Reviewer’s report

Title: Does LDL-cholesterol Induce Inflammation? If So, Does It Matter? Current Insights and Future Perspectives for Novel Therapies

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Reviewer: Norbert Gerdes

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Jukema: Does LDL-cholesterol induce inflammation? Does it matter?

This is an interesting opinion piece summarized by Jukema et al. The authors provide a comprehensive overview of the "lipid hypothesis" of cardiovascular disease and summarize established and novel therapeutic strategies to combat hyperlipidemia. They continue to introduce the "immune concept" of atherosclerosis before combining and connecting both and describing hypercholesterolemia/hyperlipidemia as the main propagators of vascular immune reactions.

The opinion is very well-balanced. It should be mentioned, however, that the entire process of atherosclerosis and vascular dysfunction is not only based, as so often suggested, on local vascular inflammatory response but is rather a consequence also of a continuing systemic chronic hyper-inflamed state. Overall, the manuscript addresses an important and clinically relevant topic that has gained a lot of attention recently. The article is well-structured and logically connected.

A few minor issues may be addressed:

The title is very attention-catching. That is good. However, the reader is looking for clear answers to these defined questions. Yet, those are given neither in the conclusions of the abstract nor the main text.

The paragraph referring to references 36 and 37 is somewhat out of focus and could be omitted without great loss. In the same paragraph: Is the ASSAIL-MI trial investigating STE-MI. If understood correctly, the previous study (ref 51) already investigated acute MI?

When the authors refer to tocilizumab (p12) they should mention that this is a IL-6R antagonizing antibody. When referring to co-stimulatory molecules as further interesting targets the relevant original publication should be mentioned.

The text requires some proof reading. For example, use of singular and plural should be controlled. Check the sentence p7, line 33. Spelling of IL-1b should be controlled and adhere to uniform standard.
Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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