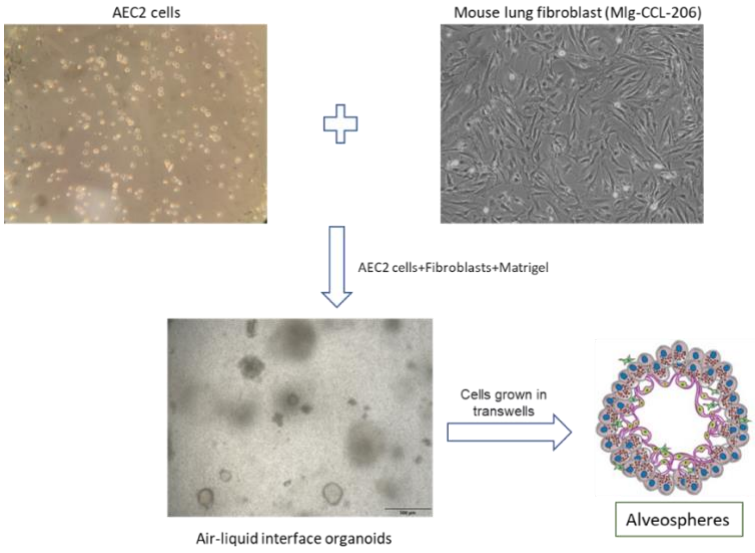
INFRAFRONTIER Complex *In Vitro* Models:

Air liquid interface (ALI) lung organoids

Brief description:

Lung organoids are three-dimensional, miniaturized models that recapitulate key structural and functional features of the lung.

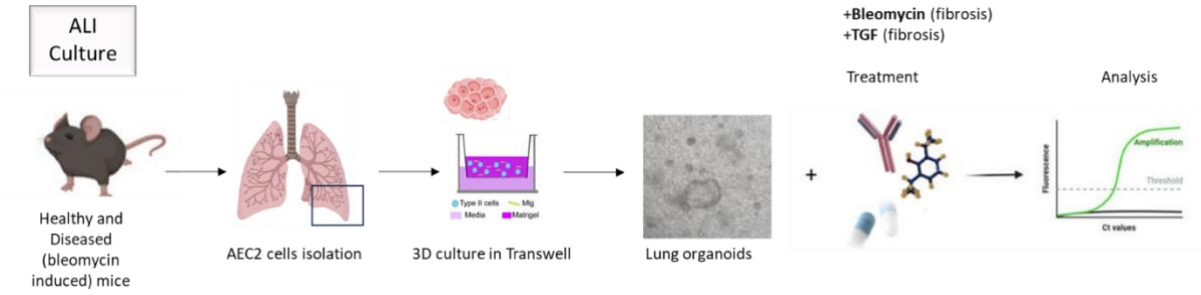
With the overall aim to establish a robust preclinical *ex vivo* model for the investigation of lung fibrosis, we have developed an advanced air–liquid interface (ALI) lung organoid system that closely reflects the alveolar structure and microenvironment. This model captures the remarkable plasticity of alveolar cells, a property that is essential for lung development, homeostasis, and regeneration. The system is established through a co-culture approach, combining alveolar epithelial type II (AEC2) cells with mouse lung fibroblasts to form intricate three-dimensional assemblies that closely mimic in vivo cellular interactions and responses[1]. AEC2 cells play a central role in this model, as their capacity for self-renewal and differentiation into other alveolar cell types makes them ideal progenitors for the formation of alveolospheres[2].



Within the ALI setup, the basal surface of the cells is maintained in contact with a liquid culture medium, while the apical surface is exposed to air, thereby more accurately reproducing the physiological conditions of the lung epithelium.

How is the model generated?

1. A first step involves the isolation of AT2 epithelial-like stem cells from the alveolar region of mouse lungs from healthy and bleomycin-induced mice using MACS technology for $CD45^+$ cells depletion and subsequent EpCAM-positive cells selection.
2. Isolated AEC2 cells are combined with mouse lung fibroblasts (Mlg-CCL-206, ATCC). The mixture is supplemented with an equal volume of Matrigel and the final cell suspension is cultured for up to three weeks on the filter surface of a three-dimensional transwell system, the lower chamber of which contains medium supplemented with insulin–transferrin–selenium (ITS), that supports the formation, growth and differentiation of lung organoids.



3. Fibrotic conditions can then be induced using stimuli such as **bleomycin or TGF**, allowing the study of fibrosis-related cellular responses[3]. The final step involves molecular analysis, including **gene expression assays**, to evaluate **fibrotic markers** and assess treatment responses within this organoid-based platform.

Potential applications:

Our goal is to develop a preclinical platform in which air–liquid interface organoids are used as an ex vivo model to study lung diseases, such as fibrosis, and to enable the preclinical evaluation of novel therapeutic approaches.

Who provides this model?

Biomedcode
Priming drugs for success

Biomedcode Hellas SA is a highly innovative Contract Research Organization (CRO) that since 2006 offers a diverse array of advanced preclinical evaluation platforms ideal for the development of human therapeutics.

Biomedcode offers state-of-the-art drug evaluation services based on a unique portfolio of spontaneous and induced mouse models expressing humanized therapeutic targets, including TNF, TNFR1, IL-17, RANKL, IL-23A, IL-12B, and TL1A. These models closely replicate the pathology and complexity of human inflammatory diseases such as rheumatoid arthritis, spondyloarthritis, osteoporosis, psoriasis, intestinal inflammation, interstitial pulmonary fibrosis and multiple sclerosis.

In parallel with its service activities, Biomedcode maintains a strong R&D program focused on the development and standardization of novel humanized preclinical platforms. More recently, the Company has expanded into organoid-based systems, enabling rapid and efficient screening of human therapeutics.

Biomedcode's integrated approach, combining organoid systems with validated in vivo models, provides clients with a powerful and flexible platform for accelerating therapeutic development while reducing translational risk.

Contact: info@biomedcode.com // +30 2109655366

References:

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INFRAFRONTIER, the European Research Infrastructure for Modelling Human Diseases, is a non-profit organisation dedicated to advancing disease understanding and treatment through cutting-edge models. Operated by a network of over 20 leading biomedical research institutes, it empowers research on human health and disease. Committed to excellence, INFRAFRONTIER adheres to rigorous scientific benchmarks and prioritises animal welfare. Through collaboration with other infrastructures, it fosters global data sharing and contributes to tackling significant health challenges. INFRAFRONTIER serves as a platform for innovative technologies and knowledge exchange, leveraging the power of disease modelling to improve human health.