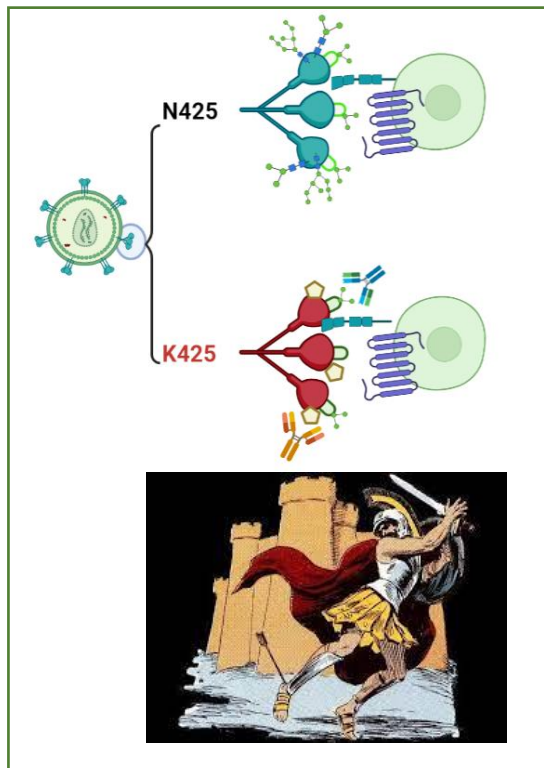


HIV-1_{A74}K425 VLP vaccination Induced HIV-specific Tcm and Tscm cells and Potent Humoral Responses

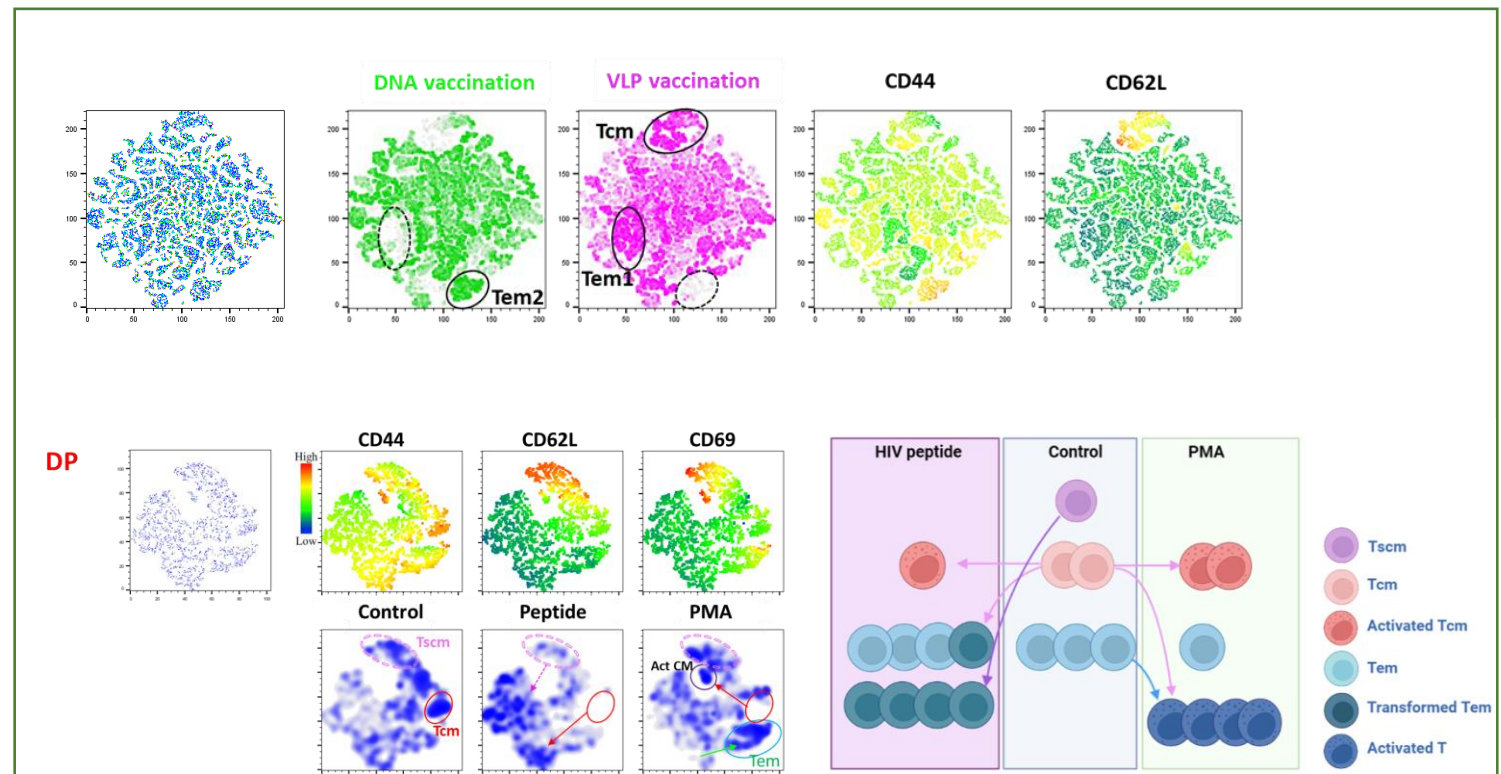
Lei Qi¹, Yue Li¹, Joshua Pankrac¹, Eric Arts¹

