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Title: Expression of matrix metalloproteinases and TIMP inhibitors in circulation/lung in patients with chronic obstructive pulmonary disease

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Body: In chronic obstructive pulmonary disease (COPD), increased expression of matrix metalloproteinases (MMPs) and their inhibitors (TIMPs) has been repeatedly reported. Some of MMPs/TIMPs, e.g. MMP9, have been investigated both in serum and lung; others were measured only in one of these localisations. To extend the profile of MMPs/TIMPs systemic / local expression in COPD, we created two pilot cohorts of COPD patients and control healthy subjects, both comprising 20 subjects. Protein expression of MMP2,8,9 and TIMP1,2,3,4 was determined in parallel in serum and in BronchoAlveolar Lavage Fluid (BALF) by a microsphere multiplex assay. To complement protein measurements, mRNA expression was evaluated in BAL cells which were available from 13 COPD patients and 18 controls. Compared with controls, in patients MMP9 levels were increased systemically (serum protein: $p=0.03$) as well as locally (BALF protein: $p<0.001$, mRNA in BAL cells: $p=0.002$). MMP2 and 8 mRNA were upregulated in BAL cells ($p=0.001$ and $p=0.03$, respectively); MMP8 protein was elevated in BALF ($p<<0.001$). Serum concentrations of TIMP4 paralleled increase of MMP2 and 9 mRNA in BAL cells ($p=0.005$ and $p=0.007$, respectively). The number of TIMP1 transcripts correlated with the number of months free of exacerbation(s) during 2-years follow-up after the BAL sampling ($p=0.03$) In conclusion, distinct expression profiles of MMPs/TIMPs were observed at systemic and local level in our COPD patients. These pilot data will be subject to further extension and verification, including subanalyses according to the GOLD stage. Grant support: IGAPU_LF_2012_07, CZ.1.05/2.1.00/01.0030.