

Bleomycin-Induced Lung Injury/ Pulmonary Fibrosis

Bleomycin is a chemotherapeutic agent used to treat cancers such as Hodgkins lymphoma. One of the side effects is pulmonary toxicity, which can be life threatening in approximately 10% of patients.

The mechanism of bleomycin-induced lung injury includes oxidative damage via oxidant-mediated DNA breaks, causing inflammatory reactions in the lungs.

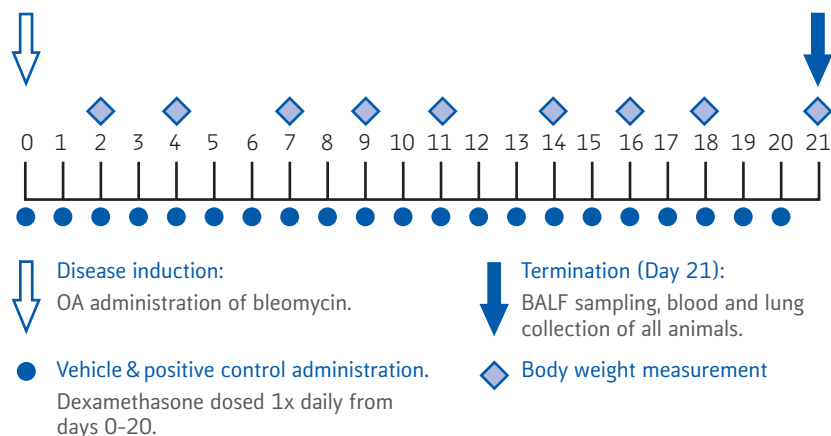
Bleomycin has also been used to induce lung injury in rodents for basic research into pulmonary fibrosis for over a decade. At MD Biosciences, we have refined the oral aspiration administration to allow for more even distribution of disease throughout both right and left lungs, making bleomycin-induced injury in mice a reliable model for research.

Experimental Overview

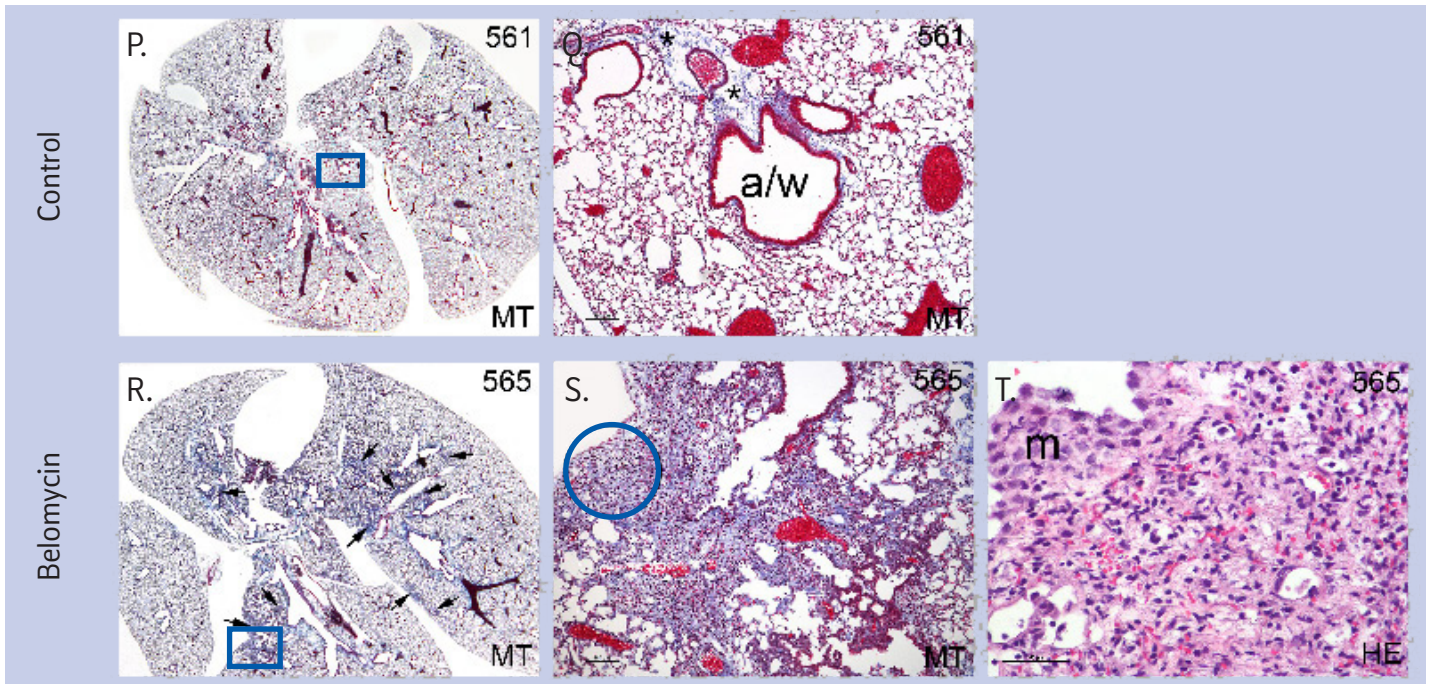
Animal Strain:	Male C57Bl/6 mice
Study Duration:	21 Days
Number/group:	10*
Positive controls:	Dexamethasone **
Standard Assessments:	Body Weights Lung Histology: H&E and MT Clinical Observations
Add-on Assessments:	BALF/Lung Tissue Cellularity BALF/Blood Biomarkers (i.e.TGF-β) Tissue IHC

