Reviewer’s report

Title: Measurement of MMP-9 and -12 degraded elastin (ELM) provides unique information on lung tissue degradation

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Reviewer: Yong Lin

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Review manuscript ‘Measurement of MMP-9 and 12 degraded elastin (ELM) provides unique information on lung tissue degradation” by Helene Skjot-Arkil, etal.

In the manuscript, the authors performed in vitro enzymatic degradation of elastin from human aorta by MMPs, cathepsins, aggregcanases and identified elastin derive peptides by proteomic mass spectrometry. An epitope VPGVGISPEA was select to generate a monoclonal antibody, which was used to develop EIISA and showed the presence of the epitope in plasma of both COPD and IPF patients and claimed to provide unique information on lung tissue degradation.

While the study suggests an effective approach to study biochemical elastin degradation relevant to disease process, the experimental methods which lead to the conclusion is not clear and incoherent. The main questions to be asked are

1. The peptide identifications were studied in three different laboratories. One lab identified 114 peptide using a large group of MMP, cathepsins, and aggregcanases. The results was used to analyzed the mode of cleavages in elastin (Table 1). The other labs were working only with MMP-9 and 12 and said to identify 441 peptides, but only few selected peptides are present in Table 2 and 3. There is no explanation to comparison or correlate the identified peptides between the labs.

2. The most important question should be asked is the selection of VPGVGISPEA. The peptide is identified in the digestion of vascular elastin by MMP-9 and 12 and selected to generate monoclonal antibody as biomarker for elastin degradation of lung extracellular matrix in COPD and IPF. The elastin derived peptides from lung and vascular system are not likely identical. It has been shown that well studied antigenic elastin peptides VGVAPG isolated from aorta or ligamentum nuchae are not present in the same digestion from lung. (He J etal, Exp Lung Res 2010; 36: 548). In addition neutrophil elastase is the major protease involves in lung elastin degradation in COPD, although macrophage has also partially involve in the disease. Several recent publications have shown desmosine and isodesmosine as a promising biomarker for the lung degradation in COPD. The statement in the manuscript (4th paragraph of Instruction) that “Desmosine and isodesmosine has not proven accurate or precise predictor of COPD” is not accurate.
3. Soluble lung and soluble aorta have been used to compare the generation of peptide. (Fig3). Definition of soluble lung and aorta and the source or how are they obtained need to be clarified.