Author's response to reviews

Title: Human antimicrobial peptide LL-37 is present in atherosclerotic plaques and induces death of vascular smooth muscle cells: a laboratory study

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Dear Editor,

Please find enclosed a revised version of our manuscript "Human antimicrobial peptide LL-37 is present in atherosclerotic plaques and induces death of vascular smooth muscle cells: a laboratory study" by Cristina D. Ciornei, Hans Tapper, Anders Bjartell, Nils H. Sterbny and Mikael Bodelsson.

We are grateful for the constructive criticism given by the two Referees and we have tried to address all the points raised as detailed below. We hope the manuscript is now acceptable for publication in BMC Cardiovascular Disorders.

RESPONSE TO REFEREE 1, Adrian H. Chester:

The lesions studied represent an early stage of the disease, fibroatheromas, and we did not study any association between the location of LL-37 and the severity/stability of the lesion. Furthermore, we did not investigate any association between LL-37 and apoptotic cells in the atherosclerotic lesion. However, it is well established that macrophages, cells capable of releasing LL-37, accumulate adjacent to thinning or rupture of the fibrous cap of advanced lesions (see Prog Cardiovasc Dis 2002, 44:357-368). At this location smooth muscle cell apoptosis is predominant. This is discussed in the revised manuscript (p. 19, first paragraph).

RESPONSE TO REFEREE 2, Dennis Bruemmer:

1. We are grateful for calling the paper by Edfeldt et al. in ATVB to our attention. This is cited and discussed in the revised manuscript (p. 18, second paragraph - p. 19, first paragraph).

2. We agree with the referee that we have not investigated the expression of LL-37 in different stages of atherosclerosis such as in the fibrous cap of an advanced lesion. Thus, we do not have any direct evidence for an involvement of LL-37 in advanced disease and plaque rupture. However, it is well established that macrophages, cells capable of releasing LL-37, accumulate adjacent to thinning or rupture of the fibrous cap of advanced lesions (see Prog Cardiovasc Dis 2002, 44:357-368). At this location smooth muscle cell apoptosis is predominant. This is discussed in the revised manuscript (p. 19, first paragraph).

The CD68 staining was performed on the same lesions as represented by the lesion in figure 1A but from separate sections. This is pointed out in the revised manuscript (p. 6, first line). Serial staining has been performed by Edfeldt and colleagues (Arterioscler Thromb Vasc Biol 2006, 26:1551-1557). Their results are discussed in the revised manuscript (p. 18, second paragraph).
Yours sincerely
Mikael Bodelsson