# GMMCDD2023

## April 17-19, 2023 |Osaka, Japan

*Global Meet on Medicinal Chemistry, Drug Discovery & Drug Delivery*

**Abstract Book**

**PRIME MEETINGS**
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# FOREWORD

Dear attendees of the Global Meet on Medicinal Chemistry, Drug Discovery & Drug Delivery,

It is with great pleasure that we welcome you to Global Meet on Medicinal Chemistry, Drug Discovery & Drug Delivery for this year's event. On April 17, experts from around the world will come together to share their knowledge and insights on the latest developments in Medicinal Chemistry, Drug Discovery & Drug Delivery. We are excited to have you join us for this international gathering, which promises to be a forum for new ideas, meaningful discussions, and collaborations. With a diverse range of topics and presenters, we are confident that this event will be a rich and valuable experience for all attendees.

Sincerely,
Jessica Paul
Prime Meetings
GMMCDD2023

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# Salvia Miltiorrhiza Related Synthesized Derivative Attenuates Obesitinduced Diabetic Disorder Syndrome via ATF3 Pathway

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## Abstract

Pharmacological studies indicate that Salvia miltiorrhiza extract (SME) can improve cardiac and blood vessel function. However, there is limited knowledge regarding the effects (exerted through epigenetic regulation) of SME and newly derived single compounds, with the exception of tanshinone IIA and IB, on obesity-induced metabolic disorders. Here, we demonstrated that SME treatment significantly reduced body weight, fasting plasma glucose, triglyceride levels, insulin resistance, and adipogenesis/lipogenesis gene expression in treated mice compared with controls. In addition, SME also improved urinary albumin in a DBA mouse model of obesity-induced diabetic nephropathy. Transcriptome array analysis revealed that the expression of numerous transcriptional factors, including activating transcription factor 3 (ATF3) and C/EBP homologous protein (CHOP), was significantly higher in the SME group. ST32da db, synthetic ATF3 inducer isolated from Salvia miltiorrhiza, promoted ATF3 expression to downregulate adipokine genes and induce adipocyte browning by suppressing the carbohydrate-responsive element-binding protein–stearoyl-CoA desaturase-1 axis. Furthermore, ST32da, db increased white adipose tissue browning and reduced obesity, insulin/glucose resistance, TG, and

creatinine level in HFD feeding mice via ATF3 dependent pathway. Finally, ST32da also can ameliorate renal function in obesity induced diabetic nephropathy DBA mice model.Our study identified the ATF3 inducer ST32da, db as a promising therapeutic drug for treating diet-induced obesity and related metabolic disorders.

## Keywords
*Salvia miltiorrhiza; ATF3; obesity induced diabetic disorder syndrome*

## Biography
Dr. Lin is Professor and Director of the Department of Physiology, Department of Medicine, Taipei Medical University. He is also a scholar who studies drug applications in kidney disease. He has about 20 years of experience in biotechnology and academic drug discovery (about 6 years). In the past few years, my research has focused on the role of Chinese herbal medicine,Salvia miltiorrhiza extract (SME), in obesity or obesity metabolic syndrome such as obesity induced diabetic nephropathy and developed drugs targeting the inducer of ATF3 [e.g., Commun Biol. 2019 Oct 24;2:389,Cells. 2022 Mar 17;11(6):1022. ]. In addition, in order to translational medicine of kidney or urology-related studying, Dr Lin si also actively involved in a special assay method for urinal microRNA based on acute kidney injury or uterus cancer which were established and applied for patents in the United States and Taiwan [e.g., see Analyst . 2018 Sep 24;143(19):4715-4722].

# Novel Anticancer Compounds Targeting Norepinephrine Transporter and Human Copper Transporter 1 for Theranostic Cancer Imaging and Therapy

**FangyuPeng**
Department of Radiology, 2Advanced Imaging Research Center, and 3Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX, U.S.A

## Abstract

Theranostics is a combination of therapeutics and diagnostics. Theranostics in nuclear medicine, or nuclear theranostics, uses radioactive compounds targeting same biomarkers on cancer cells, such as receptors or transporters for cancer imaging and therapy. Pairing with radiopharmaceuticals for cancer imaging, anticancer compounds targeting imaging-related cell transporters hold potential for theranostic use incancer therapy.Neuroblastoma is the most common extracranial cancer in childhood and often occurs in very young children. Meta-iodobenzylguanidine (MIBG), a small molecule, has been widely applied as an imaging agent in the diagnostic imaging and radionuclide therapy of neuroendocrine tumors, such as neuroblastoma, pheochromocytoma, and carcinoid tumor, based on its high-affinity binding to norepinephrine transporter (NET). Novel Meta-iodobenzylguanidine-Based Copper Thiosemicarbazide1-guanidinomethylbenzyl Anticancer Compounds Targeting NET were synthesized and found to have potent anticancer activity against Neuroblastoma. Moreover, novel steroid-based compounds were synthesized and found to reduce copper uptake and suppress prostate cancer cell proliferation by targeting human copper transporter 1 (hCtr1) highly expressed on prostate cancer cells. These novel anticancer compounds targeting NET in neuroblastoma and hCtr1 in prostate cancer hold potential for theranostic use in cancer therapy, pairing with radiopharmaceuticals targeting NET or hCtr1 for cancer imaging .

## Biography

FangyuPeng, M.D., is an Associate Professor of Radiology at UT Southwestern Medical Center and a member of its Nuclear Medicine Division. He also serves as the Director of Positron Emission Tomography (PET) Translational Imaging, and holds a secondary appointment in the Advanced Imaging Research Center. His clinical interests include general nuclear medicine,

PET imaging, and computed tomography (CT), with a particular interest in oncology and neurology. Dr. Peng earned his medical degree at Jiangxi Medical College in Nanchang, China. He then earned a master's degree in molecular virology at Chinese Academy of Preventive Medicine's Institute of Virology in Beijing. He earned a doctoral degree in microbiology and immunology at the University Of South Florida College Of Medicine in Tampa. He then completed a research fellowship program in hematopathology at Ball Memorial Hospital in Muncie, Indiana, before completing his residency in pathology at Upstate Medical University in Syracuse, New York. Dr. Peng then completed a residency in nuclear medicine at the University of Connecticut Health Center in Farmington, and in anatomic pathology at Hartford Hospital. He completed his formal training with a fellowship program in nuclear medicine and molecular imaging at the National Institutes of Health in Bethesda, Maryland. Before being recruited in 2008 to enhance the Nuclear Medicine Division's translational research, Dr. Peng served as an Assistant Professor of Radiology and Pediatrics at Wayne State University School of Medicine in Detroit. At UT Southwestern, he troubleshoots and improves imaging protocols, and actively participates in educational endeavors, in addition to his regular clinical responsibilities. Dr. Peng focuses his research on inherited and acquired copper metabolism disorders in Wilson's disease, Alzheimer's disease, and traumatic brain injury, and investigates copper metabolism as a theranostic target for molecular imaging and cancer treatment. His research has been published in more than 50 peer-reviewed publications. He also invented and received a patent for intracellular trapping of radionuclides by enzyme-mediated reduction.

# Design and Measurement of Drug Tissue Concentration Asymmetry and Tissue Exposure-Effect (Tissue PK-PD) Evaluation

**Richard Zang, Ph.D**
DMPK and Clinical Pharmacology, IDEAYA Biosciences
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## Abstract
The "free drug hypothesis" assumes that, in the absence of transporters, the steady state free plasma concentrations equal to that at the site of action that elicit pharmacologic effects. While it is important to utilize the free drug hypothesis, exceptions exist that the free plasma exposures, either at Cmax, Ctrough, and Caverage, or at other time points, cannot represent the corresponding free tissue concentrations. This "drug concentration asymmetry" in both total and free form can influence drug disposition and pharmacological effects. In this review, we first discuss options to assess total and free drug concentrations in tissues. Then various drug design strategies to achieve concentration asymmetry are presented. Last, the utilities of tissue concentrations in understanding exposure-effect relationships and translational projections to humans are discussed for several therapeutic areas and modalities. A thorough understanding in plasma and tissue exposures correlation with pharmacologic effects can provide insightful guidance to aid drug discovery.

