ABSTRACT BOOK

9 TH INTERNATIONAL BAU DRUG DESIGN CONGRESS

NOVEL METHODS AND EMERGING TARGETS IN DRUG DISCOVERY & PATENTED DRUG DEVELOPMENT

İSTANBUL - TÜRKİYE

NOVEMBER 29 – DECEMBER 02, 2023

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INVITED SPEAKERS

IS-1
BÜLENT ÖZPOLAT
Short Biography

Dr. Ozpolat has expertise in Immunology, Cancer biology, Gene therapy, Experimental Therapeutics, Nanotechnology, and development of targeted cancer therapeutics. After getting his M.D. degree Dokuz Eylul University, Izmir, Turkey, Dr. Ozpolat received his Ph.D. degree in Immunology from The University of Texas- MD Anderson Cancer Center Houston, TX, USA and completed post-doctoral training on Cancer biology, cancer genetics, nanotechnology, targeted cancer therapeutics.at MD Anderson Cancer. After serving as a faculty for more than 15 years at MD Anderson Cancer Center and Dr. Ozpolat currently works as a Professor at Houston Methodist Research institute Houston, USA and at Neil cancer Center where he leads Innovative Cancer Therapeutics. Dr. Ozpolat's translational research focuses on 1) identification of novel molecular targets and oncogenic pathways in highly aggressive cancers such as triple-negative breast cancer, drug-resistant ER+ and HER2+ breast cancer, pancreatic, lung and ovarian cancers, melanoma 2) Development of highly targeted therapeutics for oncogenic survival pathways including EF2K, AXL, FOXM1, KRAS and FOXM1, and non-coding oncogenic RNAs (microRNAs and long-noncoding RNAs) as potential targets using gene silencing therapies and small molecule inhibitors. Dr. Ozpolat has 5 patents for development of targeted therapeutics and published more than 137 publications (H-index 39) (90 research papers, 20 book chapter sand 24 review articles) in peer-reviewed high impact journals.

Abstract

IS-2
THOMAS MAVROMOUSTAKOS
Short Biography

I have completed my Bachelor studies in the Chemistry Department of National Kapodistrian University of Athens, in 1985. I then moved to University of Connecticut, USA where I pursed graduates studies in the Medicinal Chemistry Section of Pharmacy Department. After continuing with one more year Postgraduate studies with Professor A. Makriyannis I returned back to Athens in 1991. I served as a research director in the Laboratory of Molecular Analysis of Institute of Organic and Pharmaceutical Chemistry in the National Hellenic Research Foundation for sixteen (17) years. In 2007 I was elected as an Associate Professor in the Laboratory of Organic Chemistry and in 2012 I was promoted to Full Professor. I served also for several years as a President to a Research Center in Cyprus oriented to develop new natural products. I was awarded by Academy of Greek science for the best research in 1998 related to hypertension. I have received fellowships from Royal Society, Fulbright and Institute of Federal Fellowships in Greece to exert research activities in England, USA and Germany. I have been funded by several European and National Programs to exert my research activities. I have also been funded to use the European Facilities (i.e Trieste Elettra, BMRZ in Frankfurt, x-ray diffractometers in Graz Austria, NMR center in Ljubljana Slovenia). My research interests include: (a) Rational Drug Design; (b) Understand the molecular features responsible for drug activity through Molecular Docking, Molecular Dynamics and Quantitative Structure Activity Relationships; (c) Drug delivery aspects; (d) Drug;membrane interactions. I have been teaching for several years Organic Chemistry courses and the optional course of the Rational Design providing to students the principles that govern the production of a new drug. I have collaborated with Synergix company writing a part of Molecular Conceptor that is now a commercial product. I have educated more than 70 graduate students and 60 undergraduate ones. I published 323 articles and chapters with h-index=39. I have also published more than 150 articles in national Greek scientific and public journals. I had received European and National funding's as Principal Investigator and Participant. I gave many invited speeches in International and National Conferences as well as Theology Speeches as I have also gained a Ph.D. degree in Theology. I served in many European and National committees for proposal evaluations. I served also as an evaluator in high esteem journals (J.Med. Chem., European J. Med. Chem., Mini Reviews of Medicinal Chemistry, Current Medicinal Chemistry, Biophysica Biochimica Acta etc). I served in more than 70 committees for obtaining Ph.D. and Msc diplomas and had educated more than 100 ptyxiakes (undergraduate) research works.

Abstract

Discovery of Old and New Drugs

The discovery of a drug is a tedious and long process. It starts usually from in silico studies and leads to successful clinical ones. Few successful examples from the existing drugs will be given in order to drive important messages and provide impetus to young researchers for applying intensive effort to synthesize new potential drugs. Additional examples will be given from our research activity referred to AT1 antagonists that act as antihypertensive drugs, metallotherapeutics that can act as antimicrobial drugs, MAO inhibitors and anticancer agents. Chemist resembles the painter that can paint its own picture that contains the approach and content for developing a new drug. Examples fromour research aim to show the versatility that can be applied in the rational drug design.

IS-3
CANAN ATILGAN
Short Biography

Canan Atılgan received her BS degree from the Department of Chemical Engineering of Boğaziçi University in 1991, and her PhD degree from the same institution in 1996. She was a postdoctoral research fellow at the Supercomputer Computations Research Institute of Florida State University through 1999. Since then, she has been a faculty member at the Faculty of Engineering and Natural Sciences of Sabancı University. She is the recipient of Boğaziçi University PhD Thesis (1996), TÜBİTAK Encouragement (2002), Turkish Academy of Sciences Young Scientist (2004), L'Oréal Turkey For Women in Science (2005) Awards. She is an elected member of the Science Academy and is the current President. She is also Biophysical Society's Ambassador to Turkey.

Dr. Atılgan's expertise is on the computational and theoretical investigation of complex molecules. Her focus is on disclosing dynamical features of soft matter systems that lead to unique behavior identified, but not explained, through experiments. Protein dynamics, manipulation of protein conformations, understanding the antibiotic resistance problem at the scale of the three-dimensional structure of single proteins are areas of current interest for her.

Abstract

Making Sense of Antibiotic Resistance in the TolC Efflux Pump

We study the dynamics of homotrimeric TolC, an outer membrane efflux protein in Gram-negative bacteria that has a critical role for defence against antibiotics. We carry out extensive molecular dynamics (MD) simulations on this 140 Å long channel. In particular, the potentials of mean force calculated via a series of steered MD simulations for the passage of carbenicillin, piperacillin, or oxacillin provide a molecular level explanation for the varied response observed in deep mutational scanning experiments in the presence of these three beta-lactam antibiotics. We conclude by offering design strategies for derivatives of these molecules so as to bypass antibiotic resistance that otherwise emerges in the efflux pump.

IS-4
HASAN DEMİRCİ
Short Biography

I completed my B.Sc. at Bosphorus University in 2002 and later obtained a Ph.D., in Molecular Biology, Cell Biology, and Biochemistry at Brown University in 2007. Before joining Koc University in August 2019, I was a member of the Biosciences Division at SLAC National Accelerator Laboratory and affiliated with the Non-Periodic Imaging group at Stanford PULSE Institute. My research focuses on the structural biology of mutant prokaryotic ribosomes, where I am interested in characterizing the function and dynamics of these mutants, with an eye toward answering questions in the structure and dynamics of ribosomes resistant to some of today's commonly used antibiotics. My current research efforts also include methods development for time-resolved ambient-temperature X-ray crystallography of large and challenging biomacromolecules at 4th-generation light sources like the Linac Coherent Light Source at SLAC.

Abstract

IS-5
TUĞBA BAĞCI ÖNDER
Short Biography

Prof. Tuğba Bağcı Önder graduated from the Department of Molecular Biology and Genetics, Bilkent University in 2002. She then earned her Ph.D. degree in Neuroscience at Sackler School of Graduate Biomedical Sciences at Tufts University in 2008. She pursued her postdoctoral work at Harvard Medical School, Massachusetts General Hospital on the development of tumor-specific pro-apoptotic therapies in animal models of brain cancer. In 2012, she joined Koç University School of Medicine and established the Brain Cancer Research and Therapy Laboratory. Her research group is currently working on the understanding of epigenetic regulation of cell death, therapy resistance and progression of cancers. Her work is supported by FP7 Programme-Marie Curie Career Integration Grant, TÜBİTAK, TUSEB, Royal Society-UK and Koç University Research Center for Translational Medicine (KUTTAM). Prof. Bağcı Önder is also a recipient of Barbara Talamo Trainee (2008), UNESCO-L'oreal Women in Science (2013), BAGEP (2014), Sedat Simavi Heath Sciences (2021), International Cell Death
Society Rising Women in Science (2022), Eczacıbaşı (2023) and IBG Science Medal (2023) awards.

Abstract

IS-6
SERKAN KIR
Short Biography

Dr. Serkan Kır received his PhD degree from the University of Texas Southwestern Medical Center at Dallas in 2011. After his postdoctoral studies at Dana-Farber Cancer Institute/Harvard Medical School, he joined Koç University in 2017 as an Assistant Professor in the Department of Molecular Biology and Genetics. Dr. Kır's research interests include adverse effects of tumors on the host metabolism. His ongoing studies address tumor-induced hypermetabolism and the loss of adipose and skeletal muscle tissues. Dr. Kır identified PTHrP, a tumor-derived hormonal factor, as a prominent driver of energy wasting and adipose tissue atrophy. His recent work demonstrated that the EDA2R-NIK signaling promotes muscle atrophy in response to tumors. Kır laboratory continues to investigate molecular mechanisms underlying cancer-associated wasting.

Abstract

EDA2R/NIK Signaling Promotes Muscle Atrophy Linked To Cancer Cachexia

Skeletal muscle atrophy is a hallmark of the cachexia syndrome that is associated with poor survival and reduced quality of life in cancer patients. Muscle atrophy involves excessive protein catabolism and loss of muscle mass and strength. An effective therapy against muscle wasting is lacking as mechanisms driving the atrophy process remain incompletely understood. Our gene expression analysis in muscle tissues revealed upregulation of Ectodysplasin A2 Receptor (EDA2R) in tumor-bearing mice and cachectic cancer patients. Here we show that activation of EDA2R signaling promotes skeletal muscle atrophy. Stimulation of primary myotubes with EDA2R ligand, EDA-A2, triggered pronounced cellular atrophy via inducing the expression of muscle atrophy-related genes Atrogin1 and MuRF1. EDA-A2-driven myotube atrophy involved activation of the noncanonical NFκB pathway and depended on NIK kinase activity. While EDA-A2 overexpression promoted muscle wasting in mice, the deletion of EDA2R or muscle NIK protected tumor-bearing mice from the loss of muscle mass and function. Tumor-induced Oncostatin M upregulated muscle EDA2R expression and muscle-specific Oncostatin M Receptor (OSMR) knockout mice were resistant to tumor-induced muscle wasting. Our results demonstrate that EDA2R/NIK signaling mediates cancer-associated muscle atrophy in an OSM/OSMR-dependent manner. Thus, therapeutic targeting of these pathways may be beneficial in preventing muscle loss.

IS-7
MERT GÜR
Short Biography

Assoc. Prof. Mert Gur is currently serving as the Executive Director of the Computational Biomedicine & Biotechnology M.S. Program at the University of Pittsburgh (Pitt) School of Medicine (SOM), where he is a Visiting Associate Professor in the Computational and Systems Biology Department, and a tenured faculty at Istanbul Technical University (ITU) Mechanical Engineering (ME) Department. He earned his B.S. in ME (2006) and Ph.D. in Computational Science and Engineering (2010). His research focuses on Computational Structural Biology, Computational Biomedicine, and Mechanical Engineering. Dr. Gur boasts 16+ years of experience in biomolecular simulations and modelling gathered in various top academic and research institutions in Turkey and US. He published 34 papers in prestigious journals including Nature, Science and Nature Communications. He's been a principal investigator in 19 grants, spanning Turkey, US, and EU. His extensive leadership includes a total of five years of Vice Dean for undergraduate and graduate education at ITU. Dr. Gur has taught more 47 courses across various undergraduate and graduate programs, including those at IITU, the Pitt SOM graduate programs, and the Pitt ME undergraduate program. He received several awards in Turkey.

Abstract

IS-8
PETER KOLB
Short Biography

After studies in Biochemistry and Theoretical Chemistry at the University of Vienna and Karolinska Institute, I did my Ph.D. in Computational Biochemistry with Amedeo Caflisch at the University of Zurich. My work there focused on fragment-based docking for kinase ligands as well as chemoinformatic method development. After a short continuation as a postdoc in the same group, I joined the lab of Brian K. Shoichet at the University of California, San Francisco. This coincided with the publication of the structure of the first pharmacologically relevant G protein-coupled receptor, a unique opportunity to carry out one of the first studies of xray-structure-based ligand design for this protein class. Besides docking to GPCRs, I worked on the prediction of substrates for enzymes of unknown function and have as such been contributing to the Enzyme Function Initiative.
From April 1, 2011, until October 2016, I was an Emmy Noether Junior Group Leader at Philipps-University Marburg. From May 2013 until April 2017, I was chairing COST Action CM1207 "GLISTEN: GPCR-Ligand Interactions, Structures, and Transmembrane Signalling: a European Research Network", which connected more than 210 scientists from 31 European countries.
In March 2015, I was awarded the "Innovation Prize in Medicinal/Pharmaceutical Chemistry" by the Medicinal Chemistry sections of the Society of German Chemists (GDCh) and the German Pharmaceutical Society (DPhG). This was followed by the "Silver Jubilee Award" of the Molecular Graphics and Modelling Society (MGMS) in November of the same year.
Since October 2016, I have been Full Professor of Pharmaceutical Chemistry, funded by the Heisenberg programme of the German Research Foundation DFG. My Erdős number is 4.

Abstract

IS-9
VİKTORYA AVİYENTE
Short Biography

EDUCATION

Ph.D. in Chemistry Boğaziçi University 1983
M.S.in Chemistry Boğaziçi University 1977
B.S.in Chemistry Boğaziçi University 1973
High School Notre Dame de Sion French High School 1968

POST-DOC EXPERIENCE

Prof. Chava Lifshitz -Hebrew University
Prof. Ken Houk- University of California at Los Angeles
Prof. Michael Feig and Prof. Kenneth Merz – Michigan State University

PROFESSIONAL APPOINTMENTS AND POSITIONS

Professor Boğaziçi University 1995-2017
Emeritus Professor Boğaziçi University 2017-present

RESEARCH TOPICS

The following topics are being investigated in the Aviyente research group with computational methods involving the use of hybrid quantum and classical mechanics:

· Determination of the effects of structure, catalyst and solvent effects on polymerization rates in free radical polymerization reactions of acrylate derivatives.
· Examination of stereoselectivity in organic reactions
· Modelling mechanisms of removal of organic pollutants in wastewater
· Design of conductive materials for solar cells
· Effects of ionic liquids on hydrogenation reactions
· Design of potential drug molecules for photodynamic therapy
· Modeling of the catalytic properties of monoatomic metal catalysts

AWARDS AND GRANTS

· Grants from
Koç Foundation, 1979-1983
NATO, 1996-1999
NIH (FIRCA), 2000-2003
European Research Grant, 2005-2008
British Council Grant, 2004
Tübitak
Boğaziçi University Research Foundation
· Kriton Curi Award to the best paper in BU, 1998.
· Best master thesis awarded to the mentee Dr.Nurcan Şenyurt Tüzün, 1998.
· Best Ph.D. thesis award granted to the mentees
Dr.Bülent Balta 2003
Dr.Şaron .Catak 2008
Dr.Nihan Çelebi Ölçüm 2009
Dr.Burcu Çakır Dedeoğlu 2016
· Achievement Award in Research (Boğaziçi University Foundation) 2000 and 2010
· Ranked among the 100 Turks Directing the "Chemistry Science in Turkey" based on to the results of the "Golden Molecule", 2022.
· Published more than 200 articles in SCI indexed journals (h-index=30).

Abstract

Quantum-Mechanical Prediction Of The Dissociation Constants For Drug-Like Molecules

A high degree of ionization is essential for good water solubility of a drug molecule, and is required for drug-receptor interactions, whereas the non-ionized form improves a drug's lipophilicity, allowing the ligand to cross the cell membrane. The penetration of a drug ligand through cell membranes is mainly governed by the pKa of the drug molecule and the membrane environment.

First, we present an accurate protocol for the fast prediction of pKa's of carboxylic acids based on the linear relationship between computed atomic charges of the anionic form of the carboxylate fragment and their experimental pKa values. By reporting the calculated atomic charge of the carboxylate form into the linear relationship derived (M06L/6-311G(d,p) with R2 = 0.955 it should be possible to accurately estimate the amino acid's pKa's in a protein environment [1].

Next, with the aim of predicting the acetonitrile pKa's (pKa (MeCN)) of 8 drug-like thiazol-2-imine derivatives, we propose a very accurate and computationally affordable protocol. Highly well correlated pKa values were obtained with the isodesmic method (M06-2X/6-31G**-SMD) for nitrogen-containing heterocycles. The protocol established in this study is very satisfying and promising in terms of its applicability to more diverse drug datasets for future validations [2].

Finally several quantum mechanical-based computational approaches – charges, descriptors, isodesmic reactions - have been used with succcess in order to propose accurate protocols for predicting the pKa's of quinazoline derivatives, which constitute a very important class of natural and synthetic compounds in organic, pharmaceutical, agricultural and medicinal chemistry areas [3].

IS-10
ÖZLEM KESKİN
Short Biography

Currently, Ozlem Keskin is a professor in the Chemical and Biological Engineering Department at Koc University, Istanbul. Before, she was a postdoctoral fellow at the National Cancer Institute-National Institutes of Health, U.S.A., during 1999– 2001. She received her Ph.D. degree in Chemical Engineering in 1999, at Bogazici University, Istanbul. She is a member of the Science Academy, Turkey and 13ecipient of several awards including the TUBITAK Science Award, Turkey, 2012 and UNESCO-L'OREAL Co-Sponsored Fellowship Award for Young Women in Life Sciences, 2005. She is an associate editor in Plos Comp Biol, Plos One and BMC Structural Biology. Her work focuses on understanding the principles of protein–protein interactions (PPIs), the molecular mechanisms, physical principles and dynamics of macromolecular systems. She co-heads the Computational Systems Biology (COSBI) group aiming to construct protein interactomes by integrating atomistic details of protein-protein interfaces. (http://home.ku.edu.tr/~okeskin). Her work received more than 9000 citations according to Google scholar (as of 2019).

Abstract

IS-11
PHIL BIGGIN
Short Biography

Philip Biggin is a Professor in Biochemistry at the University of Oxford and a Tutorial Fellow of Lady Margaret Hall, Oxford. After a BSc in Computer-aided Chemistry and a D.Phil in ion channel biophysics, he undertook post-doctoral work with Senyon Choe at the Salk Institute in California with the award of a Wellcome Trust Prize International Travelling Fellowship. He returned to Oxford in 2000 and took up an RCUK fellowship in 2007 which converted to a lectureship in 2012. He became a Full Professor in 2016. His research interests are in the application of computational methods to understand biochemical problems with a particular focus on membrane proteins and their interactions with small molecules and drugs. He is a charted chemist (CChem), a member of the British Biophysical Society, the Biophysical Society and a Fellow of the Royal Society Chemistry (FRSC). He is also a founder member of Comp Chem Kitchen (http://compchemkitchen.org/), which organizes events open to academics and industry focussed on all aspects of computational chemistry. He was the Chair of the Molecular Graphics and Modelling Society for over ten years and sits on the committee of the high-end consortium for biomolecular simulation (HECBioSim). He served on Main Panel A (Biological Sciences unit of assessment) of the UK's REF-2021 exercise and is the Director of the Computational Discovery PhD programme.

Abstract

IS-12
ABDULKADİR KOÇAK
Short Biography

Dr. Kocak got his BSc degree from Ondokuz Mayıs University in 2004. With the scholarship from Turkish Ministry of Education, he has been awarded a PhD degree from Chemistry Department at University of Massachusetts-Amherst. He has been working in Chemistry department at Gebze Technical University in the field of physical chemistry. His research is focused on non-covalent interactions using molecular dynamics simulations at QM/MM/ML levels.

Abstract

Revisiting MMPBSA by Adoption of MC-Based Surface Area/Volume, ANI-ML Potentials, and Two-Valued Interior Dielectric Constant

ML potentials with their great capability of learning multidimensional potential energy surfaces (PES) at the DFT level are promising due to their efficiency and scalability to large systems. We explore the use of ANI-ML potentials in drug discovery so as to calculate binding/solvation free energies from molecular dynamics (MD) trajectories or rescoring molecular docking and quick estimation of the lowest energy conformer of a given small organic compounds/drugs. Previously, we have reported so called ANI_LIE method for binding and solvation free energies from post-MD simulations. Here, we thoroughly revisited molecular mechanics Poisson–Boltzmann surface area (MMPBSA) calculations by adoption of ANI-ML potentials in replacement of MM terms, the use of solvent-accessible surface area (SASA) and volume (SAV) values from the Monte Carlo sampling of the probe, and introducing two different interior dielectric constants for electrostatic interactions of protein–ligand (P–L) and polar solvation term in the MMPBSA calculations. We also present the future directions of ANI-ML potentials in drug discovery.

References:

1- E.Akkus, O. Tayfuroglu, M. Yildiz & A. Kocak, *The Journal of Physical Chemistry B,* **2023** *127* (20), 4415-4429, DOI: 10.1021/acs.jpcb.3c00834

2- M. Temel, O. Tayfuroglu & A. Kocak, *Journal of Computational Chemistry,* **2023**, 44(4), 559-569, DOI: 10.1002/jcc.27022

3- E. Akkus, O. Tayfuroglu, M. Yildiz & A. Kocak, *Journal of Chemical Information and Modeling* **2022** *62* (17), 4095-4106, DOI: 10.1021/acs.jcim.2c00601

IS-13
ENGİN ULUKAYA
Short Biography

He was graduated from Cerrahpasa Medical Faculty of Istanbul University (Turkey) in 1987, became a clinical biochemist in 1995 and then gained a PhD degree in Biochemistry and Molecular Biology from University of Leeds (the UK) in 2000. His research interests are anticancer drug development, translation of cell death into clinics, cancer stem cells, tumor chemosensitivity assays on spheroids. Among his achievements is the prediction of the response to chemotherapy in cancer patients by translating basic knowledge of apoptosis into medical oncology. He is the president of association for molecular cancer research (MOKAD) in Turkey. He is also a council member of EACR (European Association for Cancer Research) as well as full member of PathoBiology and PAMM groups of EORTC. He was awarded as the most promising laboratory physician of the year with the WASPALM Medal at WASPALM congress held in South Korea in 2003. He has 32 awards about 170 publications in peer-reviewed international journals with around 5713 citations with H index of 42 (Google Scholar, June 2023). He was the founding head of Health Sciences Institute, Dean of Health Science Faculty, and the vice rector of Istinye University. He has been the head of Molecular Cancer Research Center of the same university and a full professor of medical biochemistry since 2017.

Abstract

Critical Considerations on Preclinical Evaluation of Newly Synthesized Anticancer Compounds

Anticancer drug discovery is a long way which consists of mainly two parts, preclinical and clinical phases. The success rate of clinical phase is influenced by the quality of preclinical stages. Classically, one in 10.000 compounds may take a place on the shelves of a pharmacy after spending about 12-14 years of research. To enhance this ratio, the preclinical phase should rely on quality assurance-quaranteed, standardized and well-defined approaches. Although in silico designation of candidate drug molecules reduce the discovery period and seems trendy currently, the conventional methods are still in use. There are many considerations to be careful with. First of all, not all types of the compounds are good candidates for cancer drug development such as reactive molecules, thermal or photo labile molecules (e.g. mustards, acyl halides, α-halo carbonyl compounds, reactive Michael acceptors). High MW pegylated or similarly derivatized agents are also other examples for such compounds. Those compounds are called PAINS (Pan assay interfering compounds). Chemical or metabolic stability of the compounds is to be checked carefully in the first place. These are some examples of physicochemical properties of the compounds. However, mechanism of action studies is of particular importance. On the evaluation of antigrowth effect of any compound, it is desired to look for a spesificity towards certain type of malignancy. Otherwise, killing all kinds of cancer types may be a sign of a poison, rather than a proper anticancer drug. When it comes to the evaluation of mode of cell death, apoptosis-inducers may not be fasinating compounds as apoptotic machinary is known to be disrupted in cancer cells. Therefore, necrosis-inducers could be selected for the next stage, omitting apoptosis or autophagy-inducers. Elucidation of mechanism of action could also be the other tricky aspect. General cytotoxics are sometimes considered that they are at the end of the road. Therefore, efforts on new discoveries on such cytotoxics may be discussed. However, this may be wrong because the combination of targeted therapies with general cytotoxics seems to result in better outcomes, compared to targeted therapy alone or general cytotoxic alone. To me, development of general cytotoxics should carry on in a different approach (e.g. their being packed in a nanopartical). Animal experiments are the next stage before the human clinical phases. In silico and AI seem to replace this part. However, new experimental models are also emerging (e.g. The In Ovo Chick Chorioallantoic Membrane (CAM) Assay). It is a beautiful assay for the evaluation of compounds' antiangiogenic effects.

IS-14
NUR MUSTAFAOĞLU
Short Biography

Abstract

IS-15
SEDA ÜNSALAN
Short Biography

Seda ÜNSALAN graduated from Marmara University Faculty of Pharmacy in 1993. After graduation, she worked as an academician at the same university in pharmaceutical chemistry department. She had a scholarship from TÜBİTAK Münir Birsel Foundation during her PhD. She had been in Germany for two years. In the meantime she won a scholarship from DAAD (Deutscher Akademischer Austaushdienst). After returning from Germany, she took the exam for associate professor and passed it. At the end of 2008, she had a new position as clinical research chief at Nobel Pharmaceuticals and as of 2016, she managed the clinical research department of Nobel Pharmaceutical. In 2021, she retired from an amazing professional journey of 14.5 years in academia and 12.5 years at Nobel Pharmaceuticals. She has been teaching at Istanbul Medipol University Faculty of Pharmacy since 2022 as a professor.

Abstract

The Requirements for Bioequivalence Studies of Immediate Release Formulation

The comparative bioavailability assessment of two or more formulations of the same active ingredient to be administered by the same route is termed bioequivalence. In bioequivalence studies, the plasma concentration time curve is generally used to assess the rate and extent of absorption. Selected pharmacokinetic parameters and preset acceptance limits allow the final decision on bioequivalence of the tested products [1].

Generic medicines can only enter the market following the expiration of the patent for the innovator medicine. As clinical trial data on the safety and efficacy of the active ingredient is already available from the innovator, these expensive, lengthy studies are not required for a generic. Instead, bioequivalence studies, performed to strict internationally agreed standards, are accepted by regulatory authorities worlwide.

In Europe “Guideline on the Investigation of Bioequivalence” represents the most progressive bioequivalence guideline currently available in the ICH region [1]. This guideline specifies the requirements for the design, conduct, and evaluation of bioequivalence studies for immediate release dosage forms with systemic action The current guidelines for bioequivalence study in Turkey are consistent with this guideline described the principles of bioequivalence studies [2,3]. Bioequivalence study should be performed in compliance with Good Clinical Practice (ICH-GCP) [4], the Declaration of Helsinki [5] as well.

[1] Guideline on The Investigation of Bioequivalence. CPMP/EWP/QWP/1401/98 Rev.1/Corr., London, EMA, 2010.

[2] Beşeri Tıbbi ürünlerin biyoyararlanım ve biyoeşdeğerliğinin incelenmesi hakkında kılavuz-13.05.2022

[3] İyi Klinik Uygulamaları Kılavuzu- 13.11.2015

[4] ICH E6 (R2) Guideline for good clinical practice -01.12.2016. EMA/CHMP/ICH/135/1995

[5] Declaration of Helsinki, Fortaleza, 2013

IS-16
SERDAR DURDAĞI
Short Biography

Research Group of Prof. Durdağı applies computational chemistry methods to biological systems. Inter-disciplinary research of group focuses on protein modeling and dynamics, ligand- and structure-based drug design, investigation of molecular mechanisms of protein/drug, protein/protein, protein/DNA interactions and optimizations protocols for rational drug design. For this aim, together with applications of biophyscial approaches and molecular modeling applications research Lab of Prof. Durdağı also develops programing codes for several biological problems.

Prof. Durdağı published two books and seven book chapters on computer-aided drug design. He has around 180 research articles in top peer-reviewed medicinal chemistry and computational biophysics journals with h-index of 39. He has also more than 20 international patents and patent applications. The total citations of Prof. Durdağı's research articles are more than 4000.

Prof. Durdağı received his PhD degree in Freie Univ. Berlin in 2009 and his PhD studies is supported by EU FP6 Marie Curie Research Fellowship and his PhD thesis was graded with summa cum laude (with highest honor) degree. He also received many prestigiousresearch grants (i.e., Max Planck Inst., Canadian Institute of Health Research-CIHR, Alberta Innovates Health Solutions-AIHS). Prof. Durdağı worked as postdoctoral fellow (2009-2013) and senior researcher (2012-2013) in University of Calgary (Canada) and Max-Planck Institute (Germany), respectively.

The group of Dr Durdağı works on several projects for better understanding the drug-receptor and protein-protein, protein-DNA interactions of different systems using several computational modeling approaches and designing novel therapeutic compounds. Prof Durdağı’s research group carried out many national and international projects so far (TUBITAK, H2020, FP6 and FP7). Prof. Durdağı received many prestigious national and international awards including The Scientific and Technological Research Council of Turkey-TUBITAK's Incentive Award in Health Sciences (2016); Contribution to Science Awards (2016, 2021); Health Institutes of Turkey - TUSEB's Aziz Sancar Incentive Award (2017); Science Academy's Young Scientist Award (2014). Prof. Dr. Durdağı is also the Founder and CEO of Istanbul MedChem.

Abstract

IS-17
İSMAİL TUNCER DEĞİM
Short Biography

Prof. Dr. İsmail Tuncer DEĞİM graduated from Ankara University Faculty of Pharmacy in 1985. He completed his master's degree at Gazi University Faculty of Pharmacy in 1988. He completed his Ph.D. thesis in 1996 at Cardiff University, Cardiff School of Pharmacy, the University of Wales in the UK. He became a Professor at Gazi University Faculty of Pharmacy in 2009 and served as the Dean of Gazi University Faculty of Pharmacy between 2012-2016. He has been working at Biruni University Faculty of Pharmacy since 2016. He has been serving as the Dean since 2020.
He has more than 70 national and international articles; He has various book chapters, has been on the referee board of Hacettepe University Journal of the Faculty of Pharmacy, Journal of Biophysical Chemistry, and is currently on the referee board of Pharmaceutical Science and Technology, Asian Chemistry Letters, Austin Chromatography, ACTA Pharmaceutica Sciencia, Pharmaceutical Drug Regulatory Affairs Journal. and serves on the Advisory Board of the Turkish Clinics, Journal of Pharmacy Sciences.
He is invertor of Method for measuring blood urea level by reverse iontophoresis, (US7231242, EP1526891, AT480296, CN100431641), Cartridge for electrodialysis (US8057680, RU2323015, TR200401118, CN100518837), Extended release fluvastatin tablet (TR200800634).
It works with controlled release systems, iontophoresis, the passage of active substances through the skin, drug formulations, generic formulation development, bioequivalence and pharmacokinetics, application of optimization techniques to pharmaceutical technology, nanotechnology, aerospace pharmacy, carbon nanotubes, boron nitride nanotubes, and quantum dots.

Abstract

Pharmaceutical Drug Design through Formulation Evolution for Nanocomposites: Nanobang

A brief description of nanoparticulate systems will be given and some hurdles for formulations will be mentioned and explained. During this presentation, emphasis will be placed on the potential for nanoparticles to induce modifications in the characteristics of water molecules within formulations, potentially leading to the acquisition of distinctive properties within nanoparticulate systems. A thorough investigation into recent captivating revelations will be conducted, alongside the exploration of strategies that offer the utmost efficacy in formulation within the realm of nanoparticle integration. This discourse will encompass forefront insights and innovative conceptual frameworks that serve as the foundation for the progression of optimal approaches to formulation.

IS-18
KAYA BİLGÜVAR
Short Biography

Kaya Bilgüvar, MD, PhD, is a human geneticist and an Assistant Professor and Chair of Medical Genetics, leads the Translational Medicine PhD program, and is a member of the boards of Rare Disease and Orphan Drugs Research Center and MDPhD Program at the Acibadem University. He is also an Associate Professor Adjunct of Genetics and Neurosurgery, and a member of the Yale Center for Genome Analysis and Yale Program on Neurogenetics at the Yale University.

His major research interests include the identification of genetic bases of human diseases affecting the structure and function of the nervous system, and elucidation of underlying disrupted biological processes using patient-derived, induced neuronal systems. His latest efforts are concentrated on the studies of cortical malformations, schizophrenia, early-onset neurodegenerative syndromes and migraine. From 2013 to 2021, he served, first as associate director then as the director of the Yale Center for Genome Analysis where he contributed to many large-scale human genetics efforts along with development of diagnostic applications utilizing next-generation omics technologies which he continues to advance for profiling the tumors of the central nervous system.

Abstract

Common diseases, rare variants, unique patients: towards individualized treatments

Our understanding of the genetic basis of neurodevelopmental disorders and brain tumors have only recently made considerable strides thanks to the advances in next generation omics technologies. In addition, scientific achievements made in re-programming of somatic cells into pluripotency followed by targeted differentiation provided a new path of investigation for disease modelling. Dr. Bilguvar will provide highlights from his and colleagues' efforts on the discovery research they performed towards the elucidation of genetic determinants underlying rare developmental and common complex disorders along with the tumors of the nervous system. In addition, development of novel applications such as monitoring of tumor presence and progression through profiling of the cell-free DNA, and patient tumor derived culture models for advancing personalized treatment options will be discussed.

IS-19
ALİ MAXIMILIAN ERTÜRK
Short Biography

Prof. Ali Ertürk is the CEO and founder of Deep Piction, as well as a W3 Professor at LMU Munich and the Director of the Institute for Tissue Engineering & Regenerative Medicine at Helmholtz Munich. His research focuses on developing and combining AI-based technologies for improved diagnostics and therapeutics, with particular interests in imaging, spatial omics, organoids, neurodegeneration, cancer, metabolism, and drug delivery.
Prof. Ertürk completed his PhD at the Max Planck Institute of Neurobiology and postdoctoral training at Genentech. He has obtained around 22.5 million Euros in research funding over the past 8 years as a group leader and institute director. He is an award-winning scientist who has given over 100 invited talks including a TEDx talk, and received considerable media coverage for his innovative research advancing whole-organ imaging and AI-enabled tissue analysis including by BBC and New York Times.
Some of Prof. Ertürk's recent high-impact publications utilize machine learning for whole-brain vasculature mapping and antibody-enabled whole-body tissue clearing and imaging. His work developing methods for cellular interrogation of intact human organs also made the cover of Cell. Beyond his groundbreaking research, Prof. Ertürk is an avid photographer and has exhibited his art internationally.

