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IOMEDICINE EYOND OUNDARIES

BOOK OF ABSTRACTS

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0 WELCOME MESSAGE

It is with great pleasure that I support the VIII iBiMED Symposium: Biomedicine Beyond Boundaries. This symposium is a key part of iBiMED's research program, fostering collaboration, open discussions, and showcasing the latest advancements in biomedical and clinical research. Last year's success proved its value in bringing together researchers, clinicians, and students to engage in meaningful discussions and forge new collaborations. This year promises to be just as impactful, providing a unique opportunity to engage with leading national and international experts.

In the past year, iBiMED's research program has continued to evolve, further solidifying its role in advancing biomedical science. Our researchers have made meaningful contributions that strengthen both the national and international standing of our university's Health Sciences Program. With a strong commitment to innovation and societal impact, we remain dedicated to conducting research that is not only scientifically rigorous but also relevant.

A key milestone in our journey has been the expansion of collaborative efforts within the newly established Academic Clinical Centre, by deepening our partnerships with key healthcare institutions, including the hospitals of Aveiro (CHBV), Sta. Maria da Feira (CHEDV), Gaia/Espinho (CHVNG/E), along with several health centers in the Aveiro and Aveiro-Northern regions, we are enhancing research infrastructure, fostering clinical and translational research, and creating valuable opportunities for young scientists.

I extend my gratitude to the organizing committee, speakers, scientific committee, and participants who make this event possible. I encourage all attendees to actively participate, exchange ideas, and take full advantage of the networking opportunities.

I look forward to another successful symposium and the valuable contributions it will bring to our scientific community.

Bruno Bernardes de Jesus
The coordinator of iBiMED

SESSION 1

PUBLIC HEALTH & CLINICAL RESEARCH

Factors influencing digital health literacy among Portuguese users: a nationwide cross-sectional study

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Introduction: Digital health technologies are increasingly used in Portugal, offering benefits for healthcare access, efficiency, and patient empowerment. However, the successful use of these technologies relies heavily on individuals' ability to effectively find, evaluate, and apply digital health information – a concept known as digital health literacy (DHL). Aim: This study aims to characterize the demographic and digital usage patterns of individuals in Portugal who currently use digital health tools, and to explore the associations between these characteristics and DHL. Methods: This cross-sectional study included participants 18 years or older. Data were collected using an online survey, including questions assessing demographic characteristics, digital health usage patterns, and DHL. This study obtained ethical approval (46-CED/2024) and was conducted according to RGPD regulations. Results: A total of 1047 participants were included. Higher levels of digital health use were associated with higher scores across all measures of DHL. Older age was associated with lower DHL scores. Being of foreign nationality was associated with lower functional DHL. Conclusion: These findings highlight the critical role of frequent digital engagement in fostering DHL among Portuguese adults. Interventions aimed at improving DHL should prioritize strategies to promote regular use of digital health tools, particularly among older adults and individuals of foreign nationality.

Keywords: Digital health, Cross-sectional, Portugal, Digital health literacy

Funding: This research was funded by an individual grant by FCT (ref 2021.05141.BD).

Dose-Dependent Effects of Luanda PM10 on Lung cells Viability and Cell Cycle dynamics

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Atmospheric particulate matter lower than 10 μm (PM10) can reach the deeper parts of our respiratory system and increase DNA damage and cell death. PM10 genotoxic, mutagenic, and carcinogenic characteristics can lead to major health problems. Luanda, the capital of Angola, is a highly polluted city, yet there are currently no studies connecting its air quality to health consequences. The purpose of this study was to examine the effects of organic extracts from PM10 collected in Luanda on the cell viability and cell cycle dynamics of A549 cells following a 72-h exposure. From June to November 2023, daily PM10 samples were collected using a high-volume sampler in the city centre. A549 cells were subjected to increasing doses of the PM10 extracts from representative filters of each month. After 72 h of exposure, cell viability was assessed using the MTT assay, and cell cycle changes were evaluated using flow cytometry. As the concentrations of PM10 extracts increased, cell viability decreased, with the lowest viability observed after exposure to samples collected in October and July. Substantial alterations in the A549 cell cycle were observed only with extracts collected in September and October, particularly at the highest concentrations. These findings support the need for air quality monitoring and intervention measures to improve the overall health of the population.

Keywords: PM10, Luanda, A549, Cell viability, Cell cycle

Funding: An acknowledgment is given to the Portuguese Foundation for Science and Technology (FCT) for funding the PhD grants 2020.04826.BD, 2023.02059.BD, SFRH/BD/04992/2021 and SFRH/BD/08461/2020 and the research contract under the Scientific 742 Employment Stimulus to H.O. (DOI 10.54499/CEECIND/04050/2017/CP1459/CT0023). This work was supported by the project APAM - “Air Pollution in an African Megacity: Source Apportionment and Health Implications” (2022.04240.PTDC), financially supported by national funds (OE), through FCT/MCTES (DOI: 10.54499/2022.04240.PTDC). The financial support to CESAM by FCT/MCTES (UID Centro de Estudos do Ambiente e Mar (CESAM) + LA/P/0094/2020), through national funds, is also acknowledged.

A Dangerous Cocktail?! Assessing the Eco-toxicological Threats of Nano/Microplastics Mixed with pharmaceuticals

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Chloroquine (CQ) is an antimalarial drug that has shown selective toxicity in tumor models, but its effects on liver cancer remain unclear. Meanwhile, the widespread use of plastics raises concerns about the release of micro- and nanoplastics (MNPs), which can adsorb pharmaceuticals like CQ, altering their bioavailability and eventual toxicity. Understanding MNP-pharmaceutical interactions is crucial, yet poorly studied, emphasizing the need for further eco-toxicological research. This study aimed to evaluate and compare the cytotoxic effects on HepG2 cells following exposure to single and binary mixtures of MNPs in combination with CQ. Cell viability was assessed using the MTT assay after 72h. NPs and MPs were tested at concentrations ranging from 12.5 to 600 µg/mL, and CQ at 0.8 to 19.2 µg/mL. Binary mixtures were prepared by combining the IC_{20} and IC_{50} of each compound using the MIXTOX model. Results show that CQ follows a concentration- and time-dependent cytotoxic effect, with high cell viability at lower doses. MPs follow a similar trend, with significant viability reduction at ≥200 µg/mL over time, suggesting cumulative toxicity. NPs induce a slight decrease in viability across all concentrations. We hypothesize that MNPs co-exposure with CQ influences toxicity. This study provides valuable insight into how MNPs can impact human health and interact with CQ, highlighting the importance of assessing their combined toxicity to understand potential risks and implications.

Keywords: Mixture toxicity, cell lines, Concentration addition, Independent action, Human and environmental health

Funding: This work was supported by the project VitroTox (PTDC/CTA-AMB-0126-2020; DOI: http://doi.org/10.54499/PTDC/CTA-AMB/0126/2020), supported by the Foundation for Science and Technology in its State Budget component (OE). MP and FR are funded by national funds through the FCT – Fundação para a Ciência e a Tecnologia, I.P. under the Scientific Employment Stimulus - Individual Call (CEEC Individual) - 2023.06417.CEECIND/CP2840/CT0014 (DOI: https://doi.org/10.54499/2023.06417.CEECIND/CP2840/CT0014) and 2022.04220.CEECIND/CP2840/CT0014 (DOI: https://doi.org/10.54499/2023.06417.CEECIND/CP2840/CT0014), respectively. We acknowledge financial support to CESAM by FCT/MCTES (UID Centro de Estudos do Ambiente e Mar (CESAM) + LA/P/0094/2020), through national funds. F. Rosário thanks the financial support of FCT through the individual CEEC with reference 2022.04220.CEEC and DOI identifier http://dx.doi.org/10.13039/100007689.

Impact of nutrition in Prostate Cancer: preliminary results of a case-control study

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Background: Prostate cancer (PCa) is a prevalent oncological condition. Evidence suggests that modifiable factors such as nutrition and lifestyle may contribute to its onset and progression. Aim: To explore associations between lifestyle, dietary intake and PCa in a Portuguese male population. Methods: A matched case-control study was conducted after ethics approval (Center Regional Health Administration). One hundred participants (20 PCa cases, 80 controls) recruited from primary healthcare units. Cases were matched to 4 controls by age (±5 years). Sociodemographic, lifestyle, and dietary data were collected. Age matching was assessed via paired t-tests and Shapiro-Wilk tests. Cochran's Q test and logistic regression were used for categorical data. A linear mixed model included matched sets as random effects. Results: No significant age differences were found ($p=0.3371$), confirming adequate matching. Years in the last occupation were similar. Cochran's Q test revealed a significant difference in occupation type (manual vs. sedentary; $p=0.010$), but logistic regression did not support a significant association ($p=0.702$). No significant associations were found between dietary variables and PCa, although trends were observed for white meat ($p = 0.064$) and fish ($p = 0.070$). Conclusion: This preliminary analysis suggests a potential link between occupation type and PCa, though not confirmed by regression. Trends in dietary patterns warrant further investigation in a larger sample.

Keywords: Prostate cancer, Case-control study, Nutrition, Occupation, Risk factors

Acknowledgements: We would like to thank all the physicians for their invaluable assistance in patient recruitment and questionnaire administration.

Funding: This work was funded by an individual grant from Fundação para a Ciência e Tecnologia (grant numbers UI/BD/151352/2021).

Cytotoxicity assessment of polyethylene terephthalate micro- and nanoplastics in intestinal and liver cells

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Plastic pollution has become a major environmental concern due to the rapid increase in plastic production over the last few decades. Once released into the environment, plastics undergo continuous degradation, breaking down into small particles known as microplastics (<5 mm in diameter) and nanoplastics (<100 nm in diameter). Polyethylene terephthalate (PET), one of the most widely produced plastics, is commonly used in food and beverage packaging. The widespread distribution of micro- and nanoplastics is a global concern, however, their toxic effects on human cells remain largely unknown. In this study, we assessed the cytotoxic effects of PET particles of two different sizes (600-700 nm vs. 12 µm) on Caco-2 (human colon adenocarcinoma) and HepG2 (human hepatocellular carcinoma) cell lines after 24, 48, and 72 hours of exposure. Our findings revealed a significant decrease in cell viability at the highest concentrations, with HepG2 cells exhibiting greater sensitivity to both PET particle sizes than Caco-2 cells. These results highlight the importance of understanding the potential toxic effects of PET micro- and nanoparticles. Since different cell lines exhibit varying sensitivities, assessing toxicity across multiple cellular models is crucial for a comprehensive evaluation of their potential health risks. In future studies other markers of cellular alterations, such as cell death and inflammatory processes, should be investigated.

Keywords: Microplastics, Nanoplastics, Cytotoxicity, Cellular models

Funding: This work was supported by the BMRex -Biocatalytic membranes for micro/nano plastic degradation within waste water effluents- project, funded by European Union´s Horizon Europe EIC Pathfinder Open program under Grant Agreement N. 101099528 and supported by the UK Innovation funding agency (UKRI) under Grant Agreement N. 10062709. The financial support to UID Centro de Estudos do Ambiente e Mar (CESAM) + LA/P/0094/2020, through national funds, is also acknowledged. Catarina Cunha acknowledges for the Research Grant (BI/UI88/11875/2024) under the project BMRex - Biocatalytic membranes for micro/nano plastic degradation within waste water effluents, funded by European Union´s Horizon Europe EIC Pathfinder Open program under Grant Agreement N. 101099528.

"Often the carer is neglected" - importance of assessing the preparedness and the needs of Informal carers of people with chronic respiratory diseases

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Informal carers (IC) of people with chronic respiratory diseases (CRD) provide a wide range of support, however, their preparedness and needs to fulfil their role are rarely assessed. This study aimed to understand the perspectives of IC on the importance of assessing their preparedness and needs for caring. In this qualitative study, individual semi-structured interviews were conducted with IC of people with CRD in three Portuguese institutions. Audios were transcribed, translated and analyzed thematically. Sixteen IC (75% female; 55±14 years; 44% partners) participated. Assessment of preparedness and needs was considered "fundamental", "useful", and important (n=15) because of the necessity for empowerment, endorsement, and being linked to patients. IC emphasized the importance of "feeling ready", having "knowledge", "knowing what they are doing", and having "responsibility". The need of being supported was also highlighted, since "if the person who provides care isn't well, they won't have the capacity to care for someone else" and "there are many needs and not much support", as well as the impossibility to "disassociate the IC from the patient (...) Because it's the person who is always there with them and who provides the most support". IC of people with CRD find it essential to assess their preparedness and needs. This study highlights the need to acknowledge IC in a comprehensive assessment in healthcare research and clinical practice.

Keywords: Informal carers, Chronic respiratory diseases, Preparedness for caregiving, Needs assessment

Funding: This work was funded by the Fundação para a Ciência e a Tecnologia (Portuguese Foundation for Science and Technology, FCT), grant number PRT/BD/154726/2023.

