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cBIOS
UNIVERSIDADE LUSÓFONA
RESEARCH CENTER IN BIOSCIENCES & HEALTH TECHNOLOGIES

Science Sessions 2022

Catarina Rosado and L. Monteiro Rodrigues, eds.

CBIOS Science Sessions 2022

Integration of NEW Imaging Solutions from Optoaccoustic Tomography

Integração de Soluções Inovadoras de Imagem obtida com a Tomografia Optoacústica

Tiago Granja

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

7 January 2022

Abstract

This session will address the multiplicity of optoacoustic imaging. Imaging analysis has been prominent into Tiago Granja career and pivotal in actual bench to bedside research.

The clinical demand for optoacoustic technology will be discussed together with its extended possibilities compared to other well-established tomography imaging strategies. Developments required for deep tissue image acquisition, processing and analysis will be presented. Common anatomical structures and their relationship to natural chromophores will be highlighted.

The most used optoacoustic chromophores in clinical environment will be shown together with their most used applications and routes of administration.

The CBIOS seminar presented by Tiago Granja will engage the audience with research carried in CBIOS over the new ways to study microvasculature compared to clinical standards (e.g.,laser-doppler-fluorimetry and (LDF) and TiVi regional Changes in Red Blood Cell Concentration (CRBC)). Engaging possibilities of acquiring deep-tissue 3D images and guidelines for image processing and evaluation will be given. Ultimately, future perspectives will be presented and new applications proposed for clinical and pharmacological scenarios.

Lecturer's resumé

Tiago Granja has graduated in Biotechnology engineering at Lusófona University (Lisbon, Portugal), and later took a Master graduation in Molecular and Cellular Biology at Coimbra University (Coimbra, Portugal), from where he moved to Bristol, UK to start his PhD at the MICF – Myocardial Inflammation and Cellular Function Research group at the Bristol Royal Infirmary. Together with Professor Zackarowski he has contributed with new insights on the role of innate immune receptor TLR4 in synchronization of the HPA axis and the myocardial homeostasis. For implementation of animal models in Goethe University Frankfurt - Frankfurt am Main – Germany, Tiago Granja accomplished his PhD in Theoretical Medicine within a consortium with Tübingen University Klinik – Germany. Together with Professor Rosenberger in Tübingen he has connected the concepts of neuro-immune synapse to inflammation of shock organs using animal models of acute and chronic inflammation. From those early observations, Tiago Granja has built a body of research dedicated to the role of Neuronal guidance Proteins in innate immunity, platelet function, monocyte recruitment, macrophage differentiation, to pathophysiology signaling of ARDS (Acute Respiratory Distress Syndrome) or IRI (Ischemia/reperfusion Injury). In 2021 Tiago Granja joined CBIOS at Lusófona University where he has embraced the chance of starting new research in immunology and microcirculation pathophysiology.

Toward the targeting of cancer biomechanical compliance: the biophysical toxicology approach

Rumo à conformidade biomecânica do cancro como alvo: a abordagem da toxicologia biofísica

Giorgia del Favero

University of Vienna, Vienna, Austria

21 January 2022

Abstract

Motility and response to mechanical cues benchmark cell physiological function. Likewise, modification of biomechanical compliance is related to disease progression. This is evident, for instance, in the onset of fibrotic lesions, scar formation, and pathological modification of tissue architecture. Most importantly, mechanotransduction can tune cell metabolism, proliferation and sensitivity to drugs/bioactives *via* activation of mechanically-driven biochemical pathways [1, 2]. Similarly, it is plausible that xenobiotics (comprising pharmaceuticals as well as noxious compounds) could exert beneficial/harmful effects on cell mechanotransduction as part of their mechanism of action. The presentation will focus on models for the assessment of cell mechanotransduction *in vitro* and on the use of biomechanical compliance as an endpoint for the evaluation of cellular sensitivity after exposure to chemicals.

References

1. Del Favero, G. and A. Kraegeloh, *Integrating Biophysics in Toxicology.* Cells, 2020. **9**(5): p. 1282.
2. Park, J.S., et al., *Mechanical regulation of glycolysis via cytoskeleton architecture.* Nature, 2020. **578**(7796): p. 621-626.

Lecturer's resumé

- In 2008 degree in Pharmaceutical Chemistry and Technology (Single cycle advanced degree, Faculty Pharmacy- University of Trieste, Italy). PhD obtained from the same university in 2012.
- From 2012 to 2014 Post-doctoral fellowships (University of Trieste and University of Arizona)
- European Registered Toxicologist since 2014
- Since 2014 at the University of Vienna and since 2019 Head of the Core Facility Multimodal Imaging of the Faculty of Chemistry and PI-Biophysical Toxicology Unit.
- *Venia docendi* (Habilitation) in the subject Toxicology obtained in 2021.

Key areas of expertise include molecular pathophysiology and toxicology, Development of novel imaging workflows and microscopy-based tools and Integration of proteomics/metabolomics workflows with imaging for systems toxicology and biophysics.

