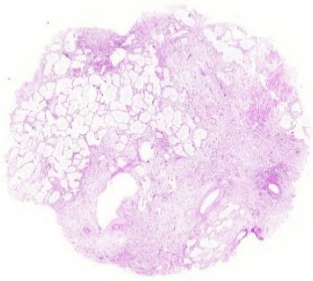
Fraunhofer ITEM

FRAUNHOFER INSTITUTE FOR TOXICOLOGY AND EXPERIMENTAL MEDICINE ITEM

PULMONARY FIBROSIS: EX-VIVO MODEL FOR RESEARCH AND DRUG TESTING

Ex-vivo lung tissue (precision-cut lung slices; PCLS) represents a relevant system to elucidate the pathogenic mechanisms of pulmonary fibrosis. The lung tissue slices can be stimulated with relevant pro-fibrotic mediators to induce important early fibrotic biomarkers in non-fibrotic human lung tissue. In addition, end-stage diseased tissue from patients with pulmonary fibrosis can be prepared with high translational relevance.



PCLS offer the possibility for ex-vivo investigation of profibrotic biomarkers and preclinical drug testing.

Our service for your research

Highly controlled and standardized models suitable for efficacy testing of drugs. Development or customization of the validated system to specific problems and requirements. We ensure availability of expertise tailor-made to the specific demands of a task. Performance of studies and analyses of the most different kinds in the context of anti-fibrotic drug testing. The PCLS ex-vivo culturing system enables pharmacological drug testing and preclinical development of new medications with high translational relevance.

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Use of lung tissue in preclinical pharmacology and toxicology:

From bench to in vivo

- Testing of substances before in-vivo studies
- Prediction of safe doses in animals

From cells to organs to living organisms

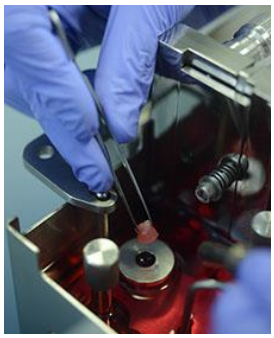
- Efficacy testing in the most complex tissue model before in vivo

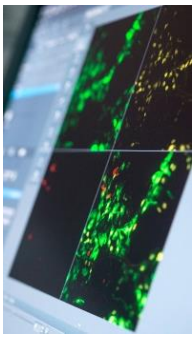
From mouse to human

- Translational testing of substances in mouse, rat, non-human primate and human tissue
- Selection of the appropriate species for further preclinical testing

High translational relevance by investigation of human lung tissue

- Fresh and vital human lung tissue for ex-vivo studies
- Non-diseased or end-stage diseased tissue available





Typical endpoints for testing of drug efficacy

- Gene expression, cytokine response and other biomarkers
- Histology and immunohistochemistry

Established ex-vivo systems to study pulmonary fibrosis

- **Ex-vivo induction of early fibrotic biomarkers**
  Various important early fibrotic mediators are upregulated in non-diseased human lung tissue after stimulation with pro-fibrotic growth factors.
- **Bleomycin-induced lung fibrosis**
  PCLS prepared from rats treated with bleomycin to induce pulmonary fibrosis display upregulation of important pro-fibrotic genes.
  PCLS prepared from these animals retain this pattern in culture for 2 to 5 days.
- **Induced pattern in both systems represents clinically relevant target genes**
  The markers include important extracellular matrix components and other pro-fibrotic tissue factors.
- **Ex-vivo pharmacological treatment (e.g. with pirfenidone) is effective**