DRUG DISCOVERY

BOOK OF ABSTRACTS

SCHOLARS CONFERENCES

SCHOLARS WEBINAR ON: THE ROLE OF NEW TECHNOLOGIES

DRUG DISCOVERY, DEVELOPMENT AND LEAD OPTIMIZATION

24-25 MAR 2021

WEBINAR

SCIENTIFC PROGRAM

DAY 1 | 24 MARCH | Wednesday

11:00-17:00 (GMT)

11:00-11:10 Introduction

KEYNOTE FORUM

11:10-11:45 **11:10-11:45** (Speaker Local Time)

Title: Implementing fully automated kinase inhibitor characterization for AI-driven drug discovery using a robotic system

Martin-Immanuel Bittner, Arctoris, UK

11:45-12:20 **13:45-14:20** (Speaker Local Time)

Title: In silico discovery of multitargeted drug candidates

Amiram Goldblum, Hebrew University of Jerusalem School of Pharmacy, Israel

12:20-12:55 **12:20-12:55** (Speaker Local Time)

Title: Structural biology, bioinformatics and drug discovery: from cancer to bacterial infections and Covid-19

Tom Blundell, University of Cambridge, UK

12:55-13:30 **15:55-16:30** (Speaker Local Time)

Title: The current trends in Bioentrepreneurship and Biotechnology Innovation Investments in USA, Europe, Turkey & Emerging Markets

Yavuz Selim Silay, Istanbul Consulting Group, Turkey

13:30-13:50 - REFRESHMENTS BREAK

13:50-14:25 **09:50-10:25** (Speaker Local Time)

Title: A Quantum Revolution in Drug Discovery

Shahar Keinan, Polaris Quantum Biotech, USA

SCIENTIFIC SESSION

14:25-14:55 **14:25-14:55** (Speaker Local Time)

Title: A computational study on the hydration-shell properties of antifreeze and non-antifreeze

Akash Deep Biswas, Scuola Normale Superiore, Italy

14:55-15:25 **23:55-00:25** (Speaker Local Time)

Title: Beyond structural diversity of organic molecules: electron configuration fingerprint for inorganic bulk materials and engineered nanomaterials

Hyun Kil Shin, Korea Institute of Toxicology, South Korea

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20:55-21:25 **08:55-09:25** (Speaker Local Time)

Title: A potential target for diabetic cardiomyopathy

Sanjay K Banerjee, NIPER, India

15:55-16:05 - REFRESHMENTS BREAK

16:05-16:35 **13:05-13:35** (Speaker Local Time)

Title: Evaluation of the potential teratogenic and toxic effect of the herbicide 2,4-D (DMA® 806) in bullfrog embryos and tadpoles (Lithobates catesbeianus)

Cristina Viriato, Unesp, Brazil

16:35-17:05 **16:35-17:05** (Speaker Local Time)

Title: Pluripotent stem cells as models of neurodegenerative diseases to support drug discovery programmes

Mark Treherne, Talisman Therapeutics Ltd, UK

17:05-17:30 - B2B MEETINGS AND NETWORKING

DAY 2 | 25 MARCH | Thursday

11:00-17:00 (GMT)

11:00-11:10 Introduction

KEYNOTE FORUM

11:00-11:35 **07:00-07:35** (Speaker Local Time)

Title: Improving on Cannabinoids in Nature in Terms of Safety, Specificity, Bioavailability, and Efficacy

William Kinney, Neuropathix, Inc., USA

11:35-12:10 **04:35-05:10** (Speaker Local Time)

Title: Genomic medicine as a powerful discovery engine for gene and CRISPR therapies

Oscar Segurado, ASC Therapeutics, USA

12:10-12:45 **08:10-08:45** (Speaker Local Time)

Title: The Dark Cancer Kinome: Targeting Understudied Kinases for the Treatment of Cancer

Stephan Schurer, University of Miami (UM), USA

SCIENTIFIC SESSION

12:45-13:15 **08:45-09:15** (Speaker Local Time)

Title: Caribbean Small Ruminant Importation Requirements in an Era Of Widespread Anthelmintic Resistance

Brandy Darby, St. Matthew's University, School of Veterinary Medicine, USA

SCIENTIFC PROGRAM

13:15-13:30 - REFRESHMENTS BREAK

13:30-14:00 **08:30-09:00** (Speaker Local Time)

Title: Toxicity study of oral docetaxel nanoformulation

Xiaowei Dong, University of North Texas Health Science Center, USA

14:00-14:30 **10:00-10:30** (Speaker Local Time)

Title: TBA

Daniel Gruffat, Nanome Inc., USA

14:30-15:00 **22:30-23:00** (Speaker Local Time)

Title: Exploring various approaches to improve and accelerate AD drug development: A technical insight

Yatinesh Kumari, Monash University, Malaysia

15:00-15:30 **21:00-21:30** (Speaker Local Time)

Title: Synthesis, computational and molecular docking study of some 2, 3-dihydro-benzofuran and its derivatives

Ashutosh Nath, Bangladesh University of Engineering and Technology (BUET), Bangladesh

15:30-16:00 **16:30-17:00** (Speaker Local Time)

Title: Mechanistic insights into the inhibitory activity of FDA approved Ivermectin against SARS-CoV-2: Old Drug with New Implications

Sehrish Naz, University of Karachi, Pakistan

16:00-15:30 **12:00-12:30** (Speaker Local Time)

Title: Fully Functionalised Fragments: A new paradigm in phenotypic screening for rapid target identification

Aarti Kawatkar, AstraZeneca, USA

E-POSTER

16:30-16:45 **22:00-22:15** (Speaker Local Time)

Title: Drug Discovery, Development and Lead Optimization

A Systemetic Review on Antidepressive Effect of Simvastatin in Rodents

Shoebul Haque, King George Medical University, India

16:45-17:00 - Networking and B2B Meetings

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KEYNOTE SPEAKERS
Day 1

DRUG DISCOVERY

Martin-Immanuel Bittner
Arctoris Ltd, United Kingdom

Biography

Martin-Immanuel Bittner is the CEO of Arctoris, the world's first fully automated drug discovery platform that I co-founded in Oxford in 2016. My background is in medicine and cancer research, having completed my MD at the University of Freiburg, and my DPhil as a Rhodes Scholar at the University of Oxford.

Implementing fully automated kinase inhibitor characterization for AI-driven drug discovery using a robotic system

About 50 kinase inhibitors have been approved by the FDA for different indications so far. On the way from target validation to approval, the biochemical characterisation of a novel kinase inhibitor is a tedious, yet absolutely critical task. High resolution, kinetic molecular profiling can enable better data-driven decision making early on in the drug discovery process, not only saving time and resources, but also leading to superior molecular design – especially when combining human with machine intelligence.