Gut-skin axis: modulation by probiotics

Eixo intestino-pele: modulação por probióticos

Emilia Alves

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

4 March 2022

Abstract

Ingestion of probiotics has shown beneficial effects on skin health, thus supporting the potential gut-skin axis. Kefir is a traditional fermented food with numerous putative health benefits, thereby presenting itself as a probiotic of the utmost interest in the gut-skin relationship.

Ingestion of kefir produced under household conditions promoted an improvement in the cutaneous barrier function in both healthy and atopic skin, with an additional improvement in the degree of severity of atopic dermatitis, and also an improvement on functional gastrointestinal symptoms, all of which were verified only in the groups that ingested kefir, on both healthy and atopic skin subjects.

Overall, this work contributes to establishing a link between regular consumption of kefir in the diet and better skin health, thus reinforcing the hypothesis of the beneficial effect of kefir on the skin through the gut-skin axis.

Lecturer's resumé

Emilia Alves has a degree in Nutrition Sciences and Chemical Engineering from Instituto Superior Técnico and a postgraduate degree in Metabolic Diseases and Eating Behavior from the Faculty of Medicine of Lisbon. She has been an assistant professor at Universidade Lusofona since 2014 and is completing her PhD. in Health Sciences at CBIOS – Research Center in Biosciences and Technologies. Emilia Alves is a member of the PIMENTO cost action CA 20128 "Promoting the Innovation of Fermented Foods" and her main areas of research concern the impact of food on human health, especially functional foods such as fermented foods.

Emilia Alves has more than 10 years of experience as a nutritionist in the clinical area and has been part of the clinical staff of the NutriAção project – Clinica de Nutricão e Alimentação at Universidade Lusofona, since it started in 2017.

Emilia Alves publishes in several international peer-reviewed journals and is a reviewer for several international Q1 and Q2 journals.

Histopathology features in ARDS models. What to measure and How?

Características histopatológicas nos modelos ARDS. O que medir e como?

Pedro Faísca

Instituto Gulbenkian Ciência; CBIOS Lusófona's Research Center for Biosciences and Health Technologies, Lisbon, Portugal

18 March 2022

Abstract

Acute respiratory distress syndrome (ARDS) is a severe pulmonary reaction, incited by many causes (including SARS-CoV-2) that result in common histopathological alterations to the lungs, collectively termed diffuse alveolar damage.

A few years ago, a consensus was available regarding the criteria of ARDS that should be evident in an experimental animal model, including mice. However, in our opinion, the methodology involved in the histopathology assessment is prone to bias as well as inter and intra-observer variability.

Unbiased and accurate quantification of lung lesions is crucial for making valid comparisons in experimental studies. Stereology is considered the gold standard in microscopical quantitative studies, as it relies on mathematical principles for obtaining representative sampling and estimating 3D parameters from 2D sections.

Here, we present an optimization of a protocol designed for stereological quantification in mouse lungs, focused on the estimation of different lung volumes, surface area, and blood-air barrier thickness in B6 mice to serve as control for future ARDS murine models.

Lecturer's resumé

- Médico Veterinário pela Universidade de Trás-os-Montes e Alto Douro em 2000.
- DEA pela Universidade da Bélgica em 2002, na área da Patologia Experimental.
- Doutorado em Ciências Veterinárias pela Universidade de Liège, Bélgica na área da Patologia Veterinária em 2007.
- Professor auxiliar na Faculdade de Medicina Veterinária desde 2005 nas unidades curriculares de Anatomia Patológica.
- Responsável pelo Laboratório de Histopatologia da FMV-ULHT desde 2010.
- Responsável pelo Departamento de Histopatologia do Laboratório DNAtech, desde 2007.
- Chefe do serviço de Histopatologia do Instituto Gulbenkian de Ciência desde 2017 e Patologista Experimental do mesmo serviço desde 2015.
- Publicou mais de 30 de artigos em revistas científicas internacionais indexadas com revisão por pares e dois capítulos em livros científicos.
- Foi Presidente da Sociedade Portuguesa de Patologia Animal entre 2015-2019
- Membro da Sociedade Europeia de Patologia Veterinária desde 2005
- Editor da Revista Lusófona de Ciência e Medicina Veterinária desde 2007
- Co-Presidente da Comissão Organizadora Local do Encontro Europeu Conjunto da ESVP-ECVP-ESVCP-ECVCP Lisboa 2023

Culicoides - A multidisciplinary case

Culicoides - Um caso de multidisciplinariedade

David Ramilo

Faculdade de Medicina Veterinária, Universidade Lusófona de Humanidades e Tecnologias, Lisbon, Portugal

28 March 2022

Abstract

Na palestra Culicoides – Um caso de multidisciplinariedade falarei do trabalho que desenvolvi durante o meu trabalho de doutoramento, realçando a importância da colaboração com várias equipas científicas, nacionais e internacionais, que permitiram, entre outros resultados, a descoberta de uma nova espécie para a ciência.

