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MEETING ABSTRACTS **Open Access**

Center for Interdisciplinary Research in Health (CIIS) National Meeting 2023

Lisbon, Portugal. 31 March - 01 April 2023

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Paulo J. G. Bettencourt[1,2], Ana Mineiro[1,3], Paulo Alves[1,4], Nuno Rosa[1,5], André Correia[1,5], Marlene Barros[1,5]
[1] Universidade Católica Portuguesa, Center for Interdisciplinary Research in Health, Portugal; [2] Universidade Católica Portuguesa, Faculty of Medicine, Lisboa, Portugal; [3] Universidade Católica Portuguesa, Instituto de Ciências da Saúde, Lisboa, Portugal; [4] Universidade Católica Portuguesa, Instituto Ciências da Saúde, Escola Enfermagem (Porto), Portugal; [5] Universidade Católica Portuguesa, Faculty of Dental Medicine (FMD), Viseu, Portugal
Correspondence: Paulo J. G. Bettencourt (pbettencourt@ucp.pt)
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The Center for Interdisciplinary Research in Health (CIIS) is the research center of the Universidade Católica Portuguesa (UCP) focused on health care. The Center is organized in five platforms, and distributed in four geographies across Portugal: Lisbon, Porto, Viseu and Sintra (Table 1). The center has currently 155 active researchers and attracted funds exceeding 10M€.

For the first time ever, CIIS has organized a National Event that included researchers from all platforms and disciplines, in a truly interdisciplinary and translational scientific event, counting 117 registered participants and 120 abstracts. The meeting took place at the Faculty of Medicine, in the Sintra campus, on the 31st March and 1st April 2023. The Scientific Committee of the CIIS National Meeting decided that the theme for the meeting is *Interdisciplinary Health Care*. Rather than clustering researchers by platform or discipline, we decided to create three working sessions that are inclusive to everyone and not restricting the presentations by discipline, being therefore, interdisciplinary. These are: 1 – *Translational Care*; 2 – *Clinical Care*; and 3 – *Community Care*.

The meeting was held in the presence of the Universidade Católica Portuguesa Rector Professor Isabel Capeloa Gil, the Vice-Rector Professor Peter Hanenberg, the Director of the CIIS, Professor Marlene Barros, the Director of the Faculty of Medicine, Professor António Almeida and the guest speaker Professor Tomáš Zima, Charles University, Prague, Czech Republic, and hosted by the Deputy Director of the CIIS, Professor Paulo J. G. Bettencourt.

For two days, papers were presented by invited speakers within each session, and posters were presented by CIIS researchers and students, in a highly anticipated poster session. All abstracts were peer-reviewed. To bring further excitement to the poster session, the Meeting´ Scientific Committee selected the best poster from each platform to receive the Best Poster Award. Finally, the CIIS platform coordinators presented their plans and vision for the future.

Following the success of this meeting, the Scientific Committee of the National Meeting, decided to implement yearly meetings of the Center.

We would like to acknowledge all CIIS members, staff and students that accepted the challenge of participating in this event, presenting their most recent data, sharing their knowledge, and making this truly an interdisciplinary health care event.

We hope this meeting has contributed to share the latest scientific achievements of all members and promoted the beginning of new collaborations for the future, keeping in mind the main goal of improving health care with an interdisciplinary view, to ultimately improve quality of life, with humanity and spirituality at the center of all scientific quests.

Acknowledgements
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Table 1 Platforms of the Center for Interdisciplinary Research in Health

Name	Location	Head
Neurosciences	Lisbon and Porto	Prof. Ana Mineiro
Nursing	Lisbon and Porto	Prof. Paulo Alves
CatólicaMed	Sintra	Prof. Paulo Bettencourt
SalivaTec	Viseu	Prof. Nuno Rosa
Precision Dental Medicine	Viseu	Prof. André Correia

