DATASHEET

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.

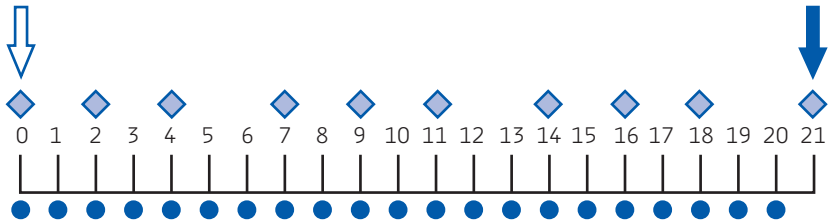
Bleomycin has also been used to induce lung injury in rodents for basic research into pulmonary fibrosis for over a decade. At MLM Medical Labs, we have refined the oral aspiration administration to allow for more even distribution of disease throughout both right and left lungs, making bleomycin-induced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



Disease induction:
OA administration of bleomycin.

Termination (Day 21):
BALF sampling, blood and lung collection of all animals.

Vehicle & positive control administration.
Dexamethasone dosed 1x daily from days 0-20.

Body weight measurement

Results

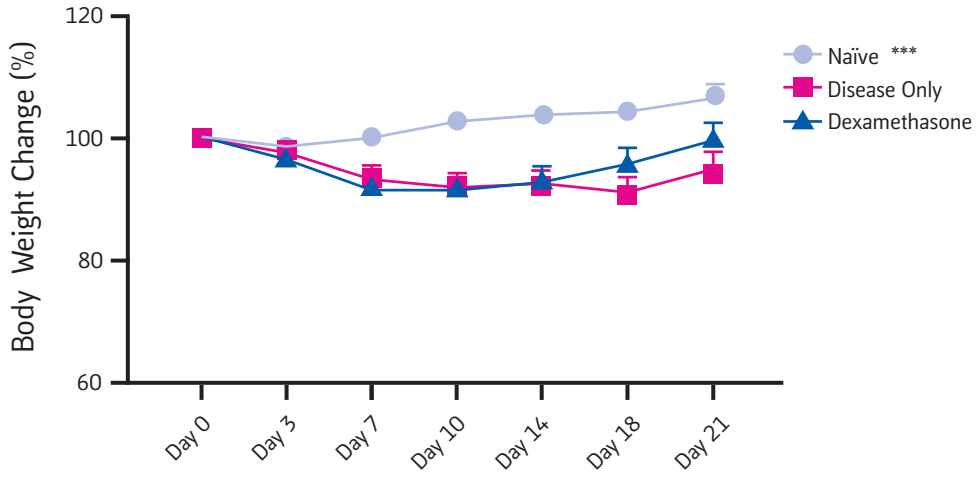


Figure 1. Body weight change.
Body weights are displayed for each day as a percent of their starting body weight. Mean values for each group are displayed ± SEM * p<0.05; ** p<0.01; *** p<0.001 vs Disease only.

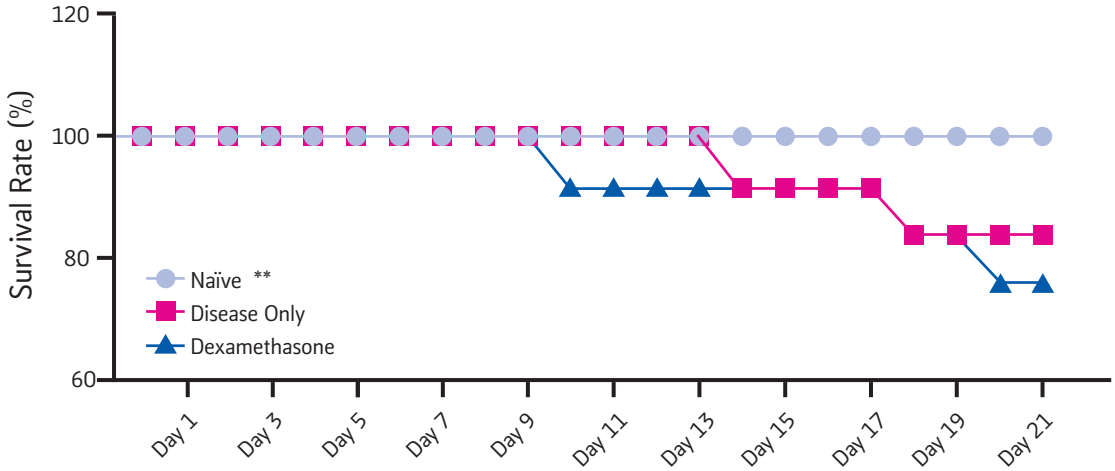


Figure 2. Survival rate. * p<0.05; ** p<0.01; *** p<0.001 vs Disease only.