## Keywords
*free drug hypothesis, drug concentration asymmetry, exposure-effect.*

## Biography
Richard Zang is a Vice President, head of DMPK and Clinical Pharmacology at IDEAYA Biosciences. With over 20 years of industrial experience, he has had impactful contributions to the development of multiple small molecules and mAb from discovery to market. Before IDEAYA Biosciences, he worked at Global Blood Therapeutics, Genentech, Novartis, Pfizer, and Neurocrine Biosciences in different therapeutic areas. He is a recipient of multiple Novartis and Genentech awards for his contribution to oncology and anti-infectious diseases research and development projects. His Research interests include ADME-PK, PK-PD and PBPK .

# Triazole-modified Nucleosides, Nucleotides and Nucleic acids for Pharmacological Applications

**Dagmara Baraniak**
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## Abstract
This subject exploits triazole-modified nucleosides, nucleotides, and nucleic acids in the range of biology and chemistry to medicine. The 1, 2, 3-triazole unit, which is obtained via click chemistry approach, shows valuable and unique properties. For example, it does not occur in nature, constitutes an additional pharmacophore, and can be considered as a rigid mimetic of amide linkage. Herein, it is presented a whole area of useful artificial compounds, from the clickable monomers and dimers to modified oligonucleotides, in the field of nucleic acids sciences. Such modifications of internucleotide linkages are designed to increase the hybridization binding affinity toward native DNA or RNA, to enhance resistance to nucleases, and to improve ability to penetrate cell membranes. The insertion of an artificial backbone is used for understanding effects of chemically modified oligonucleotides, and their potential usefulness in therapeutic applications. I describe the state-of-the-art knowledge on their implications for synthetic genes and other large modified DNA and RNA constructs including non-coding RNAs.

## Keywords
*Triazole-Linkage; Clickable Nucleosides and Nucleotides; Triazole-Modified Oligonucleotides; Synthetic Genes*

## Biography
Dr . Dagmara Baraniak is an assistant professor at the Institute of Bioorganic Chemistry of the Polish Academy of Sciences. She studied chemistry at the Adam Mickiewicz University in Poznań (Poland), where she received her M.Sc. in 2007, working on fluorinating adducts of L-proline derivatives under the guidance of prof. Henryk Koroniak. During her studies, she moved for one academic year to Germany (Organic Chemistry Institute of the University of Münster), where she studied and took an advanced course in organic chemistry and biochemistry under the supervision of prof. Günter Haufe. During the scholarship she also decided to practice in carbohydrate chemistry in the laboratory of prof. Hartmut Redlich. This

experience turned her interest into the chemistry of natural compounds. She received her Ph.D. in 2012 under the guidance of prof. Lech Celewicz, working on the synthesis of new nucleoside and nucleotide conjugates using copper(I) catalyzed reactions (click reactions) at the Faculty of Chemistry AMU. In the same year, she joined the Institute of Bioorganic Chemistry PAS on the adjunct position, working in the group of prof. Jerzy Boryski. Currently she is appointed as a research associate at IBCH PAS, engaged in research on the synthesis, properties, and applications of chemically modified nucleosides and nucleotides. She develops methods to synthesize biologically important nucleosides analogues, as well as creates tools to modify nucleic acids for therapeutic applications. In 2020, she was nominated to the Polish Intelligent Development Award 2020.

# Therapeutic and Diagnostic Potential of Ruthenium Polypyridyl Complexes

**Eimer Tuite**
School of Natural Science, Newcastle University, Newcastle upon Tyne, NE7 7RZ, UK

## Abstract
Emissive ruthenium polypyridyl complexes that strongly to DNA have potential uses as structural and mismatch probes, therapeutics, and imaging agents. Archetypical complexes re those that intercalate DNA through the expended dppz (dipyrido[3,2-a:2',3'-c]phenazine) ligand. Intercalation induces emission switch-on, and complexes in this class have been demonstrated to be excellent STED fluorophores for superresolution intracellular imaging, as well as potential therapeutics that interfere with cellular process both the in absence and presence of light.
Recently, novel mono- and di-nuclear ruthenium(II) complexes (Figure 1) have been revealed as cyctotoxic agents for a variety of cancers. We have shwon that these complexes interact with DNA, and we have explored their photophysics and DNA binding. We have found that different subsitutions on the extended ligand lead to different modes of binding to DNA. The mononuclear complex provides a core framework in which Ru(II) is complexed with three dipyridyl ligands, and the pyridine ring of the extended ligand is functionalised at different sites. Dinuclear complexes can also be formed where a second metal centre is incorporated with cyclometallation, which gives rise to compounds with dual emission.

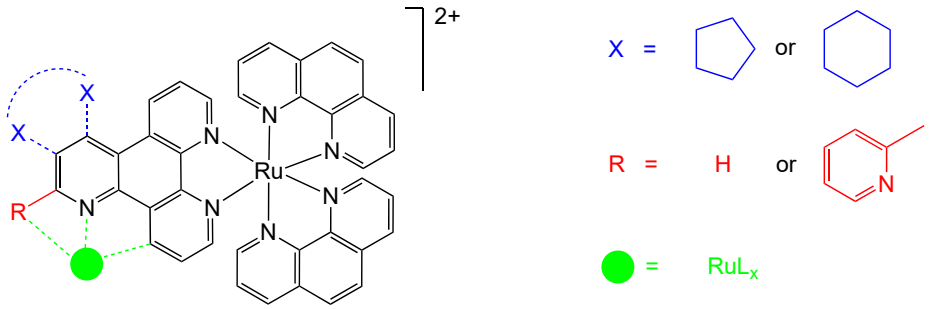



Figure 1. The core framework for a series of new DNA-binding ruthenium complexes.

## Keywords
*Metallodrugs; DNA targetting; photodynamic therapy*

## Biography

The Tuite Lab works at the interface of life and physical sciences, applying chemical and physical tools to biological, materials, and environmental problems.

We have particular interests in the chemistry, dynamics, and recognition of DNA in the context of nano-assembly, synthetic biology, molecular diagnostics, and photodynamic therapy. Another research line involves optical spectroscopy, photophysics, photochemistry, and photobiology. Together with the Pike Group, we form the Bioinspired Molecular Engineering Group.

In April 2021, assisted by Innovate UK, we jointly spun out NunaBio Ltd to provide provide DNA solutions for microbial detection and biochemical research.

My undergraduate and postgraduate studies were at Trinity College Dublin. In 1992, I completed my PhD in the School of Chemistry with Prof John Kelly on photosensitized damage of DNA. I then moved to Gothenburg on the Swedish west coast for postdoctoral work with Prof Bengt Norden at Chalmers University of Technology in the field of biomolecular recognition, and subsequently accepted an Assistant Professorship there. In 2000 I moved to a lectureship at Newcastle where I have continued to expand my research in Biophysical Chemistry.