Arctoris developed a robotics-enabled process for fully automated kinase inhibitor characterisation on its Ulysses technology platform, providing an unparalleled depth of data capture, going beyond the current state-of-the-art of biochemical assay setup. We validated our technology platform establishing assays against four members of the Janus Kinase family (JAK1, JAK2, JAK3, TYK2), profiling a set of JAK inhibitors. Of note, several JAK inhibitors with prior FDA approval for other indications entered clinical trials for COVID-19 treatment, making this target class particularly relevant for an in-depth study.

Reagent validation, assay development, calibration, and optimisation were expedited through systematic multifactorial experimental design, high density assay plate formats and versatile automated liquid handling. Fully automated protocols were optimised, validated, versioned, and explicitly encoded.

Robust potency measurements of all inhibitors were established against each of the JAK targets, enabling the identification of molecules within the JAK inhibitor set that exhibit a range of kinetic properties.

Our in-depth biochemical characterisation and profiling process generates more than 100x more data per assay compared to conventional manual laboratory operations, leading to significant improvements in data generation and data capture. These improvements are of particular importance for AI-driven drug discovery programmes, where access to structured, reproducible, and well annotated, data is of critical importance for model training and validation.

Amiram Goldblum
The Hebrew University of Jerusalem, Israel

Biography

Amiram Goldblum is Studied Chemistry and Physics followed by a PhD in Organic Chemistry at the Hebrew University of Jerusalem (With Prof. R. Mechoulam). Subsequently a postdoctoral fellow at the Institute for Physico-Chemical Biology in Paris, studying Quantum Biochemistry (with Profs. Alberte and Bernard Pullman), at Pomona College, Claremont, CAL studying Quantitative Structure-Activity Relations (with Prof. Corwin Hansch) and at Stanford University, Palo Alto, CAL, studying computational reaction mechanisms of enzymes (with Dr. Gilda Loew). Goldblum is currently the head of the Molecular Modeling and Drug Design unit at the Institute for Drug Research of the Hebrew University of Jerusalem, and a member of the Fraunhofer Project center for Drug Design and Delivery. Goldblum invented a prize winning algorithm (American Chemical Society, 2000, Kaye Innovation prize 2017) which his group employs for all drug discovery projects.

In silico discovery of multitargeted drug candidates

Our prize-winning algorithm called "Iterative Stochastic Elimination" (ISE) has already proven immense success in discovering novel drug candidates. We construct in silico models that distinguish between known bioactive molecules on a specific target ("True Positives", TP(diluted a hundred-fold and more by inactive molecules that are picked randomly from chemical databases ("True Negatives", TN) in order to mimic "real life". ISE produces models which identify the differences in molecular properties between TP and TN and constructs "filters" which enable superfast screenings of many millions of molecules. All molecules are scored by their ability to pass those filters, and the top scored ones are picked for subsequent processing and have been shown to be effective in nanomolar or low micromolar concentrations (PMID: 30705343, 31433190, 28215669, 27537371). Nearly all our discovered candidates have novel scaffolds, are highly diverse, and have not been mentioned in literature or patents. When applied to several relevant protein targets for a specific disease condition, screening these millions of molecules allows to compare scores of molecules for the different targets and to identify multitargeted single molecules rather than picking a single drug for each target. Best molecules may be docked to the target protein structures, if available. We initially screen commercially available molecules, so that the top scoring molecules would be easily purchased and outsourced for measuring solubility, caco-2 permeability and microsomal stability.

Tom L Blundell
Cambridge University, UK

Biography

Tom Blundell is a Director of Research in the Department of Biochemistry, University of Cambridge, where he was between 1996 and 2009 Sir William Dunn Professor and Chair of School of Biological Sciences. He has previously held positions in the Universities of London, Sussex and Oxford.

Tom began his research career in Oxford, working with Nobel Laureate Dorothy Hodgkin on the first structure of a protein hormone, insulin. He has made major breakthroughs on the structural and computational biology and biophysics of hormones and growth factors (insulin, glucagon, NGF, HGF, FGF), receptor activation, signal transduction and DNA repair, important in cancer, tuberculosis and familial diseases. He has produced many widely used software packages for protein modelling and design, including Modeller (~12,500 citations) and Fugue (~1400 citations), and for predicting effects of mutations on protein stability and interactions (SDM & mCSM), to understand cancer & drug resistance. He has published ~650 research papers, including ~40 in Nature and Science, and has an H-factor of 119.

Tom has developed new approaches to structure-guided and fragment-based drug discovery. In 1999 he co-founded Astex Therapeutics, an oncology company that has several drugs in clinical trials and two on the market and that was sold in 2013 as Astex Pharma to Otsuka for $886 million. In parallel in the University of Cambridge he has developed structure-guided fragment-based approaches to drug discovery for difficult targets involving multiprotein systems and protein-protein interactions. He has also been targeting Mycobacterium tuberculosis proteins as part of the Gates HIT-TB consortia, M leprae for American Leprosy Mission and M. abscessus for Cystic Fibrosis Trust, including structural and biochemical studies of resistance mutations to first-line drugs.

Tom was a member of PM Margaret Thatcher's Advisory Council on Science & Technology (1988-1990), Founding CEO of Biotechnology and Biological Sciences Research Council, 1991-1996 (Chair 2009-2015), Chairman, Royal Commission on Environment (1998-2005), Deputy Chair of Institute of Cancer Research 2008-2015 and President of UK Science Council, 2011- 2016.

Structural biology, bioinformatics and drug discovery: from cancer to bacterial infections and Covid-19

Knowledge derived from genome sequences of humans and pathogens has the potential to accelerate diagnosis, prognosis and cure of disease. We are moving quickly into an era of precision medicine, not only in familial diseases where a mutation in a human gene is important, but also for understanding somatic mutations in cancer. Equally important, the genome sequences of pathogens, for example in tuberculosis, leprosy or SARS CoV-2, can give clues about the choice of protein targets including those of existing drugs, repurposing of others, and the design of new ones to combat the increasing occurrence of drug resistance.