* This model has an overall mortality of ~20%.
** Dexamethasone is an anti-inflammatory steroid targeting initial inflammatory insult, thus its effect is mild and may be variable across parameters.

Example Experimental Schematic

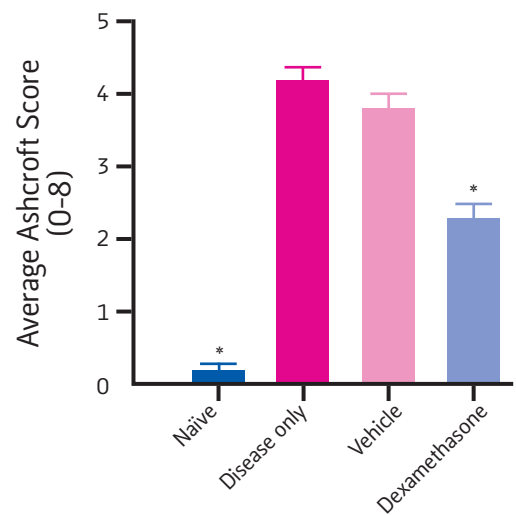
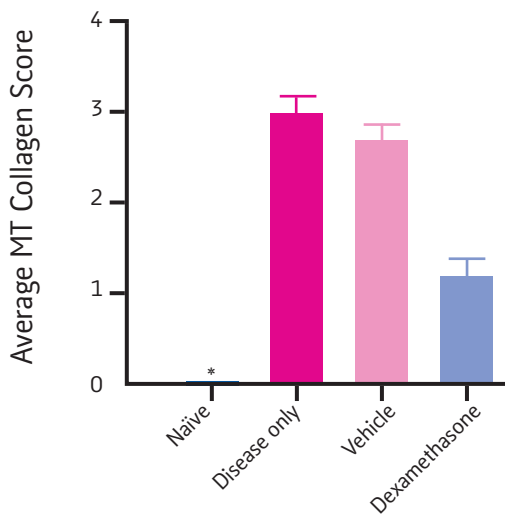


Standard Disease Severity Readouts: H&E and MT Lung Histology



Late Stage Histology: Control & Bleomycin-Treated Mouse Lungs On Day 21.

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).

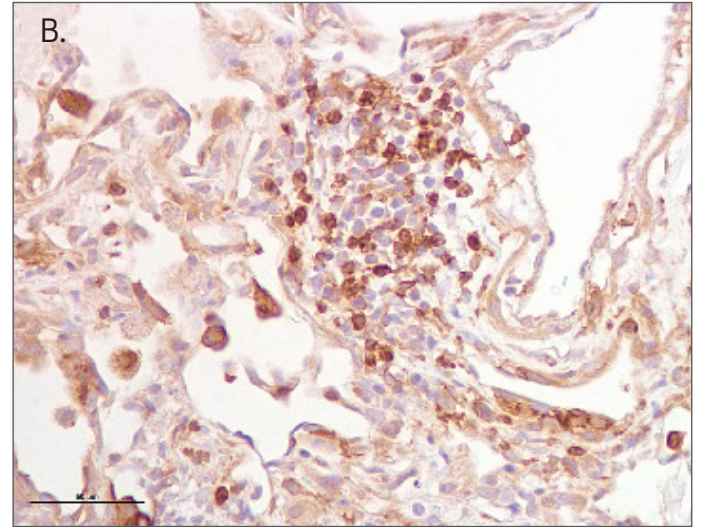
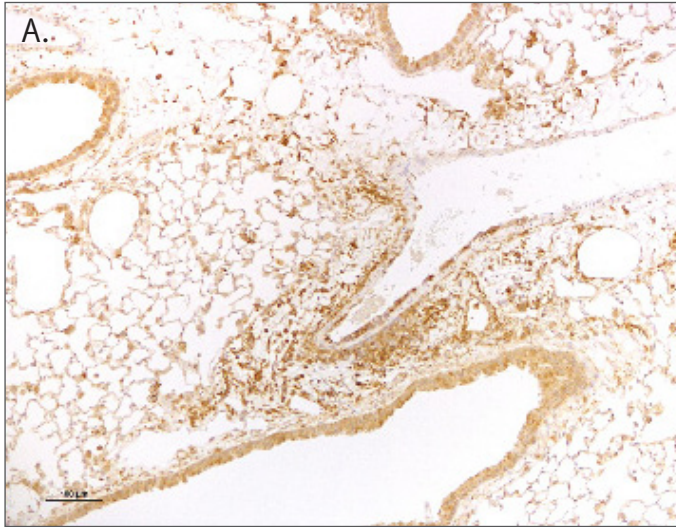