# Interaction of Platinum Drugs with Extended Telomeric DNA

**Kane Thynne Lama Alharthi**[1], Brondwyn S. McGhie[2], Janice-Aldrich-Wright[2], Andrew Pike[1], Eimer Tuite[1]

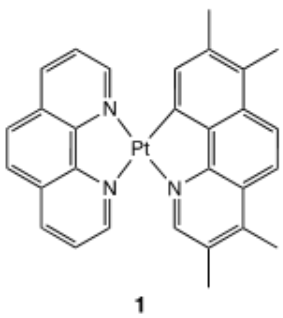
School of Natural Science, Newcastle University, Newcastle upon Tyne, NE7 7RZ, UK

School of Science, Western Sydney University, Locked Bag 1797 Penrith South DC, Penrith, NSW 2751, Australia

## Abstract

In the field of cancer research, development of innovative therapeutic methods and drugs to overcome resistance and side-effects is an on-going endeavour. Four-stranded G-quadruplex (Q-DNA) is emerging as an alternative chemotherapeutic target in cancer, since sequences that form this non-canonical structure are present in telomeres and some proto-oncogenes (e.g. c myc). In many types of cancer, tumour cells survive through the extension of their telomeric DNA by over-expression of telomerase enzyme. The binding and stabilisation of human telomere Q-DNA by drugs has been shown to prevent the action of telomerase.

Most studies that investigate the binding of small molecules to Q-DNA are carried out using inter- and intra-molecularly assembled short oligonucleotide sequences that are designed to fold into different Q-DNA conformations, stabilized by interstitial metal ions. However, in telomeres, Q-DNA-forming sequences are not isolated in this way.Human telomeres(h tel) comprise a tract of duplex tandem repeats (2-50kbp; 300-8000 repeats) of the sequence 5' TTAGGG-3', terminating with a 3' terminal single-stranded overhang of 75-300 nucleotides. This single-stranded overhanghas the capacity to fold into quadruplex structures. To better represent the native sequence and conformation of telomeres,we have used our published methods [1]for enzymatic synthesis ofds- and ss-DNA containing multiple5' TTAGGG-3' repeats. The single-stranded DNA is then folded with potassium to produce Q-DNA.

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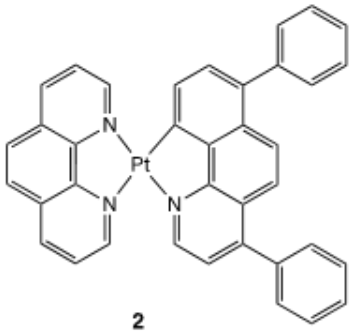


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The Aldrich-Wright research team at WSU has described a series of non-covalent binding, emissive cyclometallated platinum complexes that bind single h tel Q-DNA motifs [2]. Of these, we report the interaction of complexes 1 and 2with extended DNA containing hundreds of repeats of the h tel sequence, which are designed to fold into multiple Q-DNA structures

## Keywords
*Quadruplex DNA; Q-DNA; G4-DNA; Anti-Cancer Platinum Drugs; Telomeres.*

## Biography
Kane Thynne is agraduate research student in Chemistry at Newcastle University.

# Identification of Small Molecule Inhibitors for Blocking SARS-CoV-2 Entry

**Pui-Kai Li,** Enming Xing[1], YuexiuZhang[2], Rajni Kant Shukla[2],ValarmathyMurugaiah[2], Jianrong Li[2], andAmit Sharma[2,3]

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## Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a novel and highly pathogenic coronavirus and is the causative agent of COVID-19, an ongoing pandemic that has posed a serious threat to public health and global economy. Delays in vaccine deployment at a global scale, vaccine hesitancy, and ongoing evolution of the virus is leading to emergence of SARS-CoV-2 variants that are potentially more transmissible and pathogenic. Thus, there is a pressing need for therapeutic interventions that target essential viral proteins that regulate virus spread and replication. SARS-CoV-2 virions display the characteristic club-shaped projections formed by trimers of viral Spike glycoprotein on their surface.To invade the host cell, the receptor-binding domain (RBD) of Spike protein binds to the host cell's ACE2 receptor, followed by cleavage events that allow the Spike protein to fuse with the host cell membrane. Thus, the essential role of Spike protein in ACE2 receptor binding and viral fusion makes it a prime target for therapeutic interventions.

The objective of our work has been to screen a panel of small molecules to identify candidate inhibitors that effectively block the interaction of Spike protein with ACE2. A commercially available library with 93,835 drug-like compounds was screened for binding to RBD using molecular docking. Ligands that showed considerable occupancy in RBD pocket and a relatively stable pose were selected. Using this methodology, ten lead compounds were identified.
We evaluated the inhibitory potential of these compounds using SARS-CoV-2 Spike-pseudotypedlentiviruses for down selection to a lead small molecule. Using this approach, we identified "SAI4" as a candidate small molecule, which inhibited SARS-CoV-2 pseudovirus entry with IC50 value of ~18 μM. We also empirically determined the binding affinity between RBD and SAI4 using a competitive ELISA-based assay. We determined that SAI4 binds

RDB with a Kd of ~20 µM. Using cells engineered to express ACE2 and cells that express physiological levels of ACE2, we found that SAI4 inhibited SARS-CoV-2 pseudovirus entry at both engineered and physiological ACE2 levels. We validated the antiviral potential of SAI4 against genuine SARS-CoV-2 and HCoV-NL63, which is another coronavirus that uses ACE2 as its entry receptor. Lastly, we demonstrated antiviral potential of SAI4against four SARS-CoV-2 variants of concern (α, β, γ, and δ) using SARS-CoV-2 Spike-pseudotypedlentiviruses.

## Biography

Pui-Kai Li is an academic researcher from Ohio State University. The author has contributed to research in topic(s): Cancer & Steroid sulfatase. The author has anhindex of 45, co-authored 144 publication(s) receiving 5991 citation(s). Previous affiliations of Pui-Kai Li include Duquesne University.

# Microphyiological Systems: In Vitro 3D Models for Safety, Efficacy and Precision Medicine Studies

**Danilo A. Tagle**
Director,Office of Special Initiatives, NCATS, NIH

## Abstract
Approximately 30% of drugs have failed in human clinical trials due to adverse reactions despite promising pre-clinical studies, and another 60% fail due to lack of efficacy. A number of these failures can be attributed to poor predictability of human response from animal and 2D in vitro models currently being used in drug development. To address these challenges in drug development, the NIH Tissue Chips or Microphysiological Systems (MPS) program is developing alternative innovative approaches for more predictive readouts of toxicity or efficacy of candidate drugs. Tissue chips are bioengineered 3D microfluidic platformsutilizing chip technology and human-derived cells and tissues thatare intended to mimic tissue cytoarchitecture and functional units of human organs and systems. In addition to drug development, these microfabricated devices are useful for modeling human diseases, and for studies in precision medicine and environment exposures. Presentation will elaborate in the development and utility of MPS and in the partnerships with various stakeholders for its implementation.

## Biography
Dan Tagle is the director of NCATS' Office of Special Initiatives. He also recently served as the Center's acting deputy director, as well as the acting director of NCATS' Office of Grants Management and Scientific Review, now the Division of Extramural Activities, and as executive secretary to the NCATS Advisory Council and Cures Acceleration Network Review Board. Prior to joining NCATS, Tagle was a program director for neurogenetics at the National Institute of Neurological Disorders and Stroke (NINDS), where he was involved in developing programs concerning genomics-based approaches for basic and translational research in inherited brain disorders.Prior to joining NINDS in 2001, Tagle was an investigator and section head of molecular neurogenetics at the National Human Genome Research Institute and has been involved in the highly collaborative effort toward the positional cloning of genes for Huntington’s disease, ataxia-telangiectasia and Niemann-Pick disease type C. He has served on numerous committees and advisory boards, including the editorial boards of the journals Gene and the International Journal of Biotechnology.

Tagle obtained his Ph.D. in molecular biology and genetics from Wayne State University School of Medicine in 1990. He was an NIH National Research Service Award postdoctoral fellow in human genetics in the laboratory of Francis S. Collins, M.D., Ph.D., at the University of Michigan. Tagle has authored more than 150 scientific publications and has garnered numerous awards and patents.

