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Science Sessions 2024
Book of Abstracts

Catarina Rosado and L. Monteiro Rodrigues, eds.

UNIVERSIDADE LUSÓFONA
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Science Sessions 2024

Antracycline-induced Cardiotoxicity: a Question of Power and Clocks?

Paulo J. Oliveira

CNC – Center for Neuroscience and Cell Biology, University of Coimbra, Portugal

Abstract

Doxorubicin (DOX) is a highly effective anticancer anthracycline drug, with a broad spectrum of anti-neoplastic activity. Unfortunately, its use is associated with the development of dose-dependent, cumulative, and irreversible selective cardiotoxic side-effects. The occurrence and scale of DOX cardiotoxicity results from alterations of cardiac mitochondrial metabolism, including oxidative damage to mtDNA and inhibition of oxidative phosphorylation machinery, resulting in inhibition of respiration and ATP decrease. Interference with mitochondrial metabolism was demonstrated by us in rodent models and cell models, including H9c2 cardiomyoblasts and induced-pluripotent stem cell (iPSC)-derived mouse cardiomyocytes. We also demonstrated that DOX inhibits multiple gene expression patterns, affecting mitochondrial-relevant transcripts, as well as nuclear epigenetic regulation, as well as disrupts the oscillation of multiple circadian genes in a rodent model, which may contribute to the development of the characteristic delayed toxicity. In fact, epigenetic modifications are dependent on mitochondrial metabolites that act as co-factors or substrates for many epigenetic enzymes, which creates an inhibitory loop that contributes to the development of anthracycline-induced cardiotoxicity. DOX-mediated alterations in cardiac mitochondrial metabolism may affect the epigenetic landscape and may contribute to explain persistent DOX cardiotoxicity, manifested long after drug administration. We also present evidence that nanomolar DOX pretreatment induces a beneficial and possibly epigenetic-based mitochondrial adaptation, raising the possibility that an early sub-therapeutic DOX treatment can be used as a preconditioning and protective approach during anticancer therapies.

Lecturer's resumé

Paulo J. Oliveira is currently Principal Investigator with "Agregação" (Habilitation) at the CNC – Center for Neuroscience and Cell Biology, University of Coimbra, Portugal. He is the current leader of the "Mitochondria, Metabolism and Disease" group and of the MitoXT: Mitochondrial Toxicology and Experimental Therapeutics laboratory. He received his Bachelor of Science in Biochemistry from the University de Coimbra in 1999. In 2003, he completed his PhD in Cellular Biology from the same University. After completing his doctorate, Paulo Oliveira spent more than three years working at the University of Minnesota Medical School, Duluth, USA, where he collaborated with several researchers and contributed to the publication of several peer-reviewed manuscripts. Paulo Oliveira's current research focuses on mitochondrial biology, investigating the alteration of cardiac mitochondrial function by physical activity and diet, cardiac mitochondrial dysfunction and cell death caused by anti-neoplastic agents, mitochondrial alterations during cancer stem cell differentiation and carcinogenesis or rational designing and validation of mitochondria-directed antioxidants. Paulo has over 300 peer-reviewed publications and many collaborations in Europe, Africa, and the USA. He has also received several prizes from the Portuguese Cardiology Society for his work on cardiac mitochondrial research. Besides research, Paulo Oliveira is often involved in teaching at the Department of Life Sciences, University of Coimbra, as well as in other Universities in Portugal and elsewhere, besides in numerous science communication activities. Of importance, he has maintained a consistent primary role in the organization of national and international scientific meetings, including the International Courses in Toxicology (2005-2010 in Coimbra), Annual Meeting of the European Society for Clinical Investigation (2013, Albufeira, Portugal and 2019, Coimbra, Portugal), the 2014 Meeting of the Portuguese Biochemical Society, and FEBS Advanced Lecture Courses in Oncometabolism (2017, Figueira da Foz, Portugal and 2019 Luso, Portugal). From May 2019 to June 2022, Paulo Oliveira was also President of the European Society for Clinical Investigation, after being its Vice-President for 2 years. Paulo Oliveira has also been a reviewer for more than 40 scientific journals and over 10 different funding agencies, including the European Commission (Research

Executive Agency) and the Portuguese Foundation for Science and Technology. His research group is supported by competitive national and international funding agencies, including the Portuguese Foundation for Science and Technology, the European Commission, and private foundations. Paulo is also co-founder of the start-up MitoTAG and is co-inventor in three patents. Since 2020, Paulo is Vice-President of the CNC – Center for Neuroscience and Cell Biology, University of Coimbra, Portugal and Coordinator of the Doctoral Program in Experimental Biology and Biomedicine at the same University.