¹Department of Microbiology and Immunology, Schulich School of Medicine and Dentistry, The University of Western Ontario

N425 VS K425



DNA vaccination VS VLP vaccination

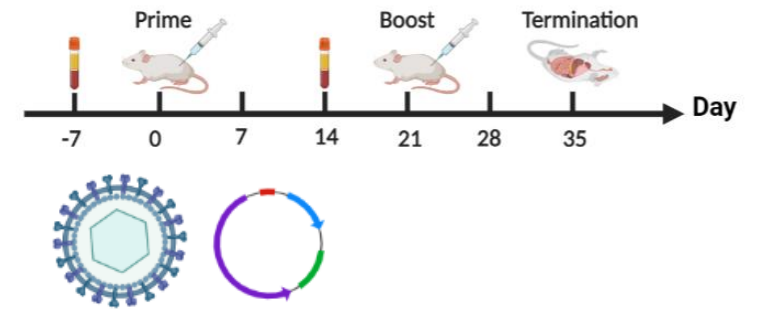


HIV-1 vaccination

Humoral responses: VLP vaccination > DNA vaccination

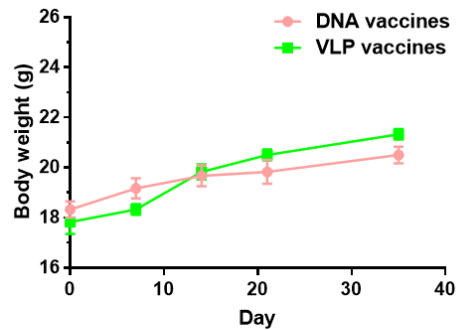
Method: Balb/c mice IM immunization with HIV-1 DNA or VLP vaccination

Results: VLP vaccination induced more potent binding and neutralizing HIV-specific antibodies than DNA vaccination



Safety:

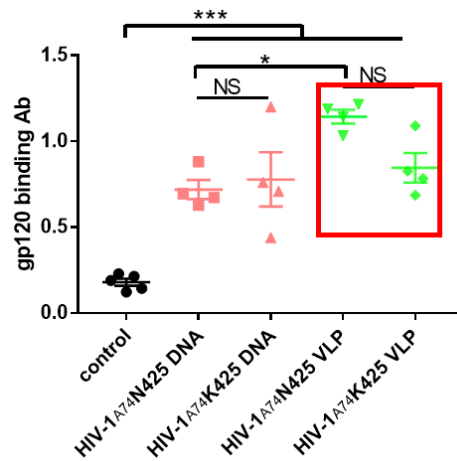
- No clinical signs
- Body weight ↑



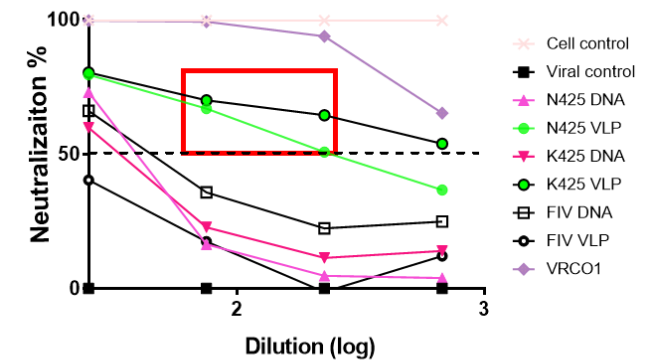
Humoral responses:

