

MEETING ABSTRACTS

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

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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 31<sup>st</sup> March and 1<sup>st</sup> 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 Capelo 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



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

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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<sup>V617F</sup> 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

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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:  $1.42 \pm 0.80 \text{ mm}^3$ ; prMTA:  $2.27 \pm 1.67 \text{ mm}^3$ ;  $P=0.049$ ).

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

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The emergence of resistance to antibiotics and antimicrobials 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

two recent identified species of marine fungi, *Penicillium lusitanum* and *Aspergillus affinis*. *Candida* spp. and *Enterococcus faecalis* isolated from oral pathologies were included to evaluate the antimicrobial potential of the marine fungi by the disk diffusion assay. The cytotoxicity of the effective concentrations of the extract was tested using the Vero cell line (ECACC 88020401, African Green Monkey Kidney cells, GMK clone), according to the ISO 10993-5. The extracts of *P. lusitanum* and *A. affinis* were active against *C. albicans* and *E. faecalis*, respectively. *Penicillium lusitanum* active extracts are non-cytotoxic, in contrast to *A. affinis* extracts that showed high cytotoxic effects on Vero cells, for all concentrations tested. The results on the biological characterization of the *P. lusitanum* extract are promising and support the development of new disinfecting solutions that may be used during root canal therapy cleaning and shaping.

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#### P9

##### - Antimicrobial properties and bioactivity potential of smart nanoparticles for dental applications

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Tooth decay is one of the greatest causes of tooth loss in the world. This not only affects the patient's quality of life but also carries an economic burden associated with the need for multiple reinterventions. Endodontic treatment aims to preserve teeth by cleaning, disinfecting and filling/sealing the root canal. Despite the high success rate of endodontic treatment, failures do occur in a large number of cases. Several new biomaterials for dentistry have been developed, however their bioactivity is often misunderstood. Our work focuses on the biological characterization of novel bioactive glass nanoparticles, including the evaluation of their antimicrobial and biocompatibility properties. *Candida albicans* (ATCC 11225) and *Enterococcus faecalis* (ATCC 29212) were included to evaluate the antimicrobial potential by the drop plate method [1]. The cytotoxicity was tested using the MC3T3-E1 cell line, through the resazurin reduction assay. The novel bioactive glass nanoparticles demonstrated antimicrobial activity against *C. albicans* and *E. faecalis*, being able to inhibit their growth but also, in some incubation times, decreased the survival of these microorganisms. After 24 h of incubation of MC3T3-E1 osteoblast cells with bioactive glass nanoparticles conditioned medium, around 48% cell viability was achieved. These novel bioactive glass nanoparticles have shown promising properties which may find applications on different areas of clinical dentistry.

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#### P10

##### - Should thermoplastic resins be used in removable dentures?

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#### Background

Removable dentures are the most popular rehabilitation treatment for edentulous patients. However, due to the presence of retentive elements and metallic structures in the aesthetic areas, several patients have reported both aesthetic and psychological problems. In addition, this type of dentures has low ductility and, therefore, low resistance to fracture. These limitations favored the development of flexible resins for use in conventional oral rehabilitation, which provide greater comfort and aesthetics for the patient.[1-3]

The aim of this investigation is to evaluate if the fabrication of denture bases with thermoplastic flexible resins provides superior mechanical and physical results in comparison with conventional acrylic resin (polymethylmethacrylate).

#### Materials and methods

After registering the research protocol in PROSPERO, the same was conducted using the PubMed/Medline®, Cochrane® Library, Web of Science® and Scopus® databases, where a combination of MeSH and free text terms were combined with Boolean operators AND and OR. The selection of articles was carried out by two independent investigators, according to the PRISMA flowchart, and the agreement was evaluated by Cohen's kappa coefficient, being later analyzed, and evaluated according to the established inclusion and exclusion criteria.

#### Results

In the 10 analyzed studies in this systematic review, 431 specimens were evaluated, being 310 of flexible thermoplastic resin and 121 of conventional acrylic resin. The studies included are in vitro and compare the mechanical properties and physical characteristics between the different types of resin. The production of removable prosthetic bases in flexible thermoplastic resin presents excellent mechanical results, but combined with poor physical characteristics, may not present superior long-term results, compared to conventional acrylic resin.

#### Conclusions

Given the results obtained, the option for these materials may not yet be an alternative to polymethylmethacrylate. More research is needed to optimize and validate these materials for intra-oral use.

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