Reviewer’s report

Title: Immunity, atherosclerosis and cardiovascular disease

Version: 1 Date: 28 January 2013

Reviewer: Antonino Nicoletti

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The proposed review is not sufficiently focused, too many aspects are being addressed. It should rather be orientated towards a limited number of issues. As a consequence, the author takes several ‘shortcuts’ and the general feeling is a lack of in-depth analysis of inflammation and immunity in the context of atherosclerosis. Out-of focus (or appearing as such) considerations are presented (for instance, effect of aging in human and animal studies) without a clear link with what is supposed to be central to the review: the interaction of inflammation, immunity and atherosclerosis.

Major Compulsory Revisions

1/ The impact of inflammation/immunity is presented as it was contributing equally to atherogenesis and plaque complication and no clear definition is given to these terms: what is inflammation as compared to immunity?

2/ While the contribution of immune effectors is clearly demonstrated in atherogenesis in experimental models of hypercholesterolemic animals (especially in mice), it is much less clear for human early lesions, even though many reviews repeat this statement. Again, the contribution of immune effectors in the genesis of plaque should be split from their effects on plaque complications.

3/ Immune modulation strategies are presented as anti-inflammatory treatments. The target of the immune response and the effector mechanisms triggered will define whether the immune modulation will result in reduction or exacerbation of inflammation: detoxification of oxLDL by anti-oxLDL antibodies is beneficial and reduces plaque inflammation; targeting HSP-expressing stressed endothelial cells is pro-inflammatory and pro-atherogenic. These two immune modulation cannot be considered as anti-inflammatory. Indeed, the author should consider splitting the immune modulation strategies that have been used to understand the pathophysiology and those that are being tested as therapeutic options.

4/ New immuno-pathophysiological mechanisms of atherosclerosis currently discussed in the field are not presented by the author: adventitial immune response, local and systemic B cell response, intraplaque hemorrhage and neovascularization of the vessel wall, crossroads between metabolic and inflammatory pathways...There are many new existing findings linking inflammation, immunity and plaque progression that could be presented in such a
review.

5/ There are (too) many misspellings in this ms.

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.