VLP vaccination > DNA vaccination

HIV-1 gp120 binding Ab



Neutralization assay

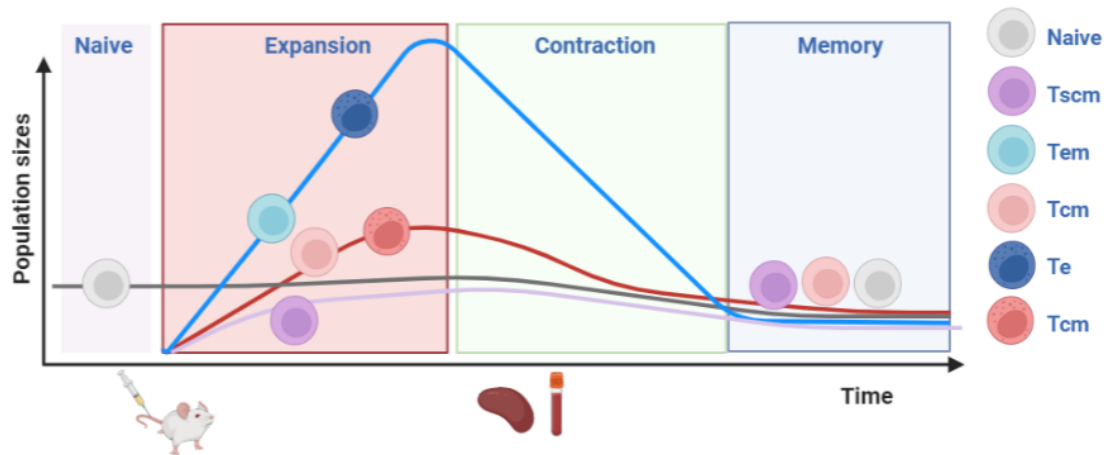


HIV-1 vaccination

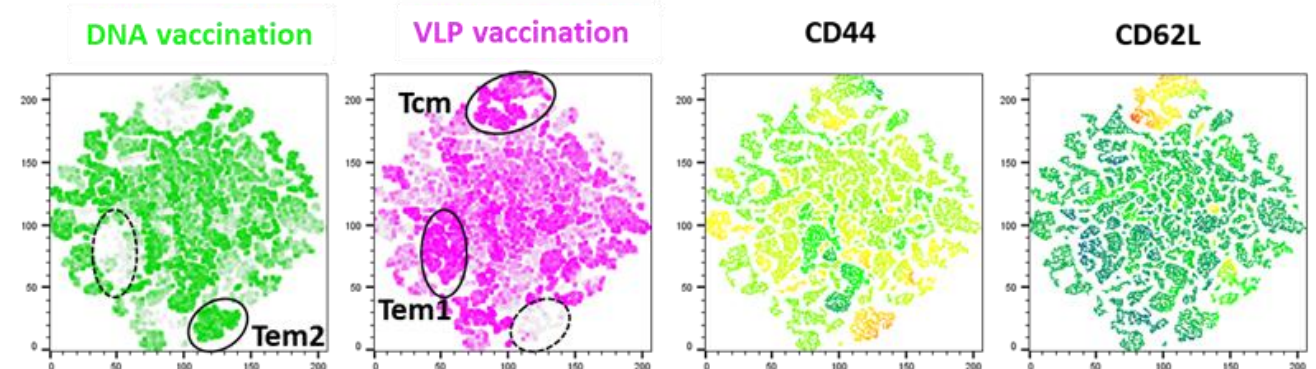
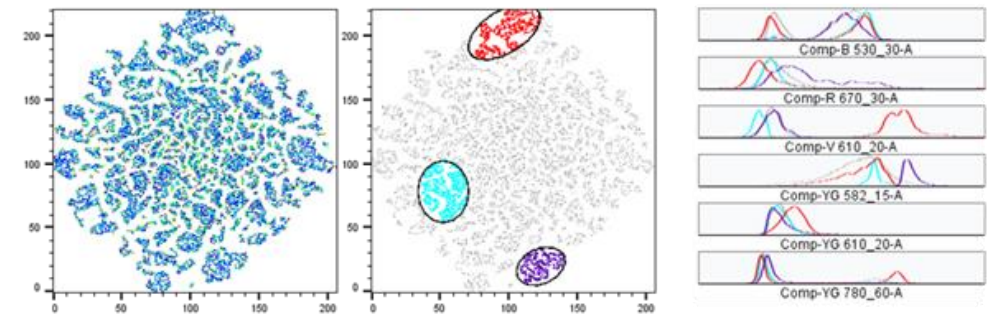
Cellular responses: VLP vaccination > DNA vaccination