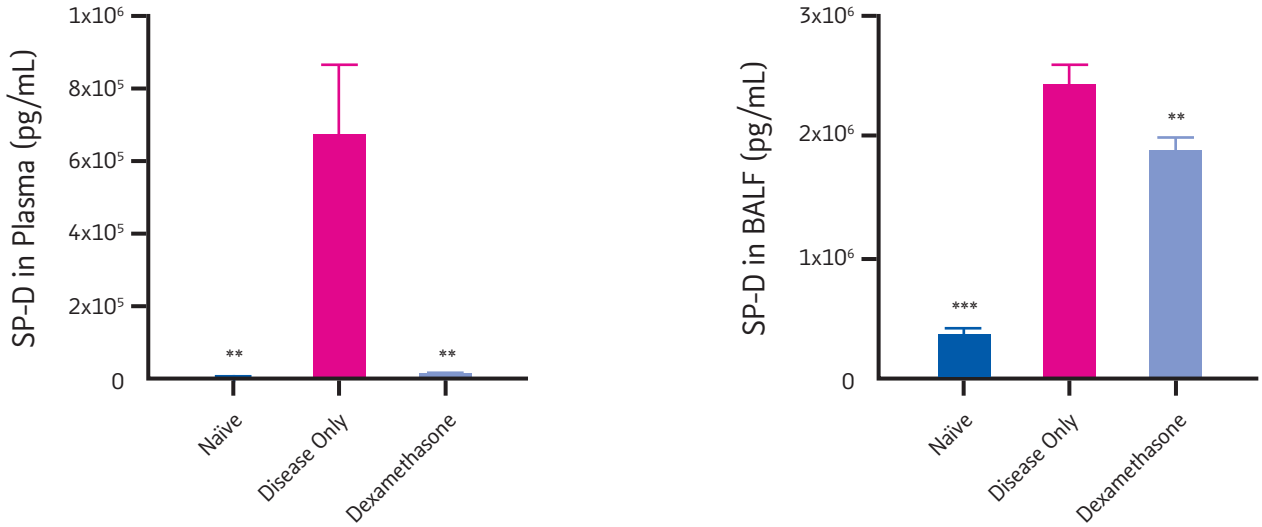
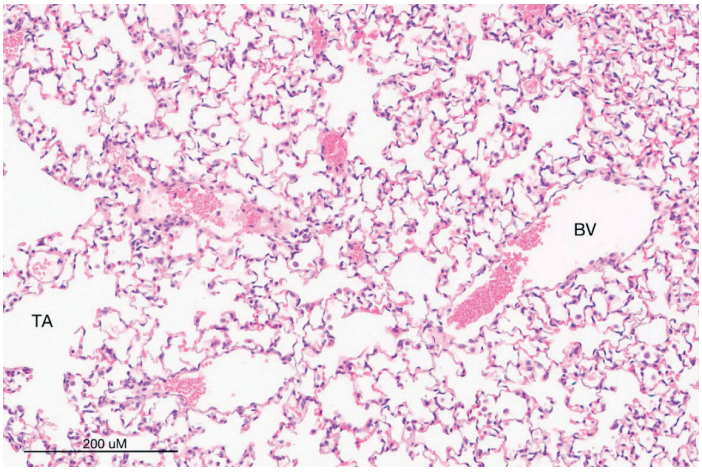
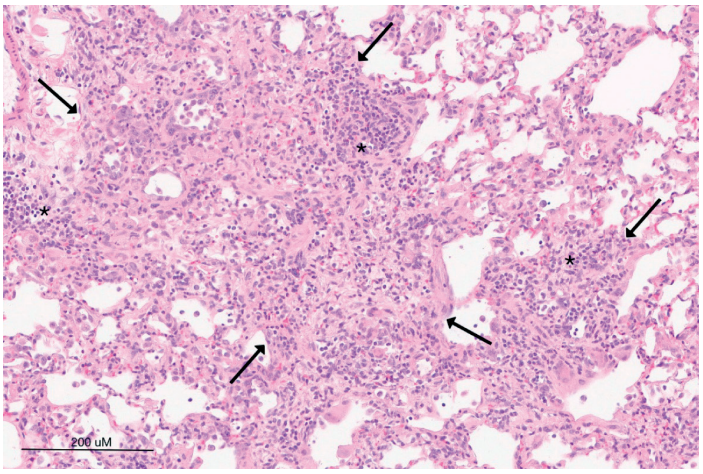