P3

- Development of a new mRNA vaccine platform for tuberculosis

Laura Matarazzo[1,2], Laura Taina-González[3,4], Ricardo Pinheiro[2], David Pires[1,2,5], María de la Fuente[4,6,7], Paulo J. G. Bettencourt[1,2]
[1] Center for Interdisciplinary Research in Health, Universidade Católica Portuguesa, Lisboa, Portugal; [2] Universidade Católica Portuguesa, Faculty of Medicine, Rio de Mouro, Portugal; [3] Universidad de Santiago de Compostela (USC), 15782 Santiago de Compostela, Spain; [4] DIVERSA Technologies, Santiago de Compostela, Spain; [5] Host-Pathogen Interactions Unit, Research Institute for Medicines, iMed-ULisboa, Faculty of Pharmacy, Universidade de Lisboa, Lisboa, Portugal; [6] Nano-Oncology and Translational Therapeutics Group, Health Research Institute of Santiago de Compostela (IDIS), SERGAS, Santiago de Compostela, Spain; [7] Cancer Network Research (CIBERONC), Madrid, Spain
Correspondence: Paulo J. G. Bettencourt (pbettencourt@ucp.pt)
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Background
Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*M.tb*), is the first cause of death by an infectious disease worldwide, killed 1.6 million people in 2021. Bacillus Calmette-Guerin (BCG) is the only approved vaccine for TB to date. However, while BCG is effective in preventing severe forms in children, its efficacy in adults is inconsistent and it does not prevent transmission, highlighting the need for new vaccine development [1]. The recent success of COVID-19 vaccines raised the interest for mRNA-based vaccines, as they are effective, safe and easy to produce. This project aims to develop a new mRNA vaccine platform for TB, based on mRNA coding for antigenic peptides from BCG and *M.tb* identified by immunopeptidomics [2], and formulated with a patented technology of lipid nanoemulsions (NE) (WO2019138139A1), adapted for efficient intracellular delivery of mRNA [3].
Materials and methods
We tested different prototypes of NE-mRNA formulations, coding for EGFP, *in vitro.* Human alveolar basal epithelial cells (A549), human monocytic cells (THP-1), and primary human monocyte-derived macrophages, were transfected with NE-mRNA formulations. Transfection efficiency was assessed by measuring the percentage of transfected cells, and the intensity of GFP fluorescence. The cytotoxicity of the formulations was evaluated using AlamarBlue, and by 7-AAD viability staining.
Results
In vitro preliminary data using EGFP-mRNA-NE formulations indicate that NE formulations can efficiently deliver mRNA and induce expression of the encoded protein in different cell types, with low cytotoxicity.
Conclusions
The NE technology presented here is safe, stable, and can efficiently deliver mRNA to various cell types. Selected NE formulations will be used as a carrier for a new vaccine candidate against TB, based on mRNA encoding relevant antigenic peptides. These will be tested in mice for safety, immunogenicity, efficacy and dose optimization in order to generate an effective and sustained humoral and cellular immune response against TB. The mRNA vaccines are rapid and relatively simple to produce. The vaccine platform described here could be adapted to develop vaccines against other infectious diseases, particularly to quickly respond to emerging pathogens.

Ethical statement
Human monocyte-derived macrophages were obtained from buffy-coats of healthy donors provided by the national blood institute (Instituto Português do Sangue e da Transplantação, Lisbon, Portugal).

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P4

- Implementation of a pre-Good Laboratory Practice management system for academic research

Ricardo Pinheiro[1], Cloé Abreu[1], Paulo J. G. Bettencourt[1,2]
[1] Universidade Católica Portuguesa, Faculty of Medicine, 2635-631 Rio de Mouro, Portugal; [2] Universidade Católica Portuguesa, Center for Interdisciplinary Research in Health, 1649-023 Lisboa, Portugal
Correspondence: Paulo J. G. Bettencourt (pbettencourt@ucp.pt)
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The implementation of quality control procedures, at an academic laboratory, relies on a system that flows information to scientists, staff, and students in a clear and accountable manner.
The organization and implementation of new methodologies, in a new laboratory, implies the definition of a work culture and structure from inception to completion. Establishing and maintaining a new work philosophy is demanding and requires constant and close supervision of all laboratory actions. Particularly, when the methods are innovative and require a significant change of work culture from users.
By establishing a system that standardizes common laboratory protocols to facilitate training while simultaneously tracking progress, we successfully implemented a pre-Good Laboratory Practices (pre-GLP) facility at the Faculty of Medicine of the Universidade Católica Portuguesa (FM).
The pre-GLP system is an adaption of the system adopted by the Jenner Institute, University of Oxford. Briefly, the new users are trained on Standard Operations Procedures (SOP), provided by a competent user. Once training is successfully completed, the user is approved and qualified as competent user. All training actions are recorded in the researcher's internal record. The internal records are internally verified by the laboratory manager, and laboratory director, and externally audited.
The SOPs are regularly updated and improved to reflect any significant updates on procedures, equipment, and reagents. Updated SOP´s are reassessed and follow the pipeline of approval. Implementation of this laboratory management system is a step forward in quality assurance and standardization of methodologies towards good laboratorial practices, increased health, and safety, and quality data production.
Finally, the implementation of this quality assurance method at the FM, provides an additional layer of health and safety protection for users, simultaneously assuring reproducibility and reliability of protocols across the campus.

