Reviewer’s report

Title: CRISPR-Cas9-mediated knockout of SPRY2 in human hepatocytes leads to increased glucose uptake and lipid droplet accumulation

Version: 0 Date: 29 Aug 2019

Reviewer: Kabirullah Lutfy

Reviewer's report:

The current manuscript reports on the role of SPRY2 in regulation of glucose uptake, fat droplet accumulation, and genes involved in energy metabolism in HepG2 cells. The authors used CRISP-Cas9 genome editing to reduce the expression of SPRY2 and showed that this treatment increased uptake of glucose and accumulation of fat droplets in HepG2 cells. However, there was no changes in phosphorylation of key proteins in glucose and fat metabolism, such as AKT, MAPK, etc). They also used transcriptome profiling and found changes in genes related to cholesterol synthesis, cell cycle regulation and cellular signaling pathways. Overall, the manuscript is well written but difficult for the laypeople to understand it. It would also benefit the readers if a paragraph or schematic diagram to link SPRY2 to glucose and fat metabolism or at least how its reduction led to glucose uptake and fat droplet accumulation in HepG2 cells. As the authors indicate that this work will benefit from addition of in vivo experiments but I leave that to the discretion of the editor of the journal.

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?
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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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I am able to assess the statistics
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