherichia coli pathogens continue to pose significant challenges in clinical treatment (Chauhan et al., 2024). One of the primary mechanisms by which E. coli acquire antibiotic resistance is through efflux pumps, the AcrB system, which actively transport antibiotics from within bacterial cells to the external environment. A promising strategy for enhancing antibiotic efficacy and the effects of treatments involves the development of effective derivatives that can inhibit these pumps, potentially overcoming E. coli resistance (Chauhan et al., 2024). Therefore, in this study, we aimed to determine the most potent inhibitor of AcrB through molecular docking analysis. Material and Methods For this purpose, the three-dimensional structure of the AcrB protein (PDB ID: 2dhh) was obtained from the RCSB PDB database. Three AcrB inhibitory ligands (with PubChem CID: 13806, 222528, and 2993) and 10 analogs for each ligand were retrieved from the PubChem databases. The protein and inhibitory ligands were prepared for docking using Molegro Virtual Docker version 6.0. After docking, the best interaction with the lowest energy binding was analyzed through Molegro Molecular Viewer v.7 software. Finally, the pharmacokinetic properties of the ligand were evaluated using the SwissADME server. Results and Conclusion Through all inhibitory ligands for AcrB protein, the best ligand was 2-[3,6-bis(dimethylamino)-2,7-diphenylxanthen-10-ium-9-yl]benzoic acid (Pumchem CID: 101886889) with a molecular weight of 539.64 g/mol and binding energy of -132.82 kcal/mol. This ligand created seven steric interactions with the AcrB protein residues of Gly97(A), Ala100(A), Asp101(A), Gln106(B), Thr98(B), Asp99(B), and Asp99(A), one hydrogen bond with Asp99(A) residue, and two electrostatic interactions with Asp99(A) and Asp101(A). In addition, the ADME results demonstrated that this ligand has a water solubility score (logS) of -7.37, a hydrophilic score (LogP) of 1.64, a polarity score (TPSA) of 56.92 A, and lastly, hydrogen bond donors of 1 and hydrogen bond acceptors of 3. These results indicated that 2-[3,6-bis(dimethylamino)-2,7-diphenylxanthen-10-ium-9-yl]benzoic acid (Pumchem CID: 101886889) is a promising candidate for inhibiting Escherichia coli resistance, although further in vitro and in vivo studies are required to confirm its potential as therapeutic agents.

Keywords: Escherichia coli, AcrB protein, molecular docking, 2-[3,6-bis(dimethylamino)-2,7-diphenylxanthen-10-ium-9-yl]benzoic acid.

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Comparative Analysis of Enzybiotic Gene Abundance Across Environmental Microbiomes with Varied Plastic Pollution Levels

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Enzybiotics, a unique class of antimicrobial enzymes originating from bacteriophages or bacterial sources, hold immense potential for addressing multidrug-resistant pathogens(Danis-Wlodarczyk et al., 2021; Thallinger et al., 2013; Wang et al., 2023). This study investigates the abundance of enzybiotic genes in whole metagenomic datasets derived from 15 environmental microbiomes, spanning aquatic and terrestrial ecosystems affected and unaffected by plastic pollution. A comparative analysis was conducted to understand the ecological roles and distribution patterns of these genes. We developed a comprehensive computational pipeline that processes raw metagenomic data through multiple stages, including quality control, assembly, and annotation, utilizing enzybiotic-specific databases. Gene detection and identification employed a bitscore threshold of ≥75 for initial screenings and ≥100 for high-confidence annotations. The pipeline also integrates statistical methods to compare enzybiotic abundance across environments. Our findings reveal a significantly higher prevalence of enzybiotic-related genes in environments contaminated by plastic, regardless of aquatic or non-aquatic classification, compared to their uncontaminated counterparts. This pattern highlights potential adaptive responses or selective enrichment of microbial communities in polluted habitats. These results not only underscore the ecological impact of plastic pollution on microbiomes but also provide insight into the functional metagenomics of enzybiotics, suggesting their biotechnological relevance in such settings. This study lays the groundwork for leveraging enzybiotics in environmental biotechnology and microbial ecology, emphasizing their importance in adapting to pollution-driven ecosystem changes.

Keywords: Enzybiotics, environmental microbiomes, metagenomic analysis, plastic pollution, antimicrobial enzymes

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ICB13 -1206

Gut Proteomics Reflecting Extraintestinal Organ Involvement in IBD

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Inflammatory Bowel Disease, including Crohn's Disease (CD) and Ulcerative Colitis (UC), is a chronic gastrointestinal disorder characterized by inflammation. About 25% of IBD patients are pediatric (Rosen et al., 2015). Pediatric IBD is of concern due to aggressive progression, nutritional deficiencies, growth failure, and complications from early disease onset (Ishige, 2019). Additionally, pediatric IBD care is more costly than adult care (Kappelman et al., 2008). IBD affects not only the gastrointestinal tract but also other organs, referred to as extraintestinal complications. These can involve the musculoskeletal system, skin, hepatobiliary tract, and eyes, significantly impacting patients' quality of life (Rogler et al., 2021). Also, extraintestinal complications present challenges for healthcare providers in managing IBD. We employed proteomics data from a cohort of pediatric patients, consisting of 22 CD cases, 18 UC cases, and 22 healthy controls from mucosal luminal interface samples of the colon (Zhang et al., 2018). Raw MS data were preprocessed using MaxQuant and differentially expressed proteins among CD, UC, and healthy controls were identified using the DEP package in R. We focused on proteins significantly altered in IBD patients compared to healthy controls as well as those distinguishing subtypes of IBD. Enrichment analysis was conducted to identify tissues and gene ontologies associated with the significant proteins. Our findings suggest that intestinal proteomics data reflects the potential links between other organs and IBD, which may offer insights into the broader physiological effects of the condition.

Keywords: pediatric inflammatory bowel disease (PIBD), Extraintestinal Organ Involvement, Proteomics, Differentially Expressed Proteins, Enrichment Analysis.

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Unlocking the Hidden Potential of Leuconostoc: Insights from Genomic Analysis

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Leuconostoc is gram-positive, non-motile, and heterofermentative of lactic acid bacteria with genome sizes ranging from 1 to 2.5 Mb. These bacteria produce various metabolites, including bacteriocins (Stiles, 1994), organic acids, and aroma compounds such as acetoin, acetaldehyde, and diacetyl (Jay, 1982; Vedamuthu, 1994), which are crucial in food and health biotechnology. However, there are a few studies on the genome mining of their metabolic activities. In this study, we employed antiSMASH (Blin and Shaw, 2023), a bioinformatics tool for bacterial, fungal, and plant genome-wide analysis of secondary metabolite biosynthetic gene clusters (BGCs), to analyze whole genomes of the valid species classified under the Leuconostoc genus. We also utilized the Bacterial Diversity Database (BacDive) (Schober and Koblitz, 2024) and related articles to retrieve related information, focusing on their environmental distribution, pathogenicity, biosafety levels, and associated annotations. Our analysis revealed 18 regions across these strains, with lengths ranging from 10 to 42 Kb, corresponding to five distinct product types, including type III polyketide synthases (PKSs) (39%), ribosomally synthesized and post-translationally modified peptides (28%), terpenes (11%), betalactones (5.5%), heterocyst glycolipid synthase-like PKSs (hgIE-KS) (5.5%), arylpolyene (5.5%), and furans (5.5%). Notably, all species contained at least one region encoding PKSs. Considering various applications of polyketides in pharmaceutical biotechnology with antibiotic, anticancer agents, and antimetabolites activities (Nivina and Yuet, 2019), which are typically obtained from actinobacteria (Robertsen and Musiol-Kroll, 2019). It appears that the potential of Leuconostoc in biotechnology extends far beyond food biotechnology and the production of fermented food. Another interesting result of the current research is the presence of heterocyst glycolipid synthase-like PKSs in L. gasicomitatum, which is typically found in cold-stored, modified atmosphere packaged foods. The hglE-KS enzymes are similar to PKSs but are specifically adapted for the synthesis of heterocyst glycolipids. These glycolipids are typically found in cyanobacteria (Bauersachs and Compaoré, 2009) and form a protective layer around heterocysts, the specialized cells responsible for nitrogen fixation in these organisms. The glycolipid protects nitrogenase enzymes from oxygen. Some types of these glycolipids appear to protect L. gasicomitatum, a psychrotrophic-aerotolerant bacterium, against certain stress factors such as toxic oxygen species and cold conditions. This study highlights the biosynthetic potential of the Leuconostoc genus and its application in biotechnology.

