Reviewer's report

Title: Slow CCL2-dependent translocation of biopersistent particles from muscle to brain

Version: 1 Date: 11 December 2012

Reviewer: Carlo Perricone

Reviewer's report:

The paper by Khan et al. evidences that the long-term biodistribution of alum, an important nanomaterial as well as one of the most common adjuvants, is dependent on MCP1/CCL2. The injection of alum-containing vaccine seems to be associated with appearance of Al deposits in organs (spleen and then brain) even after one year after injection. It is possible that alum transportation is driven by MO-lineage cells to DLNs, blood, and spleen, and then, through CCL2, penetrates the brain.

This evidence suggests that the burden of alum, as an adjuvant at escalating doses in determining ASIA especially in those patients with immature/altered blood brain barrier

Minor essential revisions:

In key words
- Single Nucleotide Polymorphisms instead of Single Nucleotid Polymorphisms

In abstract
- Please change the methods paragraph. The patients involved and their number have not been specified and in the introduction session mention the ASIA syndrome since it represents a key part of the study

In the Introduction
- When first citing MCP-1/CCL2 please use the extended name

In patients paragraph
- Summarize the demographic and clinical features of the patients in one table
- Please provide state and province of R&D system (ELISA for fractalkine)

In the results
- It is not clear why the authors use MCP-1 or CCL2, please specify and possibly use italic when referring to the gene.

In abbreviations
- Single Nucleotide Polymorphisms instead of Single Nucleotid Polymorphisms

Please refer also to:
Disparate adjuvant properties among three formulations of "alum"
Cain DW, Sanders SE, Cunningham MM, Kelsoe G. Vaccine. 2012 Nov 28.

Adjuvant immunization induces high levels of pathogenic antiphospholipid antibodies in genetically prone mice: another facet of the ASIA syndrome.


Responses to multiple injections with alum alone compared to injections with alum adsorbed to proteins in mice.


Vaccination in patients with chronic or autoimmune rheumatic diseases: the ego, the id and the superego.


Discretionary revisions
- Please specify whether the patients fulfilled the proposed criteria for ASIA, or, if not, discuss briefly in the discussion paragraph

**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