Lecturer's resumé

Mestrado Integrado em Medicina Veterinária em 2008 com o título: "Subtipificação do Parvovírus canino e felino", FMV, Universidade Técnica de Lisboa.

Doutoramento em Ciências Veterinárias em 2016 com o título; "Phenotypic and genetic characterization of Culicoides (DIPTERA: CERATOPOGONIDAE) in Portugal and comparison of the effect of pyrethroid insecticides in their control", FMV-ULisboa.

Pós-doutoramento (2017-2020): Continuação dos estudos morfológicos de insetos Culicoides e ação de inseticidas nos seus órgãos sensoriais

Pós-graduação em Pedagogia no Ensino Superior (2019-2020): 20 valores

Professor Auxiliar na Faculdade de Medicina Veterinária da Universidade Lusófona nas seguintes UCs: Biomatemática, Imunologia, Higiene, Segurança e Saúde I, Patologia e Clínica das Doenças Parasitárias II, Uma Só Saúde – One Health (Opcional) e Estágio (Apoio estatístico).

Residente do Colégio Europeu de Parasitologia Veterinária

Presidente da Comissão de Ética e Bem-Estar da Faculdade de Medicina Veterinária, Universidade Lusófona

Membro da direção dos Veterinários sem Fronteiras Portugal – Tesoureiro

Disclosing the mechanisms underlying the beneficial effects of berries-driven (poly)phenols in *in vitro*, as well as *in vivo* cardiovascular models

Descobrindo os mecanismos subjacentes aos efeitos benéficos dos (poli)fenóis de bagas in vitro, bem como em modelos cardiovasculares in vivo

Andreia Gomes

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

8 April 2022

Abstract

Cardiovascular diseases (CVD) constitute a major health problem accounting for about 30% of deaths worldwide. Diet, one of the most important lifestyle risk factors, can strongly influence CVD progression and might afford a promising prophylaxis. Epidemiological studies have shown a consistent beneficial relationship between the consumption of fruits and vegetables, rich sources of (poly)phenols, and a reduced risk of CVD susceptibility. In the present study, the beneficial effects a berry mixture in hypertensive rats was explored, namely the metabolic fate of (poly)phenols, the effects of a (poly)phenol-enriched diet and a high salt diet in the modulation of the rat's gut microbiota as well as their beneficial effects in kidney disease progression. Finally, the possible mechanisms of action for some of the (poly)phenol metabolites identified in rats, that were also found in circulation in humans that consumed the same berry mixture were evaluated in vitro towards an inflammatory insult in endothelial cells.

Lecturer's resumé

Andreia Gomes graduated in biochemistry and completed her master's in biotechnology by FCT-UNL. During her PhD in Molecular Biosciences, she focused on the understanding of the molecular mechanisms underlying the beneficial effects of (poly)phenol enriched diets in in vitro and in vivo cardiovascular models. Her work was awarded with 2 best oral communications, 2 best young poster communications and an honorable mention from Food and Nutrition awards in 2020. She offers proficiency in cell biology, particularly with different cell lines and primary cell culture techniques, and in different omics techniques: proteomics (2D-electrophoresis, Western blotting, size exclusion chromatography), metabolomics (UPLC-MS/MS, NMR, 16s rRNA gene sequencing).

Currently, Andreia is a postdoctoral researcher at the Translation Biology Laboratory at CBIOS-ULHT and through a multi-omics approach she wants to evaluate the capacity of (poly)phenol metabolites to mediate pancreatic islet cell reprogramming into insulin producers.

Skeletal muscle aging in different fiber types

Envelhecimento do músculo esquelético em diferentes tipos de fibra

Raquel Fernando

Universidade de Berlin, Berlin, Germany

22 April 2022

Abstract

O envelhecimento é um fenómeno irreversível caracterizado pela acumulação de stress oxidativo crónico, dano celular e agregados proteicos. O músculo esquelético é um dos primeiros tecidos afetados pelo envelhecimento, com perda progressiva de função e massa muscular a partir dos 30 anos de idade. Vários estudos demonstraram a acumulação de agregados proteicos em tecido muscular em diferentes modelos animais, bem como em seres humanos, sugerindo uma perda de proteostasia, especialmente no que diz respeito aos sistemas de degradação. Assim, este projecto foca-se em desvendar as diferenças entre fibras lentas oxidativas (do músculo Soleus) e fibras rápidas glicolíticas (presentes no músculo Extensor digitorum longus (EDL)) em termos de sistemas de degradação e como lidam com o stress oxidativo durante o envelhecimento. Estes músculos foram extraídos de ratinhos de 4 e 24 meses. No entanto, para além da perda de proteostasia, existem outros mecanismos que influenciam o envelhecimento do músculo. Para compreender estas alterações de uma forma sistémica, fizeram-se análises ao transcriptoma e metaboloma destes músculos. Estas abordagens fornecem certamente um quadro mais amplo do genoma e do network metabólico das fibras musculares. Sabe-se que as fibras do tipo IIb, representadas no músculo EDL, são conhecidas por serem mais susceptíveis ao envelhecimento e de facto, o músculo EDL revelou um maior número de genes e metabolitos alterados com o envelhecimento. Surpreendentemente, os processos mais afectados estão relacionados com vias de obtenção de energia. Deste modo, este trabalho investiga detalhadamente os possíveis mecanismos moleculares responsáveis por esta vulnerabilidade (manuscrito em preparação).

