MODEL TO *IN VITRO* STUDY MONO-SPECIE AND MULTI-SPECIE ORAL BIOFILMS IN REAL TIME

DESCRIPTION OF THE TECHNOLOGY

Microorganisms colonizing oral cavity are attached to surfaces living in complex microbial communities termed biofilms. Biofilms can build up on soft surfaces as the tongue, or on hard surfaces like the tooth, varying in both its bacterial diversity and abundance, and by conditioning its formation. Therefore, when dysbiosis occurs between the microbial communities that conform the biofilm, a healthy biofilm can turn into a pathogenic one and develop oral diseases of polymicrobial etiology as caries, periodontitis or halitosis.

To study the biofilm formation in the oral cavity and the bacterial associations yielded, a new *in vitro* model has been developed. It permits simulate the *in vivo* conditions in real time and without further manipulation. This information, provided by the study of microorganisms in conditions closest to their ecosystem, will lead us to a better understanding of what actually happens *in vivo* with practically non-existent sample handling.

The system is based on the impedance technology that allows to quantify the biofilm growth and the kinetics of its formation in real time, avoiding the loss of information from the use of static models, the need to invest high processing time and the use of expensive equipment. In addition, it allows performing technical and biological replication of the experiments.

Moreover, it is possible to characterize the sample according to its origin (saliva, dental plaque, tongue,…) and the dynamics of biofilm formation. In this regard, identify the different development steps of the each biofilm-types could provide valuable information for the design of new treatments with targets focused on blocking each of these steps.

On the other hand, the model could be used as a tool for screening of new oral health substances or substances with antiplaque activity; or for determine the effectiveness of commonly prescribed antibiotics or antiseptics for odontogenic diseases treatment, directing the treatment towards a personalized therapy.

MARKET APPLICATION SECTORS

Companies in the oral health sector for the study of biofilms formation in the oral cavity, interested in using the model as both a diagnostic and preventive tool.

Companies in the pharmaceutical and/or cosmetics industry for analysis and evaluation of antibiotics, antiseptics, probiotics or products destined to the prevention and/or treatment of odontogenic diseases.

Companies in the food or biomedical industry, interested in studying the formation of different types of biofilms, and/or their removal.

TECHNICAL ADVANTAGES AND BUSINESS BENEFITS

For *in vitro* study of complex biofilms, different models have been developed, differentiated by the type of study sample or by the equipment used. According to the type of sample, some models use natural or real samples, or contrary, samples defined by specific bacterial associations. Although some of them permit simulate the *in vivo* conditions, they are laborious and expensive tools, and in general, do not allow the study of biofilm formation in real time. Through this new model, it is possible to study the dynamics of the different oral biofilms formation without the requirement for any further manipulation or resort to sophisticated equipment. Thereby, it also avoids the need for long processing times to observe the results.

Identify the biofilm composition, the interactions between the microbial communities living in it and its development can help to establish both the effectiveness of the treatment and predict the establishment of the disease, being of particular interest as diagnostic and therapeutic application in periodontal, dental or tongue diseases. This type of *in vitro* tests is also much faster and less expensive than tests on animal models or clinical trials, and therefore, it represents a first step, economic and functional, to decide whether a product is promising for its development and as a proof of concept of its efficacy.

CURRENT STATE OF DEVELOPMENT

The model has been validated in oral samples from different origin and under different biofilm growth conditions, allowing to quantify the mono-species (for example, *Streptococcus mutans*, *Staphylococcus aureus* or *Candida albicans* biofilms) and multi-species (saliva, dental plaque or tongue) biofilms growth, and establish the dynamics of biofilm formation in each case.

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The protocols have been standardized and we have reference patterns according to the type of study sample and its correlation with different dental diseases. On this regard, the antibiotic effect on mono-specie and multi-specie biofilms have been studied, differentiating patterns of different effectiveness to the treatment.

Finally, the system allows measuring biochemical parameters in the culture supernatant (e.g. pH, lactate, ammonium, etc.) and retrieving the biofilm for its further study (bacterial composition by DNA sequencing, gene expression by RNAseq or qPCR, etc.).

INTELLECTUAL PROPERTY RIGHTS

The knowledge generated by the research group allows offering the technical and scientific assessment from the design of the research project to the interpretation of the results.

This knowledge has been financed with the collaboration of ACEA Biosciences Inc.

COLABORATION SOUGHT

Collaboration with other groups or research projects, both national and international, in the field of oral health, that need to simulate an artificial mouth as study model for the oral biofilms formation.

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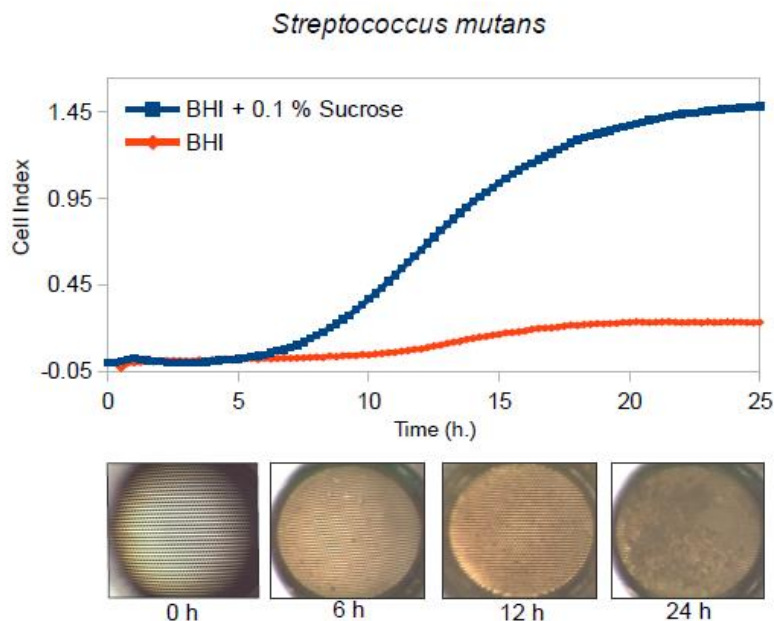
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