Histology scoring.

The lung was collected and fixed in formalin on day 21. Resulting slides were stained with H&E to evaluate inflammation and cell infiltration or Masson’s Trichrome to evaluate collagen deposition. * represents P value < 0.05 versus vehicle.

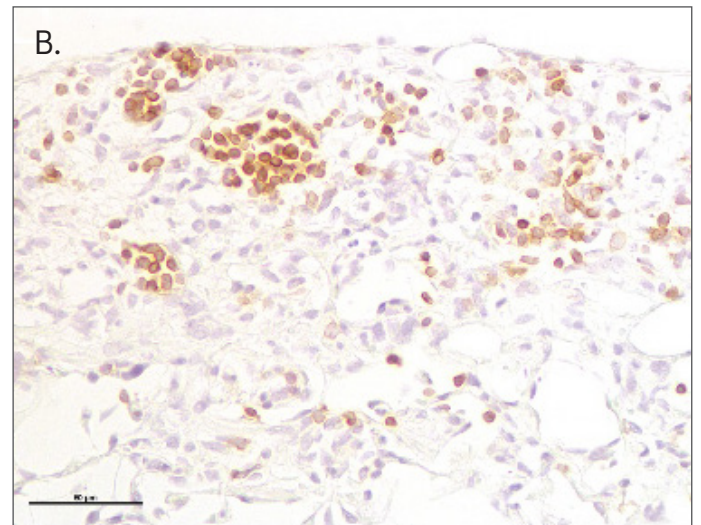
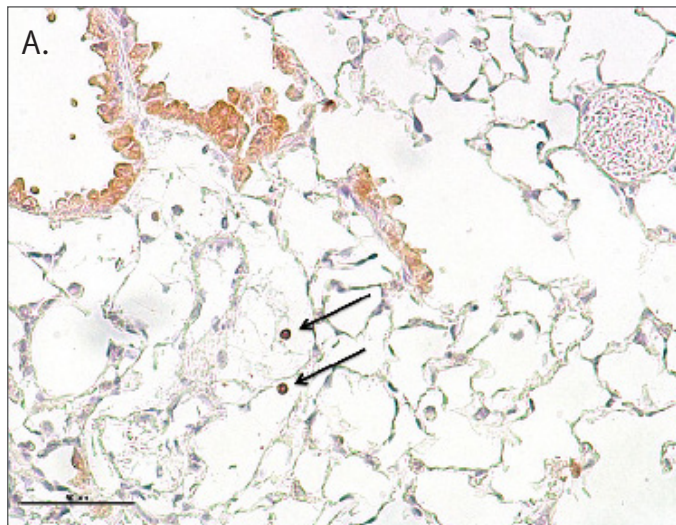
Optional IHC Assessments

IHC Staining: Anti-CD11b For Macrophage Detection



- A. Medium magnification of interstitial perivascular infiltrates showing staining for CD11b-positive cells (macrophage-specific marker).
- B. High magnification of interstitial perivascular infiltrates of CD11b-positive cells.