Imagiologia molecular: da química à clínica

Antero Abrunhosa

ICNAS - Instituto de Ciências Nucleares Aplicadas à Saúde
Universidade de Coimbra, Coimbra, Portugal

Abstract

A Imagiologia molecular tem a capacidade de gerar imagens paramétricas quantitativas que descrevem vias metabólicas e interações moleculares no corpo humano. Na base desta ciência multidisciplinar está a utilização de moléculas, como os radiofármacos, capazes de agir como biomarcadores de imagem que nos permitem estudar os processos moleculares subjacentes às doenças humanas. Os radiofármacos são uma poderosa ferramenta de translação entre a química e a clínica. Podem ser usados para identificar alvos moleculares para terapêutica, confirmar mecanismo de ação, ajudar no desenvolvimento pré-clínico de novos medicamentos, abrir a porta para os estudos em humanos, fornecer parâmetros farmacocinéticos críticos e ajudar a determinar a eficácia e a segurança em todas as fases clínicas. Nesta apresentação, vamos dar exemplos de como, utilizando técnicas de imagem molecular como a PET (Tomografia por Emissão de Positrões), os radiofármacos podem ser utilizados em todas as fases da investigação translacional, da química à clínica.

Lecturer's resumé

Antero Abrunhosa é licenciado em Bioquímica (1992) e Mestre em Eng. Biomédica (1996) pela Universidade de Coimbra. Realizou os estudos de Doutoramento no centro PET do Hospital de Hammersmith em Londres sob a supervisão do Prof. Terry Jones (2002). Entre 2000 e 2009, ajudou a projetar e supervisionou a construção do Instituto de Ciências Nucleares Aplicadas à Saúde (www.uc.pt/icnas), uma Unidade Orgânica de Investigação da Universidade de Coimbra (UC) dedicada à Imagiologia Molecular e à Investigação Translacional. É atualmente Diretor do Instituto e responsável pelo Laboratório de Radioquímica e Radiofarmácia.

Mentor da ICNAS Pharma, uma empresa do Grupo UC, é Gerente e Diretor de Produção desde a sua fundação em 2009. A empresa foi pioneira em Portugal na produção de radiofármacos para a PET com a introdução no mercado nacional em 2012 da Fluodesoxiglucose [18F] UC, à qual se seguiram outros 6 produtos, um dos quais, entretanto também aprovado em Espanha Membro da Farmacopeia Europeia (Grupo 14), é perito da Agência Internacional da Energia Atómica (IAEA) em diversas comissões técnicas e missões internacionais. Tem atualmente patentes ativas na Europa, nos Estados Unidos e no Japão.

Glioblastoma Game-Changers: cutting-edge treatment using superselective nanoparticles

Diana Matias

iMM - Instituto de Medicina Molecular João Lobo Antunes
Lisbon, Portugal

Abstract

Glioblastomas are highly lethal and incurable primary brain tumors that affect both adults and children. The failure of traditional therapies can be attributed to the presence of the blood-brain barrier (BBB). This selective gatekeeper controls the transport of brain-specific molecules and restricts the entry of non-brain cells, including immune cells. However, due to aggressive tumor growth, glioblastoma cells modulate the BBB, forming a complex network of blood vessels known as the blood-tumor barrier (BTB), which supports their proliferation. Our research has demonstrated that transport mechanisms within the BTB are affected, potentially influencing treatment outcomes. To overcome these challenges, we have explored how polymeric nanoparticles (NPs) can circumvent BTB restrictions. Furthermore, glioblastomas are characterized by a "cold" immune profile, hindering progress in glioblastoma immunotherapies. This is primarily due to the regulatory recruitment of immune cells, limited infiltration of cytotoxic T cells, and the release of immunosuppressants that enable tumors to evade immunological surveillance.

Our strategy involves activating T cells and modulating the immunosuppressive tumor microenvironment to trigger a potent antitumor immune response. Nevertheless, leveraging the immune system's potential to combat brain tumors presents challenges and opportunities for pioneering therapeutic approaches. As a result, our research is focused on developing superselective biodegradable nanoparticles and promoting T cell activation and engagement with tumor cells, ultimately leading to the induction of glioblastoma cell death.

