Characterization of spontaneous airspace enlargement in mice lacking microfibrillar-associated protein 4 (MFAP4)

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Aim MFAP4 is an extracellular matrix molecule with high pulmonary expression and localization to elastic fibers. We set out to explore MFAP4’s potential involvement in elastic homeostasis and development of pulmonary emphysema.

Results MFAP4-dependent changes in lung parameters were detectable at 6 months and 8 months but not at 3 months of age in female mice. Significant changes included increases in total lung capacity and compliance, and a decrease in tissue elasticity (Figures 1 and 2). Using in vivo breath-hold gated micro-CT to assess 8-month-old MFAP4−/− mice, we found that the mean density of the lung parenchyma of the MFAP4−/− mice was decreased, and the percentage of low-attenuation areas was significantly increased by 14 % (Figures 3 and 4). Transmission electron microscopy (TEM) did not reveal apparent differences in the organization of elastic fibers in the alveolar septa (Figure 5). Likewise, there was no change in elastin content (not shown). Stereological analysis showed that the alveolar surface density in relation to the lung parenchyma and the total alveolar surface area inside of the lung were both significantly decreased in MFAP4−/− mice by 25 % and 15 %, respectively (Figure 6).

Conclusion The data did not support an essential role of MFAP4 in elastic fiber organization. Yet, MFAP4−/− mice developed a spontaneous loss of lung function, which was evident at 6 months of age, and moderate airspace enlargement, with emphysema-like changes.