Retrovirology

Poster presentation

P17-25. A model for coverage of T-cell HIV vaccines: where are we and where do we need to be?

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Background

A central concept for the development of an effective HIV vaccine that induces T-cell responses is coverage – the extent to which reactive epitopes in vaccinees are represented in circulating viruses to which the vaccinees will be exposed.

Methods

We developed a model for epitope coverage of a target viral population by a T-cell vaccine that expresses coverage as a function of breadth of response (number of epitopes recognized) and the frequency with which vaccine-induced epitope responses are represented in the targeted viral population. This model was used to analyze epitope mapping data from 2 study populations: participants who received the Merck Ad5 HIV vaccine (insert: clade B gag, pol, nef) and participants who received the VRC multigene Ad5 HIV vaccine (insert: clade B gag-pol and clades A, B, C env).

Results

Results from these analyses include: 1) Recipients of the Merck vaccine demonstrated limited breadth in their CD8+ T cell responses to subtype B HIV (median 2 epitopes per vaccineee). These responses were infrequently directed against the most highly conserved portions of the *gag* or *nef* genes, despite the inclusion of these regions in the vaccine insert. The resultant low coverage may have been a primary factor underlying lack of efficacy seen in the Step trial; 2) Our analyses indicate that increasing breadth of response has greater potential to improve coverage than shifting the set of reactive epitopes to more conserved specificities.

Conclusion

We suggest that epitope mapping data be obtained routinely in early phase clinical evaluation of T-cell HIV vaccine candidates and that an analysis of coverage be explicitly considered in the decision to advance the candidate to efficacy evaluation. We also recommend that increased emphasis be placed on developing vaccine designs that increase breadth of response.