Lecturer's resumé

Raquel Fernando concluiu o curso de Ciências Farmacêuticas da Universidade Lusófona de Humanidades e Tecnologias de Lisboa em 2016. Após o término da tese de mestrado na área de investigação sobre propriedades biofísicas e biomecânicas da pele, ingressou num estágio internacional durante três meses, no departamento de Biologia, Química e Farmácia da Freie Universität em Berlim onde integrou um projeto de tecnologia farmacêutica relacionado com o desenvolvimento de implantes subcutâneos biodegradáveis com libertação prolongada de proteínas. Em Maio de 2016, começou como assistente de investigação no departamento de Toxicologia Molecular no Instituto de Nutrição Alemão, em Postdam. Desenvolveu dois projetos em paralelo, relacionados com o impacto do stress oxidativo e disfunção mitocondrial na formação de agregados proteicos e diminuição do processo de adipogénese, respetivamente. Em 2017, deu início ao doutoramento no mesmo grupo de investigação, onde se encontra atualmente. Durante o seu doutoramento, publicou três artigos científicos originais como primeira autora. A sua investigação foca-se no envelhecimento muscular, mais especificamente nas diferenças moleculares entre as fibras musculares.

Nanobiotechnology applied to chronic diseases: cases of cancer and diabetes

Nanobiotecnologia aplicada às doenças crónicas: os casos do cancro e da diabetes

Karina Marangoni

Institute of Experimental and Technological Biology – iBET, Lisbon, Portugal

29 April 2022

Abstract

The use of nanobiotechnology in chronic diseases therapy represents a major challenge in modern medicine. Nowadays, there are available a panoply of organic and inorganic nanomaterials, adjustable techniques, and instrumentation allowing the creation of a diversity of nanocarrier delivery systems (NDSs) with different forms and sizes. Despite the good progress of these nanomedicines, active targeting approaches are necessary to improve their therapeutic efficiency and to reduce systemic toxicity. To do that, a targeting moiety, as RNA aptamers - nucleic acid antibody-like, supplies a promising alternative to the common problems related to therapeutic molecules (ThM) delivery by NDSs. The site-directed delivery of ThM is made by the functionalization of these specific ligands on the NDSs surface, thereby creating specificity for the special characteristics of cell membranes or for an overexpressed target/receptor exposed to those cells. In the last decade, despite the continuous improvement, the functionalization of NDSs and the fabrication of “smart” nanocapsules is still in its early stage and numerous challenges are expected to impact this technology.

Lecturer’s resumé

Scientific researcher with a Ph.D. and master’s degree in Genetics and Biochemistry (conferred by the Universidade Nova de Lisboa), with 4 years of postdoctoral focusing on Oncobiology. With 18 years of experience in Research, Development, Innovation and Projects in the following areas: Nanobiotechnology, Bioengineering, Biochemistry, and Molecular and Cellular Biology. In the last years, I kept constantly updated by taking courses with an emphasis on different themes (production, maintenance, and use of experimental animals - training by REBIOTERIO | USP | CNPq, Brazil, immunotherapy, biosafety, cloning, NGS, molecular diagnostics of COVID-19, among others). I also acquired experience in co-supervised Master's and Ph.D. students, participating in examining boards, and ad hoc advisory, and collaborating with the preparation and management of projects approved with financial support, aiming the scientific and technological development and innovation of the country. I worked for more than 6 years as a professor at the Federal University of Uberlandia, teaching Genetics and Evolution, Molecular Biology, Toxicology, and Cell Culture subjects for Medicine, Biomedicine, and Biotechnology bachelors and postgraduate courses. I am currently part of the editorial board of 4 high-impact international journals. I committed myself intensively to the production of scientific knowledge and with that, I received numerous invitations to lectures around the world in this way, I was recognized as one of the 6 most voted scientists as one of the leading national and international leaders to receive the 1st Scientist and Entrepreneur Award of the year of the NanoCell Institute. I participated in the publication of 20 scientific articles in international indexed journals (with 249 citations and an H-index equal to 10), 1 book chapter, 1 book, and 2 patents, thus collaborating with translational scientific research institutions. Until January 2022, I worked as a contracted researcher at the Institute of Bioengineering and Biosciences of the Instituto Superior Técnico of the University of Lisbon, developing research activities within the scope of the scientific project "Delivery of penetrating cell-mediated p28 peptide nanomedicine for cancer treatment ". I am currently a contracted researcher at the Institute of Experimental and Technological Biology - iBET performing research within the project entitled “Islet Amyloid polypeptide (IAPP) Oligomerization and Diabetes”.

