

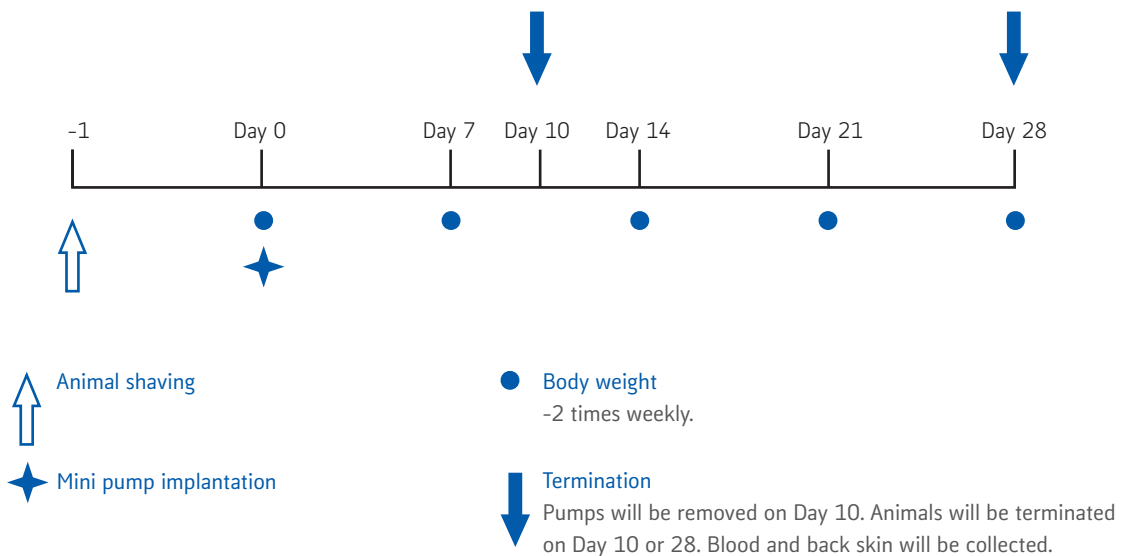
Systemic Sclerosis

Systemic Sclerosis (SSc) is an autoimmune disease characterized by vasculopathy, fibrosis of the skin and internal organs, inflammation and general immune system abnormalities. MLM Medical Labs is using the chemotherapeutic antibiotic bleomycin, to induce SSc in CD-1 mice as a model to explore the pathogenic mechanisms involved in SSc. Implementing the use of osmotic minipumps containing bleomycin allows for a more stable and convenient SSc murine model that encompasses multiple features of human disease. This model may be used in therapeutic programs related to SSc, and more broadly, fibrotic diseases. Model validation includes multiplex cytokine profiling, histological analysis and additional fibrotic disease assessments.

Experimental Overview

Animal Strain:	CD-1 Mice
Study Duration:	28 days
Standard Assessments:	Body weight Histopathology of skin and lung (H&E, M&T) with scoring
Additional Assessments:	Biomarkers (serum/plasma, tissue, BALF) IHC of skin and lung Flow cytometry

Experimental Schematic



Histology images below are representative of microscopic findings in the skin at 10 days. All images are from H&E samples.

