From *in silico* to saliva point-of-care devices and individual empowering

Salivary diagnostics is a less invasive and therefore simpler and patient empowering strategy promoting involvement in disease prevention and treatment processes.

SalivaTec is committed to fulfil the scientific ambition of the **Centre for Interdisciplinary Research in Health (CIIS)** namely: 1- Contribute to the knowledge on Precision Health focusing on chronic disease and on vulnerable groups; 2- Promote digital innovation in diagnostics, monitoring, intervention and resolution in Health.

Saliva and other oral fluids, which can be easily collected avoiding the risk and expenses involved in blood sampling, are being explored both as determinants and an indicator of **oral dysbiosis and/or systemic alterations**. By using innovative molecular medicine techniques **SalivaTec** focus on developing **oral biomarkers** to screen a variety of human disorders or conditions. These approaches are especially relevant for **early diagnosis and monitoring** the clinical course of disease which reflect on patient well-being and support solutions to be applied at the individual level (personalized medicine) but with impact at the community level.

One of the advantages of saliva is to provide a wealth of biomarkers for the host as well as for the microbiome. Saliva and other oral fluids are a source of nucleic acids, proteins and metabolites, **which can reflect host physiology, microbiome structure and evidence of the interactions established**.

SalivaTec is actively involved in the standardization of procedures and correlation between salivary biomarkers and health and/or dysbiotic states. This knowledge is fundamental for **point-of-care devices** design.

SalivaTec also develops research in **Computational Biology and Bioinformatics** including annotation of health data, development of bioinformatic strategies for data integration and functional interpretation and identification of biomarker panels and/or new therapeutic targets.

SalivaTecDB the unique database developed by **SalivaTec is** dedicated to collecting, curating and disclosing information on saliva. SalivaTec DB includes information about human and microbial proteins, microorganisms and microRNAs. This database has enabled the rebuilding on existing omics data and is an important tool **for research on mechanisms and salivary biomarkers**.

OralInt produced by **SalivaTec** is an innovative bioinformatics tool that allows for the prediction of inter-organism Protein-Protein Interactions and supports an additional skill of SalivaTec geared towards **Interactomics** analysis.

As a summary SalivaTec provides:

A - *In* silico approach

Bioinformatic analysis

- Development of omics databases.
- Biomarker prediction and biomarker panel proposal.
- Prediction of genes/ proteins' functions and molecular mechanism.
- Prediction of the structural and functional impact of mutations.
- Prediction of inter-species and intra-species protein-protein interactions.
- Comparative genetics and genomics, interactomics and network analysis.

B - Wet lab approach

Genotyping and characterization of genetic and epigenetic markers

- A suite of molecular approaches (short tandem repeats, single nucleotide polymorphisms, insertion deletion polymorphisms, methylation status, among others).
- A wide-ranging set of multiplex genotyping strategies comprising informative markers for human disorders/diseases.
- Total bacterial load and specific microbial group identification.

Omics analysis

- Sample preparation for Omics.

Biological qualitative and quantitative analysis

- Salivary biomarkers panels validation.
- Protein identification and quantification including with multiplex technology.
- Protein purification and characterization.

- Characterization of advanced materials within biologically relevant matrices and environments.
- Identification of lead candidate materials through toxicity analysis *in vitro* and *ex vivo* (antimicrobial and cytotoxic assays).
- Antimycotic and antibiotic susceptibility testing (Minimal Inhibitory Concentrations) for fungi and bacteria.
- Enzymatic analysis of tissues/cells.
- Testing of bioactive compounds with antimicrobial or antioxidant action, from natural sources.

C - Community empowerment

Health literacy

- Interventions in the community by means of science-based, and creative source of engaging educational programs and materials (especially, in vulnerable populations).

The projects in the community have been recognized namely through endorsement and funding of the Municipality (Pequenos Grandes Sorrisos e Sorrisos Especiais), national agencies (BPI Infância - Ser Criança) and through national awards (4 th edition of the Rui Osório de Castro/Millennium bcp Award). We have also been collaborating with municipalities as partners of Municipal Projects such as Atividade Sénior and STEMAcademy@Mangualde)

Salivatec Researchers

Marlene Maria Tourais Barros; ORCID ID: 0000-0003-0631-4062

SalivaTec Director

Maria José Serol de Brito Correia; ORCID ID: 0000-0002-6141-9089

Associate Professor at the Católica-Viseu, lecturing in the BSc and MSc courses. She completed her PhD in Biology- sub program Ecology, Evolution and Behavior at the City University of New York in 2001.

Research interests: are in Microbial Molecular Ecology, especially applied to the human oral microbiome. Her work has focused mainly on the study of the oral biofilm and its relationship with health and disease. She has also explored the nucleic acids present in saliva as biomarkers both for the host and the microbiome. She has also participated actively in projects with and for the community promoting health literacy and population characterizations through several health determinants.

Contribution for Science: understand microbial ecology of the oral ecosystem and the role of the “healthy” core oral microbiome.

Ana Cristina Esteves; ORCID ID: 0000-0003-2239-2976

Assistant Professor at the Católica-Viseu, lecturing BSc and MSc courses.

