Reviewer’s report

Title: Effect of Pegylated Phosphatidylserine-Containing Liposomes in Experimental Chronic Arthritis

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Reviewer: Bart Crielaard

Reviewer’s report:

The authors describe a thorough investigation into the effect of phosphatidylserine liposomes in a mouse model of arthritis. PSLs were evaluated at three different doses, but no anti-inflammatory effect compared to control was observed.

I think it is commendable that the authors took the time and effort to complete the complete study, even though probably during the study it already became apparent that no groundbreaking findings would result from it.

The main pitfall with negative outcomes in therapeutic studies (i.e. no observed effect) is that other experimental setups (such as dosages, group sizes and administration routes) could still have an effect – thereby making it impossible to conclude the study with ‘this therapy is not effective’ – the authors recognized this, and formulated their conclusion well balanced, in my opinion.

I believe this is a well set-up study with strong data. I am convinced it can assist other researchers working in this field, and publication is therefore warranted.

I do have, however, one issue that I feel really need to be addressed:

Major Compulsory Revision

1. The discussion reads like a short review of the importance of different cytokines in arthritis, rather than discussing their findings in relation to other studies. This should be improved.

E.g. the role of TGF-B1 is extensively discussed, but this is not related to any of the presented findings. If there are results that contrast with other studies (e.g. the group of Nakanishi), why not elaborate on the differences with these studies and how this could be explained. Such as the setup: PEGylated liposomes & subcutaneous administration vs non-PEGylated & intramuscular. Are there significant differences in dosing? Why the choice for PEGylation in this study? PEG shields the liposome from opsonization and phagocytosis, and isn’t phagocytosis by macrophages in fact of the therapeutic mechanism of PS?

Minor Essential Revisions

2. First line of introduction: ‘phophatidylserine liposome (PSL) is a phospholipid’. This should be ‘phosphatidylserine (PS) is a phospholipid’.

3. In the introduction the authors speak of dosing in terms of mg/mL – this must
be mg/kg (probably).

Discretionary Revision
4. the authors should reorganize the data
   a. move the important data from tables to plots (e.g. table 3)
   b. limit the tables that display purely statistical outcomes (table 4-8)

Level of interest: An article whose findings are important to those with closely related research interests

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