Keywords: lactic acid bacteria (LAB), Leuconostoc, antiSMASH, polyketide synthases, glycolipids

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ICB13 -1209

A Knowledge Graph-Based Approach for Drug Repurposing Using Graph Neural Networks and Language Models

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Drug repurposing offers a cost-effective and time-efficient strategy for discovering new therapeutic applications for approved drugs, reducing development timelines from 10-15 years to 3-5 years. Knowledge graphs (KGs) have emerged as powerful tools for representing complex biomedical relationships, integrating molecular interactions, pathway information, and clinical outcomes. Their ability to capture multifaceted drug-disease-target interactions makes them particularly valuable for drug repurposing, as they can reveal hidden patterns and potential therapeutic applications through network analysis. However, conventional approaches, particularly random walk-based methods, face significant limitations: they are inherently stochastic, lack comprehensive contextual understanding, and often fail to fully utilize the topological and semantic richness of KGs, especially in sparse graph regions. We propose a novel framework that harnesses Graph Neural Networks (GNNs) for drug repurposing applications. GNNs can effectively learn hierarchical representations by systematically aggregating both local and global graph information through multiple message-passing layers, enabling the capture of complex interaction patterns across biological scales. To enhance node embeddings, we integrate semantic features extracted from large language models (LLMs), including BioBERT (Lee et al., 2019) and GPT (Yenduri et al., 2023), addressing a critical gap in traditional approaches by incorporating unstructured textual information from biomedical literature. Our validation uses Alzheimer's disease as a case study, chosen for its complex pathophysiology and urgent need for effective treatments. The model was evaluated on two benchmark datasets, MSI (Ruiz, Zitnik and Leskovec, 2021) and PrimeKG (Chandak, Huang and Zitnik, 2023), achieving a 6% improvement in F1 score compared to baseline methods in predicting drug-disease associations. Pathway analysis using t-tests on the top 10 ranked drugs revealed statistically significant differences ($p < 0.003$) between high-ranked and lower-ranked drugs, specifically in pathways implicated in Alzheimer's disease, including amyloid-beta processing and neuroinflammation. Ablation studies demonstrated that LLM derived features contributed to a 4% improvement in prediction accuracy compared to using graph structural features alone. Our integrated GNN-LLM framework presents a robust solution for computational drug repurposing, with potential applications across diseases with complex pathological mechanisms. Future work will focus on incorporating temporal dynamics and patient-specific factors for personalized drug repurposing strategies.

Keywords: drug repurposing, Alzheimer's disease, knowledge graphs, graph neural networks, link prediction, large language models

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ICB13 -1210

In-silico investigation of bioactive peptides with anti-Alzheimer potential derived from bovine milk αs1-casein protein

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Milk is the main source of energy, protein, and fat in the human diet (Gigli, 2016). Cow's milk contains about 32 g of protein per liter, and about 80% of milk protein is casein. αs1-casein is the most abundant casein. Bioactive peptides derived from milk proteins have been the subject of numerous studies in the past two decades due to their various biological properties in human health (Haug, Høstmark and Harstad, 2007). Alzheimer's disease (AD), which has become a global problem due to the aging population and the lack of effective treatments, urgently needs innovative treatments based on natural substances (Wang et al., 2023). According to reliable sources, bioactive peptides with antioxidant properties have anti-Alzheimer's potential (Gupta and Singh, 2024). Also, by inhibiting acetylcholinesterase, it is expected that systemic and circulating acetylcholine levels will increase. Thus, the availability of acetylcholine to stimulate brain receptors for normal cognitive functions will increase. As a result, one of the preferred therapeutic strategies for the management of neurological conditions is the use of acetylcholinesterase (AChE) inhibitors (Ji et al., 2022). The effect of 13 protease enzymes on bovine milk αs1-casein was simulated in silico. In this process, 21 (non-toxic) peptide fragments with antioxidant properties were generated, and the abundance, potential activity, and digestive absorption of these peptides were also investigated. The enzymatic degradation by chymotrypsin A yielded the highest number of antioxidant peptides (5 fragments) compared to other enzymes. Subsequently, a docking test was performed between the obtained antioxidant peptides and the active site of acetylcholinesterase. Comparison of the docking results showed that the highest binding energy was related to the YFYPEL peptide. The results of this study can be used, with further investigation, for the manufacture of drugs or dietary supplements.

Keywords: Bioactive peptides, casein protein, Alzheimer's disease, antioxidant, bioinformatics

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ICB13 -1211

Phylogenetic Insights into Enzybiotic with Novel Properties

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The evolution of enzymes is crucial for the development of novel therapeutic agents against multidrug-resistant bacteria. This study explored a diverse set of enzymes, including amidases, lysozymes, and proteases, with known antimicrobial properties, sourced from uncultured bacterial strains(Iqbal et al., 2014) and species, such as Enterococcus faecium and Lysobacter capsici(Afoshin et al., 2022). Using Clustal Omega for multiple sequence alignment, we constructed a high-resolution phylogenetic tree to investigate evolutionary relationships and functional diversity within this enzyme cohort. Phylogenetic analysis revealed distinct clustering patterns among the enzyme families. M23 metallopeptidase enzymes from Lysobacter capsici showed strong conservation of catalytic residues and tight clustering, suggesting an evolutionary pressure to preserve their peptidoglycan-degrading activity. In contrast, amidases exhibited significant divergence, especially those from uncultured bacteria, implying adaptive modifications in their active sites to target structurally diverse bacterial cell walls. Proteases are split into two major clades, reflecting variations in substrate specificity and structural domains. Enzymes from uncultured bacterial strains formed unique clades that were distinct from known sequences, suggesting previously uncharacterized antimicrobial mechanisms. Notably, enzymes, such as N-acetylmuramoyl-L-alanine amidase, were identified as phylogenetic outliers, indicating potential evolutionary transitions that may broaden their activity spectrum(Premetis et al., 2023). These findings underscore the potential of uncultured microbiota as reservoirs of novel enzymatic functions. By integrating phylogenetic analysis with functional predictions, we have provided a comprehensive understanding of the structural and functional evolution of antimicrobial enzymes. Our study offers a valuable framework for discovering and optimizing bioactive enzymes, with future research incorporating structural bioinformatics and functional assays to explore their mechanistic roles in combating antimicrobial resistance.

Keywords: antimicrobial enzymes, phylogenetic analysis, enzyme evolution, uncultured bacteria, Bioinformatics

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ICB13 -1212

Boosting Healing ThroughStabilized Fibrin Clot: Structural BioinformaticsExploration of Collagen's Potential as a Sustained-Release Carrier for TranexamicAcid

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The growing demand for efficient and cost-effective strategies in biomedical research highlights the importance of computational tools in optimizing systems before transitioning to experimental settings. These tools significantly reduce the time, costs, and resources spent on trial-and-error approaches in the laboratory. Drug delivery systems play a pivotal role in modern medicine, ensuring precise and controlled administration of therapeutics. Among these, sustained release systems, comprising a carrier and a cargo, demand a delicate balance of binding energies to form stable interactions while enabling controlled cleavage for release. Structural bioinformatics has emerged as an indispensable tool in this domain, offering valuable insights into molecular interactions that can guide experimental designs with unparalleled efficiency and accuracy. In this study, we utilized structural bioinformatics to investigate the feasibility of collagen as a matrix for the sustained release of tranexamic acid at a targeted injury. Collagen, a well-known biomaterial with excellent biocompatibility, is widely used in drug delivery systems for its structural stability and adaptability (Zheng and Wang, 2023). Tranexamic acid, an antifibrinolytic agent extensively used in emergency settings via intravenous administration, reduces excessive bleeding by inhibiting fibrin degradation (Colomina and Contreras, 2022). However, localizing its presence through a sustained release system could enhance therapeutic efficacy and reduce systemic side effects (Ausen and Fossmark, 2022). In our work, the localization of tranexamic acid extends beyond its hemostatic application, aiming to leverage its antifibrinolytic properties for enhancing wound healing. By stabilizing the fibrin clot, tranexamic acid prolongs clot presence, creating an ideal natural scaffold for wound repair (Richter and Ku, 2023). The fibrin clot provides a dynamic substrate that binds and releases various growth factors, induces angiogenesis, supports cellular adhesion as a provisional matrix, modulates inflammatory responses, and fulfills its essential hemostatic role (Barbosa and Martins, 2018). This multifaceted bioactivity underscores the significance of designing a sustained release system to harness these benefits. In this context, the 3D molecular structures of collagen (PDB ID: 1BKV) and tranexamic acid (converted to PDB format from SDF using OpenBabel software) were retrieved from the RCSB database (Berman and Westbrook, 2002). Following retrieval, the files underwent further preparation, including the conversion of PDB files into PDBQT format using MGLTools software. Molecular docking was performed using AutoDockTools (Morris and Huey, 2009) with the following parameters: 50 genetic algorithm runs, a maximum of 50,000,000 evaluations, and the output