Abstract

IS-20
ERDEN BANOĞLU
Short Biography

Prof. Banoğlu is a Bachelor of Pharmacy from Gazi University in 1989 and received his PhD degree from the Department of Medicinal Chemistry at the University of Iowa, USA, in 1997. He also carried out short-term research activities at Aberdeen (Scotland), Kumamoto (Japan) and Rhode Island (USA) Universities. Prof. Banoglu still continues his research in the Department of Pharmaceutical Chemistry at Gazi University. He is also co-founder of Icosyn Therapeutics and OncoCube Therapeutics, which carry out studies on developing innovative drug molecules for the treatment of chronic inflammation and cancer. Prof. Banoğlu is a member of the Turkish Academy of Sciences (TÜBA). One of his developed molecules has recently moved to the in-human Phase-I Clinical trials in the USA against cancer.

Abstract

Targeting Cancer Cells by Inhibition of Transforming Acidic Coiled-Coil Protein 3 (Tacc3): A Novel Therapeutic Strategy For The Treatment of Various Cancers

The transforming acidic coiled-coil 3 (TACC3) is often upregulated in a broad spectrum of cancers, including breast, colon, and over cancers. TACC3 is overexpressed in cancers with centrosomal amplification and has critical roles in microtubule stability and centrosome integrity, which is frequently deregulated in cancers, and targeting TACC3 is a promising strategy as a new therapeutic modality for cancer. Recently, we discovered BO-264 as a new chemotype targeting TACC3 function. BO-264 showed potent antiproliferative activity against breast cancer subtypes, basal and HER2+, and caused mitotic arrest, DNA damage, and apoptosis while demonstrating negligible cytotoxicity towards normal breast cells. In addition, BO-264 oral administration significantly impaired tumor growth in immunocompromised and immunocompetent breast and colon cancer mouse models, confirming BO-264 as a promising lead compound for development of drug-like TACC3 inhibitors. A detailed investigation of SAR around BO-264 skeleton led to the development of an advanced lead compound for further development of improved TACC3 inhibitors.

IS-21
AMIRHOUSHANG BAHRAMI
Short Biography

I am a German biophysicist based at UNAM, Bilkent University as assistant professor and affiliated to Max Planck society. I did my PhD in soft matter physics in TUBerlin and North Carolina state university (2013) during which I was working at Max Planck institute (MPI) for colloids ad interfaces. I then moved to MPI for biophysics in Frankfurt where I worked as a postdoctoral scholar for six years in the department of theoretical biophysics. In 2018, I moved to MPI for dynamics and self-organization to start my own group as a group leader. Since 2020 I have joined UNAM, Bilkent university as an assistant professor and the leader of the first Max Planck partner group in Bilkent. Our group is funded by Max Planck society and European molecular biology organization (EMBO). Our research focuses on theoretical and computational biophysics with particular emphasis on biomembranes interactions with proteins, particles, and viruses.

Abstract

Cellular Uptake of Nano Drug Containers with Different Shapes And Sizes

Recent advances in nanotechnology have led to promising perspectives for design and fabrication of nanoparticles for therapeutical applications. Understanding cellular uptake of nanoparticles not only helps designing novel drug containers for drug delivery but also shed light on the mechanisms by which viral particles such as HIV, Covid19, and influenza viruses enter the cell. A wide range of nanoparticles and viruses gain entry into the cell via endocytic pathway where the cell membrane wraps around the nanoparticle. This wrapping that depends on the size and shape of the particle proceeds by a competition between membrane bending and membrane-particle binding. We explore the underlying physical principles of cellular uptake of nanoparticles with different shapes and sized by bilayer and vesicle membranes. We also study the cooperative wrapping on nanoparticles and investigate the role of membrane curvature on particle wrapping. For single particles, we report curvature-mediated wrapping of internal and external particles and orientational endocytosis of elongated nanoparticles. We also observe aggregations and tubulation of several nanoparticles on vesicles. Our finding highlight the significant role of membrane bending energy and membrane curvature on cellular uptake of nanoparticles and viruses and have immediate applications for drug delivery using nanoparticles.

IS-22
TAMER ÖNDER
Short Biography

Tamer Önder received his undergraduate degree in Molecular Biology and Genetics from Cornell University. He completed his PhD thesis work (2002-2008) on metastasis and cancer stem cells under the supervision of Robert Weinberg at the Whitehead Institute and the Massachusetts Institute of Technology (MIT). From 2008-2012, Dr. Önder was a postdoctoral research fellow in George Daley's group at the Harvard Medical School and Children's Hospital Boston, where he studied somatic cell reprogramming and induced pluripotent stem cells. Dr. Önder's work on cancer biology and stem cells has been published in journals such as Cell, Nature, and Nature Chemical Biology. Dr. Önder is currently a professor at Koç University School of Medicine and his research focuses on epigenetic mechanism of reprogramming and generation of pluripotent stem cells (https://scl.ku.edu.tr/). He is the recipient of TUSEB Aziz Sancar Award, iBG Science Medal, Sabri Ülker International Science Award and TÜBİTAK Young Investigator award. Research in Dr. Önder's laboratory has been supported by the EU Marie Curie program, EMBO Installation Grant, Royal Society Newton Fund and TÜBİTAK.

Abstract

IS-23
BERT DE GROOT
Short Biography

Education and professional experience

1989-1994	Chemistry studies at the university of Groningen, the Netherlands. Specialisation: Biophysical chemistry. Supervisor: prof. H.J.C. Berendsen.
1994-1998	PhD student a the the university of Groningen, the Netherlands, the department of biophysical chemistry. Promotor: prof. H.J.C. Berendsen. Subject: Native state protein dynamics studied by a variety of computer simulation techniques.
1998-2003	Postdoctoral fellow in the theoretical molecular biophysics group headed by Dr. Helmut Grubmüller, at the Max-Planck Institute for Biophysical Chemistry, Göttingen, Germany. Subject: Structure and function of aquaporins, studied by Molecular Dynamics and other computational techniques.
1997-2005	Extensive research visits to Rome university, EMBL Heidelberg, the Basel Biocentre and Nijmegen university.
2004-	Head of the computational biomolecular dynamics group, Max-Planck Institute for Biophysical Chemistry, Göttingen, Germany.
2009-	adjunct Professor, physics faculty, university of Göttingen, Germany.

Teaching and advanced training

- Computational Biophysics I and II for third and fourth year physics and chemistry students, university of Göttingen, since 2006;
- Advanced simulation course (lectures+practicals) "Computersimulation biomolekularer Prozesse" for third year physics and chemistry students, university of Göttingen, 2004-2006;
- education of first and second year chemistry and physics students in practical courses university of Groningen, 1994-1998;
- participation in numerous courses/workshops/masterclasses among which C/C++ programming, protein folding, molecular modelling, advanced techniques in Molecular Dynamics.

Abstract

Alchemical Binding Free Energy Calculations And Machine Learning Based Chemical Space Navigation

Alchemical free energy calculations have come of age. Based on rigorous first principles of statistical mechanics, these calculations explore physical paths not experimentally accessible and provide unprecendented accuracy in the prediction of processes as diverse as protein thermostability and ligand binding free energies. Based on the pmx framework coupled to the GROMACS molecular dynamics engine, results of high-throughput relative as well as absolute ligand binding free energies are presented.

IS-24
EMRAH EROĞLU
Short Biography

Emrah Eroğlu is a Principal Investigator and Deputy Director at Istanbul Medipol University's Research Institute for Health Sciences and Technologies (SABITA) in Türkiye. With a background in biotechnology and molecular biology, Eroğlu is a dedicated researcher focused on developing innovative tools to gain insights into cellular processes at the single-molecule level. At Istanbul Medipol University, Eroğlu's research laboratory is at the forefront of developing genetically encoded biosensors and chemogenetic tools. These advancements allow for the visualization of reactive oxygen species (ROS) and reactive nitrogen species (RNS) in vascular cells, contributing to the understanding of their implications in signaling processes and their connection to neurodegenerative diseases. Eroğlu has made significant contributions to the field of biosensors and chemogenetic tools, publishing numerous research papers and review articles. His expertise extends to the development of multiparametric highcontent imaging approaches, enabling the simultaneous study of multiple signaling molecules. His academic journey includes positions at prestigious institutions such as Harvard Medical School and MedUni Graz. In 2019, he joined Sabancı University as a Faculty Member and established a live-cell imaging laboratory. In 2022, Emrah relocated his lab to Istanbul Medipol University to collaborate with partner labs at SABITA, a premier research facility and high-end imaging core in Eurasia. Emrah's accomplishments have been recognized with several awards, including the EMBO Installation Grantee, the Leopold Flohé Redox Pioneer Young Investigator Award, and the Young Scientists Award Program by the Science Academy Turkey. He has also received prestigious fellowships such as the Erwin Schrödinger Fellowship and the TUBITAK 2232 International Fellowship.

Abstract

Cellular Symphony: Decoding Drug Actions Using Genetically Encoded Biosensors

This lecture explores the application of genetically encoded biosensors in the realm of drug screening and testing, focusing on their pivotal role in advancing multiparametric imaging techniques for the assessment of cellular redox signaling events. These genetically encoded tools offer unprecedented spatial and temporal resolution, facilitating intricate visualization of biological processes in vitro and in vivo. Despite these advancements, there exists untapped potential within these methodologies, particularly in the context of drug screening. This lecture aims to shed light on recent progress and future prospects of these genetic toolkits, emphasizing their potential in bridging existing knowledge gaps. Specifically, the discussion will explore how these genetically encoded biosensors can be harnessed in drug screening and testing processes, offering insights into the cellular dynamics. The integration of these innovative tools holds promise for enhancing our understanding of cellular responses to various drugs and toxins, paving the way for the development of more effective and targeted therapeutic interventions.

IS-25
GÖZDE KORKMAZ
Short Biography

Gözde Korkmaz holds a bachelor's degree in Molecular Biology and Genetics from Istanbul Technical University and a Ph.D. from the Sabancı University Department of Biological Sciences and Bioengineering, completed in 2012. Following her doctoral studies, she conducted post-doctoral research at the Netherlands Cancer Institute in Reuven Agami's laboratory. In 2020, she joined Koç University School of Medicine as an assistant professor, where she established her own laboratory. Notably, she is a distinguished recipient of the TÜBİTAK 2232 International Fellowship for Outstanding Researchers Program and has garnered prestigious awards, including The Science Academy Society of Turkey – BAGEP and Turkish Academy of Science – Outstanding Young Scientist (GEBİP) awards in 2021. Moreover, she has been honored with the Dr. Nejat F. Eczacıbaşı Medical Awards – Scientific Research Support Award on Personalized Medicine. Dr. Korkmaz's research focuses on transcriptional regulation and epigenetics, focusing on their intricate roles in cancer development and drug resistance. Her lab's research methodology primarily involves the integration of advanced techniques based on CRISPR, specifically tailored made CRISPR-based screens, and next-generation sequencing methodologies. The overarching objective of her lab is the identification of novel therapeutic targets in the field of cancer research.

Abstract

Precision Medicine in Breast Cancer: Harnessing Synthetic Lethality and ERalpha Detection

Breast cancer, globally recognized as the most prevalent malignancy and leading cause of cancer-related mortality in women, presents an evolving landscape of treatment modalities. Despite advancements in therapeutic options aimed at overcoming resistance and minimizing side effects, recurrence afflicts up to 30% of patients, often proving incurable due to resistance mechanisms against diverse therapeutic agents. Notably, studies have delineated various mechanisms of drug resistance in breast cancer, underscored by tumor heterogeneity, wherein distinct cell populations exhibit diverse genetic alterations and reliance on disparate signaling pathways for survival, proliferation, and metastasis. ARID1A emerges as a focal point in breast cancer research, with mutations identified in 4% of cases and copy number loss prevalent in 13 – 35% of instances. Our ongoing project endeavors to elucidate the synthetic lethal partners of the ARID1A gene, with the ultimate goal of devising personalized therapeutic approaches for breast cancer patients bearing ARID1A gene mutations.

IS-26
ADİL MARDİNOĞLU
Short Biography

Professor Adil Mardinoglu is an expert in the field of Systems Medicine, Systems Biology, Computational Biology and Bioinformatics. He has been recruited as a Professor of Systems Biology in Center for Host-Microbiome Interactions, King's College London, UK, where he leads a computational group. He also works as group leader in Science for Life Laboratory (Scilifelab), KTH-Royal Institute of Technology in Sweden and led a team of 25+ researchers working in the area of computational biology, experimental biology and drug development to develop new treatment strategies for Metabolic diseases, neurodegenerative diseases and certain type of cancers.

Abstract

IS-27
NURHAN ÖZLÜ
Short Biography

Prof. Nurhan Özlü is a faculty member at Koç University in the Faculty of Science, Department of Molecular Biology and Genetics, as well as at the Koç University School of Medicine. Her research, which focuses on cancer cell division mechanisms, utilizes mass spectrometry-based proteomic methods and involves developing new techniques. Her publications have been cited more than 2,400 times. After completing her undergraduate studies in the Department of Molecular Biology and Genetics at Bilkent University, Prof. Özlü earned her doctorate at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, Germany, in 2005. During her doctoral studies, she investigated the mechanisms of spindle assembly during cell division in the laboratory of Prof. Anthony Hyman. Following her doctorate, she conducted postdoctoral research at Harvard Medical School in the laboratory of Prof. Mitchison and at the Proteomics Center of Boston Children's Hospital with an EMBO long-term postdoctoral fellowship. In 2010, Prof. Özlü joined Koç University as a faculty member. She has received support from various organizations such as the European Molecular Biology Organization Installation grant, EU eRARE, EU Marie Currie, and Newton Advanced fellowships, and has also been awarded the L'Oréal Young Women in Science, TUBITAK Encouragement, and TÜBA Young Scientist awards. Currently, Prof. Nurhan Özlü is a visiting scientist at the University of Michigan while continuing her scientific work at the Koç University Cell Biology and Proteomics Laboratory.

Abstract

IS-28
EMEL TİMUÇİN
Short Biography

Emel Timucin obtained her BSc in Molecular Biology and Genetics from Middle East Technical University in 2007, and PhD in Biological Sciences and Bioengineering from Sabancı University in 2012. Currently, she is a professor at Acibadem University in the Department of Biostatistics and Medical Informatics. Her research focuses on computational modeling of biomolecules to understand their functions and implications in diseases.

Abstract

Computational completion of the Aurora interaction region of N-Myc in the Aurora a kinase complex

Motivated by the gaps in the crystal structures, we undertook the task of modeling the complete structure between AurA and N-Myc. We conducted comprehensive molecular dynamics simulations to analyze the behavior of both the incomplete and complete N-Myc in the complex. The simulations of the incomplete PDB complex (5g1x) consistently revealed partial dissociation of the short N-Myc fragment (61–89) from the kinase. To address the missing N-Myc fragment (19–60), we modeled it using the N-terminal lobe of AurA as the protein-protein interaction surface, which is also known to bind TPX2, another partner of AurA. Through relative binding free energy calculations and flexibility analysis, we confirmed that the complete AIR of N-Myc stabilizes the complex. This underscores the significance of the N-terminal lobe of AurA as a binding site for the missing N-Myc fragment (19–60). Additional models, consisting of only the missing N-Myc (19–60), as well as the fused form of TPX2 (7–43) and N-Myc (61–89), demonstrated more stable interactions with the N-terminal lobe of AurA compared to the incomplete N-Myc fragment (61–89) in the 5g1x complex. Collectively, this study offers structural insights into the involvement of the N-terminus of the AIR of N-Myc and the N-terminal lobe of AurA in forming a stable complex. This highlights the potential for effectively targeting N-Myc through these interactions.

IS-29
MUSTAFA GÜZEL
Short Biography

Dr. Guzel graduated from Hacettepe University School of Engineering with a B. Sc degree in Chemistry in 1987 and completed his M. Sc. and Ph. D. Degrees on Organic/Medicinal Chemistry at Clemson University, Clemson, SC in 1996 and 2001 respectively. He worked as organic lab coordinator at Northeastern University and later joined to ArQule Inc.as Sr. Synthetic Organic Chemist upon his graduation. He then joined to TransTech Pharma Inc, in High Point, NC and assumed various positions in Medicinal Chemistry Department between 2001 and 2014. In 2014 he started working as an Assistant Professor at International School of Medicine in Department of Medical Pharmacology at Istanbul Medipol University. In 2017 he was promoted to Associate Professor in medical pharmacology acting as a chair. In 2019 he was appointed as the department chair of Molecular Medicine and Biotechnology. In January 2020, he then became the director of Drug Discovery and Development Research Center in newly established Health Sciences and Technologies Research Institute, currently leading two critical drug development projects for Covid-19 with a local pharma company as well as several domestic and European granted drug discovery projects in Molecular Discovery and Development laboratories of the university.

Abstract

IS-30
TUNCA DOĞAN
Short Biography

Dr. Tunca Doğan is a faculty member at the Dept. of Computer Science and AI Engineering at Hacettepe University, Turkey, and the PI of the Biological Data Science Lab at the same place. Dr. Doğan also works as a research associate at the UK's European Bioinformatics Institute (EMBL-EBI). Before this, he was a post-doc in the UniProt protein database team, again in EMBL-EBI, and Cambridge University, working on automated protein annotations. He has a background in process engineering (BSc) and bioinformatics (PhD). He and his group are working on developing machine/deep learning-based predictive methods for (I) the integration and representation of heterogeneous biomedical data, (ii) the prediction of the functional properties of proteins, and (iii) discovering/designing new drug candidate small molecules. His group has lately been interested in representation learning and generative AI, with multiple ongoing projects.

Abstract

IS-31
KADİRCAN KESKİNBORA
Short Biography

Born in 1959-Mardin, Keskinbora completed his primary and secondary education at Hacettepe Medical School in the city where he was born. He became an expert in Ophthalmology in 1987, an associate professor in 1999, and a professor in 2007. In addition to ophthalmology, he completed his second Ph.D. in "Deontology, History of Medicine and Ethics" in 2006.
In 2007, he left Namik Kemal University, where he was the Founding Dean of the Faculty of Medicine, in 2012 and was appointed to the Medical Faculty at Bahçeşehir University. She continues her teaching membership at the same institution.
He was awarded the International Ibn Sina Prize in France/Paris in 2016 for his work on ibn Sina.
He has published 15 books in the fields of Eye Diseases, Medical History, and Literature, 16 books in National and International Published Books, and numerous articles in national and international scientific journals. At national and international congresses, scientific or informational meetings, universities, schools at various levels, and radio and television channels, she has held numerous events and speeches as a speaker, panelist, course instructor, or conference host.
As a national and international scientific, social, and civil society organization member, Keskinbora speaks English, German, and Arabic.

Abstract

IS-32
ŞARON ÇATAK
Short Biography

Education:
Joint Ph.D.
Theoretical Chemistry Chemical Informatics, Chemistry - University of Lorraine, Boğaziçi University - 2008
M.S.
Chemistry - Boğaziçi University - 1999
B.S.
Chemistry - Boğaziçi University – 1997

Research Areas:
Computational Chemistry
Molecular Modeling
Molecular Dynamics
Biological Reactions
Reaction Mechanisms
Chemical Reactivity

Abstract

IS-33
ÇAĞATAY AYDIN
Short Biography

Çağatay Aydın is a senior scientist at the Neuro-Electronics Research Flanders (NERF). He received his bachelor's degree in Electronic Engineering from Işık University and his master's degree in biomedical engineering from Boğaziçi University. He completed his doctorate in cognitive and molecular neuroscience track at KU Leuven University in Belgium in 2019. His main areas of interest are designing and developing next-generation neural implants and the interpretation of the complex data obtained using artificial intelligence in the context of understanding the impact of fundamental neuronal networks on our behavior. Recently, with an international consortium, he developed high-resolution neural implants and produced new prostheses that will enable high-resolution data collection on test animals for months. These studies have been published in prestigious journals such as Nature and Science. In addition, last year, he was selected as Belgium's most promising young scientist, together with a Turkish colleague. His ultimate aim is to implement personalized brain therapies with the devices he develops in the future.

Abstract

Unraveling dru g related electrophysiological footprints using high density neuronal probe

Neuropsychiatric and neurodevelopmental diseases manifest through clinical symptoms that result from abnormal functioning of specific brain circuits. Significant advancements have been achieved in comprehending the specific brain regions implicated and the chemical mechanisms accountable for these disorders. Nevertheless, the primary obstacle in developingnovel treatments is the constrained utility of behavioral animal models. While alterations in behavior may suggest an enhancement in the clinical phenotype, they may not necessarily represent an improvement in the fundamental circuitry. However, theycould be attributed to unrelated structural modifications. In addition, although preclinical models serve as valuable tools for research, their capacity to accurately forecast results in humans is frequently uncertain, posing a substantial challenge to theadvancement of drugs. The recent advancements in electrophysiology[1] have made it possible to monitor the activity of individual neurons on a wide scale and with great precision in freely moving mice andopenup the opportunity to find patterns of neural activity in situations that cause diseases. We consistently record from more than 250 neurons simultaneously over numerous days using a single Neuropixel 2.0 probe[2] implanted using lightweight 3D-printed fixtures[3]. We administered Dizolcilpine (MK-801), a potential medication that acts as an uncompetitive antagonist of the N-Methyl-D-aspartate (NDMA) receptor4. We assessed the temporal modulation of neuronal activity by administering varying doses of MK-801. We discovered substantial disparities between the control group and each group that received different concentrations, regardless of animal behavior. Subsequently, we inquired about the feasibility of using only electrophysiological footprints to forecast the administered concentration of dizocilpine. We employed temporal variations in the spike statistics of individual neurons and built a multiclass classifier. Subsequently, we accurately forecasted the concentration of the supplied medication to be above 70%. In conclusion, our existing platform paves the way for advancements in drug development and personalized treatment.

Bibliography

1. Jun, J. J. *et al.*Fully integrated silicon probes for high-density recording of neural activity. *Nature***551**, 232–236 (2017).
2. Steinmetz, N. A. *et al.*Neuropixels 2.0: A miniaturized high-density probe for stable, long-term brain recordings. *Science (80-.).***372**, eabf4588 (2021).
3. van Daal, R. J. J. *et al.*Implantation of Neuropixels probes for chronic recording of neuronal activity in freely behaving mice and rats. *Nat. Protoc.*(2021) doi:10.1038/s41596-021-00539-9.
4. Zemanova, A. *et al.*Visuospatial working memory is impaired in an animal model of schizophrenia induced by acute MK-801: An effect of pretraining. *Pharmacol. Biochem. Behav.***106**, 117–123 (2013).

IS-34
ONUR SERÇİNOĞLU
Short Biography

Dr. Onur Serçinoğlu completed his BSc in Bioengineering at Ege University in 2008, and his MSc in Biotechnology in 2011 at Hamburg University of Technology, supported by a TEV/DAAD scholarship, with a focus on mathematical modeling of mammalian cell culture applications. Dr. Serçinoğlu earned his PhD from Marmara University in 2018, specializing in the computational characterization of human Major Histocompatibility Complex (MHC) proteins.

Since then, Dr. Serçinoğlu has expanded his research portfolio, actively participating in and leading various national projects, including in-depth studies on the dynamics and structural bioinformatics of MHC proteins, particularly in relation to autoimmune diseases such as Type 1 diabetes mellitus. He is involved in projects exploring the ligand specificity and promiscuity of bacterial efflux pumps, drug repurposing for allosteric ERK5 inhibitors, bioinformatics-based polypharmacological drug discovery for personalized therapy approaches. He has 11 publications in peer-reviewed international journals and presentations at international symposiums. He has also contributed chapters to several academic books.

Currently, he holds a faculty position at Gebze Technical University, and has previously served at Recep Tayyip Erdoğan University and Marmara University.

Alongside his research work, Dr. Serçinoğlu is also committed to teaching, offering courses in structural bioinformatics, bioinformatics fundamentals, and computational biomolecular dynamics on undergraduate as well as graduate levels. His educational approach is grounded in his research experience, aiming to provide students with a solid understanding of complex biological systems and their implications in human health.

Abstract

Exploring Autoimmune Disease Mechanisms: A Structural Bioinformatics View of MHC Class I Diversity

The extensive polymorphism of human Major Histocompatibility Complex class I (MHC I) alleles plays a pivotal role in adaptive immunity, balancing the body's defense against pathogens with the potential development of autoimmune diseases. This polymorphism, critical for presenting antigenic peptides to T cells, intricately affects immune response regulation and contributes to the complexity in autoimmune disease etiology. This presentation seeks to elucidate the structural and dynamic complexities of MHC I allele polymorphism and its implications in autoimmunity through the lens of three focused studies we have conducted over the last five years. The first study analyzes the dynamic differences between HLA-B subtypes differentially associated with Ankylosing Spondylitis., specifically focusing on how a single amino acid substitution can significantly influence dynamic residue coupling and the stability of the peptide-MHC complex. In the second study, a local frustration analysis of numerous HLA I alleles is performed to explore the sequence-structure-function relationships. This analysis sheds light on the conserved structure of MHC I despite extensive polymorphism and its impact on interactions with T-cell receptors and other immune system components. Finally, the third study examines the polymorphism in the F pocket of HLA-B39 alleles, particularly in relation to type 1 diabetes, by utilizing a combination of molecular dynamics simulations and in vitro experiments. By comparing alleles with different disease associations, insights were obtained into how variations in peptide binding and stability may drive autoimmune disease mechanisms. These studies provide a comprehensive understanding of MHC I diversity and its critical role in the pathogenesis of autoimmune diseases, potentially guiding future therapeutic interventions.

IS-35
AHMET GÜL
Short Biography

Abstract

IS-36
ELİF NUR FIRAT KARALAR
Short Biography

Dr. Elif Nur Firat-Karalar studied molecular biology and genetics at Bilkent University, Turkey. She then moved to US for her PhD work at the University of California, Berkeley and her postdoctoral studies at Stanford University. In the “Cytoskeleton Research Laboratory”, Dr. Firat-Karalar and her team studies the biogenesis and function of centrosomes and cilia and aims to develop new diagnostic and therapeutic approaches for rare developmental disorders and cancer. Research in the Dr. Firat-Karalar’s laboratory is supported by an ERC Starting Grant, EMBO installation grant, Royal Society Newton Advanced Fellowship, EMBO Young Investigator Award and Installation Grant and TUBITAK.

Abstract

PRESENTATIONS

Targeting AT1R with RNA Aptamers to manage Retinal Degeneration

by Ioannis Papazoglou | Bahcesehir University

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Presenter Name: Ioannis Papazoglou
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Angiotensin receptor type 1 (AT1R) is a G protein-coupled receptor (GPCR) which mediates the effects of the renin-angiotensin system (RAS). While its primary role is well-established in the cardiovascular system, experimental research suggests its abundance and increased activity in the brain as well. However, activation of AT1R by its endogenous angiotensin peptide ligand there triggers inflammation-inducing signal pathways, an event particularly observed in the context of retinal degeneration. Recent literature suggests that blocking AT1R locally in the retina could offer neuroprotective benefits by inhibiting inflammation and mitigating retinal impairment. In an approach to achieve this, drawn by RNA therapeutics efficacy and specificity, we aim to create an RNA aptamer that targets AT1R activation.

To achieve this, we curated the experimentally resolved structure of its inactive conformation, reconstructed the apo membrane-receptor system, and conducted extensive long molecular dynamics (MD) simulations in order to validate its robustness. Then, for the design of the RNA aptamers targeting the receptor, we generated libraries of k-mer sequences (ranging from 2 to 10 bases) encompassing all possible base combinations, modeled their 3D conformations and performed molecular docking. After simulating the best-docked poses and ensuring the system stability based on free-energy results, we planon elongating the chain of the most promising oligomer to design the final aptamer. While our work is computational in nature, we aim to proceed in experimental validation of our results in the future.

Neural Relational Inference Models for Optimized Virtual Screening of Large-Scale Small Molecule Libraries using Dynamic Structure-based Pharmacophore Models for the Treatment of YB-1 Mediated Drug Resistance

by Lalehan Oktay | Serdar Durdağı | Computational Drug Design Center (HITMER), Bahçeşehir University, Istanbul, Turkey | Molecular Therapy Lab, Department of Pharmaceutical Chemistry, School of Pharmacy, Bahçeşehir University, Istanbul, Turkey

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Presenter Name: Lalehan Oktay
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Hybrid strategies, like structure-based pharmacophore models, aim to merge the strengths of both ligand-based drug design and structure-based drug design methods for faster and more accurate screening of large-scale ligand libraries. Challenges persist in these models, particularly in capturing dynamic binding interactions. To address this, we have developed dynamic structure-based pharmacophore models to accurately simulate the dynamic nature of protein-ligand binding. Our study focuses on the multifunctional protein Y-box binding protein 1 (YB-1), linked mainly to acquired cancer treatment resistance. Utilizing a known YB-1 inhibitor (SU056) bound to RNA-binding sites, we employed dynamic structure-based pharmacophore models derived from all-atom molecular dynamics (MD) simulations. Representative optimized pharmacophore models were utilized to revolutionize conventional virtual screening methods and screen large-scale chemical libraries. Top-scoring drug candidates were handpicked for steered molecular dynamics (sMD) simulations and subsequent umbrella sampling (US). Long-MD simulations and enhanced sampling methods can provide valuable knowledge on protein-ligand binding effects, however they require rigorous computational power. Keeping this in mind, we will feed collected dynamics data from simulations to build a neural relational inference (NRI) model, designed to learn and thereafter recreate protein-ligand binding effects, extending simulation time without exhaustively using computational resources. The method will be able to predict the most common pharmacophore sites of the YB-1 binding region, providing an enriched representative pharmacophore hypothesis with dynamic character. Furthermore, the change in free energy upon different pharmacophore site activation by ligand protein interactions can easily be calculated to encover the native binding modes of the YB-1/inhibitor complex.

Targeting miRNA for Colorectal Cancer: In Silico Identification and De Novo Modelling of Oncogenic miR-135b for Small-Molecule Based Therapy

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Presenter Name: Berat Demir
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Colorectal cancer is one of the leading causes of cancer deaths worldwide. In the current study, we have identified miR-135b, a microRNA to be differentially expressed in colorectal cancer, through an analysis of the differentially expressed miRNAs from the Gene Expression Omnibus database. Subsequently, the target genes associated with miR-135b were pinpointed, and pathway and functional enrichment analyses were performed to gain a comprehensive understanding of the underlying biological processes involved. A de novo three-dimensional model of its tertiary structure was created for small-molecule targeting at the Dicer cleavage site. Dicer binds to terminal loop region of the pre-miRNA and cleaves to generate double stranded miRNA duplex. The miRNA duplex is unwound, one of the strands (guide miRNA) is loaded into the RNA-induced silencing complex (RISC) for miRNA-mRNA target interaction and post-transcriptional gene silencing. Following results from molecular docking experiments initiated with the ChemDiv miRNA targeted small molecule library (~20,000 compounds), top-scoring compound commercial analogues were searched within the ZINC library using SwissSimilarity. These analogues were docked to the Dicer cleavage site and their optimized docking scores were obtained. These top-scoring molecules were then subject to all-atom molecular dynamics simulations and post-simulation analyses were conducted to assess the dynamic interactions between the miRNA and the selected ligands.

Keywords: miRNA, molecular dynamics simulation, de novo modelling.

A novel approach for precise manipulation of intracellular pH

by Asal GHAFFARI ZAKI1,2, Seyed Mohammad MIRI1,2, Şeyma ÇIMEN1, Tuba AKGÜL ÇAĞLAR1,2, Esra N. YIĞIT1, Mehmet Ş. AYDIN1, Gürkan ÖZTÜRK1,3, and Emrah EROĞLU1,2 | 1Regenerative and Restorative Medicine Research Center (REMER), Research Institute for Health Sciences and Technologies (SABITA), Medipol University, Istanbul, Turkey

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Presenter Name: Asal Ghaffari Zaki
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Implications of pH in development of various diseases such as cancer and neurodegeneration is well established. However, due to the lack of proper tools for manipulation of pH in specific (sub) cellular locales, the exact underlying mechanisms remained a mystery. We recently introduced Chemogenetic Operation of iNTRacellular prOton Levels (pH-Control) approach, as a novel alternative to previously established methods to manipulate pH with a high spatio-temporal resolution. In our study, we characterized pH-Control both *in vitro* and *in cellulo* using a genetically encoded biosensor for pH, called SypHer3s. Besides, we showed that with the help of pH-Control we can change the pH precisely in sub-cellular compartments such as mitochondria, nucleus, and cytosol of HEK293T cells. Furthermore, activity of pH-Control in dorsal root ganglion (DRG) neurons decreased the membrane potential.

This innovative pH manipulation technique holds an immense promise for advancing our understanding of the intricate interplay between pH dynamics and cellular function. By offering significant precision in manipulating pH within specific cellular compartments, pH-Control plays a key role for unraveling the integrate role of pH in health and disease. We anticipate that the insights gained through this approach will contribute significantly to the evolving landscape of drug development, providing new avenues for targeted therapeutic interventions.

DiPPI: A website including 3D structures of drug-like molecules in protein-protein interfaces

by Fatma Cankara | Simge Senyuz | Ahenk Zeynep Sayin | Attila Gursoy | Ozlem Keskin | Koç University | Koç University | Koç University | Koç University | Koç University

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Presenter Name: Simge Senyuz
Presenter Preference: Poster Presentation
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Proteins interact through their interfaces, and dysfunction of protein-protein interactions (PPIs) has been associated with various diseases. Therefore, investigating the properties of the drug-modulated PPIs and interface-targeting drugs is critical. Here, we present DiPPI (Drugs in Protein-Protein Interfaces), a two-module website that can be utilized for drug repurposing studies focusing on interface-bound drugs. On the interface module, we extracted properties of interfaces such as hotspots and post-translational modifications of drug-binding residues. On the drug side, we curated a list of drug-like small molecules and FDA-approved drugs from various databases and extracted those that bind to the interfaces. We clustered the drugs based on their molecular fingerprints and provided their drug properties, including Lipinski's rules. Using this dataset, we docked the HIV protease inhibitors tipranavir and indinavir to the EGFR-ERBB2/HER2 interface and EGFR-ERBB3/HER3 interface indicating that these drugs can be used to modulate the Ras/Raf/MEK/ERK pathway to suppress metastasis. Our dataset contains 534,203 interfaces for 98,632 proteins, of which 55,135 bind to a drug-like molecule. 2,214 drug-like molecules and 335 FDA-approved drugs are found in the interface region. DiPPI's well-curated and organized interface and drug data offer users an easy-to-follow framework for drug repurposing studies. The website can be reached in the following link: http://interactome.ku.edu.tr:8501/

Development of biocompatible and biodegradable cryogels for potential drug delivery applications

by Didem Demir | Seda Ceylan | Nimet Karagülle | Chemistry and Chemical Process Technologies Department, Mersin Tarsus Organized Industrial Zone Technical Sciences Vocational School, Tarsus University, Mersin, 33100, Türkiye | Bioengineering Department, Faculty of Engineering, Adana Alpaslan Türkeş Science and Technology University, Adana, 01250, Türkiye | Chemical Engineering Department, Faculty of Engineering, Mersin University, Mersin, 33110, Türkiye

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Presenter Name: Nimet Karagülle
Presenter Preference: Poster Presentation
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In this study, biocompatible and biodegradable chitosan/gelatin based cryogel scaffolds were fabricated by crosslinking with glutaraldehyde at cryogenic conditions, and their drug loading and release studies were evaluated for potential biomedical applications in drug delivery applications. Cryogels are suitable candidates to be used in drug release systems due to their interconnected pore structure, high surface area and high liquid absorption capacity. Therefore, we aimed to produce a cryogel to be used as drug release system. The chemical structure of the cryogel was characterized using Fourier Transform Infrared Spectroscopy and morphology was examined by Scanning Electron Microscopy. The cryogel sample was evaluated as potential drug release system by loading it with methyl orange as a model drug. The absorption capacity of the cryogels was found to be high, the cryogels were swollen in a short time, absorb the dye quickly and the cumulative release of the dye indicated that the gels were suitable for extended drug release systems. Developed cryogels are proposed to be used as drug release systems for biomedical applications.