# Effect of Methanol Extract of *Senna Occidentalis* Root on Carbon Tetrachloride Induced Hepatotoxic Albino Rats

**R. U. Hamzah,** [1]Busari, M. B., [1,2]Umar, M. Band [1]Mathew, J. O
[1]Department of Biochemistry, Federal University of Technology, Minna, Nigeria.
[2]African Center of Excellence for Mycotoxin and Food safety
Federal University of Technology, Minna, Nigeria

## Abstract
Senna occidentalis is a medicinal plant used traditionally in the treatment of liver disease and other disorders. The current study was designed to determine the effect of methanol extract of Senna occidentalis root in rats induced with carbon tetrachloride (CCl4). Phytochemical screening and extraction of senna root with methanol were determined using standard procedures. A total number of twenty (20) adult male wistar albino rats (100 - 180g) were randomly divided into five groups of four rats each. All the groups except group I were induced CCL4 and were subsequently treated thus: Group 1 served as normal control and received only normal saline. Group 2 was treated with standard drug silymarin (100 mg/kg body weight). Group 3 was induced with CCl4 but not treated. Groups 4 and 5 were treated with (100 mg/kg and 200 mg/kg) body weight respectively of the methanol root extract. Biochemical parameters such as Aspartate transaminase (AST), Alanine transaminase (ALT), Alkaline phosphatase (ALP) and antioxidant assay such as Superoxide dismutase (SOD), Catalase (CAT) and Lipid peroxidation level were determined. Phytochemical screening and quantification revealed presence of bioactive compounds such as Tannins (0.112±0.01 mg/g), Phenols (6.78±0.23 mg/g) and flavonoids (0.56±0.21 mg/g). The serum activity of Aspartate Transaminase, Alanine Transaminase, Alkaline Phosphatase was significantly ($p<0.05$) increased in the CCl4 induced but not treated group, when compared with the normal group. However, the administration of 100 mg/kg and 200 mg/kg body weight of the methanol root extract significantly decreased the level of AST, ALT and ALP. The activity of SOD and CAT were significantly decreased ($p<0.05$) in the CCl4 induced but not treated group, but was increased when treated with the methanol root extract. The lipid peroxidation level was significantly increased in the CCl4 induced but not treated rats, but was decreased on treatment with the methanol root extract.The observed results showed methanol extract of Senna occidentalis root have hepatoprotective effect in CCl4 induced hepatotoxic rats and may therefore be harnessed as an alternative therapeutic in treating liver toxicity.

## Keywords
*Carbon Tetrachloride, Phytochemicals, Antioxidants, Senna Occidentalis*

# Isolation of Pelargonium AlchemilliodesL'l her Active Compounds and Their Effect on Bacterial Growth and KeratinocytesInVivo

**F.Mtunzi**
Department of Chemistry and Biotechnology, Vaal University of Technology, South Africa

## Abstract
Pelargonium Alchemilliodes L L' Her is an evergreen shrub, cultivated principally forthe medicinal essence and decoction in Southern Africa for the treatment of skinproblems, and wounds. The aim of the study was to optimize the extraction ofphenolic and flavonoids from P. graveolens study of their proliferative and cytotoxiceffectsonhumankeratinocytes,aswellast heirantioxidantandantibacterialactivitiesandtoisolateactive compounds.

The results showed a significant ($P < 0.05$) increase in cell proliferation and viabilityw entheextractwasadministeredatconcentrationsof≤50µg/mL.Totalantioxidantcapacity and reducing power were comparable to standard gallic acid, while theantiradicalactivityhad anIC50valuesof0.18±0.03–8.98±0.15mg/mL.MICvalueof 1.56mg/mLforextractswasregi steredagainstStaphylococcusaureusandSalmonella typhi comparable to chloramphenicol. Two triterpenoid compounds 1-hydroxy-30-norlanosta-6,8-dieneand1,2,3,4,4a,8,9,10,10a-octahydro-2-(2-hydroxypent-4-enyl)-4a-vinyl-1H-benzo[c]chromen-6(10bH)-onewereisolatedfromthemethanol extracts.

## Keywords
*Pelargonium Alchemilliodes L L'Her, keratinocytes, minimum inhibitoryconcentration, cellproliferation,cytotoxicitycellproliferation, cytotoxicity*

# NovelElastin-Like Polypeptides for the delivery of αB Crystallin Peptide tothe Retina

**Sara Aly Attia1***, Alvin Phan1, Shin-Jae Lee2, J. Andrew MacKay

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Department of Biomedical Engineering, Viterbi School of Engineering, University of Southern California, Los Angeles, CA 90089, USA,

Department of Ophthalmology, Keck School of Medicine, University of Southern California, Los Angeles, CA 90089, USA

## Abstract

Oxidative stress-induced retinal degeneration is one of the leading causes of cellular death and irreversible vision loss. It accelerates the promotion of many degenerative pathologies, such as age-related macular degeneration “AMD” which is shown to affect 12.6% of Americans, according to the latest findings of the Vision and Eye Health Surveillance System “VEHSS”. Combating the oxidative stress that leads to such serious ocular dysfunctions appears a well-suited aim to be addressed.αB crystallin, a member of the small heat shock protein “sHsps” family, is a naturally secreted chaperone that has been recognized for its potential neuroprotective functionthrough a variety of biological actions, such as interfering proteins aggregations and halting inflammation, oxidative stress process, and cytoskeleton disruption. Regardless of its potential therapeutic, its delivery requires a controlled delivery platform for preventing its small molecular size from rapid filtration andlimited activity. We fused a 21-mer “GDRFSVNLDVKHFSPEELKVK” of αB crystallin peptide sequence into an elastin-like polypeptide“ELP” motiffor allowing acontrolled therapeutic outcome.ELPs technology isrecentlya smart cutting-edge discovery that enableduseful optimization and precise modifications for wide therapeutic cargos. Our study aims to modulate the hydrodynamic radius of crystallin by seamless engineering of different ELPs, assess comparativebiophysical characterization of the conjugate constructs, and evaluate the neuroprotective efficacy in retinal model. Our MacKay’s group established ELP’s construct; consisting of pentapeptide sequence, (Val-Pro-Gly-Xaa-Gly)n., at which “n”specifies the molecular weight and the guest residue“Xaa”determines the polymeric solubility. In addition to theELPs tropoelastin natural source that limits the immunogenic reactions, these ELPs are distinguished by theirtenablethermo-responsive feature. Below the physiological transition temperature“Tt”, ELPs are soluble and appear optically clear, and are easily passed through a narrow-gauge needle. Upon injection and above itsTt, the ELPs chains assemble and turn out turbid

suspensions.Suspended droplets of coacervate are immobilized in the tissues. This hinders the rapid clearance and causes the terminal half-life of the formulation in plasma to increase. Selection of ELPs length and hydrophobicity fundamentally modifies this separation phase behaviour, thus affecting the rate of dissolution and therapeutic protection. Herein, our group engineered crystallin into two different ELPs "~ 40 kDa"architectures defined as follows, S48I48 and V96. S48I48 "(VPGSG)48(VPGIG)48" isan amphiphilic di-block polymer with hydrophilic and hydrophobic guest residues; serine and isoleucine, respectively. While V96 "(VPGVG)96" is composed of 96 repetitive units using valine as hydrophobic guest residue. Both protein polymers formed temperature-dependent assembly or thermo-responsive deposits. The results demonstrated that crystallin-S48I48 and crystallin-V96 had Ttat 13°C,30°C and 37°C, respectivelywhich is expected to impact crystallin retention, and thereby desired efficacy. Below the Ttat 10°C, the dynamic light scattering results also confirmed one mass population for both constructs with a radius "< 10 nm".