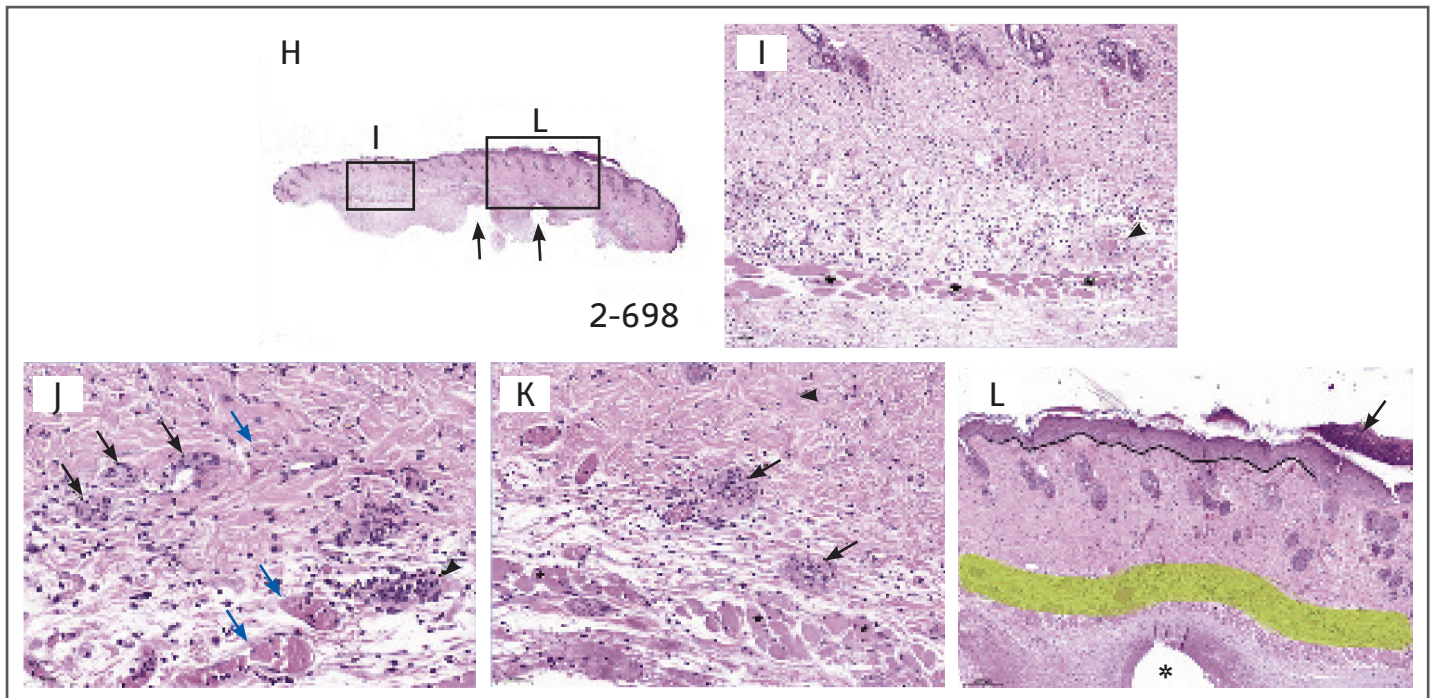


Figure 1 H-L, Bleomycin group H. The boxed areas are shown as indicated. The arrows point to indentation in the subcutis which may be due to the pump. **I.** There is diffuse moderate edema in the deep dermis and in the subcutis and moderate multifocal inflammation (dermis > subcutis). Arrow – a degenerate blood vessel. Asterisks: cutaneous trunci muscle. **J.** High magnification of changes in the deep dermis. Arrowhead: a degenerate blood vessels surrounded by, and containing in its lumen inflammatory cells. Arrows: structures consistent with degenerate arterioles. Blue arrows: dilated vessels (venules) with excessively thin walls. There is significant edema in the lower half of the field which causes the tissue to be loose. **K.** The structures to which the arrows point appear to be 2 degenerate blood vessels with mild inflammatory infiltration (top vessel > bottom), smudging of the vascular wall and vacuolation of the surrounding tissue (the last is an unusual change). There is some collagen smudging e.g. at arrowhead. Asterisks: cutaneous trunci muscle.