Computational approaches and potential drug candidates for anticancer drug discovery RAB-GTAPases

by Murat Serilmez | İsmail Erol | Serdar Durdağı | PhD | Assistant Professor | Prof.Dr

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Presenter Name: murat serilmez
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Introduction

Rab proteins oscillate between an active guanosine triphosphate (GTP)-bound state and an inactive guanosine diphosphate (GDP)-bound state.Rab proteins, in the active (GTP-bound). There are 66 Rab GTPases associated with vesicular transport in the human genome.The GEFs and GDPs make Rab GTPases act as molecular switches.Based on membrane trafficking function, Rab GTPases are important to cancer progression.

Material Method

16000 molecules were downloaded from Chemdiv Kras-Targeted Library and prepared at neutral pH. For this purpose, the LigPrep module in the Schrödinger Maestro program was used. the 5SJZ PDB coded structure was used, In the protein preparation module. Briefly, Schrödinger SiteMap was used to predict the binding pockets. The grid files were generated by the Receptor Grid Generation module and the docking was evaluated by the ligand docking function /Glide SP).The Desmond program was used for this purpose.Best scoring docked complexes were initially submerged.OPLS3e forcefield was employed for assigning parameters. Simulations are conducted at 310 K and 1 bar. Simulations were repeated two times as 500 ns and 100 ns and calculated MMGBSA values

Results

SiteMap identified 3 different binding regions, and for each region top 10 molecules (according to Glide/SP docking) were selected. Among all ligands, P950-0240 at the site2 was the tightest binder.

Conclusion

The development of small GTPase inhibitors could be a useful new treatment strategy for both non-carcinogenic and carcinogenic diseases.However, the generation of these inhibitors is a challenging issue owing to the fine regulatory roles assigned to each of the members of the small GTPases protein family.

Investigation of Synthesis and The Biological Effect Profiles of New Benzimidazole Derivative

by Hasan Tahsin ŞEN | Ofcan OFLAZ | Gülgün AYHAN KILCIGİL | Lokman Hekim Univesrty, Faculty of Pharmacy, Deparment of Pharmaceutical Chemistry | Lokman Hekim Univesrty, Faculty of Pharmacy, Deparment of Basic Medical Sciences | Ankara Univesrty, Faculty of Pharmacy, Deparment of Pharmaceutical Chemistry

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Topic: General
Presenter Name: Hasan Tahsin ŞEN
Presenter Preference: Poster Presentation
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Benzimidazole is important heterocyclic system that shows biological activity against a range of pathogens and physical disorders. For this preliminary study, benzimidazole derivative containing oxadiazole side chain at the first position was synthesized. The thiosemicarbazide were converted to 1,3,4-oxadiazoles using mercuric (II) acetate. This synthesized derivative is likely to be active and therefore proteins with which it could interact well were investigated. The active compound's putative target proteins were analyzed using the bioinformatics tool Swiss Target Prediction, developed by the Swiss Institute of Bioinformatics. This tool operates through an algorithm based on human genome-derived proteins. According to the results of the Swiss Target Prediction analysis, the protein family with high likelihood of binding was subjected to molecular docking processes. Molecular docking analyses were conducted using the bioinformatics tool CB-Dock developed by AutoDock Vina. CB-Dock is designed for the prediction of protein-ligand interactions within a three-dimensional space. Protein Ligand Interaction Profiler (PLIP) is tool designed to facilitate the facile identification of non-covalent interactions between biological macromolecules and ligands. The protein groups with a high likelihood of binding, as determined by the Swiss Target Prediction analysis, are depicted in the graph below. According to the analysis results, it is hypothesized that the active compound may directly interact with protease enzymes. In light of these findings, the Mycobacterium tuberculosis homologous proteins “Cannabinoid receptor 2 (CNR2), Muscarinic acetylcholine receptor (CHRM1), Protein farnesyltransferase subunit beta (FNTB), Calpain-1 catalytic subunit (CAPN1)" have been selected for molecular docking and PLIP analysis.

Discovery of small molecules as potential therapeutics for NAFLD and HCC

by Shazia Iqbal | Trustlife Labs,Drug Research & Development center, Istanbul

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Topic: General
Presenter Name: Dr. Shazia Iqbal
Presenter Preference: Oral Presentation
Status: Accepted

Non-alcoholic fatty liver disease and its more severe form, non-alcoholic steatohepatitis (NASH), manifest in genetically susceptible individuals who experience excessive nutrient intake. The incidence rate of hepatocellular carcinoma (HCC) is progressively rising among individuals diagnosed with NAFLD. As of now, there is no FDA-approved drug reported to treat either NAFLD or NASH. Liver pyruvate kinase (PKL) is a major regulator of metabolic flux and ATP generation during glycolysis in liver cells and has been explored as a potential target for the treatment of non-alcoholic fatty liver disease (NAFLD). In this work, we designed a new class of JNK inhibitors, that affect PKL expression level selectively. Based on molecular docking studies, a list of attenuated analogues was synthesized, and their activities on PKL expression, cell viability, triacylglyceride (TAG) levels, and the expressions of steatosis-related proteins were tested in the HepG2 cell line. Afterwards, we ranked their effectiveness by examining their effects on the ratio of TAG level/cell viability in an in vitro steatosis model for NAFLD. Among the newly discovered drug candidates, compound **152** proved to be the most efficient in significantly reducing TAG levels and demonstrated lower toxicity in HepG2 cells. Additionally, we assessed the impact of all the synthesized compounds on the HepG2 cell line to determine their anti-cancer properties, and compound **171** exhibited the highest level of toxicity. To summarize, compound **152** shows potential as a drug candidate for treating NAFLD, while compound **171** holds promise as an effective drug candidate for HCC therapy.

Discovery of Novel Hsp90 Inhibitors Bearing 2H-Triazole Ring

by Tugba TAS | Ozgur Fırat OZPOLAT | Deryanur KILIC | Atatürk University, Faculty of Science, Department of Chemistry, Erzurum, Turkey | Computer Sciences Research and Application Center, Atatürk University, Erzurum, Turkey | Atatürk University, Faculty of Science, Department of Chemistry, Erzurum, Turkey

Abstract ID: 120
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Topic: General
Presenter Name: Tugba TAS
Presenter Preference: Poster Presentation
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Introduction: Hsp90 is an evolutionarily conserved molecular chaperone in eukaryotes that modulates multiple cellular processes through signaling pathways regulated by Hsp90-related proteins such as proliferation, cell cycle, and gene expression. Therefore, targeting Hsp90 today is a promising strategy for developing a new anticancer drug.

Methods: In the present work, structure- based approaches were used for virtual screening of a library of ~1000000 compounds (containing 2H-triazole ring), which was downloaded from ZINC-15 database. GLIDE modules such as HTVS (high throughput virtual screening), SP (Standard precision) and XP (Extra precision) were used as molecular docking tools for virtual screening. The ADME (absorption, distribution, metabolism, and excretion) properties of the best Glide XP compounds were evaluated, and elimination was made based on the #stars values. The remaining complexes were then examined by molecular dynamics simulations using Desmond.

Results and Discussion: Hit compounds (ZINC000286820133, ZINC000286803821, ZINC000286977413 and ZINC000286894825) were determined as a result of virtual screening and ADME, and molecular dynamics simulations (200 ns) of Hsp-90-hit complexes were carried out. The findings revealed that hit compounds were stable in the binding pocket.

Conclusions: The stable HSP90-hit complexes were discovered in this study, and the hit molecules were computationally determined to be potential Hsp90 inhibitors. In the wet lab, the anticancer effects and HSP90 protein interactions of the hit compounds will be examined in the wet lab.

TÜBİTAK (Project number: 221Z272) funded this research.

Keywords: Hsp90, Virtual Screening, Molecular Simulation

SUBSTRATE SPECIFICITY DETERMINATION OF FRAGARIA ANANASSA L. PROTEASE

by Esma Hande ALICI | Gulnur ARABACI | Sakarya University | Sakarya University

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Topic: General
Presenter Name: Esma Hande ALICI
Presenter Preference: Poster Presentation
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Proteases enzymes that catalytically cleave peptide bonds play integral roles in diverse physiological processes such as food digestion, intricate signaling cascades, the blood coagulation cascade, etc. The extensive array of biological functions is evident through the highly specialized substrate specificities exhibited by proteases. While some display remarkable promiscuity by cleaving various substrates, others exhibit pronounced specificity for particular substrate sequences. The substrate specificity of a protease is determined by molecular interactions occurring at the protein-protein interface within the binding cleft of the protease [1].

In this study, specificity of purified *Fragaria ananassa* L. protease towards natural substrates, modified substrate azocasein and p-nitroanilide (p-NA) conjugated synthetic substrates was investigated. To determine the activity of the enzyme in the presence of some natural substrates; bovine serum albumin, casein, hemoglobin and gelatin were used as substrates. The protease activity towards azocasein, a chemically modified protein that was designed as a substrate for proteolytic enzymes, was also determined and compared with natural substrates activities. Synthetic peptide substrates conjugated with p-nitroanilide that were tested in the study were L-Leu-pNA, N-Suc-Ala-Ala-Ala-pNA, Nα-Benzoyl-DL-Arg-pNA (DL-BAPNA) and N-Suc-L- Phe-pNA. The activities were determined spectrophotometrically under standard conditions. The activity of the substrate that showed the highest activity among all substrates was accepted as 100% and the activities of the other substrates were calculated as relative (%) activity according to this value.

References

1. Schauperl M, Fuchs JE, Waldner BJ, Huber RG, Kramer C, Liedl KR, PLoS One. 2015, 10(11), e0142658.

Silk Fibroin as a Promising Vehicle for Sulfonamide Drug Formulations

by Makbule Beyza ŞEN | Hasan Tahsin ŞEN | Semih Çalamak | Lokman Hekim Univesrty, Faculty of Pharmacy, Deparment of Biochemistry | Lokman Hekim Univesrty, Faculty of Pharmacy, Deparment of Pharmaceutical Chemistry | Lokman Hekim Univesrty, Faculty of Pharmacy, Deparment of Pharmaceutical Basic Sciences

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Topic: General
Presenter Name: Makbule Beyza Şen
Presenter Preference: Poster Presentation
Status: Accepted

Anticoagulant compounds play important role in treating thrombosis. Researchers aimed to create novel synthetic material with anticoagulant or antithrombotic properties that mimics heparin structure and function. Anticoagulant activity is primarily achieved through the presence of ionic functional groups, anticoagulant materials typically consist of ionic polymers containing sulfate, sulfamide, carboxylic acid groups. Research has shown that the anticoagulant properties of the polymer can be modified by incorporating sulfate and sulfonate groups into the polymer. Bombyx mori silk (SF) is widely used biomaterial in several biomedical applications. Moreover, SF is also highly biocompatible, highly oxygen permeable, biodegradable, minimally inflammatory, morphologically versatile, has strong mechanical properties. Sulfamethoxazole and sulfadimethoxine, recognized antibacterial agents, are classified as sulfonamide drugs. These drugs inhibit the proliferation and growth of many different types of bacteria that colonize wounds, the respiratory tract, the urinary tract. In this study, we investigated potential binding pathways between SF, sulfamethoxazole, and sulfadimethoxine using in silico approaches. Molecular docking studies were performed using the Glide module of Schrödinger software version 2023-1, results were interpreted for binding to SF. After in silico studies, SF solution was prepared and then mixed with specific concentrations of the drugs sulfamethoxazole and sulfadimethoxine to perform the experimental studies. Viscosity measurements were used to characterize the physical and chemical binding mechanisms. The overall results indicated that molecular and binding interactions could lead to further experimental studies to validate specific drugs, as well as to study the potential of using silk fibroin as carrier system in the design of anticoagulant materials.

Investigation of the Effects of 3-Carene on Neuronal Excitability: An ex vivo electrophysiological study

by Cansu YILMAZ, İsmail ABİDİN | Cansu Yılmaz is a senior undergraduate student at Yıldız Technical University, İsmail Abidin is a professor at Karadeniz Technical University

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Presenter Name: Cansu YILMAZ
Presenter Preference: Poster Presentation
Status: Accepted

Introduction: 3-Carene is a monoterpene obtained from woody plants of the pine genus. 3-Carene has antioxidant and anti-inflammatory effects. Besides, it has as anxiolytic effects and regulates sleep cycles. 3-Carene strengthens currents mediated by GABA-A receptors responsible for rapid inhibition in the central nervous system. Based on this existing knowledge , we hypothesized that 3-Carene, could affect the excitation/inhibition balance and neuronal excitability in the central nervous system.

Methods: We investigated the effects of two different doses of 3-carene (10 and 50 µM), on excitability of hippocampal circuitry. Horizontal hippocampal slices were obtained from 6-8 weeks old mice. Electrophysiological activities were recorded from CA1 region by glass micropipette electrodes. Artificial epileptic activity was induced with 4AP (100 µM). The properties of baseline oscillatory powers and epilepsy-like activities obtained before and after 3-Carene administration were compared.

Results and Discussion: Effects of two different doses of 3-Carene on i. baseline neuronal activity and ii. Synchronous seizure like events were calculated. Power of baseline activity (mV 2 /Hz) was also investigated in five different band ranges similar to common EEG bands. The changes of frequency, amplitude and duration of seizure-like events upon 3-Carene application were also determined.

Conclusions: Based on its previously reported neuronal effects and the present findings, we can suggest that 3-Carene may have a modulatory effect of neuronal excitability. Further in silico studies and experiments will help identify the related mechanism.

This study is supported by TUBİTAK 2209-A program.

Keywords: 3-carene, excitability, ex vivo brain slices, electrophysiology, Mouse

SYNTHESIS AND FUNCTIONALIZATION OF NANOSIZED METAL-ORGANIC FRAMEWORK (MOF) FOR TARGETED CONTROLLED RELEASE CANCER THERAPY

by Maha MORAL | Güliz AKYÜZ | Mübbera ANDAÇ | Nanoscience and Nanotechnology MD, Nanoscience and Nanotechnology PhD Student, Ondokuz Mayis University | Nanotechnology and Nanoscience PhD, Ondokuz Mayis Univesity, Post Doctoral researcher at University of Aveiro | Professor, Ondokuz Mayıs University, Department of Chemistry

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Topic: General
Presenter Name: Maha Moral
Presenter Preference: Oral Presentation
Status: Accepted

Metal-organic frameworks (MOFs) are coordination polymers consisting of inorganic metal ions joined together by organic bridging ligands to form a three-dimensional structure, with distinct physicochemical characteristics as a single unit.

By utilizing various organic linkers and synthesis techniques, structures with different size ranges, compositions, morphologies and chemical characteristics can be constructed with the desired features required for optimal drug delivery. Their surface can be easily modified to functionalize them for active targeting. They can also be engineered and tailored using different composition and structure to obtain responsive chemical and physical properties that can be used for stimuli-responsive controlled drug release.

The design of a drug-loaded MOF that is stimuli responsive to the acidic environment of cancer cells causes the MOF to decompose and release medication in a passive stimuli responsive manner together with its functionalization to act by active targeting as well, binding to the overexpressed receptors on cancer cells and releasing the drug only within cancer cells upon MOF disintegration.

A nanosized CoBDC MOF loaded with the hydrophobic anticancer Quercetin and functionalized with folic acid was successfully synthesized to active target cancer cells that have overexpressed folic acid receptors and to release the drug upon disintegration in response to the acidic pH characteristic to cancer cells in a passive responsive manner.

Characterization with XRD, FTIR and SEM confirmed successful synthesis and functionalization of a nanosized Quercetin-loaded CoBDC MOF, and the drug release study emphasized the pH-sensitivity of our MOF and confirmed our MOF's combined passive stimuli-responsive targeting strategy.

Synthesis of Novel Quinone Derivatives as Promising Antioxidant Agents

by Ayşe Nur ÖNEM | Sibel ŞAHİNLER AYLA | Mustafa ÖZYÜREK | Istanbul University-Cerrahpaşa, Department of Chemistry | Istanbul University-Cerrahpaşa, Department of Chemistry | Istanbul University-Cerrahpaşa, Department of Chemistry

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Presenter Name: Ezgi BİRDAL
Presenter Preference: Poster Presentation
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Studies and applications on synthetic quinone derivatives, which have an important place in many applications from cosmetics to pharmaceutical chemistry, have always gained great importance. In this study, the synthesis and characterization of some quinone compounds were carried out. (1-2) The antioxidant capacity of newly synthesized compounds were performed according to the original CUPRAC method, described by Apak et al [2]. The calibration curves of the related compounds were constructed, and their Trolox equivalent antioxidant capacities (TEACCUPRAC coefficients) were calculated (TEACCUPRAC=εsample/εTrolox). Ascorbic acid was used as a positive control. TEACCUPRAC values of compound (1) (2.55±0.02) and compound (2) (2.38±0.07) were found to be greater than ascorbic acid (TEACCUPRAC: 1.00).

Reference

1. K., Sandeep, K., Nikhil, R., Partha, S., M. Sham, 2013, Efficient synthesis of piperazine-2,6-dione and 4-(1*H*-indole-2-carbonyl)piperazine-2,6-dione derivatives and their evaluation for anticancer activity, MEDICINAL CHEMISTRY RESEARCH, vol. 22, 4600-4609.

2. ŞAHİNLER AYLA, S. And Gonul, G. P. 2022. Synthesis and characterization of some 2-quinonyl piperazine derivatives. PHOSPHORUS SULFUR AND SILICON AND THE RELATED ELEMENTS , vol.197, no.9 , 943-951.

3. R. Apak, K. Güçlü, M. Özyürek, S.E. Karademir, Novel total antioxidant capacity index for dietary polyphenols and vitamins C and E, using their cupric ion reducing capability in the presence of neocuproine: CUPRAC method, J. Agric. Food Chem., 52 (2004)7970-7981.

New Biologically Active Hybrid Indole Compounds

by Tarık Emre Öztürk | İstanbul Universtiy

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Presenter Name: Tarık Emre Öztürk
Presenter Preference: Poster Presentation
Status: Accepted

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Introduction: Cancer, which is described as abnormal cell Growth, the health-threatening cause of which for centuries is not exactly known, is a disease whose cure has still not been discovered despite number of researches carried out.

Today, a wide variety of chemotherapeutic compounds are used for cancer treatment. However, since cancer is an individual-specific disease, new and specific compounds for treatment should be established and these compounds should be evaluated for possible antitumoral and antimetastatic properties.

The compounds carrying the indole and hydrazinecarbothioamide (thiosemicarbazide) structure have attracted the attention of researchers due to their ability to demonstrate various biological activities in the literature and have been the subject of various researches especially due to their antitumoral activities.

Method: In this study, from the thesis that the new structures which are being formed by combination of two separete groups, each of which is known in literature by their antitumoral activity, can show higher anticancer activity, the novel hydrazinecarbothioamide compounds have been synthesized from hydrazide compound. After the structural determinations conducted by elemental analysis and spectral methods (IR, ^{1}H-NMR, ^{13}C-NMR, MS), the anticancer activities against various cell lines will be evaluated.

Results and Discussion: The spectral data and elemental analysis results approved the formation of novel compounds.

Conclusion: Further studies on diverse cell lines will be conducted to better understand the anticancer activity of the synthesized compounds.

Keywords: Synthesis, indole, hydrazinecarbothioamide

Synthesis of new N-(1,3-dioxolo[4,5-f]benzothiazol-2-yl)-2-(substituted)acetamide/propanamide and evaluation of their AChE and BChE activities

by Beyzanur TUTUŞ | Aybüke Züleyha KAYA | Yonca BAZ | Asaf Evrim EVREN | Begüm Nurpelin Sağlık | Leyla YURTTAŞ | Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey. Hatay Mustafa Kemal University, Kırıkhan Vocational School, Hatay, Turkey | a Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey. | a Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey. | a Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey, cBilecik Seyh Edebali University, Vocational School of Health Services, Pharmacy Services, Bilecik, Turkey | a Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey. | a Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Eskişehir, Turkey.

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Alzheimer hastalığı (AH), son yıllarda görülme sıklığı giderek artan nörodejeneratif bir hastalıktır. AD'nin henüz radikal bir tedavisi yoktur. Mevcut ilaçlar yalnızca semptomatik rahatlama sağlar ve nörodejenerasyonu durdurma özelliğine sahip değildir. Bu nedenle AD tedavisinde kullanılacak ve seyrini yavaşlatacak yeni bileşiklere ihtiyaç duyulmaktadır. Asetilkolinesteraz (AChE) ve bütirilkolinesteraz (BChE) inhibitör aktivitesi AD'de kullanılan stratejilerden biridir. Benzotiyazol halkası, doğada ve tedavi edici etkileri olan birçok bileşikte bulunan bir heterosiklik halkadır. Ayrıca çeşitli çalışmalar, benzotiyazol halkasının güçlü kolinesteraz inhibitör aktivitesine sahip olduğunu göstermiştir. Bu bilgilerin ışığında, bir dizi N-(1,3-dioksolo[4,5-f]benzotiyazol-2-il)-2-(sübstitüe)asetamid/propanamid (**3a-3k**) türevleri sentezlendi. 3,4-(metilendioksi)anilinden. Sentezlenen bileşiklerin *in vitro* Ellman yöntemi kullanılarak AChE ve BChE enzim inhibisyon aktivite çalışmaları devam etmektedir. *Ayrıca in vitro* çalışmalar sonucunda belirlenen en aktif bileşik için moleküler yerleştirme çalışmaları gerçekleştirilecek .

Using combination of different sets of features of molecules for improved prediction of solubility

by Muhammet Baldan | Acıbadem University

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Presenter Name: Muhammet Baldan
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Generally, absorbtion and bioavailability increase if solubility increases therefore, it is crucial to predict them in drug discovery applications.

Molecular descriptors and Molecular properties are traditionally used for the prediction of water solubility. There are various key descriptors that are used for this purpose, namely Drogan Descriptors, Morgan Descriptors, Maccs keys, etc., and each has different prediction capabilities with differentiating successes between different data sets. Another source for prediction of solubility is structural features; they are commonly used for prediction of solubility, howewer there are little to no studies that combine three or more properties or descriptors for prediction to produce a more powerful prediction model.

Unlike available models, we used a combination of those features in a random forest machine learning model for improved solubility prediction to better predict and, therefore, contribute to drug discovery systems.

ENZYMATIC AND NON-ENZYMATIC ANTIOXIDANT PROFILE OF BITTER DOCK PLANT GROWN IN SAKARYA REGION OF TURKEY

by Esma Hande ALICI | Gulnur ARABACI | Sakarya University | Sakarya University

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Presenter Name: Esma Hande ALICI
Presenter Preference: Poster Presentation
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During regular metabolic processes, the body can produce highly reactive compounds known as free radicals in the form of reactive oxygen species (ROS) that interact with cellular components and leading to their denaturation. These interactions contribute to the development of various pathological conditions in living organisms such as cancer and failures in immune and endocrine functions. Living organisms have developed antioxidant defense systems, consisting of various enzymatic (such as superoxide dismutase, catalase, peroxidase, etc.) and non-enzymatic components (such as glutathione, flavonoids, phenolic acids, etc.) to counteract the harmful effects of ROS accumulation. Consequently, when an excessive ROS production occurs, the antioxidant defense system steps in to regulate and express these enzymes and the other antioxidants, thereby mitigating the damage [1, 2]. Since fruits and vegetables are rich in antioxidants, they serve as effective protectors against various diseases [3]. Therefore, antioxidant properties of plants are intensively investigated for disease prevention.

In this study, the antioxidant potential of the bitter dock was examined. The study observed the enzymatic antioxidant capabilities of this plant, including peroxidase, catalase, superoxide dismutase, and polyphenol oxidase. The optimal pH and temperature conditions for each enzyme were identified spectrophotometrically to assess their activities under ideal circumstances. The non-enzymatic antioxidant activity of two different solvent fractions of the plant was determined by using DPPH radical scavenging and Reducing power activity.

References

1. Krishnamurthy P, Wadhwani AM. Antioxidant Enzyme. 2012;3-18.
2. Mates JM, Perez-Gomez C, De Castro IN. Clin Biochem. 1999;32(8):595–603.
3. Rahman K. Clin Interv Aging. 2007;2(2):219–236.

Exploring N-Ferrocenylmethylaniline Derivatives as Potent Anti-Breast Cancer Agents: Insights from Computational Chemistry, Pharmacokinetics, and QSAR Analysis

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Topic: General
Presenter Name: Nadjiba Zegheb
Presenter Preference: Poster Presentation
Status: Accepted

Breast cancer is the most common cancer in women in front of colorectal cancer and lung cancer. Ferrocene derivatives have proved their efficiency against breast cancer cells. In this study we aimed to find new ferrocene derivatives having pharmacochemistry properties as potential drug candidates against human breast cancer cells. A series of 29 N-ferrocenylmethylaniline derivatives (FMA) were optimized using DFT/ B3LYP method with 6-311 ++ G (d,p). The Pharmacokinetics and ADME properties were also studied. The anti-proliferative activity of the studied derivatives against both hormone-dependent (MCF-7) and independent (MDA-MB 231) human breast cancer cell lines were performed using MTT test. Moreover, the binding affinity between FMA derivatives and MCF-7 was further studied by molecular docking using AutoDock 4.2 software, using both estrogen and progesterone receptors as targets. Finally, the anti-proliferative activity of FMA derivatives against MCF-7 cell lines was used to predict a Quantitative Structure–Activity Relationship (QSAR) model.

The FMA derivatives have shown an important cytotoxicity effect against MCF-7 cell lines, which was explained using molecular docking by the interaction of the compounds with the ERα and PR. The QSAR model indicates that these descriptors (HOMO, E, MR, MV, HF, POL, TPSA, qC11 and qN1) have significant relationships with the observed bioactivity. The model was internally validated using Leave One Out method (LOO) to proves its successful application against MCF-7 cell line.

Conformational Effects of Post-Translational Modifications in MtrA

by Nur Eksi | Istanbul Medipol University

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Presenter Name: Nur Eksi
Presenter Preference: Poster Presentation
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Tuberculosis (TB) remains an enduring global health challenge caused by *Mycobacterium tuberculosis* (MTB). This infectious disease remains a significant threat to human health worldwide and is a critical concern for public health. The data from the World Health Organization underscore the magnitude of the issue, with millions of new TB cases and TB-related deaths reported annually. MTB utilizes two-component systems (TCS), such as MtrB/MtrA, to adapt to environmental changes and develop antibiotic resistance. While acting as a response regulator, MtrA undergoes complex post-translational modifications (PTMs) that significantly influence its activity. Understanding the role of these PTMs in MtrA is crucial. This research delves into the impact of specific PTMs, namely acetylation and methylation, on MtrA's conformation and functionality. The findings reveal that PTMs act as modulators of MtrA activity, influencing its DNA binding affinity and potentially affecting TB drug resistance. In addition, experimental investigations provide compelling evidence that suppressing MtrA results in heightened susceptibility of *Mycobacterium tuberculosis* cells to antibiotics targeting the cell wall and high-molecular-weight drugs. Simultaneously, these studies underscore the indispensable role of MtrA in the survival of *Mycobacterium tuberculosis*, emphasizing the potential of MtrA as a promising drug target. Computational structural analyses decode PTM-induced conformational changes in MtrA, providing valuable insights for TB drug development. In summary, this research enhances our understanding of PTMs' effects on MtrA in *Mycobacterium tuberculosis* and their potential implications for more effective TB treatments.

Evaluation of Antioxidant Properties of Casir (Prangos Ferulacea (L.) Lindl.) and Phenolic Profile by HPLC

by Rana Arıduru | Gülnur Arabacı | Sakarya Üniversitesi | Sakarya Üniversitesi

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Topic: General
Presenter Name: Rana Arıduru
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Casir *(Prangos Ferulacea (L.) Lindl.)* grows in the Artvin, Turkey were investigated about antioxidant activities. It is grown in the town of and used as a therapeutic in various forms by the people against diseases. Prangos belonging to the Apiaceae family is a perennial genus and found widespread in Turkey.[1] In Yusufeli region, fresh shoots of 10-20 cm are consumed in early spring. It is usually boiled in water or eaten or brined. It is also consumed in various forms in daily life such as breakfast. In some regions, the dried casir roots are mixed with honey and then consumed as aphrodisiac.[2] The body and roots of the plant have been proven to be effective especially in the treatment of digestive disorders. It has also been widely observed to help heal wounds and stop bleeding.[3]

In this study, first of all, the body parts of Casir *(Prangos Ferulacea (L.) Lindl.)* plant were extracted with methanol. Then, The total phenolic components of all extracts were analyzed by Folin Ciocalteu method[4] and were supported by HPLC [5]. The results showed that methanol-extract of Casir plant total phenolic contents with Folin-Ciocaltaeu method (66,55±0,35mg GAE/g extract). After determining the antioxidant values of Casir, HPLC analysis method was used to and identify the phenolic compound profile. Gallic acid and chlorogenic acid compounds were detected in methanol extracts of the plant. A general examination of activity studies in this study show that methanol is a suitable solvent for the plant results can be obtained with such selectivity.

Design, synthesis and antifungal activity of new monoterpene-containing azoles

by Nikolai Li-Zhulanov | Suat Sari | Keriman Ozadali-Sari | Dolunay Gülmez | Suna Sabuncuoğlu | Sevtap Arikan-Akdagli | Konstantin Volcho | Nariman Salakhutdinov | N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry SB RAS, 9 Akademika Lavrentieva Ave., Novosibirsk, 630090, Russia | Department of Pharmaceutical Chemistry, Hacettepe University Faculty of Pharmacy, Sihhiye, Ankara 06100, Turkey | Department of Pharmaceutical Chemistry, Hacettepe University Faculty of Pharmacy, Sihhiye, Ankara 06100, Turkey | Department of Medical Microbiology, Hacettepe University Faculty of Medicine, Sihhiye, Ankara 06100, Turkey | Department of Pharmaceutical Toxicology, Hacettepe University Faculty of Pharmacy, Sihhiye, Ankara 06100, Turkey | Department of Medical Microbiology, Hacettepe University Faculty of Medicine, Sihhiye, Ankara 06100, Turkey | N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry SB RAS, 9 Akademika Lavrentieva Ave., Novosibirsk, 630090, Russia | N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry SB RAS, 9 Akademika Lavrentieva Ave., Novosibirsk, 630090, Russia

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Presenter Name: Nikolai Li-Zhulanov
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Fungal diseases are a major public health concern as about 600 fungi species can cause human disease, and there are no licensed vaccines to prevent them. Fungal diseases have a significant impact on public health, with over one million humans dying every year from them. World Health Organization published WHO Fungal Priority Pathogens List to Guide Research in 2022 to underline the need for action [1]. The number of cases of fungal infections is increasing, particularly in immunocompromised patients, and current treatments are expensive and toxic. The development of antifungal drugs is challenging because fungi are eukaryotes and many potential treatment targets also occur in humans, increasing the risk of toxicity. There are four main families of antifungals: polyenes, azoles, echinocandins, and pyrimidine analogues. However, these antifungals are associated with therapeutic failures and antifungal resistance, making treatment difficult.

The present work aimed at creating new derivatives of azoles, for the first time including natural monoterpene fragments, which, as known, themselves have antifungal potential. The new synthesized hybrids show superior activity compared to the control drug fluconazole against both azole-susceptible and azole-resistant strains of *Candida* spp [2]. Many of these molecules have excellent minimum inhibitory concentration (MIC) values, which are 100-fold lower than the values of MICs of fluconazole.

The research was financially supported by the Russian Science Foundation, RSF grant 22-73-00046. Biological and modeling studies were funded by TSA-2023-20443.

1. *WHO fungal priority pathogens list to guide research, development and public health action*; WHO: Geneva, Switzerland, 2022.
2. N. Li-Zhulanov et al. Antibiotics, 12, 5: 818.

The effect of MEIS Inhibition in Cardiac Regeneration and Protection

by Fatih Kocabas | Yeditepe University

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Topic: General
Presenter Name: Aynura Mammadova
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We have recently shown that regulators of quiescence or cell cycle arrest could be targeted to modulate cardiomyocyte renewal.Notably,*Meis1*, which belongs to TALE-type class of homeobox gene family, appeared as one of the key regulators of cardiomyocyte cell cycle arrest and a potential therapeutical target.However, small molecule inhibitors of MEIS1 remained unknown.This led us to determine inhibitors of MEIS1 that could reactivate cardiomyocyte proliferation.We have used our previously constructed library of homeobox family inhibitors and implemented a high-throughput in silico screening approach targeting theMEIS homeodomain protein, leading to the identification of potential MEIS inhibitors(MEISi) without anticipated cytotoxicity and cardiotoxicity,as validated by PubChem bioassay analysis and hERG1 channel docking assessments. This was followed by *in-vitro* validation of putative MEIS inhibitors using MEIS-dependent luciferase reporter assays and analysis in the *ex-vivo* expansion of neonatal cardiomyocytes.We have shown that small molecules that we named MEISi-1 and MEISi-2 induce neonatal cardiomyocyte proliferation(Ph3+TnnT cells) and cytokinesis(AuroraB+TnnT cells).Intriguingly, our investigation delves deep into the genetic landscape, unveiling a substantial surge in the expression of cardinal cardiac-specific genes following extended post-MEISi treatment with(IPSCs). This transcriptional upregulation significantly impacts both cardiac mesoderm(CMs) and cardiac progenitor(CMPs) cells, underscoring the potential of MEIS inhibitors as master regulators of cardiac gene expression.Besides, this study has implications for cardiac tissue engineering using hIPSC-CMs and potential cardioprotection against doxorubicin-induced cardiotoxicity. In-vivo models will clarify the effects on apoptosis and ROS generation, with clinical relevance. In summary, this study advances our understanding of MEIS-inhibitors in cardiac biology, offering opportunities for regeneration, protection, and therapy.

Pharmacodynamic and pharmacokinetic studies of potential bioactive natural products in two Achillea species found in Greece

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Abstract ID: 104
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Presenter Name: Thomas Mavromoustakos
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The use of medicinal plants and their products as a mean to cure diseases is a practice that continues even to this day and has it's roots to the early history of mankind. The development of molecular docking alongside the rise of novel computational technologies has managed to considerably reduce the cost of drug development. Thus, molecular docking can be used to predict whether the natural products found in medicinal plants could potentially act as bioactive compounds that could lead to the development of novel drugs. In the present study the chemical compounds that are found at *Achillea Millefolium L.* and *Achillea Holosericea Sibth. Sm.,* which grows at the geographic area of Epirus, Greece, are collected and examined regarding their pharmacodynamic and pharmacokinetic properties, as well as their potential use as bioactive compounds. The compounds that show the desired properties are then examined *in silico,* using the AutoDock software, in order to determine their ability to effectively bind to two proteins, MAO-A and MAO-B.