Structure-guided approaches, both in academia and large pharma, have informed drug discovery for five decades. More recently fragment-based screening structure guided techniques have proved effective in lead discovery in Astex, a company I cofounded with Harren Jhoti and Chris Abell. Applications have been not only for classical enzyme targets such as protein kinases, but also for less "druggable" targets such as protein-protein interfaces. Initial screening involves small fragments with very low, often millimolar affinities, and biophysical methods including X-ray crystallography are used to explore chemical space of potential ligands. The approach involves a fast initial screening of a library of around 1000 compounds, followed by a validation step involving more rigorous

use of related methods to define three-dimensional structure, kinetics and thermodynamics of fragment binding. The use of high throughput approaches does not end there, as it becomes a rapid technique to guide the elaboration of the fragments into larger molecular weight lead compounds. I will discuss progress in using these approaches for targets in cancer and in mycobacteria tuberculosis, abscessus and leprae and SARS CoV-2 infections. I will discuss the impact of the Resolution Revolution in cryo-EM.

I will also review our computational approaches using both statistical potentials (SDM) and machine learning methods (mCSM) for understanding mechanisms of drug resistance. We have demonstrated that resistance does not only arise from direct interference of the resistance mutation to drug binding but can also result allosteric mechanisms, often modifying target interactions with other proteins. This has led to new ideas about repurposing and redesigning drugs.

Yavuz Selim Silay

Istanbul Consulting Group & Co-Founder of MAIN (MaQasid Angel Investors Network), Turkey

Biography

Dr. Yavuz Selim Silay is the Chairman of Istanbul Consulting Group & Co-Founder of MAIN (MaQasid Angel Investors Network) and international TV Show Host known as 5TN (5 Technology News) , WHN (World Health News) and ITB (Idea to Business) broadcasting to more than 22 countries with 500 million viewers.

Dr. Silay is currently working on establishing several VC and PE funds in healthcare and biotechnology. ICG (Istanbul Consulting Group) which was founded in 2013 and provided guidance to the Turkish ministry of health as part of a World Bank project. Yavuz is currently the Co-Founder of BioCube Istanbul Bioentrepreneurship & Innovation Center and Corporate Communication Director of several healthcare companies. He previously managed the largest distributor of Siemens Healthcare in Turkey managing 250 employees and director of Avcilar Hospital R&D Center, Chief Medical Officer of Lifematrix GmbH. Previously he worked as the Market Access & Health Policy Director for AIFD in Turkey.

Yavuz previously worked as the Vice President of IPSEN pharmaceutical and Director of Teva pharmaceutical in USA managing large clinical trials as well as Investigator Initiated Trials and developing relationships with Key Opinion Leaders. Previously, Yavuz was the Associate Director at KV Pharmaceuticals and Director in Clinical Development department at Forest Laboratories

Yavuz earned his MD from the Faculty of Medicine, University of Ankara in Ankara, Turkey. He completed a clinical internship at Baylor College of Medicine in Houston, followed by continued research training at The University of Texas MD Anderson Cancer Center in Houston. He recently completed his Executive MBA at the Olin Business School at Washington University in St. Louis. Yavuz currently resides with his wife Dr. Kamile Silay and their two daughters and one son in Ankara, Turkey.

The current trends in Bioentrepreneurship and Biotechnology Innovation Investments in USA, Europe, Turkey & Emerging Markets

International TV Host Show in Healthcare, Technology and Business. Interaction with FDA. Development of generic and branded regulatory strategic plans for new product development, life cycle management of marketed products. Evaluation of potential products & in-licensing opportunities. Participate in all aspects of clinical development & study management, providing scientific, medical, and logistical direction and support to studies. Market Access to USA, Africa, Turkey & Europe. Clinical development in Medical Device & Pharmaceutical including Oncology/ CNS/ Pain . Managing Phase 2-4 clinical trials.

Shahar Keinan
Polaris Quantum Biotech, USA

Biography

Dr Shahar Keinan is the cofounder and CEO of Polaris Quantum Biotech. She has over 20 years of extensive experience in the field of computational and theoretical chemistry and published over 50 peer-reviewed manuscripts in the fields of in-silico drug design and discovery, as well as molecular materials design and computational methods development. Shahar has received a Ph.D. in theoretical chemistry from The Hebrew University of Jerusalem, after which she moved to Northwestern University and Duke University for a post-doc positions. Previously she was CSO of Cloud Pharmaceuticals and has been instrumental in the development of the Quantum Molecular Design process since its inception at Duke University, and has pioneered the use of computational chemistry algorithms to optimize electro-optical materials and small molecule drugs.

A Quantum Revolution in Drug Discovery

Polaris Quantum Biotech (POLARISqb), the first drug discovery platform built on a quantum computer, is transforming health for people everywhere by revolutionizing drug design with the acceleration of lead time for preclinical drug candidates. Drug development begins with drug discovery – a three year and $4 million dollar process. The POLARISqb drug design platform enables real-time adaptability by compressing the lead time for preclinical drug candidates from years to months. We are using quantum computers to solve a quadratic unconstrained binary optimization (QUBO) problem by identifying lead compounds from virtual libraries of billions of molecules. Here we will discuss previous work on rapid design of lead-like compounds for the Dengue viral RNA-dependent-RNA polymerase (RdRp) and how we can apply the POLARISqb platform to other targets.

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SCIENTIFIC TRACKS & ABSTRACTS

Day 1

DRUG DISCOVERY

Akash Deep Biswas
Scuola Normale Superiore, Italy

Biography

Akash Deep Biswas is a Ph.D. in Methods and Models for Molecular Sciences from Scuola Normale Superiore di Pisa, Italy. By using Molecular Dynamics simulation and implementing mathematical models, he focuses to characterise the hydration shell around the antifreeze proteins, notes the similarity and dissimilarity with the non-antifreeze proteins. Before joining his Ph.D. he did his masters in Biosciences and Bioinformatics from Tezpur University, later worked as a Junior Research Fellow in the Department of Biosciences and Bioengineering at IIT Guwahati, and as a Project Associate in the Department of Mechanical Engineering at IIT Kanpur.

A computational study on the hydration-shell properties of antifreeze and non-antifreeze

Here, we present a computational approach based on molecular dynamics (MD) simulation to study the dependence of the hydration-shell density on the size of the several protein molecules including 8 antifreeze proteins (AFPs) and 10 non-antifreeze proteins (Non-AFPs). AFPs have the ability to inhibit ice growth by binding to ice nuclei. Their ice-binding mechanism is still unclear, yet the hydration layer is thought to play a fundamental role. Thus, the hydration-shell density of eighteen different proteins were calculated. The results obtained shows that an increase in the hydration-shell density, relative to that of the bulk (range of 4–14%) for all studied proteins and that this increment strongly correlates with the protein size, while it does not depend on the type of the protein. In particular, a decrease in the density increment is observed for decreasing protein size. Through a simple model we show that the hydration-shell density increase is located in grooves and pockets of the protein surface. Further investigating the local properties of the hydration shell around the Ice-Binding Surface (IBS) of two AFPs, we found that the hydration-shell density of the IBS is always higher than the bulk density, indicates no ice-like layer. However, the local water-density around the IBS is lower than that around the non-IBS, this difference correlates to the higher hydrophobic character of the IBS w.r.t. the non-IBS. We hypothesize that the lower solvent density at the IBS can pave the way to the protein binding to ice-nuclei, while the higher solvent density at the non-IBS might provide protection against ice growth. We tested our hypothesis by studying the dependence of the antifreeze activity of 8 AFPs on various structural and chemical properties of the IBS and non-IBS and found that the activity strongly correlates with the difference in the local hydration-shell properties of IBS and non-IBS.