Lecturer's resumé

Diana Matias has acquired diverse knowledge and skills in various fields, particularly in biological and material sciences, focusing on nanomedicine. Her interest in biomedical research began during her undergraduate studies in biochemistry at Evora University in Portugal. She was awarded a scholarship that allowed her to conduct a project exploring stem cells in glioma at the Institute of Biomedical Sciences in Brazil. After returning to Portugal, she pursued a master's in biomedical research at the University of Coimbra. During this time, she delved into neurobiology, specifically studying brain tumours and their resistance to therapies. She also gained experience as an assistant lecturer in Molecular and Cell Biology at the University of Coimbra. After completing her master, she pursued a Ph.D. in morphological sciences at the Institute of the Brain and the Federal University of Rio de Janeiro in Brazil. Her Ph.D. thesis focused on GB heterogeneity, therapeutic approaches, stem-like cancer cells, and signalling pathways involved in microenvironment interactions. She contributed significantly to understanding the proteins involved in glial to mesenchymal transition and the interaction between GB and microglial cells. Throughout her academic journey, she has published several research papers and review articles in esteemed journals, covering topics such as the Wnt signalling pathway, the role of Sox2 and connexins in GB stem-like cells, and novel therapeutic approaches for GB treatment. She has received recognition for her research, including an honourable mention for their Ph.D. thesis and an indication for a prestigious award in Brazil. In addition to her research work, she has actively participated in international projects, managed the laboratory, and demonstrated solid scientific writing skills. She has also held roles as a postdoctoral researcher, collaborating on multidisciplinary projects in cancer and neuroscience. She expanded her expertise in nanomedicine during her postdoc position at University College London, focusing on developing targeted drug delivery systems for glioma treatment. Diana has been actively involved

in collaborations with experts in the field and has established her research line in the lab. Furthermore, she has demonstrated leadership skills by supervising masters and Ph.D. students and establishing collaborations with various institutions and sectors, including healthcare systems and pharmaceutical companies. Diana's critical writing skills are evident through their publication record, including scientific articles, book chapters, and reviewer and guest editor contributions. Diana has a rich academic and research background, expertise in multiple disciplines, and a strong track record of contributions to neuro-oncology and nanomedicine. She was recently awarded "la Caixa"; Junior Leader fellowship by the La Caixa Foundation, which allowed her to establish her research line at IMM (Lisbon, Portugal). She has been developing new nano-immunotherapies for brain tumors.

pBAE polymers: a new nano-delivery platform of nucleic acids for targeted therapies applications

Cristina Fornaguera Puigvert

Insitut Químic de Sarrià (IQS)
Ramon Llull University, Barcelona, Spain

Abstract

Immunotherapies and targeted therapies are becoming the next-generation standard of care therapeutics for many unmet medical needs. Although traditional small molecules could be used for these purposes, in the last days, there is no doubt on the enhanced performance that nucleic acids could bring to this field. Beyond the application of viral vectors for monogenic diseases treatment and mRNAs for infectious diseases prophylaxis, it is now the time they can be used for neural diseases therapeutics, rare disorders treatments and tumor therapeutic vaccination, among others.

However, nucleic acids have still some drawbacks to be overcome. Their stability in biological environment is compromised by the presence of nucleases. In parallel, being bigger macromolecules as compared to small drugs, they are easier recognized by the immune system and prematurely cleared up from circulation. Thus, the use of a nanometric carrier system that can overcome both issues, while ensuring a safe and efficient therapy is an urgent need.

Among possible nanocarriers, polymeric nanoparticles, and specifically, our proprietary oligopeptide end-modified poly (beta-aminoester) polymers (pBAE) stood as promising carriers, not only for nucleic acids, but also for different type of viral vectors that can be used for therapeutics. Thus, pBAE polymers stand as a novel platform with demonstrated safety and efficacy for the direct in vivo delivery of nucleic acids for therapeutics. We have already demonstrated the possibility to selectively target the nanoparticles to different cells of interest (i.e. tumor cells) while allowing a non-invasive administration thanks to their enhanced crossing of biological barriers (i.e. blood-brain barrier). Additionally, we have demonstrated the potential of our technology for various diseases, such as oncolytic virotherapy and blood-brain barrier crossing.

Lecturer's resumé

Dr. Fornaguera is a biotechnologist by training. After finishing her final degree thesis, she completed a master's degree in respiratory medicine, entering into what would later become her area of expertise: the use of nanomedicine as a controlled release system for drugs, mainly for respiratory diseases. Her doctoral thesis focused on the design of polymeric nanoparticles to cross physiological barriers, the blood-brain barrier in that case, thus avoiding the use of highly invasive administration routes and allowing non-invasive treatments. She then completed an industrial postdoctoral degree, during which she consolidated her knowledge and came into contact with her other two passions: teaching and tech transfer. Since 2018, the year in which she achieved a professor position at IQS, she has combined research and teaching in nanomedicine, biomaterials, and immunology.