Assessment of KRAS Inhibitors through Pharmacophore-Based Virtual Screening, Molecular Docking and AI-Enhanced ADMET Profiling via the Pharmit Server

by Yiğit Akkan | Defne Eşkin | Beril Uras | Mazlum Türk | Harun Nalçakan | Gülbin Kurtay | Hacettepe University | Ankara University | Hacettepe University | Hacettepe University | Ankara University | Hacettepe University

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Topic: General
Presenter Name: Yiğit Akkan
Presenter Preference: Poster Presentation
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KRAS, HRAS, and NRAS are members of the RAS protein family, which plays the role of binary molecular switches important for the control of key cellular signaling pathways governing essential cellular activities such as differentiation, proliferation, and survival. Particularly, KRAS stands out as the leading oncogene with the highest frequency of mutations in human cancer. The designation of RAS as a "undruggable" target, however, because of prior futile attempts to regulate it pharmacologically, has traditionally paralleled this distinction. However, recent technological developments and novel methods for drug discovery have revived optimism, providing a glimmer of hope for the doable creation of a direct KRAS inhibitor.

To find effective KRAS inhibitors, a versatile computational approaches were utilized such as pharmacophore-based virtual screening with Pharmit server. Particularly, a pharmacophore model based on the AMG510/KRAS co-crystallized receptor structure (PDB ID: 6OIM) was used to search the 103,302,052 compound-containing PubChem database. 38 intriguing compounds are found after applying Lipinski's and pharmacophore filters, which would be used in further molecular docking simulations. ADMET analyses are performed using SwissADME, OSIRIS, Molinspiration to gauge the effectiveness of the compounds and their compatibility with druglike properties. To assess the toxicity analysis of the candidates, AI-guided Syntelly and Toxtree software were employed. Using the SAMSON platform/2022-R2 and OneAngstrom/AutoDock Vina Extension, molecular docking simulations were ran simultaneously to reveal the potential of these screened candidates as powerful KRAS inhibitors.

Guiding TRK Inhibition Strategies: Revelations from Pharmacophore-Based Virtual Screening, Molecular Docking Analysis, and AI-Facilitated In Silico ADMET Profiling

by Beril Uras | Defne Eşkin | Yiğit Akkan | Mazlum Türk | Harun Nalçakan | Gülbin Kurtay | Hacettepe University | Ankara University | Hacettepe University | Hacettepe University | Ankara University | Hacettepe University

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Presenter Name: Beril Uras
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Status: Accepted

The tropomyosin receptor kinase (TRK) receptors, encompassing TRKA, TRKB, and TRKC isoforms, hold considerable promise as targets for therapeutic intervention in various types of malignant human cancers. These receptors have garnered significant attention due to their tendency to undergo diverse mutations that confer significant resistance to inhibitors, which are encoded by the neurotrophic receptor tyrosine kinase (NTRK) genes. In this perspective, various small molecules have been proposed in the literature although their efficacy has not yet been evaluated.

Therefore, we have employed several computational methods including pharmacophore-based virtual screening via the Pharmit server to identify potent TRK inhibitors. In this scope, The ZINC database, comprising 13,127,550 compounds, was screened using a pharmacophore model based on the co-crystallized receptor structure of 4EK/Tropomyosin Kinase (PDB ID: 4YNE). Pharmacophore and Lipinski's filter was executed and 818 hit compounds were identified for subsequent molecular docking simulations. In addition, ADMET inquiries were executed, encompassing an evaluation of the compounds' efficacy and their alignment with drug-like attributes. Therefore, the AI-centric Syntelly platform and Toxtree software for toxicity evaluation of the ligands, along with SwissADME, OSIRIS, and Molinspiration, were harnessed. In parallel, molecular docking simulation was conducted (via the SAMSON platform/2022-R2 and OneAngstrom/AutoDock Vina Extension), unraveling the binding potentials of the screened candidates as potent TRK inhibitors.

Crafting Excellence in LIM Kinase 1 Inhibition: Pharmacophore-Based Virtual Screening and AI-Boosted ADMET Insight in Molecular Docking Investigation

by Defne Eşkin | Yiğit Akkan | Beril Uras | Mazlum Türk | Harun Nalçakan | Gülbin Kurtay | Ankara University | Hacettepe University | Hacettepe University | Hacettepe University | Ankara University | Hacettepe University

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Presenter Name: Defne Eşkin
Presenter Preference: Poster Presentation
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The LIM kinases (LIMKs), which are made up of the two enzymes LIMK1 and LIMK2, are a group of protein kinases that play a crucial role in the control of actin dynamics. LIMK1 carefully regulates the dendritic spine density and size in a healthy brain. A worsened LIMK1 enzyme activity, on the other hand, causes structural deterioration in these spines in people with dementia. As a result, LIMK1 inhibition in dementia improves dendritic spine density and size, hence lessening the impact of Alzheimer's disease (AD). In this perspective, a number of small compounds have emerged as fruitful treatment targets for AD in the literature.

A variety of computational methods, including pharmacophore-based virtual screening with the Pharmit server, were used to uncover potent LIMK1 inhibitors. To search the 103,302,052 compound-containing PubChem database, a pharmacophore model based on the 9DB/LIMK1 co-crystallized receptor structure (PDB ID: 5NXC) was specifically used. After applying the Lipinski's and pharmacophore filters, 34 compounds were discovered that will be employed in additional molecular docking simulations. Consequently, SwissADME, OSIRIS, Molinspiration, were used for ADME assessments and toxicity analysis were employed using Syntelly (AI-guided tool) and Toxtree platform. Additionally, molecular docking simulations were run simultaneously using the SAMSON platform/2022-R2 and OneAngstrom/AutoDock Vina Extension to highlight the potential of these screened candidates as potent LIMK1 inhibitors.

Probing the MAO enzymes with novel quaternary propargylamine derivatives

by THOMAS MAVROMOUSTAKOS | NKUA

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Presenter Name: THOMAS MAVROMOYSTAKOS
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A versatile family of quaternary propargylamines was synthesized through the KA2 multicomponent reaction, involving the coupling of an amine, a ketone, and a terminal alkyne. Sustainable synthetic procedures employing transition metal catalysts were employed in all cases. The inhibitory activities of these molecules were evaluated against hMAO-A and hMAO-B enzymes, and they displayed significant inhibitory activities. The IC50 values for hMAO-A ranged from 765.6 to 861.6 uM, while the IC50 values for hMAO-B ranged from 152.1 to 164.7 uM. Furthermore, these compounds complied with the Lipinski's rule of 5 and exhibited no predicted toxicity. To understand their binding properties with the two target enzymes, key interactions were studied using molecular docking, molecular dynamics (MD) simulations, and MM/GBSA calculations. These molecules exhibit promising potential as leads for the treatment of neurodegenerative diseases such as depression, Parkinson's disease, and Alzheimer's disease.

Chalcones derivatives as potential anti-inflammatory agents

by THOMAS MAVROMOUSTAKOS | NKUA

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Presenter Name: THOMAS MAVROMOUSTAKOS
Presenter Preference: Poster Presentation
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The framework 1,3-diphenylprop-2-en-1-one (Fig. 1) is well known by the generic term ‘‘chalcone,’’. It is also known as benzalacetophenone and benzylidene acetophenone. The potential of the chalcones derivatives a, b and c (Figure 2), as possible drug leads was investigated. Their structure assignment were performed via joint experimental and computational chemistry. Specifically, the structure assignment and conformational analysis were performed through homonuclear and heteronuclear 2D Nuclear Magnetic Resonance (NMR) spectroscopy (2D-TOCSY, 2D-NOESY, 2D-HSQC, and 2D-HMBC) and via Density Functional Theory (DFT). Additionally, docking and molecular dynamics simulations were performed to discover their ability to bind and stability to remain in the active site of the LOX-5 enzyme. These *in silico* experiments and DFT calculations indicated favorable binding for the enzyme under study. The atomic details of chalcones derivative’s interaction profile with LOX-5 were revealed through Saturation Transfer Difference (STD) NMR (Nuclear Magnetic Resonance). Finally, *in vitro* experiments against the enzyme of lipoxygenase revealed favorable results.

Antioxidant efficiency and xanthine oxidase (XO) inhibition activity of newly synthesized piperazine derivatives

by Menekşe GÜNGÖR | Pınar KÖSE | Kevser Zehra AKSU | Ayşe Nur ÖNEM | Mustafa ÖZYÜREK | Sibel ŞAHİNLER AYLA | Istanbul University-Cerrahpaşa, Department of Chemisrty | Istanbul University-Cerrahpaşa, Department of Chemisrty | Istanbul University-Cerrahpaşa, Department of Chemisrty | Istanbul University-Cerrahpaşa, Department of Chemisrty | Istanbul University-Cerrahpaşa, Department of Chemisrty | Istanbul University-Cerrahpaşa, Department of Chemisrty

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Topic: General
Presenter Name: Şeyma ÖNNER
Presenter Preference: Poster Presentation
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In present study new piperazinyl substituted quinone derivatives were synthesized. The structures of compounds were charcterized by using spectroscopic techniques such as NMR, FT IR and mass spectroscopy.

These newly synthesized compounds were also evaluated for antioxidant efficiency and xanthine oxidase (XO) inhibition activity. Among the newly synthesized compounds, **(1)** had the highest antioxidant capacity ($TEAC_{CUPRAC}$= 2.63±0.01) and the TEAC value of this compound was found to be higher than that of ascorbic acid ($TEAC_{CUPRAC}$: 1, 00). XO enzyme was effectively inhibited by the newly synthesized Q-compounds with % inhibition values in the range of 54–66%.

Protective Effect of Selective mTORC2 Inhibition on Zymosan-Induced Hypotension in a Rat Model of Non-Septic Shock: Contribution of IKKα/IKB-α/NF-KB Pathway

by Zainab Sabrie | Meryem Temiz-Resitoglu | Taskın Kalkan | Banu Kılıc | Bahar Tunctan | Seyhan Sahan-Firat | Mersin University | Mersin University | Mersin University | Mersin University | Mersin University | Mersin University

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Topic: General
Presenter Name: Zainab Ali Mohamud Sabrie
Presenter Preference: Oral Presentation
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Mammalian target of rapamycin (mTOR) has very important basic cellular functions and has been extensively studied in different pathologies. This study aims to investigate the contribution of mTORC2 to zymosan-induced hypotension in rats and the role of IKKα/IκB-α/NF-κB pathway by using selective mTORC2 inhibitor JR-AB2-011. Rats were divided into four groups: (1) Control group (SF, 4 ml/kg, i.p.), (2) Zymosan group (500 mg/kg, i.p.), (3) JR-AB2-011 group (1 mg/kg), and (4) Zymosan + JR-AB2-011 group. The rats ' mean arterial pressures and heart rates in all groups were measured before saline or zymosan injection and at 1st, 2nd, 3rd, and 4th hours. JR-AB2-011 was administered to rats 1 hour after saline or zymosan injection. After the experimental protocol, all animals were sacrificed, and the kidney, heart, thoracic aorta, and superior mesenteric arteries were collected. Rictor, Akt, IKKα, IκB-α, NF-κB p65, and β-actin protein expression and/or phosphorylation were measured in the tissue samples. We reported an increase in mTORC2 activity in zymosan-administered rats shown by increased phosphorylation of Akt and Rictor expression. Additionally, zymosan caused an increase in the expression of p-IκB-α, p-IKK-α, NF-κB p65, and p-NF-κB p65 with a decrease in IκB-α protein expression. JR-AB2-011 reversed all these changes induced by zymosan. Our results demonstrate for the first time that selective mTORC2 inhibition by JR-AB2-011 reverses zymosan-induced hypotension and IKKα/IκB-α/NF-κB pathway activation seems to contribute to this process. Therefore, we suggest that JR-AB2-011 could be a novel pharmacological approach for non-septic shock.

Keywords: zymosan, hypotension, mTORC2, rat, non-septic shock.

Development and Optimization of a Novel “Chimeric Protein Reporter” Screening Assay for TGFb-SMAD Signaling

by Nilay Çolak | Hacettepe University School of Medicine, Dept. of Medical Biology, Ankara, Turkey

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Topic: General
Presenter Name: Nilay Çolak
Presenter Preference: Oral Presentation
Status: Accepted

Introduction: TGFβ (Transforming-growth-factor-□) signaling initiates wound healing and regulates context dependent processes including apoptosis, proliferation, migration, and differentiation. Over-active TGFβ signaling is associated with irreversible fibrosis and pivotal in cancer, autoimmune diseases and atherosclerosis. Thus, assessment of TGFβ signaling is key in development of any therapeutic means. We aimed to develop an innovative cell-based SMAD responsive dual reporter assay to express SEAP (Secreted Alkaline Phosphatase) and GFP fusion peptide to profile TGFβ signaling in vitro.

Methods: The GFP protein was cloned into the C-terminus of SEAP by using the “Overlap Extension PCR” method and so a chimeric open reading frame to express dual reporter proteins. The vector was transfected into the C2C12 cells and SEAP enzyme activity was assayed in supernatant, GFP expression was quantitated using fluorimetric measurements.

Results and Discussion: Following the transfection limited GFP was observed in cells, but SEAP activity was not detectable (following 24, 48 and 72 hours). Based on these, in silico modeling approaches were used to engineer the “linker region” in the chimeric structure. Better reporter functionality was obtained following meticulous optimization of the connecting "linker region".

Conclusions: While transient expression studies pinpoint the functionality of the chimeric constructs, our ultimate aim is to obtain a stable cell line to be used as an in vitro screening assay to monitor TGFb signaling towards high-throughput screening. This model is a key to screening and optimization of anti-TGFb compounds and support drug development efforts towards augmentation of TGF-β signaling.

Keywords: TGFβ, GFP, SEAP, reporter

The Effect of Conformational Dynamics on Calmodulin-Mediated Sensor Activity

by Büşra Tayhan | Melike Berksöz | Ali Rana Atilgan | Canan Atilgan | Sabancı University | Sabancı University | Sabancı University | Sabancı University

Abstract ID: 94
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Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Büşra Tayhan
Presenter Preference: Oral Presentation
Status: Accepted

Genetically Encoded Fluorescent Biosensors(GEFB) are molecular tools of precision and sensitivity to monitor protein interactions and enzyme activity. An example of these tools is Ca2+ biosensors, with Calmodulin(CaM) being a calcium-binding protein that has been effectively integrated as a sensing domain in fluorescent calcium sensors. The ability of CaM to undergo conformational changes upon calcium binding makes it a valuable component for biosensor applications, enabling effective indicator of cellular processes. Structural transitions of CaM depend on different environmental variables and chemical modifications of the protein therefore, our aim is to investigate the dynamics of CaM to achieve the best designs.

We perform 1-μs-long Molecular Dynamics(MD) simulations under physiological/low ionic-strength(IS) for apo/holo CaM. Then we utilize two essential degrees of freedom, linker end-to-end distance and torsion angle to project the CaM conformations into low dimensional space. Furthermore, we explore the dynamics of CaM with a modification of our perturbation-response scanning(PRS) technique, by aiming to identify the sensitive residues for removal of calcium ions.

Our analyses indicated that the conformational states sampled by the protein are influenced by ion concentration. Lowering the IS significantly reduced the region visited by apo/holo CaM. The mobility of the N-terminal domain is affected by calcium, regardless of IS, which acts as the point of connection to fluorescent protein in CaM-based sensors.

Based on our results, we propose that the dynamics of holo/apo transition of sensing domains can reveal the potential sites of linkage to fluorescent protein to achieve the highest level of allosteric modulation of fluorescence.

Proteomic-bioinformatic characterisation of an antimicrobial peptide isolated from the nontoxic fraction of scorpion venom

by Djelila Hammoudi-Triki | .USTHB, Laboratory of Cellular and Molecular Biology, Faculty of Biological Sciences, USTHB, BP 32, El Alia, Bab Ezzouar, 16111, Algiers, Algeria.

Abstract ID: 93
Submitted: September 2, 2023
Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Djelila Hammoudi-Triki
Presenter Preference: Poster Presentation
Status: Accepted

Currently, the use of different proteomic approaches and their association with in silico techniques have made it possible to better exploit natural biomolecules as prototypes to design new therapeutic agents. In this light, scorpion venoms are an interesting example of rich sources of diverse biomolecules that could be of great therapeutic potential. The non-toxic fraction from the scorpion, venom had shown anti-infectious activity in a mouse model of intraperitoneal infection, by *Bacillus cereus.* The active fraction was able to reduce bacterial growth and inflammatory profile. The purification of the anti-infective molecule is carried out using a proteomic approach using RP-HPLC and LC-MS/MS followed by *in silico* structural characterization. The bioactive molecule is a sodium channel inhibitor automatically annotated only by gene model, under the name of G-TI classified by *in silico* similarity as a sodium channel blocker. It includes a "Knot" domain rich in cysteine and also present in defensins, trypsin inhibitors of the "Kunitz" family and other protein families. The determination of the physicochemical parameters of G-TI showed that it's made up of 68 amino acids, the first of which at the N terminal end is a valine. Its amino acid composition is diverse without noting a blatant predominance of a particular amino acid. It has a molecular weight of 7391.33 Da, an extinction coefficient at λ280 nm of 1.14 M-1cm-1 and an overall charge of +2 and a pHi 8. Proteomic and bioinformatics analyses proved for the first time the proteomic evidence of the sodium neurotoxin G-TI.

Activation Mechanism of AKT: A Control Point of Cell Fate

by Meryem Eren | Özlem Keskin | Hyunbum Jang | Attila Gürsoy | Ruth Nussinov | Koç University | Koç University | NCI | Koç University | NCI

Abstract ID: 92
Submitted: September 2, 2023
Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Meryem Eren
Presenter Preference: Poster Presentation
Status: Accepted

AKT (PKB) is a crucial regulator that functions as a molecular switch by orchestrating intricate signaling cascades. It has pivotal roles in cell survival, growth, and proliferation through PI3K/AKT/mTOR pathway. This makes AKT a prime therapeutic target for diverse cancer types. In this study, we used molecular dynamics simulations to further our understanding of AKT activation mechanism. We particularly investigated the aftermath of PH-domain detachment from the kinase domain, focusing on the interplay between the phosphorylation events and the intramolecular contacts between linker and C-tail. We seek to unveil the role of these molecular events in modulating AKT's activity and their potential implications in cancer signaling.

We utilized multiple AKT1 models, including different phosphorylation states (Thr308, Ser473), along with ATP/ADP-binding and C-tail truncation. We analyzed the trajectories to inspect key elements for activation: αC-helix and DFG motif orientations, spine motif formations, and intramolecular interactions. Our comparative analysis reveals that only the fully phosphorylated AKT-ATP exhibits a distinctive stabilization of the kinase domain. Notably, we observe the most stable R-spine and C-spine formation, highest salt-bridge occupancies, and critical residue contacts between N-lobe and C-lobe of the kinase domain in this system. C-tail interactions appear to allosterically contribute to the AKT activity, even after PH-domain removal and ATP-binding. These suggest they are collectively required for the protein’s functional state and allosterically regulate its activity. Overall, our study provides a deeper understanding of how AKT is activated, which may be useful in further improving therapeutic targeting of AKT with drugs.

Manganese (Mn) doped Fullerenes as a MR imaging material for anticancer drug : Thiotepa : A DFT Study

by Serap Şentürk Dalgıç | Dilek Kuzaliç Bürücü | Fatma Kandemirli | Department of Physics, Faculty of Science, Trakya University | Electric and Electronic Engineering Dept., Faculty of Engineering & Architecture, Beykent University | Biomedical Engineering Department, Faculty of Engineering & Architecture, Kastamonu University

Abstract ID: 91
Submitted: September 1, 2023
Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Dilek Kuzaliç Bürücü
Presenter Preference: Oral Presentation
Status: Accepted

Abstract

We have presented a Density Functional Theory (DFT) calculation on the Thiotepa (THIO) drug adsorption properties on the Manganese (Mn) doped Fullerene by comparison with the other metal-doped Fullerenes in previous calculations. It was first considered for the thiotepa adsorption. All the probable positions of THIO adsorption on Mn-doped Fullerenes were investigated to find which one is energetically favourable.

The charge analysis indicates that charge transfer is from the adsorbed THIO to the pristine and Mn-doped carbon fullerenes Cn. However, the results suggest that those Mn-Cn can serve as promising sensors in practical applications to detect, recognize and carry THIO drug for its medicinal drug delivery applications.

Keyword: Mn-doped Fullerenes, Thiotepa (THIO), DFT calculations, Sensors, drug carrier, drug delivery vehicle, carbon fullerenes

Elucidating the Conformational Dynamics and Activation Mechanism of CHK2 via Molecular Dynamics Simulations

by Clara Xazal Buran | Ceren Kilinc | Gizem Dinler Doganay | Levent Doganay | Mert Gur | Department of Mechanical Engineering, Istanbul Technical University, Istanbul, Turkey | Department of Biochemistry and Molecular Biology, Michigan State University, USA | Department of Molecular Biology and Genetics, Istanbul Technical University, Istanbul, Turkey | Gastroenterology and Hepatology Unit VM Pendik Medicalpark Teaching Hospital, Istanbul, Turkey ; Department of Internal Medicine Bahçeşehir University (BAU), Istanbul, Turkey | Department of Mechanical Engineering, Istanbul Technical University, Istanbul, Turkey ;Department of Computational and Systems Biology, University of Pittsburgh, Pittsburgh, PA, USA

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Topic: General
Presenter Name: Clara Xazal Buran
Presenter Preference: Poster Presentation
Status: Accepted

Cancer is a leading global cause of death, and checkpoint kinase 2 (*CHEK2*) plays a vita role in cancer prevention. Its protein product, CHK2, maintains genomic stability by regulating DNA repair and cell cycle checkpoints. While it is established that CHK2 mutations are linked to various cancers, full details of its catalytic cycle remain elusive.

Normally, CHK2 exists as an inactive monomer in cell nucleus. Upon double-strand DNA breakage, CHK2 is phosphorylated and forms dimer. Subsequent phosphorylation of activation loop (A-loop) triggers further conformational changes, leading to disassociation of the CHK2 homodimer into fully active monomers.

Our study employed comprehensive all-atom Molecular Dynamics (MD) simulations, utilizing insights from partial crystal structures available in the Protein Data Bank. Prior to MD simulations homology models built on the partial available structures were constructed and used as starting conformations. Our simulations explored various states of CHK2, including its phosphorylated and ADP-bound forms and uncovered its conformational dynamics during activation process. Importantly, our work elucidates the positions of FHA domain, C-helix, and A-loop within monomeric CHK2 throughout its catalytic cycle. We also generated a comprehensive free energy surface covering a significant portion of this cycle.

This research lays the molecular groundwork for better understanding CHK2's essential role in genomic stability and offers avenues for potential therapeutic interventions. By elucidating the CHK2 activation mechanism, we contribute to the ongoing efforts to develop new strategies for treating CHK2-related disorders and enhancing our grasp of its complex regulatory mechanisms.

This work was supported by TUBITAK Grant 318S129.

Binding Strengths and Molecular Interactions of Self-Peptides with HLA-B*51:01

by Sema Zeynep Yılmaz | Derman Basturk | Ahmet Gul | Burak Erman | Mert Gur | Department of Mechanical Engineering, Istanbul Technical University (ITU), 34437, Istanbul, Turkey | Department of Mechanical Engineering, Istanbul Technical University (ITU), 34437, Istanbul, Turkey | 2Division of Rheumatology, Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey | Chemical and Biological Engineering, KocUniversity, Istanbul, Turkey | Department of Mechanical Engineering, Istanbul Technical University (ITU), 34437, Istanbul, Turkey; Department of Computational and Systems Biology, University of Pittsburgh, Pittsburgh, PA, USA

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Submitted: September 1, 2023
Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Sema Zeynep Yılmaz
Presenter Preference: Poster Presentation
Status: Accepted

Human Leukocyte Antigen (HLA) proteins are crucial to the immune system, aiding the transfer of peptides from cells' interiors to their surfaces for presentation to CD8+ T cells. Specific alleles, such as HLA-B*51, are strongly linked to diseases like Behçet's disease, an autoinflammatory disorder of unknown etiology. Incompatibility between HLA-B*51 and certain peptides can result in unstable complexes, triggering inflammation.

In our study, we selected peptides that interact with HLA-B*51:01 from an immune epitope database, focusing on those that meet specific criteria: a length of eight to 11 residues and the inclusion of key binding residues. Despite HLA-B*51:01's capacity to bind thousands of peptides, limited data exists on their binding poses and dynamics. To fill this gap, we analyzed the interactions between HLA-B*51:01 and 33 self-peptides using molecular dynamics (MD) simulations. Binding affinities were determined with NetMHCpan 4.1, and strengths were assessed through steered MD simulations (i.e. *in silico* pulling experiments) performed at loading rates comparable to those in high-speed atomic force microscopy experiments.

Using all-atom MD simulations we obtained a deeper understanding of the dynamic structural aspects of HLA-B*51:01 and its interactions with self-peptides. This novel knowledge may contribute to clarifying the molecular link between HLA-B*51 and Behçet's disease, potentially laying the groundwork for targeted therapeutic strategies.

This work was supported by TUBITAK, Grant No: 119Z553

Effect of Microtubule Curvature on Dynein Binding Explored through Molecular Dynamics Simulations

by Derman Basturk | Mert Golcuk | Ahmet Yildiz | Mert Gur | Department of Mechanical Engineering, Istanbul Technical University (ITU), Istanbul, Turkey | Department of Mechanical Engineering, Istanbul Technical University (ITU), Istanbul, Turkey | Physics Department, University of California, Berkeley, CA, USA; Department of Molecular and Cellular Biology, University of California, Berkeley, CA, USA | Department of Mechanical Engineering, Istanbul Technical University (ITU), Istanbul, Turkey; Department of Computational and Systems Biology, University of Pittsburgh, Pittsburgh, PA, USA

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Topic: General
*Presenter Name: Derman Başt*ürk
Presenter Preference: Poster Presentation
Status: Accepted

Motile cilia, whip-like projections on cells, rhythmically beat to propel sperm, drive fluid flow, and mediate cell signaling. The cilium's core, the axoneme, features nine outer microtubule doublets surrounding two central ones. Understanding self-coordinated ciliary motion aids ciliopathy comprehension. Inner arm and Outer arm dynein motor proteins (IADs and OADs) induce microtubule sliding for effective bending. Alternating active/inactive dyneins on opposite sides propel bending. Coordinating negative feedback mechanisms governing dynein activity within axonemes remain enigmatic, holding the key to ciliary malfunctions and broader implications.

We performed all-atom molecular dynamics (MD) and steered MD (SMD) simulations of the OAD microtubule binding domain (MTBD) in the presence of tubulin to elucidate the mechanisms regulating ciliary beating. OAD binding to tubulin and structural rearrangements in MTBD and tubulin upon binding were simulated for microtubules with no curvature, positive curvature, and negative curvature to test OAD binding sensitivity to microtubules curvature.

We observed that when left near tubulin without curvature OAD MTBD was able to bind the microtubule within several 100 nanoseconds, while OAD MTBD was not to bind to microtubule having positive or negative curvature during the simulation durations of 1000 nanoseconds.

This work was supported by TUBITAK Grant 122N045.

Insights from Molecular Dynamics Simulations on TAU and MAP7 Unbinding Mechanisms

by Reyhan Metin Akkaya | Mert Gölcük | Ahmet Yildiz | Mert Gür | Department of Mechanical Engineering, Istanbul Technical University (ITU), Istanbul, Turkey | Department of Mechanical Engineering, Istanbul Technical University (ITU), Istanbul, Turkey | Physics Department, University of California, Berkeley, CA, USA ;Department of Molecular and Cellular Biology, University of California, Berkeley, CA, USA | Department of Mechanical Engineering, Istanbul Technical University (ITU), Istanbul, Turkey; Department of Computational and Systems Biology, University of Pittsburgh, Pittsburgh, PA, USA

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Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Reyhan Metin Akkaya
Presenter Preference: Poster Presentation
Status: Accepted

Microtubule-associated proteins (MAPs) play a crucial role in maintaining microtubule stability and facilitating motor protein function. However, investigating these proteins is challenging due to their intrinsically disordered conformation. This complexity poses obstacles in terms of experimental characterization and resolving their intricate three-dimensional structures and their movements at atomic resolution.

In this study, we conducted conventional all-atom molecular dynamics (MD) simulations and steered MD simulations to elucidate the mechanisms of unbinding from the microtubule surface for TAU and MAP7 proteins. AlphaFold model was used to predict the unresolved regions of the MAP7 bound to the microtubule crystal structure (PDB ID:7SGS). For TAU, the crystal structure of TAU (PDB ID:6CVN) was utilized and its missing R1-R4 repetitive microtubule binding domain was constructed based on R2 segment. To accommodate the larger size of the MAP7 and TAU proteins compared to their crystal structures, the microtubule structure was modelled to comprise 10 tubulin doublets, including their highly fluctuating and structurally unresolved C-terminal tails. First conventional MD simulations were performed to explore the interactions between these MAPs and microtubule, which was followed by constant velocity-steered MD simulations to model MAP7 and TAU unbinding mechanisms and binding strength.

Our simulation revealed that the highly charged C-terminal tails establish robust interactions with both TAU and MAP7. Notably, we observed that when TAU and MAP7 underwent partial unzipping, the unzipped parts interacted with the C-terminal microtubule tails, rendering the separation challenging or leading to re-interactions after unbinding.

This work was supported by PRACE (Grant:2021250119) and TUBİTAK (Grant:121C283)

Manganese (Mn) doped Fullerenes as a MR imaging material for anticancer drug : Thiotepa : A DFT Study

by Serap ŞENTÜRK DALGIÇ | Dilek Kuzalic Burucu | Fatma Kandemirli | Department of Physics, Atomic and Molecular Physics Branch, Faculty of Science, Trakya University, 22030 Edirne, Turkey | Electric and Electronic Engineering Dept., Faculty of Engineering & Architecture, Beykent University, Turkey | Biomedical Engineering Department, Faculty of Engineering & Architecture, Kastamonu University, Kastamonu.

Abstract ID: 86
Submitted: September 1, 2023
Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Dilek Kuzalic Burucu
Presenter Preference: Oral Presentation
Status: Accepted

Enter description here.

This oral presentation will be presented Dr. Dilek Kuzalic

Metal doping and Size effect on the drug detection and delivery of the Carbon Nanotubes (CNTs): Theoretical studies and perspectives.

by serapd@trakya.edu.tr | Department of Physics, Atomic and Molecular Physics Branch, Faculty of Science, Trakya University, 22030 Edirne, Turkey

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Submitted: August 31, 2023
Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Serap ŞENTÜRK DALGIÇ
Presenter Preference: Oral Presentation
Status: Accepted

Prof. Dr. Serap ŞENTÜRK DALGIÇ

Short Biography

She is a Professor in the Atomic and Molecular Physics of the Physics Department at Trakya University in Edirne, Turkey. She has received a BS (1984) degree at Istanbul University, MS (1987) and PhD (1992) degrees in Physics. She was in a post-doctoral position at East Anglia University in Norwich-England. She visited ICTP-Italy many times. She was in the Physics Department of the University of Valladolid, Spain, for long and short periods to give courses and participate in projects. She became a Professor in 2003 at Trakya University. She was a director/a member of various Academic and administrative units of Trakya University. She is the author of over 48 scientific articles published in SCI journals and more than 150 conference studies at national and international conferences. Her publications received more citations (h-index 10). She was also the researcher or director of some international and national projects.

She has studied modelling and atomistic simulations on Molten Salts, Liquid Metals, Nano surfaces, nanomaterials, Nanomaterials, Nanomaterials, and Carbon-based nanomaterials. Recently, she has focused on DFT studies on molecules, atomic clusters, drug delivery systems, and molecular interactions in ionic liquids. She has done 20 master's/10 doctorate studies in Physics. She won the Turkish Physical Society 2021 Honorary Award.

Identification of Dickkopf-1 Antagonist Candidates using Virtual Screening

by Sahra Setenay Baran | Yusuf Şimşek | Aylin Sepici Dinçel | Gazi University, Graduate School of Health Sciences, Ankara, Türkiye | Gazi University, Vocational School of Health Services, Ankara, Türkiye | Gazi University, Vocational School of Health Services, Ankara, Türkiye

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Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Sahra Setenay Baran
Presenter Preference: Poster Presentation
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The Wingless/Int-1 (Wnt) signaling pathway plays an important role in the regulation of many biological processes such as cellular growth, tissue repair, and cancer. Dickkopf-associated protein-1 (DKK-1) is one of the natural extracellular inhibitors of the Wnt pathway due to its interaction with LRP5/6 (Low-Density Lipoprotein Receptor-Related Protein 5/6) receptors. Therefore, targeting the inhibition of the interaction of DKK-1 and LRP5/6 is a good approach for studies that aim to activate the Wnt signaling pathway such as osteoblast differentiation. It was aimed to investigate the potential of small molecules to be DKK-1 inhibitor candidates. In order to determine the interaction between our small molecules library downloaded from online databases and DKK, the Glide module of Shrödinger software was used. The thermodynamic stability of molecular interactions was studied by the Prime MM-GBSA program. The results show that the 1-(beta-D-Ribofuranosyl)-4-fluoro-1H-indole, 3,5-Bis[6-(hydroxymethyl)pyridine-2-yl]-1H-pyrazole and 4-[3,5-Bis(hydroxymethyl)phenylethynyl]benzoic acid are compounds that can strongly inhibit the interaction of DKK-1 with LRP5/6. Compounds of aromatic heterocyclic structure can be potential candidates in the treatment targetting DKK-1 and LRP5/6 interaction. Therefore, their effects need be investigated by *in-vitro* and *in-vivo* studies.

Keywords: anti-DKK-1, LRP5/6, small-molecules, virtual screening

Unraveling Potential: Tailoring Liver Pyruvate Kinase Inhibitors via Structural Guided Optimization

by Sajda Ashraf | Trustlife Labs

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Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Sajda Ashraf
Presenter Preference: Oral Presentation
Status: Accepted

The liver isoform of pyruvate kinase (PKL) has attracted attention due to its potential role in regulating fatty acid synthesis, a process implicated in the progression of non-alcoholic fatty liver disease (NAFLD) [1, 2]. JKN-IN-5A has previously emerged as a potential therapeutic agent for fatty liver diseases, particularly NAFLD, by effectively reducing PKLR expression and lowering triglyceride (TAG) levels. The optimization of JKN-IN-5A derivatives was guided by modeling and structural biology. A study investigating the structure-activity relationship among 75 newly synthesized derivatives highlighted PKL inhibitors that exhibited the most significant impact on curbing TAG accumulation. Despite the challenges inherent in probing a binding site, these derivatives encompass a broader range of structural diversity and chemical compositions, potentially enhancing their inhibitory potency against PKL. The findings contribute to a deeper understanding of the specific structural prerequisites governing interactions with PKL's ADP-binding site.

Design, synthesis, and antimicrobial evaluation of novel thiazole derivatives: In vitro and in silico approaches

by Aybüke Züleyha Kaya | Asaf Evrim Evren | Ülküye Dudu Gül | Leyla Yurttaş | Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, 26470, Eskişehir, Turkey. | Bilecik Seyh Edebali University, Vocational School of Health Services, Pharmacy Services, Bilecik, Turkey | Bilecik Seyh Edebali University, Faculty of Engineering, Department of Bioengineering, Bilecik 11230, Turkey | Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, 26470, Eskişehir, Turkey.

