Functional Characterization of a Porcine Emphysema Model

Lung emphysema is a central feature of chronic obstructive pulmonary disease (COPD), a frequent human disease worldwide. Cigarette smoking is the major cause of COPD, but genetic predisposition seems to be an important factor. Mutations in surfactant protein genes have been linked to COPD phenotypes in humans. Also, the catalytic activities of metalloproteinases (MMPs) are central in the pathogenesis of emphysema/COPD. Especially MMP9, but also MMP2, MMP7, and MMP12 seem to be involved in human emphysema. MMP12−/− mice are protected from smoke-induced emphysema. ITGB6−/− mice spontaneously develop age-related lung emphysema due to lack of ITGB6-TGF-β1 regulation of the MMP12 expression. A mutated pig phenotype characterized by age-related lung emphysema and resembling the ITGB6−/− mouse has been described previously. To investigate the emphysema pathogenesis in this pig model, we examined the expression of MMP2, MMP7, MMP9, MMP12, and TGF-β1 by quantitative PCR (qPCR). In addition, immunohistochemical stainings of the lungs with SP-B, SP-C, MMP9, and MMP12 antibodies were performed. The haematologic/immunologic status of the pigs also was studied. The qPCR study showed no difference between pigs with and without emphysema, and no systemic differences were indicated by the haematologic and immunologic studies. However, the immunohistochemical stainings showed an increased expression of MMP9 and MMP12 in older, mutated pigs (with emphysema) compared with normal and young mutated pigs (without emphysema). The pig model is comparable to human emphysema patients and the ITGB6−/− mouse model with respect to both morphology and functionality.