## Keywords
*Crystallin; Elastin-like polypeptide; Transition temperature; Guest residue*

## Biography
SaraAttia is a Ph.D. graduate student at the University of Southern California, School "USC" of Pharmacy, Los Angeles, California, USA. Attia graduated from the Alexandria School of Pharmacy, Egypt in 2018. In December 2018, Attia got a scholarship to join Northeastern University in USA as a pre-doctoral fellow, working primarily on designing and delivering various lipid/polymer nanoparticles into different resistant cancer cell models. In 2021, Attia started her doctoral studies at USC. Her doctoral responsibilities are focusing on translational mediated approaches for targeting cancer lines and ocular tissues. Attia is very passionate and keen on inventing new protein/ polymer drug delivery systems and exploring their molecularly targeted approach.Attia had more than 12 publications in peer-reviewed highly-indexed journals.Attia is very interested in Asian Culture and Asian cuisines with a particular interest in the Japanese culture. Attia visited Tokyo previously in 2018 to present her research work in the International Society of Nephrology and she is looking forward to seeing all scientists and researchers in Osaka.

# Carbohydrate-based Biopolymers: Biologically Active Poly[3-(3,4-Dihyd-Roxy¬¬Phenyl)¬Glyceric Acid] —the Paradigm of a Multi-Target Biopolyether with Applications in Prostate Cancer Prevention and Treatment

**Vakhtang Barbakadze**

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## Abstract

Carbohydrate-based biopolymer is the main chemical constit¬uent of high molecular (>1000 kDa) water-soluble preparations from Symphytumasperum, S. caucasicum, S. officinale, S. grandiflorum, Anchusaitalica,CynoglossumofficinaleandBoragoofficinalis (Boraginaceae). According to data of liquid-state 1H, 13C NMR, APT, 1D NOE, 2D 1H/13C HSQC, 2D DOSY and solid-state13C NMR spectra of this biopolymer was found to be poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl)ethylene] that is poly[3-(3,4-dihydroxy¬phe¬nyl)¬glyceric acid] (PDPGA). The polyoxyethylene chain is the backbone of this polymer with a residue of 3-(3,4-dihydroxyphenyl)glyceric acid as the repeating unit. 3,4-dihydroxyphenyl and carboxyl groups are regular substituents at two carbon atoms in the chain. This compound represents a new class of natural polyethers, namely caffeic acid-derived biopolyether. PDPGA as a 3,4-dihydroxyphenyl derivative of poly(2,3-glyceric acid ether) belongs to a rare class of carbohydrate-based biopolymer, namely poly(sugar acids) as well. Poly(2,3-glyceric acid ether) chain is the backbone of this polymer and 3,4-dihydroxyphenyl groups are regular substituents at carbon atoms in the chain. Its basic monomeric moietyglyceric acid is an oxidative form of aldotrioseglyceraldehyde. PDPGAas a unique natural polyether contains aliphatic ether groups in its polymer backbone. Naturally occurring ethers include small molecules such as antibiotics, or aromatic polymer such as lignin. Lignin contains ether links between two aromatic rings or between an aromatic ring and an aliphatic moiety. However, reports concerning polymers that contain aliphatic ethers as repeating unit are missed. Every repeating structural unit of PDPGA contains three reactive functional groups, two phenolic hydroxyl groups in ortho-position and one carboxyl group. Multifunctionality of PDPGA should be a reason of its wide spectrum of biological activities. PDPGA is endowed with intriguing pharmacological

activities as immunomodulatory (anticomplementary), antioxidant, anti-inflammatory, burn and wound healing and anticancer properties. The monomer was synthesized via asymmetric dihydroxylation of trans-caffeic acid derivative using a potassium osmate catalyst. Synthetic methylated derivative of PDPGA was synthesized via ring opening polymerization (ROP) of 2-methoxycarbonyl-3-(3,4-dimetho¬xy¬phenyl)oxirane using a cationic initiator BF3•OEt2. Oligomers of PDPGA were synthesized by "green" chemistry ROP enzymatic polymerization of methyl 3-(3,4-dibenzyloxyphenyl)¬glycidate using lipase from Candida rugosa and further deprotection. Hyaluronidase (Hyal-1) degrades high molecular mass hyaluronic acid into smaller fragments which stimulate inflammation. PDPGA possesses the ability to inhibit the enzymatic activity of Hyal-1 completely. Consequently, PDPGA exhibited anti-inflammatory efficacy. PDPGAand its synthetic monomerDDPPA suppressed the growth and induced death in androgen-dependent (LNCaP) and -independent (22Rv1) human prostate cancer (PCA) cells, with comparatively lesser cytotoxicity towards non-neoplastic human prostate epithelial cells PWR-1E. PDPGA induced apoptotic death by activating caspases, and also strongly decreased androgen receptor and prostate specific antigen (PSA) expression. In 22Rv1 xenograft model male athymic nude mice with 22Rv1 xenografts was administered orally of PDPGA. The tumor volume was decreased by 88%. Plasma analyses revealed that PDPGA administration caused a strong dose-dependent decrease in PSA levels by 87%. Anticancer efficacy of PDPGA against human PCA cells is more compared to its synthetic monomer. Methylated PDPGA did not show any activity against PCA. Overall, this study identifies PDPGA as a potent agent against PCA without any toxicity.

## Keywords

*Poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl)ethylene]; Poly[3-(3,4-dihydroxy¬phe¬nyl)¬glyceric acid]; Caffeic acid-derived biopolyether; Carbohydrate-based biopolymer*

## Biography

Vakhtang Barbakadze has his expertise in isolation and structure elucidation of a new series of plant polyethers, which are endowed with pharmacological properties as immunomodulatory, antioxidant, antiinflammatory, wound-healing and anti-cancer agents. Besides, he interested in enantioselective synthesis and biological activities of basic monomeric moiety of these biopolyethers, synthesis of enantiomerically pure epoxides as chiral building blocks for the production of synthetic analogues of natural polyethers by chemical and enzymetic catalysis. He has received PhD degree in Chemistry and DSci degree in Biology in 1978 and 1999 from Institute of Organic Chemistry, Moscow, Russia and Institute of Biochemistry and Biotechnology, Tbilisi, Georgia, respectively. He is Head of the Department of Plant Biopolymers and Chemical Modification of Natural Compounds at Tbilisi State Medical University I.Kutateladze Institute

of Pharmacochemistry. In 1996 and 2002 he has been a visiting scientist at Utrecht University, Departments of Pharmacognosy and Medicinal Chemistry, Utrecht, The Netherlands, by University Scholarship and The Netherlands organization for scientific research (NWO) Scholarship Scientific Program, respectively. He is also an organizing committee member and renowned speaker for many reputed scientific conferences. He has published more than 100 papers in reputed journals. In 2004 he was Georgian State Prize Winner in Science and Technology.