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Submitted: August 31, 2023
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Topic: General
Presenter Name: Aybüke Züleyha Kaya
Presenter Preference: Poster Presentation
Status: Accepted

Fungal infections are still one of the most serious diseases that threaten human health today. It is frequently seen in people whose immune system is weakened due to various diseases, diabetes patients, and people hospitalized in intensive care units. There is an urgent need to develop novel antimicrobial agents that can overcome drug resistance. For this purpose, 3,4-disubstituted-*3H*-thiazole derivatives were synthesized to obtain antimicrobial activity. Structural analysis of the final compounds (**4a**-**4p**) was performed by APCI and NMR techniques. Then, the antimicrobial activities of the substances were investigated using bacterial and fungal strains. As a result, it was determined that compound **4o** is as potent as standard drugs (voriconazole and fluconazole) against *C. albicans* and *C. glabrata* strains. The target protein, lanosterol demethylase (LDM), is currently under investigation via molecular docking and dynamics simulation studies. Experimental studies are planned based on these studies for the active compounds.

DESIGNING PEPTIDES TO PREVENT YAP-TEAD COMPLEX FORMATION BY INTEGRATION OF NON CANONICAL AMINO ACIDS INTO ROSETTA COMMONS

by Emre Can BULUZ | İsmail Hakkı AKGÜN | Department of Biotechnology, Institute of Science and Technology, Ege University, 35100, Bornova, İzmir, Türkiye | Department of Bioengineering, Faculty of Engineering, Ege University, 35100, Bornova, İzmir, Türkiye

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Topic: General
Presenter Name: Emre Can BULUZ
Presenter Preference: Poster Presentation
Status: Accepted

Introduction:

Non canonical amino acids can be defined as amino acids that are not genetically encoded by living organisms (1). The peptidomimetic studies to be performed with this type of amino acids are very promising (2). In the study carried out by Gfeller et al., the rotamer library and force field parameters of approximately 200 unnatural amino acids were compiled (3). Renfrew et al. developed a protocol for compiling various parameters of Non canonical amino acids using Rosetta Commons software. With the protocol they developed, they carried out both molecular modeling and wet laboratory studies of peptides that could be inhibitors of the Calpain/Calpastatin complex (4). In this study, we focused on integrating the rotamer library compiled by Gfeller et al. into Rosetta Commons software, calculating energy parameters, and finally performing molecular modeling studies using Non canonical amino acids. Using the compiled library of non canonical amino acids, it was aimed to develop YAP/TEAD complex inhibitors that initiate oncogenic transcriptional programs that are very important in tumor development, metastasis and drug resistance (5).

INVESTIGATION OF CELLS AND CYTOKINES INVOLVED IN DEMYELINATION AND REMYELINATION PROCESS VIA THE MULTIPLE SCLEROSIS CUPRIZONE MODEL USING HEMATOPOIETIC STEM CELL TRANSPLANTATION

by Müge Didem ORHAN | PhD Candidate

Abstract ID: 80
Submitted: August 31, 2023
Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Müge Didem ORHAN
Presenter Preference: Oral Presentation
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The aim of this study is to explore novel potential IL-17A inhibitors by using diverse applications involving in silico, in vitro and in vivo model of multiple sclerosis (MS).

In silico techniques involve the mapping of IL-17A and its receptor structures using the Protein Data Bank (PDB), assessing critical amino acids for ligand-receptor binding, and preparing structures for simulations. FDA-approved drugs are screened based on binding sites, binding affinity scores, MM/GBSA score, therapeutic activity, and compatibility with critical amino acids. Lead compounds were selected from relevant libraries. Inhibitory effects of selected compounds on reporter HEK cells overexpressing IL17Rs, monitoring NFkB and AP1 activation were analyzed through in vitro analysis. Three of twelve drugs showed no inhibitory effect at the highest concentration (100µM), while the others exhibited almost 100% inhibition of IL-17A/IL17RA interaction. Additionally, three drugs displayed inhibition at 100µM, though the lowest concentration showed limited effect. Six drugs demonstrated over 50% inhibition at 10µM. In vivo experiment was conducted using selected active compounds by using cuprizone mice model of MS to observe demyelination and effect of IL17A inhibitors on specific cytokines.

Twelve drugs wre identified as potential anti-IL17A candidates for receptor-ligand binding points among the 2300 FDA-approved molecules screened. Berotralstat, Epirubicin, and Mitaxantrone showed the maximum inhibitory efficiency with IC_{50} values of 4.5µM, 2.2µM, and 0.7µM, respectively, indicating effective inhibition of IL-17A/IL-17RA interaction at lower concentrations, while other drugs demonstrated inhibitory activity at higher concentrations. Following in vitro and in vivo studies confirmed the inhibitory activities of selected compounds.

Synthesis, Characterization and Antimicrobial Activities of Tetra-Paraben Substituted Monospiro Cyclotriphosphazenes

by Perihan Kızılkaya | Elif Şenkuytu | M. Özkan Baltacı | Gönül Yenilmez Çiftçi | Department of Chemistry, Trakya University, Edirne, Türkiye. | Department of Chemistry, Atatürk University, Erzurum, Türkiye. | Department of Molecular Biology and Genetics, Atatürk University, Erzurum, Türkiye. | Department of Chemistry, Gebze Technical University, Kocaeli, Türkiye.

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Topic: General
Presenter Name: Perihan Kızılkaya
Presenter Preference: Poster Presentation
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Cyclotriphosphazenes, $N_3P_3Cl_6$, one of the most precious members of inorganic ring systems, are deeply preferred in the design and development of new molecules having different physical and chemical properties for using diverse applications depending on the side groups replacing their chlorine atoms [1,2].

Parabens, belong member of esters of p-hydroxybenzoic acid, are used as the preservative or antimicrobial agents against fungi, bacteria and yeast for pharmaceutical and cosmetic industries. Besides, parabens derivative compounds also exhibit several biological properties such as highly cytotoxic activity on cancer line and DNA interaction [3-5].

In this study, firstly, the mono-spiro 2-Mercaptoethanol that contains both a hard oxygen donor and a soft sulfur donor derivative of cyclotriphosphazene was synthesized to use as starting compound. Then, the reactions of this compound with methyl paraben, ethyl paraben, and propyl paraben respectively were caried out for first time. All newly synthesized compounds were purified and their structures were characterized with different spectroscopies technique such as single crystal X-ray diffraction, mass spectrometry, ^{1}H, and ^{31}P NMR spectroscopies. The antimicrobial activities of the all compounds were investigated.

References

1. Allen, C. W. Chem. Rev., 1991, 91, 119–135.
2. Greish Y.E., Bender J.D., Lakshmi S., Brown P.W., Allcock H.R., Laurencin C.T., Biomaterials, 2005, 26, 1.
3. Şenkuytu, E., Kızılkaya, P., Ölçer, Z., Pala, U., Davarcı, D., Zorlu, Y., Erdoğan, H., Yenilmez Çiftçi, G., Inorganic Chemistry, 2020, 59, 2288–2298.
4. Şenkuytu E., Akbas N., Yildirim T., Yenilmez Çiftci G., New Journal of Chemistry, 2022, 46, 2453-2464.
5. Park, C.J., Nah, W.H., Lee, J.E., Oh, Y.S., Gye, M.C., Andrologia, 2011, 23.

Design and Synthesis of Novel 1,3,4-Oxadiazoles as Potential Anticancer Agents

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Introduction

An intensive study is carried out around the world to develop new drugs that can act against cancer. 1,3,4-oxadiazole derivatives also draw attention as molecules with a very strong potential in these drug development studies. The 1,3,4-oxadiazole structure, which is currently used in the structures of various drugs, is also being tested against cancer in drug development studies.

Methods

Synthesis of novel 1,3,4-oxadiazole compounds was carried out in four steps. In the first step, 2-thioether benzaldehyde derivatives to be used as the starting compound were obtained as a result of the nucleophilic aromatic substitution (S_NAr) reaction between thiophenol derivatives and 2-fluorobenzaldehyde. In the second step, benzylidene acyl hydrazones were synthesized from the reaction of synthesized aldehyde compounds and hydrazine derivatives. In the third step, new 1,3,4-oxadiazole compounds were obtained by I_2-catalyzed intramolecular cyclization of hydrazones.

In the last step, 1,3,4-oxadiazole compounds synthesized were reacted with m-chloroperbenzoic acid, and sulfonyl groups were added to the structures.

Results and Discussion

The synthesized compounds were purified by column chromatography. Their structures were elucidated by IR, ^{1}H NMR, ^{13}C NMR and Mass spectroscopic methods. The dose- and time-dependent anticancer activity of novel 1,3,4-oxadiazole derivatives was examined

against breast (MCF7), lung (A549), and colon (HCT 116) cancer cells.

Conclusions

With the results obtained, more detailed studies will be carried out on candidate molecules that show activity on the proliferation of cancer cells, and it will be possible to reveal which molecular pathways cause this effect.

Keywords: 1,3,4-oxadiazole, hydrazone, cyclization, anticancer activity.

Investigation of Viomycin Pass Through MscS Ion Channel, an Antibacterial Drug Target

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Aim: The small conductivity mechanosensitive ion channel (MscS) may be an antibacterial drug target, but the mechanism of cell access of solutes from EcMscS ion channels is not clear yet. In this study, we aimed to determine whether an antibiotic can pass through the channel by binding to this channel.

Methods: Cell viability was determined using CFU counting on MscS expressed and non-expressed E.coli strains in Viomycin concentration-dependently. Ligand binding sites (PDB-code:6RLD) were determined by the Proteins-Plus program, and Viomycin (PubChem-code:135398671) was placed in the MscS by blind docking using ClusPro2.0. Ligand-bound and unbound constructs were inserted into the lipid bilayer with CHARMM-GUI. After minimization and equilibration, 500ns MD simulations were made using the CHARMM36m force-field with the GROMACS2020.1 version. An EEF of 0.02V/Å was applied to the ligand to simulate the viomycin transition. Ligand-protein interaction and ligand pass-through-the-channel analyses were performed with trajectory files.

Results: Our in-vivo findings showed that viomycin reduced cell viability in wild-type EcMscS-containing strains dose-dependently. It was observed that the EcMscS channel maintained its closed conformation for 500ns in ligand-bound and unbound states. When EEF was not applied to the Viomycin, it remained bound to the B, C, D monomers in the extracellular-part of the channel pore, but when EEF was applied, it was observed to pass into the cytosolic space at 20ns during simulation.

Conclusion: Due to the potential of MscS as an antibacterial drug target, it is thought that the passage of different drugs through the channel should be investigated.

Keyword: MscS, Viomycin, Cell viability, MD simulation.

New Ibuprofen-based prodrug from tert-butyl alpha-hydroxymethacrylate

by Simay Denizkuşu / Burcu Balaban | Aleyna Esenturk | Seckin Altuncu | Duygu Avci | Bogazici University | Bogazici University | Bogazici University | Bogazici University

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Presenter Name: Simay Denizkuşu
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Introduction: Ibuprofen (IBU) is one of the most widely used nonsteroidal anti-inflammatory drugs (NSAIDs). Unfortunately, high systemic dosage of this drug can result in side effects such as heart attack, stroke and stomach ulcers. Therefore, localized and targeted delivery is the major obstacle to effective use of this drug. The development of polymeric prodrugs which can improve the bioavailability of a drug, decrease their toxicity, facilitate administration, enable better control of drug release, or deliver the drug to specific tissues is an important strategy. In this work, a novel IBU functionalized alkyl alpha-hydroxymethacrylate and poly(ethylene glycol) methyl ether methacrylate (PEGMA)-based copolymeric prodrug was synthesized and the release properties were investigated.

Methods: The drug (MA-IBU-*co*-PEGMA) was synthesized by polymerization of PEGMA (80 mol%) and IBU functionalized *tert*-butyl alpha-hydroxymethacrylate (20 mol%) in bulk using AIBN, followed by cleavage of *tert*-butyl groups by trifluoroacetic acid. Its nanoparticles were prepared by nanoprecipitation method and characterized by FTIR, SEM, DSC and XRD analysis. The drug release studies were performed in PBS (pH 7.4) using dialysis method and the amount released was determined using a UV spectrophotometer.

Results: The amphiphilic copolymer was observed to self-assemble to form nanoparticles in aqueous solution. This prodrug did not show a significant burst release in PBS, which is a drawback for the usually used small molecule IBU.

Conclusions: The prodrug may increase bioavailability and decrease side effects of IBU.

Acknowledgment: This study was supported by ADP (50003) of Bogazici University.

Keywords: alkyl alpha-hydroxymethacrylates; drug delivery; Ibuprofen; polymer-drug conjugate

Design and synthesis novel oxadiazole-thiadiazol as aromatase inhibitors: In vitro and in silico evaluation

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In the search for new anticancer agents, our group aimed to design and synthesize novel thiazole derivatives carried on thiadiazole-oxadiazole hybrid as core. Final compounds (**5a–5i**) were obtained via steps reaction and analyzed via NMR and HRMS techniques. The pharmacokinetic profile of the final compounds was predicted via in silico calculations. Their anticancer properties were determined using MTT method against MCF7 and A549 cell lines. Compounds with small group substitutions (**5a**, **5b**, and **5c**) were found more active against MCF7 cells than A549 cells while they were not cytotoxic on L929 healthy cells. In general, it can be summarized that acetamide moiety has a pivotal role in anticancer activity. For further studies, their aromatase inhibitory activity was evaluated. After the determination of all these features, the binding modes of the active compounds and the stability and relation of the ligand-enzyme complex were investigated using molecular docking and dynamics simulation studies. In vitro and in silico studies suggest two important structure-activity relationship (SAR) points that at least one azole ring is essential, and if there is approximately 8.0 ± 0.5 Å distance between the H-bond rich zone of ligand and the heteroaryl ring system of ligand has a major impact on aromatase inhibitory activity. Compounds with small group substitution on thiazole ring derivatives are suggested as candidates that may be used for the treatment of anti-breast cancer orally.

Match Score Motif Representation to Design Novel Antimicrobial Peptides

by Ümmü Gülsüm Söylemez | Malik Yousef | Zülal Kesmen | Burcu Bakir-Gungor | Department of Software Engineering, Faculty of Engineering, Muş Alparslan University, Muş, Turkey | Department of Information Systems, Zefat Academic College, Zefat, Israel | Department of Food Engineering, Faculty of Engineering, Erciyes University, Kayseri, Turkey | Department of Computer Engineering, Faculty of Engineering, Abdullah Gul University, Kayseri, Turkey

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Topic: General
Presenter Name: Burcu Bakir-Gungor
Presenter Preference: Oral Presentation
Status: Accepted

Introduction: Researchers are interested in antimicrobial peptides (AMPs) because they provide a substitute for conventional antibiotics in the fight against antibiotic resistance and display additional pharmaceutically significant features. Computational studies in this field aim to explore the biological cues or qualities that govern activity, and also aim to understand how antibacterial activity is conducted in a machine learning scenario.

Methods: In this study a novel approach based on motif representation, motif match score and machine learning was put forward. The main idea behind the match score-based feature extraction method is to identify significant patterns that are present in AMPs. We combine the top five motifs to produce new peptides based on feature significance scores. Novel AMP sequences with potential antibacterial activities against i) Gram-positive, and ii) Gram-negative bacteria have been designed separately. "DBAASP: strain-specific antibacterial prediction based on machine learning approaches and data on AMP sequences" program is also used to validate the antimicrobial activity of the designed peptide sequences.

Results and Discussion: We get 98% accuracy and 99% AUC for Gram-negative and 96% accuracy and 98% AUC for Gram-positive datasets. The model that we have proposed in this study could pave the way to the precise prediction and the design of antimicrobial peptides that are highly effective against bacterial pathogens.

Conclusions: Before synthesizing de-novo AMPs, here we propose a method to computationally evaluate the antimicrobial activity of the candidate peptides. Future studies could also generate novel antifungal, antiviral, antiprotozoal, and anticancer peptides using the proposed techniques.asal

In Silico Assessment of Nigella Sativa Phytochemicals Targeting Key Proteins in Aspergillus fumigatus

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Presenter Name: Khawaja Faheem Shahid
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Abstract

Background: Aspergillus fumigatus stands as the predominant species within the aspergillus genus, bearing a significant burden in the escalation of invasive aspergillosis (IA). This formidable ailment has ushered in a distressing surge in mortality rates, soaring to an alarming 90% within the afflicted patient cohort

Methods: This study employs a comprehensive methodology, initiating with molecular docking of Nigella sativa phytochemicals against critical pathogenic targets in Aspergillus fumigatus. PubChem and Protein Database (PDB) provide structural inputs for phytochemicals and proteins, respectively. MOE software facilitates intricate docking simulations. Next, high-affinity phytochemicals undergo assessment for drug-like attributes using ADMET SAR and SWISS ADME tools. Molecular Simulations (MD Simulations) through GROMACS software follow, elucidating intermolecular dynamics and complex stability.

Results: Thymoquinone emerges as an exemplar due to its remarkable efficacy, boasting an impressive repertoire of attributes encompassing anti-bacterial, anti-cancerous, and anti-oxidant activities. This multifaceted nature positions Thymoquinone as a frontrunner, anticipated to exhibit a notable propensity for high-affinity interactions with the pathogenic targets intrinsic to Aspergillus fumigatus. The amalgamation of its potent bioactivities with its structural features suggests a promising avenue for efficacious engagement against the pathogenicity associated with Aspergillus fumigatus.

Conclusion: Within the realm of botanical resources, Nigella sativa emerges as a reservoir of potential phytochemicals that hold promise as potent anti-fungal agents against the formidable Aspergillus fumigatus. This unique botanical composition harbors compounds with the potential to effectively counteract the pathogenic influence of Aspergillus fumigatus, ushering in a new avenue of exploration for combating fungal infections.

In Silico Identification of Sclerostin Inhibitors

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Presenter Name: YUSUF ŞİMŞEK
Presenter Preference: Oral Presentation
Status: Accepted

Sclerostin (Scl) and dickkopf-1 (DKK1) are primary inhibitors regulating the Wnt signaling pathways. Both molecules have important roles in the formation of the hard tissues such as bone, tooth enamel, dentin, and cementum. Also, they are critical molecules for hard tissue related diseases. Neutralization of Scl with drug-like molecules was studies as a therapeutic target in bone diseases. To prevent protein-protein interaction between the LRP6 and Scl structure, residues 91-97 (PNAIGR motif) on the Scl loop 2 must be capped with drag-like molecules. However, Scl loop 2 appears to be relatively flexible and is highly mobile in solution. Therefore, we performed molecular dynamics simulation before screening study, and an ensemble of receptor composed of eight distinct geometrical structures of the Scl was obtained from 50 ns MD simulation. Structure-based virtual screening protocol implemented in Schrodinger software has been performed to identify hits among DrugBank compounds. Combination of molecular docking, MD simulation and MM-GBSA methods were successfully used for screening the DrugBank compounds to inhibit flexible PNAIGR motif in loop 2 region of the Scl. Compound DB02675 has been identified to have the most binding affinity toward the PNAIGR motif after MM-GBSA analysis of MD trajectories. Besides, DB15238, DB04226, DB03325 and DB05644 have significant binding energies and number of molecular interactions.

Computational Evaluation of potent SGLT1 Inhibitors: Sotagliflozin Derivatives Explored with Pharmacophore-Based Virtual Screening, Molecular Docking, and AI-Guided ADMET Assessment

by Harun Nalçakan | Mazlum Türk | Gülbin Kurtay | Müşerref Önal | Ankara University | Hacettepe University | Hacettepe University | Ankara University

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Presenter Name: Harun Nalçakan
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Diabetes mellitus (DM) is a metabolic disorder characterized by elevated blood glucose levels, a condition known as hyperglycemia. The deleterious effects of hyperglycemia can result in tissue and blood vessel damage, ultimately leading to severe complications. Recently, the sodium-dependent glucose cotransporter (SGLT) has emerged as a promising target for managing diabetes due to its unique mechanism of action. The SGLT family, encompassing primarily SGLT1 and SGLT2, facilitates the active transport of extracellular glucose into the cell cytoplasm via the electrochemical potential of sodium ions. While several selective SGLT2 inhibitors have gained clinical approval, their efficacy in diabetes management remains limited. Therefore, there is a growing interest in blood glucose control by targeting SGLT1, offering an alternative approach that is not contingent upon renal function.

Based on this perspective, a detailed computational investigation including pharmacophore-based virtual screening was conducted to reveal potential selective SGLT1 inhibitors. In this scope, sotagliflozin, which is a promising SGLT1 inhibitor was used as a pharmacophore model via Pharmit server and PubChem database (103,302,052 compounds) was employed for virtual screening. After, applying pharmacophore filter and Lipinski's filter, 207 hit candidates were identified for further investigations. Additionally, ADME assessments were conducted to gauge the compounds' efficacy and druglikeness. Therefore, SwissADME, OSIRIS, and Molinspiration, was employed. In addition, toxicity assessments were conducted using Toxtree software and Syntelly, which is and AI-driven platform. Simultaneously, molecular docking simulations were executed (via the SAMSON platform/2022-R2, OneAngstrom/AutoDock Vina Extension), elucidating the binding affinities of the screened compounds as potent SGLT1 (PDB ID: 7WMV) inhibitors.

Pol Theta Inhibitors in Cancer Therapy : Molecular Mechanisms and Therapeutic Potential

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Presenter Name: Ekin CÜCÜ | Atakan AYDIN
Presenter Preference: Poster Presentation | Poster Presentation
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This review highlights the importance of Pol Theta in DNA repair and its prospects for cancer therapy. Pol Theta inhibitors, which are derived from the synthetic lethality concept, are proving to be effective anti-cancer drugs, but they are still in the early stages of development. The design, synthesis, and intricate binding details of many classes of these inhibitors, including novobiocin, carboxamidobenzimidazoles, and ART558, are examined. Molecular interactions, binding affinities, and pharmacokinetic characteristics of these inhibitors are investigated using computational techniques and cross-validated with results from experiments. For the best clinical trial candidates, in vitro tests give insights into the inhibitors' potency, selectivity, and cytotoxic properties, matching predictions with actual data. The study also explores Pol Theta inhibitor methods and resistance factors, emphasizing the drugs' potential for treating a variety of malignancies, including ovarian, breast, prostate, and pancreatic cancers. Adverse reactions and biomarkers like BRCA statusserve as indicators for therapeutic response. Future prospects include medicines that are integrated with other medications, although certain unmet needs call for more study. In conclusion, Pol Theta inhibitors show potential as a cancer treatment and demand thorough investigation.

DNA AND EGFR PROTEIN DOCKING OF HEXAHISTIDINE

by Alparslan Numan Yıldız | Soykan Ağar | E. Esra Kasapbaşı | Mine Yurtsever | Ana yazar

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Histidine oligomers (His-tags) are mostly used in purification steps of recombinant proteins in molecular biology and genetic studies due to their high affinity and selective binding to bivalent metal-NTA resin **[1].** Due the catalytic effect metal coordination, the cleavage of polypeptide bond occurs. The first row transition metal cations such as Co^{+2}, Ni^{+2}, Cu^{+2}, and Zn^{+2}, present in the human body are known to facilitate the binding upon coordinating to the basic nitrogen atoms of the imidazole moiety of the histidine molecules. Recently, the other effects like modulation effect of His-tags on the DNA activity was also reported **[2].** In this study, the hexahistidine (His_6) chain and its coordination complexes with M^{+2}-NTA resin were modelled for M^{+2} = Ni^{+2}, Cu^{+2}, and Zn^{+2}, realistically. The nature of the coordination and the impact of metal type on protein binding was studied via the model structures by using DFT methodology at B3LYP/6-31g (d,p) level. We determined that the presence of metal cation improved the protein binding capacity of His_6 and Ni^{+2} was the most efficient metal due to its smaller size and $3d^8$ configuration in its outermost subshell. The complex bearing Ni^{+2} was found to be the most stable coordination complex with high affinity towards hexahistidine with amino acid tail **[3].**

Exploring of Interaction Between Bcl-2 Protein and Novel BH3 Mimetics with X-ray Crystallography

by Merve YILMAZ | Koc University

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Presenter Name: Merve YILMAZ
Presenter Preference: Poster Presentation
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The Bcl-2 protein family plays a crucial role in regulating programmed cell death and maintaining the balance between cell survival and death. This study primarily focuses on comprehending the structural intricacies of the Bcl-2 protein, a critical regulator of cellular equilibrium, by employing X-ray crystallography. In addition, our investigation focuses on BH3 mimetics, a class of inhibitors emulating the pro-apoptotic BH3 domain, which show promise in sensitizing cancer cells, particularly in B cell lymphoma. These mimetics disrupt the interactions between anti-apoptotic proteins like Bcl-2 and their pro-apoptotic counterparts, potentially enhancing therapeutic approaches.

The core aim of our study is to uncover the interaction mechanism between Bcl-2 and these recently identified BH3 mimetics. Through comprehensive analysis of molecular interactions and dynamic structural features, we intend to clarify how these mimetics bind to Bcl-2, ultimately impacting its function.

Our research significantly enhances our comprehension of Bcl-2's structure through X-ray crystallography and sheds light on its interplay with novel BH3 mimetics. The implications of these findings hold substantial promise in advancing therapeutic strategies for B cell lymphoma and other malignancies characterized by disruptions in apoptosis pathways.

ANTIPROLIFERATIVE EFFECT OF ASTRAGALOSIDE-IV IN A CELL CULTURE MODEL OF PSORIASIS

by Serhat SEVGİ | Zeynep DEMİR ÖKSÜZ | Elif GÜN | Ayşe BÜYÜKTAŞ | Canan ÇAKIR ÇOBAN | Tuba DİNÇER | Karadeniz Technical University Drug and Pharmaceutical Technology Application and Research Center (KTU İLAFAR), Karadeniz Technical University Faculty of Pharmacy, Department of Pharmacology | Karadeniz Technical University Drug and Pharmaceutical Technology Application and Research Center (KTU İLAFAR) | Karadeniz Technical University Drug and Pharmaceutical Technology Application and Research Center (KTU İLAFAR), Karadeniz Technical University Faculty of Pharmacy, Department of Pharmacology | Karadeniz Technical University Drug and Pharmaceutical Technology Application and Research Center (KTU İLAFAR), Karadeniz Technical University Faculty of Pharmacy, Department of Pharmacology | Karadeniz Technical University Drug and Pharmaceutical Technology Application and Research Center (KTU İLAFAR) | Karadeniz Technical University Drug and Pharmaceutical Technology Application and Research Center (KTU İLAFAR), Karadeniz Technical University Faculty of Medicine, Department of Medical Biology

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Presenter Name: Elif GÜN
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Introduction: Psoriasis, a chronic multifactorial skin disease, is characterized by hyperproliferation and abnormal differentiation of epidermal keratinocytes. Current therapeutics for psoriasis have limited efficacy and tolerability, thus alternative agents are needed. Astragaloside-IV (AS-IV) is a herbal compound that is widely used in Chinese medicine. Recently, AS-IV has been shown to prevent UVB-induced oxidative damage and inflammatory response in HaCaT cells, however its effect in psoriasis is unknown. HaCaT cells gain hyperproliferative properties when treated with lipopolysaccharide (LPS) and this is commonly used as an in vitro model of psoriasis. We investigated the effect of AS-IV on LPS-induced proliferation of HaCaT cells.

Method: HaCaT cells were incubated with LPS (100 ng/ml) and AS-IV (12,5-25-50-100 μM) or vehicle (DMEM, as control). Cell proliferation was measured with WST-1 colorimetric assay.

Results: Proliferation was significantly reduced ($p<0.05$) in LPS-treated HaCaT cells co-treated with 12.5 and 25 μM AS-IV compared to vehicle. In contrast, in non-LPS-treated cells, 50 μM AS-IV increased proliferation ($p<0.05$) compared to vehicle.

Conclusion: AS-IV demonstrated a significant concentration- dependent antiproliferative effect only in HaCaT cells treated with LPS. Role of cytokines (such as IL-1β, IL-6) in the mechanism of action of AS-IV is currently under investigation. Future studies involving animal models will pave the way for development of AS-IV as a new therapeutic agent in psoriasis. *This study was supported by the TUBITAK 2209A University Students Domestic Research Projects Support Program (Project no 1919B012111805 to AB).*

Key words: therapeutic, astragaloside, LPS, proliferation.

REPOSITIONING OF TRIMETAZIDINE: EFFECTS IN AN IN VITRO MODEL OF PSORIASIS

by Berkay DEMİRÇİ | Elif GÜN | Zeynep DEMİR ÖKSÜZ | Serhat SEVGİ | Yeşim KAYA YAŞAR | Seçkin ENGİN | Tuba DİNÇER | Karadeniz Technical University Drug and Pharmaceutical Technology Application and Research Center (KTU İLAFAR), Karadeniz Technical University Faculty of Pharmacy, Department of Pharmacology | Karadeniz Technical University Drug and Pharmaceutical Technology Application and Research Center (KTU İLAFAR), Karadeniz Technical University Faculty of Pharmacy, Department of Pharmacology | Karadeniz Technical University Drug and Pharmaceutical Technology Application and Research Center (KTU İLAFAR) | Karadeniz Technical University Drug and Pharmaceutical Technology Application and Research Center (KTU İLAFAR), Karadeniz Technical University Faculty of Pharmacy, Department of Pharmacology | Karadeniz Technical University Faculty of Pharmacy, Department of Pharmacology | Karadeniz Technical University Faculty of Pharmacy, Department of Pharmacology | Karadeniz Technical University Drug and Pharmaceutical Technology Application and Research Center (KTU İLAFAR), Karadeniz Technical University Faculty of Medicine, Department of Medical Biology

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Topic: General
Presenter Name: Berkay DEMİRÇİ
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Status: Accepted

Introduction: Psoriasis is a lifelong inflammatory skin disease. Since cytokines (IL-1β, IL-6) are important in its pathophysiology, agents that reduce the cytokines is a logical approach for the development of new therapeutics. Trimetazidine (TMZ), an antianginal drug with a favorable safety profile, demonstrates antiinflammatory properties by reducing IL-1β activity in experimental studies, however it has not been examined in an inflammatory skin disease model. This study aims to investigate the antiinflammatory and antiproliferative effects of TMZ on HaCaT cells, a keratinocyte *cell line* from adult human skin.

Method: HaCaT cells were incubated with lipopolysaccharide (LPS; 1 µg/ml for 24 hours) to induce in vitro psoriasis. During LPS incubation, cells were treated with TMZ (25-50-75-100 µM) or vehicle (DMEM, as control). Cell proliferation and IL-1β were measured with WST-1 colorimetric assay and commercially available ELISA, respectively.

Results: TMZ (50, 75,100 µM) concentration-dependently inhibited LPS-induced proliferation of HaCaT cells ($p<0.001$). At 75 and 100 µM concentrations, TMZ also decreased viability of non-LPS treated cells ($p<0.05$). IL-1β did not change in cells treated with both LPS and TMZ. In contrast, 50 and 75 µM of TMZ increased IL-1β ($p<0.05$) in non-

LPS treated cells.

Conclusion: TMZ demonstrated a strong antiproliferative effect in LPS- treated HaCaT cells with an unexpected change in IL-1β in non-LPS treated cells. Potential of TMZ as an antipsoriatic agent and mechanism of action on cytokines requires further studies. *This study was supported by the TUBITAK 2209A Support Program (Project no 1919B012112223 to BD).*

Key words: psoriasis, HaCaT, trimetazidine, inflammation

Determination of Novel and Non-Competitive MRP4 Inhibitors by Structure-Based Virtual Screening and Drug Discovery Methods

by Öyküm Önel | Elif Bengü Kızılay | Onur Serçinoğlu | Gebze Technical University | Gebze Technical University | Gebze Technical University

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Presenter Name: Öyküm Önel | Elif Bengü Kızılay
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MRP4 is a transmembrane protein affiliated with the ATP-Binding Cassette (ABC) transporter family. It serves the dual function of transporting organic anions and recognizing pivotal signaling molecules. In the context of diseases such as cancer, viral infections, and cardiovascular diseases, the MRP4-driven drug efflux mechanism holds a crucial role in multidrug resistance. Previous efforts to identify inhibitors for MRP4 yielded several small molecules, but most of these either interfered with other ABC transporters or became substrates themselves. This led to a scenario where these inhibitor molecules competed with the protein's natural substrates at the active site, thereby diminishing their efficacy. This study's core objective was to identify novel MRP4 inhibitors that do not engage in orthosteric binding. First, coarse-grained membrane molecular dynamics simulations of MRP4 were conducted using an AlphaFold2 model of MRP4 as starting structure and the MARTINI force-field with ELNEDYN restraints. Subsequent exploration of MRP4's allosteric pockets using DoGSiteScorer 2.0 unveiled potential binding sites. From these, pockets on MRP4's Nucleotide-Binding Domain (NBD) were selected as potential binding sites for non-competitive ligands. Then, molecular docking simulations were conducted, incorporating both FDA-approved drugs and a diverse library of small molecules. Finally, compounds that exhibited superior binding affinities when compared to Ceefourin-1, the most potent known MRP4 inhibitor, were identified. These compounds are considered promising candidates for potential non-competitive MRP4 inhibitors.

Targeting the C-SH2 domain of the Syk kinase by virtual drug screening to identify potential anticancer candidates

by Merve Şansaçar | İsmail Akçok | Hüseyin Güner | Emel Başak Gencer Akçok | Abdullah Gül University | Abdullah Gül University | Abdullah Gül University | Abdullah Gül University

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Spleen Tyrosine Kinase (SYK) which is a non-receptor kinase crosstalk pivotal signaling pathways such as PI3K, NFκB and JAK/STAT that play a role in pathogenesis of various cancers. Syk is composed of two SH2 domains at the amino terminus, followed by a catalytically active kinase domain. In this study, we aim to target the C-SH2 domain of Syk to prevent cancer progression. We employed a virtual screening of a mid-scale chemical library provided by COCONUT with 407,270 unique natural products. The chemical files of the library were converted into 3D structure files using RDKIT as preparation step for molecular docking via Smina. The target protein was selected as the crystal structure of the protein complex (PDB entry: 18A1). The existing heteroatoms and the conjugated peptide molecule were cleared, then the target binding region located on C-SH2 domain was determined using Fpocket utility to prepare the protein molecule for docking. The docking experiments yielded 25 ligand poses with a docking score less than -7.5. Three lead candidates were selected and further tested with Molecular Dynamics simulations via Gromacs for a duration of 100 ns. Post analysis of trajectories of three complexes revealed one of the hit molecules is a more promising lead candidate, which is called Preussomerin B. The multidrug resistance and poor prognosis reveal the requirement of more effective treatments for cancer. Here, we suggested a novel strategy to target Syk by *in silico* studies.This project was supported by the Health Institutes of Turkiye (TUSEB) with grant ID of 22905

IL-23 as a Key Player in psoriasis: New Approache For Psoriasis treatment

by Raghad Sharbaji | Pinar Siyah | department of bioengineering, faculty of biomedical engineering, Bahçeşehir Üniversitesi, istanbul, Turkey. | department of Biochemistry, faculty of pharmacy, Bahçeşehir Üniversitesi, istanbul, Turkey.

