**Reviewer's report**

**Title:** Systemic inflammation links to atherosclerosis via C3aR1; results of a human in vivo LPS infusion study.

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**Reviewer:** daniel belstrøm

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Review of the manuscript entitled, Systemic inflammation links to atherosclerosis via C3aR1; results of a human in vivo LPS infusion study

This study deals with the role of systemic inflammation as part of the pathogenesis in atherosclerosis. The study which is very interesting and for the most part very well documented and well executed is the continuation of a prior in vitro study performed by the same group.

The authors successfully identify differences in the transcriptome of circulating monocytes after infusion of LPS in healthy volunteers. Furthermore they confirm 7 candidate genes which they had already identified in the corresponding in vitro study.

The authors postulate that the discovered differences in gene expression could have important implications in the understanding of the pathogenic mechanisms of atherosclerosis.

The authors focus much of the role of C3aR1 as a candidate gene, documenting the role of monocytes in inflammation and atherosclerosis. The hypothesis is certainly interesting and sufficient documented in articles published in high-impact journals.

This group adequately identifies the deficiencies of their study such as a small study population, as well as the identification of two candidate genes, traditionally looked upon as having anti-inflammatory potential. However the strict control procedures in the study verifies the correctness of their discoveries.

The manuscript is very well written with, and the written language is at a high academic level.

Unfortunately the methods used in this study lies beyond my expertise as a researcher. Because of that I have only been able to review the article as a layman. Therefore I strongly encourage the editorial team to have this paper reviewed also by an expert in the field of genetics, mostly in respect of the delicate work performed by this group of researchers.

Sincerely
Daniel Belstrøm
Level of interest: An article of importance in its field

Quality of written English: Acceptable

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