21. Analysis of Lung Injury Models by Using Human MUC1 Transgenic Mice

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Rationale. KL-6 (Krebs von den Lungen 6) is an epitope exclusively expressed on MUC1 mucin of the pulmonary epithelial membrane surface. KL-6 has been shown to be a sensitive marker for interstitial pneumonia. Despite its usefulness and significance, this epitope has only been found in primates, and is not present in rodents; thus, a practical experimental animal model for KL-6 has yet to be established. Interestingly, we have found that KL-6 is present in human-MUC1 transgenic (MUC1-tg) mice (C57BL/6) sera, as well as bronchoalveolar lavage fluid (BALF), as measured by ELISA (enzyme-linked immunosorbent assay).

Methods. To establish a standard animal model, we characterized KL-6 status in MUC1-tg mice. Levels of KL-6 in both sera and BALF were measured by ELISA, and KL-6 expression was detected by immunohistochemistry. The bleomycin-induced lung injury model using these mice was also evaluated.

Results. Serum concentrations of KL-6 in unstimulated MUC1-tg mice showed similar levels as in healthy adult humans. In addition, levels of KL-6 in BALF from these mice were much higher than those in sera. Similarly to humans, KL-6 was expressed in alveolar epithelial cells in these mice as determined by immunohistochemistry. Bleomycin (2 mg/kg) was administered via the trachea. As reported previously with C57BL/6 mice, MUC1-tg mice showed lung inflammation and finally developed fibrotic changes in the lungs. Levels of serum KL-6 increased by approximately 7.6-fold when compared with unstimulated MUC1-tg mice in the inflammation phase, whereas those of BALF decreased to one third. In contrast, in the fibrotic phase, serum KL-6 levels decreased gradually, but remained 2-fold higher than in unstimulated mice, while BALF KL-6 levels returned to the levels in unstimulated mice. These observations resemble the pathological changes in KL-6 during lung diseases in humans.

Conclusion. This model, in which KL-6 can be easily measured by ELISA, is a unique animal model for the further evaluation of lung injuries.