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IL-23 considers the dominant cytokine and is associated with several autoimmune diseases including psoriasis. Psoriasis is a chronic inflammatory skin disease that significantly impacts the patient's quality of life. Studies showed that the agents of IL-23 (P19 & P40) are well tolerated, highly effective -90% reduction in the psoriasis area- and most likely have mild side effects. Current data suggest targeted IL-23/IL-23R inhibitors may have more sustained efficacy in the long term than IL-12, IL-17 & IFN. Targeted small molecules represent an attractive alternative to the current psoriasis treatment because they are much smaller, taken orally, easier to produce, less expensive and target specificity. Several small molecule inhibitors (SMI) treating psoriasis are either FDA approved drugs or under development. However, existing SMIs do not directly target IL-23 and may come with various side effects. This research aims to evaluate FDA-approved molecules through computer-based screening techniques such as Molecular Docking, Dynamics, and MM/GBSA to identify small molecules with the highest affinity, selectivity, and minimal toxicity for inhibiting IL-23/IL-23R.

1- Chunlei Tang, Shu Chen, et al. (2011). Interleukin-23: as a drug target for autoimmune inflammatory diseases. Immunology. v1-13.

2- Joseph Dodson, et al.(2022). Biologics and Small Molecule Inhibitors: an Update in Therapies for Allergic and Immunologic Skin Diseases. Springer link. 183–193.

3- George Martin.(2023). Novel Therapies in Plaque Psoriasis: A Review of Tyrosine Kinase 2 Inhibitors. Springer link. 417–435.

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IL-23 considers the dominant cytokine and is associated with several autoimmune diseases including psoriasis. Psoriasis is a chronic inflammatory skin disease that significantly impacts the patient's quality of life. Studies showed that the agents of IL-23 (P19 & P40) are well tolerated, highly effective -90% reduction in the psoriasis area- and most likely have mild side effects. Current data suggest targeted IL-23/IL-23R inhibitors may have more sustained efficacy in the long term than IL-12, IL-17 & IFN. Targeted small molecules represent an attractive alternative to the current psoriasis treatment because they are much smaller, taken orally, easier to produce, less expensive and target specificity. Several small molecule inhibitors (SMI) treating psoriasis are either FDA approved drugs or under development. However, existing SMIs do not directly target IL-23 and may come with various side effects. This research aims to evaluate FDA-approved molecules through computer-based screening techniques such as Molecular Docking, Dynamics, and MM/GBSA to identify small molecules with the highest affinity, selectivity, and minimal toxicity for inhibiting IL-23/IL-23R.

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Synthesis, Purification and Characterization of Spike-Angiotensin Converting Enzyme-2 Targeted Drug Candidate Peptides against SARS-COV-2

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Topic: General
Presenter Name: Sümeyra Ayan
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Abstract

Peptide, which is one of the leading compound in drug discovery, is molecularly stable. In recent years, peptide-based drug studies have been work has accelerated. SARS-COV-2, which led to one of the deadliest epidemics in the 21st century, infects humans in three common ways, which are accepted through larger respiratory droplets, airborne/aerosol, and direct contact with patients. The virus attaches to the cell membrane by binding the Spike (S) protein to the Angiotensin Converting Enzyme-2 (ACE2) receptor. In this study, modeling studies were carried out to determine peptide sequences, and then S-ACE2 targeted FKRN, WRWA, and KYLW peptides have been synthesized by using the Solid Phase Peptide Synthesis (SPPS) method, purified by Reverse Phase High-Performance Liquid Chromatography (RP-HPLC) and characterized by Liquid Chromatography-High Resolution Mass Spectrometry (LC-HRMS/MS) for use in drug development for Covid-19. All peptides have been successfully synthesized, purified and characterized.

Keywords: Covid-19 outbreak, drug delivery, SARS-COV-2, peptide, solid-phase peptide synthesis

Acknowledge: This study was supported by the Scientific and Technological Research Council of Türkiye (TUBITAK) 2247-C Intern Researcher Scholarship Program (STAR).

IN SILICO AND IN VITRO ANALYSIS OF THE INTERACTION OF THYMOQUINONE AMONG SOME ONCOGENIC DRIVER PROTEINS

by Aycan Sezan | Sehreen Tory | Mojahidur Hasan | Yağız Çapanoğlu1 | Ege Özkan | Senanur Taş | Burcu Saygıdeğer Demir | Yasemin Saygıdeğer | Department Of Biotechnology, Institute Of Natural And Applied Sciences, Cukurova University | Department Of Translational Medicine, Institute Of Health Sciences | Department Of Translational Medicine, Institute Of Health Sciences | Department Of Biotechnology, Institute Of Natural And Applied Sciences, Cukurova University | Department Of Bioinformatics And Genetics, Faculty Of Engineering, Kadir Has University | Department Of Biotechnology, Institute Of Natural And Applied Sciences, Cukurova University | Department Of Biotechnology, Institute Of Natural And Applied Sciences, Cukurova University | Department Of Biotechnology, Institute Of Natural And Applied Sciences, Cukurova University, Department Of Translational Medicine, Institute Of Health Sciences, Cukurova University, Department Of Pulmonary, School Of Medicine, Cukurova University

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Presenter Name: Aycan Sezan
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Aim: In this study, the structural interaction between oncogenic driver proteins and TQ (TQ/2-methyl-5-isopropyl-1,4-benzoquinone) -targeted therapy was investigated in silico, and its cytotoxicity on some type of cancer cell lines in vitro was analyzed.

Methods: The 3D structure of the ligand (TQ) was obtained from PubChem and converted to pdb format using the software Discovery Studio 2016 (BIOVIA). Autodock Vina was used to mark the active site for docking analyses. The results were compared with the online analysis program Swissdock and CB-Dock2. The IC50 value of TQ on some cancer cell lines was determined by performing MTT analyzes in vitro and HER2 expressions of these cancer cell lines were investigated.

Results: Examined proteins are listed in Table-1. HER2 formed the only covalent bond whose binding energy was compatible with this interaction (Figure-1). IC50 (μM) values of TQ in A549, MCF7, SW620, HCT116 and HT-29, Calu-1 cell lines, respectively; 175.9, 29.39, 77.09, 41.83, 20.05, 79.27 (Fig. 2A). HER2 expressions of cancer cell lines are shown in Figures 2B and 2C.

Conclusion: The results of this in-silico study showed that TQ might be interacting with several oncogenic proteins to possess its anticancer activity and HER2 was found as the most potent target of this compound.It was observed that TQ had different effects on different cancer cells and when the IC50 values were examined, it showed an anti-cancer treatment feature in almost every cancer cell line.

Extraction and rapid recovery of bioactive constituents from C. sativum seeds.

by Iqra Akhtar, Sumera Javad | Lahore College for Women University, Lahore, Pakistan

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Presenter Name: Iqra Akhtar
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The extraction of bioactive compounds from plants has gained significance in various fields, including pharmaceuticals and healthcare, due to their potential antimicrobial properties. This study explores the use of two extraction methods, microwave-assisted extraction (MAE) and Soxhlet extraction of seeds of *Coriandrum sativum* for obtaining bioactive compounds and assessing their antimicrobial activity. This study indicated that a 5-minute session of microwave-assisted extraction (MAE) yielded the highest amounts of phenolics (275 mg) and flavonoids (229 mg). In comparison the Soxhlet extraction (SE) method necessitated a lengthy 5-hour duration to achieve its peak yield. GC-MS analysis revealed that MAE generated 15 compounds, while SE produced 11 compounds. Notably, the major constituent in the MAE-derived extract was identified as Apiol, constituting 52.55% of the compound profile. Conversely, the primary component in the SE-derived extract was recognized as linalool, comprising 39.97% of the composition. HPLC analysis revealed a diverse range of phenolics and flavonoids within the microwave-assisted extraction samples, in contrast to the Soxhlet extraction. The MAE extracts exhibited notably higher levels of antioxidant activity (82%) and antifungal potential (with an impressive 89.3% inhibition rate) compared to SE extracts (showcasing values of 54.32% and 60.7% respectively). This study strongly indicated that MAE has the capability to extract bioactive constituents from *C. sativum* seeds while preserving their biological activities. This implies that analytical laboratories considering the utilization of MAE can confidently adopt this technique to expedite the extraction of desired phytochemicals, a process that can be further optimized by modifying the extraction parameters.

Investigation of Emulsification Formulations of Pemetrexed Loaded Polymeric Nanoparticles

by Gamze Liman | Serap Mert | Department of Stem Cell, Institute of Health Sciences, Kocaeli University, 41001, Kocaeli, Turkey | Center for Stem Cell and Gene Therapies Research and Practice, Kocaeli University, 41001, Kocaeli, Turkey

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Presenter Name: Serap Mert
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Introduction: In lung cancer, the most commonly diagnosed cancer type worldwide, it is very difficult for drugs to reach cancer cells in sufficient doses with traditional methods such as chemotherapy and radiotherapy. To overcome this disadvantage, polymeric nanoparticles (PNPs), providing controlled drug delivery systems, attract attention with their biodegradable, biocompatible, small size, easy to produce and targetable properties. In addition to PLGA, which is widely used in the literature, polydiisopropylglycolide (PDIPG) is also used in drug delivery systems. In this study, loaded PLGA and PDIPG-NPs were developed using Pemetrexed-disodium (PEM) used in lung cancer treatment.

Methods: Single emulsion and double emulsion were applied for PEM loaded PNP's preparation because of PEM's solubility in water and methanol. The encapsulation efficiency (EE) and size of the obtained NPs were compared. Furthermore, appropriate drug-polymer, surfactant and solvent ratios were optimized for high EE, low size and PDI and drug releases of PEM from PNP's were also performed in PBS.

Results and Discussion: In this study, for the first time PEM-PNPs were prepared by single emulsion with high EE, low size and PDI, while more successful results were obtained in single emulsion than that of DE. A controlled release of PEM was achieved by encapsulating with PNPs.

Conclusions: It was found that the EE of PEM-PNPs obtained with single emulsion under optimized conditions was higher than that of double-emulsion and PEM-loaded PNPs exhibited a controlled release profile.

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Keywords: Pemetrexed-disodyum, Single Emulsion, Lung Cancer

Synthesis and Characterization of Peptide Molecules Targeting TMPRSS2 for COVID-19 Drug Studies

by Kübra ARANCI ÇİFTÇİ | Özgür YILMAZ | Materials Technologies, Marmara Research Center, TUBITAK, 41470, Gebze, Kocaeli, Turkey | Materials Technologies, Marmara Research Center, TUBITAK, 41470, Gebze, Kocaeli, Turkey

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Presenter Name: Kübra ARANCI ÇİFTÇİ
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Abstract

Coronavirus Disease 2019 (COVID-19) is a highly dangerous infectious disease that spreads rapidly and causes a pandemic. Although many precautions have been taken for the disease, the primary treatment in drug development studies is still symptomatic. The development of peptide and peptide-based drugs as an alternative to conventional drugs is very popular. Peptides have many advantages due to their high selectivity, low side effects and easy production. The main purpose of this study is to synthesize, characterize and purify peptides that can bind to the Transmembrane protease serine 2 (TMPRSS2) receptor- is responsible for viral entry and spread of coronaviruses- with high affinity. In this context, peptide sequences determined as a result of molecular docking analysis and were synthesized using Solid Phase Peptide Synthesis (SPPS), purified by Reverse Phase High Performance Liquid Chromatography (RP-HPLC) and characterized by Liquid Chromatography-High Resolution Mass Spectrometry (LC-HRMS/MS). Within the scope of the study, it was determined that **HWRY, NYYF** and **QKWY** peptides were synthesized with 97%, 99% and 98% purity, respectively, according to HPLC chromatograms. It was observed that the average molecular weights of the peptides were very similar to the molecular weights obtained from the mass spectrum. Peptides have been successfully synthesized. In future studies, the affinity of the peptides to the relevant region will be evaluated and *in vitro* studies will be performed.

Keywords

COVID-19, Drug design, Molecular docking, Peptide synthesis

Acknowledgements

This study was funded by Scientific and Technological Research Council of Turkey (TUBITAK) 2247-C Intern Researcher Scholarship Program (STAR).

DE NOVO ANTIMICROBIAL PEPTIDE DESIGN AGAINST DRUG-RESISTANT STAPHYLOCOCCUS AUREUS

by Zülal Kesmen | Şeyma Aydın | Nurullah Okuyan | Dilara Herdem | Erciyes University, Engineering Faculty, Department of Food Engineering, Kayseri /Türkiye | Erciyes University, Engineering Faculty, Department of Food Engineering, Kayseri /Türkiye | Cumhuriyet University Gürün Vocational School Sivas/Türkiye | Erciyes University, Engineering Faculty, Department of Food Engineering, Kayseri /Türkiye

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Presenter Name: Dilara Herdem
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Antimicrobial peptides (AMPs) become increasingly popular alternatives due to their broad spectrum of activity, versatile mechanisms of action, and low potential for resistance development compared with conventional antibiotics. Therefore, in this study, we developed a novel strategy for effective AMP design against Multidrug-resistant (MDR) *Staphylococcus aureus* strains. First, we developed a regression-based machine learning approach to predict the experimental minimal inhibitory concentration (MIC) of peptides that inhibit MDR-*S. aureus*. For this purpose, AMPs active against drug-resistant *S. aureus* were selected from the DBAASP database (Database of Antimicrobial Activity and Structure of Peptides) and a positive data set (MIC<50µg/ml) and a negative data set (MIC>100µg/ml) were generated according to the experimental MIC values. The best model for prediction was obtained using the cubic SVM algorithm with an R^2 value of 0.88 and RMSE of 0.016. Second, we developed a motif-based approach for designing effective AMP against MDR *S. aureus* strains. For this purpose, conserved motifs in peptides of the positive data set were identified using the motif discovery tool MEME Suite 5.5.0, and 5 motifs with the lowest E value (E<0.0001) were selected. *De novo* peptides were designed with the triple combination of the selected motifs, and their MIC values were estimated using the developed model. The regression-based SVM model estimated the MIC values of thedesigned peptides between 4.99 and 127.5 µg/ml with an R^2 value of 0.84 and an RMSE of
0.018. Among them, 5 peptides with the lowest MIC values were subjected to *in-silico* testing of physicochemical properties.

Drug repurposing against PolTheta driven PARPi resistance in HR-deficient cancers

by Ekin CÜCÜ | Atakan AYDIN | Pınar SİYAH | Faculty of Medicine, Bahçeşehir University, Istanbul, Turkey | Faculty of Medicine, Bahçeşehir University, Istanbul, Turkey | Department of Biochemistry, Faculty of Pharmacy, Bahçeşehir University, Istanbul, Turkey

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Presenter Name: Ekin CÜCÜ | Atakan AYDIN
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BRCA1, BRCA2 and PARP-1 genes are crucial for cell survival. Mutations in these genes can contribute to cancer development. While BRCA1 and BRCA2 mutations alone aren't fatal to cells, the combined mutations with mutations in the PARP-1 gene can kill cells, a mechanism that PARP inhibitors (PARPi) rely on. However, certain types of ovarian and breast cancers develop resistance to PARPi by upregulating the POLQ gene that codes DNA polymerase theta (POLθ), which has synthetic lethality with Homologous Recombination (HR) deficient cancers. Tumors that develop resistance to PARPi by increased POLQ levels still remain vulnerable to POLθ inhibitors such as Novobiocin (NVB). High-throughput small molecule screenings found that the antibiotic NVB is a POLθ inhibitor, eliminating HR-deficient cancer cells by combatting PARPi resistance. Currently, no FDA-approved POLθ inhibitors are used in treatment of PARPi resistant HR-deficient cancers to our knowledge. We aim to identify potential drugs for POLθ inhibition that are better than NVB in terms of efficiency, adverse effects, cost-effectiveness. In our study, FDA-approved molecules from various databases will be examined through in silico methods. We'll utilize techniques like Molecular Docking, MD simulations, and MM/GBSA evaluations on the protein-ligand complexes. Based on the collected data, we'll develop QSAR and pharmacophore models to dive deeper into several databases, including SPECS, OTAVA, and ZINC. By applying docking, MD simulations, and MM/GBSA tests on the recently discovered molecules, we'll conduct an in-depth study of their therapeutic potential and safety in treating cancer, aiming to recognize promising drug candidates.

Unveiling New Therapeutic Avenues: Targeting Cancer via Focal Adhesion Kinase Inhibition

by Pınar Siyah | Department of Biochemistry, School of Pharmacy, Bahcesehir University

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Presenter Name: Pınar Siyah
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Synthetic lethality, involving the simultaneous deactivation of two genes, plays a critical role in disrupting vital cellular functions or prompting cell death. This study delves into the impact of synthetic lethality within cancer research, specifically examining the interplay between the Focal Adhesion Kinase (Fak) and Neurofibromin 2 (NF2) genes. While deactivating Fak or NF2 individually has minimal impact, their combined deactivation highlights the pivotal significance of their synthetic lethal interaction. Hence, the principal aim of this study is to direct our efforts towards the inhibition of the Fak gene, a venture of notable significance. The NF2 gene is responsible for producing merlin, a tumor suppressor protein that is often deactivated in schwannoma, meningioma, and malignant mesothelioma. The inhibition of the Fak gene is pivotal, given its pivotal role in the synthetic lethal interplay with NF2/Merlin, promising substantial prospects for the progression of cancer treatment strategies. This investigation has the capacity to propel forward inventive therapeutic methodologies, harnessing the potential of synthetic lethal interactions within cancer cells, and forging a path towards more refined and efficacious interventions in cancer treatment. Employing docking, molecular dynamics (MD) simulations, we evaluated Fak inhibitor complex stability, unveiling intricate interactions. Through MD simulations and MM/GBSA calculations, we identified effective Fak inhibitors for diverse cancer types. This study lays a foundation for novel therapeutics, holding promise for diverse cancer treatments through our computational framework.

Reference : Shapiro, Irina M., et al. "Merlin deficiency predicts FAK inhibitor sensitivity: a synthetic lethal relationship." *Science translational medicine* 6.237 (2014): 237ra68-237ra68.

Computational Analysis of Epileptic Encephalopathy Disease Mutations

by Sinem Nur Açıkgöz | Gebze Teknik Üniversitesi

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Presenter Name: Sinem Nur Açıkgöz
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Mutations in the KCNQ2 protein, which forms the voltage-gated potassium channel, are responsible for autosomal dominant benign familial neonatal seizures (BFNS) and epileptic encephalopathy(EE) [1].The KCNQ2 potassium channel has homotetramer structure and consists of six topological regions(S1-S6)(Figure 1). The aim of this study is to reveal the structural effects of R213Q mutation in the S4 region and T274M mutation in the pore region on KCNQ2 channel. These two mutations are predicted to have a greater effect on channel function than a total of seven mutations known to have dominant-negative effects[1]. Firstly, a cell membrane structure containing 128 DPPCs was obtained from the website of Tieleman research group to be used for this purpose[2]. It was symmetrically replicated using the YASARA Structure [3] programme and a new structure containing 512 DPPCs was created and Molecular Dynamics simulation was applied (Figure2). KCNQ2 protein structure x-ray crystal structure[4](PDB code: 7CR0) used in the project was obtained from Protein Data Bank. Using YASARA Structure [4] programme, both mutations were applied to KCNQ2 channel in different combinations and crystal structure and the mutations in different combinations were compare. To compare structures, distances between residues in the pore, s6 and s4 regions were calculated and cavity of the pore region was revealed with Cavity Plus[5,6].As a result, when upon T274M mutation in A-C (reciprocal chains), a closure is observed in the channel region and an opening is observed in the S6 region. This structural rearrengement will most likely affect the ion concentration passing through the channel.

Synthesis, Characterization, and Molecular Docking Studies of Novel 1,3-thiazoline Derivatives

by Sema Şenoğlu | Sevgi Karakuş | semasenoglu34@gmail.com | -

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Presenter Name: sema şenoğlu
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Introduction: Topoisomerase enzymes are of critical importance for DNA, which is the hereditary material of living things, to replicate and for cells to divide, and thus for the cell to remain alive with a protected and intact DNA. Since topoisomerase enzymes are increased in proliferating cells such as cancer cells, DNA topoisomerase enzymes are increasingly important for anticancer drug targets. Therefore, here in this study, new molecules which may possess topoisomerase inhibition activity were synthesized.

Methods: Novel compounds were prepared from substituted thiosemicarbazide in chloroacetone under reflux. All the synthesis compounds were monitored by TLC. The compounds were characterized by IR, LC-MS, ^{1}H-NMR, and ^{13}C-NMR methods. The docking studies were performed in the Auto Dock, Chimera 1.16, and PyRx program. The crystal structures of the Topoisomerase II were downloaded from the protein data bank (PDB code: 1zxm).

Result and Discussion: The Synthesis compounds of 1,3 thiazolines derivatives showed remarkable Topoisomerase II inhibitory activity compared to the Etoposide. The F atoms contained in the active compound showed conventional hydrogen bond interaction with ALA167, ASN 91 and LYS 168. At the same time, conventional hydrogen bond formation was observed between the sulfur atom in the thiazole group and the amino acid ARG 98. Besides, binding energy was found as -9.1 kcal/mol. This value is thought to be a candidate molecule of the active compound with a good binding energy.

Conclusion: The synthesized 1,3-thiazoline derivatives have great potential to be the Topoisomerase inhibitors for cancer treatment.

Keywords: Topoisomerase**,** 1,3-thiazoline, molecular docking, synthesis

Luteolin disrupts cell health as a pro-oxidant agent against PC3 metastatic castration-resistant prostate cancer cells

by Isil Ezgi Eryilmaz | Ceyda Colakoglu Bergel | Nuseybe Huriyet | Bilge Arioz | Gulsah Cecener | Unal Egeli | Bursa Uludag University, Faculty of Medicine, Medical Biology Department, Bursa, Turkey | Bursa Uludag University, Faculty of Medicine, Medical Biology Department, Bursa, Turkey | Bursa Uludag University, Faculty of Medicine, Medical Biology Department, Bursa, Turkey | Bursa Uludag University, Faculty of Medicine, Medical Biology Department, Bursa, Turkey | Bursa Uludag University, Faculty of Medicine, Medical Biology Department, Bursa, Turkey | Bursa Uludag University, Faculty of Medicine, Medical Biology Department, Bursa, Turkey

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Presenter Name: Isil Ezgi Eryilmaz
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Luteolin, a dietary flavonoid molecule, is shown to be a promising anticancer agent against various human malignancies. However, the selective anticancer mechanism of luteolin through its ROS-inducing pro-oxidant effect has yet to be investigated. In the present study, we aimed to evaluate the association between luteolin's apoptotic and ROS-inducing effects in PC3 metastatic castration-resistant prostate cancer cells and WPMY-1 prostate normal cells for the first time. After the colorimetric cell viability and Annexin V tests, the ROS-inducing effects were analyzed using morphological ROS staining and a Muse Cell Analyzer in the luteolin-treated cells. The results showed that luteolin selectively decreased PC3 viability in dose and time-dependently and significantly triggered more apoptotic death than normal cells, ranging apoptosis to 19.3% and 63.2% at 40 and 80 µM for 72 h (p<0.01), respectively. However, in WPMY-1, the total apoptotic cells were detected as 33.3% at 80 µM treatment (p<0.01). Additionally, luteolin significantly increased the endogenous ROS levels from 4.6% to 30.6% (p<0.01) in PC3 cells treated with 80 µM luteolin 24 h before the apoptotic effect. However, the ROS-positive cells at 80 µM were 13.3% in WPMY-1 normal cells. Based on the morphological oxidative stress analysis, we also showed that luteolin has a more pro-oxidant effect on PC3 than WPMY-1 cells. These preliminary results indicated that ROS-related mechanisms may also be associated with the selective anticancer effect of the agent. Thus, further studies are needed to understand the critical molecular actors of the selective pro-oxidant effect of luteolin.

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NIK Signaling and Exercise-Dependent Drug Targets

by Serkan Kır | Sevgi Döndü Özen | Koç University | Koç University

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Presenter Name: Sevgi Döndü Özen
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Background: Cancer cachexia poses a complex and severe challenge, compromising patient well-being and treatment tolerability Although exercise holds potential as a remedy for alleviating cachexia, its viability is constrained for a substantial patient subset Therefore, molecular pathway research for exercise-induced signaling pathways are required for exploring novel targets for pharmacological intervention. EDA2R and NIK has been previously reported as cachexia-inducing genes in cancer models. Systemic inflammation mediated by IL-6, a proinflammatory cytokine, is known to be the central actor of cachexia. Increased FOXO1 level is associated with muscle atrophy, and it's known to be downregulated after chronic exercise. Lastly, PGC1α has crucial roles for adapting muscles to physical activity like regulation of mitochondrial biogenesis, and insulin sensitivity.

Methods: Wild-type (WT) and NIK knockout mice underwent an 8-week involuntary treadmill running regimen. Grip strength tests were performed pre-sacrifice, followed by qPCR analyses of PGC1α, IL-6, and FOXO1 in gastrocnemius muscle cDNA.

Result: Grip strength force for the WT mice were 120 newtons for control and 165,3 for the HIIT group. NIK KO control and HIIT groups showed no difference. In the chronic exercise model, IL-6 and FOXO1 mRNA expression levels were downregulated, but the drop was more drastic for the NIK-KO mice. Also, upregulation of PGC1α was seen in HIIT group but the more pronounced increase was observed in the NIK-KO mice.

Conclusion: High-intensity interval training (HIIT) enhanced grip strength, indicating muscle hypertrophy. Exploring links between exercise markers and EDA2R-NIK signaling may unveil valuable drug targets.

DRUG REPURPOSİNG AGAİNST LASSA VİRUS PROTEİNS BY USİNG IN SİLİCO METHODS

by Handan Simsek | Seref GUL | Istanbul University | Istanbul University and Bezmialem Vakıf University

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Lassa fever virus (LASV), one of the arenaviruses, infects ~500,000 people each year in Africa and ~5000 people die due to this infection. LASV has been found to spread in other countries. LASV is a single-stranded ambisense RNA virus with two genomic RNA segments encoding four genes. The nucleoprotein (NP) of LASV encapsulates viral genomic RNAs in ribonucleoprotein complexes and is required for both RNA replication and transcription. NP also suppresses the immune signaling pathways in the host. To date, there is no approved drug for this virus. Repositioning of FDA-approved drugs in emerging diseases is a frequently used method to speed up the drug discovery process. Structure-based in silico approach is the first step in drug repositioning studies when structural information of the target protein is available. In our study, we selected NP as the drug target to reposition FDA-approved drugs in silico. The affinities of the FDA-approved drugs were calculated by docking to the catalytic site of NP. Among drugs with the best binding energies, we selectedthe ones with low side effects and widely used for further analysis. The selected NP-drug complexes obtained from docking analysis have been studied in detail by moleculardynamics studies by simulating for 100 ns. The binding energies were calculated using the MM-GBSA method. Critical amino acids for NP-drug binding were determined by performing silico point mutations and recalculating the binding energies. Our analysis showed that eltrombopag, paliperidone, amaryl, lurasidone, and doxazosin can inhibit LASV infection by blocking the NP active site.

Computational Construction LbpA - LbpB - lf Triple Complex

by Gizem Nur DURAN | Gebze Technical University

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Submitted: August 15, 2023
Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Gizem Nur DURAN
Presenter Preference: Poster Presentation
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Bacterial meningitis is still a serious health threat for earthlings and the mortality rates are extremely high among toddlers(1). The bacterium requires iron (Fe^{3+}) ion for its survival/virulence and acquires it from human host. Fe^{3+} ion is carried by two transporter proteins in human blood serum, transferrin (hTf) and lactoferrin (lf) (2). The ion is imported by the bacterium through two specialized ion transfer protein systems, transferrin binding proteins (Tbp) and lactoferrin binding proteins (Lbp). Due to the lack of TbpA/B-hTf and LbpA/B-lf complex 3-D structures, iron import mechanism by the bacterium hasn't been elucidated in atomistic level of detail.

In this study, the 3-D structure of the Lbp system is revealed. For this purpose, the homology model of LbpA was obtained (3). Equilibrated 3-D structures of LbpB and lf obtained from 200 ns-long classical MD simulations. The LbpA/B-lf were docked manually by aligning complex by previously modelled TbpA/B-hTf(4). At previously study due to conformational change of TbpA same replaced to LbpA (5).Thus, the interactions that lead to the formation of complexes have been revealed in atomic dimension and the basis for the studies of drug molecule design that will prevent these interactions have been formed.

A Polypharmacological Approach Unveiling Subtype-Specific Drug Candidates for Alzheimer's Disease and Liver Cancer

by Simge Şengül BABAL | Ronald Regan ODONGO | Pınar PİR | Onur SERÇİNOĞLU | Tunahan ÇAKIR | Gebze Technical University | Gebze Technical University | Gebze Technical University | Gebze Technical University | Gebze Technical University

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Topic: General
Presenter Name: Şuara ŞAHİN
Presenter Preference: Poster Presentation
Status: Accepted

Heterogeneity refers to the presence of variation or diversity within a particular system. In the context of neurodegenerative conditions and cancer, heterogeneity implies that these patients exhibit distinct molecular and clinical characteristics. This manifest as differences in genetic mutations, disease progression rates, response to treatment, and overall prognosis. Understanding this heterogeneity is crucial because it can have significant implications for disease management and treatment strategies. By identifying and classifying subtypes based on these diverse profiles, researchers can develop more targeted and personalized approaches to diagnosis and therapy selection. However, research focusing on the identification of specific drug targets and the development of appropriate drug candidates for different disease subtypes is limited.

In our study, we developed an innovative polypharmacological approach to uncover subtype-specific drug candidates for the complex and heterogeneous diseases of Alzheimer's and liver cancer. By analyzing transcriptome profiles of patients, we identified distinct disease subtypes. To pinpoint potential drug targets for each subtype, we integrated the transcriptome data with gene regulatory networks and protein interaction networks. For each target both from Protein Data Bank and AlphaFold Structure database, we obtained experimental and modeled protein structures, respectively. Utilizing these models, we identified druggable pockets on the protein surfaces using DogSiteScorer 2. Furthermore, we quantified the similarities between these pockets using PocketMatch 2. The findings demonstrated the presence of multiple druggable pockets for each subtype, exhibiting highly similar binding pockets. These results highlight the significant potential of polypharmacological approach for the discovery of subtype-specific drugs against Alzheimer's and liver cancer.

Novel Anticancer Peptide Design; Computational Point of View

by Esra Albayrak Karahan | Sude Büyükkurt | Özal Mutlu | Faculty of Science, Department of Biology, Marmara University, Istanbul, Turkey | Faculty of Science, Department of Biology, Marmara University, Istanbul, Turkey | Faculty of Science, Department of Biology, Marmara University, Istanbul, Turkey

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Presenter Name: Esra Albayrak | Sude Büyükkurt
Presenter Preference: Poster Presentation | Poster Presentation
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GLOBOCAN has estimated the number of new cancer cases from 2020 to 2040 will be 30.2 million. Although significant improvements in cancer research, treatments like chemotherapy and radiotherapy are still limited and have considerable side effects. This has led to exploring new routes for treatment, like anticancer peptides. These 10-60 amino acid long positively-charged peptides display distinct mechanisms of action in disrupting negatively-charged cancer cell membranes while not harming the healthy ones. This study seeks to design novel anticancer peptides using the unique family of Temporins as templates [Temporin-1RNa and Temporin-1RNb] and investigate their properties through computational methods. The AntiCP-2.0 web server was used to generate peptides with altered amino acids. Novel peptides were evaluated for net charge, anticancer activity, cell - penetrating activity, hemolytic activity, and hydrophobicity. The best ten novel peptides were selected for further research. For 2D structure prediction, the PEP2D server and for 3D structure prediction the PEP-FOLD3.5 server was used, and all were predicted as helix. To glimpse how the peptides respond in water and in a hydrophobic solvent environment, 250 ns molecular dynamics simulations were conducted. RMSD analyses were carried out after the simulations. In conclusion, while peptides are predominantly in the random form when water is used as the solvent in the simulations, they acquire a 3D helix form when in hydrophobic conditions. This suggests, when peptides interact with the membrane they gain a helix form and will have a disruptive effect on the integrity of the membrane.

Keywords: Cancer, Anticancer Peptides, Molecular Dynamics Simulations

Computational evaluation of cell membrane destruction by Bacteriophage-K holin protein

by Nurgül Kaya | Gebze Technical University

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Presenter Name: Nurgül Kaya
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Methicillin-resistant *Staphylococcus aureus* (MRSA) is gram-positive bacterium that causes infectious diseases. Antibiotic resistance is serious obstacle for MRSA infection treatment[1]. Increasing antibiotic resistance has made use of bacteriophages widespread for treatment[2]. Bacteriophages are bacterial viruses. Specific ability of phages to recognize their hosts allows bacteriophages to be used as antimicrobial agents in various fields[3]. Bacteriophage-K facilitates the pathogenic staphylococci lysis including *S.aureus*[4]. The phage employs a cell membrane protein, holin. Holins accumulate in bacterial inner membrane and form holes[5]. It has been stated that the C-terminal domain of holin has important role in cell membrane degradation and type-II holins can perform bacterial lysis even though endolysin enzymes are not present[6]. This provides an insight that holin can cause cell membrane destruction.

This study aimed to examine structural effects of holin, involved in bacterial lysis mechanism of bacteriophage-K, on inner membrane of *S.aureus* by molecular dynamics (MD) simulations and computational analyses. Observation of the structural effects of holin on cell membranes will enable to evaluate potential of holin as an anti-microbial agent against *S.aureus* infections. In addition, understanding the effects of holin on the cell membrane structure will allow the use of holin-like protein products as therapeutic agents. In this context, 3-D structure of bacteriophage-K holin protein will be modelled and structural effects of holin on *S.aureus* cell membrane will be analyzed by computational techniques for the first time in the literature.

In silico analysis of phytochemicals for use in COVID-19 treatment and assessment of binding properties of potential drug candidates

by Ezgi Keskin Taldari | Tosin Fajembola | Sami Doğanlar | Muse Oke | Anne Frary | İzmir Yüksek Teknoloji Enstitüsü | İzmir Yüksek Teknoloji Enstitüsü | İzmir Yüksek Teknoloji Enstitüsü | İzmir Yüksek Teknoloji Enstitüsü | İzmir Yüksek Teknoloji Enstitüsü

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Presenter Name: Ezgi Keskin Taldari
Presenter Preference: Oral Presentation
Status: Accepted

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has had serious consequences such as pneumonia, acute respiratory failure, multiple organ failure, septic shock, and death. Shortly after the outbreak of COVID-19, it spread around the world and turned into a global pandemic.
Although numerous vaccine studies have been initiated, the emergence of new variants has made it difficult to control the pandemic. In addition to vaccines, the search for drugs should be stepped up to prepare for future SARS-CoV-2 or other coronavirus outbreaks.
Plant compounds possessing antiviral and anti-inflammatory properties are important sources for drug development. Because testing all plant metabolites is impractical, computer-aided drug design studies can screen these compounds for potential effects. Due to their crucial role in the pathogenicity of SARS-CoV-2, the spike (S) protein and chymotrypsin-like protease (3CLpro) enzyme are selected as targets. The study aims to screen the anti-viral and anti-inflammatory properties of about 5660 phytochemicals from MPD3 databases using Autodock Vina for molecular docking and GROMACS for molecular dynamics simulations. These phytochemicals will be assessed based on their binding energies to the target proteins. Compounds will be ranked and filtered using the admetSAR to assess their pharmacokinetic properties. Selected plant compounds will be evaluated on their binding efficiency to targets with fluorescence-based thermal shift assay and surface plasmon resonance. As a result, we will get distinct S protein and 3CLpro inhibitors which could act as foundational structures to control the transmission of COVID-19 and further coronavirus infections.