Empowered by her experience, knowledge and proactivity to pursue with biomedical research, she started an industrial postdoc at the startup Sagetisa. Currently, she is the leader of the NanoImmunoTherapies Unit, at Insitut Químic de Sarrià (IQS), from the Ramon Llull University (URL), where, in addition to the numerous research projects she is leading, she also develops teaching, innovation, and dissemination. She is the coordinator of the Biomedical Science undergraduate degree.

Efeitos bioquímicos e metabólicos da administração de farinha de bagaço de uvas em modelo animal de Diabetes Mellitus Tipo 2

Raphaella Cassol Piccoli

Universidade Federal de Pelotas
Brasil

Abstract

Concurrently, there has been a growing interest within the scientific community in investigating the effects of natural compounds on non-communicable diseases, such is diabetes, prompting attention to grapes (Vitis sp.), a widely cultivated crop primarily for winemaking purposes. Notably, 'Arinto' and 'Touriga Nacional' are prominent grape varieties in Portugal, renowned for their consumer acceptance. Grape pomace (GP), a by-product of winemaking, comprising skins, stems, seeds, and other residues, is rich in bioactive compounds and dietary fibers. GP can be processed into grape pomace flour (GPF) through drying and grinding. Its natural origin, easy application, and abundant bioactive compounds and fiber make it an intriguing subject for further investigation in T2DM research. Our study using Adult male Wistar rats aims to explore GPF's from 'Arinto' and 'Touriga Nacional' varieties potential in developing preventive or adjunct therapeutic interventions for individuals affected by this metabolic disorder.

Lecturer's resumé

Raphaela, having graduated from the Federal University of Pelotas (UFPEL) in 2022 with a degree in Nutrition, continued her academic journey by earning a Master's degree in Nutrition and Foods from UFPEL in 2023, specializing in the field of experimental nutrition. Currently, she is pursuing her doctoral studies in the Program of Postgraduate Studies in Biochemistry and Bioprospecting at the same institution. Since her undergraduate studies, she has been dedicated to investigating the effects of natural products in treating metabolic disturbances. Throughout her academic journey, she has gained extensive experience in conducting bioassays, proficiently managing and utilizing laboratory animals, designing and implementing experimental models to study metabolic diseases, and formulating and administering experimental diets. Her contributions include numerous presentations at scientific conferences, honorable mentions, and a published review article. In recent years, she has focused on studying the effects of administering grape pomace flour (from the Arinto and Touriga Nacional grape varieties) in animal models of metabolic diseases, exploring their diverse manifestations.

A patient-derived hepatocellular carcinoma multicellular spheroid model for screening of anti-cancer treatments

Nuno Almeida

HookeBio
Shannon, Ireland

Abstract

Liver cancer is among the leading and fastest rising cause of cancer-related death worldwide. Hepatocellular carcinoma (HCC) is the most frequent liver cancer and arises in the context of chronic fibrotic liver diseases. Current treatment options for HCC are still unsatisfactory. While several new compounds for HCC treatment have been recently approved, the overall response rate remains limited. HCC is characterized by high heterogeneity among the tumors and the HCC disease biology following treatment is still only partially understood. To better understand the mechanisms of treatment response and resistance, we developed a novel patient- derived spheroid model. Using a large series of different readouts, we show that patient-derived HCC spheroids recapitulate the heterogeneity of HCC and model the tumor microenvironment. Applying functional studies, we show that this patient- derived HCC spheroids can be used to study response to cancer therapeutics and their effect of cellular signaling. In conclusion, this simple and robust model will be useful to better understand the tumor biology in patients and may ultimately contribute to novel approaches treatment approaches including the development of strategies for personalized medicine.

Lecturer's resumé

Nuno Almeida holds a BSc (2014) and a MSc (2016) in Biochemistry, both obtained at Faculty of Sciences and Technology, University of Coimbra (FCTUC), Coimbra, Portugal. He was also a research fellow in the Pharmacology and Therapeutics group at Center for Biosciences & Health Technologies (CBIOS), Lisbon, Portugal (2017-2018). In 2023, he completed a PhD in life sciences at the University of Strasbourg, France, focusing on the study of liver cancer patient-derived spheroid models for drug screening. His research expertise is based on the field of oncology and in vitro 3D models, covering several areas in oncobiology and cancer therapeutics. Currently, he is a Senior Research Scientist at HookeBio, an Irish start up company working in the field of microphysiological systems for drug screening.