Indeterminate Cytopathology in Thyroid Nodules: A Cross-Sectional Study of Predictive Factors in the Aveiro Region

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Thyroid nodules (TNs) are highly prevalent and often incidentally detected, with diagnostic uncertainty in indeterminate cytology remaining a clinical challenge. This study aims to characterize a cohort of patients with TNs from the Aveiro region and identify predictors of indeterminate cytology. A prospective cross- sectional study was conducted, including 311 adults referred for fine-needle aspiration biopsy between May 2021 and March 2024. Most nodules were benign (63.3%), 22.8% were indeterminate, and only 1.3% were malignant. Malignant patients were notably younger (48.25±7.50 years) compared to other groups. A female predominance was observed across all categories, with the malignant group being exclusively female. Dietary habits showed significantly lower vegetable and meat intake in the indeterminate and malignant groups, with fewer malignant cases reporting tea consumption ($p<0.05$). Exercise frequency was significantly lower in the malignant group ($p=0.001$). The indeterminate group presented the highest mean TSH levels (2.98±8.74 µIU/mL) and largest nodule size (26.70±14.68 mm), while malignant nodules were smaller, predominantly solitary, and more frequently located in the left lobe. While certain sociodemographic and clinical factors are associated with TNs, none reliably distinguish indeterminate cases from benign or malignant ones. Further research is needed to identify biomarkers for improved diagnostic accuracy.

Keywords: Thyroid nodules, Cohort characterization, Bethesda classification, Indeterminate cytology, Predictive factors

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Evaluation of salivary biomarker cortisol in patients with Temporomandibular Disorder

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Introduction: It is recognized that cortisol, a hormone produced by the adrenal glands, is a marker found at elevated levels in patients with psychological disorders, particularly anxiety. On the other hand, Temporomandibular Disorders (TMD) are a condition with a multifactorial etiology, in which emotional disorders play a crucial role. Aim: The objective of this study is to evaluate whether patients with TMD present higher levels of salivary cortisol compared to a control group consisting of individuals without TMD. Methods: This study was conducted at the Dental Medicine Area of the Faculty of Medicine of Coimbra and the Instituto de Investigación Biomédica Salamanca. Based on the DC/TMD, participants were classified into two groups: a study group composed of 50 patients with TMD and a control group consisting of 50 individuals without the disorder. Data on age and gender were collected. All participants received a detailed explanation of TMD and the study objectives. Each participant was evaluated using the DC/TMD, assigned an alphanumeric code to ensure anonymity, and had their salivary samples collected for subsequent laboratory analysis. Preliminary Results: Initial findings suggest that cortisol levels are higher in the study group Conclusion: Current evidence indicates that TMD symptoms are strongly linked to emotional factors like anxiety and stress, which may trigger the overactivation of the hypothalamic-pituitary-adrenal axis and result in increased cortisol.

Keywords: Cortisol, Temporomandibular disorder, Stress, Salivary biomarker

SESSION 2

OMICS & BIOINFORMATICS

Exploring Calcium Dysregulation and Potential Therapeutic Targets in Myotonic Dystrophy Type 1

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Myotonic Dystrophy Type 1 (DM1) is the most common adult-onset muscular dystrophy, affecting 1 in 3,000 to 8,000 individuals. It is caused by an abnormal CTG repeat expansion in the Dystrophia Myotonica Protein Kinase (DMPK) gene, leading to myotonia, muscle wasting and atrophy, as well as multisystemic complications. Dysregulated protein phosphorylation has been implicated in DM1, but the underlying mechanisms remain unclear. This study investigates molecular alterations contributing to calcium dysregulation and muscle dysfunction in DM1, identifying key proteins and signaling pathways to uncover potential therapeutic targets. Quantitative mass spectrometry-based proteomics and phosphoproteomics were used to analyze protein expression and phosphorylation changes in DM1 patient-derived fibroblasts. Findings were validated by immunoblotting and immunofluorescence analyses to assess protein expression and localization in fibroblasts and in the DMSXL transgenic mouse model. Significant alterations were identified in the protein levels and phosphorylation of a cation channel involved in calcium signaling and muscle contraction-relaxation. The underlying dysregulated pathways may contribute to sustained intracellular Ca^{2+} elevation, potentially linking to myotonia. This study highlights calcium dysregulation as a key factor in DM1 pathophysiology and identifies a potential therapeutic target, providing a foundation for novel treatment strategies for DM1.

Keywords: Myotonic Dystrophy Type 1, Neuromuscular disorders, Calcium dysregulation, Proteomics, Therapeutic strategies

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Radioprotective effects of losartan against short and long-term irradiation-induced testicular damage

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Testicular dysfunction is a side effect of radiotherapy (RT) due to off-target damage to germ cells, while Sertoli and Leydig cells, though resistant, still sustain damage, impairing spermatogenesis and steroidogenesis. With rising cancer rates in young patients, fertility preservation strategies are crucial. Losartan (LOS), an antioxidant, may mitigate this damage. This study evaluated whether RT induces short- and long-term testicular metabolic changes and if LOS can restore function. Male Wistar rats received ionizing scrotal radiation. LOS-treated rats received 34 mg/kg twice daily before, during, and after irradiation. Animals were euthanized 2 and 60 days post-irradiation to assess short- and long-term effects. Reproductive organs were weighed, serum hormones measured (ELISA), sperm parameters analyzed (WHO guidelines), mRNA expression quantified (qPCR), and oxidative stress assessed (slot-blot). Metabolomic profiles were obtained via 1H-NMR. Short-term irradiation reduced seminal vesicle weight, increased FSH, and reduced sperm count. Long-term, it reduced testicular and epididymal weight, impaired sperm quality, increased oxidative stress, and altered metabolism. LOS mitigated short-term weight loss but not sperm decline. Long-term, it improved sperm quality, reduced oxidative stress, and promoted adaptive metabolic responses. RT causes structural and functional testicular damage, while LOS is a putative radioprotector against radiation-induced male infertility.

Keywords: Losartan, Angiotensin receptor blocker, Renin-angiotensin system, Spermatogenesis, Radiotherapy

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Exploring anthocyanin-enriched fractions from Callistemon citrinus as promoters of Leydig cells viability, metabolic function, and steroidogenesis

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The transition from a linear to a circular economy searches for sustainable bioactive compounds with clinical applications. Polyphenols and flavonoids antioxidant properties makes them promising candidates for conditions where oxidative stress (OS) occurs (i.e. as male infertility). This study evaluates the effects of an anthocyanin-enriched fraction from Callistemon citrinus (Lemon bottlebrush) flowers and cyanidin 3-O- glucoside (cya-3-O), on Leydig cells viability, metabolic function, and steroidogenesis. A green extraction method of Callistemon citrinus was performed and characterized via RP-HPLC-DAD-ESI-MS/MS, revealing a predominant anthocyanin profile. TM3 Leydig cells were exposed to extract and cya-3-O (0.01, 0.1, 1 µg/ml and 0.5, 5, 50 µM, respectively) for 24 hours. Cytotoxicity assays, assessment of mitochondrial potential and ROS production were assessed. Results show that the extract modulated Leydig cell metabolic activity, and exposure to cya-3-O promoted a dose-dependent increase in LDH release. No statistical differences were detected in mitochondrial membrane potential and intracellular ROS production. An exometabolome analysis will be performed using 1H-NMR and steroidogenesis assessed. More studies will be needed to fully evaluate the potential of anthocyanin-enriched fractions as promoters of Leydig cells viability, metabolic function, and steroidogenesis.

Keywords: Circular economy, Anthocyanins, Oxidative stress, Steroidogenesis, Metabolomics

Proteomic Profiling of Pericardial Fluid for the Identification of Coronary Artery Disease Biomarkers

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Cardiovascular diseases (CVDs) are the leading cause of death globally, with coronary artery disease (CAD) as the most prevalent form. CAD develops silently is often only diagnosed at advanced stages, emphasizing the need for early diagnostic strategies. Biomarkers offer a promising route to fill this gap, by reflecting early molecular changes in disease progression, often before structural damage is detectable by imaging (e.g. coronary angiography). This study focuses on pericardial fluid (PF), a plasma ultrafiltrate with reduced systemic background that, due to its direct contact with the coronary arteries, offers a uniquely enriched and localized source for the discovery of CAD-specific biomarkers. A cohort of 26 patients undergoing cardiac surgery, consisting of 13 CAD and 13 non-CAD patients, was matched for several comorbidities, where the PF samples were processed with albumin/IgG depletion columns to minimize the minimize albumin's interference. This approach yielded albumin-rich and albumin-poor fractions, each individually analyzed by MS-based proteomics, which revealed the presence of hundreds of unique proteins in each fraction (593 in ALBR, 849 in ALBP). S100A12, SOD3, FSTL1, and PLOD1 showed significant statistical results ($p < 0.05$, Cohen's $d > 0.8$, AUC
> 0.7) and strong biological relevance in pathways related to inflammation, oxidative stress, extracellular remodeling, and vascular integrity - hallmarks of CAD - further supported by bioinformatic analysis.

Keywords: Proteomics, Coronary Artery Disease (CAD), Biomarkers, Bioinformatics

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Uncovering the proteogenomic landscape of head and neck squamous cell carcinoma through urine analysis

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Background: Head and neck squamous cell carcinoma (HNSCC) is a significant clinical challenge due to its aggressive nature and poor prognosis in advanced stages. Despite treatment advances, survival rates for late- stage HNSCC remain low, primarily due to delayed diagnosis. Early detection is critical, but current methods are invasive and unsuitable for early-stage detection. Aim: This study aimed to identify non-invasive diagnostic techniques for detecting molecular biomarkers of HNSCC. Methods: A proteogenomic approach was used to analyze urinary samples from 19 male HNSCC patients to identify distinct proteomic profiles for early detection and prognostic accuracy. Mass spectrometry identified 1427 proteins, with 730 common to both patients and healthy controls. Machine learning techniques, including Principal Component Analysis and Partial Least Squares Discriminant Analysis, were used to differentiate patient samples from controls. Results: Key proteins like RNASE1, LRG1, and CD44, with prognostic significance, were identified. Pathogenic variants, such as GAA p.(Trp746Cys) and SIAE p.(Pro210Leu), were identified as potential markers of advanced disease. Functional analysis revealed protein clusters linked to epithelial-mesenchymal transition and neutrophil degranulation. Conclusion: This study demonstrates the potential of urinary proteomics as a non-invasive tool for early HNSCC detection, offering promising implications for improved clinical outcomes.

Keywords: Head and neck cancer, Urine proteome, Variant, Biomarker, Early diagnosis

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Embryo Quality Evaluation: Metabolomic Approach Using Fourier Transform Infrared Spectroscopy

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Background: Struggles with infertility are common, affecting about one in six people worldwide. Despite the development of various assisted reproductive techniques, pregnancy success rates remain relatively low, therefore, it is essential to develop more effective methods for selecting viable embryos. While microscopy- based morphological evaluation remains the standard approach, its limitations have driven interest in alternative strategies, such as metabolomic profiling. Aim: This study aims to analyze the metabolomic composition of embryo culture media, using vibrational spectroscopy, to assess embryo quality and its potential impact on reproductive success. Methods: The culture media of 8 embryos with different quality grading, obtained from one couple doing IVF, was analyzed using FTIR spectroscopy followed by multivariate analysis using Unscrambler X software. Results: There were differences in the metabolomic profile of the embryonic culture medium, particularly in the 1200-900 cm -1 region. The results suggest that the 1170 cm - 1 peak (C –O stretching of carbohydrates) could serve as a spectroscopic marker for low quality embryos. Contrarily, the 952 cm -1 and 923 cm -1 peaks (C –N+ –C stretching of nucleic acids) could be indicative of high quality embryos. Conclusion: It is possible to conclude that vibrational spectroscopy metabolomics approach has potential to complement conventional morphological criteria to identify the most viable embryo.

Keywords: FTIR spectroscopy, Embryo culture media, In vitro fertilization, Metabolism

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Characterization of tissue-specific proteomic signatures identifies significant age-related shifts in abundance and solubility in mice.

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As cells age, protein homeostasis (proteostasis) progressively declines, leading to the widespread aggregation of misfolded insoluble proteins, a hallmark of age-related diseases. We hypothesize that protein aggregation also occurs during natural tissue ageing due to an age-associated decline of proteostasis responses responsible for misfolded protein degradation. In this study, we performed SWATH mass spectrometry analysis to detect age-related shifts in protein abundance that occur in the total proteome, detergent-soluble and insoluble protein fractions of young, middle-aged, and old aged female C57BL/6J mice. Tissue-specific SWATH profiles were produced for the liver, skeletal muscle, and cortex. Our results found that proteins with significant changes in the total protein extract are involved in oxidative stress response across all tissues. In triton- insoluble fractions, most proteins with significant changes in abundance across the tissues in middle- and old aged mouse groups are largely involved in peroxisomal transport, stress response, and proteasomal degradation while soluble proteins are involved in cell redox homeostasis and translation-related processes. Future studies will examine the eligibility of these proteins as targets for anti-aging therapeutic strategies.