IHC Staining: Anti-CD3 For Lymphocyte Detection



- A. Rare CD3+ cells (arrows, non-specific staining in epithelium in upper left corner of image).
- B. Subpleural infiltrate which includes CD3+ lymphocytes

Optional Flow Cytometry and Biomarker Assessments

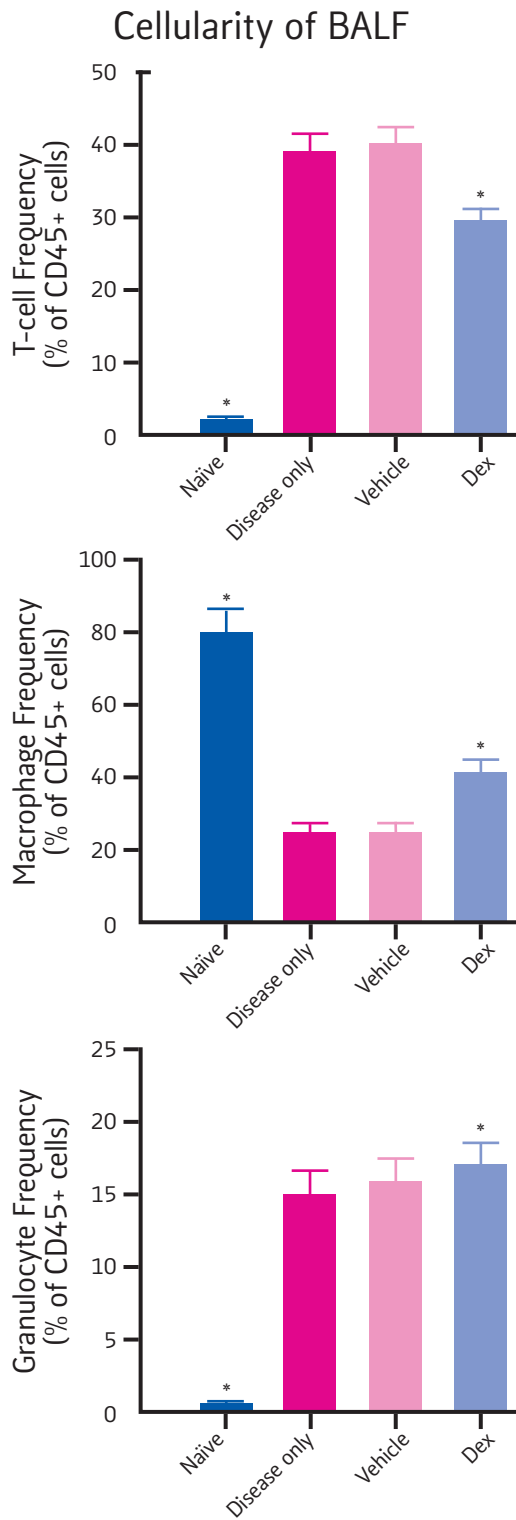


Figure 1. Cellular distribution of immune cell populations. The BALF was collected on study day 21 and differentiated cellular populations were analyzed via flow cytometry with surface markers. * represents P value <0.05 versus vehicle.

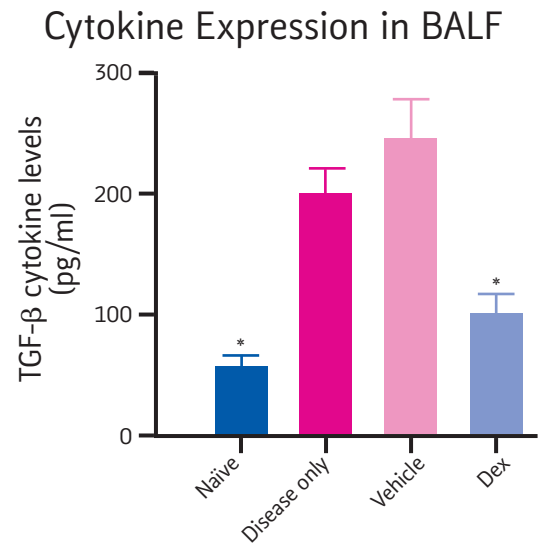


Figure 2. BALF TGF-β cytokine levels. The level of TGF-β in BALF collected on study day 21 was measured by Luminex technology. * represents P value <0.05 versus vehicle.

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... MLM Medical Labs 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 Company

About MLM Medical Labs

MLM Medical Labs is a leading specialty and central laboratory with comprehensive research services and diagnostic capabilities in Europe and the United States. Offering a range of standard and fully customizable analytical services across a variety of therapeutic areas, we add value at every stage of the drug development process from non-clinical/preclinical through phase IV clinical trials that serve to augment and accelerate research programs to their next stages and milestones. Each disease area is supplemented extensively by different models and batteries of in vitro and ex vivo analyses, offering answers to your therapeutics' effect on different parameters. With our strong reputation for scientific expertise, passionate approach to customer care, and adherence to quality data, we empower clients ranging from emerging biotech to Top Ten Global Pharma companies to reach confident clinical decisions that ultimately serve to improve patient lives.

If you'd like to discuss a particular study or speak with a scientist, please reach out to us!

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