based on the Lamarckian Genetic Algorithm (version 4.2). Blind docking simulations were conducted to evaluate the binding affinities and clustering of docked poses. The results revealed binding energies ranging from -4.16 to -5.05 kcal/mol, with the most abundant cluster at -4.87 kcal/mol, categorized as moderate interactions (Varadwaj and Marques, 2020). These moderate interactions indicate a suitable balance for developing a sustained release system, where stable bonding ensures matrix integrity while enabling controlled release of tranexamic acid. These findings suggest that collagen exhibits a promising binding profile for sustained release applications of tranexamic acid, offering a localized delivery system that stabilizes the fibrin clot and accelerates wound healing by enhancing the natural repair process.

Keywords: Collagen, tranexamic acid, sustained-release system, molecular docking, structural bioinformatics.

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ICB13 -1214

Exploring Vaginal Microbiome Diversity in Early Pregnancy: Implications for Healthy Pregnancy and Miscarriage

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Recent research has unveiled the critical role of the microbiome composition during pregnancy in regulating inflammatory responses and immune functions, potentially exerting a significant impact on pregnancy outcomes (Liu et al., 2021). This study focuses on investigating the vaginal microbiome in the early stages of pregnancy among three distinct groups of women: those with healthy pregnancies, individuals undergoing dydrogesterone treatment, and women who have experienced miscarriages. The study involved the collection and analysis of samples from the vaginal microbiomes of 51 Eastern European women between the 8th and 11th week of pregnancy (Gryaznova et al., 2023). Microbiome analysis utilized 16S rRNA sequencing and Qiime2 software (Bolyen et al., 2019) for taxonomic analysis, as well as PICRUSt2 (Douglas et al., 2020) for functional assessments. The findings from this investigation reveal significant differences in the composition of the vaginal microbiome among the different groups during the initial stages of pregnancy. Although no significant variations were noted in within-group alpha diversity, beta diversity analysis (between groups) demonstrated substantial species diversity among the cohorts, with an adjusted p-value of 0.04. Women who had experienced miscarriages exhibited the highest richness and evenness in their vaginal microbiome compared to the other groups. The study's results highlight the crucial roles of Gardnerella vaginalis and Mycoplasma girerdii in miscarriage pathology, while Lactobacillus iners and Bifidobacterium longum were identified as protective factors in early pregnancy. Furthermore, the research indicates that progesterone treatment exerts significant effects on the composition of the microbiome.

Keywords: 16S rRNA sequencing, early pregnancy, miscarriage, vaginal microbiome, Qiime2, PICRUSt2.

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ICB13 -1215

Identification of potential RNA interference targets in bladder cancer through bioinformatics approaches

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Bladder cancer is a urothelial carcinoma with histological heterogeneity, making it difficult to manage. High recurrence rates and the lack of effective targeted therapies highlight the need for less invasive therapeutic options. In the present study, we aim to identify potential miRNAs to suppress upregulated key genes related to bladder cancer using bioinformatics approaches to pave the way for more effective treatment strategies. Microarray data of bladder cancer and normal tissues were retrieved from the Gene Expression Omnibus (GEO) database (GSE121711). After preprocessing the data, differentially expressed genes (DEGs) were identified using the R/Bioconductor package limma, focusing on upregulated genes for further analysis. A protein-protein interaction (PPI) network was reconstructed to explore interactions among upregulated hub genes, based on centrality scores within the network. Gene expression levels of the identified hub genes were confirmed using GEPIA. Additionally, NetworkAnalyst was employed to analyze hub gene interactions with miRNAs, constructing gene-miRNA interaction networks. A total of 9,781 differentially expressed genes were identified. The PPI network nodes were ranked using four topological analysis methods from the CytoHubba plugin in Cytoscape: Degree, Maximal Clique Centrality (MCC), Closeness, and Betweenness. Additionally, the MCODE (Molecular Complex Detection) plugin of Cytoscape was used to determine gene clusters in the constructed network. The hub genes identified were TOP2A, NUSAP1, TPX2, CENPF, ASPM, MKI67, CCNB2, CENPE, CDC6, ANLN, and PRC1. The results from GEPIA also confirmed the differential expression of these hub genes across multiple bladder cancer datasets. Notably, miRNAs such as hsa-miR-192-5p, hsa-miR-215-5p, hsa-miR-193b-3p, hsa-miR-92a-3p, and hsa-miR-218-5p demonstrated substantial associations and regulatory interactions with the identified hub genes. In this study, we identified several miRNAs that target key biomarkers related to bladder cancer through bioinformatics approaches. These miRNAs may serve as potential biomarkers and therapeutic targets in future bladder cancer treatments.

Keywords: Bladder cancer, hub gene, systems biology, bioinformatics

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ICB13 -1216

BiogenExplorer: A Robust Solution for Rapid Gene Presence Detection and Allelic Diversity Analysis in large Genomic Datasets

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In the era of genomic research, understanding genetic variability is pivotal for advancing health diagnostics, disease prevention, and biotechnological innovations. The analysis of gene presence-absence and allelic diversity provides critical insights into evolutionary dynamics, population genetics, and the functional potential of organisms. However, the management and analysis of large genomic datasets can be daunting, often hampered by inefficiencies and a high likelihood of human error. To address these challenges, we introduce BiogenExplorer—a powerful and user-friendly tool designed to streamline the analysis of gene presence across complete genomes. With its robust integration of BLAST+, SQL, and Python, BiogenExplorer empowers researchers to efficiently analyze extensive datasets while ensuring high accuracy and speed. BiogenExplorer employs BLAST+ for precise sequence alignment, SQL for optimized data storage and querying, and Python for automation of workflows. Genomic sequences are systematically processed to identify the presence of specific genes across multiple samples. After establishing gene presence, the tool assesses allelic diversity by analyzing sequence variation within the identified genes. The system is engineered to manage large datasets while minimizing human intervention, facilitating rapid analysis, even with extensive sample cohorts. BiogenExplorer was evaluated using various genomic datasets encompassing a range of sample sizes. The tool exhibited exceptional accuracy in detecting gene presence and delivering reliable assessments of allelic diversity. Its enhanced performance demonstrated notable advancements in speed and scalability when compared to traditional analytical methods, particularly beneficial for large sample numbers. BiogenExplorer emerges as a fast, reliable, and scalable solution for analyzing gene presence and allelic diversity in genomic studies. Its ability to efficiently manage large datasets provides profound value in health-related research and industrial applications alike. By automating the analysis process, BiogenExplorer significantly reduces human error and enhances throughput, establishing itself as an invaluable resource for large-scale genomic analysis.

