

Supplementary Materials: The following

Table S1. Comparison of results of hyperresponsiveness to methacholine, cells of bronchoalveolar lavage fluid, inflammatory markers, remodeling markers, oxidative stress markers and signaling pathway, in airways and alveolar septa, between SAL and SAL-pep-BbKI control groups.

| Hyperresponsiveness to methacholine (%) | SAL | SAL-pep-BbKI | p * | Inflammatory marker (cells/10 ⁴ µm ²) | SAL | SAL-pep-BbKI | p * |
|---|------------|---------------------|------------|--|---------|--------------|-------|
| %Rrs | 113.7±14.8 | 161.0±14.3 | 0.125 | IL-1β - Airways | 0.4±0.1 | 0.5±0.1 | 0.407 |
| %Ers | 77.3±7.5 | 52.7±8.7 | 0.110 | IL-1β - Alveolar septa | 0.2±0.1 | 0.4±0.1 | 0.476 |
| %Raw | 96.4±16.2 | 159.6±35.9 | 0.106 | IL-4 - Airways | 1.5±0.5 | 2.5±0.7 | 0.306 |
| %Htis | 39.0±5.6 | 25.1±2.8 | 0.137 | IL-4 - Alveolar septa | 1.7±0.3 | 1.8±0.4 | 0.940 |
| %Gtis | 54.4±9.9 | 85.2±13.6 | 0.091 | IL-5 - Airways | 1.7±0.2 | 1.2±0.3 | 0.220 |
| Bronchoalveolar lavage fluid (x10⁴cells/mL) | SAL | SAL-pep-BbKI | p * | IL-5 - Alveolar septa | 1.2±0.2 | 0.8±0.2 | 0.150 |
| Total cells | 0.8±0.1 | 0.7±0.1 | 0.745 | IL-6 - Airways | 0.7±0.4 | 0.8±0.1 | 0.838 |
| Eosinophils | 0.2±0.05 | 0.1±0.03 | 0.221 | IL-6 - Alveolar septa | 0.4±0.1 | 0.4±0.1 | 0.927 |
| Macrophages | 0.2±0.03 | 0.1±0.03 | 0.343 | IL-10 - Airways | 2.1±0.2 | 2.0±0.2 | 0.701 |
| Neutrophils | 0.1±0.02 | 0.1±0.03 | 0.410 | IL-10 - Alveolar septa | 3.2±0.3 | 2.4±0.3 | 0.084 |
| Lymphocytes | 0.2±0.05 | 0.1±0.02 | 0.141 | IL-13 - Airways | 1.7±0.2 | 1.9±0.3 | 0.768 |
| Remodeling markers | SAL | SAL-pep-BbKI | p * | IL-13 - Alveolar septa | 2.6±0.4 | 2.0±0.3 | 0.262 |
| MMP-9 - Airways (cells/10 ⁴ µm ²) | 0.2±0.03 | 0.3±0.1 | 0.256 | IL-17 - Airways | 2.1±0.2 | 1.6±0.2 | 0.138 |

| MMP-9 - Alveolar septa (cells/10 ⁴ μm ²) | 0.5±0.1 | 0.3±0.1 | 0.08 8 | IL-17 - Alveolar septa | 1.5±0.2 | 1.0±0.2 | 0.13 5 |
|---|------------|--------------------------|------------|---|--------------|--------------------------|------------|
| MMP-12 - Airways (cells/10 ⁴ μm ²) | 1.3±0.2 | 1.1±0.2 | 0.49 8 | IFN-γ - Airways | 0.7±0.2 | 0.4±0.1 | 0.12 5 |
| MMP-12 - Alveolar septa (cells/10 ⁴ μm ²) | 0.4±0.1 | 0.5±0.1 | 0.72 8 | IFN-γ - Alveolar septa | 0.7±0.2 | 0.5±0.1 | 0.37 0 |
| TGF-β - Airways (cells/10 ⁴ μm ²) | 0.8±0.3 | 0.8±0.1 | 0.85 4 | TNF-α - Airways | 1.7±0.4 | 3.2±0.9 | 0.07 7 |
| TGF-β - Alveolar septa (cells/10 ⁴ μm ²) | 0.1±0.07 | 0.2±0.1 | 0.36 1 | TNF-α - Alveolar septa | 1.3±0.2 | 2.0±0.2 | 0.06 0 |
| Collagen fibers - Airways (%) | 1.6±0.4 | 2.1±0.5 | 0.55 3 | | | | |
| Collagen fibers - Alveolar septa (%) | 2.4±0.2 | 2.7±0.2 | 0.43 2 | | | | |
| Signaling pathway (cells/10⁴μm²) | SAL | SAL-pep- BbKI | p * | Oxidative stress markers | SAL | SAL-pep- BbKI | p * |
| NF-κB - Airways | 0.4±0.1 | 1.0±0.2 | 0.34 3 | iNOS - Airways (cells/10 ⁴ μm ²) | 3.3±0.5 | 2.1± 0.2 | 0.06 7 |
| NF-κB - Alveolar septa | 0.2±0.1 | 0.3±0.1 | 0.50 9 | iNOS - Alveolar septa (cells/10 ⁴ μm ²) | 2.6±0.4 | 2.8 ±0.4 | 0.75 1 |
| | | | | Exhaled Nitric Oxide (ppb) | 12.3±2. 1 | 18.5±0.3 | 0.06 9 |

Note: Rrs, respiratory system resistance; Ers, respiratory system elastance; Raw, airway resistance; This, tissue elastance; Gtis, tissue resistance; IL, interleukin; IFN, interferon; TNF, tumor necrosis factor; MMP, metalloproteinase; TGF, transforming growth factor; iNOS, inducible nitric oxide synthase; NF, nuclear factor.

* p value.