Neutrophil protease 3 is present in human atherosclerotic lesions and modifies LDL and HDL particles

Su Duy Nguyen¹, Katariina Maaninka¹, Mikko I. Mäyränpää², Katariina Nurmi¹, Jari Metso^{3,4},
Matti Jauhiainen^{3,4}, Petri T. Kovanen¹, Katariina Öörni¹

¹Wihuri Research Institute, Haartmaninkatu 8, 00290 Helsinki, Finland

²Pathology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

³Minerva Foundation Institute for Medical Research, Biomedicum, Helsinki, Finland

⁴National Institute for Health and Welfare, Helsinki, Finland

Objective

Protease 3 (PR3), a major neutrophil protease present in neutrophil azurophilic granules, is a multifunctional enzyme involved in the regulation of pro-inflammatory processes but its role in atherosclerosis remains unexplored. Here, we aim to identify, whether PR3 is present in human atherosclerotic lesions and to examine how PR3 affects structure and functions of LDL and HDL.

Methods and Results

1. PR3 is present in advanced atherosclerotic lesions of human coronary arteries

2. PR3 induces rapid degradation of apoB-100 in LDL

3. Modification of LDL by PR3 leads to change in LDL structure and LDL aggregation

4. PR3-modified LDL binds strongly to human aortic proteoglycans

5. Modification of LDL by PR3 induces foam cell formation

7. PR3 degrades apolipoproteins in mature spherical HDL

8. PR3 reduces the ability of apoA-I and HDL to promote cholesterol efflux

6. PR3 induces degradation of apolipoproteins of HDL

Conclusion

The present data demonstrate that PR3 is a novel protease found in human advanced atherosclerotic lesions, and suggest that PR3 may have a role in the development of atherosclerosis by modifying both LDL and HDL particles.