Reviewer’s report

Title: Impact of naturally occurring amino acid variations on the detection of HIV-1 p24 in diagnostic antigen tests

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Reviewer: Jesse Kwiek

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Vetter et al. have shown in a previous publication (DOI: 10.1371/journal.pone.0111552) that some HIV Gag virus like particles (VLP) are not detected by some commercial HIV ELISA kits. In this manuscript, the authors test the hypothesis that Gag sequence polymorphisms cause the ELISAs to fail.

This well written manuscript uses sequence alignments to identify polymorphic amino acid positions that correlate with assay failure; subsequent mutagenesis experiments confirm the in silico results. The experiments are simple, well controlled, and provide conclusive evidence that specific amino acids at positions 16 and 170 in p24 (HXB2 coordinates) can cause ELISA failure. They present a fair and balanced discussion of the results, and make reasonable conclusions.

Minor essential revision.

There are no methods describing the sequence alignment (although there are a few hints in the results section). How were sequences chosen from LANL, and were they cleaned prior to inclusion in the dataset? If they were cleaned, how were they cleaned (what were the inclusion/exclusion criteria). For example, often there are multiple sequences from the same participant. We all sequences included in table 1 or just one per patient? Were the sequences translated to amino acids and codon aligned? Assuming yes, which programs/parameters were used?

Level of interest: An article of outstanding merit and interest in its field

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.