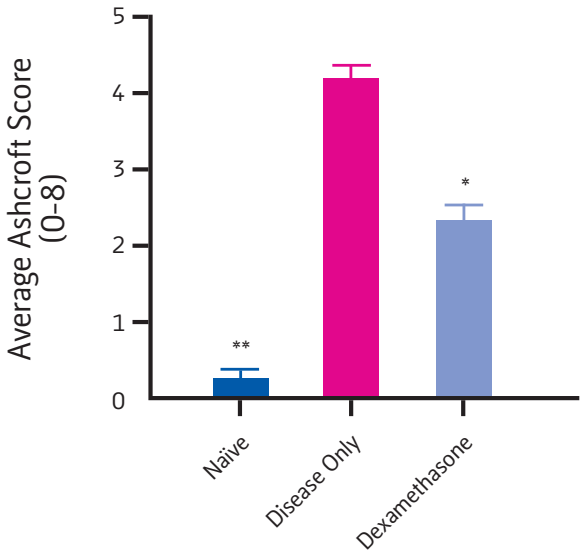
Figure 3. Pulmonary surfactant protein D in plasma and bronchoalveolar lavage fluid (BALF)
*** p<0.05; ** p<0.01; *** p<0.001 vs Disease only.**

Naïve



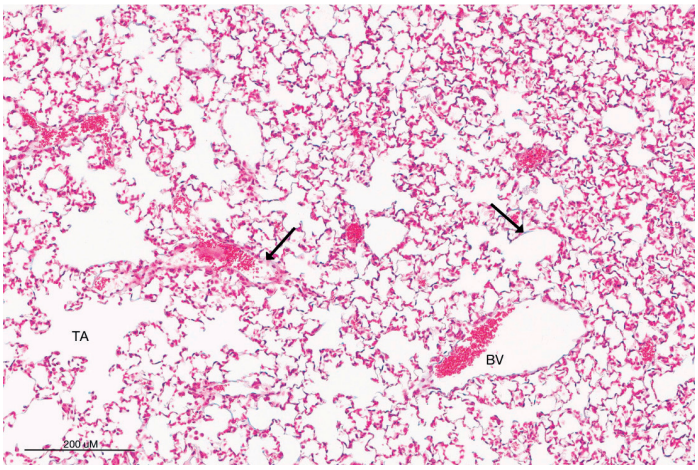
Disease



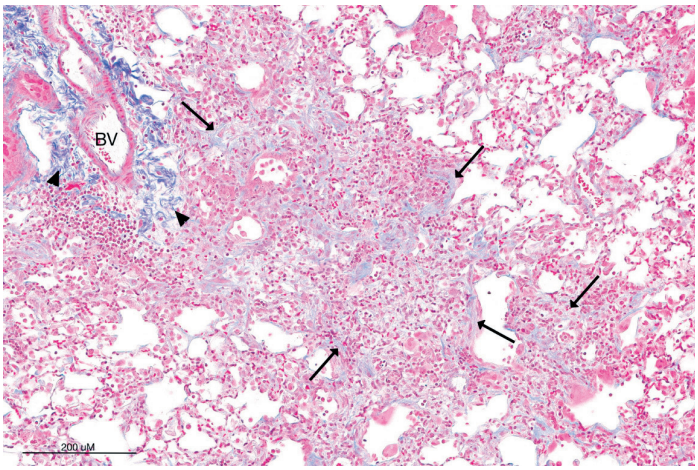


Figur 4. H&E staining of lung tissue. Non-lesioned lung (Naïve): Alveoli/air spaces are open and alveolar walls are thin. Bronchi/bronchioles (Br), terminal airways (TA) and blood vessels (BV) are indicated. Diseased lung: Expansion/replacement of alveolar walls by fibrous tissue (black arrows) is primarily evident toward the hilus adjacent to bronchi/bronchioles (Br). Alveoli/air spaces are obliterated by a mass of fibrous tissue (black arrows) and lympho-cyte aggregates (*). * $p<0.05$ vs Diseasere only.