Identification and characterization of a nutraceutical protein isolated from lupine seeds, with anti-inflammatory and anti-tumor activities

Identificação e caracterização de uma proteína nutracêutica isolada de sementes de tremoço, com atividades anti-inflamatórias e anti tumorais

Ana Lima

FMV- ULHT Faculdade de Medicina Veterinária, Universidade Lusófona de Humanidades e Tecnologias, Lisbon, Portugal

6 May 2022

Abstract

Matrix metalloproteinases 9 (MMP-9) are regarded as important clinical targets due to their nodal-point role in inflammatory and oncological diseases; however effective non-toxic inhibitors have been difficult to find. We have isolated and characterized a small protein from Lupinus albus seeds exhibiting a potent inhibition against MMP-9 activities, both *in vitro* and *in vivo*.

The MMP-9 inhibitor (MMPI) was found to be an oligomer comprising fragments derived from two Lupinus seed storage proteins: δ-conglutin and, to a lower extent, β-conglutin. *In vitro* studies showed that this novel gelatinase inhibitor successfully impaired cancer cell invasion whilst reducing MMP-9 activity in a dose-dependent manner and with an EC50 of 10 µg.mL-1. *In vivo* studies showed the MMPI protein maintained its activities throughout digestion and significantly reduced colitis lesions. Moreover, in zebrafish cancer models the novel MMPI induced a significant reduction in cancer development and metastasis.

Overall, this novel type of MMPI was found to be edible, non-toxic, soluble in water, heat resistant, survives digestion and effectively reduces MMP-9

activities *in vivo,* strongly suggesting a high potential for functional/therapeutic diets.

Lecturer's resumé

Ana Lima is an assistant professor at the Faculty of Veterinary Medicine, Lusófona University. She completed her PhD degree in 2010 at University of Aveiro and developed her Postdoc in the area of food anticancer bioactivities at Instituto Superior de Agronomia. Her expertise resides mainly on proteomics and metabolomics, with a particular focus on bioactive compounds from food and plants for human and animal health, mainly focusing on inflammation and cancer preventive/ curative diets and natural alternatives to antibiotics and food disinfectants. She also works in the area of nutraceutical incorporation in functional foods. She participated in a total of 15 funded research projects, both national and European and has supervised several PhD, post-doc, and MSc students. She holds more than 40 publications, including book chapters and peer-reviewed papers. She has received the Born from Knowledge Award from the Food Nutrition Awards in 2018 and holds 3 international patents from her discoveries.

Molecular biophysics applied to the study of human healthy ageing

A biofísica molecular aplicada ao estudo do envelhecimento humano saudável

Maria João Sarmento

IMM - Instituto de Medicina Molecular, Lisbon Portugal

13 May 2022

Abstract

Aging is a major risk factor for many human pathologies. At a time when we are living longer than ever before, untangling the mechanisms of this biological deterioration is absolutely critical if we aim at providing a better quality of life for aging individuals. The loss of nuclear integrity, and the consequent defects in nuclear mechanics, are already among widely considered hallmarks of aging. In mammalian cells, the structural properties of the nucleus are maintained by the nuclear lamina (NL), especially lamin A (LA), and its interaction with the nuclear envelope (NE). The NE is mainly composed of phosphatidylcholine (PC) and phosphatidylethanolamine (PE) phospholipids, together with a series of other minor components, such as phosphatidylinositol phosphates (PIP), phosphatidylserines (PS) and sphingolipids (SL). However, the link between variations on the NE lipid content and altered biological functions within the nuclear compartment is only now starting to be explored. Here, we start to elucidate the role of specific lipid classes in maintaining the proper nuclear integrity during healthy aging. To that end, we isolated nuclei from human primary fibroblasts prepared from healthy individuals of young and old age, and Hutchinson-Gilford Progeria Syndrome (HGPS) patients. Cells from male and female individuals were used to account for any gender-related variability. Nuclei isolation was confirmed through atomic force microscopy (AFM), confocal microscopy, histology and transmission electron microscopy (TEM). Upon lipid extraction, lipidomics analysis through liquid (and gas) chromatography coupled with mass spectrometry (LC(GC)-MS) was carried out. Our results show significant differences in NE lipid composition as age progresses. Interestingly, there seems to be a general decrease in ether lipids in aged individuals. Ether lipids, especially plasmalogens, are known antioxidant molecules, and their decrease with age can be directly linked to the loss of nuclear integrity/ function. Moreover, other lipid classes such as sphingolipids appear to be altered, suggesting that aged cells might contain nuclei with significantly different bulk biophysical properties that could in principle affect many biological processes, from diffusion to the mechanical properties of the overall nuclear lamina.