Plants4Health: da etnomedicina às soluções de saúde baseadas em plantas

Célia Cabral

CBIOS Lusófona's Research Center for Biosciences and Health Technologies
Universidade Lusófona, Lisbon, Portugal

Abstract

Segundo dados da Organização Mundial de Saúde (OMS) estima-se que 65-80% da população mundial dependa das plantas medicinais no que se refere à atenção primária em saúde, e uma grande parte tem inclusive nas plantas a única fonte de medicamentos. Estes dados comprovam que as plantas medicinais constituem uma enorme fonte de moléculas potencialmente bioativas. Prova disso também é a percentagem considerável de medicamentos que exigem prescrição médica e que têm na sua constituição moléculas derivadas de plantas. São enumeradas apenas a título de exemplo, alguns princípios ativos bem conhecidos derivados de plantas: morfina (analgésico isolado em 1816 da Papaver somniferum L.); quinina (antimalárico isolado em 1820 da Cinchona pubescens Vahl e da Cinchona calisaysa Wedd.); colquicina (antigotoso isolado em 1820 do Colchicum autumnale L.); atropina (midriático isolado em 1831 da Atropa belladonna L.); efedrina (broncodilatador e descongestionante isolado em 1887 de espécies do género Ephedra L.); vincristina e vimblastina (citostáticos isolados nos anos 50 do séc. XX do Catharanthus roseus (L.) G. Don); galantamina (inibidor da acetilcolinesterase, usado na doença de Alzheimer isolado em 1952 do Galanthus woronowii Losinsk.) e paclitaxel (citostático isolado em 1971 do Taxus brevifolia Nutt.).

Todavia, há um longo caminho desde que se identifica uma planta com propriedades medicinais, até se caraterizar quais os constituintes que têm potencial terapêutico e até efetivamente se poder produzir e comercializar um medicamento, mas essa investigação é fundamental para se conseguirem obter novos constituintes mais efetivos e com menor número de efeitos secundários. Os estudos farmacognósicos que ligam o passado e o presente das plantas com interesse medicinal são de grande relevância uma vez que constituem uma articulação importante entre a história da farmácia e da medicina e o atual interesse na identificação e validação de novos compostos naturais bioativos.

O grupo de investigação liderado por Célia Cabral, o Plants4Health: Phytochemicals, Metabolism and Disease, dedica-se à identificação de compostos bioativos provenientes de plantas medicinais com comprovada segurança e eficácia, e o estudo dos seus mecanismos de ação, com o objetivo da sua possível incorporação em formulações, desenvolvendo assim soluções de saúde baseadas em plantas, com fins farmacêuticos, cosméticos e alimentares (nutracêuticos).

Lecturer's resumé

Célia Cabral é doutorada em Biologia com especialização em Sistemática e Morfologia (2008), e tem uma carreira de quase 20 anos, com um percurso científico multidisciplinar e um historial de publicações sobre taxonomia vegetal, plantas medicinais, etnobotânica, fitoquímica , doenças não transmissíveis, soluções de saúde baseadas em plantas e comunicação de ciência.

É investigadora na Faculdade de Medicina da Universidade de Coimbra (FMUC) e professora convidada na Universidade Lusófona, Lisboa. Na FMUC coordena o grupo de investigação Plants4Health: phytochemicals, metabolism and disease, focado no estudo de fitoquímicos de origem natural, pretendendo desenvolver soluções de saúde à base de plantas.

Segundo a Scopus, tem 56 artigos, 1512 citações e índice h 19. Orienta vários alunos nacionais e internacionais de doutoramento, de mestrado e vários alunos de licenciatura. É revisora de quase 50 periódicos e pertence ao conselho editorial de diversas revistas, incluindo Pharmaceuticals e Phytomedicine. É avaliadora de organismos de financiamento, incluindo Federação Valónia-Bruxelas (Bélgica), CFCA (Letónia), ANI (Portugal), UEFISCDI (Roménia), Centro Nacional de Ciência (Polónia) e Comissão Europeia. Foi PI do projeto recentemente finalizado: CôaMedPlants - COA/BRB/0019/2019 e é membro da equipa de diversos projetos em execução.