Keywords: gene presence, Allelic diversity, bioinformatics automation, BLAST

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PTE-MED: AI-based Early Detection of Pulmonary Embolism

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Timely diagnosis of pulmonary embolism (PE) is a significant challenge in clinical medicine, mainly due to the condition's non-specific symptoms. The PTE-MED artificial intelligence system has been developed to accurately predict the likelihood of PE by analyzing clinical data. Current research indicates that over 50% of suspected PE cases undergoing CT angiography yield negative imaging results (Li et al., 2021). This not only results in unnecessary exposure to contrast agents and radiation but also poses serious risks for vulnerable populations, including patients with renal conditions and pregnant women. The PTE-MED system employs advanced machine-learning algorithms to analyze critical variables such as age, gender, medical history, and clinical symptoms. Imaging results from CT angiography are also incorporated as vital inputs for predictive modeling (Valente Silva et al., 2023). This approach enables PTE-MED to provide early predictions regarding the probability of PE, generating interpretable results for individual patients through AI-driven analytical tools. By supporting healthcare professionals in making informed decisions, PTE-MED has the potential to enhance the management of this complex and urgent medical condition. To improve accessibility for healthcare providers, a mobile application named PTE-MED is being developed. This application will allow physicians and specialists to input patient symptoms and medical history and subsequently receive predictive insights about the likelihood of PE. Preliminary modeling results demonstrate that the CatBoost model achieves an Area Under the Curve (AUC) of 0.768, an accuracy of 71.1%, a precision of 74.0%, a recall of 71.0%, and an F1 score of 72.0%. In conclusion, this system assists healthcare providers in making better-informed treatment decisions by increasing the accuracy of predictions, addressing a key concern for emergency physicians, surgeons, cardiologists, infectious disease specialists, and obstetricians. The PTE-MED artificial intelligence system not only improves diagnostic accuracy but also potentially reduces the financial and temporal burdens associated with unnecessary diagnostic procedures. By implementing this system, healthcare providers can mitigate the risks associated with invasive diagnostic methods and contribute to enhanced public health outcomes.

Keywords: Pulmonary embolism, artificial intelligence, machine learning, diagnosis, medical informatics, emergency medicine

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ICB13 -1219

Machine Learning for Enhanced Diagnosis of Endometriosis: Challenges and Opportunities

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Endometriosis is a chronic and complex condition that significantly affects the quality of life for over 190 million women globally. Delayed diagnosis can lead to serious complications such as infertility and chronic pain. This study explores the challenges and opportunities of employing machine learning and deep learning models to enhance the diagnosis of endometriosis and improve healthcare outcomes. Key challenges include the variability and complexity of clinical symptoms, a lack of high-quality data, the necessity for specialized knowledge in algorithm implementation, and the absence of standardized evaluation metrics for comparing models (Ellis et al., 2022). Artificial intelligence can potentially reveal hidden patterns in clinical and imaging data. At the same time, machine learning algorithms can facilitate the development of non-invasive screening tools and generate more accurate predictions of treatment outcomes. These advancements are likely to improve diagnostic accuracy and reduce healthcare costs. The study examines various input data, including clinical information, imaging data (MRI and laparoscopic images), and laboratory results (biochemical markers such as CA125 and VEGF1) (Goldstein & Cohen, 2023). It evaluates various models, including deep learning models like ResNet50 and classical models, including decision trees, random forests, logistic regression, and AdaBoost (Zhang et al., 2023). The findings demonstrate that the AdaBoost model performs best in diagnosing endometriosis, achieving an accuracy of 94% and a sensitivity of 93% (Balica et al., 2023). In comparison, the ResNet50 model achieves an accuracy of 91% and a sensitivity of 82% (Visalaxi & Muthu, 2021) To further enhance research in this field, it is recommended that datasets be expanded to incorporate more diverse patient populations and that models be compared across various conditions and similar contexts. Furthermore, clear guidelines for applying artificial intelligence in diagnosing and treating endometriosis are essential. Despite existing challenges, machine learning and deep learning use in analyzing and predicting endometriosis presents significant potential, necessitating ongoing research to refine model performance and increase confidence in their clinical applications.

Keywords: endometriosis, machine learning, deep learning, diagnosis, artificial intelligence, healthcare

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ICB13 -1220

Drug repurposing for brain cancer

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Health and wellbeing are a crucial component for quality of society and life, one of the worries is cancer. Brain cancer has a highly negative emotional toll on patients and caregivers, the patient may lose their productivity and it has huge costs. Brain tumors can start in the brain or cancer can spread to the brain from other parts of the body and tumor treatment options depend on the type of brain tumor you have, as well as its size and location. Common treatments include surgery and radiation therapy. Drug reproposing is a way to re-use well-known drugs to control the undesirable genes expressed and as an immunological treatment, it helps the immune system to beaten the cancer. We chose a database on GEO and compared with significant genes on CoreMine using two statistical condition, p-value and |log FC|, there are 869 genes remain of over 16000. Then we used STRING to find PPI network, now we have the PPI network of the most important genes according to two databases. In this step we made a 5-cluster graph out if the PPI network and sorted the genes by node degree, then we picked 10 higher degree genes as hub genes. Using DGIdb database, we chose the effective drugs on these 10 hub genes and picked the approved by FDA. Then sort them by interaction score and made a list of hub genes and drugs. We considered the side effects of these drugs using Drug Bank database. The final result is the effective drugs with considering side effects that potentially can be used as a treatment for brain cancer, namely: CINNARIZINE, CLOFIBRATE, ZANUBRUTINIB, AFATINIB, OBINUTUZUMAB, TRIFLURIDINE, PIRTOBRUTINIB, MOBOCERTINIB, DACOMITINIB ANHYDROUS.

Keywords: brain cancer, network-based analysis, drug repurpose, hub genes, PPI Network

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ICB13 -1221

A computational approach to identify the biomarker based on the RNA sequencing data analysis for Alzheimer's disease

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Alzheimer's disease (AD) is a progressive neurodegenerative disease. AD affects at least 27 million people and is associated with a high impact on the life of the patient's family and a huge financial cost to society. RNA sequencing (RNA-seq) is one effective approach to finding the heterogeneous gene expressions of diseases that helps discover new functional genes as prognostic biomarkers. Besides, It is well-known that microRNA (miRNAs) biomarkers have emerged as a powerful screening tool, as they are highly expressed in AD patients and easily detectable in several biological samples. The bioinformatics method is cost-effective and time-saving when studying the role of miRNAs-mRNA. Therefore, in this study computational models were used to identify AD-related biomarkers by RNA-seq analysis. The RNA sequencing of 40 AD samples with 8 healthy control tissue from the occipital lobe under the accession code GSE203206 were obtained from the GEO database (https://www.ncbi.nlm.nih.gov/geo/). The differentially expressed genes (DEGs) between AD and normal tissues were obtained by using GEO2R. The 1000 top up regulated genes were imported into the STRING (version 12.0, http://string-db.org) database to identify the interactive association between the proteins. Then, all interactions with a significant combined score >0.4 were selected for further analysis. The appropriate gene with the highest degrees of connectivity were selected as hub genes. The targetScan database is a specialized collection of microRNA-mRNA targeting relationships. These databases were used to obtain hub gene-associated miRNA. This study identified 4150 genes with |log2FC|>0.5 and P-value <0.01 as DEGs: 1279 upregulated and 2871 downregulated genes. γ-aminobutyric acid receptors β2 subunit gene (GABRB2) was identified as one of the best hub genes in STRING which hsa-miR-9-5p can suppress the GABRB2 expression in AD. GABRB2 has a pivotal role in the central nervous system. Several studies also reported alterations in GABA levels, typically a reduction in total neurotransmitter concentration in several regions of the post-mortem AD brain. As recorded, miR-9-5p is found to be downregulated in the brain of the AD patients. Overexpression of miR-9-5p modulates neuroinflammation in the central nervous system. Of note, these bioinformatic results confirmed that targeting GABRB2 is an important mechanism of AD function improving by miR-9-5p in AD. Moreover, TargetScan indicates that the seed region of miR-9-5p contains 2 complementary sites within position 4645-4652 and 4726-4732 of GABRB2 3′ UTR. Taken together, our findings from RNA sequencing analysis provide the first clues regarding the role of miR-9-5p as a modulator of the progression of AD by inhibiting GABRB2 translation. The results also provide valuable insights into the regulation of miR-9-5p and GABRB2 for future research and therapeutic development. These can be used as a specific diagnostic

index and therapeutic target for patients with AD.