Lecturer's resumé

MJS was awarded her PhD (2016, University of Lisbon) on membrane biophysics, with the main goal of understanding PIP2 organization in membrane mimetics and live cell membranes. Her PhD also included a 2-month stay at King's College London to perform time-resolved fluorescence anisotropy imaging, a setup that she later helped to implement at the home laboratory. To pursue the scientific topic of her interest, MJS moved to IIT (Genoa, Italy) and carried out her first PostDoc (2016-2017) on the application of STED-based approaches to the visualization of different nuclear structures within intact cell nuclei. She later moved to the J. Heyrovský Institute (Prague, Czech Republic) where she used single-molecule fluorescence microscopy and spectroscopy to unravel the molecular details behind the protective role of gangliosides on the membrane-mediated oligomerisation of amyloidogenic peptides involved in the onset of neurodegenerative diseases. MJS was also involved in the development and implementation of new FRET-based approaches to study membrane organization and lipid nanodomain formation. In 2019, she was awarded both the CEECIND (FCT funding, national PT) and a Marie-Curie fellowship, to study the molecular determinants of healthy human aging. MJS then moved back to Lisbon in June 2020, to Instituto de Medicina Molecular (iMM), where she is currently working to address lipid-lamin interactions in the nuclear compartment and their effect on the loss of nuclear structural integrity during age progression. She has now solid expertise in advanced and quantitative state-of-the-art biophysical approaches, including several fluorescence microscopy techniques (confocal, FRET, FLIM, FCS, FAIM, STED) and steady-state/time-resolved ensemble average fluorescence spectroscopy.

HLA-DR-expressing Cytotoxic T lymphocytes: a novel approach to improve Breast Cancer management

HLA-DR-expressor de linfócitos T citotóxicos: uma nova abordagem para melhorar a gestão do cancro da mama

Guadalupe Cabral

CEDOC - Centro de Estudos de Doenças Crónicas, Lisbon, Portual

27 May 2022

Abstract

Breast cancer (BC) is the most common malignancy in women worldwide. Despite the abundant ongoing research efforts, globally, BC remains a challenging disease to treat.

Neoadjuvant chemotherapy (NACT), where patients receive systemic therapy before surgery, is the standard treatment for locally advanced or inflammatory tumors. However, NACT still fails to benefit the majority of patients selected for this treatment and could potentially worsen the disease. Therefore, the implementation of predictive biomarkers and new tailored therapies to NACT non-responder patients are urgently needed.

A high frequency of tumor infiltrating lymphocytes (TILs) have been associated with improved outcome in patients submitted to NACT. Yet, the utility of global TILs quantification remains questionable, due to the likelihood of finding immunosuppressive factors in the tumor microenvironment that spoil antitumor responses of those lymphocytes, hence contributing to therapeutic failure.

Recently, we reported that more than TILs per se, it is the expression level of HLA-DR in the subset of cytotoxic T lymphocytes (CTLs), that discriminates accurately patients that will respond from patients that will not respond to NACT treatment. Thus, we proposed CTLs expressing high levels of HLA-DR (HLA-DRhiCTLs) as a highly sensitive, specific, independent and validated predictive factor of NACT response and developed a predictive probability model of the response to NACT based on the analysis of this immunological feature.

Additionally, using 3D co-cultures with BC cell lines and patients' peripheral blood mononuclear cells (PBMCs) we have shown that the addition of NACT-responders' PBMCs decreases the viability of cancer cells in the co-culture while PBMCs from NACT non-responders did not contribute to cancer cells' loss of viability, corroborating in vitro our clinical observations. Interestingly, we also observed that HLA-DR level in CTLs can be modulated ex-vivo, boosting their capacity to kill tumor cells synergistically with doxorubicin (a drug used in NACT). Thus, we believe that the modulation of the immune system in order to upsurge these HLA-DRhiCTLs in patients that lack or have very few of these cells, seems a promising approach to improve NACT response of BC patients. Therefore, currently we are developing strategies to increase HLA-DRhiCTLs, aiming to contribute to the implementation of more efficient therapeutic approaches for individual BC patients.

Lecturer's resumé

MG Cabral is an invited assistant professor at NOVA Medical School and a researcher at CEDOC, who has been developing research in the Immunology field for the last 15 years, increasingly focusing on a deeper understanding of the immunobiology of Breast Cancer, which is believed to be a critical step towards the implementation of more personalized treatments for this disease.

MG Cabral graduated in Biology at Faculdade de Ciências/Universidade de Lisboa and developed her PhD at Instituto Superior Técnico. After a post-doc on Glycoimmunology at CEDOC/NMS, in 2016, she started an independent line of investigation, at the same institute, focused on translational Cancer Immunology.

Although recently established, this research line already led to relevant contributions to the field (6 papers in peer-reviewed journals and several communications in national/international conferences) and was honored with the Medicine Research Prize 2018 (by Tagus Tank Consortium), the Terry Fox Research Grant 2019 (by Liga Portuguesa Contra o Cancro), the Prize in Clinical Research 2019 (by Pfizer/Sociedade das Ciências Médicas) and the Scicare Health Science Accelerator Award 2020 (by Novartis).