Hyun Kil Shin
Korea Institute of Toxicology, South Korea

Biography

Dr. Hyun Kil Shin is an expert in cheminformatics particularly in development of machine learning (ML) or deep learning (DL) model based on molecular structure datasets. His strong support on safe-by-design concept led him to participate in diverse research projects such as drug-induced liver toxicity prediction model development, biocidal active substance neurotoxicity prediction model development, and development of AI model designing safe compounds. He is currently a researcher in Korea Institute of Toxicology (KIT). As image data is one of most abundant data set, he also works with image data in research projects such as smartphone deployable animal skin disease diagnosis model development and atopy dermatitis region detection model development.

Beyond structural diversity of organic molecules: electron configuration fingerprint for inorganic bulk materials and engineered nanomaterials

Artificial intelligence (AI) models have been broadly applied in drug discovery; however, applicability domain (AD) of AI models is mainly focused on organic molecules so far since 1) majority of available database is composed of organic molecules, and 2) cheminformatics tools mainly handle organic molecules alone. Particularly, lack of appropriate cheminformatics tools for inorganic molecules becomes a significant technical obstacle that should be overcome in order to expand AD of AI models over wider range of chemical space beyond structural diversity of organic molecules. In order to provide more cheminformatics tools for inorganic compounds, electron configuration fingerprint (EC FP) was developed as a first fingerprint designed for inorganic compounds. Furthermore, size-dependent EC FP (SDEC FP) is designed by considering particle size in EC FP calculation to develop fingerprint for engineered nanomaterials (ENMs) whose structural diversity is much complicated than bulk inorganic materials due to compositional complexity in core, doping, and coating part of ENMs in different sizes. By applying EC FP, artificial neural network (ANN) models for prediction of physicochemical properties of inorganic compounds were developed based on composition of inorganic compounds alone. The models were developed with dataset containing almost all atoms in the periodic table to make reliable prediction on inorganic compounds with diverse atomic compositions. ANN models with EC FP outperformed other possible descriptors calculated from composition of inorganic compounds. SDEC FP was applied to develop prediction models for cytotoxicity and zeta potential of ENMs in diverse composition and shapes. Given that previous studies developed models applicable for one specific type of ENMs such as metal oxide, metal, coated, or carbon-based ENMs, the models developed with SDEC FP achieved breakthrough by developing general models applicable to any composition and shape of ENMs.

Sanjay K Banerjee
National Institute of Pharmaceutical Education and Research, India

Biography

Sanjay Kumar Banerjee is an Associate Professor and In-Charge at National Institute of Pharmaceutical Education and Research (NIPER), Guwahati, Assam, India. He completed, his PhD in Pharmacology from All India Institute of Medical Sciences, India. His research goal is to identifying and validating novel targets and therapeutic intervention for cardiovascular and metabolic disorders. His laboratory is mostly interested to understand molecular mechanisms of insulin resistance and cardiac complication in diabetes, and identify nutritional agents/natural products to reduce the disease progression. Overall goal is to bridge the gap between observations in the basic research laboratory and the clinical bedside. Sanjay K Banerjee studies will be an integral part in "translating" new discoveries into therapeutic initiatives.

A potential target for diabetic cardiomyopathy

Several targets are being explored to reduce cardiac disorder in diabetes. Sirtuins, a group of deacetylases, are potential targets that can regulate cellular metabolism, oxidative stress, and mitochondrial health. Data showed that sirtuins, specially Sirt1 and Sirt3 activation can prevent or reverse the progression of several chronic metabolic diseases through the regulation of multiple histone and non-histone proteins. In the present study, we aimed to evaluate the effect of Sirt1, Sirt3 and combined activation in high fructose diet-induced insulin resistance rat heart and assessed the cardiac function focusing on mitochondrial health and function. We administered the Sirt1 activator; SRT1720 (5mg/kg, i.p.), Sirt3 activator; Oroxylin-A (10 mg/kg i.p.) and the combination; SRT1720+Oroxylin-A (5mg/kg and 10 mg/kg i.p.) daily from 12th week to 2oth weeks of study. We observed significant perturbations of most of the cardiac structural and functional parameters in high fructose diet-fed animals. Administration of SRT1720 and Oroxylin-A improved perturbed cardiac structural and functional parameters by decreasing insulin resistance, oxidative stress, and improving mitochondrial function by enhancing mitochondrial biogenesis, OXPHOS expression and activity in high fructose diet-induced insulin-resistant rats. However, we could not observe the synergistic effect of SRT1720 and Oroxylin-A combination. Similar to in-vivo study, perturbed mitochondrial function and oxidative stress observed in insulin resistant H9c2 cells were improved after activation of Sirt1 and Sirt3. We observed that Sirt1 activation enhances Sirt3 expression and mitochondrial biogenesis, and the opposite effects were observed after Sirt1 inhibition in cardiomyoblast cells. Taken together our results conclude that activation of Sirt1 alone could be a potential therapeutic target for diabetes-associated cardiac complications.

Cristina Viriato
São Paulo State University (UNESP), Brazil

Biography

Cristina Viriato endeavors to apply her experience in the field of ecotoxicology, evaluating pesticides exposed to aquatic organisms. The aim of her studies is to evaluate the herbicide 2,4-D and its commercial formula, which is a widely used herbicide and one of the most used pesticide in Brazil, using bullfrog (Lithobates catesbeianus) and zebrafish (Danio rerio) as model aquatic organisms. Currently, she is doing a PhD in São Paulo State University (UNESP), where she collaborates with TOXICAM (Nucleus of Environmental Impact Assessment on Human Health) group, which performs studies regarding to toxicological tests using different types of pesticides and other substances. Her current work involves embryos and adults of zebrafish exposed to 2,4-D (DMA® 806) and its components separately.