Keywords: Alzheimer's disease; RNA sequencing; miRNA; miR-9-5p; GABRB2

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ICB13 -1222

Prediction of E8 mpox virus protein structure: a potential to design inhibitor

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The World Health Organization (WHO) has classified the Monkeypox outbreak as a public health emergency due to the absence of specific therapeutic interventions for the Monkeypox Virus (MPXV). This virus is classified as a rare zoonotic pathogen within the Orthopoxvirus genus of the Poxviridae family. The entry of MPXV into host cells involves several key proteins. This study aims to perform a structural analysis of the E8 envelope protein, which plays a crucial role in the virus's pathogenesis and its ability to bind to host cells.(Martínez-Fernández, Fernández-Quezada et al. 2023) (Das, Bhattarai et al. 2024) (Lu, Xing et al. 2023) To investigate the structural properties of the E8 protein, including its amino acid composition and domain structure, various bioinformatics tools were employed, such as InterPro, ProtPram, and PSIPRED. For modeling the E8 protein of Monkeypox Virus (MPXV), we utilized SWISS-MODEL, Robetta, and AlphaFold. Analysis of the generated models revealed that the AlphaFold model provided the most accurate representation of the E8 protein and may serve as a foundational framework for future drug design efforts..

Keywords: Monkeypox virus (MPXV), viral structure, E8, structural prediction

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ICB13 -1223

Distribution and Allelic Diversity of Outer Membrane Proteins in Helicobacter pylori: Implications for Vaccine Development and Therapeutic Approach

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Helicobacter pylori is a pathogen that affects over half of the global population, thriving in the acidic gastric environment due to the diversity and adaptability of its antigenic structures. Among these structures, outer membrane proteins (OMPs) are critical for bacterial adhesion, immune evasion, and antibiotic resistance, significantly contributing to the bacterium's pathogenicity and persistence. Despite extensive research, the genetic diversity and distribution of OMPs, particularly in high-prevalence regions such as Iran, remain underexplored. This study investigates the presence and diversity of OMP genes in H. pylori using whole-genome sequencing to provide insights into its evolutionary dynamics and potential therapeutic targets. Gastric biopsy samples from 30 Iranian patients were used to isolate H. pylori strains, which were subjected to whole-genome sequencing at a UK-based facility. A custom Python-based automated alignment tool integrated with BLAST+ was developed to analyze the sequences of 61 identified OMP genes regarding their presence, absence, and genetic novelty. This comprehensive approach enabled the identification of patterns in gene distribution and diversity. Analysis revealed substantial variation in the 61 OMP genes. Notably, hopC, hopV, horA, and horJ showed 100% prevalence, while babC, hopO, and hopU were absent in all strains. The average gene presence across all analyzed strains was 75%, with the identification of 611 novel alleles. Among the investigated genes, nine exhibited the highest diversity, each contributing 14 novel alleles. These findings highlight the extensive genetic variability in H. pylori OMPs and the evolutionary pressures influencing their distribution. This study demonstrates significant genetic variation and distribution patterns in H. pylori OMP genes, with some genes consistently present and others entirely absent. The observed diversity underscores the critical roles of these genes in bacterial adaptation, pathogenicity, and potential resistance mechanisms. These findings provide valuable insights for therapeutic and vaccine development, offering targets for managing H. pylori-related diseases in high-prevalence populations. By identifying both conserved and variable OMP genes, this work lays the foundation for future strategies aimed at combating this globally significant.

Keywords: helicobacter pylori, outer membrane proteins, genetic diversity, whole-genome sequencing, bioinformatics analysis, therapeutic targets

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1. Comparative Genomics of Helicobacter pylori: Analysis of the Outer Membrane Protein Families

2. Analysis of Surface-Exposed Outer Membrane Proteins in Helicobacter pylori
3. In Vivo Sequence Variation in HopZ, a Phase-Variable Outer Membrane Protein of Helicobacter pylori
4. HopE and HopD Porin-Mediated Drug Influx Contributes to Intrinsic Antimicrobial Susceptibility and Inhibits Streptomycin Resistance Acquisition by Natural Transformation in Helicobacter pylori
5. The Role of Helicobacter pylori Outer Membrane Proteins in Adherence and Pathogenesis

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Novel Potential Peripheral ECM Biomarkers for Prognosis and Therapeutic Approaches in Liver Cirrhosis Based on Microarray Analysis

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Liver cirrhosis is a significant global health concern, with incident cases rising by 16.7% from 2009 to 2019 and contributing to nearly 1.5 million deaths globally by 2019 (Lan et al., 2023). Its pathogenesis involves excessive collagen deposition and extracellular matrix accumulation, leading to hepatocellular dysfunction and portal hypertension. Consequently, the identification of reliable biomarkers for diagnosis and prognosis has become paramount in clinical research (Ismaiel et al., 2024). To address this urgent need, we utilized microarray analysis to examine gene expression profiles and identify differentially expressed genes (DEGs) associated with disease progression. Dataset GSE97083, obtained from the Geo database, includes 10 male Wistar rat liver tissue samples, five normal control livers, and five cirrhotic liver models with DEN/TAA treatment (Romualdo et al., 2017). GEO2R analysis confirmed dataset normalization, and DEGs were screened based on adjusted P-value < 0.05 and |logFC| ≥ 1. A Protein-Protein Interaction Network of DEGs was constructed using the STRING database, beside Cytoscape software identified 12 hub genes (Agxt, Plg, Apoa5, Vtn, Akr1c6, Slc27a5, Serpinc1, Lipc, Lcat, Hrg, Pon1, Mbl1) based on betweenness centrality (BC), closeness centrality (CC), eigenvector centrality (EGC), and degree centrality (DC). Expression locations of the hub genes were identified using UniProt and DAVID databases, with genes expressing intracellularly excluded. Based on literature review, from the eight genes with secreted products to ECM and expression in liver cells reported by Enrichr, a panel of four genes—Plg, Apoa5, Mbl1, and Serpinc1—was suggested as putative diagnostic and prognostic biomarkers for liver cirrhosis and potential therapeutic targets to mitigate its pathological features. The plasminogen (Plg) gene may be involved in processes related to liver cirrhosis and hepatocellular carcinoma (HCC). Overexpression in HBV-induced HCC is hypothesized to promote tumor progression via the Hippo signaling pathway through SRC activation (Hu et al., 2021). The Apolipoprotein A5)Apoa5(gene, which is primarily associated with triglyceride metabolism, may enhance triglyceride hydrolysis and remnant lipoprotein clearance in plasma. Its intracellular role could potentially contribute to triglyceride-rich lipid droplet accumulation, aggravating non-alcoholic fatty liver disease (NAFLD) (Ress et al., 2011; Forte and Ryan, 2015). Elevated Apoa5 expression is suggested to correlate with hepatic triglyceride storage in human and rat NAFLD livers (Feng et al., 2015). The Mannose-Binding Lectin (MBL) gene may play a role in immune defense and complement activation via the lectin pathway (Lo, Austin and Freeman, 2018). Mutations in the MBL gene, particularly at codon 54, are thought to be associated with the progression of chronic hepatitis B and increased risks of cirrhosis and spontaneous bacterial peritonitis (Yuen et al., 1999). Lastly, the Serpin family C member 1 (Serpinc1) gene is hypothesized

to play a crucial role in regulating blood coagulation, modulating inflammatory responses, and maintaining vascular integrity, which may collectively influence hemostasis and fibrosis. Its potential role in platelet activity and cellular interactions suggests it could be significant in managing complications such as coagulopathy and variceal bleeding in cirrhotic patients (Kademani, Subramanian and Nelaturi, 2024; Pontisso and Parola, 2024).