Keywords: Healthy aging, Protein aggregation, Proteostasis

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Differential Interactome of Phosphorylated Amyloid Precursor Protein at Serine 655 and Its Role in Neuronal Differentiation

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Amyloid Precursor Protein (APP) is a transmembrane glycoprotein essential for neuronal development and function, both in its full-length form and as proteolytic fragments such as Abeta, implicated in Alzheimer's disease. APP phosphorylation regulates its trafficking, cleavage, and protein interactions. One site of interest is Serine 655 (S655), located within the YTSI basolateral sorting motif. In this study, we used differentiated neuronal cells overexpressing either wild-type APP or S655 phosphomutants. Following immunoprecipitation, APP-associated proteins were identified via mass spectrometry and the data was treated using Proteome Discoverer. Protein-protein interactome comparisons between phosphorylated and dephosphorylated-APP forms were performed using Cytoscape and the statistical analysis was performed in R. Additionally, we integrate known databases to annotate and visualize enriched pathways, biological and molecular functions across the groups in two differentiation timepoints. Results confirm that phosphoS665 APP has specific interactors with impact on APP neuronal functions.

Keywords: Amyloid Precursor Protein (APP), Serine 655 phosphorylation, Neuronal differentiation, Interactome, Alzheimer's Disease

Deciphering the importance of peroxisomes in the context of viral infections through transcriptomic analyses

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Viral infections remain a major health challenge, with mutations often undermining the efficacy of virus- specific treatments. Hence, there is a growing interest in identifying host cell mechanisms as targets for the development of novel antivirals. Peroxisomal mechanisms are promising candidates, as these organelles have been pinpointed as key players during viral infections. However, detailed knowledge on the underlying mechanisms is still scarce. In this study, we performed a transcriptomic analysis of peroxisomal genes at several stages of infection by influenza A virus (IAV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), and dengue virus (DENV). Raw RNA-seq datasets were retrieved from publicly available repositories and processed through a standard pipeline, involving STAR and StringTie, to obtain gene-level read counts, which were then analyzed with the DESeq2 R package. Exploratory data analysis was performed to evaluate sample variability and condition-specific clustering, followed by differential expression analysis across the different infection stages. Our findings show transcriptional changes between infected and non-infected samples, with significant up- or downregulation in genes encoding peroxisomal proteins. These variations, particularly affecting genes involved in lipid metabolism, were more pronounced at specific infection stages. These results provide key insights for identifying peroxisome-related targets against IAV, DENV, and SARS-CoV-2.

Keywords: Viruses, Peroxisomes, Influenza A virus, Dengue virus, Severe acute respiratory syndrome coronavirus 2

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Effects of Physical Exercise on the Metabolome of Patients with Heart Failure

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HF is a complex syndrome with symptoms from structural/functional cardiac abnormality, confirmed by elevated natriuretic peptide and/or pulmonary/systemic congestion; it often involves cardiac/systemic metabolic changes. Physical exercise is recommended in HF management, but its metabolomic effects are poorly understood. This study investigated exercise effects on plasma metabolomic profiles in HF patients, using FTIR spectroscopy. Plasma samples from 82 HF patients, who completed a 3-month supervised exercise program (home or center-based), were analyzed by FTIR spectroscopy. Key spectral regions linked to lipid (3050–2800 cm^{-1}), protein structure (1800–1500 cm^{-1}), and nucleic acid/carbohydrate/protein (1500–900 cm^{-1}) signatures were examined. The plasma metabolomic profile was analyzed with PCA and PLS-R. No significant changes occurred in global metabolomic profiles after 3 months, with no differences between groups. However, significant correlations were found between specific FTIR spectral regions and clinical markers (VO2 peak, 6MWT, CRP, proBNP). VO2 showed the best correlation (R^2 = 0.429; R^2 = 0.448; R^2 = 0.553). The results indicate that while short-term exercise may not induce global metabolomic shifts detectable by FTIR, specific spectral features strongly correlate with key clinical markers. Future studies with longer interventions, cohorts, and multi-omics are needed to uncover metabolic signatures and identify biomarkers sensitive to exercise response in HF.

Keywords: Heart failure, Physical exercise, Metabolomic profile, FTIR spectroscopy, Multivariate analysis

Spectroscopic Analysis of Proteome Changes in Neuronal Differentiation and Optineurin Mutations

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Amyotrophic Lateral Sclerosis (ALS) is a neurological disorder that affects motor neurons. A hallmark of ALS is the accumulation of protein aggregates in motor neurons. To investigate proteomic profiles, including protein conformational changes and post-translational modifications during neuronal differentiation, FTIR spectroscopy combined with multivariate analysis is a valuable tool (Magalhães et al., 2021). Our goal was to validate FTIR spectroscopy for characterizing neuronal differentiation models and studying the impact of Optineurin (OPTN) mutations on proteostasis. We examined changes in protein secondary structures and post- translational modifications during differentiation and in OPTN mutant-transfected neurons. Primary cortical neurons from rat embryos (Rattus norvegicus) were cultured for 14 days, and cells were harvested every two days. Neurons were transfected with wild-type (WT) OPTN or the E478G-mutated OPTN. Spectra were acquired from samples of differentiated and transfected neurons and analysed in triplicate. PLS-R analysis showed a strong correlation(R=0.93) between spectra and neuronal differentiation and distinguished maturation stages. It also revealed clear separation between OPTN-WT and OPTN-E478G-transfected neurons, highlighting significant protein modifications. Our results suggest alterations in protein conformation and post- translational modifications during differentiation and provide insight into proteome changes in OPTN mutation models.

Keywords: FTIR, Spectroscopic profile, Neuronal development, Cortical neurons, Proteomics

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Automated Laboratory Workflow for Personalized Medicine in Candidiasis: A Comparative Study

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Introduction: Personalized medicine in candidiasis requires precise and efficient diagnostic methodologies to optimize clinical decision-making and avoid antimicrobial resistance. Conventional manual laboratory procedures are time-consuming and prone to variability, necessitating the development of automated workflows. Aim: This study aims to evaluate an automated laboratory workflow for identifying Candida species, by assessing its efficiency, reliability, and scalability compared to manual methods. Methods: An automated wet-lab workflow covering DNA extraction, qPCR analysis for species identification, library preparation for next generation sequencing (NGS), and data analysis was developed. Clinical isolates of Candida sp. from patients were analyzed using both automated and manual methods. Performance parameters, were compared. Results: Automation demonstrated greater scalability and reproducibility, reducing hands-on time and error rates. initial costs were higher, cost analysis revealed that automation is more efficient for high-throughput testing.The optimized qPCR protocol enhanced Candida species identification, improving diagnostic accuracy. Conclusion: The study underscores the significance of automated workflows in personalized medicine for candidiasis, enhancing efficiency, accuracy, and scalability. This approach supports clinical diagnostics and antimicrobial stewardship by enabling rapid, cost-effective and reliable pathogen identification.

Keywords: Candidiasis, Personalized medicine, Laboratory automation, DNA sequencing, qPCR

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SESSION 3

BIOMEDICAL THERAPEUTICS

Enhancing Orthodontic Biomaterials: A Biocompatibility in vivo and in vitro Study of DLC-Based Coatings

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The use of pure metals and first-generation metallic biomaterial alloys remains prevalent in medicine, particularly in orthopedics and orthodontics. Stainless steels (SS) and Nickel-Titanium (Ni-Ti) alloys are favored for their mechanical properties and biocompatibility. However, in vivo corrosion is inevitable, particularly in the oral cavity, where pH fluctuations accelerate metal ion release. Elements like Nickel (Ni) and Chromium (Cr) may cause allergic or cytotoxic effects, raising concerns about long-term safety. To mitigate this issue, diamond- like carbon (DLC) coatings are being explored for their corrosion resistance and biocompatibility. This study, a collaboration between iCBR/CIBB (FMUC) and CEMMPRE (FCTUC), focuses on functionalizing orthodontic alloys with DLC coatings to enhance durability and reduce ion release. The study assessed in vitro and in vivo biocompatibility. In vitro tests included saliva immersion and cytotoxicity (MTT assays) to evaluate cell viability, while in vivo tests involved subcutaneous implantation in mice. Inflammatory responses were monitored through microPET imaging and histopathology. MTT analysis showed DLC1 performed best. All coatings improved corrosion resistance over uncoated SS316L, though Si/DLC2 had higher SUV values, suggesting lower biocompatibility. Despite some inflammatory responses, DLC coatings show potential for enhancing orthodontic biomaterials by improving longevity and reducing adverse reactions.

Keywords: DLC, SS316L, In vitro studies, In vivo studies, easyPET.3D

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Exploring mitochondrial therapy in the context of neurodegeneration: characterisation of isolated mitochondria and transplantation optimisation

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Mitochondrial dysfunction severely affects high-energy organs like the brain and is linked to neurodegenerative diseases such as Alzheimer's and Parkinson's. These conditions exacerbate mitochondrial damage by increasing oxidative stress and disrupting energy balance. This study explores mitochondrial transplantation as a therapeutic approach to enhance cellular fitness and homeostasis against ageing-, pathology-, and metabolism-associated insults. Using a neural cell line as an in vitro model for future applications in neurodegenerative disease research, donor mitochondria (modulated in terms of redox status) were isolated and characterized. Mitochondria were transplanted into acceptor cells to allow the assessment of its effects on physiological pathways, providing insights into its potential neuroprotective benefits. The characterisation of isolated mitochondria allowed the identification of proteins of interest that can be playing hereto undescribed crucial roles determining pathological vs. pathological fate. Additionally, mitochondrial transplantation appears to increase acceptor cell resilience to pathology-related insults. Being so, this concept demonstrates promising results, seriously impacting the understanding of mitochondrial dysfunction and its implication on pathology. This work will expand the therapeutic potential of mitochondrial transplantation, particularly its applicability in neurodegenerative pathologies.

Keywords: Alzheimer's Disease, Mitochondria, Mitochondrial transplantation, Neurodegeneration, Metabolism

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easyPET.3D in the Longitudinal Assessment of Acute Cocaine and Quercetin Exposure in BALB/c and C57BL/6J Mice

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Cocaine use remains a major public health concern, with rising consumption and severe socioeconomic consequences. In 2022, an estimated 23 million people used cocaine, reflecting a 20% increase over the past decade. Despite its widespread impact, there are no approved/effective treatments for cocaine addiction. Quercetin, a flavonoid, has emerged as a promising candidate, targeting the same brain receptors as cocaine and potentially reducing cravings while exerting cytoprotective effects. This study investigated the metabolic and histopathological effects of low-dose cocaine exposure in 2 mouse strains (BALB/c(+) and C57BL/6J) and the therapeutic potential of quercetin. Using easyPET.3D - a microPET imaging system designed for small rodents -and [18F]-FDG, the metabolic activity of key brain regions affected by cocaine was assessed: hippocampus, amygdala, prefrontal cortex, thalamus, and striatum. Histopathological analyses were also done. Cocaine induced metabolic and structural changes, with C57BL/6J mice showing higher sensitivity. Quercetin restored baseline metabolic activity in BALB/c(+) mice but had limited effects in C57BL/6J, particularly in the amygdala and prefrontal cortex. Histologically, cocaine caused dose-dependent damage, partially mitigated by quercetin. While quercetin could not fully reverse structural damage, its ability to restore metabolic function suggests potential for promoting neuronal recovery and improving outcomes in cocaine addiction treatment.

Keywords: Cocaine, Flavonoids, Quercetin, easyPET.3D, [18F]-FDG

Acknowledgements: A special thank you to: Hospital Center of the University of Coimbra (CHUC), iCBR-FMUC Vivarium, Biophysics Institute-FMUC, Experimental Pathology Laboratory-FMUC, University of Aveiro and RI.TE.

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Embodiment and Performance Impact of Virtual Exoskeleton in Brain-Machine Interfaces

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Recent studies highlight the potential of Virtual Reality (VR) in Motor Imagery (MI) Brain-Machine Interfaces (BMIs), particularly in improving decoding performance. Immersive VR scenarios, used to promote neuroplasticity in conditions such as paraplegia and chronic pain, have been shown to enhance MI performance by strengthening the Sense of Embodiment (SoE). SoE describes the human sensation of being in control of a different body, such as the ability to feel in real control of a virtual avatar and perceive it as one's own. This study evaluated the impact of the presence versus absence of a virtual exoskeleton on SoE while subjects controlled an Electroencephalogram (EEG)-based MI-BMI. Sixteen healthy volunteers (10 females, 6 males, mean age = 23.69 ± 5.02) were tested. After the session, they completed the Sense of Embodiment Questionnaire (QCCPIC) and the Simulator Sickness Questionnaire (SSQ). Decoding accuracy showed a decrease in performance with the introduction of the virtual exoskeleton on the avatar (virtual exoskeleton: 60.17±2.85%, avatar without virtual exoskeleton: 67.33±3.40%, Mean±SEM, Paired samples t-test: 2.294, df=13, P=0.0391). Participants reported high SoE (37.94±2.49, min=15, max=51) and low-mild simulator sickness (mean = 8.63±1.69, min=3, max=30). These preliminary results suggest that a virtual exoskeleton may reduce BMI performance. Further research exploring alternative designs and multimodal modulation are needed to optimize VR-BMI integration.

