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Unique IL-4R antagonist and IL-13Ra2 adjuvanted pox viral vector-based HIV vaccines

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We have shown that the efficacy of a heterologous, poxvirus prime-boost immunization is strongly influenced by the cytokine milieu at the priming vaccination site, where endogenous IL-4/IL-13 is detrimental to the quality of the HIV specific CD8 T cells induced. We have recently developed two novel HIV vaccines that co-express i) IL-13R α 2 which can transiently inhibit IL-13 activity, and ii) an IL-4R antagonist that can bind to IL-4 type I and II receptors with high affinity, and transiently prevent the signalling of both IL-4 and IL-13 activity at the vaccination site. Following intranasal/intramuscular recombinant fowl pox prime, recombinant Modified Vaccinia Ankara virus booster followed by an gp140 Env protein booster these vaccines were able to induced not only high avidity poly-functional mucosal/systemic gag-specific CD8 T cell immunity but also B cell immunity compared to the unadjuvanted vaccine strategy. Whilst IL-13R α 2 adjuvanted strategy only induced p55gag-specific IgG1 antibodies, the IL-4R antagonist vaccine was able to induce excellent long-lived p55gag-specific IgG1 and IgG2a antibody differentiation. Moreover, following 3-6 weeks post Env protein booster vaccination only the 13R α 2 adjuvanted strategy, was able to induce elevated env-IgG1 antibody responses. But, at 16-20 weeks both novel vaccines were able to induce elevated env-specific IgG1 antibody responses of high avidity. Collectively, the IL-4R antagonist adjuvanted vaccine strategy was able to induce excellent triple action CD8 T and B cell (gag & env) immunity, similar to HIV elite controllers and the responders in the RV144 trial, which offer good promise for a future HIV-1 vaccine. This strategy also has high potential as a platform technology against may other chronic mucosal pathogens.

Biography

Charani Ranasinghe completed her PhD from University of Western Australia. She is the Group Leader of the Molecular Mucosal Vaccine Immunology Group at the JCSMR, Australian National University. She was the first to discover that IL-13 plays an important role in modulating CD8 T cell avidity in a vaccine route dependent manner. Her team has recently developed two novel IL-4R antagonist and IL-13Ra2 adjuvanted vaccine platforms that can induce high quality systemic/ mucosal CD8 T and B cell immunity.

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