From computational drug discovery to protein design

Bruno Lourenço da Silva Víctor

FCUL
Lisbon, Portugal

Abstract

In this talk Bruno L. Victor will overview two different projects. The first delves into the intricate world of aquaporin proteins, seeking out novel active molecules poised to revolutionize cancer treatment. Meanwhile, the second expedition charts a course against African swine fever, wielding computational protein engineering as a potent tool to forge innovative vaccines and diagnostic solutions.

Lecturer's resumé

Bruno L. Victor is currently a Computational Medicinal Chemist at CoLab AccelBio, an Invited Auxiliar Professor at Departamento de Química e Bioquímica, Faculdade de Ciências, Universidade de Lisboa (FCUL) and a Principal Investigator at BioISI research center.

He got his degree in Biochemistry from the Faculdade de Ciências e Tecnologia da Universidade de Coimbra and his PhD in Biochemistry from Instituto de Tecnologia Química e Biológica (ITQB), Universidade Nova de Lisboa (UNL). After performing an initial Post-Doc also at ITQB-UNL, he then moved to BSIM therapeutics, as a computational chemist. He was then awarded with two Post-Doc fellowships at FCUL and Faculdade de Farmácia da Universidade de Lisboa (FFUL), until he returned to FCUL as an Principal Researcher. In 2023 he joined Zymbol Biomodeling, a biotech company dedicated to Protein discovery and engineering for Biotechnological applications. In 2024, he became a Computational Medicinal Chemist at CoLab AccelBio, where he is responsible for applying computational medicinal chemist methods to boost early-stage drug discovery projects to future technological transfer applications.

Beating hard-to-treat cancer with a first-in-class inhibitor of DNA damage response

Lucilia Saraiva

Faculty of Pharmacy, University of Porto
LAQV/REQUIMTE
Porto, Portugal

Abstract

Our team produced, characterized, and patented new anticancer agents, of which BBIT20 is the lead. BBIT20 is a first-in-class disrupter of the BRCA1/BARD1 interaction, leading to BRCA1 degradation and subsequent depletion of homologous recombination DNA damage repair. In vitro and in vivo data showed its great potential against wild-type- or mutBRCAs triple- negative breast, ovarian, prostate, and pancreatic cancer. BBIT20 is also a strong inhibitor of the multidrug resistant P-glycoprotein. This singular mode of action justifies its high efficiency against a broad range of cancer patients (regardless of BRCA status), also overcoming the emerging resistance to standard-of-care therapy. BEAT Therapeutics intends to bring BBIT20 closer to the clinic, gathering additional data relating to its toxicity and pharmacokinetics in clinically relevant cancer models.

Lecturer's resumé

Lucília Helena Ataíde Saraiva is Associate Professor with Aggregation at the Faculty of Pharmacy of University of Porto, and Principal Investigator at the REQUIMTE Research Centre, leading the Drug Discovery & Development Unit.

She is focused on cancer pharmacology and drug discovery. She has disclosed new anticancer drug candidates for personalized therapy (such as BBIT20), which are the basis of one international and two national patents granted, and four international patent applications. She is co-founder and CSO of the startup Beat Therapeutics, which explores the anticancer drug candidate BBIT20 aiming to take it into clinical trials. She received 37 awards related to innovation and entrepreneurship. She had 26 funded projects and successfully coordinated 13. She published 107 indexed peer-reviewed international papers. She has successfully concluded the supervision of 20 Master students and 16 PhD students. She is Editor of three international journals with scientific refereeing in Pharmacology, Oncology and Biotechnology.

Non-canonical targeting of non-conventional targets

Mattia Mori

Siena University
Siena, Italy

Abstract

G-quadruplex (G4) are non-canonical DNA or RNA secondary structures that are emerging as prosing targets in the development of innovative anticancer and antibacterial agents. In the search of selective G4-targeting chemotypes, natural compounds have been thus far poorly explored, though representing appealing candidates due to the high structural diversity of their scaffolds. A high diversity in house library composed of ca. one thousand individual natural products was investigated through a combination of molecular modelling and experimental assays.