Professional relationship between nursing and criminal investigation in dealing with child victims of sexual abuse: an exploratory review

Relação profissional entre a enfermagem e a investigação criminal, na abordagem a crianças vítimas de abuso sexual: uma scoping review

Nuno Coelho

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

3 June 2022

Abstract

Sexual abuse crimes adapt and evolve, following the development of social norms and standards, bringing high consequences for physical, mental, and social health, with high economic costs for society. The statistical reality is under-represented in official figures. Victims of sexual abuse and their families seek help from criminal law enforcement agencies and health professionals for justice and care. Liaison and coordination between systems are often weak, making victims feel tired and alone. The World Health Organization has recognized the importance of interdisciplinary collaborative working to ensure successful healthcare delivery. Although not a new concept for health professionals, the operationalization of the concept in practice has been a challenge, and there continue to be variations in the qualities that constitute interdisciplinary collaboration, potentiating the emergence of barriers in relationships, and obstructing its implementation in the provision of care. The complexity, between police institutions and health services, which are not used to developing collaborative

work, due to the difference in roles and objectives, highlights conflicts. The very concept of the victim does not gather consensus among these professionals. Criminal investigation teams often have the perception that doctors and nurses obstruct justice while providing care to the victim; in the same way, doctors and nurses perceive the police as invasive to the privacy of patients, or as a pressure factor in the provision of care during the investigation process. To know through a scoping review, of the professional relationship between nursing and medicine with a criminal investigation in the approach to victims of sexual abuse, in the numbers of studies and their characteristics, which means, what barriers and facilitators influence this relationship, is important, because of the implications it has for networking, as well as, the impact it has on the victim, on society, and justice. A conceptual framework was used, based on the two-part model developed by Bronstein, in which five elements of ideal collaboration are described.

Os crimes de abuso sexual adaptam-se e evoluem, seguindo o desenvolvimento de normas e padrões sociais, trazendo elevadas consequências para a saúde física, mental e social, com elevados custos económicos para a sociedade. A realidade estatística está sub-representada nos números oficiais. As vítimas de abuso sexual e as suas famílias procuram ajuda nos órgãos de polícia criminal e nos profissionais de saúde, para a obtenção de justiça e cuidados de saúde. A ligação e coordenação entre os sistemas é muitas vezes fraca, fazendo com que as vítimas se sintam cansadas e sozinhas. A Organização Mundial da Saúde reconheceu a importância do trabalho colaborativo interdisciplinar para garantir o sucesso da prestação de cuidados de saúde. Embora não sendo um conceito novo para os profissionais de saúde, a operacionalização do conceito na prática, tem sido um desafio, continuando a existir variações nas qualidades que constituem a colaboração interdisciplinar, potenciando o surgimento de barreiras nas relações, obstruindo a sua implementação na prestação de cuidados. A complexidade, entre as instituições policiais e os serviços de saúde, que não estão habituados a desenvolver um trabalho colaborativo, pela diferença de papéis e objetivos, evidencia conflitos. O próprio conceito de vítima não reúne o consenso entre estes profissionais. As equipas de investigação criminal, muitas vezes têm a perceção de que os médicos e enfermeiros obstruem a justiça enquanto prestam cuidados à vítima; da mesma forma, os médicos e enfermeiros entendem a polícia como invasiva para a privacidade dos pacientes, ou, como um fator de pressão na prestação de cuidados durante o processo de investigação. Conhecer através de uma scoping review, a relação profissional entre a enfermagem e a medicina com a investigação criminal na abordagem a vítimas de abuso sexual, nos números de estudos e as suas características, o que significa, que barreiras e facilitadores influenciam essa relação, é importante, pelas implicações que tem para o trabalho em rede, bem como, o impacto que tem na vítima, na sociedade e na justiça. Foi utilizada uma estrutura conceptual, baseada no modelo de duas partes desenvolvido por Bronstein, em que se descreve cinco elementos de colaboração ideal.

Lecturer's resumé

Nuno Bastos Coelho, PhD student in Health Sciences at the University of Alcalá, Madrid, Spain and member of CBIOS (PhD Student) - Universidade Lusófona's Research Center for Biosciences & Health Technologies, has been developing research in the area of the professional relationship between health teams and criminal investigation in crime situations, which is believed to be necessary for the establishment of the truth and better care to the victim, their families and society.

Nuno Bastos Coelho, graduated in Nursing from the Escola Superior de Enfermagem S. Vicente de Paulo and obtained a master's degree in Legal Medicine and Forensic Sciences, at the Faculdade de Medicina de Coimbra. In his doctoral thesis, he is developing research on the professional relationship between doctors and nurses with the criminal investigation in situations of sexual abuse.

Nuno Bastos Coelho, aluno de doutoramento em Ciências da Saúde, na Universidade de Alcalá, Madrid, Espanha e membro do CBIOS (PhD Student) – Universidade Lusófona's Research Center for Biosciences & Health Technologies, tem vindo a desenvolver investigação na área da relação profissional entre as equipas de saúde com a investigação criminal em situações de crime, que se acredita ser necessário para o apuramento da verdade e melhores cuidados à vítima, suas famílias e sociedade.