Naïve



Disease



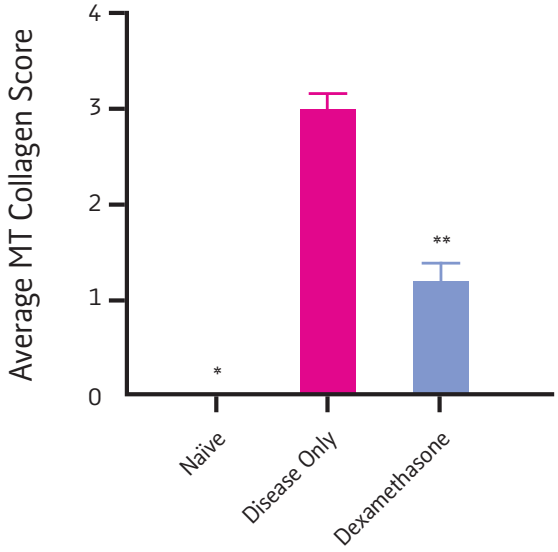


Figure 5. Masson's trichrome staining of lung tissue. Non-lesioned lung (Naïve): Thin rims of collagen (blue staining; black arrows) are visible surrounding blood vessels (BV) and in alveolar or terminal airway (TA) walls. Diseased lung: Collagen expanding alveolar walls stains blue with trichrome (black arrows). Endogenous collagen (black arrowheads) surrounds blood vessels (BV). * $p<0.05$; ** $p<0.01$ vs Disease only.

