PeerJ

Thank you for your submission to PeerJ. I am writing to inform you that your manuscript, "Adeno-associated virus Type 2 Rep proteins mediate integration of lentiviral vectors" (#2014:03:1848:0:1:REVIEW), has been rejected for publication.
The comments supplied by the reviewers on this revision are pasted below. My comments are as follows:

Editor's comments

Both reviewers find that the experimental results are not adequate to support the conclusion that integration occurs at a specific site. In addition, the discussion does not address any of the issues raised by the data. For instance, why are there multiple bands from a nested PCR reaction? Even if the PCR products observed did come from the AAV integration site, how does this data address possible integrations elsewhere? Altogether, these objections make the paper unacceptable.
Jeremy Bruenn
Academic Editor for PeerJ

Reviewer Comments

Reviewer 1

Basic reporting

The abstract is obscure and written for the expert, not general audience. For example, it is unclear to the non-expert that Rep68 & Rep78 are both encoded by the same gene, much less the rep gene, as I was forced to surmise. More significantly, the conclusion cited in the abstract, i.e., that all lentiviral vectors integrated and AAVS1, is based on my analysis of the data, not completely accurate. Moreover, the conclusion is also in opposition to the observed findings.

Experimental design

It is unclear to the reviewer why use of a nested PCR strategy was necessary. If indeed the integration was highly specific, as suggested by the authors, a simple one step PCR strategy should be sufficient.

Validity of the findings

The authors conclude from the results in figures 1 and 3 that the rep proteins can specifically direct integration to AAVS1. However, inspection of figures 1 and 3 indicates that reactions mediated by the rep proteins result in multiple integrations. The authors do not comment on the source or reason for the multiple bands they observe in these figures. From my understanding of the assay, the findings they report limit the utility of the proposed use of the rep proteins to mediate specific integration of non-AAV2 DNA with free ads into a specific location.

At the very least, the authors need to acknowledge the evidence indicating multiple integrations shown in the presented results and to provide evidence that all of these integrations are within AAVS1 and/or identify the off target sites.

Reviewer 2

Basic reporting

Article meets Peer J basic reporting

Experimental design

Experimental Design is not adequate to make the conclusion as authors have determined. Example PCR analysis to determine viral integration after 24 & 48 hr post infection does not in a meaningful way determine actual true integrations, but only reflects on PCR products that can be derived under the experimental conditions. So these exp are not carried out in the rigor and high technical standard accepted by field, (e.g. isolation of single clone integrants to confirm PCR observations-- major weakness). These flaws make it difficult to accept these results for publications.

Validity of the findings

Major concern about the current findings is the fact that similar data has been published previously (acknowledged by authors in intro) but not significant enough to justify publication.

Comments for the author

Generate some single clones and confirm PCR data.