Reviewer’s report

Title: Limitations in high-throughput drug screening on a cellular model for Friedreich ataxia

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Reviewer: Ioav Cabanchik

Reviewer’s report:

The authors should be complemented for the elegant system they developed and the quality of their state of the art work in relation to the technologies applied. Despite the authors arguments, I am still to be convinced of its relevance to the scientific question posed or the pharmacological goal that is sought to be achieved.

The 2 stumbling blocks are the lack of resemblance of the model cells to those affected in the disease (even in basic biochemical or physiological parameters) and the analytical parameters used for assessing properties relevant to frataxin-deficiency, the hallmark of F ataxia. The fact the engineered cells have a stable phenotype that can be used for HTS of agents aimed at rescuing the particular phenotype is important, if the cells resemble pathophysiologically those affected in the disease. Whether or not the genuine F ataxia-phenotype can be revealed in non stressful conditions is a matter of contention, which at this point can not be dismissed (as was done by the authors).

I strongly believe the work as presented is most suited in journals dealing primarily with methodological aspects, many of good reputation and high impact factor.

Level of interest: An article of limited interest

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