Evaluation of the potential teratogenic and toxic effect of the herbicide 2,4-D (DMA® 806) in bullfrog embryos and tadpoles (Lithobates catesbeianus)

Pesticides are one of the causes implicated in the decline of amphibians, which are frequently used as a biological indicator of environmental health status due to their life cycle in both aquatic and terrestrial habitats. The current agricultural production systems are contaminating the southern waters, which is one of the most important surface waters of South America. In Brazil, the herbicide 2,4-D is indiscriminately used throughout the entire country and studies demonstrate a high ecological risk. The study of the herbicide 2,4-D in its commercial formula 2,4-D (DMA® 806) allows for a better knowledge of the potential teratogenic and toxic effects of this pesticide on bullfrog (Lithobates catesbeianus) embryos and tadpoles. The result of the present study contributed to more data analyses regarding to healthiness, hematology, and histopathology of tadpoles exposed for 49 days and also values of LC50-144h (Median Lethal Concentration), EC50-144h (Median Effective Concentration), MCIG (Minimum Concentration to Inhibit Growth) and TI (Teratogenic Index) for embryos exposed to this pesticide using FETAX (Frog Embryo Teratogenesis Assay Xenopus) assay. This study showed that the herbicide 2,4-D (DMA) is not acutely toxic to embryos and tadpoles of L. catesbeianus. Nevertheless, the chronic toxicity test (49 days) demonstrated physiological stress and dehydration, characterizing this pesticide as a respiratory allergen for L. catesbeianus tadpoles. More studies on 2,4-D are needed, mainly in its commercial formulas. Currently, working on the same formula and also its components separately using zebrafish (Danio rerio) as a model organism.

Mark Treherne
Talisman Therapeutics Ltd, UK

Biography

Mark Treherne is a Director and the Chairman of Talisman Therapeutics. He is responsible for the business strategy of Talisman.Mark has over 25 years' experience in the discovery of novel treatments for diseases of the central and peripheral nervous systems, including Parkinson's and Alzheimer's diseases. Mark formerly worked with Pfizer where he was responsible for research into neurodegenerative diseases, including using stem-cell derived lines for screening compounds. In 1997, Mark set up Cambridge Drug Discovery as Chief Executive, which he sold to BioFocus in 2001. Mark has worked with many early-stage biotechnology companies, including CDD, Xention, Ampika, Population Genetics Technologies, Domain Therapeutics, Cyclofluidic and NeuroSolutions.Mark was formerly Chairman of ERBI for 3 years, which represents the biotechnology companies in the East of England (now One Nucleus). He was also Chief Executive of the Life Sciences Organisation of UK Trade & Investment and helped define the national investment strategy for dementia research in the UK. Mark is an author of over 70 articles published in the scientific and trade press.Mark obtained his PhD in receptor neuropharmacology from Cambridge University.

Cell & molecular biology of neurodegeneration

Alzheimer's disease is the most common neurological disease, affecting half of the World's population over 85. The World Alzheimer Report estimated that the $604bn (£388bn) costs associated with dementia in 2010 amounted to more than one percent of the world's gross domestic product. About 70% of these costs occur in Western Europe and North America. There are no disease-modifying drugs currently available to treat the initiation or progression of AD, with currently approved products only providing temporary symptomatic relief. There is an immediate unmet need for the development of new treatments that target the underlying causes of Alzheimer's disease and allow early intervention before irreversible pathological changes occur. Meeting this need is a focus of Talisman's work.

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KEYNOTE SPEAKERS
Day 2

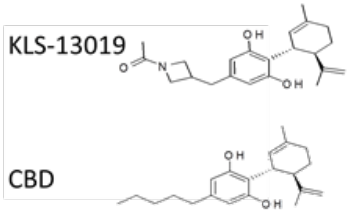
DRUG DISCOVERY

William A Kinney
Neuropathix, Inc., USA

Biography

Dr. Kinney began his industrial career as a medicinal chemist at Wyeth, where he invented the unique NMDA antagonist perzinfotel that progressed to Phase II clinical trials for pain. At Magainin Pharmaceuticals, he was an inventor of squalamine, a shark-derived natural product that advanced to clinical trials. In 2000, he joined Johnson & Johnson, where he pursued drug targets for cardiovascular indications. He is Founder of IteraMed Consulting, a company focused on medicinal chemistry, drug discovery, and small business development. In this capacity he invented KLS-13019 for Kannalife Sciences, a company focused on cannabinoid therapeutics. Most recently, Dr. Kinney co-founded Enterin Inc., where he is leading the manufacturing of squalamine phosphate for Parkinson's Disease.

Improving on Cannabinoids in Nature in Terms of Safety, Specificity, Bioavailability, and Efficacy



Neuropathic pain remains a challenging neurologic disorder that adversely affects quality of life and presents a large unmet medical need. Chemotherapy-induced peripheral neuropathy (CIPN) is a chronic, severely debilitating consequence of cancer therapy for which there are no effective management strategies. Upwards of 80-97% of CIPN patients reported using prescription opioids for this pain management. Mitochondrial dysfunction, oxidative stress, and inflammation have all been implicated in CIPN etiology. In a mouse model of paclitaxel-induced pain sensitivity, we have previously reported that cannabidiol (CBD) is effective in preventing the onset of this treatment consequence. Now a new CBD analogue (KLS-13019) has been discovered in our laboratory that has improved drug-like properties in comparison to CBD, while retaining neuroprotective properties. Both CBD and KLS-13019 were equi-effective and equi-potent following oral administration. However, in the reversal studies, CBD did not attenuate mechanical sensitivity when administered after CIPN was induced by paclitaxel treatment. KLS-13019 significantly and dose-dependently attenuated tactile sensitivity in the reversal paradigm and was more potent and effective than treatment with morphine. Importantly, KLS-13019 also attenuated the reinforcing properties of morphine in a mouse model of morphine self-administration. In vitro, we have shown that KLS-13019 and CBD protect against paclitaxel-induced oxidative stress in dorsal root ganglia cultures, and that a mechanism underlying this neuroprotection is regulation of intracellular calcium via the mitochondrial Na+/Ca++ exchanger-1 (mNCX-1). Our central hypothesis is that administration of CBD or KLS-13019 preserves Ca2+ homeostasis by promoting activity of the mNCX-1. Furthermore, our new data demonstrates that an additional target is induced following paclitaxel treatment and contributes to sensory neuron toxicity and inflammation that can be reversed by KLS-13019, but not CBD. We predict bi-modal pharmacological effects of KLS-13019 that can both increase viability of sensory neurons exposed to paclitaxel acutely and decrease long-term neuroinflammation.

Oscar Segurado
ASC Therapeutics, USA

Biography

Oscar Segurado is the Chief Medical Officer for ASC Therapeutics, a fast-growing biotechnology company focused on developing curative gene-based therapies for inherited blood disorders, initially focusing on hemophilia A and B and Beta-Thalassemia. As a leading biopharma discovery company with over 12 years of experience in gene editing and stem cell technologies, we have created an end-to-end platform for gene therapy and gene editing.