Keywords: Brain-Machine Interfaces (BMIs), Virtual Reality (VR), Exoskeleton, Electroencephalography (EEG), Embodiment

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Assessing the therapeutic potential of tRNAs in Alzheimer's disease using humanized 3D cellular models

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by cognitive decline, amyloid plaques and neurofibrillary tangles. Increasing evidence suggests that dysregulated translation and impaired proteostasis also contributes to AD pathology. Our group has recently found that specific tRNA modifications are dysregulated in AD models and that wobble uridine hypomodification of tRNA-LysUUU, tRNA-GluUUC and tRNA-GlnUUG contributes to proteotoxic stress. We have observed that transfection of a plasmid encoding tRNA-LysUUU recovers proteostasis in AD cellular models, namely SH-SY5Y cells expressing the AD Swedishmutation (SH-SWE), without disrupting other tRNAs, suggesting that tRNA manipulation can have a therapeutic potential. To further test this hypothesis, we are now developing AD 3D cell culture models, namely spheroids to develop a humanized screening platform to test the therapeutic potential of synthetic tRNAs in AD. Our preliminary data show that we can form spheroids from both SH-SY5Y control cells and SH-SWE cells with and without previous tRNA transfection. Spheroids obtained from transfected tRNA-LysUUU SH-SWE cells apparently recover proteostasis when compared to spheroids obtained from non-transfected SH-SWE cells. This indicates that tRNAs have the potential to be used as therapeutic agents to restore proteostasis in neurodegeneration Future work will include testing tRNA therapeutic potential in 3D cellular models obtained from AD-derived iPSCs.

Keywords: tRNA modifications, ELP3, Neurodegeneration, Alzheimer's Disease, 3D cell models

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Development of Cellular and Animal Models for Mucopolysaccharidosis Type III

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Mucopolysaccharidosis type III (MPS III) is a rare, monogenic neurological disorder caused by mutations in hydrolases responsible for degrading heparan sulfate, leading to its accumulation. Currently, it has no available therapy. Over the last years, our group has developed RNA-based therapies for MPS III, and evaluated their potential in patient-derived fibroblasts. Now, we want to study their efficacy in neurological disease models, both in vitro and in vivo. But we must generate them first. Thus, we have established two independent MPS III-derived induced pluripotent stem cell (iPSC) lines for neuronal differentiation, and we also seek to develop a zebrafish (Danio rerio) model. Previously generated iPSCs obtained from two fibroblast cell lines from MPS III patients were neurodifferentiated for subsequent genetic and biochemic characterization. The zebrafish model was generated by CRISPR/Cas9-mediated knockout of the naglu gene and its phenotypic and biochemical characterization is ongoing. We have characterized MPS III-derived iPSCs and successfully neurodifferentiated two lines. In the in vivo model, knockout efficacy was confirmed by molecular and biochemical analyses. Additionally, the knockout zebrafish exhibited both developmental and behavioural alterations compared to wild-type controls. So far, all our preliminary data on both models support the assumption they may later qualify as valuable tools for disease modelling as well as a platform for drug screening.

Keywords: Lysosomal storage diseases, iPSC, Neurons, Zebrafish, Therapies

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In-House Engineered Cosurface Capacitive Electrodes For Customized Neuronal Electrical Stimulation

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Introduction. Neuroregeneration after Central Nervous System lesions is limited, lacking effective therapies. Electrical stimulation (EStim) promotes neuronal differentiation, plasticity, and regeneration. This study examines two capacitive electrodes: (1) copper (Cu), known to promote osteoblast differentiation, and (2) silver (Ag), to enhance neuronal differentiation and neuritogenesis. Aims. This study investigates Cu electrodes' effects on in vitro sensory neuron differentiation, identifying optimal stimulation parameters. Additionally, it optimizes Cu electrodes, developing flexible, biocompatible Ag electrodes, and evaluates their EStim performance. Methods. Sensory neurons differentiated for four days under varying voltage waves, frequencies, and exposure times. Ag electrodes were screen-printed and tested using optimal Cu electrode parameters. Results. Cu electrodes applied EStim via V0/10 and V-5/5 waves, differing in field direction. Morphometry showed Cu electrodes increased neurite number (+48%) and length (+70%) at 50 Hz V0/10. Western blot and immunocytochemistry revealed EStim-induced changes in neuritogenic targets. Ag electrodes were flexible, biocompatible, and enhanced metabolic activity (+80%) over four days. Finite element analysis showed Cu electrodes generated 0.2–1.0*10-4 mV/mm fields, while Ag electrodes delivered higher fields (0.5–2.5*10-4 mV/mm). Conclusions. These electrodes show potential to integrate next-generation stimulation devices.

Keywords: Central nervous system, Electrical stimulation, Capacitive coupling, Neuritogenesis, Neuroregeneration

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Exploring the bioactivity of Pedobacter lusitanus NL19 extracts using the prized Caenorhabditis elegans model

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Pedobacter lusitanus NL19 is a bacteria first isolated from the sludge of a uranium mine in Quinta da Bispo (Viseu, Portugal). Its bioactive potential has been investigated, but only regarding its antimicrobial properties. The current study examined the bioactivity of P. lusitanus extracts related to antioxidant protection, benefits on development, and neuroprotection (associated with tau proteins, a hallmark of Alzheimer's disease) using the experimental model Caenorhabditis elegans. Two types of bacteria extracts were considered: i) a n-butanol extract (BUT) and ii) a filtration of the previous extract (BUT-F). ABTS radical and FRAP assays revealed the extract's antioxidant capacity. Additionally, the N2 C. elegans strain was treated with both extracts (25, 50, and 100 µg mL-1) and assessed for their effects on the percentage of survival, egg viability, and growth. Extracts seemed to have a relevant effect on the worm's size, suggesting benefits on C. elegans development. Moreover, the intracellular reactive oxygen species (ROS) and tau proteotoxicity were evaluated in a mutant C. elegans strain (BR5706) exposed to BUT and BUT-F (50 µg mL-1). A significant reduction of ROS content was detected in both conditions. Extracts had a positive effect on worms' size, but no statistical differences were found for motor parameters (e.g., swimming speed). This study confirms the antioxidant capacity of P. lusitanus extracts, suggesting their relevance in health-related applications.

Keywords: Pedobacter lusitanus NL19, Bioactive natural compounds, Antioxidant protection, Neuroprotection, Caenorhabditis elegans

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Advances in Gene and Regenerative Therapies for Epidermolysis Bullosa and Xeroderma Pigmentosum: A Decade of Progress.

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Introduction: Rare, hereditary skin conditions with a substantial clinical burden and few available treatments are epidermolysis bullosa (EB) and xeroderma pigmentosum (XP). While XP results in high UV sensitivity and early-onset skin cancer, EB causes extremely fragile skin. Until recently, care was mainly supportive, highlighting the need of treatments targeting the genetic causes. Aim: This structured review aims to assess the advancements in gene and regenerative therapy development for EB and XP from 2015 to 2025. Methods: Peer-reviewed studies on gene therapy, stem cells, and genome editing for EB and XP(2015-2025) from PubMed and Scopus were reviewd. Results: Notable clinical developments for EB include the FDA-approved topical gene therapy B-VEC, successful grafting, and ex vivo correction of epidermal stem cells, both of which have greatly enhanced wound healing and long-term skin regeneration. Gene therapies, on the other hand, are still in the preclinical stage for XP. Viral gene transfer and new CRISPR technologies successfully restore DNA repair in XP models, according to encouraging experimental results. Conclusions: Gene therapy has developed into a practical clinical treatment for EB, providing patients with better results. Even though gene therapy for XP has not yet been used in clinical settings, current research indicates that breakthroughs may be possible in the future.

Keywords: Epidermolysis Bullosa, Xeroderma Pigmentosum, Gene therapy, Regenerative medicine, CRISPR

Stem Cell Osteogenic Differentiation Probed by Atomic Force Microscopy-Infrared Nanospectroscopy: Sub-cellular Biochemical Characterization

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Mesenchymal stem cells (MSC) osteodifferentiation is a promising toll in regenerative medicine of bone tissue. However, challenges in bioengineered bone adequacy and biocompatibility are still an issue. Thus, a deeper understanding of MSC osteodifferentiation is crucial. This study aimed to probe sub-cellular events of the differentiation process, using photothermal Atomic Force Microscopy-Infrared (AFM-IR) measurements, comparing both controls and osteogenic differentiation induced human adipose derived MSC (hAMSC), at different time points (0, 6 and 21 days). Spectra were acquired at the new MIRIAM/B22 end station at Diamond Light Source, with a spatial resolution of ca 100 nm and a spectral resolution of 10 cm^(-1). AFM-IR osteodifferentiation monitoring of hAMSC is a pioneering study. It provided both morphological and chemical information, from the AFM topography images and IR nanospectra, respectively. The biomarker band at ca. 1060 cm-1 of IR spectra evidenced hydroxyapatite (HA) deposition, a key indicator of mineralization associated with osteogenesis of MSC. HA was observed at osteogenic induced MSC on day 21, but also as early as day 6. The results provided accurate information on chemical differences in hAMSC cellular samples at distinct stages of osteodifferentiation, allowing their correlation with the spatial arrangement at the sub-cellular level. This knowledge is expected to contribute to a more effective use of MSC as key players in bone tissue regeneration.

Keywords: Mesenchymal stem cells, Osteogenic differentiation, Nanospectroscopy, Photothermal Atomic Force Microscopy-Infrared, Bone tissue engineering

Acknowledgements: This work was partly developed within the scope of the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020, financed by national funds through the FCT/MEC (PIDDAC). FCT is also acknowledged for BetterBone project 2022.04286.PTDC.

Effects of upconversion nanoparticles with a thermoresponsive nanovalve loaded with doxorubicin in melanoma cells

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Melanoma skin cancer has an increasingly higher incidence, and when detected in advanced stages, tumour eradication is often incomplete, contributing to poor prognosis with conventional treatments. Upconversion nanoparticles (UCNPs) have unique properties, such as excitability under near-infrared (NIR) excitation light, which confers a relatively high penetration depth in tissue, that allow their effective use in several biomedical applications. Mesoporous silica nanoparticles (MSN) with nanovalves or derived coatings have widely been used for triggered and targeted drug delivery in the past. Anticancer drugs can be loaded into the pores of MSN, enabling controlled drug release. In this work, UCNPs were coated with a mesoporous silica shell yielding UCNP@MSN core-shell nanoparticles which were equipped with thermoresponsive retro-Diels-Alder nanovalves and then loaded with DOX, a chemotherapeutic agent for melanoma treatment (UCNP@MSN- DOX). Subsequent DOX release from this drug delivery system was triggered by 980 nm NIR light. Melanoma cells exposed to UCNP@MSN-DOX or the NIR laser exhibited no change in ROS production, while the combination of both induced an increase in ROS production. This combination of conditions also induced changes on apoptosis and necrosis levels. These findings underscore the potential use of UCNP@MSN drug delivery systems with thermoresponsive caps as effective drug delivery platforms for melanoma therapy.

Keywords: UCNP, Melanoma, Cell viability, ROS production, Apoptosis

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Targeting Pancreatic Cancer: Synergistic Potential of Vinblastine and Doxorubicin

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Pancreatic cancer (PC) is one of the most lethal solid tumors, with an increasing incidence and poor survival rates despite advancements in therapy. Vinblastine (VBL), a microtubule inhibitor, and doxorubicin (DOX), a DNA damage agent and a topoisomerase II inhibitor, are widely used in cancer treatment. However, their effectiveness is often limited by severe cytotoxicity. Thus, the aim of this work was to evaluate the combined effects of VBL and DOX in Panc-1 PC cells. Cells were treated with VBL (0.05-10 nM) or DOX (0.1-10 µM) for 24, 48 and 72h and cell viability was assessed by the MTT assay. Furthermore, IC50 was determined, and cells were exposed to 1/16-2 times the IC50 of each drug alone or in combination for 48 and 72h. Then, cell cycle and intracellular ROS levels were assessed by flow cytometry. Results showed that both drugs reduced cell viability in a time and concentration dependent manner. Synergy was observed at 1/16 and 1/8 of the IC50 after 48h. Cell cycle analysis revealed that both 1/16 and 1/8 of the IC50 of DOX alone or in combination induced a cell cycle arrest at the G2/M phase, with no additional effect from the combination. Similarly, intracellular ROS levels showed an increase caused by 1/8 of the IC50 of drugs combined, but DOX alone had a greater effect. Further investigation is needed to elucidate the mechanisms underlying the observed synergy.

Keywords: Panc-1 cells, Synergy, Chemotherapy, Cytotoxicity

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Biomaterial Development for Axonal Regeneration Regarding Spinal Cord Injury

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Spinal Cord Injury, despite extensive research, remains a challenging neurological disorder due to the lack of methods for regeneration and function restoration. Patient recovery depends on axonal regeneration and current treatments cannot significantly induce regeneration. The objective of the study was to develop a controlled drug release biomaterial to be implanted in situ promoting targeted axon regeneration after injury. Two natural polymers, chitosan and alginate, were tested due to their biocompatibility and biodegradability. A plasticizer and cross-linkers were employed to enhance mechanical performance and control degradation rate. The drug, to promote axonal regeneration and functional recovery, was encapsulated as a nanoparticle. Other nanoparticles were explored to assess anti-inflammatory and antioxidant properties. The materials have proved to be easy to manipulate, and presented several interesting characteristics such as the possibility to integrate nanoparticles in their composition and their biocompatible and non-toxic behaviour. Drug- encapsulated nanoparticles were found to aggregate in one of the membranes, which can be a good way to enable gradual drug release. Membranes were examined in in vitro setting, and none of the materials appeared to be harmful or toxic to neural cells. This study has helped to create a novel drug delivery system, showing promising results in improving the pharmacological regeneration capabilities of already-approved drugs.

