Bleomycin-induced Lung Injury/ Pulmonary Fibrosis

Bleomycin-induced lung injury has been used as a model for basic research into pulmonary fibrosis for over a decade. A single dose can consistently induce pulmonary fibrosis via oxidant-mediated DNA breaks causing inflammatory cytokine release.

Fibrosis occurs 21 days following administration making it a reliable and acute model for research. The oral aspiration route of administration used by MD Biosciences allows for more even distribution of disease throughout both right and left lungs.

**Experimental Overview**

- **Animal Strain:** Male C57B1/6 mice
- **Study Duration:** 21 Days
- **Numbers/group:** 10
- **Positive controls:** TBD
- **Standard Assessments:** BALF cellularity, Body weights, Clinical signs
- **Add-on Assessments:** Collagen levels, Histology, BALF cytokine

**T cell frequency in lymphocytes from BALF.**

BALF lymphocytes were sorted as follows: CD45⁺; Non-autofluorescent; Gr-1⁻; CD3⁺. * represents P value < 0.001.

**Neutrophil cell frequency in lymphocytes from BALF.**

BALF lymphocytes were sorted as follows: CD45⁺; Non-autofluorescent; Gr-1⁻; CCR3⁻. * represents P value < 0.001.

**B cell frequency in lymphocytes from BALF.**

BALF lymphocytes were sorted as follows: CD45⁺; Non-autofluorescent; Gr-1⁻; B220⁺.
DATASHEET: BLEOMYCIN-INDUCED LUNG FIBROSIS

Macrophage frequency in lymphocytes from BALF. BALF lymphocytes were sorted as follows: CD45⁺; Non-autofluorescent; CD11c⁻; CD11d⁺. * represents P value < 0.001.

BALF TGF-β cytokine levels on day 21. * represents P value < 0.001.

Percent change in body weight. Body weights are expressed as percent change from Day 0. * represents P value < 0.001.

Validation Date: March, 2015
Verification Date: November, 2015
**DATASHEET: BLEOMYCIN-INDUCED LUNG FIBROSIS**

**Control**

A) Low (1x) magnification (mag) of control lung. Boxed area is shown in B. B) A small amount of collagen is present in the interstitium (*) around an airway (a/w). C) 10X mag of well-inflated normal parenchyma. D) At 1X mag, only a small area is consolidated (stains darker) - boxed and shown in E. E) Consolidated focus (2) is densely cellular and the alveolar spaces are obliterated. The lesion is contained within the lobe. The adjacent lobe (1) is normal. Boxed area is shown in F1+F2. F1) 10X mag shows increased cellularity and loss of alveolar architecture in the inflamed lobe (2). F2) An adjacent field stained with MT shows hazy bluish staining due to early collagen deposition. Abbreviations: Mason’s trichrome (MT), haematoxylin & eosin (HT), interstitium (*) and airway (a/w).

**Bleomycin**

Histology from control & bleomycin treated mouse lungs on Day 7. A) Low (1x) magnification (mag) of control lung. Boxed area is shown in B. B) A small amount of collagen is present in the interstitium (*) around an airway (a/w). C) 10X mag of well-inflated normal parenchyma. D) At 1X mag, only a small area is consolidated (stains darker) - boxed and shown in E. E) Consolidated focus (2) is densely cellular and the alveolar spaces are obliterated. The lesion is contained within the lobe. The adjacent lobe (1) is normal. Boxed area is shown in F1+F2. F1) 10X mag shows increased cellularity and loss of alveolar architecture in the inflamed lobe (2). F2) An adjacent field stained with MT shows hazy bluish staining due to early collagen deposition. Abbreviations: Mason’s trichrome (MT), haematoxylin & eosin (HT), interstitium (*) and airway (a/w).

**Control**

P) 1X mag of a normal lung. Boxed area shown in Q. Q) 10X mag of control lung. R) Multiple, small consolidation foci are detected (arrows). Boxed area shown in S. S) Parenchyma in the central -low region is consolidated (stains blue)- 10X mg. Circled area shown in T. T) Normal parenchymal architecture is obliterated and is replaced by fibrous tissue admixed with inflammatory cells- 40X mag. Collagen shown as fibrillar pink material and inflammatory cells as dark dots. Overlying pleura is hypertrophic (m= mesothelium). Note the progression in blue staining - its intensity and confluence between F2 and S. Abbreviations: Mason’s trichrome (MT), haematoxylin & eosin (HT), interstitium (*), airway (a/w) and mesothelium (m).
Our clients say...

“The performance of your team far exceeded our expectations. The study was performed well and we appreciate all your input into the study design. Your responsiveness and feedback during the study and following in the data interpretation was extremely helpful to guide our next steps. That’s something we don’t find with every CRO.” - S.G., Toxicologist, Biotech Company

“Of all the CROs that I have used over the years...MD Biosciences has been one of the very best in terms of scientific knowledge, data quality, timelines, flexibility and personal contacts.” - O.B., Director of Therapeutics, Pharmaceutical Company

“Throughout our relationship, you have been attentive to our needs and have completed exploratory pilot studies and three drug studies with professionalism and an understanding of tight biotech timelines that are unmatched by other CROs.” - D.Z., Director of Therapeutics, Biotech

Your needs....

We continually hear there has to be a better way. No matter what stage of your preclinical program you are in, we can think together about the best way to fulfill efficacy data. We place heavy emphasis on the scientific rationale for each study so that it not only meets the goals of the R&D program but also provides the most clinically relevant data. We feel that this will help reduce the failure rate in clinical stages and the burden upon the industry.

If you’d like to discuss a particular study or a research plan to work together long-term, we can be reached at info-us@mdbiosciences.com or by phone at 651.641.1770 (North America) or +41-44 986 2628 (International).