Former CMO for Symvivo, Myriad Genetics and CellMax Life, Vice President for Becton Dickinson and Global Medical Head for Abbott/AbbVie (Humira). Executive veteran with extensive global leadership experience in translational science, clinical development and global medical affairs.

Author and co-author of over 100 peer-reviewed publications, including Nature and Lancet, books and medical articles and member of several scientific and medical societies. Holding a tenured Professorship of Immunology at the University of Leon, Spain. Received PhD from the University of Wuerzburg, Germany and MD from the University of Salamanca, Spain.

Genomic medicine as a powerful discovery engine for gene and CRISPR therapies

Over the past 20 years, DNA sequencing throughput has progressed from 1K base pairs per day to more than 1K bases per second today. Since the first proof-of-concept human application in the early '90s, the field of gene therapy has entered an exciting stage of drug discovery, clinical translation and medical transformation.

In 2020 the first patient with sickle-cell disease was treated with ex-vivo CRISPR. This is the start of applying Nobel prize technology allowing to use enzymes able to cut and paste genes in the nucleus, the core of the generic machinery. We have discovered genes responsible for over 5K rare genetic diseases and over 100K genes associated with common diseases from diabetes to heart disease.

At this session we will discuss the principles, challenges, and future directions of discovery and development of human gene therapies, including CRISPR and base editing technologies. Genomic medicines possess the intrinsic benefit of being precise tools for manipulating human biology and are reserved for indications where there is a clear pathophysiology. While recent breakthrough therapeutics offer new hope for patients, they have also made biomedical innovation more complex, riskier, and more expensive. In the face of multiple growing uncertainties, the need for greater accuracy in predicting clinical trial outcomes has also grown. More accurate diagnostics mean fewer drug failures and faster approval times to bring new and better therapies to patients sooner.

As a case study we will discuss the experience of ASC Therapeutics for gene therapy and CRISPR therapy in hemophilia A, an optimal target due to the monogenic nature of inheritance and the observation that even minimal increases in clotting factor activity can significantly improve quality of life.

Stephan Schürer
University of Miami (UM), USA

Biography

Dr Stephan Schürer is a Professor in the Department of Pharmacology, Director of Drug Discovery at the Center for Computational Science, and a Member of the Sylvester Comprehensive Cancer Center at the University of Miami. With a background in synthetic chemistry and informatics, Dr Schürer applies data science to chemistry and biology problems in drug discovery, such as target prioritization, prediction of drug sensitivity, -mechanism of action, -specificity, -promiscuity and -polypharmacology, drug combinations, and lead discovery and -optimization. He is Principal Investigator in several national research consortium, including the Library of Integrated Network-based Cellular Signatures (LINCS), Big Data to Knowledge (BD2K), and Illuminating the Druggable Genome (IDG).

The Dark Cancer Kinome: Targeting Understudied Kinases for the Treatment of Cancer

The approval of the first kinase inhibitor, Gleevec, in 2001, ushered in a paradigm shift for oncological treatment—the use genomic data for targeted, efficacious therapies. Since then, about 50 additional small molecule kinase inhibitors have been approved, solidifying the case for kinases as a highly druggable and attractive target class. Despite the established role deregulated kinase activity plays in cancer, only 8% of the Kinome has been effectively "drugged". Moreover, a quarter of the more than 600 human kinases are vastly understudied. We have developed a comprehensive scoring system, the Clinical Kinase Index (CKI), which utilizes differential gene expression, clinical and pathological parameters, overall survival and mutational hotspot analyses to rank and prioritize clinically-relevant kinase targets across 17 solid tumor cancers from The Cancer Genome Atlas. These findings suggest that dark kinases have potential clinical value as biomarkers or as new drug targets, which warrant further study.

To identify small molecules that directly target and inhibit dark kinases, for the development of chemical probes or drug leads, we have developed a pipeline that combines AI (artificial intelligence) models trained on activity data from across the Kinome with structure-based simulations.

We have applied this computational workflow to identify novel small molecule for dark kinases with no known small molecule binders and no protein structure. For a novel pseudokinase with no data, we have now developed advanced lead compounds.

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SCHOLARS WEBINAR ON: THE ROLE OF NEW TECHNOLOGIES

DRUG DISCOVERY, DEVELOPMENT AND LEAD OPTIMIZATION

MARCH 24-25, 2021 | WEBINAR

SCIENTIFIC TRACKS & ABSTRACTS

Day 2

DRUG DISCOVERY

Brandy J Darby
St. Matthew's University, School of Veterinary Medicine, USA

Biography

Brandy Darby graduated as a Doctor of Veterinary Medicine from Louisiana State University in 2007. She worked in mixed animal practice for three years before transitioning to academia in 2010. Dr. Darby taught at St. Matthew's University, School of Veterinary Medicine, in the Cayman Islands for nine years. In 2016, she completed a Master's in Public Health from Michigan State University, with a focus on communicable diseases. In 2019, she joined the Virginia Department of Health as the Veterinary Epidemiologist in the Division of Surveillance and Investigation.

Caribbean Small Ruminant Importation Requirements in an Era of Widespread Anthelmintic Resistance

Resistance of small ruminant gastrointestinal parasites to available classes of anthelmintic drugs is a widespread problem. As such, use of these drugs needs to be applied in a judicious manner in order to protect animal health. A case of drug-resistant gastrointestinal nematodes in goats imported to the Cayman Islands led to the development of a survey to explore the potential for similar occurrences within the region. The survey was distributed to seventeen English-speaking Caribbean countries in March 2017 to assess the importation requirements for small ruminants and showed that universal administration of anthelmintics to small ruminants is a common pre-requisite for importation to the Caribbean region, though very few countries require any proof of drug efficacy. Such requirements are discordant with current recommendations for judicious anthelmintic use in domestic animal species and promote the continued development of anthelmintic resistance. While this survey focused on small ruminants, similar policies are often in place for the importation of a variety of animal species, including cattle, horses, and companion animals. Given that anthelmintic resistance is also recognized in parasite populations that impact these species, it may be time for the international community to revisit live animal importation requirements in the age of anthelmintic resistance. Some recommendations and considerations are put forward to help preserve animal health, animal welfare, and developing animal agricultural industries.