Keywords: Spinal Cord Injury, Biomaterial, Regeneration

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Developing a Model to Study Spinal Cord Injury Genetic Targets in Drosophila melanogaster

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Spinal cord injury (SCI) is a devastating neuropathology with major impact on patient's life quality. SCI remains untreatable and a major challenge in regenerative medicine due to the CNS's limited repair capacity. Innovative and effective therapies are needed, likely focusing on gene/molecular strategies targeting regeneration- associated genes (RAGs). In a previous transcriptomic-based preclinical study of our group (GoBack project), candidate RAGs were identified and their neuritogenic capabilities confirmed in vitro. To further address their regenerative potential, in vivo studies are needed. Drosophila melanogaster has emerged as a powerful animal model to investigate neural regeneration, including the function and therapeutic value of RAGs. However, its potential in SCI research remains underexplored. In this study, we aimed to establish and characterize a SCI-like crush injury model in D. melanogaster. A mechanical contusion was applied to the ventral nerve cord, targeting the metathoracic ganglion, to mimic mammalian SCI. Flies were then selected based on third leg dragging 24h after injury, and their recovery was monitored. Immunohistochemical analyses will be further performed to confirm the lesion site status. The establishment of this model will enable in vivo RNAi- based assessment of GoBack genes' regenerative capacity and will support future genetic studies on RAGs, validating Drosophila as a cost-effective model for SCI research.

Keywords: Ventral nerve cord (VNC), Spinal cord injury (SCI), RAGs

REPAIR – REPAIRING ISCHEMIC STROKE. CELL MODEL AND STEM CELL THERAPY

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Ischemic stroke (IS) occurs when an artery supplying blood to the brain becomes occluded, leading to neuronal damage. Current treatments, including mechanical thrombectomy and thrombolytic therapy, aim to restore blood flow but have significant limitations. The penumbra, a dynamic region surrounding the infarct core, contains neurons that, despite morphological changes, remain viable and represent a key target for neuroprotection. However, more physiologically relevant in vitro models are needed to mimic distinct penumbra microenvironments. These models should incorporate essential cell types, such as neurons and glial cells, and better replicate physiological conditions. Culturing cells under physioxia (2–6%O_2) rather than standard normoxia (18–21%O_2) better reflects in vivo conditions, significantly influencing cellular responses and protein expression. Mesenchymal stem cells (MSCs), particularly those derived from the umbilical cord (UC-MSCs), show promise in IS treatment due to their neuroprotective and immunomodulatory properties. However, optimizing MSC survival, homing, and functional integration remains a challenge. Quantitative proteomics is a powerful tool for advancing IS research. It enables protein characterization in the penumbra, supports the development of physiologically relevant in vitro models, and aids in the validation of UC-MSC- based therapies. Leveraging proteomics-driven insights could pave the way for more effective neuroprotective strategies in IS.

Keywords: Ischemic Stroke, MSCs, Co-Culture, Physioxia, Proteomics

New Approaches against Breast Cancer: Assessment of Drug Cytotoxicity through Vibrational Microspectroscopy

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Breast cancer (BC) is the most common cancer in women, with a high mortality. TNBC is a biologically aggressive tumour, characterized by high rates of metastasis. Improved chemotherapeutic approaches against BC are therefore an urgent clinical need. Raman and Fourier transform infrared (FTIR) spectroscopies are complementary techniques with high specificity. Coupled to optical microscopy, they allow to interrogate biological samples with unmatched sub-cellular spatial resolution. This study aims to assess the metabolic impact of a Pd(II) complex with spermidine (Pd3Spd2, Spd=H2N(CH2)4NH(CH2)3NH2), as well as of a Pt(II) complex with putrescine (Pt2Put2(NH3)4, Put= H2N(CH2)4NH2), on: i) TNBC cells (MDA-MB-468); ii) non-TNBC cells (MCF-7) and iii) healthy human breast cells (MCF-12A). The cells were treated with Pd3Spd2 and Pt2Put2(NH3)4 at their corresponding IC50 concentrations, respectively for 48h and 72h. Raman and FTIR spectra were acquired for both untreated and drug-treated cells, followed by pre-processing and data analysis. Upon analysis, chemical differences between the cell lines and the drugs were clearly unveiled. These results provided spectral features specific to malignancy and allowed the identification of particular spectral biomarkers that led to the discrimination between drug-treated and untreated cells. This knowledge is expected to contribute for the rational design of improved anticancer drugs, with a higher efficiency coupled to lower toxicity.

Keywords: Metallodrugs, Breast cancer, Raman microspectroscopy, FTIR microspectroscopy

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SESSION 4

MOLECULAR AND CELLULAR MECHANISMS: ORGANIC SYSTEMS

The role of Ube3A in presynaptic differentiation

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The decrease in UBE3A gene expression levels, derived from various genetic etiologies, results in Angelman Syndrome (AS), a rare neurodevelopmental disease characterized by cognitive and motor impairments, epilepsy, EEG abnormalities, lack of speech and sleep difficulties. Although the subcellular localization, targeting and dynamics of Ube3A have been explored, the specific localization and functions in the presynapse, remain to be elucidated. To characterize the subcellular organization of Ube3A in neurons we analyzed Ube3A localization and colocalization with presynaptic proteins through immunocytochemistry. To address Ube3A role in presynaptic differentiation we analyzed the levels of presynaptic proteins in AS model mice by western blot. Additionally, we downregulated Ube3A in hippocampal neurons of WT mice to evaluate the effects in presynaptic proteins abundance. In this work, we demonstrate that Ube3A is expressed in distal axons. Additionally, we show that Ube3A colocalizes with presynaptic proteins and that these tend to be decreased in AS model mice when compared to WT mice. Finally, we also show that Ube3A downregulation decreases the number of glutamatergic presynaptic terminals. Collectively, our findings underscore the presence and function of Ube3A in the presynapse, its potential involvement in the cognitive alterations found in patients with AS which supports targeted modulation of Ube3A expression as a potential therapeutic strategy.

Keywords: Ube3A, Angelman syndrome, Axon, Presynapse

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Neuroprotection by mitochondrial NAD against glutamate-induced excitotoxicity

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Excitotoxicity is a pathological process that occurs in many neurological diseases such as stroke or epilepsy, being characterized by the extracellular accumulation of high concentrations of glutamate or other excitatory amino acids. Nicotinamide Adenine Dinucleotide (NAD) depletion is an early event following excitotoxicity in many in vitro and in vivo excitotoxic-related models and contributes to the deregulation of energy homeostasis. However, the interplay between glutamate excitotoxicity and the NAD biosynthetic pathway is not fully understood. To address this question, we used a primary culture of rat cortical neurons and found that glutamate excitotoxicity alters the expression of NAD biosynthetic enzymes. Using a fluorescent NAD mitochondrial sensor, we observed that glutamate induces a significant decrease in the mitochondrial NAD pool, which was reverted when exogenous NAD was added. We also show that exogenous NAD protects against glutamate-induced decrease in mitochondrial membrane potential and cell death. Additionally, we show that NAD and NAD precursors protect against changes in mitochondria retrograde transport in neurites. Our results demonstrate that glutamate-induced excitotoxicity compromises the NAD biosynthetic pathway, particularly in the mitochondria. These results also uncover a potential role for mitochondrial NAD as a tool for Central Nervous System (CNS) regenerative therapies.

Keywords: Mitochondria, NAD metabolism, Glutamate

Sex-Specific Effects of 17β-Estradiol and Testosterone on Human Cardiac Microvascular Endothelial Cells

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Coronary microvascular endothelial dysfunction (CMED) is central to heart failure with preserved ejection fraction (HFpEF), a condition predominantly affecting postmenopausal women and older individuals, contributing to structural and functional cardiac changes. Despite clear sex differences in disease prevalence, the role of sex hormones, particularly 17β-estradiol (E2) and testosterone (T), on endothelial function remains unclear. To investigate this, human cardiac microvascular endothelial cells (HMVECs) from both sexes were treated with E2 (0, 0.01, 0.1, 1, 10 nM) and T (0, 0.01, 0.1, 1, 10 nM) for 24 hours, and their effects on cell viability and proliferation were assessed, via the resazurin and BrdU assays, respectively. Neither hormone exerted a detrimental effect on cell viability. While E2 exhibited a non-significant trend toward increased proliferation in female HMVECs, T at 1 nM significantly enhanced proliferation in male compared to female HMVECs ($p<0.05$), with a general tendency for higher proliferation in male cells, suggesting sex-specific endothelial proliferative responses. Additionally, given the complex interplay between hormonal and inflammatory factors in HFpEF, future studies should assess the impact of HFpEF patient-derived serum or pro- inflammatory stimuli, such as tumor necrosis factor-alpha, on HMVECs, employing advanced techniques, including Omic analyses, in order to elucidate CMED mechanisms and aid in developing sex-specific therapies.

Keywords: Heart failure with preserved ejection fraction, Human cardiac microvascular endothelial cells, Coronary microvascular endothelial dysfunction, 17β-estradiol, Testosterone

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The impact of Cardiomyocyte-secreted Extracellular Vesicles on cardiac cell function and Atrial Fibrillation progression

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Atrial Fibrillation (AF) is the most common sustained arrhythmia and a major cause of cardiovascular morbidity and mortality. Although it mainly affects the elderly, its increasing prevalence reinforces the need to better understand AF onset and progression. AF is associated with cardiomyocyte remodelling and atrial fibrosis, impacting the vascular system. Extracellular Vesicles (EVs) mediate crosstalk between cardiac cells, with changes in EVs cargo being implicated in cardiovascular disease progression. A hallmark of AF is proteostasis disruption in cardiomyocytes characterized by heat shock proteins (HSPs) depletion and autophagy impairment, leading to an accumulation of toxic aggrgates. We hypothesized that EVs secreted by cardiomyocytes at the onset of AF act as a compensatory mechanism to alleviate intracellular stress by releasing damaged proteins and proteostasis-related factors, while inadvertently promoting inflammation, fibrosis and vascular dysfunction. To test this, we used HL-1 cardiomyocytes subjected to normal and rapid electrical pacing. HL-1 under rapid pacing demonstrated autophagy impairment and altered HSP expression. Moreover, cardiac fibroblasts and endothelial cells exposed to HL-1 secretome and EVs exhibited changes in proteostasis markers, fibrotic phenotype and endothelial dysfunction. These findings highlight a potential role for EVs in the propagation of damage in AF and open new perspectives for therapies targeting intercellular.

Keywords: Atrial fibrillation, Extracellular vesicles, Proteostasis, Autophagy, Intercellular communication

INVESTIGATING THE ROLE OF ELP3 OVEREXPRESSION IN ALZHEIMER'S DISEASE CELLULAR MODELS

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by severe cognitive decline. Its pathophysiology is characterized by amyloidβ plaques, tau neurofibrillary tangles and gene expression alterations. However, the molecular mechanisms underlying AD onset and progression remain unclear, and no effective therapies exist. Recently, tRNA modifications, catalyzed by different tRNA modifying enzymes, have emerged as key regulators of translation, essential for accurate mRNA decoding. Disruption of tRNA modifications have been found in several neurological disorders and we have recently shown that the expression of ELP3, a tRNA modifying enzyme, and the levels of its dependent thiolated wobble uridine tRNA modifications are reduced in AD. Here, we aim to elucidate if ELP3 overexpression has a positive impact in AD cellular models, namely SH-SY5Y-appSwe cells when compared to SH-SY5Y expressing wild-type APP. After ELP3 plasmid transfection, its expression was assessed by qPCR and Western blotting in both cell lines, confirming ELP3 overexpression. Analysis of protein insoluble fractions indicate that overexpressing ELP3 in SH-SY5Y- appSwe impacts proteostasis. We are currently assessing if overexpression of ELP3 restores 2-thiolation tRNA modification levels by Northern blotting. Our preliminary data indicate that targeting tRNA modifying enzyme expression is promising in the context of neurodegeneration and can result in innovative therapeutic strategies.

