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Poster **#1** proposé par : **Epithelix**

In vitro human airway epithelial platform for the development of novel anti-bacterial drugs

Auteurs : ***Laureen Jaupart, Christine Caul-Futy, Ophelie Verbeke, Carole Bertinetti, Mireille Caul-Futy, Samuel Constant***

Respiratory bacterial infections cause frequently mild to severe diseases worldwide. To develop new anti-bacterial new relevant and efficient tools are needed. We report herein the use of 3D epithelia made of primary human airway epithelial cells, MucilAir™, for anti-bacterial drug screening. As proof-of-concept, typical disease-causing bacteria (Pseudomonas aeruginosa (Pa), Staphylococcus aureus (Sa), Streptococcus pneumoniae (Sp), Acinetobacter baumannii (Ab) and Haemophilus influenzae (Hi)) were used to infect MucilAir™ tissues. The effect of bacterial infections can be easily and accurately monitored with several endpoints: Trans Epithelial Electrical Resistance (TEER); cytotoxicity (LDH), cilia activity, mucin and IL-8 release, etc… (Pa) infection induces a loss of TEER and an increase of IL-8, while (Sa) also leads to an increase in ciliary activity. On the contrary, a strong increase in cytotoxicity upon (Ab) infection was observed. Antibiotics like Meropenem inhibits the bacterial growth and abrogates its side effects. Similarly, macrophages in co-culture decrease the growth of (Sp) and prevent the bacterium-induced increase of mucin secretion. These results suggest that MucilAir™ is a reliable tool for anti-bacterial drug development.

Contact du poster : **Samuel Constant**

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Poster **#2** proposé par : **Epithelix**

Fingerprint of the most prevalent respiratory viral strains on in vitro primary human nasal epithelium

Auteurs : ***Guy Barbin, Rosy Bonfante, Bernadett Boda, Song Huang, Samuel Constant***

Acute respiratory infection are a leading cause of death worldwide. The most prevalent causative agents includes influenza A (H1N1, H3N2), respiratory syncytial virus (RSV-A), rhinoviruses (RV-A16), human metapneumovirus (hMPV) and para-influenza virus (PIV3). Here, we used MucilAir™, an in vitro reconstituted human nasal respiratory epithelium cultured at the air-liquid interface, to develop an assay that enables the ranking of antiviral efficiency. The polarized epithelium is fully ciliated, exhibits high trans-epithelial electrical resistance and secretes mucus. For this assay, we measured the cytopathic effects of each virus on key features of the respiratory epithelium: barrier function, cell viability, secretory response, cilia motion and mucociliary clearance. Using this multiparameter approach, we established a fingerprint for each virus and mimicked systemic delivery of antivirals to measure their efficacy. We were able to determine the most efficient dose for each strain: H1N1 (Baloxavir Marboxil 0.1 µM), H3N2 (Oseltamivir 10 µM), RV-A16 (Rupintrivir 5 µM), RSV-A (Ribavirin 100 µM), PIV3 (Nirmatrelvir 30 µM) and hMPV and PIV-3 (Molnupiravir 30 µM). In conclusion, MucilAir™ can be used as a predictive in vitro screening platform to facilitate drug development, while providing an alternative to animal testing.

Contact du poster : **Samuel Constant**

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Poster **#3** proposé par : **IVPC - INRAE-Univ Lyon1**

GENERATING COMPLEX PHYSIOLOGICAL LUNG TISSUE USING 3D BIOPRINTING TO STUDY RESPIRATORY PATHOLOGIES

Auteurs : ***F Archer, A Carré, A Erny, N Lechopier, M Riva, K Moreau, E Petiot***

In view of the considerable and growing impact of respiratory diseases worldwide, the Print@Lung project aims to create a physiological model of the human lung using 3D bioprinting, in order to study the mechanisms of infection, predict their severity and validate therapeutic approaches. The complexity of the architecture and composition of the lung represents a major challenge for the creation of in vitro models. Current advances in 3D culture techniques still have limitations, such as the absence of architecture, vascular structure and an immune component. The multidisciplinary Print@Lung consortium aims to recreate this three-dimensional multicellular structure of lung tissue using 3D bioprinting technology.
The project aims are to generate a functional, differentiated model of the respiratory epithelium, incorporating vascularised connective tissue and immune system cells, while presenting the architecture of the different zones of the respiratory system (alveolus, bronchi/bronchioles). The functionality of this model will be assessed and compared with that of currently available models. Finally, these models will be used to study the response of lung tissue to bacterial infections or viral infections, as well as to atmospheric pollutant molecules. It will also be used to assess the effectiveness of various antimicrobial strategies. In the longer term, this model will open up new avenues for biomedical research, not only in the field of infectious diseases, but also in cancer, chronic respiratory diseases and genetic diseases.

Contact du poster : **Fabienne Archer**

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Poster **#4** proposé par : **SATT OUEST VALORISATION**

NEW TREATMENT TO PREVENT ASTHMA

Auteurs : ***Jean-Jacques HELESBEUX***

The invention refers to novel tocotrienol derivatives that specifically inhibit 5-lipoxygenase (5-LOX) activity and leukotrienes synthesis. Leukotrienes promote inflammation. Novel tocotrienol derivatives strongly inhibit 5-LOX activity at very low concentrations (nanomolar levels) thus preventing leukotrienes synthesis and inflammation.

A screening step has revealed many secondary metabolites isolated from Garcinia amplexicaulis and Garcinia kola as potential anti-inflammatory agents. In vitro tests highlighted one hit : α-amplexichromanol. α-AC has been administrated either intraperitoneally or by oral gavage to BALB/c mice sensitized by subcutaneous injection of ovalbumin (OVA). Treatment reduced OVA-induced airway hyperreactivity as well as peri-bronchial inflammatory cell infiltration. α-AC also reduced pulmonary leukotriene C4 levels, Ig plasma levels, lung mast cell infiltration and Th2 immune response.

Allergic diseases such as asthma affect approximately 25 % of the world's population. Asthma is a chronic airway disease characterized by reversible airway obstruction and chronic inflammation. Tocotrienol derivatives proved to be efficient molecules targeting inflammation. Preclinical tests confirmed their ability to prevent inflammation and asthma features.

Contact du poster : **Patrice MOREL**