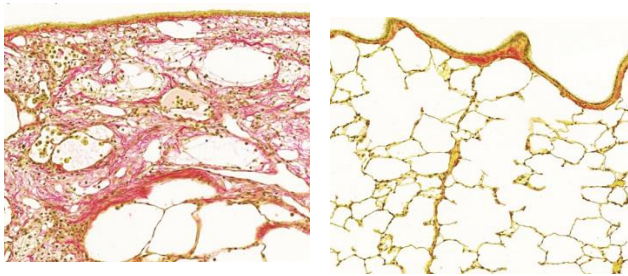


FRAUNHOFER INSTITUTE FOR TOXICOLOGY AND EXPERIMENTAL MEDICINE ITEM

# PULMONARY FIBROSIS: IN-VIVO BLEOMYCIN MODELS

The well-established bleomycin model is the standard model for idiopathic pulmonary fibrosis (IPF) research. Bleomycin is an anti-cancer drug (cytostatic) and antibiotic which provokes a production of DNA-cleaving superoxide and free radicals. Overproduction of the reactive oxygen species can lead to a pulmonary inflammation response. This inflammation triggers an activation of fibroblasts and subsequent fibrosis.



**Histomorphometric analysis (bleomycin rat model) Sirius red staining for histomorphometric analysis (quantification of collagen-positive area). Left: Bleomycin-treated rat, collagen-positive, fibrotic areas; Right: Saline-treated negative control rat**

## Our service for your research

Bleomycin rodent models for basic research and pharmacological efficacy studies. Investigation of in-vivo efficacy of therapeutic candidates for preventive or therapeutic IPF treatment. Invasive but repetitive lung function measurements for monitoring of bleomycin-induced lung injury and fibrosis without destruction of the organism. Integration of histological examination as a qualitative method to assess IPF.

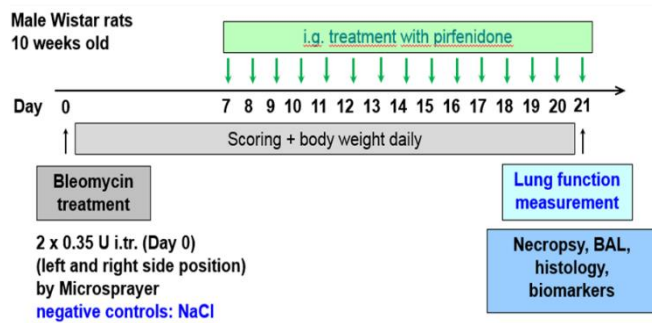
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## Bleomycin rat or mouse model



Typical study protocol of rat (Wistar WU) or mouse (C57Bl/6) bleomycin model. Induction of lung fibrosis (example): bleomycin aerosol, intratracheally on day 0 (classical single-dose regimen) or on days 0 and 1 (two-dose regimen) with a MicroSprayer® aerosolizer.

## Lung function

- Longitudinal measurements, quantification of loss of distensibility and increased airway/tissue resistance
- Measured invasively in anesthetized, orotracheally intubated but spontaneously breathing rodents
- Dynamic compliance (C<sub>dyn</sub>), lung resistance (RL), optional: recruitment maneuver by deep inspiration (up to 30 cm H<sub>2</sub>O)

## Histopathology

- Scores of interstitial lung fibrosis
- Multifocal alveolar emphysema
- Accumulation of pigment-laden macrophages
- Chronic active inflammation
- Right heart hypertrophy (Fulton index)

## Histomorphometry

- Collagen localization and quantification of collagen area

## Sampling of tissue and lavage

- Bronchoalveolar lavage (BAL) followed by cell differentiation
- Hydroxyproline content in BAL and lung tissue
- Immunological and biochemical analyses, e.g. inflammatory cell influx and biomarker levels in BAL and lung tissue, gene expression analyses