P5

- Mass spectrometry-based identification of peptides presented by major histocompatibility complex in macrophages

Hugo Mateus[1,2,3], Ricardo Pinheiro[1], Hugo M. Santos[3,4,5], Paulo J. G. Bettencourt[1,6]
[1] Universidade Católica Portuguesa, Faculty of Medicine, 2635-631 Rio de Mouro, Portugal; [2] NOVA School of Science and Technology, FCT NOVA, Universidade NOVA de Lisboa, 2829-516, Caparica, Portugal; [3] BIOSCOPE Research Group, LAQV-REQUIMTE, Chemistry Department, NOVA School of Science and Technology, FCT NOVA, Universidade NOVA de Lisboa, 2829-516, Caparica, Portugal; [4] PROTEOMASS Scientific Society, Madan Park, 2829-516, Caparica, Portugal; [5] Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [6] Universidade Católica Portuguesa, Center for Interdisciplinary Research in Health, 1649-023 Lisboa, Portugal
Correspondence: Paulo J. G. Bettencourt (pbettencourt@ucp.pt); Hugo M. Santos (hmsantos@fct.unl.pt)
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Immunopeptidomics is a field of research that has progressed in the last years due to advances in sophisticated analytical techniques based on mass spectrometry and bioinformatics. The ability to identify molecules to the extent of a single ion led to a step forward in immunopeptidomics. Mass spectrometry enables the identification of thousands of peptide sequences in a single sample, thus providing large-scale reliable information. The immunopeptidome is the entire

group of peptides presented by the major histocompatibility complex Class-I (MHC-I), at the surface of all nucleated cells and Class II, at the surface of professional antigen presenting cells. The MHC-bound peptides are recognized by T cells and constitute the immunological synapse, leading to the initiation of the adaptive immune response. Under pathological conditions, peptides originating from the proteolysis of pathogen proteins are presented to the cells of the host immune system via MHC. Thus, the identification of pathogen peptides through immunopeptidomics is an unbiased method for understanding the generation of adaptive immune responses against pathogens.
Here we describe the establishment of a new mass spectrometry-based immunopeptidomics platform for peptide identification in physiological and pathological conditions. Using the macrophage cell line with THP-1, with a known HLA-type, we were able to identify a total of 2913 unique MHC-I bound peptides. The peptide length distribution, NetMHCpan-4.1 rank affinity, and best match HLA binding allele for each peptide will be presented.
Finally, identifying MHC-I and MHC-II peptides under physiological and pathological conditions could uncover the most relevant peptides able to stimulate the right type of T-cell response for vaccine design and development.

P6

- CD137 drives therapeutic resistance to JAK inhibition therapy in Myeloproliferative Neoplasms

Bruno Martins[1], António Medina Almeida[1,2], Bruno António Cardoso[1]
[1] Universidade Católica Portuguesa, Faculdade de Medicina, Centro de Investigação Interdisciplinar em Saúde, Lisbon, Portugal; [2] Hospital da Luz, Lisbon, Portugal
Correspondence: Bruno António Cardoso Bruno António Cardoso
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The BCR-ABL-negative myeloproliferative neoplasms (MPN) are clonal myeloid malignancies that rely on constitutive JAK-STAT signaling as a consequence of the $JAK2^{V617F}$ mutation. However, despite the recent advances in understanding MPN pathophysiology and the efficacy of JAK inhibitors in the clinical practice, bone marrow transplantation remains the only curative option. Unfortunately, resistance to chemotherapy is a frequent event in myeloid malignancies and the bone marrow (BM) microenvironment provides the perfect protective milieu for leukemic cells to thrive and proliferate. Research from our own group demonstrated that the BM protects from the cytotoxic effects of JAK inhibition (Ruxolitinib) in MPN cells, and such effects rely on the activation of PI3K-Akt and JNK/SAPK signaling networks.
MPN patient derived cell lines (SET-2 and HEL) were incubated cultured *in vitro* (no stroma) alone, with HS-5 bone marrow cell line and with HS-5 conditioned media medium in the presence of Ruxolitinib and CD137 neutralizing antibody. The cellular viability was analyzed by staining with Annexin-V/7-AAD and CD45-APC (to distinguish MPN cells from the HS-5 cells) staining. Furthermore, cells were also stained with a CD137-PE antibody and lysed for RNA extraction. cDNA was synthesized and gene expression evaluated by quantitative real-time polymerase chain reaction (qPCR) and normalized to the expression levels of *HPRT1* gene.
Interestingly, in a screen to search for novel modulators of BM-mediated protection to JAK inhibition in MPN disease we identified the *TNFRSF9* gene. The *TNFRSF9* gene encodes for the CD137 receptor that receptor belongs to the Tumor Necrosis Factor Receptor Superfamily (TNFRSF) and is involved in tissue homeostasis by regulating inflammation. We found that the contact of MPN cells with BM in the presence of Ruxolitinib upregulated the *TNFRSF9* transcript levels and the surface expression of the CD137 receptor. Importantly, the inhibition of the CD137 receptor with a neutralizing antibody dampened the BM protective effect to the cytotoxic action of Ruxolitinib.
Overall, our preliminary results identify the CD137 death receptor as a putative novel regulator BM-mediated protection in the context of MPN disease and we are currently intensifying our studies to further exploit the therapeutic applications of this receptor as well as the molecular mechanisms behind it.

