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The time-course of cardiac and pulmonary matrix metalloproteinase-2 and -9 activities after chronic cigarette smoke exposure in mice
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Background: Gelatinase-type matrix metalloproteinases (MMP-2 and -9) have crucial role in inflammatory diseases, e.g. chronic obstructive pulmonary disease as well as in cardiovascular pathology. It is known that chronic smoke exposure increases MMP-2 and -9 activities in the lung. However, the smoke-induced alterations in MMP-2 and -9 activities in the heart and the time-course of their pulmonary and myocardial activity during chronic smoke exposure have not been examined.

Purpose: Therefore, the aim of this study was to characterize the time-course of cardiac and pulmonary MMP-2 and -9 activities during chronic tobacco smoke exposure.

Methods: Eight week-old male C57Bl/6 wild type mice (25-30 g; n=5-6/group) were exposed to whole body tobacco smoke with a manual system twice a day for 30 min throughout periods of 1, 2 and 3 months. Age-matched mice without smoke administration were used as controls. Then hearts and lungs were isolated at the end of each month, rinsed in PBS and snap-frozen in liquid nitrogen. MMPs activities were determined by gelatin zymography.

Results: The myocardial activity of 72- and 75 kDa-MMP-2 showed an increasing tendency after 3-month smoke exposure compared to the time-matched control group, however, the difference did not reach statistical significance. Although MMP-9 yielded weak signals from heart samples, MMP-9 activity decreased significantly at the end of the second month compared to the corresponding controls (7,140 ± 3,809 and 2,266 ± 750 AU, p=0.008), and showed a mild increase after 3 months. In the lung, we have found a non-significant decrease in the activity of both MMP-2 isoforms in the 3-month smoking group when compared to the time-matched controls. MMP-9 activity was significantly lower after 3-month smoke exposure compared to the control mice (35,476 ± 6,628 and 28,424 ± 2,578 AU, p=0.03 respectively). Tobacco smoke administration for 1 or 2 months did not influence MMP-2 or -9 activities in either the heart or the lung compared to the respective controls.

Conclusion: MMP-9 activity decreased after 3-month tobacco smoke exposure in the lung, while MMP-2 activity showed only a tendency of decrease. Meanwhile, in the heart, a moderate increase was observed in the activity of both MMPs. Further experiments are needed with longer smoke exposure to evaluate the time-dependent alterations and possible roles of MMP-2 and -9 in tobacco smoke-induced cardiac and pulmonary changes.