Author's response to reviews

Title: Evidence for Transmission of HIV-1 Infection from an Elite Controller to a Patient who Progressed to AIDS: a case report

Authors:

Michael S Killian (scott.killian@ucsf.edu)
Girish N Vyas (girish.vyas@ucsf.edu)
Rochak Mehta (rochak.mehta@roche.com)
Karen Young (karen.young@roche.com)
Osman Ebrahim (osman.ebrahim@telkomsa.net)

Version: 4 Date: 25 April 2012

Author's response to reviews:

April 22, 2012

Dear Editor:

We thank the reviewers for their additional critiques. The manuscript has been further revised as detailed in the following responses. As a result, we hope that our manuscript can now be accepted for publication in Journal of Medical Case Reports.

Reviewer: Klaus Korn

We are pleased that Dr. Korn finds this case worth reporting and that the added information has addressed several of his concerns.

1. "How was sequencing accomplished in the male partner when "On at least eight separate occasions spanning this 10 year period, MM tested negative for HIV DNA by PCR."?"

In comparison to the standard Roche Amplicor 1.5 HIV-1 DNA qualitative assay (Figure 1), a more intensive effort was made to amplify HIV-1 from MM for sequencing. Nested PCR was not used in the standard assay, but was used to amplify HIV-1 gag DNA for sequencing. These details have been added to the revised text.

2. "A phylogenetic analysis capable of demonstrating that the two sequences are indeed epidemiologically linked would have to include the 20 or so most closely related sequences from e.g. the LANL database (ideally also some local sequences) and would need only one "outgroup" sequence from another clade like for example B. ... a thorough phylogenetic analysis is in my opinion absolutely necessary..."

The results from a thorough Maximum Likelihood-based phylogenetic analysis are now included in the manuscript.
Reviewer: Hauke Walter

We appreciate that Dr. Walter has found the manuscript to be much improved and that the case is worth reporting.

1. …the title of the manuscript is misleading and should reflect the remaining limitations of the conclusion. E.g.: Evidence for Transmission of HIV-1 infection by an Elite Controller to a Patient who progressed to AIDS: a case report.

The title has been changed as suggested.

2. Abstract: “His plasma HIV-1 RNA levels were measured and have remained undetectable for the past decade.” This phrase could be misunderstood indicating that the “past decade” is dated before the transmission occurred. If so, the direction of transmission would be obvious. But this is not the case, so the phrase is misleading. Exchange “past” by “next”.

The wording has been changed.

3. Results: … show a more detailed analysis for the exceptionally interesting area of sequences with 6 or less nucleotides difference to the reference strain in the figure. It is ok to argue for the group of 6 or less bases differences together (in the text), because the data covers the maximal difference of FF’s and MM’s sequences...

The results from a thorough Maximum Likelihood-based phylogenetic analysis are now included in the manuscript.

4. Discussion: …I strongly suggest to provide an honest and cautious argumentation about the two relevant questions, simply admitting that as long as you believe FF and MM that they had no other sexual contacts in the relevant time, and if you take into account that FF was sero-negative approx. one year before she was diagnosed (with AIDS!), in comparison to MM who could be infected for decades because he obviously is an elite controller, the high homology of their sequences supports the idea that FF was infected by MM, an elite controller.

The discussion has been modified fully disclose the limitations/interpretations of the report and to address this concern.