a) Five hit binders of telomeric and oncogenic G4s, i.e., Bulbocapnine, Chelidonine, Ibogaine, Rotenone and Vomicine were identified. Biophysical studies unambiguously demonstrated the selective interaction of these compounds with G4s compared to duplex DNA. The rationale behind the G4 selective recognition was suggested by molecular dynamics (MD) simulations. From biological assays, Chelidonine and Rotenone emerged as the most active compounds of the series against cancer cells, also showing good selectivity over normal cells. In a follow-up optimization study, some analogues of bioactive G4 binders were tested. Among them, Dicentrine was found to thermally stabilize telomeric and oncogenic G-quadruplexes without affecting the control duplex. MD simulations indicated that Dicentrine preferentially binds the G-quadruplex groove or the outer G-tetrad for the telomeric and oncogenic G4s, respectively. Finally, biological assays proved that Dicentrine is highly effective in promoting potent and selective anticancer activity by inducing cell cycle arrest through apoptosis, preferentially targeting G-quadruplex structures localized at telomeres.

b) A combination of MD and biophysics and mutagenesis experiments is currently exploited in the elucidation of structural details of bacterial G4s, with the aim of designing specific and effective stabilizers endowed with antibacterial properties.

Taken together, these data further validate G4s as profitable targets in anticancer therapy as well as candidate targets in antibacterial drug discovery.

Lecturer's resumé

Mattia Mori is an Associate Professor in medicinal chemistry at the University of Siena, Department of Biotechnology, Chemistry, and Pharmacy since August 2021. Prior to this, he was a Senior Researcher at the same university from 2018 to 2021, a Researcher at the Italian Institute of Technology (IIT) from 2017 to 2018, and a postdoc at IIT from 2012 to 2017. His research focuses on understanding the structural and conformational features of target macromolecules, such as proteins, nucleic acids, and biological membranes, for pharmacological interventions. He aims to identify and optimize small molecules that can modulate the activity of these targets in pathological contexts, using computational and biophysical tools.

Mattia Mori earned his degree in medicinal chemistry from the University of Florence in 2004 and completed his PhD in structural biology at the same university in 2009, with co-tutorship by the Universities of Utrecht and Frankfurt. In 2022, Mattia Mori obtained the National Qualification (Abilitazione Scientifica Nazionale) as Full Professor in Medicinal Chemistry, sector 03/D1 (CHIMICA E TECNOLOGIE FARMACEUTICHE, TOSSICOLOGICHE E NUTRACEUTICO-ALIMENTARI).

He is a member of the American Chemical Society (ACS) and the Italian Chemical Society (SCI). His scientific achievements include more than 25 invited presentations, over 140 peer-reviewed publications, 5 patents, and 3 book chapters. He has an H-index of 31 and has received 2,750 citations according to Scopus.

Antitumor studies of different diterpenoids and derivatives from Plectranthus spp

Eva Dominguez

CBIOS Lusófona's Research Center for Biosciences and Health Technologies, Universidade Lusófona
Lisbon, Portugal

Abstract

Cancer is a complex disease often treated with surgery, chemotherapy, radiation, and biological drugs, which can lead to adverse effects and drug resistance. Glioblastoma (GB), a common brain tumor, is particularly resistant to Temozolomide (TMZ), resulting in a poor prognosis. Thus, new treatments from natural sources are needed.

This presentation explores natural products, including plant-derived terpenes and compounds from animals (Zoopharmacognosy), as potential new drug sources. Plectranthus plants, rich in abietane diterpenes like 7α-acetoxy-6β-hydroxyroyleanone (Roy) and 6β,7β-dihydroxyroyleanone (DiRoy), will be presented. Bio-guided isolation from P. hadiensis identified Roy and DiRoy as major compounds with significant antiproliferative effects on GB cell lines.

Parviflorone D (ParvD) from P. ecklonii showed stronger anti-GB activity than TMZ, inducing apoptosis in tumor cells and inhibiting enzymes related to skin pathologies. Current studies focus on optimizing extraction, synthesizing derivatives, and understanding their mechanisms in vivo to develop these terpenes into new drugs.

In conclusion, this presentation highlights the potential of natural products, particularly terpenes from Plectranthus plants, as promising sources for new anticancer drugs. An educational practice is proposed to synthesize an improved antibiotic derivative of nalidixic acid using mechanochemistry, aiming to innovate and enhance teaching methodologies.

Lecturer's resumé

Eva Dominguez is an International Doctor with Honors in Health Sciences from University of Alcalá - UAH (Madrid, Spain) and Universidade Lusófona (ULTH) since 2023. Her thesis "Antitumor studies of different diterpenoids and derivatives from Plectranthus spp." was proposed for Extraordinary PhD Award. Currently, she works as Assistant Professor at UAH, where she participates teaching Pharmacognosy and Pharmacology in the Degrees of Pharmacy, Medicine and Nursery.