P7

- Evaluation of Extruded Material in Furcation Perforation Repair with Micro-computed Tomography

Miguel Cardoso[1], Rita Noites[1], Vitor Correlo[2], Carlos Viegas[3]
[1] Universidade Católica Portuguesa, Faculty of Dental Medicine, Center for Interdisciplinary Research in Health, Viseu, Portugal; [2] 3B's Research Group-Biomaterials, Biodegradables and Biomimetics, Department of Polymer Engineering-School of Engineering University of Minho, Gandra, Portugal; [3] Department of Veterinary Sciences University of Trás-os-Montes e Alto Douro, Vila Real, Portugal
Correspondence: Miguel Cardoso (mabcardoso@ucp.pt)
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Background
Furcation perforations are pathological conditions of complex treatment and, currently, bioceramics are good options for furcation perforations repair. The aim of this study was to compare the volume of extruded material with micro-computed tomographic (microCT) after Furcation Perforation (FP) repair with Biodentine (BDT) or ProRoot MTA (prMTA) in dogs' teeth.
Materials and methods
Forty dogs' teeth were divided into 2 groups: prMTA (n=20, FP repaired with ProRoot MTA), BDT (n=20, FP repaired with Biodentine). All animal procedures were approved by the institutional Ethical Committee and conformed with the ethical guidelines and regulations of the national Directorate-General for Food and Veterinary (Process number 0421/000/000/2014). The animals were euthanized after 4 months. The volume of extruded material was quantified using microCT images.
Statistical analysis was performed using independent-samples t-test in SPSS™. All differences were considered significant at $P \leq 0.05$.
Results
Total volume of extruded material was significantly lower in BDT group than in prMTA group (BDT: 1.42±0.80mm3; prMTA: 2.27±1.67mm3; $P=0.049$).
In both test material groups, microCT showed continuity between the extruded repair material and the surrounding bone.
Along with the study's included outcomes, further evaluation of microCT images allowed the identification of new mineralized tissue bridges over the remaining radicular pulp tissue in specimens of both test groups.
Conclusions
The greater amount of extruded material found for prMTA group is consistent with its lengthier setting time, which may contribute to the unintended compaction of the unset material into the furcation defect. Even though Biodentine presented lesser extrusion, a concomitant histologic study revealed similar results concerning mineralized tissue formation.
Keywords
Biodentine; Endodontics; Furcation perforation; *in vivo*; MTA.

P8

- Marine fungi exhibit antimicrobial activity against human oral pathogens

Bruna L. Correia[1,2], Daniela Devesas[2], Rita Noites[1,2], Ana T.P.C. Gomes[1,2], Ana Cristina Esteves[3], Artur Alves[3], Ana Sofia Duarte[1,2]
[1] Universidade Católica Portuguesa, Center for Interdisciplinary Research in Health, Viseu, Portugal; [2] Universidade Católica Portuguesa, Faculdade de Medicina Dentária, Viseu, Portugal; [3] CESAM & Departamento de Biologia, Universidade de Aveiro, Aveiro, Portugal
Correspondence: Bruna L. Correia (bcorreia@ucp.pt)
BMC Proceedings 2023, **17(9):**P8

The emergence of resistance to antibiotics and antimycotics has become a challenge in the treatment of infectious diseases, including infections of the oral cavity. Marine fungi are a source of novel biologically active compounds, namely in what concerns the development of antimicrobial and anticancer solutions. Our study aimed to test the antimicrobial activity and the cytotoxicity of the extracts of the