Exploiting Synthetic Lethality in BRCA-Mutated Cancers with Selective PARP Inhibitors: A Computational Drug Discovery Study

by Elifsu PERSİLİOĞLU | Pınar SİYAH | Serdar DURDAĞI | Department of Medicine, Faculty of Medicine, Bahçeşehir University, Istanbul, Turkey. | Department of Biochemistry, Faculty of Pharmacy, Bahçeşehir University, Istanbul, Turkey | Computational Biology and Molecular Simulations Laboratory, Department of Biophysics, School of Medicine, Bahçeşehir University, Istanbul, Turkey

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Presenter Name: Elifsu PERSİLİOĞLU
Presenter Preference: Oral Presentation
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ABSTRACT

The BRCA1 and BRCA2 genes, known as tumor suppressors, contribute to DNA damage repair. Mutations in these genes, often inherited, can drive malignant tumor formation, accounting for a significant portion of hereditary breast and ovarian cancers. Synthetic lethality, where combined gene mutations cause cell death, offers a promising cancer treatment approach. Synthetic lethality arises when both BRCA genes and PARP-1, an enzyme vital for DNA repair, are mutated. Administering PARP inhibitors to cancer cells with BRCA mutations triggers cell death by preventing DNA repair. Current FDA-approved PARP inhibitors like niraparib, talazoparib, olaparib, rucaparib lack selectivity. To address this, the study aims to screen thousands of molecules for selective PARP inhibition. Techniques such as Molecular Docking, Molecular Dynamics simulations, and MM/GBSA analysis will be used to assess protein-ligand interactions. Data will be employed to create models for detailed investigations and screenings. Through this approach, new and effective drug candidates for cancer treatment will be identified.

REFERENCES

1. Roy, R., Chun, J., & Powell, S. N. (2012). BRCA1 and BRCA2: Distinct Roles in Genome Protection. Nature Reviews Cancer, 12(1), 68–78. doi:10.1038/nrc3181
2. Narod, S. A., & Foulkes, W. D. (2004). BRCA1 and BRCA2: Evolution beyond 1994. Nature Reviews Cancer, 4(9), 665–676. doi:10.1038/nrc1431
3. Pujol, P., Barberis, M., Beer, P., Friedman, E., Piulats, J. M., Capoluongo, E. D., … Foulkes, W. D. (2021). Guidelines for BRCA1 and BRCA2 Genetic Testing. European Journal of Cancer, 146, 30–47. doi:10.1016/j.ejca.2020.12.023
4. Sahin, K., & Durdagi, S. (2020). Discovery of PARP1 Inhibitors using Text Mining and Molecular Modeling. Journal of Biomolecular Structure and Dynamics, 1–10. doi:10.1080/07391102.2020.1715

Possible molecular mimicry-based autoimmunity mechanism studied through HLA-affinity changes at Omicron(21K,21L) mutation-regions

by Yekbun Adiguzel | Yehuda Shoenfeld | Atilim University | Sheba Medical Center and Reichman University

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Presenter Name: Yekbun Adiguzel
Presenter Preference: Oral Presentation
Status: Accepted

Certain human and pathogen-shared peptides can cause molecular mimicry-based autoimmunity in susceptible individuals, upon infection. We hypothesize that mean HLA affinities of all such peptides can be another, additional mechanism of molecular mimicry-based autoimmunity. SARS-CoV-2 variants can reveal changes in the associated molecular mimicry-based autoimmunity risks and pathogenicity, as a proof-of-the-concept of our hypothesis. It can also give insights about the host-pathogen interaction related viral-evolution.

We selected human protein sequences sharing 6mers with the sequences at the mutation sites of the Omicron 21K and Omicron 21L variants, and with the respective nonmutant SARS-CoV-2 sequences at the same mutation sites. Then we predicted binding affinities ofthose human peptide sequences to 12 HLA supertype representatives. We evaluated the cumulative changes in the predicted HLA affinities of the Omicron-similar peptide sequences, compared to that of the SARS-CoV-2-similar peptide sequences at the same mutation sites.

Omicron-similar human peptide sequences had decreased mean HLA affinities with a skewed change in the means and medians. Combined results of the affinities to different alleles revealed that Omicron 21K-similar human sequences with increased affinities was significant. In relation, mean predicted-affinity for the HLA-B*15:01 allele was significantly higher. Omicron 21K-similar human sequences at the viral mutation sites have different mean predicted-affinity changes than that of the human sequences mimicking the sequences with Omicron 21L-specific mutations. Trend of changes in the mean HLA affinities of the combined data revealed lowered mean affinities.

Our observations can involve an evolutionary mechanism, providing a mechanistic basis.

Keywords

HLA; peptide-similarity; SARS-CoV-2; COVID-19; disease susceptibility

Investigation of the Effect of Dioncophyllin A on DNA through Molecular Dynamics Simulation

by Yağmur Yeşilyurt | Osman Doluca | Izmir University of Economics | Izmir University of Economics

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Topic: General
Presenter Name: Yağmur Yeşilyurt
Presenter Preference: Oral Presentation
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Dioncophyllin A is a natural product found in Ancistrocladus abbreviatus, Triphyophyllum peltatum and Ancistrocladus barteri. Dioncophyllin A is notable for its natural composition in plants and is potentially of interest for various biological interactions and roles. DNA intercalators, also known as linking agents, are chemical compounds that integrate into the DNA chain by separating base pairs in the molecular structure, usually between two nucleotides of cellular DNA. This study aims to investigate the interaction of Dioncophyllin A, a potential DNA intercalator, with DNA through molecular dynamics simulation (MD simulation). The target ligand was manually inserted between the middle two bases of the 108D PDB model using Avogadro. MD simulations were performed to reveal the details of ligand-DNA interactions. GROMACS 2018.1, AMBER99SB-ILDN force field and NA ions were used, and simulation times of 10 ns were preferred. The interactions of the ligand-DNA complexes were visualized, and Gibbs free energy analysis was performed with gmxMMPBSA for information on the binding affinities of these interactions. The simulation results reveal in detail how the ligand binds to the DNA helix and how it can alter the DNA structure. The ligand behaves as an intercalator, and the intercalation mechanism of the ligand suggests that it can affect the function of the genetic material by disrupting the helical structure of the DNA strand. This information can help us better understand the biological effects of the ligand and form the basis for future research and applications.

Broad spectrum antiparasitic activity of Organotin (IV) derivatives and its Proteomic analysis

by Nazif Ullah | Abdul Wali Khan University Mardan

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Topic: General
Presenter Name: Nazif Ullah
Presenter Preference: Poster Presentation
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Metals have been used in medicine since ancient times for the treatment of different ailments. Metal complexes have also been reported to show antibiotic and antiparasitic activity. In this context, we tested the antiparasitic potential of 10 organotin (IV) derivatives from 4-(4-methoxyphenylamino)-4 oxobutanoic acid (MS26) against eukaryotic pathogens such as *Leishmania donovani*, *Trypanosoma cruzi, Trypanosoma brucei, Entamoeba histolytica, Giardia lamblia, Naegleria fowleri and Schistosoma mansoni*. Among the compounds with and without antiparasitic activity, compound MS26Et3 stood out with a 50% effective concentration (EC_{50}) of 0.21 and 0.19 µM against promastigotes and intracellular amastigotes of *L. donovani*, respectively, 0.24 µM against intracellular amastigotes of *T. cruzi*, 0.09 µM against *T. brucei*, 1.4 µM against N. *fowleri* and impaired adult *S. mansoni* viability at 1.25 µM. In terms of host/pathogen selectivity, MS26Et3 demonstrated relatively mild cytotoxicity toward host cells with a 50% viability concentration of 4.87 µM against B10R cells (mouse monocyte cell line), 2.79 µM against C2C12 cells (mouse myoblast cell line) and 1.24 µM against HEK923 cells (human embryonic kidney cell line). The selectivity index supports this molecule as a therapeutic starting point for a broad spectrum antiparasitic alternative. LC-LC-MS^n Proteomics analysis of host cells infected with *L. donovani* after exposure to MS26Et3 showed a reduced expression of Rab7, which may affect the fusion of the endosome with the lysosome, and, consequently, impairing the differentiation of *L. donovani* to the amastigote form. Future studies to investigate the molecular target(s) and mechanism of action of MS26Et3 will support its chemical optimization

Computational Analysis of The Effect of Human Telomerase Mutations on Protein Complexation and Template RNA Binding

by Kamer Nisa BAZ | Mehmet ÖZBİL | Gebze Technical University - Institute of Biotechnology | Gebze Technical University - Institute of Biotechnology

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Topic: General
Presenter Name: Kamer Nisa BAZ
Presenter Preference: Poster Presentation
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Human telomerase enzyme prevents elongation of telomere regions and aging of cells by adding repetitive nucleotide sequences to DNA ends. The enzyme consists of H/ACA lobe and TCAB1 protein located in the H/ACA lobe is involved in transportation to Cajal (active) regions. As the 3-dimensional structure has just been elucidated, the dynamical structures of TCAB1-H/ACA and their interactions have not yet been studied. Moreover, few mutations in proteins were known to decrease telomerase activity, but their effects on protein structures and protein-protein binding energies have yet to be clarified. The aim of the project is to reveal how mutations affect protein-protein and protein-RNA interactions at atomic scale and alter protein binding energies.

Cryo-EM structure of telomerase enzyme was obtained from PDB (ID: 7bgb). The H/ACA complex and wild type and mutant (G435R, R398W, H376Y, F164L at once) TCAB1 proteins were simulated separately and together by using GROMACS software and AMBER03 force field. Then, RMSD, RMSF, Rg and SASA analyses were performed. After, WT and mutant TCAB1 proteins were docked to H/ACA complex by using ClusPro2.0 web server. After docking and molecular dynamics simulations, protein-protein interface between TCAB1 and H/ACA complex and protein binding energies were elucidated.

Structural alterations were observed between wild-type and mutant TCAB1 proteins. Upon mutations different binding modes and binding scores were obtained from protein-protein docking simulations indicating the negative effect of mutations.

Structural differences caused by disease-causing mutations were observed as computationally, and their effects on protein complexation were revealed by changes in protein-protein binding energy.

Computer-Aided Drug Design (CADD) of Multitarget-Directed Ligands (MTDLs) for Treatment of Various Neurological Disorders

by Talha Islam | Mariya al-Rashida | Department of Chemistry, Forman Christian College (A Chartered University), Ferozepur Road 54600, Lahore, Pakistan | Department of Chemistry, Forman Christian College (A Chartered University), Ferozepur Road 54600, Lahore, Pakistan

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Presenter Name: Talha Islam
Presenter Preference: Poster Presentation
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Neurological disorders are showing a consistent ascension in trend among the global population as time progresses. Etiologies of neurophysiological and neuropsychiatric disorders show that these are caused by multi-factorial and complex conditions to whichpoly-pharmacological approach could be better suited as treatment option. In this study, 2884 MTDLs (Multitarget-Directed Ligands) were generated from the 3-acetylcoumarin based chalcone scaffold. The six proteins structures selected for this study are Monoamine Oxidase A and B, Acetylcholinesterase, Butyrylcholinesterase, BACE-1, and D2 Dopamine Receptor with their PDB IDs as 2Z5X, 4CRT, 4M0F, 6EP4, 6EJ2, and 6CM4 respectively. Virtual screening was carried out using Autodock Vina. Results were sorted and the top 500 docked compounds were visualized and subjected to *in silico* ADME analysis to get an estimate of their drug likeness, especially their ability to cross the blood brain barrier (BBB) which is a crucial parameter for drugs targeting neurological disorders. Toxicity was also evaluated using ProTox-II webserver. Finally, a hit compound **Comp2443** was selected based on considering holistic approach for multiple factors including binding-energies, types of interactions, ADME profile, and toxicity. The protein-ligand complexes of **Comp2443** with all six respective proteins were subjected to molecular dynamics (MD) simulation for 50ns. Molecular dynamics results suggest that the protein complexes with **Comp2443** remain quite stable during the simulations. Overall, results indicate that **Comp2443** could be a promising MTDL lead compound for further optimization, *in vitro* and *in vivo* studies for possible treatment of neurological disorders.

Novel pyrazolidines: synthesis, characterization and antioxidant activity studies

by YAĞMUR BİLİZ | BELMA HASDEMİR | HATİCE BAŞPINAR KÜÇÜK | Istanbul University- Cerrahpaşa, Faculty of Engineering, Department of Chemistry, Istanbul, Turkey | Istanbul University- Cerrahpaşa, Faculty of Engineering, Department of Chemistry, Istanbul, Turkey | Istanbul University- Cerrahpaşa, Faculty of Engineering, Department of Chemistry, Istanbul, Turkey

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Presenter Name: YAĞMUR BİLİZ
Presenter Preference: Poster Presentation
Status: Accepted

Pyrazolidines are five-membered heterocyclic compounds containing N-N bonds. Pyrazolidine and derivatives are widely used as anticancer, antidepressant, anti-inflammatory, antioxidant, antiviral, antialzheimer, anesthetic, anticonvulsant and antibacterial agents [1-2]. In this study, novel pyrazolidine were synthesized as a result of the [3+2] cycloaddition reaction of hydrazide-hydrazones with cyclopentadiene. The structures of the synthesized molecules were determined by IR, ^{1}H-NMR, ^{13}C-NMR and GC-MS spectroscopic methods. The antioxidant activity of the novel pyrazolidine compounds synthesized was evaluated by the DPPH radical scavenging activity test using ascorbic acid (AA), butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) as standards for comparison [3].

Keywords

Pyrazolidine, antioxidant activity, synthesis

References

[1] Parashar, B.; Jain, A.; Bharadwaj, S.; Sharma, V. K. Synthesis and Pharmacological Properties of Some Novel Pyrazolidine and Pyrazole Derivatives. Medicinal Chemistry Research 2012, 21 (8), 1692–1699.

[2] Rana, M.; Arif, R.; Iqbal Khan, F.; Maurya, V.; Singh, R.; Imam Faizan, M.; Yasmeen, S.; Hussain Dar, S.; Alam, R.; Sahu, A.; Ahmad, T. Pyrazoline Analogs as Potential Anticancer Agents and Their Apoptosis, Molecular Docking, MD Simulation, DNA Binding and Antioxidant Studies. Bioorg Chem 2021, 108, 104665.

[3] Tabarsaei, N.; Hamedani, N. F.; Shafiee, S.; Khandan, S.; Hossaini, Z. Catalyst-free Green Synthesis and Study of Antioxidant Activity of New Pyrazole Derivatives. J Heterocycl Chem 2020, 57 (7), 2945–2954.

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Novel pyrazolidines: synthesis, characterization and antioxidant activity studies

by YAĞMUR BİLİZ | BELMA HASDEMİR | HATİCE BAŞPINAR KÜÇÜK | Istanbul University- Cerrahpaşa, Faculty of Engineering, Department of Chemistry, Istanbul, Turkey | Istanbul University- Cerrahpaşa, Faculty of Engineering, Department of Chemistry, Istanbul, Turkey | Istanbul University- Cerrahpaşa, Faculty of Engineering, Department of Chemistry, Istanbul, Turkey

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Pyrazolidines are five-membered heterocyclic compounds containing N-N bonds. Pyrazolidine and derivatives are widely used as anticancer, antidepressant, anti-inflammatory, antioxidant, antiviral, antialzheimer, anesthetic, anticonvulsant and antibacterial agents. In this study, novel pyrazolidine were synthesized as a result of the [3+2] cycloaddition reaction of hydrazide-hydrazones with cyclopentadiene. The structures of the synthesized molecules were determined by IR, ^{1}H-NMR, ^{13}C-NMR and GC-MS spectroscopic methods. The antioxidant activity of the novel pyrazolidine compounds synthesized was evaluated by the DPPH radical scavenging activity test using ascorbic acid (AA), butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) as standards for comparison.

Keywords

Pyrazolidine, antioxidant activity, synthesis

Acknowledgement

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Evaluation of the pharmaceutical potential of components of aniseed and flaxseed against Shigellosis through in silicio and in vitro analysis

by Tosin Fajembola | EZGİ KESKİN TALDARİ | Prof. Dr. SAMİ DOĞANLAR | Prof.Dr. Anne Frary | Izmir Institute of Technology | Izmir Institute of Technology | Izmir Institute of Technology | Izmir Institute of Technology

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Presenter Name: Tosin Fajembola
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Shigella sonnei is a human pathogen that causes Shigellosis (dysentery) disease. Due to its resistance to currently available antibiotics in the market, it has been identified as a global crisis by the World Health Organization (WHO). Hence, the need to discover and develop new drug candidates against this disease. Although there are options of synthetic/chemical drugs, their side effects and toxicity are greatly unavoidable. For this reason, plant-based drug candidates have received more attention and are more attractive to both the consumer and the pharmaceutical industry not only for the presence of wide bioactive components, but also for being easily accessible and inexpensive to grow. Therefore, it is worthwhile to investigate the bioactivity of natural compounds from such plants. For the first time, the chemical constituents of the aniseed oil and flaxseed oil will be elucidated to determine which compound(s) are responsible for antimicrobial activity and how they interact with each of the molecular target- 'the enzymes of the shikimate pathway'. The pharmacodynamics of the chemical components will be determined through molecular docking and Molecular dynamic simulation studies as well as the pharmacokinetics of the compounds through swissADME. The most promising component(s) determined will then be tested against *Shigella sonnei* in vitro by determining the minimum inhibitory and minimum bactericidal concentrations. Thus, a new plant-based drug candidate will be determined against shigellosis, which causes thousands of deaths every year and this drug candidate can be used in clinical trials.

Computational evaluation of molecular imprinting monomers that selectively bind ApoE4 protein for Alzheimer's Disease diagnosis

by Miray Cakiroglu | Msc Student

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Presenter Name: Miray Cakiroglu
Presenter Preference: Poster Presentation
Status: Accepted

Alzheimer's disease (AD) is a progressive neurological disorder predominantly marked by memory loss and dementia. The apolipoprotein E (apoE) isoform, ApoE4, is recognized as a primary genetic risk factor for late-onset AD. The only residue distinctions between the ApoE3 and ApoE4 isoforms play a critical role in understanding the disease's etiology and potential therapeutic strategies. This study seeks to computationally evaluate molecular imprinting monomers capable of selectively binding to the ApoE4 isoform, differentiating it from the ApoE3 isoform. Using molecular docking and dynamics analyses, we investigated functional monomers that can recognize various regions of ApoE4. The unique binding capabilities of these monomers were examined to ensure the selective recognition of ApoE4 over other isoforms. Initial findings highlight the identification of potential monomers with a selective affinity for the ApoE4 isoform. This offers promising prospects for the diagnosis and therapeutic targeting of AD. Utilizing computational chemistry techniques, this research elucidates potential molecular imprinting monomers that can play a significant role in discerning the ApoE4 isoform, thereby advancing the precise diagnosis and understanding of Alzheimer's disease.

INHBA is a potential biomarker and therapeutic target for patients with colorectal cancer

by Nevin Belder | Seçil Demirkol Canli | Selim Tamam | Serdar Çulcu | Berna Savas | Hakan Akbulut | Ankara University, Biotechnology Institute, Ankara, Turkey | Hacettepe University, Oncology Institute, Ankara, Turkey | Ankara University, School of Medicine, Department of Surgical Oncology, Ankara, Turkey | Ankara University, School of Medicine, Department of Surgical Oncology, Ankara, Turkey | Ankara University, School of Medicine, Department of Pathology, Ankara, Turkey | Ankara University School of Medicine, Department of Medical Oncology, Ankara, Turkey

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Topic: General
Presenter Name: Nevin Belder
Presenter Preference: Oral Presentation
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Introduction: Inhibin β A (INHBA) plays a fundamental role in various cancers. However, the exact role of INHBA in colorectal cancer (CRC) remains elusive. Thus, our objective is to explore the prognostic and therapeutic potential of INHBA in CRC.

Methods: To assess INHBA expression in CRC, we utilized the TCGA and 14 independent CRC datasets. We analyzed the association between INHBA expression and clinicopathological features, survival outcomes, and performed co-expression and enrichment analysis (GSEA) to unveil the underlying mechanisms of INHBA in CRC. Additionally, tumor and normal tissues were collected to confirm the INHBA expression pattern in CRC.

Results and Discussion: Our findings revealed significantly higher INHBA expression in cancer tissues across fifteen studies ($p<0.0001$). Elevated INHBA levels were confirmed in collected CRC patients compared to normal tissues. High INHBA expression linked to shorter overall survival ($p<0.05$), advanced CRC stages ($p<0.05$), and recurrence ($p<0.05$). A significant increasing expression trend was seen from normal tissue to polyp and cancer in five diverse CRC cohorts ($p<0.001$), introducing a novel insight for early diagnosis. Co-expression and GSEA analyses suggested INHBA's involvement in CRC carcinogenesis via hypoxia and epithelial-mesenchymal transition. High INHBA expression is also positively correlated with CMS4 subtype, macrophage and cancer-associated fibroblasts.

Conclusions: In conclusion, INHBA was highly expressed in CRC and significantly associated with a poor prognosis. Our study also suggests that INHBA could be a novel potential therapeutic target for CRC patients.
This study is supported by TUBITAK with grant number: 122S340

Keywords: colorectal cancer, INHBA, biomarker, therapeutic target

Design of Nanoparticle Integrated Chitosan Microparticles for Controlled and Sustained Ocular Drug Delivery of Anti-Angiogenesis Peptide

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Presenter Name: Zeynep Ozornek
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Neovascularization is the formation of dysfunctional new blood vessels (angiogenesis) which leads to vision loss and other complications within the eye. Vascular endothelial growth factor (VEGF) is the main biological factor regulating the ocular angiogenesis. Intravitreal injection of VEGF antagonist peptide (anti-VEGF) is the gold standard treatment. However, this drug has a short half-life and requires frequent injections which compromises the comfort of the patient and the clinician by increasing the risk of infections and complications along with a financial burden on the patient. Unfortunately, no design up to date has been developed to increase the efficiency of the anti-VEGF treatment and to decrease the frequency of the injections into the patient eye. In this study, we report a biocompatible, nanoparticle integrated chitosan microgel as a drug delivery vehicle to promote the sustained release of anti-VEGF. The controlled release of anti-VEGF will be promoted through near infrared (NIR) light stimulation of chitosan microgels which will then be upconverted into ultraviolet (UV) light by the upconverting nanoparticles (UCNPs) within the microgel. Synthesized UCNPs are encapsulated in the chitosan microparticles. Anti-VEGF peptide will be conjugated by a UV light sensitive ortho-nitro benzyl bond, where drug molecule will then be released in response to NIR. The drug release kinetics and therapeutic efficacy will be assessed by spectroscopic methods and cell culture experiments. This project proposes a novel design to solve the problems of intraocular anti-VEGF drugs, delivery of anti-VEGF peptide controlled by UCNP integrated chitosan methacrylate microgel.

Structure Activity Relationship for Antifungal Activity of Chalcone Derivatives

by sondos ALREQEB | Bengü Ergüden | GEBZE TECHNICAL UNIVERSITY | GEBZE TECHNICAL UNIVERSITY

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Topic: General
Presenter Name: Sondos ALREQEB
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Fungal infections are described as infections that are caused by fungal cells or fungi. These types of infections can be serious or life threatening in severe cases. For this reason and due to the increased number of people suffering from fungal infections, the need to discover and find new and novel antifungal agents has been raised.

Chalcones are phenolic organic substances that exist naturally in plants. These substances can be extracted from fruits and vegetables to be used in pharmaceutical drugs industry as they have properties such as having good anticancer, antibacterial, anti-inflammatory features.

Most of the existing antifungal agents target the cellular membrane of the fungal cell. Cell membrane acts as the external barrier that controls substances entering or leaving the cell. When cell membrane is disrupted by such agents the cell loses its viability. The mechanism of fungal cellular membrane disruption differs from agent to another.

The studies on the link between chalcone derivatives with different chemical structures and the fungal cell viability are very few. Thus, in this study, we aim to clarify the relationship between chalcones and its derivates on yeast cells S. cerevisiae. Many tests are applied to S. cerevisiae treated with chalcones to investigate the exact effect of these substances on yeast cells. Our study will take part in the improvement of the current knowledge regarding antifungal agents, and it will help in the discovery and development of novel antifungal agents.

Valdecoxib (VLX)-DSPC Model Membrane Interaction Explains the Ameliorative Effects of Selective COX-2 Inhibitors on Cancer Cell Lines in Terms of Biophysical Parameters

by Aysun İnan Genç | Richardas Rachkauskas | Sreeparna Banerjee | Feride Severcan | Kastamonu University | Middle East Technical University | Middle East Technical University | Altınbaş University

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Presenter Name: Aysun İNAN GENÇ
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Valdecoxib (VLX) belongs to the family of Non-steroidal anti-inflammatory drugs (NSAIDs), which is a selective COX-2 inhibitor and prescribed as an analgesic drug. VLX, as well as, other COX-2 inhibitors were withdrawn from the market for their serious side effects on gastrointestinal and cardiovascular system. After clinical trials indicated that some members of COX-2 inhibitors, such as, Celecoxib (CLX) have been used as an adjuvant and/or chemopreventive agent in cancer and it has been approved for the use as a chemopreventive agent for the Familial Adenomatous Polyposis (FAP). One of the many destructive effects of cancer is the one on the membrane lipid composition. We examined the ameliorative effect of Valdecoxib (VLX) in lipid dynamics on HT29 and SW620 colon cancer cell lines previously. Obtained results revealed that VLX decreased lipid fluidity in both cell lines. Furthermore, it affected the order parameters of the membrane lipids. To understand how VLX makes these changes, we did a complementary study on the DSPC model membrane by using differential scanning calorimetry (DSC) and fourier transform infrared spectroscopy (FT-IR) methods. We have observed that VLX alters biophysical properties of the DSPC model membrane,such as, phase transition temperature (Tm) and membrane fluidity. With these results obtained from the model membrane, study, the ameliorative effect of VLX on the cancer cell line was confirmed. These results provide us new insights into COX-2 inhibitors-lipid interactions which can help delineate further the effects of these drugs on cancer cell membrane.

VIRTUAL SCREENING, MOLECULAR DYNAMICS, AND IN-SILICO ADME-Tox ANALYSIS OF NATURAL COMPOUNDS FOR EXPLORATION OF POTENTIAL ANTIFUNGAL DRUG TARGETS

by Imane YAMARI | Oussama ABCHIR | M'hammed EL KOUALI | Abdelkbir ERROUGUI | Mohammed TALBI | Samir CHTITA | Laboratory of Analytical and Molecular Chemistry, Faculty of Sciences Ben M'Sik, Hassan II University of Casablanca, Morocco | Laboratory of Analytical and Molecular Chemistry, Faculty of Sciences Ben M'Sik, Hassan II University of Casablanca, Morocco | Laboratory of Analytical and Molecular Chemistry, Faculty of Sciences Ben M'Sik, Hassan II University of Casablanca, Morocco | Laboratory of Analytical and Molecular Chemistry, Faculty of Sciences Ben M'Sik, Hassan II University of Casablanca, Morocco | Laboratory of Analytical and Molecular Chemistry, Faculty of Sciences Ben M'Sik, Hassan II University of Casablanca, Morocco | Laboratory of Analytical and Molecular Chemistry, Faculty of Sciences Ben M'Sik, Hassan II University of Casablanca, Morocco

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Presenter Name: YAMARI IMANE
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Candida Albicans remains a significant fungal culprit in a range of human pathologies. The quest for alternative antifungal therapies becomes imperative with the surfacing of resistant forms. Our research employed a computational assessment of 297 derived natural compounds to discern molecules with optimal binding interactions to Candida Albicans' target structure (PDB ID: 1EAG). This was supplemented with an ADMET evaluation to gauge potential pharmacokinetic and toxicological outcomes. We further embarked on molecular dynamics exercises to analyze the enduring stability of these predominant compounds. This comprehensive study resulted in several natural derivatives as potential therapeutic agents against emergent resistant forms of Candida Albicans.

SVM-DO: Identification of Tumor-discriminating mRNA Signatures via Support Vector Machines Supported by Disease Ontology

by Mustafa Erhan Özer | Marmara University

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Presenter Name: Mustafa Erhan Özer
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The complex nature of tumors causes difficulty in identifying discriminatory genes. Recently, application of transcriptome datasets in supervised classification methods using support vector machines (SVMs) have become popular in this field. However, using big datasets without eliminating less effective variables causes significant decrease in SVM classification performance. Useful gene expression features among the junk data can be filtered through feature selection methods such as enrichment analysis. Linkage between cancer and chronic disorders have been hinted in various studies. Yet, there is still a few genetic genetic studies focusing on this linkage. To this end, we thought that focusing on disease-associated gene discovery could be a viable strategy to identify gene sets effective in distinguishing tumor and normal states. To acquire genes with significant disease associations, Disease Ontology (DO) enrichment analysis was applied to the differentially expressed genes. Furthermore, the removal of non-discriminative features at the data level among disease-associated genes was applied by using Wilks Lambda Criterion filtration prior to the classification method. To analyze the performance of our algorithm, we applied comprehensive RNA-Seq data of colon adenocarcinoma, lung squamous cell carcinoma, and lung adenocarcinoma. According to the results, good accuracy in discriminating tumor/normal states using lesser number of genes was acquired. In addition, acquired gene sets were observed as including potential prognostic markers. By combining gene sets for both diagnosis and prognosis, our method can improve clinical applications in cancer research. Our algorithm is available as an R package in GUI form in Bioconductor (10.18129/B9.bioc.SVMDO) and Github (https://github.com/robogeno/SVMDO).

In vitro and in silico investigation of inhibitory activities of 3-arylcoumarins and 3-phenylazo-4-hydroxycoumarin on MAO isoenzymes

by Basak Yuce-Dursun | Özkan Danış | Lalehan Ozalp | Elif Şahin | Serap Demir | Safiye Sağ Erdem | Ayşe Ogan | Marmara University | Marmara University | Marmara University | Marmara University | Marmara University | Marmara University | Marmara University

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Presenter Name: Lalehan Ozalp
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A series of 3-aryl coumarin derivatives and 3-phenylazo-4-hydroxycoumarin were evaluated for their monoamine oxidase (MAO) A and B inhibitory activity and selectivity by fluorometric enzymological assays. Among 21 coumarin derivatives, compound **21** (3-phenylazo-4-hydroxycoumarin) displayed a good inhibitory activity (0.12 ± 0.02 μM) and very high selectivity for MAO-B (SI > 833.33). The inhibition was determined as mixed-type and not time-dependent. Docking studies, molecular dynamics and molecular mechanics/Poisson-Boltzmann surface area (MM/PBSA) calculations were performed to elucidate *in vitro* results. Our results reveal that the insertion of an azo linker between coumarin and phenyl rings in 3-arylcoumarins enhances MAO-B selectivity enormously since such a linker leads to the perfect alignment of the coumarin ring in the aromatic cage and the phenyl ring in the entrance cavity of MAO-B active site. Hydrogen bond interactions with Cys172 in the active site entrance of MAO-B also contributes to the remarkably higher inhibitory activity and selectivity for MAO-B.

Acinetobacter baumannii D-Alanine-D-Alanine Ligase (AbDDL) Enzyme as a Drug Target: Molecular Modelling, Docking, Classical Molecular Dynamics (MM MD) and Quantum Mechanical (QM/MM MD) Reaction Modelling

by Can AYGÜN | Özal MUTLU | Marmara University | Marmara University

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Presenter Name: Can AYGÜN
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Among the six highly virulent, antibiotic resistant bacterial pathogens categorically grouped together, based on their proclivity for increased drug resistance over time in common, to comprise the "ESKAPE" acronym, is *Acinetobacter baumannii*. Since multi-drug resistant (MDR) strains of *A. baumannii* pose a grave threat to global health as even available treatment options such as colistin, often used as a last resort and is known for severe adverse side-effects, have been reported to fail in some cases, targeting a druggable *A. baumannii* enzyme as the basis of a computer-aided drug discovery study would be a prudent course of action. The bacterial D-Alanine-D-Alanine Ligase (DDL), the vancomycin resistance agent which catalyses the synthesis of the D-alanine dipeptide D-alanyl-D-alanine, the cross-linking terminal peptidoglycan component, could be a reasonably druggable target, with an already clinically available inhibitor, D-cycloserine, available as a reference starting point for investigating DDL inhibitor binding modes and inhibitory capacity therof. Pursuing this aim, the complete 3D *Ab*DDL apoenzyme and holoenzyme structures containing ATP, 2xMg^{+2}, 2xD-Alanine/D-cycloserine+D-Alanine were acquired by multiple template homology modelling with Modeller and molecular docking using SeeSar. Dynamics and stability of the apoenzyme and ligand-bound structures were investigated, running 1000ns MD simulations on GROMACS. Capturing the base enzymatic DDL reaction, and the phosphorylation of D-cycloserine at the active site whereby it exerts its inhibitory effect, was attempted using AMBER22 QM packages and its gpu-accelerated QUICK interface. After preliminary QM runs employing semi-empirical methods, single point DFT calculations were made to optimise the energies of reaction intermediates and transitions.

Discovery of Sars-CoV-2 3C-like protease (3CLpro) inhibitor by drug repurposing approach using biosafe Sars-CoV-2 Replicon

by Betul Orucoglu | İdil Çetin | Mehmet Rıfkı Topçul | Seref Gul | Istanbul University | Istanbul University | Istanbul University | Bezmialem Vakıf University

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Topic: General
Presenter Name: Betul Orucoglu
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Covid-19 disease caused by the SARS-CoV-2 virus resulted in a pandemic worldwide. According to reports ~622 million people were infected and ~7 million lost their life. However, an effective drug has not yet been developed. The SARS-CoV-2 genome consists of two polyproteins and four structural proteins. When the viral genome proliferates, polyproteins are cut from appropriate regions by the 3C-like protease ($3CL^{pro}$) and papain-like protease (PL^{pro}) included in these polyproteins. Therefore, these two proteases are critical to the life cycle of virus and are safe-critical targets in drug design studies since similar proteins are not found in humans. We aimed to find SARS-CoV-2 inhibitor that is effective at low doses from FDA-approved drugs in widespread use. With the help of computational studies, we determined 25 FDA-approved drugs with high binding energies to the active site of $3CL^{pro}$ that have potential to be inhibitors of this protease. After analyzing the toxicity profile of these drugs using xCELLigence system, we tested them in vitro $3CL^{pro}$ enzymatic activity assay and determined their IC50 values. Next, combination trials were conducted to identify drugs having synergistic effects and hence have high efficacy at lower doses. We determined a set of drugs that have IC50 values lower than 1μM. Recently, by using a special subgenomic non-infective SARS-CoV-2 replicon with luciferase and GFP reporters, we are testing the inhibitory effect of these drugs on the replication of SARS- CoV-2 in Calu-3 and Caco-2 cell lines.