# rRNA Platform Technology for Identifying Ligands That Target Pathogen RNA Structural Motifs

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## Abstract

Approximately half of all naturally occurring antibiotics affect protein synthesis, and most of these target ribosomes. Ribosomes are complex macromolecular structures composed of RNA (rRNA) and protein, whose function is to catalyze protein synthesis within the cell. Mutations in ribosomal RNA (rRNA) are often lethal because they affect the production of all cellular proteins. Importantly, human and pathogen rRNAs are sufficiently different to allow specific drug interactions. Thus, prokaryotic and Eukaryotic rRNA is an ideal drug target and the modular nature of rRNA facilitates the development of in vitro assays, structure determination, and molecular-modeling studies for drug design.Generation of drugs that target RNA is limited by the ability to generate three dimensional structures of organells using x-ray and NMR, key technologies in drug discovery. Such technologies are not only expensive and tedious but also slow. We have developed Platform technology,that allows the discovery and characterization of new drug target sites in ribosomal RNA. The developed platform technology, allows the generation of high resolution atomic level three dimensional pathogen ribosomes crystal structures. The high-resolution structures rapidly created using only their sequence information as input, a process that has the potential to increase the speed of scientific discovery. Through this technology platform, we demonstrate that RNA is a target of choice for the development of next-generation drugs.The platform demonstrates that the modular nature of rRNA facilitates thedevelopment of in vitro assays, structure determination, molecular-modelling, andcompound screening studies for drug design.The generated rRNA structures contain all of the ordered regions of 16S RNA and associated proteins. In the absence of the pathogen 40S ribosomal x-ray and NMR crystal structure, the models accurately depict a global topology, secondary and tertiary connections, and achieve an overall root mean square deviation (RMSD) value of less than 3 Å relative to the x-ray generated template's crystal structure. These results demonstrate that this approach has the power to identify motifs of interest in RNA and identify potential drug targets for macromolecules whose crystal structures are unknown. The results also show the utility of RNA homology modeling software for structure determination and lay the groundwork for applying this approach to larger and more complex eukaryotic ribosomes and other RNA-protein complexes. Structures generated from

this study have been used in in silico screening experiments and lead to the determination of structures for targets/hit complexes.This ribosomal structures are comparable in quality to experimentally determined X-ray crystallography, Nuclear Magnetic Resonance (NMR) spectroscopy or Cryo – Electron Microscopy (EM) crystal structures. Thus, the structure opens a new door in the approach on drug target, and will be important in the development of a new class of anti-infectives compounds. In-silico screening of ligands can be carried out to identify compounds that show binding potential on ribosome, ribosomal RNA (16S and 18S rRNA) or the ribosomal proteins. Compounds identified this way could be further studied for anti-infectives activity.

# How Artificial Intelligence enhances drug discovery?

**Sang EunJee**
XtalPi Inc., USA

## Abstract
Drug discoveryis time-consuming and expensive, largely owing to the substantial costs and long development period. It takes on average of 2.6 billion dollars and over 10 years to bring a new drug to market. Artificial Intelligence(AI) is becoming more widely adopted in the pharmaceutical industry to enhance drug discovery efficiency.At the preclinical stage, AI helps to reduce the development time and cost significantly by removing the compounds with undesirable potencybefore the synthesis and biological test. More importantly, AI can suggest a new compound possibly with desirable potency, selectivity, and PK/PD properties by virtually exploring the expanded chemical space. The key to success in AI-driven drug discoverydepends on how well it is integrated into the biology and chemistry teams of drug discovery. Our AI drug discovery technology and integrated drug discovery platform will be introduced with case studies of how we solved challenging problems with AI.

## Biography
Sang EunJee is an application scientist in the business development department and has been with XtalPi Inc. since 2022. She is responsible for Computer Aided Drug Discovery (CADD) at the preclinical stage. Her expertise is in predicting drug-protein interaction, structural changes of proteins, and virtual screening. She received her Ph. D. in the chemical &biomolecular engineering school at Georgia Tech and completed two postdoctoral training at Georgia Tech and Washington University in Saint Louis. Before joining XtalPi, she worked in Humanwell Pharmaceuticals Inc. in the United States and worked in drug discovery.

# VIRTUAL PRESENTATIONS

# Development of 3D Structured Micro needle Device for transdermal Drug Delivery

**Jufan Zhang**
Centre of Micro/Nano Manufacturing Technology (MNMT-Dublin), School of Mechanical and Materials Engineering, University College Dublin, Dublin 4, Ireland

## Abstract
Development of micro-manufacturing technology has greatly facilitated the emergence of innovative medical devices. A 3D structured hollow microneedle device was developed for transdermal drug delivery in a relatively large dosage (>2ml). Such a device utilizes the optimized internal micro-channel to regulate the hydrodynamic characteristics of the drug liquid, along with the multiple lateral outlets to reduce the hydrostatic resistance from the skin, and the profiled microneedle length distribution to mitigate the skin saturation. In vivo experiments on rabbits have evidenced injection of 1ml ethanol within 29 seconds and 1ml 5% (w/v) glucose within 56 seconds. The micropores created by microneedles closed within 4 mins after injection, without any rupture or fester left. During the injection, the rabbit didn't struggle like it did during conventional intramuscular injection, indicating the much less pain created by microneedles.

## Keywords
*Micro needle, transdermal drug delivery, dosage, 3D structure*

## Biography
Dr. Jufan Zhang received his PhD degree in 2009 from Harbin Institute of Technology, China. After working in the industry for years, he returned to the academia as the postdoctoral fellow, and then hosted several major funding as the PI. He joined the Centre of Micro/Nano Manufacturing Technology, University College Dublin (UCD), and Ireland in 2017, and now is working as the lecturer/assistant professor in UCD School of Mechanical and Materials Engineering. He is the Member of International Academy of Engineering and Technology (AET), Member of International Society for Nanomanufacturing (ISNM), Member of the Irish Manufacturing Council. He is the Chair of Organizing Committee of the 8th International Conference on Nanomanufacturing (nanoMan2022) and the 4th AET Symposium on ACSM and Digital Manufacturing (AETS2022). His research interests mainly include the design and manufacturing of medical devices and bioimplants, micro/nano functional structures, geometrical waveguide design and manufacturing, etc

# Targeting the Endocannabinoid System in the Treatment of Addiction Disorders

**David A Dawson**
Aeon Bio Health Inc, USA

## Abstract
This disquisition provides historical context illustrating the psychosocial, political, and bureaucratic barriers to applying a biomolecular approach to substance use disorders, focusing on what are arguably the most stigmatized molecules in the world. It provides a biomolecular treatment strategy designed to mitigate multiple types of addiction by influencing the dopamine and serotonin neurotransmitters' activity through phytocannabinoid supplementation of the endocannabinoid system and proposes a strategy for circumventing bureaucratic obstacles.
Aeon Bio Health Inc.

## Keywords
*Green Roofs; Green walls; Atmospheric water harvesting; Sustainability*

## Biography
David A. Dawson is a biomolecular psychologist, author, and endocannabinoid and botanic cannabinoid expert, who graduated from Macalester College and the University of Iowa and is currently completing a doctorate at National University.
Formerly the Director of Endocannabinoid Research & Development for the Integrative Pain and Rejuvenation Centers of America.

David was a Featured Speaker at the 2nd Annual Conference on Medicinal Chemistry & Drug Design and has been recognized by the Worldwide Who's Who Organization for his integrity, longevity, outstanding achievements in his field, and his innumerable contributions to society as a whole.

David is the author of the textbook Medical Cannabis: The Definitive Guide, the dramatic comedy novel Pummeled to Death by Hamburger, and regularly publishes articles on the topic of biomolecular psychology in a wide variety of scientific journals.

# Modernization of Old Drugs: Revolutionize Treatment of Acute Leukaemia

**Sin Chun Fung**
Queen Mary Hospital, Hong Kong

## Abstract

Acute leukaemia is an aggressive haematological malignancy. Intensive chemotherapy and haemopoietic stem cell transplant are the mainstay of treatment. However, a substantial proportion of patients suffered from relapse/refractory disease and their prognosis are dismal. Novel therapeutic strategies are urgently needed.

While numerous research are actively done to develop novel small molecules inhibitors or compounds, it often takes a long time from drug discovery to validation of therapeutic efficacy and safety in clinical trials setting. Hence, it can hardly meet the clinical needs of patients. Therefore, research on existing drugs that are widely used to treat other diseases becomes an attractive approach of research.