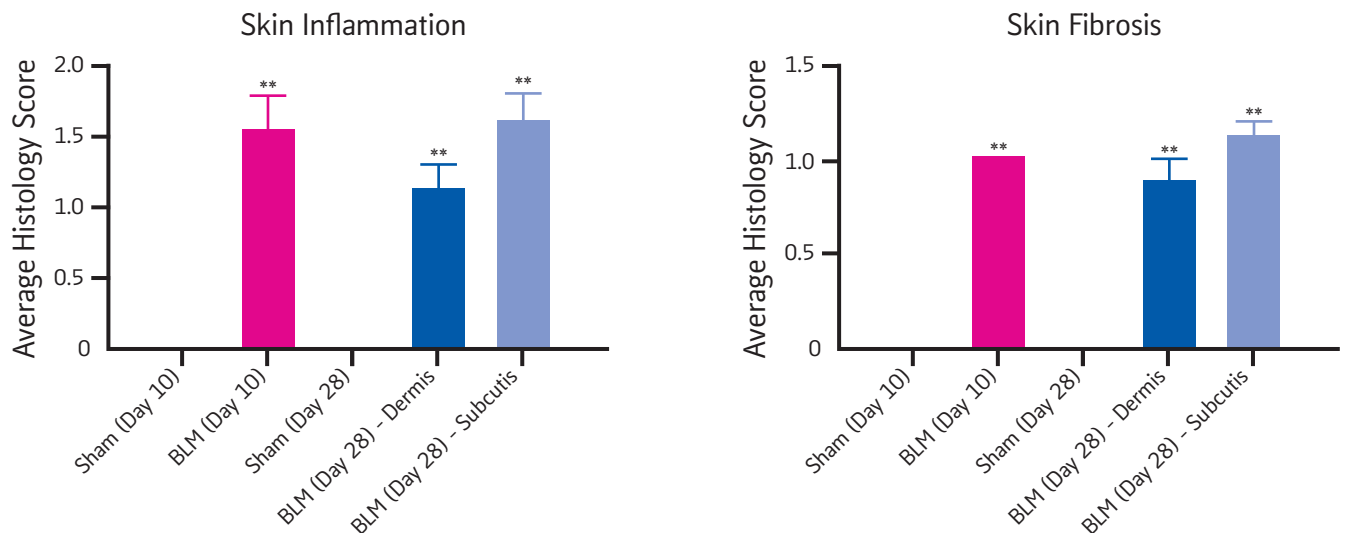


Figure 2. Graphs are representative of mean histological score of skin tissue for inflammation and fibrosis in saline control vs. BLM groups.

Histology images below are representative of microscopic findings in lungs at 4 weeks. A subgross magnification with the distribution of the lesions shaded in green is shown for each sample. Photos G, I-L are from MT-stained samples. The remaining photos are from HE-stained samples.