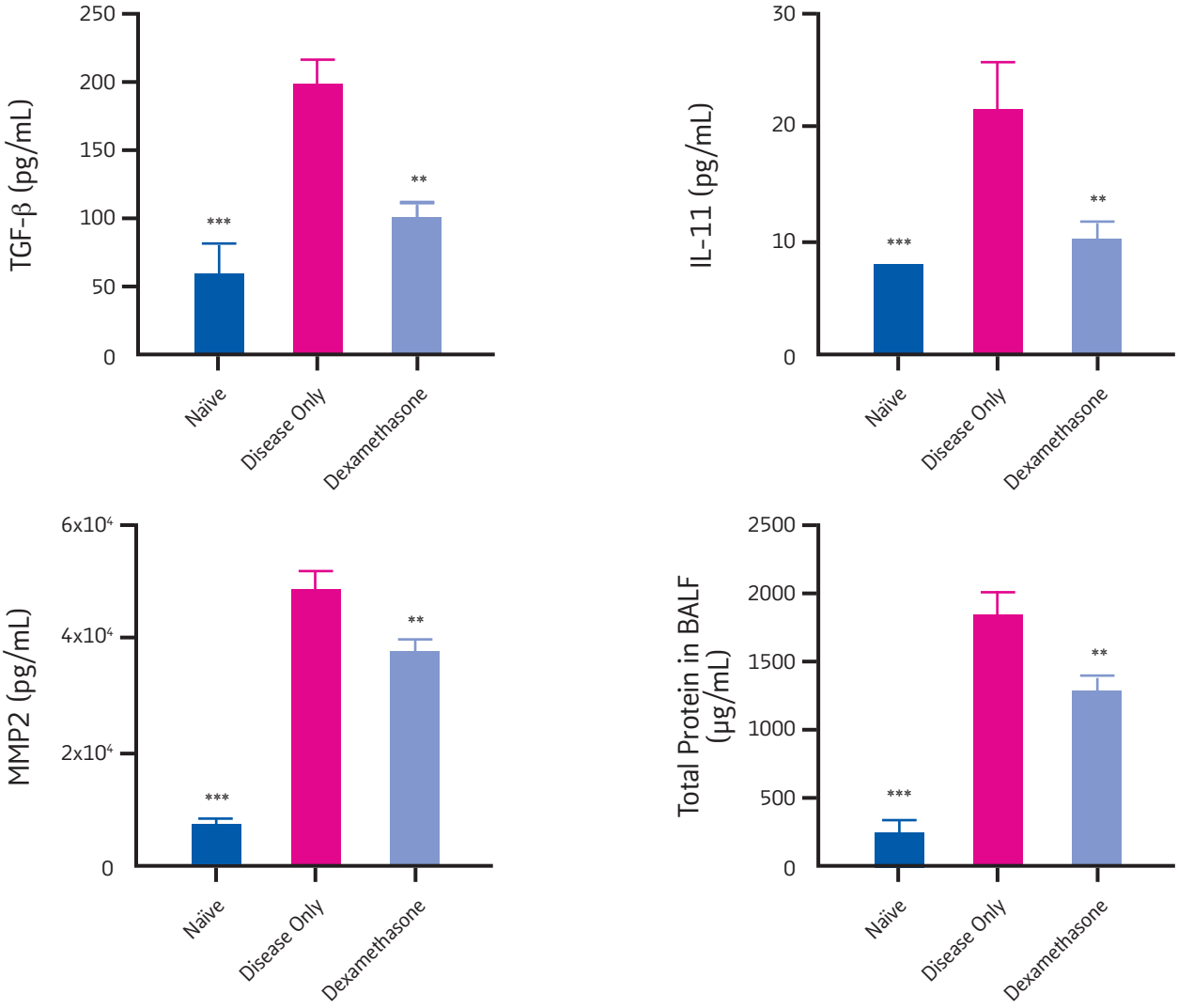


Figure 6. Levels of TGF-β, IL-11, MMP2 and total protein BALF.* p<0.05; ** p<0.01; *** p<0.001 vs Disease only.

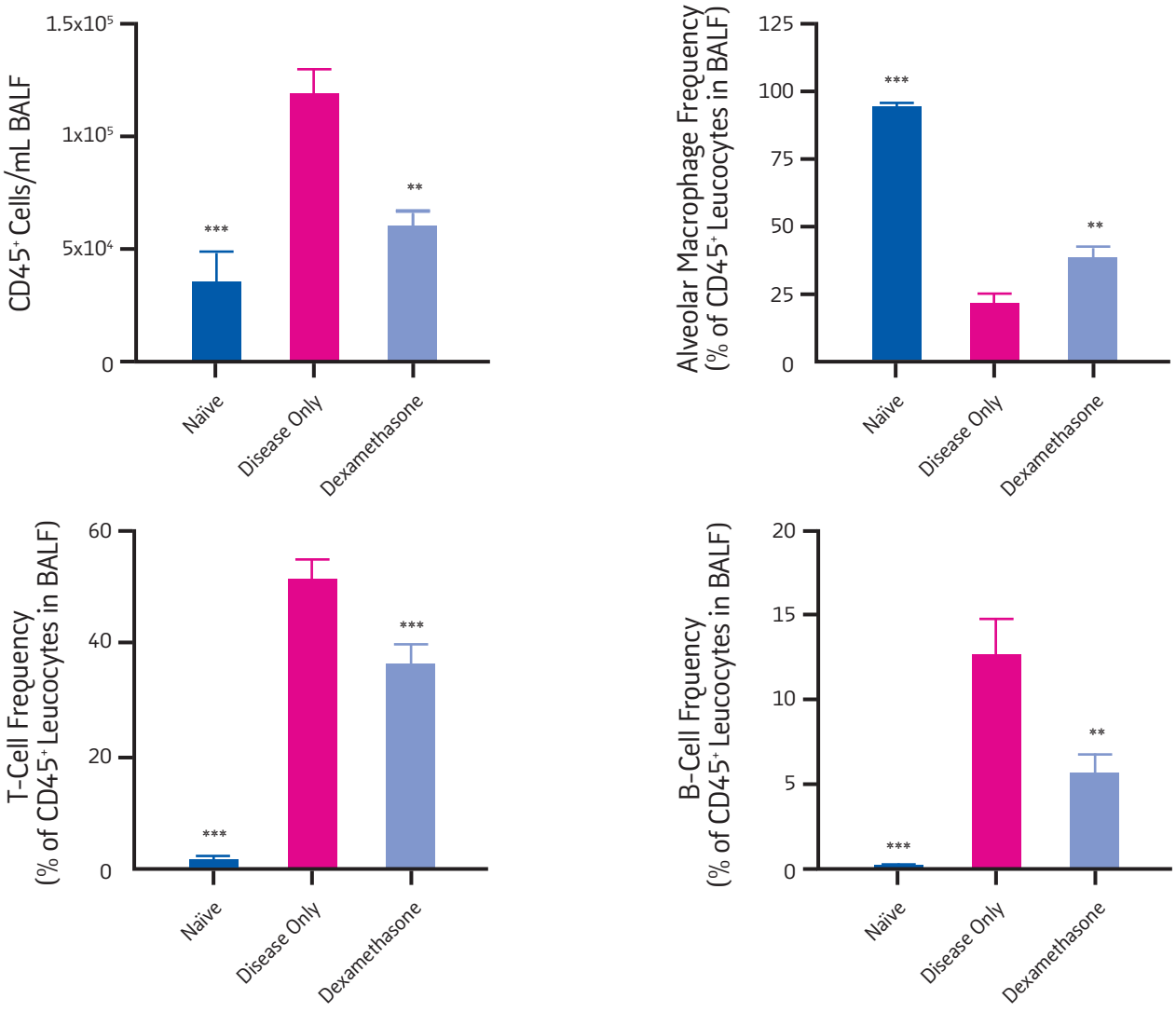


Figure 7. Inflammatory cellular infiltration in BALF * p<0.05; ** p<0.01; *** p<0.001 vs Disease only.

