

Review of: "Macrophage-Mediated Tissue Response Evoked By Subchronic Inhalation of Lead Oxide Nanoparticles Is Associated With The Alteration of Phospholipases C And Cholesterol Transporters"

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The authors present an interesting report on lead oxide nanoparticle (PbO NP) toxicity in mice. They found altered markers of lipid/phospholipid metabolism in different tissues after chronic PbO NP inhalation. The results show that PbO NP inhalation has important effects in lung, liver, kidney, and spleen. This report provides important insights into lead exposure and merits publication. The data and experimental methodologies are sound and clearly explained and the paper is well-written.

The data center wholly around one experimental in vivo setup of PbO NP inhalation. This setup has been used similarly in the authors' previous studies (refs. 5, 6, 7, 21, 77). The focus on tissue histology/qPCR limits the analysis to a descriptive report of effects of PbO NP exposure. A suggestion for future experiments would be to do in vitro studies using macrophages, either isolated using lavage for alveolar or peritoneal macrophages. This could provide additional mechanistic insight into how PbO NP triggers changes in lipid metabolism in macrophages. In particular the cholesterol crystal phenotype is intriguing and could be followed up with an array of in vitro experiments using similar techniques as in this paper, like microscopy and qPCR. However I think addition of these experiments to this paper are not crucial for publication.

Minor comments:

In Table 2 and/or the methods section, please state the LOD.

"As 11 days long inhalation..." - correct days to weeks.

I am not sure what is the significance of stating "female-like" or "male-like" in the description of kidney cells - consider removing.