The use of animal models of neuropsychiatric disorders in studies of biological effects of herbal extracts

Tatyana Strekalova

Department of Pharmacology
University of Oxford & Neuroplast BV
Maastricht the Netherlandsl

Abstract

Genetically modified rodents and environmental models of neuropsychiatric disorders using mice and rats are routinely employed in translational studies with new potential therapies including herbal extracts. The availability of low-cost herbal medicines for economically disadvantaged communities is of particular importance for providing affordable healthcare in managing a broad range of medical conditions, including cancer, autoimmune disorders, and neurological and neuropsychiatric diseases. Choosing the optimal experimental design in this type of studies often remains a challenge. Our experiments using the standard laboratory mouse line C57BL6 in the ultrasound chronic stress depression model, the modified forced swim test as a mouse paradigm of post-traumatic stress disorder (PTSD), a "Western diet" paradigm of metabolic syndrome, and genetically modified FUS-tg mutants, a model of amyotrophic lateral sclerosis, suggest the adequacy of these preclinical approaches for studying the potential therapeutic effects of herbal medicines. These paradigms allow for addressing the potential anti-inflammatory, anti-oxidative, and neurotrophic properties of herbal extracts that may underlie their beneficial anti-stress and pro-regenerative effects. In a broader context, this branch of research demonstrates the importance of considering herbal remedies as highly relevant and promising because of its high medicinal and social relevance.

Lecturer's resumé

Dr Tatyana Strekalova, MD, PhD, is a Senior researcher at the Department of Pharmacology, University of Oxford. After a completion of her medical studies as a general practitioner, Tatyana moved to Hamburg, Center for Molecular Neurobiology. She than has worked in Mannheim and Aachen on translational models in Psychiatry and Neurology and since 2008 has worked at the Dept. of Psychiatry and Neuropsychology Maastricht University.

Currently, she is also a principle Scientist of Neurplast BV in Maatricht, a biotech company specialized on the stem cell therapy.

A Peek into Animation Film Making, Incorporating Microscopic Images

Natalie Woolf
Lusófona University Lisbon, Portugal

Abstract

"AH - while we wait" is a pilot project to research how animation film can contribute to the reduction of stress in hospital waiting spaces for children and young adults. To achieve this a team combining professors and students from the Animation and Psychology departments at Lusófona are working together to, firstly, explore the types of animation and image making that will be effective in stress reduction and secondly to make a short animation film to install and test in a partner hospital in Lisbon. Many approaches and ideas were discussed, and nature was identified as the most appealing theme. In this presentation Natalie Woolf will show the work that has been developed with the help of images produce with the microscope equipment at CBIOS. Attendees with be invited to discuss the work and offer suggestions on how the theme of nature could be expanded on.

Lecturer's resumé

Natalie Woolf is an Artist/Researcher/Professor teaching at Lusófona University since 2015. Currently active in both the Animation (MA & BA courses) and Communication Design (BA) departments, an integrated researcher at CICANT. In addition to her academic role, she continues her art practice at Atelier Concorde in Lisbon. Natalie holds a PhD in Design Products from Royal College of Art, and a BA in Fine Arts/Painting from Leeds Beckett University. Her current work includes two funded research projects on the role of animation in healthcare settings, and the development of various exhibitions and publications on the theme of expanded and experimental drawing as artistic practice and research in educational contexts.

Addressing the Mechanisms of toxicity of environmental pollutants to refine risk assessment: the 3 case-studies of mercury, polycyclic aromatic hydrocarbons and nanoplastics

Vasco Branco

iMed

Abstract

This talk will provide an overview of his work, including i) the study of the role of redox active systems (glutathione and thioredoxin) and nutritional factors, namely selenium, in mercury toxicity to develop mitigation strategies for neurodevelopmental toxicity, ii) the evaluation of nanoplastic toxicity to the gut epithelia and iii) the evaluation of the toxicity mechanisms of PAHs mixtures.

Lecturer's resumé

Vasco Branco got his PhD in Pharmacy (specialization in Toxicology) at the Faculty of Pharmacy University of Lisbon (2012) where he is currently Assistant Professor. His main research interests are within the realm of Environmental Toxicology namely in understanding the mechanism of action of several environmental pollutants. He is also very much interested in biomonitoring studies that provide human data to conduct chemical risk assessment. To date he has published 48 papers in reference journals in the field, including in Redox Biology, Free Radical Biology and Medicine, Toxicology and Applied Pharmacology, Ecotoxicology and Environmental Safety, Environmental Toxicology and Pharmacology, among others.