



PROJECT

Tutor's Name	Prof.ssa Sofia Pavanello
Cotutor's Name	Dr.ssa Manuela Campisi

1) Project title

Production of Lung Organoids from Peripheral Blood Stem Cells to Investigate Cellular Conversion in Idiopathic Pulmonary Fibrosis in Response to Fibrogenic Dusts

2) Abstract (max 500 words)

Idiopathic pulmonary fibrosis (IPF) is a chronic and progressive disease characterized by the replacement of normal lung tissue with fibrotic tissue, severely compromising respiratory function. Its etiology remains poorly understood, but environmental factors such as exposure to fibrogenic dusts are believed to play a key role in its pathogenesis. However, the precise mechanisms through which these dusts induce pulmonary fibrogenesis are not fully understood.

This research project proposes the use of lung organoids derived from peripheral blood stem cells as an in vitro model to study the effects of fibrogenic dusts on cellular conversion in IPF. Lung organoids are three-dimensional aggregates of cells that replicate the structural and functional complexity of lung tissue, offering a more representative experimental system compared to traditional two-dimensional models.

The methodology of this study involves initially isolating peripheral blood stem cells (PBSCs) from IPF patients and healthy individuals as controls. PBSCs are isolated and reprogrammed into pluripotent stem cells. Subsequently, these cells are differentiated into lung organoids using specific protocols, enabling the development of three-dimensional models of lung tissue for biomedical research.

Fibrogenic dusts, representative of those found in occupational or domestic environments, will then be exposed to the lung organoids. The effects of these dusts on organoid morphology, cell proliferation, extracellular matrix production, and gene expression of pulmonary fibrosis markers will be evaluated. Additionally, initial indicators of cellular aging, such as telomeres and DNA methylation, will be analyzed to better understand their involvement in IPF pathogenesis.

Single-cell RNA sequencing (scRNA-seq) analysis will be employed to comprehensively characterize the transcriptional profiles of cells within the organoids, allowing for a deeper understanding of the molecular mechanisms involved in the response to fibrogenic dust stimulation.

The ultimate goal of this project is to identify key molecular mechanisms through which fibrogenic dusts influence cellular conversion in IPF, providing new insights into the pathogenesis of this disease and paving the way for the development of novel targeted therapies. The creation of lung organoids from PBSCs offers an innovative and promising experimental model for studying idiopathic pulmonary fibrosis and its environmental determinants, opening new perspectives in clinical and translational research.