Reviewer's report

Title: HIV-1 functional cure: will the dream come true?

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Reviewer: Christine Durand

Reviewer's report:

This is a comprehensive and up to date review of the HIV cure field however there are several issues that need to be addressed.

General
The quality of the English language is not adequate. Extensive editing is needed. Over-emphasis on basic science/ in vitro mechanistics studies without much discussion of clinical trials of latency reversing agents.

Specific comments, organized by section

Abstract
Reservoir is not defined

See later comments on the concepts of shallow and deep reservoirs.

Introduction
cART is not defined nor is HAART defined

Boston patients did continue to have detectable HIV antibody responses - this error should be corrected.

HIV Latency is the major obstacle to cure
Section I do not agree with the discussion of the concepts "shallow" and "deep" reservoirs to distinguish inducible and non-inducible viruses - this implies there is something mechanistically different about the state of latency of these infected cells. While this is theoretically possible - perhaps there are mechanisms such as amount of DNA methylation, etc - the authors don't discuss this point or make it clear in their definitions. They refer to the Ho et al. paper in Cell, in which a significant proportion of viruses were not induced in an ex vivo viral outgrowth assay with a single round of maximal T cell activation. However this may be a purely stochastic phenomenon.

Furthermore, I do not agree with the example of the three year delay in rebound viremia in the Mississippi baby as evidence of "deeper reservoirs" that would be hard to reactivate with latency reversal agents. Rather this case more likely reveals 1) the fact that there were likely very few latently infected memory CD4 T cells in the baby and 2) the normal process of immunologic memory, whereby long-lived memory T cells are quiescent until they happen to encounter their cognate antigen.

Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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