Keywords: Alzheimer's disease, tRNA modifications, tRNA-modifying enzymes, ELP3, Translation

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The impact of breast cancer-derived secretomes and extracellular vesicles on endothelial cells

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Breast cancer (BC) patients often develop cardiovascular diseases (CVD), yet the mechanisms whereby malignant cells induce damage in cardiac and vascular cells remain unclear. Given the role of extracellular vesicles (EVs) in intercellular communication, cell proliferation, and angiogenesis, evidence ascribing them a part in this interplay is increasing. Connexin 43 (Cx43) has been found on the EVs' surface and mediates their interaction with target cells and the release of EVs' cargo. This project aimed to understand the impact of secretomes and EVs secreted by BC cells on endothelial cells (ECs)' function, with a focus on the influence of Cx43 in this process. The triple-negative BC Hs578T cell line was used grounded on previous results demonstrating significant differences between wild type (WT) and Cx43 knock-out (KO) Hs578T cells regarding invasion capacity and colony formation. Our results showed that secretomes and EVs isolated from Hs578T WT and KO cells alter, at different levels, ECs' senescence and DNA damage levels. Secretome and EVs treatments modulated the expression of several proteins, including ZO-1, VE-cadherin and LC3, affecting endothelial-mesenchymal transition, integrity of the ECs monolayer, and autophagy. Lastly, both treatments led to differences in the ECs' angiogenic potential, compared to untreated controls. Overall, this project highlights the relevance of tumor-derived secretomes and EVs, as well as Cx43, in the development of BC-associated CVD.

Keywords: Breast cancer, Cardiovascular disease, Cardio-oncology, Extracellular vesicles, Connexin 43

Impact of Systemic Lipids in the Reprogramming of Mouse Induced Pluripotent Stem Cells and Cardiomyocyte Differentiation

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Cell reprogramming to induced pluripotent stem cells (iPSCs) holds great potential as a cell-based therapy for cardiovascular regeneration. However, and despite the importance in the context of cardiovascular diseases, the impact of lipids remains undisclosed. Here, we set out to determine how systemic lipids affects the reprogramming and differentiation of iPSCs into cardiomyocytes. Animals fed a high-fat diet (HFD) for 9 weeks showed a significant increase in body weight, serum glucose, and triglyceride levels compared to control (CD) diet. Reprogramming of adult ear fibroblasts (AEFs) from HFD animals into iPSCs exhibited lower efficiency. After expansion, HFD-derived iPSCs showed increase proliferation and NANOG expression and several deregulated metabolic parameters, as increased lipid droplets and lower TMRE labeled mitochondria. Importantly, HFD-derived iPSCs produce teratomas with representation of the three germ layers but a clear reduction in mesoderm-derived tissues. In vitro differentiation of HFD-iPSCs into embryoid-bodies derived cardiac lineage present a clear reduction in beating foci, lower levels of cardiac and increased expression of pluripotent markers. Our findings indicate that short exposure to systemic lipids induced a functional long- term obesogenic memory in adult fibroblast that impacted reprogramming and differentiation of mouse iPSCs and effective cell-based cardiac regeneration.

Keywords: Cell reprogramming, Obesogenic memory, Pluripotency, Cardiomyocyte differentiation, Metabolism

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Senescence-Induced Alterations of Mitochondria-Associated Membranes (MAMs) in Astrocytes

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Cellular senescence and mitochondria-associated membranes (MAMs) play a role in various neurodegenerative diseases. MAMs are close contact sites between the endoplasmic reticulum (ER) and mitochondria that regulate multiple physiologic processes. Astrocytes can develop a senescent-like phenotype contributing to neuroinflammation, neurodegeneration, and cognitive decline. This study aims to establish a model of senescence in a human astrocytic cell line and evaluate its impact on MAMs. Senescence was induced by treating astrocytes with 10 and 20 μM of Etoposide for 24h, followed by immediate analysis or a two-day recovery period. Cell viability (MTT assay), cell death (caspase 3 cleavage), and senescence markers (p53, p16, p21, γ-H2AX, Lamin B1, β-gal) were assessed (WB and ICC). MAMs structure was evaluated via TEM and WB, and ER-mitochondria Ca^{2+} transfer via single-cell calcium imaging (SCCI) with Rhod-2/AM. In recovery cells, but not in non-recovery cells, Etoposide induced a senescence-like phenotype, supported by increased lysosomal accumulation of β-gal, Lamin B1 depletion, and decreased of proliferative markers. These observations were concomitant with reduced metabolic activity and absence of caspase 3-dependent apoptosis.Under these conditions, changes in the number of ER-mitochondria close contacts were observed, as well as altered ER- mitochondria Ca^{2+} transfer. These findings suggest that senescence induction is associated with MAMs dysfunction in astrocytes.

Keywords: Senescence, Endoplasmic reticulum-mitochondria close contacts, Glia cells

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Transcription factor cooperativity at a GATA3 tandem DNA sequence determines enhancer- mediated activation of oncogenic TAL1 in T-ALL

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T-cell acute lymphoblastic leukemia (T-ALL) is a hematological malignancy characterized by dysregulation of transcription factor (TF) oncogenes, with activation of TAL1 being the most common. A novel mechanism of aberrant TAL1 activation occurs through somatic mutation of a non-coding site approximately 7.5 kb from the TSS. The mutation creates binding motifs for the TF MYB. Despite the requirement of MYB to establish the novel enhancer, it remains to be elucidated which additional TFs are required for ongoing enhancer oncogenic TAL1 expression. Using a TAL1-reporter Jurkat cell line, where TAL1 has been endogenously GFP-tagged, we employed a genome-wide CRISPR/Cas9 knockout screen. Cells with reduced GFP expression, indicating TAL1 reduced expression, were sorted for analysis. Accordingly, genomic DNA was extracted and sgRNAs were amplified by PCR and quantified upon sequencing. GATA3 scored as the strongest activator of TAL1 (log2FC = 1.8, pvalue = 1.2x10-5). Next, we tested the functionality of the GATA3 DNA binding motifs on TAL1 activation. We found that the TAL1 enhancer sequence is comprised of three GATA3 binding sites (S1, S2 and S3). Editing of these sites using CRISPR/Cas9 HDR in Jurkat cells, showed GATA3 occupancy at sites S2 and S3 determines the chromatin accessibility landscape and TAL1 activation. Overall, our data provide insights into the mechanisms of enhancer-oncogene regulation in T-ALL, thus offering an opportunity for therapeutic targeting.

Keywords: Transcription Factor cooperativity, Oncogene, TAL1, T-cell Acute Lymphoblastic Leukemia (T-ALL)

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Finding the mechanisms underlying cell intrinsic resistance to oncogenesis

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Oncogenesis arises from genetic and epigenetic changes that stimulate the uncontrolled growth of cells. However, different types of cells react differently to oncogenic stimuli. In Drosophila eye precursor epithelium, differentiated epithelial cells proliferate in response to oncogenic stimuli, while the progenitor cells resist transformation. Our hypothesis is that the progenitor cells might possess state-specific resistance mechanisms to avoid excessive response to mitogenic signals. To test this hypothesis, we determined the transcriptome of the progenitor cells and identified genes exclusively expressed in the progenitor domain. After this identification, we performed a genetic screen using CRISPRa and identified optix as a possible regulator of cancer cell proliferation. Interestingly, Optix levels impact differently on oncogenesis. In the differentiated domain, ectopic expression of Optix closer to its physiological levels results in a considerable reduction of the hyperplasia, while higher levels of Optix promote tumour growth. We are currently evaluating the role of Optix on the balance of cell proliferation and differentiation to understand how Optix function can control cell transformation according to the cellular context. Our results highlight optix as a crucial element in the relationship between cell differentiation state and oncogenesis, emphasizing the relevance of understanding these mechanisms to explore new therapeutic approaches against cancer.

Keywords: Oncogenic resistance, Progenitor cells, Eye development, Retinal determination genes

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Investigating Epigenetic Barriers to Oncogenesis in the Germline

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This research explores epigenetic landscapes that control cellular responses to oncogenic signals, focusing on how chromatin dynamics influence the proliferation of primordial germ cells (PGCs). Despite their intrinsic immortal nature and unlimited proliferative potential, germline cells exhibit a remarkable resistance to oncogenic transformation—raising fundamental questions about the epigenetic barriers that safeguard this lineage. Using the Drosophila melanogaster female germline model, we are using a mild response of PGCs to the evolutionary conserved oncogene Yki as a sensitized background to systematically target chromatin remodelers by RNAi. By using germline specific fluorescent markers, we analyzed the gonad size as a readout of germline proliferation. Our preliminary analysis indicated that the SWI/SNF and PRC complexes are important regulators of this process, where some subunits restrict PGCs proliferation and others are required for PGCs survival or determination. We are currently performing histological analysis of the larval gonads to understand the impact of these key epigenetic regulators on germline response to Hippo signaling. Understanding these epigenetic constraints could unveil novel insights into oncogenic resistance, potentially informing new strategies to limit pathological cell proliferation across cancer types.

Keywords: Drosophila, Germline, Epigenome, Germline cancer genes, Chromatin remodelers

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Understanding the contribution of BRI2 to the differentiation of SH-SY5Y cells

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BRI2 is a transmembrane protein linked to neurodegenerative disorders, with its dysregulation contributing to disease onset and progression. While previous studies from our group suggest a role for BRI2 in neuronal differentiation, its exact function and signalling pathways involved remains unclear. This study aims to clarify BRI2's role in neurite outgrowth and neuronal differentiation. CRISPR/Cas9-mediated genomic deletion was used to generate a BRI2 knockout (KO) SH-SY5Y cell line. Cells were then differentiated with retinoic acid (RA) and brain-derived neurotrophic factor (BDNF) for seven days, and BRI2 and neuronal marker expression were assessed by immunoblotting and immunocytochemistry at multiple timepoints. Western blot analysis showed reduced BRI2 levels in KO cells compared to controls, suggesting a partial KO across the population. ICC analysis confirmed these results, revealing some cells with no detectable BRI2 expression. Notably, BRI2-KO cells showed altered levels of neuronal markers, such as MAP2 and βIII-tubulin, suggesting that BRI2 deletion impact neuronal differentiation. Our findings indicate that BRI2 is necessary for proper neuronal differentiation in SH- SY5Y cells. Moreover, the correlation between BRI2 loss and the alterations observed in neuronal markers highlights a potential regulatory role for BRI2 in the neuronal differentiation process, and future studies will help elucidate the underlying molecular mechanisms.

Keywords: Neuronal differentiation, Neurodegeneration, BRI2, Knockout

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Amyloid Transthyretin Induces Lysosomal Dysfunction in Cardiac Fibroblasts

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Transthyretin cardiac amyloidosis (ATTR-CA) is a systemic disorder that often leads to chronic heart failure and death. Its heterogeneous clinical presentation and non-specific phenotype have contributed to frequent underdiagnosis. However, advances in diagnostic techniques, have significantly improved its recognition. Although interstitial deposition of amyloid transthyretin (ATTR; transthyretin pathological form) in heart is a hallmark of the disease, early cardiac cell dysfunction is believed to precede amyloid accumulation. However, the underlying mechanisms remain poorly understood. In this work, we propose that age-related proteostasis dysregulation and the lysosomal overload caused by internalized transthyretin, foster the progressive accumulation of dysfunctional lysosomes. This triggers an upregulation of lysosomal exocytosis and the release of their contents, promoting a feedforward cycle of amyloid deposition. Our results demonstrate that ATTR can be internalized by cardiac fibroblasts inducing the loss of lysosomal function and membrane integrity. Furthermore, we found that ATTR also elicits alterations in the cellular response to lysosomal damage, impairing repair mechanisms and the clearance of damaged lysosomes. Notably, we observed enhanced lysosomal exocytosis triggered by TTR-induced lysosomal damage. This work brings new insights into the interplay between lysosomes and ATTR-CA, shedding light on its physiopathology and opening new therapeutic avenues.

Keywords: Lysosomal dysfunction, Lysosomal damage-response, Cardiac amyloidosis, Transthyretin

Electrophysiological changes in cerebellar neurons caused interleukin-4

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The cerebellum is crucial for motor control and cognition, and cerebellar dysfunction is linked to Attention- Deficit/Hyperactivity Disorder (ADHD). ADHD is associated with cerebellar, basal ganglia, and prefrontal cortex (PFC) changes and it is more prevalent in people with allergies. Our prior work shows that IL-4 elevation in mice postnatal period, mimicking early-life allergies, alters the cerebellar circuit and the connection cerebellum-ventral tegmental area (VTA), a dopaminergic nuclei that regulates dopamine levels in the PFC. Here, we assessed how postnatal IL-4 alters the inhibitory tonus of the cerebellar circuit and anatomically characterized the putative circuit cerebellum-VTA-PFC, whose dysfunction may underlie ADHD. We injected a fluorescent tracer in the cerebellar nuclei (CN), which projects to the VTA, and stained for VTA dopaminergic neurons, to evaluate their colocalization. To assess how IL-4 elevation affects the cerebellum, we injected IL-4 at P6 and P8, followed by patch-clamp in young (P10-P15) and adult mice (P60+) on cerebellar Purkinje cells (PCs), and Molecular Layer Interneurons (MLI). We identified a specific VTA region receiving CN projections, with CN neurons synapsing with dopaminergic and non-dopaminergic VTA neurons. Patch-clamp data show age-dependent effects of IL-4 on MLI, hinting at a circuit (mal)adaptation. IL-4 also seems to accelerate MLI's maturation. This work highlights the impact of immune challenges on neurodevelopment.