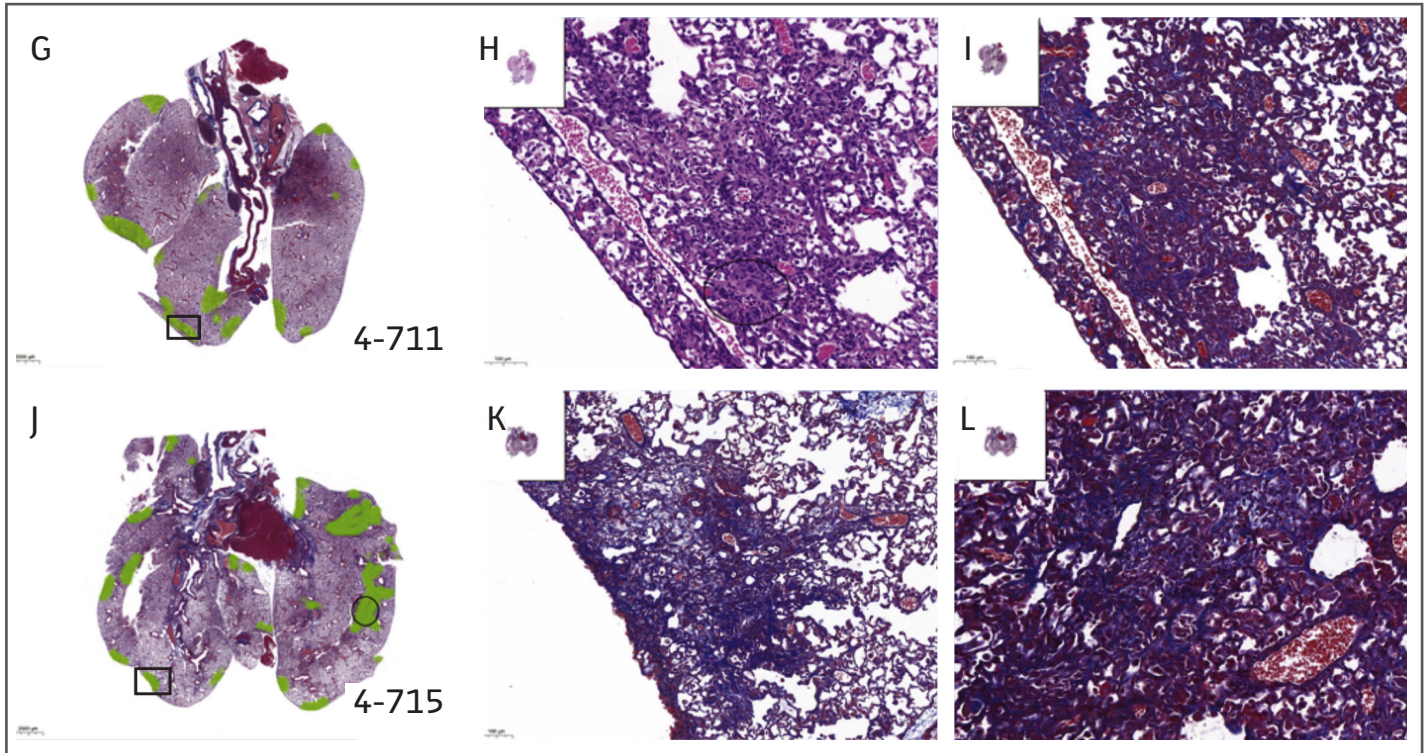


Figure 3 Bleomycin group G. The lesions are limited to the subpleural parenchyma. The boxed area is shown in H and I. H+I. There is significant fibrosis which partly obliterates the alveolar walls (e.g. circled area in H). J. This was the lung with the most widespread lesions. The boxed area is shown in K and the circled area in L. K. There is significant fibrosis with obliteration of alveolar structure in some areas (MT stain). L. This is a larger lesion but the fibrosis tends to be of the alveolar wall.

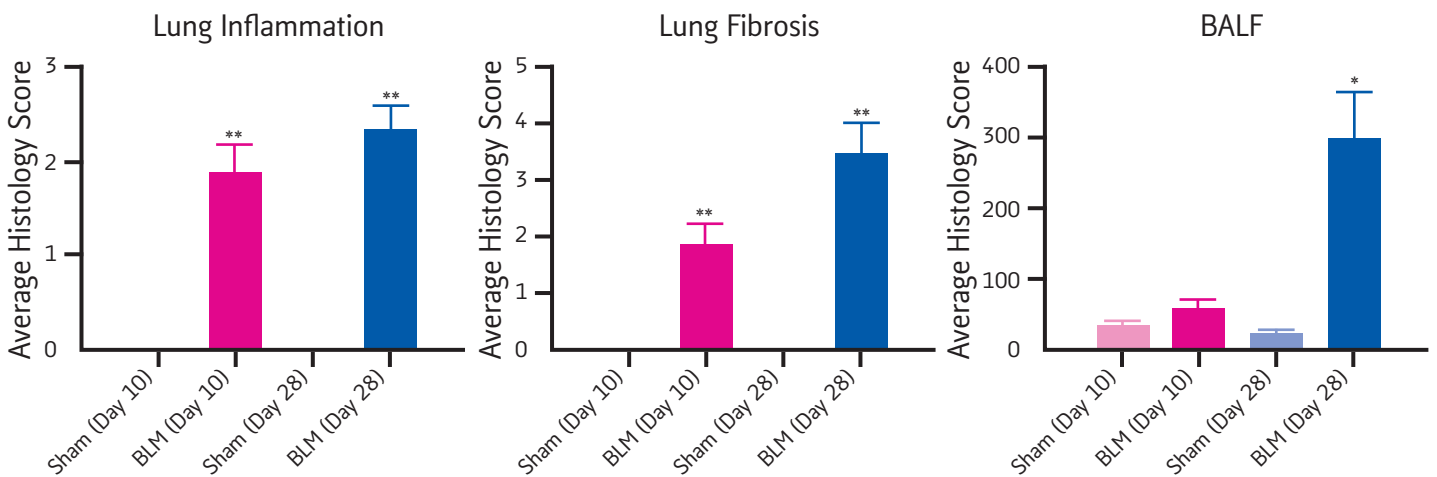


Figure 4. Graphs are representative of mean histological score of lung tissue for inflammation and fibrosis in saline control vs. BLM groups and BALF levels.

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!

info@mlm-labs.com
+1 (651) 641 1770
+49 (2161) 4642 108