Retrovirology

Poster presentation

P19-32. HIV-1 vaccine design based on human vaccine trials to improve Gag, Pol, Nef and Env specific immune responses

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Background

As recently reported, HIV-1 candidate vaccines (DNA-C; NYVAC-C) expressing an artificial polyprotein consisting of Gag, Pol and Nef (GPN) as well as a secreted from of gp120 (E) induced high levels of polyfunctional, HIV-specific CD4+ and CD8+ T-cells in phase I clinical trials (EUROVACC). Thereby, T cell responses showed some dominance of Env over Gag/Pol reponses.

Methods

To improve Gag/Pol specific immunogenicity, some modifications were included comprising (i) re-introduction of the natural gag-pol frameshift allowing budding and release of GPN particles from transduced cells, (ii) inactivation the protease and (iii) separation of Gag (+G) and PolNef (PN) on two plasmids. Following various protocols, different combinations of GPN derivatives, G, PN and Env encoding plasmids were administered i.m. into Balb/c mice to overcome competition for presentation of relevant epitopes.

Results

Budding competence increased levels of Gag specific, IFNγ producing T cells. The injection of equimolar amounts of G and PN increased Pol specific responses, whereas Gag responses remained on a constant level.

Co-administering Env in a mixture with GPN derivatives or G largely abrogated Gag-specific responses and resulted in the induction of almost exclusively Env specific T-cells, whereas injection of Env and GPN in separate muscles as well as a timely separated administration induced Gag, Pol and Env specific T-cells at substantial levels.

Conclusion

In sum, the modifications increased Gag and Pol specific T-cell responses up to 10-fold if compared to the GPN immunogens as used in the clinical trial. Such DNA vaccines may represent valuable priming immunogens for subsequent booster immunisations using second generation poxviral vectors to deliver optimised immunogens.

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