Nuno Bastos Coelho, licenciou-se em Enfermagem pela Escola Superior de Enfermagem S. Vicente de Paulo, e obteve o grau de mestre em Medicina Legal e Ciências Forenses, na Faculdade de Medicina de Coimbra. Desenvolve no seu doutoramento, investigação na relação profissional entre médicos e enfermeiros com a investigação criminal, em situações de abuso sexual.

Protein hydration and dynamics seen by fluorescence: studies on haloalkane-dehalogenases

Hidratação e dinâmica proteica vista por fluorescência: estudos sobre haloalkane-dehalogenases

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Abstract

The hydration and mobility of proteins are believed to profoundly affect their function. However, only a few approaches for monitoring these characteristics within the relevant protein regions are available. Here we describe two fluorescence methods for site-specific analysis of the extent of hydration and degree of the mobility in enzyme class of haloalkane dehalogenases. The first approach is based on recording „time dependent fluorescence shift" [1] placing the dye in the tunnel mouth of this enzyme [2]. Secondly, the "gating" dynamics of the enzymes can be traced by following the photoinduced electron transfer between the selected tryprophan and properly positioned fluorescence dye [3]. The hydration and dynamics monitored within the biologically relevant regions of the dehalogenase enzymes is then compared with the enatioselectivity as well as catalytic efficiency of various mutants, which brings fundamental insights into the functioning of such enzymes.

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Lecturer's resumé

Prof. Martin Hof is the director of the Heyrovsky Institute of Physical Chemistry of the Czech Academy of Sciences in Prague. He has his scientific roots in the development of fluorescence spectroscopy and microscopy methods, being recognized worldwide. Methods like e.g. z-scan Fluorescence Correlation Spectroscopy, Fluorescence Spectral/Lifetime Correlation Spectroscopy or time-dependent fluorescence shift approach for membrane and enzyme sciences were developed in his lab. He has kept for many years' scientific links with Universidade de Lisboa, publishing with Liana C. Silva (Faculdade de Farmácia), Maria Joao Sarmento (Instituto de Medicina Molecular, Faculdade de Medicina), or Manuel Prieto (iBB-Institute for Bioengineering and Biosciences, Instituto Superior Técnico). For the latter he also serves as a member of the External Advisory Board.

Carbohydrate chemistry in the search for new molecular entities against metabolic and neurodegenerative diseases

Química dos hidratos de carbono na procura de novas entidades moleculares contra doenças metabólicas e neurodegenerativas

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Abstract

Type 2 diabetes and Alzheimer's disease are two tightly related amyloid disorders with rising prevalence at a global level. In this CBIOS seminar, our research towards the discovery of new carbohydrate-derived compounds with therapeutic potential against these pathologies will be explored, keeping in mind the existing pathophysiological links between them.[1] First, the results of in vitro and in vivo studies focusing on the natural compound 8-β-D-glucosylgenistein (8G) will be disclosed to uncover a multiorgan and multitarget mechanism of action that culminates in significant antihyperglycaemic effects.[2] Furthermore, the rational design and synthesis of two new families of C-glucosyl polyphenols will be presented, together with data supporting their establishment as promising prototypes for further development against Alzheimer's disease or diabetes-induced dementia.[3-5] Importantly, these are the first sugar-based protein-protein interaction inhibitors (PPIIs) against Aβo-PrPC interactions,[4] as well as the first sugar-based inhibitors of Aβo-induced Fyn activation and subsequent tau hyperphosphorylation in neuronal cells.[5] They have been found to exhibit adequate physicochemical properties for blood-brain barrier (BBB) permeation, and to present negligible cytotoxicity at relevant concentrations. Moreover, in order to exclude the possibility of unwanted interactions with the cell membrane, we successfully showed that C-glucosyl derivatives of lipophilic polyphenol PAINS (resveratrol, genistein and phloretin) do not present concerns regarding membrane dipole potential alterations, contrarily to their aglycones.[6] These results highlight the potential of carbohydrate-derived compounds for therapeutic applications, opening new avenues for drug discovery and development in the context of metabolic and neurodegenerative disorders.

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Lecturer's resumé

Ana Marta de Matos completed her BSc in Biochemistry in 2011 and her MSc in Medicinal Chemistry in 2013 at the University of Lisbon, Portugal. From 2014 to 2019, she pursued her Ph.D. supervised by Professor Amélia Pilar Rauter, head of the Carbohydrate Chemistry Group of the Faculty of Sciences of the University of Lisbon, Portugal, where she specialized in Medicinal and Carbohydrate Chemistry focused on the synthesis and biological evaluation of C-glucosyl polyphenols for the treatment of Alzheimer's disease and type 2 diabetes. In 2016 and 2018 she was a visiting Ph.D. student at Eli Lilly (UK), and in 2017 at the University of Basel (Switzerland), where she had the chance to work with the Pharmacology and Medicinal Chemistry expert Professor Beat Ernst. In 2021, she started her Junior Researcher position at CQE, IMS (Portugal), where she initiated her career as an independent researcher. Ana Marta is currently interested in the development of carbohydrate-based molecules for the treatment of infections caused by Gram-negative bacteria.