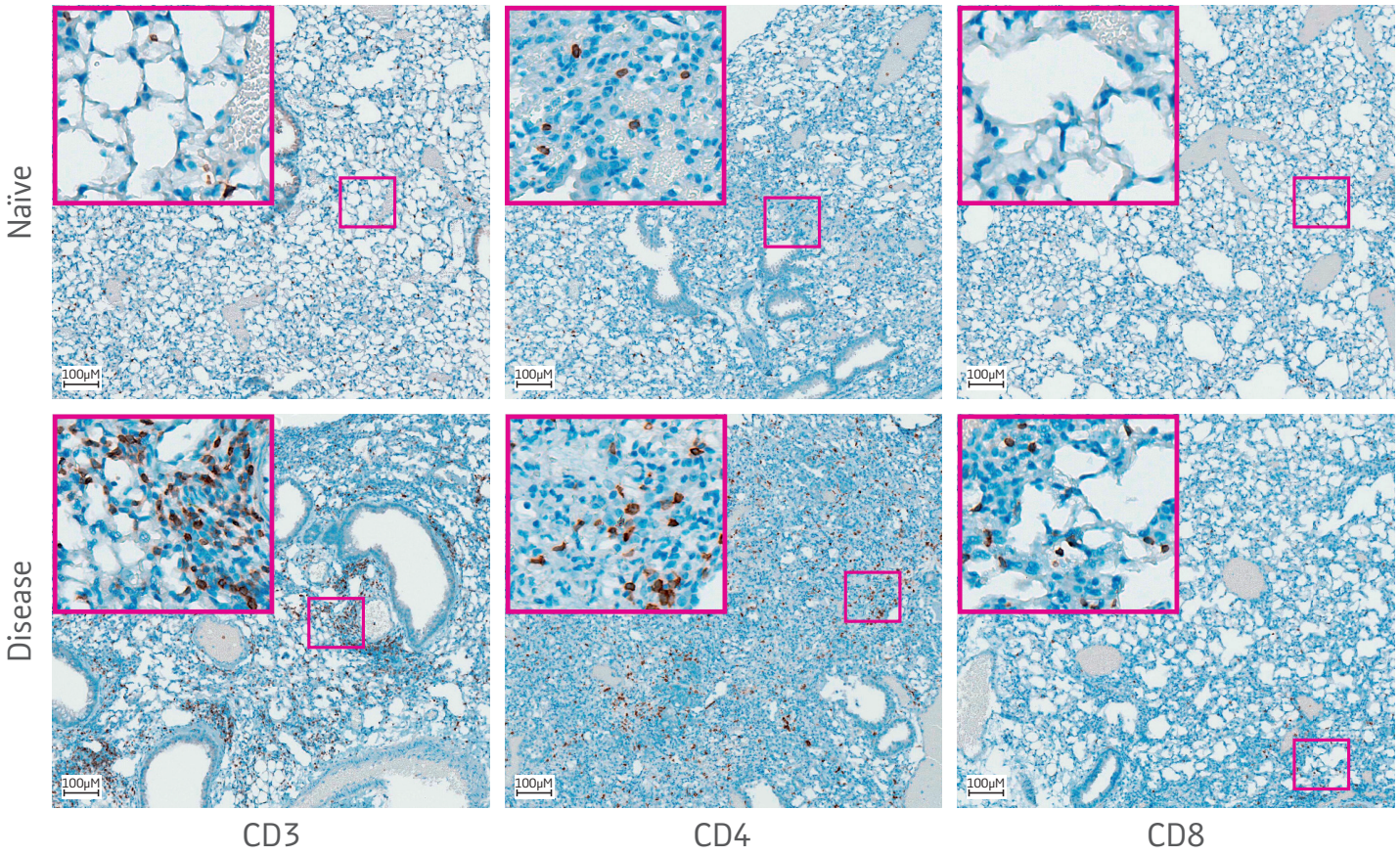


Figure 8. CD3, CD4 and CD8 IHC staining of lung tissue.

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 under- standing 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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