Research interests: focus on the molecular mechanisms of microbial pathogenicity and on the interactions of microorganisms and the environment. She has been interested in the use of Omics technologies (genomics, transcriptomics, proteomics and metabolomics) to unravel the influence of environmental conditions of the fitness and virulence of microorganisms. At the same time, ACEsteves is interested in developing and applying bioinformatic solutions for biological problems, such as interactome prediction or protein functional analysis. Another line of research is related to the characterization of microbial enzymes.

AC Esteves is also interested in the development of new eco-solutions for inhibition of microbial pathogens. Solutions compatible with the environment and with pathogen’s hosts. These solutions comprise the Biological Control Agents or the use of Photoinhibitors.

Finally, she has been involved in science communication projects and courses and is very interested in developing tools for science communication for non-scientists.

Contribution for Science: understand the molecular interactions between microbial pathogens and their hosts and environment.

Ana Sofia Duarte; ORCID ID: 0000-0001-6849-6004

Assistant Professor at the Católica-Viseu, lecturing BSc and MSc courses.

Research interests: focus on the molecular mechanisms involved in the cytotoxicity and virulence of microorganisms and their potential applications in biomedicine. She has also developed research on the characterization of polymers and nanoparticles, including the evaluation of their biocompatibility and antimicrobial properties aiming medical applications. She has complementary training in valuing intellectual property and science dissemination for non-scientists. She has participated in various initiatives of science communication in different contexts, from technology transfer to the social valorization of scientific knowledge.

Contribution for Science: unravel genetic and molecular basis for virulence and resistance of clinically relevant microorganisms for developing sustainable therapeutic solutions.

Nuno Ricardo das Neves Rosa; ORCID ID: 0000-0003-4604-0780

Assistant Professor at the Católica-Viseu, lecturing BSc and MSc courses. Is responsible for Computational Biomedicine at SalivaTec laboratory.

Research interests: are in the identification of salivary biomarker panels by *in* silico studies using bioinformatics tools developed in our group (SalivaTecDB, OralInt and SalivaPrint Toolkit) and their subsequent validation by using state of the art technology and know-how for protein identification in small saliva sample volumes.

Contribution for Science: Bioinformatic tools namely SalivaTecDB, OralInt and SalivaPrint Toolkit.

Raquel Silva; ORCID ID: 0000-0001-5926-8042

Assistant Researcher at the Católica-Viseu, lecturing BSc and MSc courses. She obtained her PhD in Biology (2005) at the University of Aveiro (UA) and took Researcher positions in Population Genetics at IPATIMUP (Institute of Molecular Pathology and Immunology of the University of Porto) and in Bioinformatics at IEETA (Institute of Electronics and Informatics Engineering of Aveiro). Between 2015 and 2018, she was an invited assistant Professor at UA.

Research interests: focus on the interplay between genetics and metabolism, namely, the dynamics of the NAD metabolic network and its roles in health and disease. Additional lines of investigation are maintained in collaboration, for the development of bioinformatics tools to detect genome rearrangements and pathogen signatures; to address the mechanisms of anti-fungal resistance in clinical isolates; and to determine the structural and functional effect of mutations in human proteins.

Contribution for Science: the research performed has implications for diagnosis and therapeutics in cancer and infectious disease and contributes to the rational design of more efficient drugs.

Anna Carolina Volpi Mello-Moura; ORCID ID: 0000-0002-9420-1721

Assistant professor at the Católica-Viseu, lecturing in MSc course. She obtained her PhD in Dental Sciences – subprogram Pediatric Dentistry in 2011 at University of São Paulo, Brazil. From 2009 until 2019 she was Associate Professor of Pediatric Dentistry at Paulista University (UNIP) and Ibirapuera University, São Paulo, Brazil. At UNIP she was also Chair of the Postgraduate course of Pediatric Dentistry, from 2012 until 2019.

Research interests: focused on the improvement of oral health and quality of life of babies and children, more specifically in endodontic therapy of primary teeth and dental trauma management. She developed and patented a new medicament filling material for endodontic treatment. Another interest is the evaluation of the oral health conditions of the community and the development of strategies for quality of life improvement.

Contribution for Science: improvement of oral health and quality of life of babies and children, more specifically in endodontic therapy of primary teeth and dental trauma management.

Cacio Moura-Netto; ORCID ID: 0000-0003-4495-1126

Assistant professor at the Católica-Viseu, lecturing in MSc course. He obtained his PhD in Dental Sciences – subprogram Endodontics in 2009 at University of São Paulo, Brazil (USP). After that, he joined a Postdoctoral fellowship at USP between 2009 and 2012, at the Cell Biology Laboratory of the Restorative Dentistry Department. From 2003 until 2019 he was Associate Professor of Endodontics at Paulista University, São Paulo, Brazil. In the same institution he was also Chair of the Postgraduate course of Endodontics, from 2009 until 2019. From 2012 until 2017 he was Associate Professor of the MSc and PhD program in Dentistry from Cruzeiro do Sul University.

Research interests: focused on development and evaluation of materials and techniques for the improvement of endodontic treatment success rate. More specifically,

he evaluated the interaction between high intensity lasers and the dental internal surfaces. Additionally, during the postdoctoral fellowship, he studied the influence of low power laser therapy on growth and differentiation of dental Stem Cells. Another interest is the use of Photodynamic therapy on disinfection processes in oral cavity.

Contribution for Science: development and evaluation of materials and techniques for the improvement of endodontic treatment success rate, specifically on the use of high and low power lasers.