Bortezomib is a 26S proteasome inhibitors and licensed by FDA to treat plasma cell myeloma and mantle cell lymphoma. Clinical studies are emerging to investigate the role of bortezomib in treating acute lymphoblastic leukaemia. Despite the efficacy and safety of bortezomib had been demonstrated in treating acute lymphoblastic leukaemia, the mechanisms are unknown. This hampered the widespread clinical use of this drug in treating acute lymphoblastic leukaemia. Latest research revealed some novel mechanisms of action of this drug on acute lymphoblastic leukaemia and provide mechanistic insights in developing optimal combination regimen.

Homoharringtonine is a protein translation inhibitor and it had been used to treat acute myeloid leukaemia in 1980s. However, the efficacy was poor when used as monotherapy. Study had shown that combined homoharringtonine and FLT3 inhibitors was effective in treating acute myeloid leukaemia with FLT3-ITD mutations. The clinical safety had been demonstrated by various clinical studies. Given the success of treating FLT3-ITD acute myeloid leukaemia, this drug is actively being investigated to treat other haematological malignancies.

From the above examples, we can extend the therapeutic use of some “old drugs” with active research on mechanisms of action and provide an alternative novel therapeutic strategies to patients. Since the clinical safety of these drugs had been well established, they can be readily translated to clinical use.

# Further Improve the Efficacy and Safety of Tumor Immunotherapy by Targeting Ctla-4

**Xuexiang Du,** Chunxia Ai1[2], Mingyue Liu[2], Yan Zhang[2], Fei Tang[2], Musleh M. Muthana[2], Pan Zheng[3], and Yang Liu

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[2]University of Maryland School of Medicine, Baltimore, USA

[3]OncoC4, Inc. Rockville, USA

## Abstract

Cancer immunotherapy is becoming a powerful and acceptable treatment to malignant tumor in addition to traditional methods such as surgery, radiotherapy and chemotherapy. Anti-CTLA-4 monoclonal antibodies confer a cancer immunotherapeutic effect (CITE) but cause severe immunotherapy-related adverse events (irAEs). How to uncouple the undesired irAEs from the beneficial CITE seen in cancer patients treated with anti-CTLA-4 and/or other immunotherapies has proven to be a daunting challenge, partially due to the lack of the understanding of the real MOA(mechanism of Action) of CITE and irAEs. First, we discovered that the immunotherapy of current anti-CTLA-4 mAbs were dependent on Fc/Fc receptor mediated intra-tumor Treg depletion rather than the widely held mechanism of checkpoint blockade, which raised the reappraisal of CTLA-4 checkpoint blockade in cancer immunotherapy; Second, we establish one realistic irAEs model and reveal one new mechanism of irAEs, while irAE-prone Ipilimumab and TremeIgG1 rapidly direct cell surface CTLA-4 for lysosomal degradation, the non-irAE-prone antibodies we generated, HL12 or HL32, dissociate from CTLA-4 after endocytosis and allow CTLA-4 recycling to cell surface. Our data establish a new paradigm for cancer research that allows for abrogating irAE while increasing CITE of anti-CTLA-4 antibodies.

## Keywords

*CTLA-4; immunotherapy; Checkpoint Blockade; immunotherapy-related adverse events.*

## Biography

Xuexiang Du. Professor in Shandong University, School of Basic Medical Sciences. He has a broad background in tumor immunology with 14 years of experience. He focuses on the molecular mechanisms of immune checkpoint molecules and their applications in cancer immunotherapy to dissociate the undesired immunotherapy related adverse events (irAE) from

the beneficial cancer immunotherapeutic effect. His recent two first author papers published on Cell Research were both selected as Sanofi-Cell Research Outstanding Research Article Award. April 25, 2022, the U.S. FDA has granted Fast Track designation to ONC-392, the next-gen anti-CTLA-4 monoclonal antibody (mAb) which he developed , as a single agent for the treatment of patients with metastatic NSCLC who have had disease progression on prior anti-PD-(L)1 therapy. He is also looking for novel immune regulatory pathways as potential immunotherapy targets or biomarker for safer and improved immunotherapy.

# When Known Therapeutic Agents Meet a Renewed Prospect - Carbon Nanotubes as a Drug Delivery Platform for Prednisolone and Doxorubicin for Anticancer Therapy

**M. R. Chetyrkina,** A. A. Abalymov[1,2], J. Cvjetinovic[1], A. E. Goldt1, F. S. Fedorov[1], D.A. Gorin[1], A. G. Nasibulin[1]

[1]Skolkovo Institute of Science and Technology, 3 Nobel Street, Moscow, 121205, Russia

[2]Science Medical Centers, Saratov State University, 410012 Saratov, Russia

## Abstract

Nowadays, cancer with different origin is the leading cause of human deaths worldwide; according to the WHO, every sixth patient is dying because of cancer. A great variety of approaches were developed to fight the disease and eliminate symptoms. However, there are a lot of complications that patients face onto their road to recovery, such as drug resistance, long-term recovery after chemotherapy, painful surgeries, etc. This stimulates the search for new drugs or drug combinations with novel treatment scenarios. From that viewpoint, drug delivery systems (DDS) are one of the leaders because they potentially can minimize negative effects. The main goal of DDS is to promote the extended drug release, better drug availability and controlled location of releasing. Carbon nanotubes (CNTs) are considered to be prospective candidates for DDS design. In the present work, we evaluated the stability and toxicity of CNT dispersions containing therapeutic agents, doxorubicin (DOX) and prednisolone (PR), for use as a DDS.

In our study, we made two dispersions of CNTs with therapeutic agents. The first one is a cytostatic drug called doxorubicin, which is broadly applied for anticancer treatment. The second one is an anti-inflammatory agent prednisolone usually utilized to suppress an inflammation response. To prepare dispersions, we used CNTs produced by CoMoCat (SigmaAldrich) or HiPco process (Nano Integris) with concentrations 5 mg/mL. The concentration of therapeutic agents was 10 mg/mL. To produce dispersions with a high quality and homogeneity, we used an ultrasonication. Zeta potential measurements, transmission electron microscopy and absorbance spectrum were done to characterize the dispersions.

We tested the prepared dispersions for their cytotoxic effects on five cell lines: Neuro2A or N2A, L929, A549, SKOV3, HEK. Cell culturing was performed in standard flasks in DMEM media. Every 2-3 days we replaced media and maintained the cells at incubator (5% $CO_2$ and 37 °C). A colorimetric cytotoxic assay, MTT, was applied to evaluate the dispersions' toxic

effects after 72 hours of incubation. Analysis was performed with a spectrophotometer.
For CNTs with PR, the most sensitive N2A cells demonstrated 70% of alive cells at a dose 7.1 µg/mL. Skov3 and L929 showed the same response with nearly 90% of alive cells. For HEK and A549, viability was at the middle between the culture with a high sensitivity (N2A) and cultures with low response (Skov3, L929). As a control, we tested just PR suspension, that showed a 100% viability. This fact means that CNTs intercalate into cells compared to the control group.
For CNTs with DOX, L929 fibroblasts and N2A cells were the most sensitive. Skov3 were almost resistant, 80% of cells stayed alive after the incubation with the agent. For HEK and A549, cells demonstrated the same viability staying in the middle between L929 and N2A. Still, just DOX itself was more toxic than our dispersion made of CNTs. Summing up, the present work is a successful demonstration of manufacturing of CNTs dispersions with therapeutic agents and their potential application in anticancer treatment.