Keywords: biomarker, liver cirrhosis, hub gene, PPI network

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Integrating Biological Networks and Deep Learning for Microbe-Disease Prediction

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The human microbiome, consisting of diverse microbial communities, plays a crucial role in health and disease. Identifying associations between microbes and diseases holds the potential to revolutionize diagnosis, prevention, and treatment strategies. Despite the high accuracy reported by many predictive models in microbe-disease association tasks, their evaluation frameworks often overlook biases and distributional challenges inherent in the datasets, resulting in unreliable performance metrics. To overcome this limitation, we propose a novel evaluation framework that systematically adjusts for node degree distribution, ensuring a more rigorous and reliable assessment of model performance. Furthermore, we present a predictive model that leverages deep artificial neural networks and graph learning algorithms, designed to be improved under these new evaluation criteria for microbe-disease association prediction. A comparative analysis with six state-of-the-art models shows that our approach consistently outperforms existing methods across both traditional and newly proposed evaluation frameworks. Our proposed evaluation framework introduces a sampling algorithm to construct test sets with nearly balanced numbers of positive and negative associations for each node, offering a more unbiased and comprehensive evaluation. Our new predictive model integrates heterogeneous biological network data through the MDKG knowledge graph, which encompasses nine biological entities, including microbes and diseases, connected by 39 distinct edge types. We employ the Node2Vec algorithm to extract meaningful features from this knowledge graph, generating rich feature representations for microbes and diseases. These features are then processed by a deep artificial neural network specifically designed for microbe-disease association prediction. In our study, we used the HMDAD dataset, a widely utilized resource that compiles known microbe-disease associations from previous research articles. This dataset is the most commonly used benchmark in this problem domain, ensuring comparability and relevance. Our model achieved an average AUC of 0.91 in the traditional evaluation framework, outperforming or matching existing models. Under the proposed evaluation framework, it achieved an average AUC of 0.73, surpassing the performance of competing models, which ranged between 0.41 and 0.67. Using the Wilcoxon signed-rank test, we demonstrated that our model significantly outperforms all other models in the new evaluation framework and outperforms five models in the traditional framework, achieving equal performance with the sixth.

Keywords: microbe-disease, deep learning, association prediction

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Exploring the Antibiotic Potential of Micromonospora

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The term "antibiotic" must be redefined because it is often used inaccurately and primarily reflects an outdated definition. Conventional understanding emphasizes antimicrobial properties. However, some data suggest that antibiotics are better characterized as "pluripotent" agents due to their multifunctional qualities. This perspective enhances our understanding by illustrating that the emergence of antibiotic resistance is not confined to their activity against bacteria but should also consider other roles, such as antifungal, anticancer, and antiviral properties. Micromonospora, a genus in the Actinomycetota phylum, is well-known for its biosynthesis of medicinal bioactive compounds (Yan et al., 2022). Non-ribosomal peptides (NRPs), a significant source of secondary metabolites with various biological functions, play a crucial role in this process (Süssmuth & Mainz, 2017). Identifying novel compounds and enhancing our understanding of their biosynthesis pathways via genome mining techniques are essential for developing new therapeutic agents (Bauman et al., 2021). In this study, we analyzed the whole genomes of nine species of the Micromonospora genus using antiSMASH, a bioinformatics platform designed primarily for identifying and characterizing biosynthetic gene clusters (BGCs) (Blin et al., 2023). Microorganisms' annotations were sourced from BacDive (Bacterial Diversity Database), the largest repository providing standardized information on bacterial and archaeal strains (Schober et al., 2024). Of the 185 identified regions containing a BGC, 45 were linked to NRP production, with their applications further extracted from PubChem, ChEBI, and relevant articles. The wide range of applications includes antibacterial (42%), siderophore (12%), antitumor (18%), antifungal (6%), antiprotozoal (6%), neuroprotective (3%), antiviral (3%), immunosuppressive (3%), antioxidant (3%), and anti-cardiovascular (1%). Some compounds, such as Lymphostatin (an immunosuppressive compound), are distributed among all nine Micromonospora species. Concurrently, certain compounds were identified only within a single species, including Capreomycins, Clifednamide A, Clipibicyclene, Coprisamide, Disgocidine, Enduracidin, Enteromycin, Frankobactins, Griseobactin, Kosinostatin, Pacidamycins, Telomycin, Trichrysobactins, and Tyrobetaine. Significantly, over half of these bioactive compounds are classified as hybrid polyketide-NRP structures, exhibiting considerably greater bioactive potential than their NRP counterparts. For instance, hybrid compounds encompass neuroprotective, antifungal, antiviral, immunosuppressive, antioxidant, and anti-cardiovascular activities, along with nearly all antitumor properties. In contrast, hybrids account for half of the identified compounds related to antibiotics and siderophores. This study elucidates the biological roles and microbial annotations within the Micromonospora genus. It also emphasizes the genus's contribution to the production of bioactive chemicals with biotechnological applications, paving the way for discovering novel therapeutic medicines.

Keywords: genome mining, Micromonospora, antibiotics, NRP, antiSMASH, BacDive.

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Astrocyte-Mediated Regulation of Neurogenesis in the Anterior Hippocampus of Alzheimer's Disease Patients

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by cognitive decline and memory loss, particularly affecting the hippocampus, a key region for memory and emotional regulation. The anterior hippocampus plays a crucial role in neurogenesis—the generation of new neurons—which is disrupted in AD, contributing to cognitive impairments (Tobin and Musaraca, 2019). Understanding neurogenesis regulation is essential for developing potential treatments for AD, as restoring neurogenic processes could alleviate cognitive decline (Young, 2020). Astrocytes, a type of glial cell, are critical in neurogenesis by maintaining the neural stem cell niche, managing inflammation, and providing metabolic support (Medeiros and LaFerla, 2013). This study investigated astrocyte-specific contributions to neurogenesis in the anterior hippocampus of AD patients using trajectory analysis and protein interaction networks based on single-cell RNA sequencing (scRNA-seq) data. scRNA-seq data from the GSE175814 dataset, which includes samples from AD patients and age-matched controls, were used to characterize neurogenic processes in the anterior hippocampus. Seurat (v5.1.0) and Harmony packages facilitated UMAP visualization, clustering, and integration to identify major cell populations. Cell type annotation was performed with the ScType package. Astrocytes were selected for trajectory analysis due to their crucial role in neuroinflammation and metabolic support, significantly altered in AD. Trajectory analysis using Monocle3 package reconstructed cellular developmental paths, revealing differentiation trajectories between normal and AD astrocytes and the gene expression changes governing neurogenesis in AD. Differentially expressed genes (DEGs) identified from this astrocyte-specific analysis overlapped with known neurogenesis-regulating genes and were further analyzed using the STRING webserver. Ten hub genes identified using CytoHubba plugin in Cytoscape from Protein-Protein interaction, included STAT3, CDH1, FGF2, CXCL12, EGFR, HIF1A, IL1B, TGFB1, MET, and PTEN, which were studied for their regulatory roles in neurogenesis. The study identified several disrupted pathways affecting neurogenesis in AD. The MAPK/ERK pathway, crucial for neural stem cell proliferation and differentiation, is impaired in AD due to dysregulation by factors such as FGF2 and EGFR (Zhu and Lee, 2002). The PI3K/AKT pathway, regulated by PTEN and influenced by growth factors, is also disrupted, compromising cell survival and proliferation (Long and Cheng, 2021). STAT3-mediated JAK-STAT signaling integrates cytokine signaling and neuroinflammation, exacerbating neurogenic impairment in AD (Rusek and Smith, 2023). The TGF-beta pathway, involving TGFB1, modulates

neurogenesis and neuroprotection but is disrupted (Wyss-Coray, 2006), while the hypoxia response pathway regulated by HIF1A supports cellular adaptation to hypoxic conditions common in AD brains (March-Diaz and Lara-Ureña, 2021). Its perturbation further impairs neurogenesis. Key interactors such as CDH1, CXCL12, IL1B, and MET were identified as critical nodes in astrocyte-mediated neurogenesis regulation, shedding light on AD pathogenesis. This study emphasizes the role of astrocytes in regulating neurogenesis in the anterior hippocampus of AD patients. Restoring neurogenic processes through targeting astrocyte-mediated pathways offers potential therapeutic strategies to alleviate cognitive decline in AD. Trajectory analysis of astrocyte differentiation revealed dynamic gene expression changes related to neurogenesis and AD pathogenesis, supporting therapeutic approaches targeting astrocyte pathways to enhance neurogenesis and combat cognitive decline in AD.