Xiaowei Dong
University of North Texas Health Science Center, USA

Biography

Dr. Xiaowei Dong has completed his PhD in Pharmaceutical Sciences from University of Kentucky and then joined Novartis Pharmaceutical Corporation working as a lead formulator for drug product development for about 4 years. In 2013, she joined UNT Health Science Center as an assistant professor in the Department of Pharmaceutical Sciences at the College of Pharmacy. Her research includes drug delivery and formulation development using nanotechnology and has special focus on novel oral formulation technology.

Toxicity study of oral docetaxel nanoformulation

Although oral delivery is the most favorable and preferred route of drug administration, many chemotherapy drugs (e.g. docetaxel) have been commercially formulated for intravenous injections because of low oral absorption. Metronomic chemotherapy, giving low doses of chemotherapy drugs on a frequent schedule over a long time, may improve outcomes and reduce side effects for cancer patients. Oral drug formulations are essential for metronomic chemotherapy. However, the toxicity of orally administrated anticancer drugs was not widely studies. In this study, the toxicity of an oral docetaxel nanoformulation was evaluated to establish the maximum tolerated dose (MTD) and identify the tissue which was affected. Docetaxel is a poorly water-soluble drug with low permeability. Thus, it is very challenging to develop oral docetaxel formulation with sufficient absorption. Recently, our lab has developed a new docetaxel granule that does not have nanoparticles, but upon contact with water the granule generated docetaxel-entrapped in situ self-assembly nanoparticles. FVB mice were administered with docetaxel granule by oral gavage once per day. A dose range from 10 -400 mg/kg of docetaxel granule was tested. Alanine Transaminase activity was measured to evaluate liver function, and blood urea nitrogen was measured for renal function. Finally, kidney, liver and lung were stained with H&E and imaged by a microscopy. The results demonstrated that the MTD of docetaxel granule was 25 mg/kg for once daily. High dose docetaxel granule reduced renal function but not liver function, which was further confirmed by histology analysis.

Dr Yatinesh Kumari
Monash University, Malaysia

Biography

Dr Yatinesh Kumari is an independent and self-directed young researcher who is interested to explore pharmacological potential of plant-based compounds to find out underlying molecular and neural pathways to understand their mechanism of action, as it is essential for the development of new therapeutic strategies in context to neurodegenerative diseases. To date she has been successfully awarded number of grants and published number of articles in reputed, high impact international journals. She has also won various awards for innovation in research, and continuously contributing to the scientific community as a peer reviewer for number of reputed international journals.

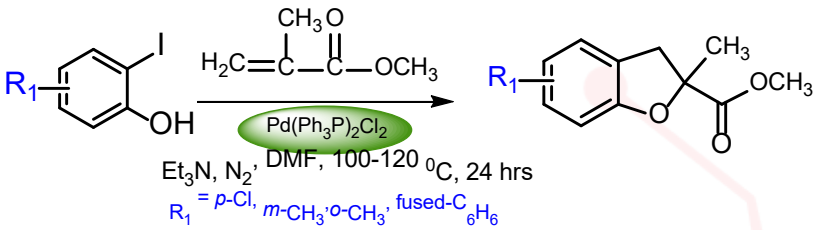
Exploring various approaches to improve and accelerate AD drug development: A technical insight

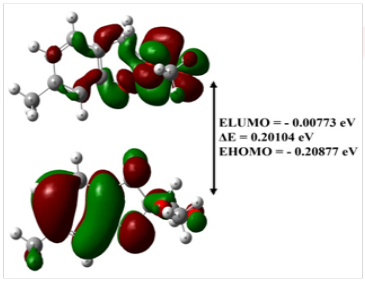
Alzheimer's disease (AD) is a progressive neurodegenerative disease and leading cause of dementia in elderly population. It is one of the largest public health and economic challenges of the 21st century. Commonly, anti-cholinesterase and NMDA antagonist drugs are used to slow down the progression of the disease. Current drugs improve symptoms but do not have profound disease-modifying effects. The biggest challenge in AD drug development is lack of understanding about the mechanisms underlying AD pathogenesis as it is a multifactorial neurodegenerative disorder and involves multiple biological pathways. Over 20 years, Amyloid cascade hypothesis has dominated the field. As a result, large number of studies have focused on removal or inhibition of amyloid beta and senile plaques, but this approach has failed to show improvements in cognition in AD patients. Therefore, it is needed to shift current paradigms of AD drug development from single target approach to multiple disease aspects. Our research focuses on the evaluation of the efficacy of potential therapeutic agent in multiple aspects to ameliorate the condition. This presentation will address emerging tools, technologies and approaches based on scientific utility criteria that are relevant to the field at present and will provide technical insight to combat the coming crisis.

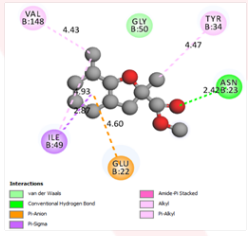
Ashutosh Nath
Bangladesh University of Engineering and Technology (BUET), Bangladesh

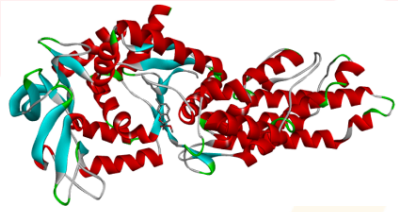
Synthesis, computational and molecular docking study of some 2, 3-dihydrobenzofuran and its derivatives

2, 3-Dihydrobenzofuran-2-carboxylates (DHBCs) derivatives were synthesized by cyclization on one pot reaction and characterized by FT-IR, 1H-NMR, and 13C-NMR spectral studies, besides we have investigated the intermolecular coupling reaction of 2-iodophenols with acrylic esters by the Pd(Ph3P)2Cl2 catalyst. The density functional theory (DFT) calculations have been executed for the DHBCs using B3LYP/6-31++G (d, p) and B3LYP/6-31++G (d, p) for obtaining HOMO and LUMO, descriptors, vibrational properties and charge distribution potential. The HOMO-LUMO gap is 0.23450, 0.20104, 0.20711, 0.16533, 0.29371 and -0.32549 Hartee for 6-11 DHBCs, respectively. The calculated IR and NMR are correlated with experimental value. Molecular docking studies predict the microbial activity of DHBCs against both fungi and bacteria calculating the binding energy, hydrogen bond, and hydrophobic interactions with proteins while binding energy is from -6.0 kcal/mol to -7.5 kcal/mol, and it is illustrated that substitute groups in 3 positions plays an important role for biological studies.