Keywords: Cerebellum, Attention Deficit/Hyperactivity Disorder (ADHD), Allergies, Patch-clamp eletrophysiology, Viral Tracing

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Oxidative Stress, Proteostasis, and Metabolism: How BIN1 Modulates Cellular Homeostasis and Amyloidogenic Pathways in Alzheimer's Disease

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Alzheimer's Disease (AD) is an incurable, progressive neurodegenerative disorder and the leading cause of dementia worldwide. Its pathology is primarily characterized by the accumulation of β-amyloid (Aβ) plaques and intracellular tau aggregates, contributing to synaptic dysfunction and neuronal loss. Bridging Integrator 1 (BIN1) is a multifunctional protein involved in membrane curvature, intracellular trafficking, and endocytosis. Notably, BIN1 plays a role in the regulation of BACE1, a key enzyme in the processing of amyloid precursor protein (APP), a crucial step determining the production and accumulation of Aβ. Disruptions in BIN1 function have been associated with increased Aβ deposition, but its mechanisms of action, namely on cellular fitness, remain hereto unexplained. This work explored the impact of BIN1 signalling and modulation in a cellular model of AD, using a combination of molecular and imaging techniques to evaluate cellular responses and determine the role of BIN1 dysfunction in AD progression and pathology. Through targeted interventions, including manipulation of redox and metabolic status, the expression and activity of BIN1 were found to affect key cellular mechanisms. By dissecting the molecular mechanism mediating the regulatory role of BIN1 in AD, this research contributes to better understanding its involvement in mechanisms resulting in neurodegeneration, identifying new molecular targets and opening new avenues for therapeutic intervention.

Keywords: Oxidative stress, BIN1, Alzheimer's disease, Cellular homeostasis

Funding: Research was supported by FCT EXPL/BTM-SAL/0902/2021 and La Caixa Foundation CI21-00276.

Drosophila@Aveiro: An in vivo iBiMED platform for pre-clinical studies

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The fruit fly Drosophila melanogaster has emerged as a powerful model organism in biomedical research, bridging fundamental biology and translational medicine. Its genetic tractability, short life cycle, and conservation of key disease-related pathways make it an invaluable tool for pre-clinical studies. Drosophila models have been successfully employed to investigate the molecular mechanisms underlying a variety of human diseases, including neurodegenerative disorders, cancer, metabolic syndromes, and rare genetic conditions. The ability to perform large-scale genetic screens, coupled with advanced imaging and high- throughput drug screening techniques, enables rapid identification of therapeutic targets and potential drug candidates. In this poster, we will showcase the resources and capabilities of the iBiMED Drosophila facility and explore how this platform can address your scientific questions in pre-clinical research and personalized medicine. By fostering collaboration between Drosophila researchers and the clinical community, we aim to enhance the translational impact of this model organism and accelerate the development of novel therapeutic strategies.

Keywords: Model organism, Drosophila melanogaster, Genetics, Pre-clinical studies, Pharmacological screens

Funding: Torcato Martins was supported by the EC Marie Curie Individual Fellowship (DOI: 10.3030/893260) and is currently supported by the FCT CEEC 5th Edition Assistant Researcher Award (DOI: 10.54499/2022.02406.CEECIND/CP1720/CT0014). This project was supported by PTDC/BIA-BID/1606/2020, and the iBiMED research unit is supported by FCT funds under UIDB/4501/2020 and UIDP/4501/2020.

SESSION 5

IMMUNOLOGY & HOST-MICROBE INTERACTIONS

Deciphering the Susceptibility of Patients with Peroxisome Biogenesis Deficiencies to Influenza A Virus Infection

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Peroxisomal biogenesis disorders (PBDs) are rare genetic disfunctions caused by defects in specific peroxisomal proteins. The most prominent subtype, the Zellweger Syndrome Spectrum, is characterized by congenital malformations and high mortality rates. Although the role of peroxisomes in the context of viral infections is well-acknowledged, the susceptibility of PBD patients to viral diseases remains largely unexplored. In this study, we specifically addressed the susceptibility of cells from a PEX10-deficient PBD child to infection by influenza A virus (IAV). Our results demonstrated that PEX10 deficiency significantly compromises the immune response not only during IAV infection, but also upon non-specific viral RNA stimulation. However, the virus is apparently not able to take advantage of this cellular condition, as a lower number of new infectious viral particles are produced in PEX10-deficient cells. These results highlight the role of peroxisomes in modulating susceptibility to IAV infections, and the implications of PBD mutations on the host cell antiviral response.

Keywords: Peroxisomes, Viruses, Influenza A virus, Peroxisome biogenesis disorders, Zellweger spectrum disorders

Funding: This work was supported by the Portuguese Foundation for Science and Technology (FCT): PTDC/BIACEL/31378/2017 (POCI 01-0145-FEDER-031378), CEECIND/03747/2017, 2024.04462.BD, UID/BIM/04501/2013, POCI-01 0145-FEDER-007628 under the scope of the Operational Program "Competitiveness and internationalization", in its FEDER/FNR component. It was also supported by the European Union through the Horizon 2020 program: H2020-WIDESPREAD-2020-5 ID 952373.

Peroxisomal MAVS activation kinetics and peroxisome-endoplasmic reticulum interaction modulate innate immunity against RNA viruses

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Peroxisomes are key antiviral and pro-viral platforms. Different viruses modulate their dynamics to evade the antiviral response and/or enhance viral propagation1. Alongside mitochondria, peroxisomes host MAVS (mitochondrial antiviral signaling adaptor protein), which, upon viral RNA recognition, oligomerizes and activates a signaling cascade to the production of antiviral effectors. Our study aims to elucidate the mechanisms that govern and distinguish the MAVS signaling at peroxisomes and mitochondria and unravel how peroxisome metabolism, morphology, and inter-organelle interactions shape immune responses against RNA viruses. Using a doxycycline-inducible system to control MAVS expression and activation at peroxisomes and mitochondria, we reveal that peroxisomes play a crucial role in rapidly triggering a strong antiviral response, driven by a highly efficient and swift oligomerization of MAVS at this organelle. Our results also show that MAVS activation induces alterations in peroxisome morphology and metabolism. Using a cell line with disrupted peroxisome-endoplasmic reticulum (ER) tethering, we have also discovered that the interaction between these two organelles is essential for MAVS oligomerization and the proper establishment of an efficient antiviral response. This data highlights peroxisomes as crucial hubs in antiviral immunity, supporting the putative targeting of specific peroxisomal mechanisms for the development of novel antiviral strategies.

Keywords: Peroxisomes, MAVS, Antiviral signaling, Viruses

Funding: This work was supported by the Portuguese Foundation for Science and Technology (FCT): PTDC/BIACEL/31378/2017 (POCI 01-0145-FEDER-031378), CEECIND/03747/2017, 2022.14102.BD, SFRH/BD/148516/2019, SFRH/BD/137851/2018, 2020.09490.BD, UID/BIM/04501/2013, POCI-01 0145-FEDER-007628 under the scope of the Operational Program "Competitiveness and internationalization", in its FEDER/FNR component. It was also supported by the European Union through the Horizon 2020 program: H2020-WIDESPREAD-2020-5 ID 952373.

Unveiling the role of peroxisome metabolism in influenza A virus infection

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Peroxisomes are ubiquitous organelles increasingly recognized as key players in viral infections, acting as both pro-viral and antiviral platforms. Viruses, as obligate intracellular parasites responsible for thousands of deaths annually, can manipulate these organelles to evade the cellular antiviral response or enhance their replication. Although the importance of peroxisomes in the context of influenza A virus (IAV) infection has been demonstrated, there is still a significant gap in the understanding of the molecular mechanisms that take place. Preliminary data from our group suggests that metabolically dysfunctional peroxisomes affect the cellular antiviral response. To unravel the role of the different peroxisome metabolic pathways in the context of IAV infection, we have infected cells lacking key peroxisomal enzymes and analysed the effect not only on the production of new IAV infectious particles, but also on the peroxisome-dependent antiviral signalling. Our findings confirm that peroxisome metabolism influences antiviral signalling and suggest that the β-oxidation of very long chain fatty acids impacts both the cellular antiviral response and IAV infection. These findings indicate that modulating peroxisome metabolism holds potential for developing innovative host-directed antiviral therapies.

Keywords: Peroxisomes, Influenza A virus (IAV), Peroxisome metabolism

Funding: This work was supported by the Portuguese Foundation for Science and Technology (FCT): PTDC/BIACEL/31378/2017 (POCI 01-0145-FEDER-031378), CEECIND/03747/2017, 2022.14102.BD, UID/BIM/04501/2013, POCI-01 0145-FEDER-007628 under the scope of the Operational Program "Competitiveness and internationalization", in its FEDER/FNR component. It was also supported by the European Union through the Horizon 2020 program: H2020-WIDESPREAD-2020-5 ID 952373.

Implementation of a GFP-reporter system to assess CUG mistranslation in Candida albicans clinical isolates.

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Mistranslation during protein synthesis leads to incorrect amino acid incorporation. The human pathogen Candida albicans exhibits intrinsic mistranslation, particularly at the CUG codon, which can be ambiguously translated as serine or leucine. This contributes to a heterogeneous proteome, enhancing the organism's adaptability under stress conditions. Despite its relevance, codon-specific error rates and the spectrum of misincorporation events in clinical isolates of C. albicans remain largely underexplored. To address this, we optimized a reporter system based on the yeast-enhanced green fluorescent protein (GFP) to detect and quantify, for the first time, CUG-related mistranslation in clinical isolates using flow cytometry. To determine whether these errors correlate with antifungal resistance, we analyzed nine C. albicans isolates from the iBiMED biobank with varying antifungal susceptibilities. Our results confirm the successful incorporation of the reporter into the Candida genome and the effectiveness of our method for mistranslation assessment. Basal CUG mistranslation in the isolates was comparable to previously reported levels in laboratory strains, which surpasses the expected level of 10-5 to 10-4 for translation errors. Stress-induced mistranslation by exposure of these clinical strains to antifungals will enhance our understanding of the relationship between mistranslation, stress adaptation, and antifungal resistance.

Keywords: CUG ambiguity, Translation fidelity, Fungal adaptation, Antifungal resistance, Candida albicans

Funding: This work is funded by grants 2022.07484.CEECIND, 2021.00329.CEECIND, and project 10.54499/PTDC/BIA-MIC/1141/2021. The iBiMED research unit is supported by FCT funds under 10.54499/UIDB/04501/2020 and 10.54499/UIDP/04501/2020.

Mechanosensing and ER Stress in Plasmacytoid Dendritic Cells: Implications for Fibrosis in Systemic Sclerosis

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Systemic sclerosis (SSc), or Scleroderma, is a rare autoimmune disease characterized by immune dysregulation, vasculopathy and fibrosis. Plasmacytoid Dendritic Cells (pDCs) have emerged as key contributors to fibrosis progression. Fibrosis is associated with alterations in the mechanical properties of tissues, which can influence the activation, migration and metabolism of immune cells. However, the role of mechanosensing in pDCs within the context of SSc remains largely underexplored. As such, we investigated how substrate stiffness and ER stress affect pDC function and metabolism, and how their interaction with fibroblasts in a co-culture setting could influence fibrotic progression. Using engineered cell models and commercially available substrates replicating physiological and fibrotic tissue stiffness, we show that stiffer environments alter pDC metabolic profiles, promoting fibroblast activation and extracellular matrix deposition. The metabolic alterations observed in response to increasing stiffness suggest a role for mechanosensing in pDC activation. However, ER stress-mediated production of type I IFN by pDCs, a key cytokine in the context of SSc, was not affected by substrate stiffness. These findings provide novel insights into fibrosis regulation in Systemic Sclerosis, highlighting the potential of pDC modulation as a target for anti-fibrotic immunotherapies.

Keywords: Fibrosis, Systemic Sclerosis, ER stress, Immunometabolomics, Mechanosensing

Funding: This work was supported by the World Scleroderma Foundation and Edith Busch Stiftung (the EBF and WSF Research Grant Programme 2022-2023). Work was also developed within the scope of iBiMED – Institute of Biomedicine and supported by FCT - Fundação para a Ciência e Tecnologia, I.P. by project references UIDB/04501/2020 (DOI 10.54499/UIDB/04501/2020) and UIDP/04501/2020 (DOI 10.54499/UIDP/04501/2020), financially supported by national funds (OE), through FCT/MCTES. FCT is acknowledged for the individual grant to M.D.M. (SFRH/2024.05442.BDANA) and the research contract under the Scientific Employment Stimulus to I.F.D. (CEECIND/02387/2018).

Unravelling the role of peroxisome fission in influenza A virus replication and propagation

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Peroxisomes, crucial organelles for multiple metabolic pathways, have also been identified as important players in viral infections, serving either as pro-viral or antiviral platforms. Viruses can modulate peroxisomes in different manners, either to support replication and/or influence the cellular antiviral responses. Our group has demonstrated the importance of peroxisomal morphology for the modulation of the peroxisome- dependent antiviral response and has shown that the manipulation of peroxisomal fission by controlling the expression of dynamin-1-like protein (DLP1) strongly influences antiviral signalling. To investigate the impact of the peroxisomal fission machinery on influenza A virus (IAV) replication and propagation, we quantified the amount of new infectious viral particles produced upon overexpression of DLP1. Our results demonstrate that enforced peroxisome fission leads to a reduction of viral propagation, alongside with a lower infection rate. Additionally, we demonstrate that viral protein translation is also directly affected by the induction of organelle fission. These findings suggest that the modulation of peroxisome morphology, specifically their fission machinery, disrupts IAV infection, and may lead to the discovery of novel cellular targets for host-directed antiviral therapy against IAV.