Keywords: Alzheimer's Disease, Neurogenesis, Astrocytes, Anterior Hippocampus, Single-cell RNA Sequencing

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Investigating the Potential of Natural Small Molecules as BDNF Mimics for Neurodegenerative Disease Treatment: A Molecular Docking Study with TrkB Receptor

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Neurodegenerative diseases, such as Alzheimer's and Parkinson's, are characterized by the progressive degeneration of neurons and dysfunction of the nervous system. A major contributing factor in these diseases is the reduced level and activity of Brain-Derived Neurotrophic Factor (BDNF), a protein essential for neuronal survival, growth, and function. BDNF exerts its effects by binding to its primary receptor, TrkB, which triggers downstream signaling pathways that protect neurons from degeneration and enhance neuroplasticity. In neurodegenerative diseases, the diminished activity of BDNF contributes to neuronal apoptosis, impaired synaptic plasticity, and reduced cognitive function, making it a promising therapeutic target (Palasz & Wysocka, 2020; Colucci-D'Amato & Speranza, 2020). Given the critical role of BDNF in maintaining neuronal health, mimicking its neurotrophic effects through small molecules presents a novel and potentially effective therapeutic strategy (Kowiański & Lietzau1, 2018; Balakrishnan, Jannat, & Choi, 2024). The primary objective of this study is to explore the potential of several natural small molecules as BDNF mimics by assessing their ability to activate the TrkB receptor. The molecules selected for investigation—Quercetin, Berberine, Baicalein, Oleuropein, Apigenin, Curcumin, and Resveratrol—are known for their antioxidant, anti-inflammatory, and neuroprotective properties. They have also demonstrated therapeutic promise in various in vitro and in vivo models of neurodegeneration (Aliakbari & Shabani,2024; Ma et al., 2014; Costa & Garrick, 2016; Schiavone & Trabace, 2018; Tian, Sharma, & Dai, 2023). To simulate interactions between these compounds and the TrkB receptor, the 3D structure of the TrkB receptor (PDB ID: 1HCF) was retrieved from the Protein Data Bank (https://www.rcsb.org), and the structures of the small molecules were obtained from the PubChem database (https://pubchem.ncbi.nlm.nih.gov).These compounds—Quercetin (CID: 5280343), Berberine (CID: 2353), Baicalein (CID: 5281605), Oleuropein (CID: 5281544), Apigenin (CID: 5280443), Curcumin (CID: 969516), and Resveratrol (CID: 445154)—were optimized using VEGA ZZ software. The TrkB receptor was also prepared for docking using AutoDockTools (ADT, version 1.5.7). Molecular docking simulations were conducted with AutoDock Vina (version 1.1.2). The simulations allowed for the evaluation of docking scores, binding modes, and the stability of ligand-TrkB complexes (Scior, 2021). The results revealed that Quercetin, Berberine, and Baicalein exhibited the strongest binding affinities for the TrkB receptor, with docking scores of -6.5 kcal/mol. These findings indicate that these natural compounds may effectively mimic BDNF's action and activate TrkB receptor signaling pathways, providing neuroprotective effects similar to those of BDNF.

In conclusion, this study highlights the potential of natural small molecules as promising candidates for therapeutic development aimed at mimicking BDNF and providing neuroprotection in neurodegenerative diseases. The findings from this in silico study provide a strong foundation for further in vitro and in vivo studies to validate these results.

Keywords: BDNF Mimetics, small molecule, TrkB, molecular docking

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ICB13 -1232

Study population structure in Iranian Arab horse breed by principal component analysis (PCA) and discriminant analysis of principal components (DAPC) methods using genomic data

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The preservation and reproduction of native animal species in any country is of considerable value and importance. Iran has native horse breeds that have deep roots in Iranian culture and civilization, so their protection is very necessary. There are various lineages in Iranian Arab horse populations that are usually classified based on morphological and genetic characteristics. The most important lineages include Kohailan, Hamdani, Seglavy, Jolfan, Shuiman, Abyan, Khersan, Hedban or hadian, Malihe, Nasmani, and Vadne. The aim of this study was to use two methods, principal component analysis (PCA) and discriminant principal component analysis (DAPC), to investigate the population structure of Iranian Arabian horses using SNP markers. . For this purpose, 109 Iranian Arabian horses from the Hamdani(19), Kahilan (9), Abyan(13), Seglavy(12), Khersan (53) and Shuiman (3), lineages were sampled. These lineages were identified based on information from the Arabian Horse Pedigree Book of the Islamic Republic of Iran Equestrian Federation. The samples were genotyped using Illumina SNP 40k chips. Data quality control steps were performed using Plink 1.9 software and none of the samples were deleted, but at maf 0.03 we saw the deletion of 2347 SNPs. Then, Python software was used to analyze the data. The results showed that in both analysis methods, the Khersan and Shuiman lineages were completely separated from other lineages, and the Abyan and Kehilan lineages were clustered close to each other, and the Seglavy and Hamdani lineages were also clustered close to each other, and DAPC provided a better picture of the relationship between lineages, which was observed using a Box plot between lineages. Given the small number of samples from different lineages such as Shuiman and the unavailability of phenotypic information of the samples, It is expected that in the future, with this information in hand, more extensive research will be able to be conducted on the Iranian Arabian horse breeds.

Keywords: population structure, iranian arab horse, PCA and DAPC methods, SNP markers

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Exploring Genetic Variability: A Bioinformatics Approach to Analyzing Reported SNPs in the cagA Gene of Helicobacter pylori

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Single nucleotide polymorphisms (SNPs) within the cagA gene of Helicobacter pylori influence the bacterium's virulence by altering the amino acid sequence and phosphorylation sites of the CagA protein, affecting its interactions with host proteins. These variations are linked to clinical outcomes such as increased gastric cancer risk and severe inflammatory responses. Understanding cagA SNPs aids in unraveling H. pylori pathogenic mechanisms and developing targeted therapies and vaccines, emphasizing the need for personalized treatment approaches. In this study, SNPs in the cagA gene were identified by comparing the sequences obtained from 30 gastric biopsy samples of patients diagnosed with H. pylori infection to validated SNPs with known positions on the reference gene HP0547. The analysis of these sequences, which were acquired through next-generation sequencing, was conducted using BLAST to detect the SNPs. The analysis revealed a mix of conserved and variable SNP patterns among the sequences. It was found that SNPs such as G2701A and G3100A were consistently present in all samples, while others, such as C1279A and C581T, were uniformly absent. Additionally, it was observed that some SNPs exhibited variable distribution; for instance, G154A was identified in only one sample, whereas A1280G was detected in all but one sequence. Variations in SNPs within the cagA gene can result in structural and functional changes in the CagA protein, which is a critical virulence factor of H. pylori. An understanding of these genetic differences is provided, offering valuable insights for the tailoring of antibiotic treatments and the development of vaccines aimed at specific H. pylori strains prevalent in Iran. The need for region-specific studies to enhance the management of H. pylori-related diseases is emphasized by this research.

Keywords: Helicobacter pylori، SNP، cagA

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Therapeutic Biomarker Identification in Methotrexate-Treated Rheumatoid Arthritis Patients

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Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation and joint destruction, significantly impacting patients' quality of life [1]. Methotrexate (MTX) remains the cornerstone of RA treatment; however, variability in therapeutic response presents a challenge, prompting researchers to explore molecular predictive biomarkers to optimize patient outcomes [2]. non-coding RNAs, such as miRNAs have recently gained attention due to their regulatory roles in gene expression [3]. Emerging evidence suggests that non-coding RNAs play crucial roles in autoimmune diseases, including RA. Gene expression profiles (GSE45867) were downloaded from the Gene Expression Omnibus. Differentially expressed genes and miRNAs were identified using the GEO2R analysis. Enrichr was used to obtain the pathway and biological process. miRTarbase database was used to receive miRNAs. The miRNA-mRNA interaction was reconstructed with Cytoscape software. Functional enrichment analysis identified several pathways and biological processes associated with PIP, including Interferon Signaling, Immunoregulatory Interactions between Lymphoid and Non-Lymphoid Cells, Signaling by Interleukins, Transforming Growth Factor Beta (TGF-β) Family Signaling, and Neutrophil Degranulation. The results of this study showed that miR-124-3p, miR-101-3p, miR-16-5p and miR-26b-5p have the most important regulatory roles. This study identifies that these miRNAs may serve as therapeutic biomarkers in predicting the response to methotrexate treatment.