## Keywords
*Carbon nanotubes; drug delivery; doxorubicin; cancer*

## Biography
Margarita graduated with honours from Lomonosov Moscow State University in 2018, getting a bachelor's degree in Biology, and from Skolkovo Institute of Science and Technology in 2020, earning a master's degree Material Science. Her bachelor's research was dedicated to the study phenomenon named epithelial-mesenchymal transition and development of new methods for prediction of cancer progression and studying of overcoming drug resistance of breast cancer. Her master's degree work was devoted to biological effects study and development of new semiconductor materials in vat dyes family, research of cytotoxic effects of water-soluble derivatives of fullerenes on in vitro models of lung cancer, and evaluation of potential toxic effects of halides used as precursors for perovskite solar cells in vitro/ in vivo.

# New and Potent Nystatin water Soluble Analog

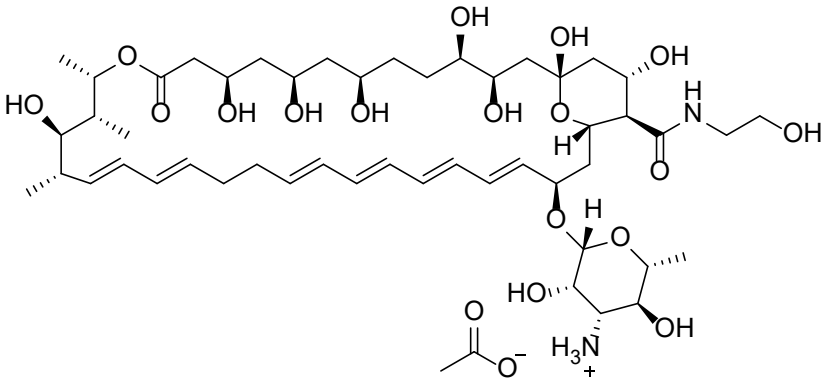
**Aviran Amir**

## Abstract

Fungal infections are worldwide threat effecting people with varied severity from skin rush to mortality. The most severe illness is raised by invasive candidiasis and aspergillosis which immunocompromised people are the most in risk. Furthermore, in recent reports, fungal infections have identified as emerging threat in intensive care units (ICU).

Polyene macrolides such as: Amphotericin B, Nystatin and Natamycin are used in the clinic to treat fungal infections. However, the polyene antifungals are not water-solubleissue that lower their bioavailability and increase their toxicity.

Recently we proposed a NY statin derivative that demonstrates high water solubility and less toxic in vitro. Moreover, the absorption to plasma proteins and stability in plasma were tested.




Reference:
https://pubs.acs.org/doi/10.1021/acsmedchemlett.1c00538

# Towards the Next Generation of Inducible Nitric Synthase Inhibitors: Challenges and Hopes

**Cristina Maccallini**[1,*], Marialucia Gallorini[1], Ilaria Bellezza[2], Amelia Cataldi[1], Rosa Amoroso[1]

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## Abstract

Nitric Oxide (NO) is a free radical signalling molecule, involved in different biological processes and produced by nitric oxide synthases (NOS). There are two constitutive NOS (the endothelial and neuronal ones) and an inducible NOS (iNOS). This last is highly involved in the innate immunity and has a role in inflammatory diseases. Moreover, in tumour biology, correlation between iNOS expression and clinical outcome associated to worse prognosis, was evaluated in different types of tumours. Therefore, inhibition of iNOS has been proposed as a targeted therapy in several cancers, including breast cancer, prostate cancer and gliomas [1]. However, no iNOS inhibitor has passed clinical trials, therefore there is the need to develop new potent and safe compounds. To this aim, in the last years we have reported several potent and selective iNOS inhibitors, and different chemical scaffolds were explored leading to new compounds with ameliorated pharmacokinetics. The most promising ones were subjected to a deep biological evaluation on glioma and breast cancer cell lines. Moreover, some compounds were also evaluated on LPS-stimulated monocites, as well as on and LPS-stimulated primary dental pulp stem cells (DPSCc) and BV2 microglia cells to ascertain their potential antiinflammatory activity. It was found that selected acetamidine-based iNOS inhibitors showed encouraging anticancer activity, moreover they were able to modulate the inflammatory response in monocytes, DPSCs, and BV2 microglia cells [2-7]. Data presented lay the ground for further investigation on the anti-inflammatory and anticancer potential of acetamidines selectively targeting iNOS in a clinical context, especially considering the deep connections between the immune system and the cancer microenvironment.

## Keywords

*Cancer; Immune System; Nitric Oxide Synthase; Targeted therapy*

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## Biography

Prof. Cristina Maccallini received her PhD in Pharmaceutical Sciences in 2002 from the University of Chieti, where she is currently associate professor of medicinal chemistry at the Department of Pharmacy. Her main research interest is focused on the design, synthesis and biological evaluation of small molecules targeting proteins involved in inflammation and cancer development, such as the inducible Nitric Oxide Synthase, the Carbonic Anhydrases, the Aromatase and PPARs. She is author of 75 publications in the Medicinal Chemistry field in peer reviewed Journals and of 1 book chapter. She is a member of the Editorial Board of various international Journals and member of the Italian Chemistry Society.

# Synthetic, Orally Bioavailable, Selective, Highly SulfatedMimetics of Heparan Sulfate as AntiCancer Agents with In Vivo Activity

**Umesh R. Desai, PhD**
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## Abstract
Glycosaminoglycan's (GAGs), such as heparan sulfate (HS), have been implicated in tumorigenic responsesincluding initiation, progression and metastasis. Earlier, we have shown that a defined 6-mer of HS, but not 4-,8-mer or longer, inhibits colorectal cancer stem cells (CSCs) by inducing activation of p38 MAPK (Oncotarget2016, 7:84608-22). Later, we showed that a synthetic mimetic of the HS 6-mer, labeled as G2.2, selectively targets CSCs over bulk adherent tumor cells (Mol. Cancer Ther. 2019, 18:51-61). We now report the design of three lipidic analogs of G2.2, which demonstrate major promise in mouse models of tumor growth (J. Med. Chem. 2023, 66:1321-38). Briefly, microarray-based screening led to identification of IGF-1R as a potential receptor of HS 6-mer (Angew. Chem. Int. Ed. 2022, 61:e202211320) and lipid-modified mimetic.Biophysical studies indicated that the preferred soluble and/or cell surface target receptors were in line with microarray results. Three different models of CSC growth in mouse were performed to test the efficacy of the lipid-modified analogs in vivo. Two of the lipid-modified analogs G2C and G5C were found to selectively inhibit CSCs in vivo and reduce tumor progression better than a combination of 5-fluorouracil and oxaliplatin (FUOX). Both G2C and G5C displayed very promising oral bioavailability and in vivo anti-cancer potential. Overall, this work presents a powerful proof of concept that synthetic GAG mimetics are unique anti-cancer therapeutics with high potential for selective elimination of the tumor initiating cells.

## Biography
Umesh Desai is the Alfred Burger Professor of Medicinal and Biological Chemistry at Virginia Commonwealth University (VCU), Richmond, VA. He also serves as the Chair of the Department of Medicinal Chemistry in the School of Pharmacy at VCU. He received his baccalaureate from the M. S. University of Baroda, and his doctorate from the Indian Institute of Technology, Bombay, India. He specializes in rational drug design with emphasis on glycosaminoglycan-based agents that function as anticoagulants and anticancer agents.

# Antibiotics in Arab Traditional Medicine, the Legacy of the Past, is it Proven by the Future?

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## Abstract
Arab history abounds with the use of folk or traditional medicine in the treatment of various infections. So while the greater part of it was firmly rooted in people's minds from what they inherited from the Arab library, we find, on the other hand, experience has a role that cannot be ignored. And with the frequent use of folk medicine in light of the era of unprecedented resistance to antibiotics, an urgent need has emerged to verify the effectiveness of this important drug in people's lives, in order to provide evidence based on scientific foundations. In this article, we will shed light on some of the traditional remedies used as antibiotics, referring to recent studies conducted to test their effectiveness against microbes.

# Thank You!

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