Reviewer's report

Title: CKR-L3, a deletion version CCR6-isoform shows coreceptor-activity for limited human and simian immunodeficiency viruses

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Reviewer: Alfredo Garzino-Demo

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This report by Islam et al describes the result of studies on the coreceptor activities of CCR6, a chemokine receptor that the same group had shown to mediate infection by a limited number of HIV isolates. Here, the group expands their observation to a variant of CCR6, CKR-L3, which differs from CCR6 as it is missing 5 aa at the N terminal region. Their result show that one HIV-2 isolate, and one SIV isolate can grow in a cell line that expresses CCR6 or CKR-L3. The HIV-2 isolate can also use CCR5 or CXCR4, and the SIV Isolate is R5-tropic. Using IFA, the authors show that the two viruses grow better on CKR-L3-expressing cells, as compared to similar cells expressing CCR6. RT assays show that the HIV-2 isolate has a kinetic of replication when grown in CKR-L3 cells faster than that observed in CCR6 cells. The authors conclude that this could be important in the pathogenesis of HIV, since strains that do not need CCR5 or CXCR4 are occasionally detected.

Major compulsory revisions

There are two major issues with this manuscript. One is that there is no information on the growth characteristics of the different cell lines. Even though all cells were derived from the same initial cell line, NP2/CD4, it is possible that different clones or transfected cells may have different growth rates. Since RT is observed more than 10 days after infection, even a small difference in cell growth rate may reflect on viral growth. So data on cell growth rates must be included to correctly interpret the data.

A second issue relates to the overall relevance of the data to pathogenesis. The authors show that only two isolates can use CKR-L3 (or CCR6- which is not new as the information was in their previous article); and RT data are shown only on one virus. However, the viruses can use also CCR5 (and CXCR4 in the case of the HIV-2 isolate), which are often coexpressed often with CCR6. Since the author show that CCR5 is a much more efficient receptor for the CRR-L3 isolates, one wonders whether the use of this additional receptor has really any impact on HIV infection/AIDS. Other coreceptor such as CCR3 had been shown to mediate HIV entry, and still overall the evidence for their role in pathogenesis is marginal. So the findings reported here on CKR-L3, while of some scientific interest, necessitate of some validation before broad conclusions on their impact. Accordingly, i recommend careful revision of the conclusions made by the authors.
Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

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