Keywords: Rheumatoid Arthritis; Methotrexate; regulatory network

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Comprehensive Computational Strategies for Multi-Target Drug Discovery in Inflammatory Bowel Disease Utilizing Bioactive Compounds

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Inflammatory bowel disease (IBD) is a chronic gastrointestinal disease that includes ulcerative colitis and Crohn's disease. Based on the pathogenesis of the disease, simultaneously targeting inflammation and the epithelial barrier could have an effective role in improving the symptoms of this disease. Previously, each of these therapeutic targets, PDE4, PHD1, and PHD2, has been investigated separately. But finding small molecules that can inhibit multi-targets is so essential for treating diseases with multi-pathways like IBD. The enzyme phosphodiesterase 4 (PDE4) plays an important role in inflammation. PDE4 is involved in the production of inflammatory cytokines by converting cAMP to AMP. Inhibition of this enzyme leads to inhibition of inflammatory cytokine production and the production of anti-inflammatory cytokines. Also, It is demonstrated that inhibition of prolyl hydroxylase domain enzymes ½ (PHD1/2) increases HIF-a levels and improves the epithelial barrier following the expression of protective factors such as mucin and β-defensin. Therefore, inhibition of PDE4B and PHD1/2 can be a potential therapeutic target for the treatment of IBD and the improvement of pathological symptoms in it. In this study, after Virtual Screening, Molecular Docking, and Molecular Dynamics, our results introduced 5 compounds including Cassiamin C, Ginkgetin, Hinokiflavone, Sciadopitysin, and Sojagol as new drug candidates for the treatment of IBD. All compounds inhibit all three targets more effectively than the reference ligands, except for Sojagol, which shows lower activity against PDE4B. Future experimental studies can validate these findings.

Keywords: inflammation, inflammatory bowel disease, , anti-inflammation, multi-target drugs

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ICB13 -1237

A Novel Approach to Antimicrobial Susceptibility Testing: Automated Disk Diffusion Analysis with Smartphone Cameras and Deep Learning Techniques

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Antibiotic diffusion tests are essential in clinical microbiology for assessing microbial resistance and antibiotic efficacy. These tests measure inhibition zones around antibiotic disks to determine microbial susceptibility. Traditional methods can be slow and error-prone, particularly when processing large sample sets, underscoring the need for a fast, automated approach. We developed a high-speed automated analysis system using OpenCV and deep learning techniques to detect and analyze antibiotic diffusion disks on plate images. The system utilizes OpenCV's contour detection for inhibition zone identification and measurement, Canny and Sobel filters for edge detection and image quality enhancement, and UNet for disk segmentation and OCR to read antibiotic labels. The method achieved a 98.7% accuracy rate in detecting and labeling antibiotic disks, accurately identified inhibition zones, and provided precise measurements. Cross-referencing with Clinical and Laboratory Standards Institute (CLSI) guidelines confirmed its effectiveness in determining antibiotic resistance or susceptibility. The system demonstrated rapid processing speeds, maintaining high accuracy even with large sample volumes.This approach provides a scalable, efficient solution for antibiotic diffusion test analysis, minimizing human error and supporting high-throughput needs in clinical and research settings. Future work will enhance adaptability to different disk formats and antibiotic types, expanding its potential for broader testing applications[1].

Keywords: deep learning،image processing،disk diffusion

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Age-Related Gene Expression Changes in Microglia: Insights from the Nygen platform and Brain-Aging Atlas

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Aging is characterized by the accumulation of molecular and cellular damage over an organism's lifespan, leading to physical deterioration and an increased risk of diseases (Filipa Gaspar-Silva et al., 2023). Brain aging involves physiological, structural, and functional changes that contribute to cognitive decline and the risk of neurodegenerative diseases (Ana Cordeiro et al., 2024). Microglia, as key non-neuronal cells, perform immune surveillance, synaptic pruning, and debris clearance, playing an essential role in maintaining neural health (William E. Allen et al., 2023). In this study, we used data from the Brain-aging-atlas on the Nygen platform, a comprehensive resource of single-cell transcriptomic data, to investigate aging-associated changes in the brain. This dataset includes gene expression profiles, spatial distributions, and pathway-level insights across various brain cell types, including neurons, astrocytes, and microglia, sampled from the frontal cortex and striatum of young (4 weeks) and aged (90 weeks) mice. Differential expression analysis revealed three key differentially expressed genes (DEGs) in aged microglia: Adamtsl1 (fold change: 74.47, score: 0.965), Kcna1 (fold change: 56.52, score: 0.964), and Klhdc4 (fold change: 53.05, score: 0.965), highlighting significant molecular changes with aging. ADAMTSL1 is a secreted glycoprotein in the ADAMTS family, playing a key role in extracellular matrix (ECM) organization, synaptic maintenance, and cellular adhesion. A GWAS study identified it as a significant genetic variant linked to Alzheimer's and Parkinson's diseases (Gabel et al., 2018). KCNA1, a voltage-gated potassium channel, is essential for neuronal excitability and synaptic transmission. RNA editing of KCNA1 by ADAR2 has been associated with Alzheimer's disease and neuronal signaling dysregulation during aging (Tassinari et al., 2023). KLHDC4 was significantly upregulated in aged microglia, indicating involvement in ubiquitin signaling, innate immunity regulation, and lysosomal and autophagy pathways, all linked to neurodegenerative processes (Aguilan et al., 2023). Its CpG methylation site (cg08734237) strongly correlated with cognitive aging, suggesting an epigenetic regulatory role in neurological signaling and neurodegeneration (Mohammadnejad et al., 2021). These findings provide valuable insights into the molecular mechanisms of brain aging, highlighting the significant roles of ADAMTSL1, KCNA1, and KLHDC4 in microglial function and their associations with neurodegenerative processes. The identification of these genes underscores the importance of extracellular matrix remodeling, neuronal excitability regulation, and epigenetic modulation in aging and age-related diseases such as Alzheimer's and Parkinson's disease. Future research should validate these pathways in animal models and human studies, paving the way for targeted interventions to address cognitive decline and

neurodegeneration in aging populations.

Keywords: brain aging, neurodegeneration, cognitive decline, Adamtsl1, Kcna1, Klhdc4

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Genome-Wide Bioinformatics Discovery and Validation of Long-Core SSR Markers for Alfalfa (Medicago sativa): Applications in Genetic Diversity and Seed Authentication

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The genetic diversity of alfalfa (Medicago sativa) significantly impacts forage and seed quality, making the authentication of its populations and varieties crucial for farmers and seed suppliers. This study employed genome-wide bioinformatics approaches to discover and validate SSR (simple sequence repeat) markers, with a focus on long-core SSR motifs, for distinguishing alfalfa populations and ensuring seed authenticity. Genomic data were obtained from the NCBI database (Project: PRJNA685277) and the Chinese Academy of Genomic Sciences (GWH: GWHBECI00000000), with the tetraploid alfalfa genome estimated at 3.1 Gb. Using Geneious R9 and Phobos software, repetitive sequences were identified, and over one million microsatellite loci were screened. Key criteria for marker selection included long-core SSR motifs (3–6 nucleotides), uniform genome-wide distribution (at least one locus per chromosome), absence of repetitive flanking sequences (within 200 bp), and loci shorter than 300 bp. Special emphasis was placed on selecting loci within 10 Mb of chromosome ends, where recombination rates are higher, enhancing their utility for genetic studies. A total of 464 loci met these criteria, with long-core SSR motifs prioritized for their higher polymorphism and stability. From these, 23 primer pairs were synthesized after rigorous screening for multiplexing compatibility, secondary structure stability ($\Delta G > -9$ kcal/mol), and absence of off-target binding. PCR optimization and validation were performed using DNA from 30 seeds of each alfalfa population. Among the 23 primer pairs, 12 demonstrated high reproducibility, polymorphism, and the ability to differentiate alfalfa populations effectively. These markers, enriched with long-core SSR motifs, were distributed across all chromosomes, with allele sizes ranging from 170 to 340 bp, ensuring broad applicability for genetic diversity studies. This study highlights the power of bioinformatics-driven approaches in developing SSR markers for alfalfa breeding and seed authentication. The selected markers provide a robust toolset for genetic diversity analysis, population differentiation, and quality control in alfalfa cultivation. Future applications include marker-assisted breeding and the development of high-yield, stress-resistant alfalfa varieties.

Keywords: Alfalfa, long-core SSR motifs, Medicago sativa, seed authentication, bioinformatic

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