Keywords: Peroxisomes, Influenza A virus (IAV), Viral replication, Peroxisome fission

Funding: This work was supported by the Portuguese Foundation for Science and Technology (FCT): PTDC/BIACEL/31378/2017 (POCI 01-0145-FEDER-031378), CEECIND/03747/2017, 2022.14102.BD, UID/BIM/04501/2013, POCI-01 0145-FEDER-007628 under the scope of the Operational Program "Competitiveness and internationalization", in its FEDER/FNR component. It was also supported by the European Union through the Horizon 2020 program: H2020-WIDESPREAD-2020-5 ID 952373.

Combined effect of phage therapy and antibiotics against methicillin-resistant Staphylococcus aureus

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The rising number of deaths from bacterial infections and increasing antibiotic resistance highlight the urgent need for new antibacterial therapies. Phage therapy alone or combined with antibiotics have emerged as a promising solution. This study aims to isolate, characterize, and evaluate the efficacy of a phage alone and combined with antibiotics against methicillin-resistant Staphylococcus aureus (MRSA), a major human pathogen that causes a wide range of infections. The phages was isolated from wastewater, tested in vitro at a multiplicity of infection (MOI) of 10 against a MRSA strain alone, and combined with ciprofloxacin and chloramphenicol at different concentrations (MIC, ½ MIC, ¼ MIC, and 1/8 MIC). The phage effectively reduced the MRSA concentration, reaching the maximum of inactivation after 10 hours of treatment. When the phage was tested combined with the antibiotic the inactivation was more effective, the inactivation was higher and observed earlier, mainly when the antibiotics were used at values below the MIC (¼ and ⅛ of the MIC, respectively, for chloramphenicol and ciprofloxacin). The high bacterial inactivation efficiency of the combined approach paves the way for depth in vivo studies to control MRSA infections and to overcome the development of resistance by bacteria.

Keywords: Bacteriophages, Staphylococcus aureus, Antibiotics, Resistance

Establishing a 3D-hydrogel model to study fibrosis mechanisms in Systemic Sclerosis

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Systemic Sclerosis (SSc) is an autoimmune disease with high mortality and morbidity. SSc is characterized by immune dysregulation, vasculopathy, and fibrosis of skin and/or internal organs. This fibrosis occurs upon differentiation of fibroblasts into myofibroblasts, which promotes secretion and deposition of extracellular matrix proteins, leading to increased tissue stiffness. The pathological mechanisms of SSc are yet to be understood and models allowing characterization of cellular behavior under varying stiffness conditions are valuable research tools. Hydrogels made from human methacryloyl platelet lysates (hPLMA) have tunable mechanical properties and a biocompatible profile, making them interesting platforms for 3D fibrosis modeling. Thus, this study aims to use hPLMA hydrogels to mimic healthy and fibrotic lung tissue, evaluating its impact on fibroblast behavior. hPLMA hydrogels at concentrations of 12.5%, 15%, and 20% (w/v) were synthetized and mechanically characterized by compression tests. Hydrogels with higher hPLMA concentrations were generally related with increased stiffnesses, i.e. higher Young's modulus values. To model lung fibrosis, lung fibroblasts were encapsulated in hydrogels. Cell viability, evaluated through Live/Dead staining, indicated decreasing survival of encapsulated fibroblasts with increasing incubation time. Protocols are currently being optimized to improve cell survival and to measure proteins of interest by Western Blot.

Keywords: 3D-Hydrogel model, Human platelet lysates, Fibroblasts, Fibrosis, Systemic Sclerosis

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Funding: This work was supported by the World Scleroderma Foundation and Edith Busch Stiftung (EBF and WSF Research Grant Programme 2022–2023). Work developed within the scope of iBiMED – Institute of Biomedicine (references UIDB/04501/2020, DOI https://doi.org/10.54499/UIDB/04501/2020, UIDP/04501/2020, DOI https://doi.org/10.54499/UIDP/04501/2020) financially supported by national funds (OE), through Fundação para a Ciência e a Tecnologia (FCT)/MCTES.

Candidiasis: identifying novel RNA-based factors as virulence determinants in Candida albicans clinical isolates

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Candida albicans is the most common cause of candidiasis, and it can lead up to 40% mortality when infections become invasive. Many attributes have been linked to its the ability to successfully colonize and infect the human host, including biofilm formation, adhesion and morphological transitions. However, the mechanisms involved in regulating its virulence remain unclear. Recently, tRNA modifications emerged as important regulators of gene expression and have been associated with various human diseases, including fungal infections. Also, studies pointed to 2-thiolation as an important tRNA wobble modification related to stress resistance in yeast models, such as Saccharomyces cerevisiae. Despite this, modulation of the epitranscriptome in C. albicans remains unexplored. For this study, we are assessing how tRNA modification levels influence virulence traits of C. albicans clinical isolates from the iBiMED biobank. The strains selected present distinct phenotypes, including pseudohyphae formation, lack of filamentation, strong biofilm production, and antifungal resistance. We are analyzing 2-thiolation tRNA modification levels by Northern blotting, and the expression of tRNA modifying enzymes, NCS2 and HMA1, by RT-qPCR. Our preliminary data show that tRNA modification and tRNA modifying enzyme levels vary in clinical isolates with different virulence traits. This association can be used to develop new antifungal therapeutic strategies.

Keywords: Epitranscriptome, tRNA modifications, NCS2, HMA1, Candida-mediated diseases

Funding: This work is funded by the grants CEECIND/00284/2018, AARG-NTF-23-1149641 and 10.54499/PTDC/BIA-MIC/1141/2021. The iBiMED research unit is supported by FCT funds under 10.54499/UIDB/04501/2020 and 10.54499/UIDP/04501/2020.

The impact of LPS induced tolerance on macrophage – Escherichia coli interaction

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Innate immune responses are crucial in shaping host–pathogen interactions. Lipopolysaccharide (LPS) is a Pathogen Associated Molecular Pattern (PAMP) that can either trigger immune cell activation or induce tolerance, depending on the dosage and/or repeated stimulation. Furthermore, immune responses can affect and be affected by an organism's microbiota. Dysbiosis, commonly associated with aging and inflammatory bowel diseases, can lead to increased gut permeability, thereby facilitating the translocation of bacterial products such as LPS. Repeated or prolonged exposure to LPS may induce endotoxin tolerance, which in turn can influence the evolution and composition of the gut microbiota. However, the exact role of LPS-induced tolerance in bacterial evolution remains unknown. In order to study this in detail, we started by establishing in vitro and in vivo models of tolerance by repeated stimulation with low doses of LPS. The in vitro model uses THP-1-derived macrophages exposed to LPS in culture conditions whereas the in vivo model uses mice intraperitoneally injected with LPS. We have collected peritoneal macrophages, which are now being tested for tolerance in vitro through the analysis of cytokine secretion. In the future, we aim to compare adaptation of E. coli in a LPS-tolerant versus non-tolerant environment both in vitro and in the in vivo conditions. With this, we hope to understand the influence of LPS tolerance in E. coli and microbiota evolution.

Keywords: Endotoxin tolerance, E. coli, Macrophage, Inflammation

Validation of antifungal resistance biomarkers in clinical isolates of Candida albicans

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Candida albicans is a major fungal pathogen responsible for both superficial and life-threatening systemic infections, particularly in immunocompromised individuals, with a mortality rate ranging from 30% to 60%. The increasing prevalence of antifungal resistance, particularly to azoles and echinocandins, represents a critical challenge in clinical settings. Antifungal susceptibility tests were completed on C. albicans isolates from the iBiMED biobank using E-tests and broth microdilution according to EUCAST guidelines. The genetic characterization of C. albicans isolates identified alterations associated with antifungal resistance, including a trisomy in chromosome 1, which harbors the FKS1 gene, the target of echinocandins. This study aims to functionally validate the impact of chromosome 1 trisomy using genetic manipulation techniques through the insertion of an additional copy of FKS1 via the CIp10 vector, mimicking the effects of trisomy in susceptible isolates and assessing its role in resistance by analyzing drug susceptibility and conducting immunochemical assays to quantify β-1,3-glucan production, a key component synthesized by FKS1. Together, these findings enhance our understanding of antifungal resistance in C. albicans, supporting the identification of reliable biomarkers and providing essential insights for improving diagnostic and therapeutic strategies.

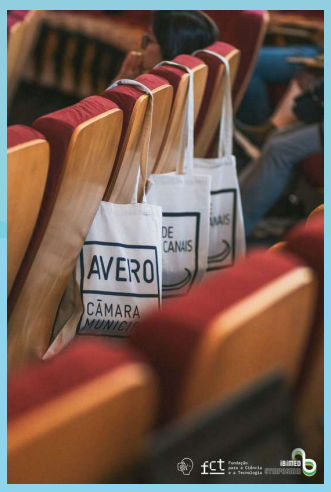
Keywords: Candida albicans, Antifungal resistance, Biomarkers, Chromosome 1 trisomy, FKS1

Funding: This work was supported by FCT – Fundação para a Ciência e Tecnologia, I.P. by project reference UIDB/04501/2020 and DOI identifier https://doi.org/10.54499/UIDB/04501/2020, project reference UIDP/04501/2020 and DOI identifier https://doi.org/10.54499/UIDP/04501/2020, and project FunResist - PTDC/BIA-MIC/1141/2021 and DOI identifier https://doi.org/10.54499/PTDC/BIA-MIC/1141/2021.

6 VENUE

CONFERENCE VENUE

The VIII iBiMED Symposium took place at the **Joaquim José da Cunha Auditorium** at the Institute of Accounting and Administration, University of Aveiro (ISCAA). The Symposium Dinner occurred on May 22nd at the University Restaurant with a special menu with several options, from appetizers to desserts.

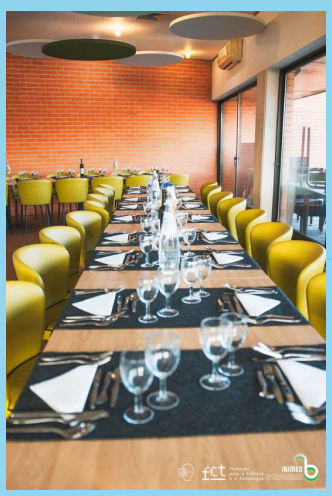


POSTER EXHIBITION

The poster session occurred at the **Exhibition Gallery** (UA Bookstore).

DINNER

The Symposium Dinner occurred on May 22nd at the University of Aveiro.



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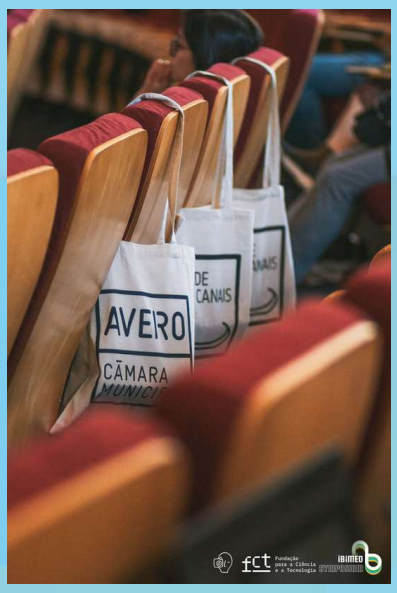

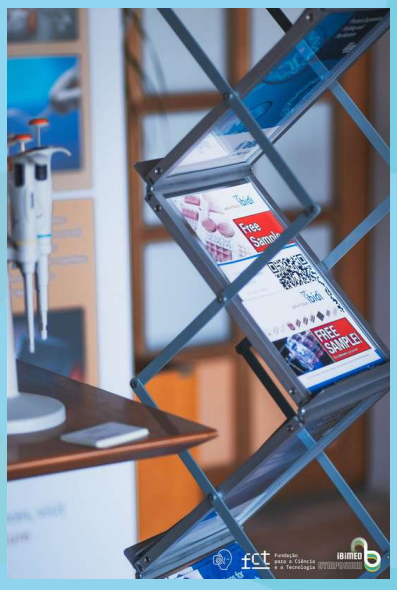

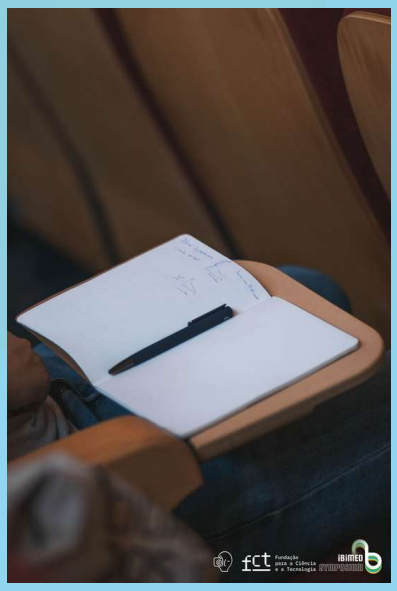

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