Reviewer’s report

Title: The effect of Lipoxin A4 on the interaction between macrophage and osteoblast: possible role of inflammation resolution in the treatment of aseptic loosening

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Reviewer: Paola Maderna

In this paper, the Authors describe the effect of LXA4 on the interaction between macrophage and osteoblast and the role in the treatment of aseptic loosening, a major problem rising in the case of total joints replacement. LXs are well defined anti-inflammatory, pro-resolution mediators and this paper show data which can extend the potential therapeutic activity of LXs.

Comments:

I would suggest that in title “inflammation resolution” could be omitted

The Authors should indicate the commercial source of the LXA4 they use in the study

In the first set of experiment the Authors use different concentrations of PMMA (from 0.1 mg/ml to 1 mg/ml). The increase in pro-inflammatory cytokine production is statistically significant at all the concentrations tested. In the following experiments, the Authors use 1 mg/ml of PMMA in the presence of LXA4. The Authors should discuss why they use this concentration in the following experiments, considering that probably the effect reaches the highest plateau, rendering more difficult to evaluate an effect of LXA4. However, even in these experimental conditions, LXA inhibits cytokine production in a range of concentrations between 10 nM and 100 nM. On the other end, the endogenous levels of LXA measured in the supernatants are about 2 nM. This concentration should be used also in the experiment when exogenous LXA is tested and probably PMMA should be used at a lower concentration.

The experiments carried out to evaluate the effect of the inhibition of 15-LO should be better described. It is not clear which cell type was target by the siRNA.

Following the results of these experiments, The Authors suggest that LXA4 is indeed the mediator responsible of the effects described in this paper. However the formation of other mediators could be inhibited by the 15-LO siRNA. The Authors should discuss this possibility.

It could be interesting to define the exact role of LXA, carrying out experiments in which an inhibitor of LX receptor (i.e. Boc compound) is used. This experiment will unequivocally demonstrate the direct involvement of LXA4.
**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**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'