Sehrish Naza
University of Karachi, Pakistan

Biography

Dr. Sehrish Naz has obtained her PhD in Computational Drug Designing under the supervision of Prof. Zaheer Ul-Haq from Dr. Panjwani Center for Molecular Medicine and Drug Research, International Center for Chemical and Biological Sciences, University of Karachi, Pakistan. She had secured Pakistani govt. funding to get an opportunity to work as guest research scholar at University of Copenhagen, Denmark. She is also recipient of Young Scientist Award by International Union of Crystallography (IUCr). She has won a number of poster and oral prizes in various national and international Conferences and workshops. She has published more than 8 research articles in top International Journals of Computational Chemistry. Her area of interest includes computational modeling, designing bio-active compounds using In silico tools, generation and screening of large commercially available compounds, and Molecular Dynamics (MD) simulation of bio-molecules. Her passion and curiosity of seeing and exploring the unseen world have led her to this path and will keep her going on, to help the humanity and contribute to the betterment of industry and academia.

Mechanistic insights into the inhibitory activity of FDA approved Ivermectin against SARS-CoV-2: Old Drug with New Implications

The novel corona virus (Covid-19) has become a great challenge worldwide since 2019, as no drug has been reported yet. Different clinical trials are still under way. Among them is Ivermectin (IVM), an FDA approved drug which was recently reported as a successful candidate to reduce SARS-CoV-2 viral load by inhibiting Importin-α1 (IMP-α1) protein which subsequently affects nuclear transport of viral proteins but its basic binding mode and inhibitory mechanism is unknown. Therefore, we aimed to explore the inhibitory mechanism and binding mode of IVM with IMP-α1 via different computational methods. Initially, comparative docking of IVM was performed against two different binding sites (Nuclear Localisation Signal (NLS) major and minor sites) of IMP-α1 to predict the probable binding mode of IVM. Then, classical MD simulation was performed (IVM/NLS-Major site and IVM/NLS-Minor site), to predict its comparative stability dynamics and probable inhibitory mechanism. The stability dynamics and biophysical analysis of both sites highlighted the stable binding of IVM with NLS-minor site by establishing and maintaining more hydrophobic contacts with crucial residues, required for IMP-α1 inhibition which were not observed in NLS-major site. Altogether, these results recommended the worth of IVM as a possible drug to limit the SARS-CoV-2 viral load and consequently reduces its progression.

Aarti Kawatkar
AstraZeneca, US

Fully Functionalised Fragments: A new paradigm in phenotypic screening for rapid target identification

Phenotypic screening faces the challenge of identifying the molecular target(s) of active compounds, especially in cases where the screening hits display moderate-low potency. Recent reports suggest that embedding photoreactive and biorthogonal reporter groups into bioactive small molecules can facilitate the chemical proteomic analysis of protein targets in cells1. AstraZeneca have recently generated a library of small molecule Fully Functionalised Fragments (FFFs), which are pre designed for compatibility with chemical proteomics, enabling a novel capability for both ligand and target identification. The additional advantage of FFFs is a demonstrated ability to bind to a diverse array of protein targets, most of which had no previously known ligands, suggesting the ligandable human proteome is larger and more untapped than previously thought1.

The following examples show how deployment of the AZ FFF library has highlighted our early successes in using FFFs to find novel targets for a diverse range of phenotypes including pancreatic β-cell redifferentiation, and downregulation of receptors driving resistance in pancreatic cancer.

FFF hits were identified which redifferentiate modified β-cells by re-establishing expression of a key β-cell marker, MAFA. Chemical proteomics identified a set of secretory granule proteins as targets of the active FFF. Subsequently, siRNA knockdown of granin protein SCG3 increased MAFA, validating SCG3 as a potential target to modulate MAFA expression and demonstrating the applicability of this approach as a target ID capability.

Application to a diverse range of phenotypic platforms was demonstrated by the identification of structurally distinct FFF hits driving a decrease in a key receptor driving resistance in pancreatic cancer and in cell lines expressing clinically relevant variants of the receptor. Chemical proteomics for both active FFFs identified unique sets of targets with functional links to the receptor biology, further demonstrating the value of FFF as a new target identification capability.

We believe FFFs will be especially useful in screens of primary or rare cell types, and are an important complement to our current methods to identify new targets.

- Parker et al., Ligand and Target Discovery by Fragment-Based Screening in Human Cells, Cell, 2017, 168, 527–541

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e-Poster

Day 2

DRUG DISCOVERY

Shoebul Haque
King George Medical University, India

Biography

Dr Shoebul Haque is a first-year resident in pharmacology and therapeutics department at King George Medical University, Lucknow. He received a bachelor's degree in Medicine from Smolensk State Medical University Smolensk, Russia in 2012. A Post graduate diploma in Maternal and Child health care from IGNOU university in 2015, Delhi and a Post graduate diploma in infectious diseases from Medvarsity in 2016.

Dr Shoebul has served as an in-charge doctor of mohalla clinic in Delhi Government and as a medical officer in Uttar-pradesh government, India. His current field placement is in pharmacology department of KGMU where he is doing research on different effect of drugs on animals in animal house of department. It works under (CPCSEA) The Committee for the Purpose of Control and Supervision of Experiments on Animals. The aim of his study to evaluate the antidepressant effect of Simvastatin which are mainly used as lipid-lowering agent.

Drug Discovery, Development and Lead Optimization A Systemetic Review on Antidepressive Effect of Simvastatin in Rodents

INTRODUCTION: Depression is one of the most common neuropsychological disorder with severe impacts on mortality and morbidity. It can be a lethal illness due to the elevated risk for suicide. Extensive use of the present antidepressant drugs usually shows no response at therapeutic levels due to neuronal adaptation. Therefore, the development of new antidepressants will be valuable in psychiatric disorders. Simvastatin, a lipid lowering drug has been shown to be effective in reducing depression in rodents. Present study aimed to investigate the potential antidepressant-like activity of simvastatin in rodents.

AIM AND OBJECTIVES: The aim of this systemic review is to assess the antidepressant effect of simvastatin in rodents.

MATERIAL AND METHODS: The study was done to find out antidepressant effect of simvastatin using the available published studies on Google scholar, PubMed. 17 studies were included for analysis.

RESULTS: Results showed that simvastatin could significantly produce an antidepressant-like effect in rodents, by different mechanisms, indicated by reduction in immobility time in both Forced Swim Test and Tail Suspension Test. Simvastatin 20mg/kg dose markedly inhibits NF-κB pathway, and probably mediated through NO-cGMP-KATP signaling system and PPAR-γ receptors.

CONCLUSION: Out of 17, nine studies revealed the antidepressant effect of simvastatin. Rest of the studies having inconclusive result. On the basis of overall analysis possible antidepressant effect of simvastatin can be proposed. Further clinical evaluation is needed to be tried in human subjects, as it will be very helpful for the patients having hyperlipidemia and depression.

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