Reviewer’s report

Title: Synthetic high-density lipoprotein nanoparticles for the treatment of Niemann-Pick Diseases

Version: 0 Date: 13 Jun 2019

Reviewer: Yongtae Kim

Reviewer's report:

This study showcasing a potential approach for the treatment of Niemann-Pick Diseases using synthetic high-density lipoprotein nanoparticle (sHDL). The study demonstrated that sHDL significantly reduce lipid storage in Niemann-Pick C and A. The overall concept and biological results are okay for the publication in BMC Medicine with broad impact potential on the field, however, more solid characterizations are required. Therefore, it is recommended that the changes below necessarily be made to improve upon the quality of the publication:

1. In Line 418 (page 19), ApoA1 peptide should be replaced with ApoA1 mimetic peptide.

2. In Figure 1c, the authors claim that the nanoparticle exhibited disc-like morphology, however, the images do not look like discoidal shape. The images need to be retaken with phosphotungstic acid (PTA) as a negative staining agent, which will give clearer stacked image of disc-like morphology.

3. TEM images of 5A-DMPC and 5A-POPC should be presented.

4. The actual composition had better to be presented. In the manuscript, the ratios of peptide and lipid were presented as a feed ratio. However, the composition should be different after the synthesis (co-lyophilization and thermocycling process) and multiple purification step.

5. The lettering in Figure 2 should be revised.

6. Although 5A-DMPC exhibits minor toxicity (Sup Fig 1b), it seems negligible. While in Figure 2a and 2b, alteration of the filipin intensity in the 5A-DMPC treated case was more than 5A-SM treated case. What if the filipin intensities are compensated with cell viability and normalized by cell viability (such as relative filipin intensity/mg protein)?
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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