Development of solid lipid nanoparticles containing budesonide for Crohn's disease based on the quality by design (QbD) approach.

by Mazen Al-Mohaya | Institute of Health Sciences, Istanbul University, Istanbul, 34216, Türkiye

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Abstract

The purpose of our study was to apply the Quality by Design (QbD) approach to develop and optimize solid lipid nanoparticles (SLNs) containing budesonide and evaluate *in vitro*, *in vivo*, and *in silico*. Firstly, to identify the critical material attributes (CMAs) and critical process parameters (CPPs) by adapting the initial risk assessment. SLNs were produced using a hot homogenization method. The ratio of Cetyl Stearyl Alcohol as solid lipid, and Cremophor® A25 and Gelucire® 44/14 as surfactant were the CMAs, and homogenization time was CPP. The design of experiment (factorial design) was employed to understand the effect of CMA and CPP on critical quality attributes (CQAs), which included particle size, polydispersity index, entrapment efficiency, and cumulative drug release after 2 h in buffered medium pH (7.5). Based on the applied experiments, the data showed that the optimum formulation can be produced using Cetyl Stearyl Alcohol at 15%, Cremophor® A25 at 5%, and homogenization time in 10 minutes. The optimum SLNs displayed mean particle size (10.15 ± 0.11), polydispersity index (0.104 ± 0.00), entrapment efficiency (99.80 ± 0.00), and cumulative drug release after 2 h (98.53 ± 8.08). The optimum SLNs were evaluated in vivo (rabbit) and in silico compared to the marketed product.

Keywords: Solid lipid nanoparticles; Budesonide; In vitro; In vivo; In silico

Virtual screening of a large set of compounds as candidate drugs against alpha amylase-activity, ADMET, and molecular dynamics simulation

by Oussama Abchir | Imane Yamari | Hassan Nour | Samir CHTITA | Abdelkbir Errougui | El Mehdi Karim | Maroua Fattouche | Chemsitry, Universite Hassan II de Casablanca, Casablanca, Morocco | Chemsitry, Universite Hassan II de Casablanca, Casablanca, Morocco | Chemsitry, Universite Hassan II de Casablanca, Casablanca, Morocco | Chemsitry, Universite Hassan II de Casablanca, Casablanca, Morocco | Chemsitry, Universite Hassan II de Casablanca, Casablanca, Morocco | Chemsitry, Universite Hassan II de Casablanca, Casablanca, Morocco | Chemistry, Biskra university, Algerie

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Presenter Name: Oussama ABCHIR
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The rising number of diabetes cases and the current medications' side effects make it necessary to develop a novel candidate drug that may block alpha-amylase as a severe means of treating diabetes cases. In this work, a large series of compounds pulled from the PubChem database was subjected to several conception-assisted drug design methods to identify that may inhibit alpha-amylase activity. Applying molecular docking, the studied ligands were docked in the protein's binding site corresponding to the alpha-amylase activity to assess their stability and reduce the size of the examined set. The ADMET study was conducted to assess the pharmacokinetics features for understanding how potential drugs penetrate, transport, and transform into the body, and how to exit the body. Also, molecular dynamics were used to confirm the obtained results of molecular docking. As a result, some compounds were suggested as candidate drugs considering their ability to form stable complexes with targets, and their good pharmacokinetics properties. We recommended in vitro, then in vivo studies to validate the obtained results.

Pore-Forming Proteins that Trigger Necrotic Cell Death as New Druggable Targets

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Presenter Name: Elif EREN
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Introduction: One of the main challenges of cancer treatment is the acquisition of apoptosis resistance to different chemotherapeutic drugs by tumor cells. Pyroptosis is an inflammatory cell death triggered by infections or danger signals and is executed by Gasdermin proteins. Upon their cleavage, Gasdermins form pores at the plasma membrane that not only constitute a conduit for IL-1beta secretion but also result in Ninjurin 1-dependent membrane rupture. Based on these properties, pyroptosis is considered as an alternative approach to kill cancer cells. However, to design effective drugs that modulate them, understanding the molecular mechanism of pore formation is crucial.

Methods: In this project, we sought to determine the role of Gasdermin in tumor cell killing. For this purpose, we evaluated pyroptosis in cancer cell lines treated with well-known apoptosis inducer drugs and assessed the underlying molecular mechanism by using cellular and molecular approaches.

Results and Discussion: Treatment of cancer cell lines with apoptosis-inducer drugs resulted in morphological and biochemical features characteristic of pyroptosis. Surprisingly, an unconventional cleaved form of Gasdermin and an unexpected subcellular localization of this cleaved fragment were observed.

Conclusions: Up to now, several drugs reducing Gasdermin activity have been tested in inflammatory disorders where pyroptosis activation and IL-1beta secretion are detrimental. However, their lack of specificity and the need of Gasdermin activation in cancer, require the discovery of new drugs. Our results provide fundamental science data for the development of effective drugs targeting Gasdermins.

Keywords: Gasdermin, Pyroptosis, Inflammasome, Cancer, Infection

Development of New 1,4-Benzoquinone Derivatives as EGFR-TK Inhibitors

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Presenter Name: Edanur Düzgün
Presenter Preference: Poster Presentation
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Epidermal growth factor receptor (EGFR; HER-1) belongs to ERBB family of receptor tyrosine kinases along with three other closely related receptors, namely HER-2, HER-3 and HER-4. Each contains an extracellular ligand-binding domain, a single hydrophobic transmembrane region and an intracellular tyrosine kinase (TK) domain. Upon ligand binding to the extracellular domain, homo- or heterodimerization of EGFR leads to autophosphorylation of the intracellular domain through TK activity and subsequent stimulation of downstream cascade that may result in proliferation, suppression of apoptosis, metastasis and angiogenesis. In particular, EGFR is commonly overexpressed in lung cancer.

In the current work, we designed and synthesized new 1,4-benzoquinone derivatives (**1-15**) via the reaction of 2-acetamido-1,4-benzoquinone with different aryl amines. EGFR-focused anti-lung cancer studies are ongoing for these derivatives. Besides, we performed molecular docking studies in order to understand the interactions of compound **1-15** in ATP binding pocket of EGFR compared to erlotinib (PDB ID: 4HJO). Results indicated that ethylenedioxy substituted compound (**14**) showed the most promising docking score and molecular interactions. Compound **14** presented two important hydrogen bonding with Lys721 and Met769 residues in the ATP binding cleft of EGFR. In a similar manner, erlotinib also established a key hydrogen bonding with Met769. The docking score of compound **14** was found as -7.419 kcal/mol compared to erlotinib (-8.895 kcal/mol).

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Targeting EGFR in Lung Cancer: Novel Inhibitors and Molecular Insights with X-ray Crystallography

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Presenter Preference: Oral Presentation
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Abstract

Lung cancer is a prevalent and serious global health issue, which leads to the development of abnormal and uncontrolled tumors in the cells of the lungs. Understanding cellular processes involving biological molecules like the Epidermal Growth Factor Receptor (EGFR) is of utmost importance in exploring treatment options. Therefore, targeting EGFR has become a significant research area for lung cancer treatment as it is a transmembrane protein presents on the cell surface, playing a critical role in fundamental cellular processes such as growth, proliferation, and survival.

Our research focuses on the determination of the three-dimensional atomic arrangement of EGFR and its interactions with our designed and synthesized hit EGFR inhibitors at the molecular level using X-ray crystallography at home source X-ray diffractometer (XRD). XRD is a powerful technique that allows us to collect diffraction data at cryo and near-physiological temperatures promises to provide new fundamental insights into the structural dynamics of the EGFR and their functional complexes. Understanding these intricate interactions can potentially lead to the development of novel and more effective EGFR inhibitors, which could be drug candidates for innovative and personalized cancer treatments, aiming to improve patient outcomes and combat drug resistance.

Acknowledgement: This work is supported by TUBITAK 1001, Grant No: 122Z775

In silico and in vivo outcomes on Cerastokunitz : A twofold potential therapeutic biopeptide with valuable pharmacological anti-thrombosis and anti-tumoral activities

by CHERIFI Fatah | USTHB, Faculty of Biological Sciences, Laboratory of Cellular and Molecular Biology, USTHB, BP 32, El-Alia, Bab Ezzouar, Algiers, Algeria

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Presenter Name: CHERIFI Fatah
Presenter Preference: Oral Presentation
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Abstract

Thrombo-inflammatory disorders are becoming characteristic complications of diverse diseases such as coagulopathies and mainly various cancers. Currently, an actual interest is increasing to isolating and characterizing new anti-thrombotic and anti-inflammatory active biomolecules which could be good candidates as substitutes for chemical drugs. In this regard, the main focus of the present study was to report the structure and the function of a new biopeptide called Cerastokunitz, from a snake venom with its multi-antithrombotic activities.

Structurally, Cerastokunitz is a hydrophilic peptide consisting of 67 cross-linked amino acid residues, stabilized by three disulphide bridges and with a low molecular weight equivalent to 7746.89 determined by mass spectrometry MALDI-MSMS, it is a with basic an isoelectric point value of about 8.48. 3D structure of Cerastokunitz undertook by SWISS-MODEL unveiled 12 % Alpha helix and 21 % Beta strand. The overall percentage of basic amino acids (Arg, Lys and His) of 16.5% is higher than that of basic amino acids (Asp and Glu) with only 9% in the entire sequence. At physiologic pH value, the whole charge of Cerastokunitz provides a cationic peptide to be +4 due to the 6 negatively charged residues (Asp and Glu) and 10 positively charged residues (Arg and Glu). In silico studies have shown that the Kunitz peptide has structural similarity to several Kunitz-like serine protease inhibitors. Functionally, three main assays laid to identify ; the effect of Cerastokunitz on platelet inhibition, by aggregometery after induction of aggregation of platelets' rich plasma by thrombin alone, followed by thrombin pre-incubated with biopeptide. Then, the IC50 value of the antiplatelet activity was determined by incubating increasing doses of Cerastokunitz with thrombin before adding the PRP in a 96-well microplate, the absorbance was recorded with microtiter reader Bio-Tek Instrument at 580 nm. The third assay was related to check the biopeptide toxicity and its in vivo anti-coagulation effect carried out on NMRI male mice after inducing the tail thrombosis induced by carrageenin (60 mg/kg). The results of this experimentation have shown that the purified Cerastokunitz is a non-toxic until 10 mg/kg. Cerastokunitz exhibits both in vitro and in vivo anti-thrombotic activity. It inhibits the thrombin-dependent platelets activity at 10 µg/mL with an IC50 value of only 1.695 µg/µL. In addition, it reduces in vivo thrombus length in a dose dependent manner more efficiently than other thrombolytic therapeutics. we opted for the carrageenin-induced mice tail thrombosis model, which is one of the most used models for the evaluation of antithrombotic and thrombolytic agents such as aspirin and heparin. The use of this

model in our study was chosen first, for ethics reasons, because of its non-invasive and non-chirurgical method of thrombus formation, that is a simple i.p injection of 60 mg/kg carrageenin dissolved on 9% NaCl. Secondly, the model elaboration protocol is very easy, uncomplicated and unexpansive. And finally, due to the visibility of the developed thrombus on the tail vein since the first post-treatment hours, the evaluation of the anti-thrombotic effects of the Apixaban and Rivaroxaban at a dose of 0.2 mg/kg and also of the studied biomolecule at different graduated dose (2, 4 and 6 mg/kg) was done by measuring the length of the formed thrombus on the tail vein of each model mouse after being treated b one of those three molecules. The results of this in vivo method were obtained by measuring the formed thrombus 24 and 48-hour post-treatment and at 48h posttreatment, comparatively to the negative control mice models treated with 9% NaCl, the measurements have shown an antithrombotic effect on a dose-dependent manner with a 75% inhibition of thrombus formation at the dose of 6 mg/kg of the tested biomolecule, whereas, the Apixaban and Rivaroxaban exerted an inhibitory effect of only 51.79% and 17.92% respectively. This data leads us to attribute an important antithrombotic activity to Cerastokunitz, with comparison to the two selective specific inhibitors of factor Xa (used as positive controls). Apixaban and Rivaroxaban interrupt both extrinsic and intrinsic coagulation pathways by the prothrombinase inhibition and thrombus formation prevention.

These two drugs, presented an antithrombotic effect, left on the model of the present study at 48h post-treatment, which is less important than Cerastokunitz. This data attribute a potential therapeutic effect to Cerastokunitz, on thrombotic disorders witch is characteristic of Kunitz type peptides showing an additional interesting anti-angiogenesis and anti-tumoral effect.

Key words: Cerastokunitz, Thrombosis, Bio-therapeutics, Anti-thrombotic, StructureFunction relationships

A system that can cross the blood-brain barrier in the treatment of Alzheimer: Donepezil hydrochloride incorporated Resomer RG 502 H nanoparticle systems

by Merve KÖMÜR | A. Alper ÖZTÜRK | Anadolu University, Graduate School of Health Sciences, Department of Pharmaceutical Technology, Eskişehir, Türkiye. | Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Eskişehir, Türkiye

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Great success has been achieved in treatments with nanoparticle (NP) systems. In this study, donepezil hydrochloride (DNP) loaded PLGA-based NPs were prepared by the 'Double Emulsification Solvent Evaporation' method and the effect of PVA concentration in the aqueous phase and probe sonication time on NP properties was investigated. It was found that increasing PVA concentration and probe sonication time resulted in a decrease in particle size. After the examinations, the I-DNP coded formulation was chosen as optimum. The particle size of the I-DNP coded NP formulation was obtained as 136.37 nm ± 0.93 and the formulation proved to be monodisperse with a PDI value of 0.122±0.011. The zeta potential value was -24.17 mV±1.21 and it was concluded that it could be stable for a long time. In the encapsulation efficiency study, a value of 69.22±4.84%, ideal for oral administration, was obtained. When the release of DNP from the I-DNP coded NP formulation was compared with the pure DNP, it was determined that the I-DNP coded NP formulation had a slower and extended 24-hour release. In line with the results obtained with DDSolver, it was concluded that the release kinetics are predominantly governed not by only a single mechanism, but by a combined Fickian and non-Fickian mechanism. As a result, NP systems that have a particle size that can pass the blood brain barrier and provide extended release have been successfully produced. This study was financed by Anadolu University Scientific Research Project Foundation (No: 2304S027).

A drug delivery system that can be used in diseases caused by oxidative damage: Preparation and Characterization of Ferulic Acid Loaded PLGA-Based Nanosystems

by Kübra Nur Arınmış | A. Alper ÖZTÜRK | Anadolu University, Graduate School of Health Sciences, Department of Pharmaceutical Technology, Eskişehir, Türkiye. | Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Eskişehir, Türkiye

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Topic: General
Presenter Name: A. Alper ÖZTÜRK
Presenter Preference: Poster Presentation
Status: Accepted

In this study, ferulic acid loaded PLGA-based nanoparticles (NPs) were prepared by the 'nanoprecipitation' method and the effects of Poloxamer 188 concentration in the aqueous phase and Span 60 concentration in the organic phase content on the NP properties were investigated. With increasing Poloxamer 188 and Span 60 concentration, an increase in particle size was detected. A-Blank coded formulation was selected optimally and ferulic acid loaded form was prepared in order to avoid excessive excipients. The particle size of the ferulic acid-loaded A-FA coded NP formulation was obtained as 174.70 nm ± 0.89 and the formulation proved to be monodisperse with a PDI value of 0.113 ± 0.006. The zeta potential value was -22.00 mV ± 0.56 and it was concluded that it could be stable for a long time. Due to the low affinity of ferulic acid to the water phase and thus its tendency to migrate to the organic phase, high encapsulation efficiency (EE%) was achieved and the EE % was 76.48 ± 3.12%. When the ferulic acid release from the A-FA coded NP formulation was compared with pure ferulic acid, it was determined that the A-FA coded NP formulation had a slower and 24-hour extended release. According to the results obtained with DDSolver, a high correlation was observed between the Peppas-Sahlin model and the Weibull model. In conclusion, in vitro results have proven successful encapsulation and extended release for oral use.

Leveraging High-Throughput Screening for Accelerated Drug Discovery: A Case Study in Targeted Cancer Therapies

by Dr. Naimat Ullah | Gomal University

Abstract ID: 10
Submitted: August 2, 2023
Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Dr. Naimat Ullah
Presenter Preference: Poster Presentation
Status: Accepted

File attached

A NOVEL DE NOVO DESIGN APPROACH FOR PROLINE-RICH ANTIMICROBİAL PEPTIDE PR26

by Zülal Kesmen | Melike Canpolat | Saime Gülsüm Batman | Erciyes University, Engineering Faculty, Department of Food Engineering | Erciyes University, Engineering Faculty, Department of Food Engineering | Stiftung Tierärztliche Hochschule Hannover

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Topic: General
Presenter Name: Melike Canpolat
Presenter Preference: Oral Presentation
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Proline-rich AMPs (PrAMPs) are a class of AMPs that kill bacteria by inhibiting their essential intracellular functions. Natural PrAMPs, which are derived from a variety of organisms, generally had low antimicrobial activity. In order to overcome this drawback of natural PrAMPs, intensive studies are being carried out on the modification of peptide sequences or de novo design. In this study, we develop a motif-based de novo peptide design method to generate novel PrAMPs with high antimicrobial activity. Therefore, PrAMPs with high antimicrobial activity (MIC < 25 μg/ml) were selected from AMP databases. The motif discovery tool (Meme Suit 5.5.1) was used to discover the motifs responsible for antimicrobial activity in these prAMPs and the motifs with the lowest E-value (< 0.001) were identified. Bioinformatic analyses were applied to the candidate peptides formed by combining the selected motifs. The Pr26 peptide "DKGSYLPRPYPRWPRWPRHPIRPGRPRPKPY" was selected for production by chemical synthesis and used for wet-lab analysis. The Pr26 peptide inhibited the growth of Escherichia coli ATCC 25922, Salmonella Typhimurium ATCC 1428, Listeria monocytogenes ATCC 7644 at 160 μg/ml, while has no hemolytic activity against against mouse erythrocytes and no cytotoxic activity toward animal fibroblast lung cells (MRC-5 cells) at >1280 μg/ml.

Identification of dysregulated mRNAs as therapeutic targets in Alzheimer's Disease and drug repurposing approaches.

by Birgül ÇOLAK AL | Nagehan ERSOY TUNALI | 1 İstanbul Medeniyet University, Dept. Molecular Bioloy and Genetics, İstanbul, Turkey; 2 İstanbul Medeniyet University, Science and Advanced Technologies Research Center (IMU-BİLTAM), İstanbul, Turkey | 1 İstanbul Medeniyet University, Dept. Molecular Bioloy and Genetics, İstanbul, Turkey; 2 İstanbul Medeniyet University, Science and Advanced Technologies Research Center (IMU-BİLTAM), İstanbul, Turkey

Abstract ID: 8
Submitted: July 31, 2023
Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Nagehan ERSOY TUNALI
Presenter Preference: Poster
Status: Accepted

Introduction: Alzheimer's Disease (AD) is a complex neurodegenerative disease. Detailed molecular analyses are required to explore advanced diagnostic and therapeutic modalities. We utilized a comprehensive bioinformatics framework to unravel the molecular intricacies and new drug targets.

Methods: We first analyzed GEO datasets to identify differential gene expression (DEG) patterns in various brain regions. We also explored the overlapping DEGs. Next, we performed functional enrichment analyses (FEA). Then, we constructed a PPI network and identified hub genes. In line with our goal to identify potential therapeutic candidates, we implemented drug repositioning strategy targeting the DEGs identified in our study. Utilizing molecular docking, we assessed the probability of drug-protein binding, which allowed us to identify potential drugs that could be repurposed for AD treatment.

Results and Discussion: 7 upregulated and 14 downregulated DEGS were first identified in the entorhinal cortex, hippocampus, frontal cortex, and temporal cortex, then shared molecular signatures across these brain regions were identified. FEA revealed disruptions in neurotransmitter regulation, organelle localization, cytoskeleton organization, vesicle transport, synaptic signaling, and neuronal development. PPI network construction revealed SNAP25 as the downregulated and GFAP as the upregulated hub proteins. Molecular docking studies indicated high binding affinity of dronabinol and permethrin to GFAP, and lestaurdinib, scriptaid, and alvocidib to SNAP25.

Conclusion: The repositioned drugs scriptaid, alvocidib and lestaurdinib act as HDAC, CDK, and tyrosine kinase inhibitors, respectively. Dronabinol and permethrin bind to cannabinoid receptor and sodium channels, respectively. More research and experimental validation are required to establish the effectiveness and safety of these drugs.

New Drug Discovery Approaches for Antibiotics in the Era of Increasing Rate of Panresistant Bacterial Isolates

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Topic: General
Presenter Name: Filiz Yarimcan
Presenter Preference: Projector
Status: Accepted

Infectious diseases are among the most common disease groups and the third most common cause of death despite the presence of the treatment: antibiotics. Pan-resistant bacteria are increasingly reported as a cause of deadly infections, and the introduction of new antibiotics is very limited. The old methods of antibiotic development are producing drugs against which bacteria are already resistant before these drugs are introduced to the market. This study aimed to compare the rate of pan-resistant bacteria isolated in the Acibadem Labmed Microbiology laboratory in 2012 and 2022 and to analyze the resistance ratios of newly introduced drugs in the pan-resistant isolates. The rate of pan-resistant isolates in 20112 was 0% and 1.02 % in 2022 (P<0.0001). The most effective newly introduced drug was ceftazidime-avibactam, with a susceptibility rate of 83% in 75 pan-resistant bacteria. These findings show an urgent need for new approaches using the algorithms generated by machine learning approaches that screen new molecules for antibacterial activity.

References

https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death

Jukic M and Bren U. Machine Learning in Antibacterial Drug Design. 2022. Frontiers in Pharmacology 13: 864412

Wohlleben W, Mast Y, Stegmann E, Ziemert N. Antibiotic Drug Discovery. 2016. Microbial Biotechnology 9: 541-548

Identification of Molecular Signatures and Therapeutic Targets for COVID-19 and PAH through Multiomics Data Integration

by Defne Çığ | Ceyda Kasavi | Bioengineering Department, Marmara University, Istanbul, Turkey | Bioengineering Department, Marmara University, Istanbul, Turkey

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Event: International BAU Drug Design Congress
Topic: General
Presenter Name: Defne Çığ
Presenter Preference: Poster
Status: Accepted

COVID-19 is caused by infection with SARS-CoV-2, spread rapidly, and resulted in approximately 6.5 million deaths. Pulmonary arterial hypertension (PAH) is a progressive and fatal pulmonary vascular disease that shows similar symptoms to cardiovascular disease. Studies showed the association between COVID-19 and cardiovascular complications and endothelial dysfunction leading to increased inflammation in pulmonary vasculature. Increase in the prevalence of PAH was also observed following COVID-19. Although PAH and COVID-19 share common risks, molecular mechanisms underlying the crosstalk between two diseases have not been fully understood. Therefore, the identification of new signatures would provide invaluable information for the discovery of novel therapeutics. In this study, a comparative analysis of transcriptome data of COVID-19 and PAH was performed to understand their relationship. Specifically, differentially expressed genes and associated molecular mechanisms were identified. Using a systems-science approach, data were integrated with biological networks (protein-protein interaction, transcriptional regulatory, and genome-scale metabolic networks) to identify molecular signatures (hub proteins, reporter transcription factors, miRNAs, and metabolites) that warrant future development as putative therapeutic targets. A drug repositioning approach was applied to determine potential drugs for both diseases. Enrichment analysis revealed significant alterations in RNA surveillance and vascular remodelling pathways in PAH, and immunity and inflammation-related processes in COVID-19. Regulation of arachidonic acid and glutathione metabolisms was prominent in both diseases. Moreover, signature-based drug repositioning analysis identified 24 common drug candidates. Our findings revealed the differences and similarities of PAH and COVID-19 at molecular level and allowed the identification of drug candidates for both diseases.

Preliminary evaluation of POFUT1 inhibitors as anti-cancer agents against head and neck cancer using in vitro models

by Neslisah Barlak | Rustem Ebiri | Derya Aktas Anil | Burcin Turkmenoglu | Serdar Burmaoglu | Oztekin Algul | Omer Faruk Karatas | Erzurum Technical University | Ataturk University | Ataturk University | Erzincan Binali Yildirim University | Ataturk University | Mersin University | Erzurum Technical University

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Topic: General
Presenter Name: Neslisah Barlak
Presenter Preference: Poster
Status: Accepted

Despite advances in diagnosis/treatment methods, there has been no remarkable increase in survival of HNSCC patients in recent years due to diagnosis of disease in later stages and frequent recurrence of primary lesions. The cause of signaling pathway irregularities associated with HNSCC initiation and progression has not yet been fully elucidated, and effective treatment methods are not yet available.

We recently identified *POFUT1* (Protein O-Fucosyltransferase 1) as an important oncogene for HNSCC and our *in vitro/in vivo* findings emphasized the necessity for discovery of small molecules to inhibit POFUT1 as a therapeutic target.

Considering the lack of commercially available POFUT1 inhibitors and comprehensive studies on synthesis of compounds with potential to effectively inhibit POFUT1; we aimed at designing, synthesizing and evaluating putative POFUT1 inhibitors efficacy, and investigating their anti-cancer potential.

A total of 34 compounds with potential to inhibit POFUT1 were designed through molecular docking studies using Schrödinger 2021-2 Glide program. Of those, Group1 molecules, comprised of 10 compounds with outperforming binding capacity for POFUT1 compared to its substrate fucose, were synthesized and tested for anticancer activities, Notch1 (target of POFUT1) and Notch pathway inhibition. Compound-7 with IC50 values of less than 2mM against HNSCC cells caused profound decrease in fucosylation of Notch1 and expression of both Notch1 and its downstream targets.

Our results demonstrated the importance of POFUT1 inhibition for treatment of HNSCC and pointed Compound-7 as a novel therapeutic agent, although further pre-clinical studies are needed to better demonstrate its potential.

In silico identification of novel Inhibitors targeting 1-deoxy-d-xylulose 5-phosphate reductoisomerase from neisseria gonorrhoeae

by Mustafa Necati Haşimoğlu | Prof. Dr. Dilek Balık | Doç. Dr. Özal Mutlu | Emrah Sarıyer | Osman Mutluhan Uğurel | Ratana Lawung | Wanchai De-eknamkul | Björn Windshügel | Sinem Koçer | Yildiz Technical University | Yildiz Technical University | Marmara University | Artvin Çoruh University | Altinbas University | Mahidol University | Chulalongkorn University | Fraunhofer Institute | Yeni Yüzyıl University

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Topic: General
Presenter Name: Mustafa Necati Haşimoğlu
Presenter Preference: Poster
Status: Accepted

Gonoccocal infection is one of the main causes of STIs, with an estimated 82 million new cases reported in 2020 by WHO. The emergence of antibiotic-resistant strains of Ng has raised concerns about the effectiveness of current treatments and Ng is included in the WHO's priority pathogen list for research and development of new antibiotics. Isoprenoids are the largest group of chemicals in living organisms. The methylerythritol phosphate (MEP) pathway involved in isoprenoid biosynthesis contains enzymes that could be targeted with drugs because of the lack of this pathway in human. 1-deoxy-d-xylulose-5-phosphate reductoisomerase (DXR) enzyme is a key enzyme in the MEP pathway and converts 1-deoxy-d-xylulose-5-phosphate (DXP) into MEP, which is the first committed step in the synthesis of isoprenoids. Inhibition of DXR activity has the potential to be an effective treatment for gonococal infections. In this study, structure-based drug design approach was used to identify compounds that could bind to and inhibit the activity of DXR in Ng. Schrödinger Maestro was used to identify possible binding poses for small molecules that could inhibit the enzyme's activity. A large library of compounds was screened, and a number of potential hits were identified. To refine the binding mode and stability of the complexes formed between the identified hits and the DXR enzyme, molecular dynamics simulations were performed. The simulations were run for 100 ns to ensure that the binding interactions were stable and specific. This research has been supported by the Scientific And Technological Research Council Of Türkiye. (TUBITAK 121N818.)

Homology Modeling and In Silico Inhibitor Screening of Lactate Dehydrogenase from Theileria annulata

by Selcan AKAR | Mustafa Necati Haşimoğlu | Özal Mutlu | Maria Orlenco | Erennur Uğurel | Dilek Turgut Balık | Yildiz Technical University, Faculty of Chemical and Metallurgical Engineering, Department of Bioengineering, Davutpasa Campus, 34210/Esenler, Istanbul, Türkiye, | Yildiz Technical University, Faculty of Chemical and Metallurgical Engineering, Department of Bioengineering, Davutpasa Campus, 34210/Esenler, Istanbul, Türkiye, | Marmara University, Faculty of Science, Department of Biology, Goztepe Campus, 34722, Kadikoy, Istanbul, Turkey | Yildiz Technical University, Faculty of Chemical and Metallurgical Engineering, Department of Bioengineering, Davutpasa Campus, 34210/Esenler, Istanbul, Türkiye, | Yildiz Technical University, Faculty of Chemical and Metallurgical Engineering, Department of Bioengineering, Davutpasa Campus, 34210/Esenler, Istanbul, Türkiye, | Yildiz Technical University, Faculty of Chemical and Metallurgical Engineering, Department of Bioengineering, Davutpasa Campus, 34210/Esenler, Istanbul, Türkiye,

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Topic: General
Presenter Name: Selcan AKAR
Presenter Preference: Poster
Status: Accepted

Tropical theileriosis, which is transmitted to cattle by ticks of the genus Hyalomma, is a major cause of economic loss and reduced productivity in the livestock sector in many regions of the world. Infection caused by theileria parasite causes fatal or clinical symptoms in cattle, while the drugs used are mostly effective at an early stage in animals. However, anti-therileral chemotherapeutic drugs are insufficient to eliminate the infection completely. Recently, it has been reported that *T. annulata* has developed resistance to buparvaquone, which is primarily used for the treatment of theileriosis. Therefore, with the increase in mutation-induced resistance reports, new drug design studies have become essential. For many parasites, lactate dehydrogenase has been chosen as a therapeutic target because it is a key player in anaerobic energy metabolism and its inhibition would cause issues with the parasite's energy dependence. The ultimate goal of this study is to identify novel inhibitor candidates using *T. annulata* lactate dehydrogenase as a drug target through structure-based drug design studies. In this study, homology modeling is performed for *Ta*LDH using the PDB structures of proteins with known three-dimensional structures as templates. Specific inhibitor candidates on *T. annulata* lactate dehydrogenase were identified by *in silico* screening of compound libraries from the PubChem database. The compounds identified by molecular docking studies on *Ta*LDH were subjected to molecular dynamics simulation analyses. Simultaneously with *in silico* studies, high purity recombinant *Ta*LDH was produced for further *in vitro* studies.

In Silico Examination of Bifenilaminoketooxime Derivatives: Unraveling Anti-Inflammatory Potential and ADMET Characteristics

by Zeliha Nur YILMAZ | Bülent DEDE | Süleyman Demirel University, Department of Chemistry, Isparta, Turkey | Süleyman Demirel University, Department of Chemistry, Isparta, Turkey

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Presenter Name: Zeliha Nur
Presenter Preference: Poster
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Generally, oximes molecules were synthesized by the condensation of hydroxylamine with aldehydes or ketones. Oximes contain azomethine group (-N=C) and hydroxyl group (-OH) in their structure. The oxime functional group contains two H-bond acceptors (nitrogen and oxygen atoms) and oxime of carbonyl groups H-bond donor (OH group). Oxime molecules are bioactive molecules with many properties such as antibacterial, anti-inflammatory, antifungal, and anticancer. For this reason, oxime group molecules play an important role in bioinformatics studies. While methods such as Q-SAR and pharmacophore analysis were used in chemoinformatic studies, molecular docking, and MD simulations were used in bioinformatics studies.

In this study, three biphenyl based aminoketoxime-derived molecules previously synthesized and characterized were used. Molecular docking simulations were performed using the AutoDock Vina 1.1.2 program. Molecular docking studies were determined docking scores, H-bond locations and lengths. In molecular docking studies, Phospholipase A2 (PDB ID: 3H1X) receptor protein was chosen as the receptor structure. Molecular Docking scores of protein-ligand complexes were calculated as -7.9 kcal/mol (Ligand1-3H1X), -7.7 kcal/mol (Ligand2-3H1X) and -7.5 kcal/mol (Ligand3-3H1X). Furthermore, molecular dynamics simulations were performed for the best docking score of complex.

Molecular dynamics calculations for 25 ns were performed to examine the stability of the complexes. AMBER force field was used for MD simulations. MD simulations were performed in the presence of 0.15 M NaCl at pH 7.4 and 300 K.
Finally toxicity parameters, druglikeness and ADME (Absorption, Distribution, Metabolism and Excretion) parameters of the ligands were calculated.

Preparation and Characterization of Salinomycin-Loaded Boron-Doped Mesoporous Bioactive Glass Nanoparticles as an Anti-Cancer Drug Delivery System

by Hatice Kurnaz | Melike GÜNEY AKKURT | Murat KAZANCİ | 1. Istanbul Medeniyet University, Department of Nanoscience and Nanoengineering, Istanbul, Turkiye 3. Halic University, Faculty of Arts and Sciences, Department of Molecular Biology and Genetics, Istanbul, Turkiye | 1.Istanbul Medeniyet University, Department of Nanoscience and Nanoengineering, Istanbul, Turkiye 2. Istanbul Medeniyet University, Department of Biomedical Engineering, Istanbul, Turkiye | 1. Istanbul Medeniyet University, Department of Nanoscience and Nanoengineering, Istanbul, Turkiye 2. Istanbul Medeniyet University, Department of Biomedical Engineering, Istanbul, Turkiye

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Presenter Name: Hatice Kurnaz
Presenter Preference: Poster
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Introduction: This study aims to characterize Boron-doped Mesoporous Bioactive Glass (B-MBG) drug delivery system for salinomycin delivery to cancer cells. B-MBG nanoparticles possess desirable properties for drug delivery due to their small size and porous structure, while boron, a trace element, is known for its significance in various biological processes.

In this study, Salinomycin, a water-insoluble chemotherapeutic agent, is loaded into B-MBG nanoparticles coated with chitosan to allow drug-release in acidic environment and decorated with Hyaluronic acid (HA) for cancer cell targeting.

Methods: The synthesis process involved using the modified sol-gel method for mesoporous silica synthesis to create B-MBG nanoparticles by incorporating boron and calcium. Further modifications included coating the APTES-functionalized nanoparticles with chitosan and subsequently attaching HA using EDC-NHS.

For particle characterization, size, morphology and elemental analysis was performed using SEM-EDS and STEM. Dimensional analysis was performed using DLS. The surface area and pore size were measured via Surface Area and Porosity Analysis. The structure was further analyzed via XRD and Raman spectroscopy.

Results and Discussion: B-MBG nanoparticles have a powder diameter of ~100 nm (SEM) and hydrodynamic diameter of ~380 nm (DLS). Chitosan-coating increases the size by ~60 nm. The synthesized B-MBG nanoparticles possess a surface area of 156.1425 m^2/g, with 4.271 nm pore size, and 0.041964 cm^3/g pore volume. XRD and Raman spectra confirm the physical and chemical structure, respectively.

Conclusions: B-MBG is a promising drug-delivery system with small, spherical structures

coated with chitosan and modified with HA. Supported-by-TUSEB, No:11985.

Keywords: Drug delivery, B-MBG Nanoparticles, salinomycin, cancer