Method: Flow cytometry, t-distributed stochastic neighbor embedding (t-SNE); n=6 mice/each group

1. **VLP vaccination** developed HIV-specific central memory T cells (Tcm) and effector memory T (Tem) #1 cluster
2. **DNA vaccination** developed Tem #2 cluster



T Cell t-SNE map



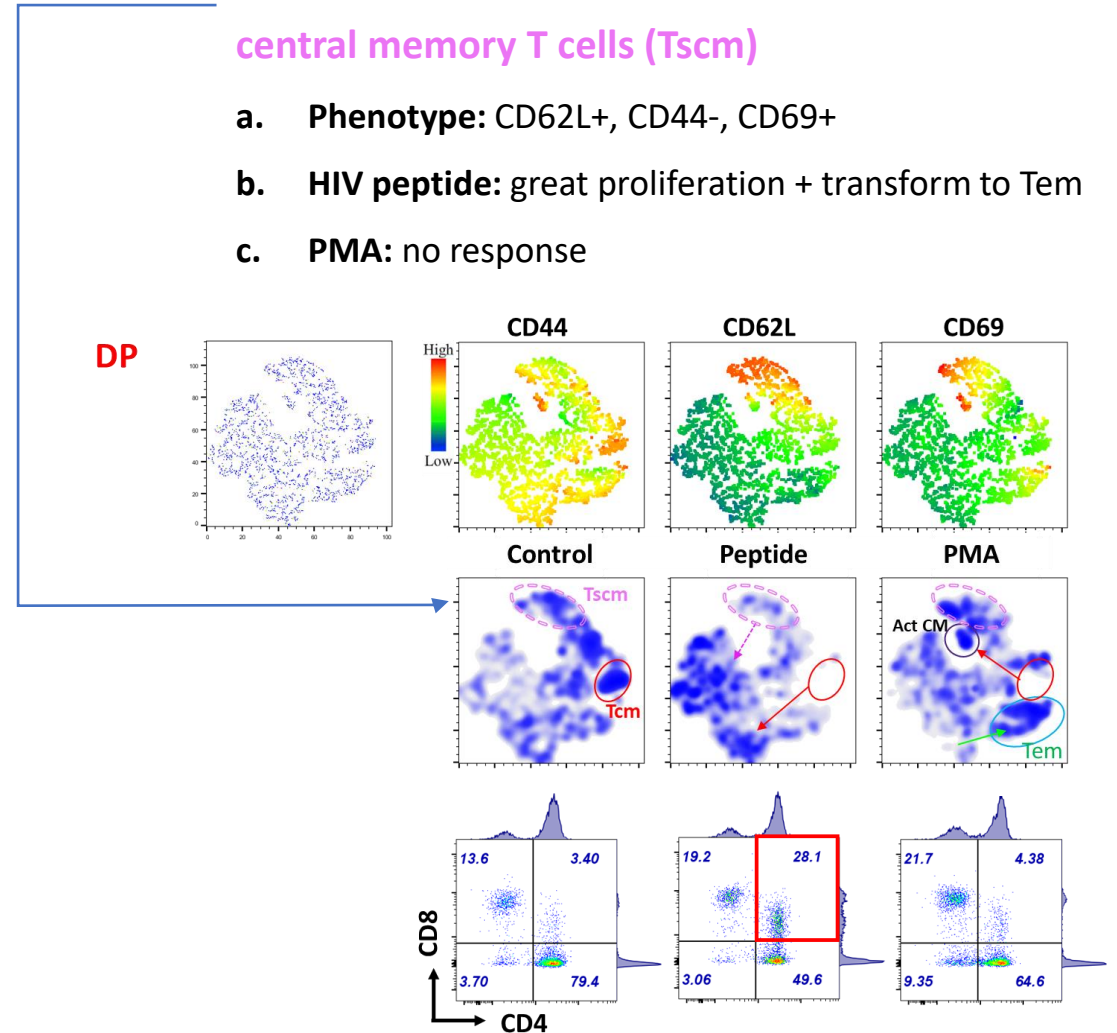
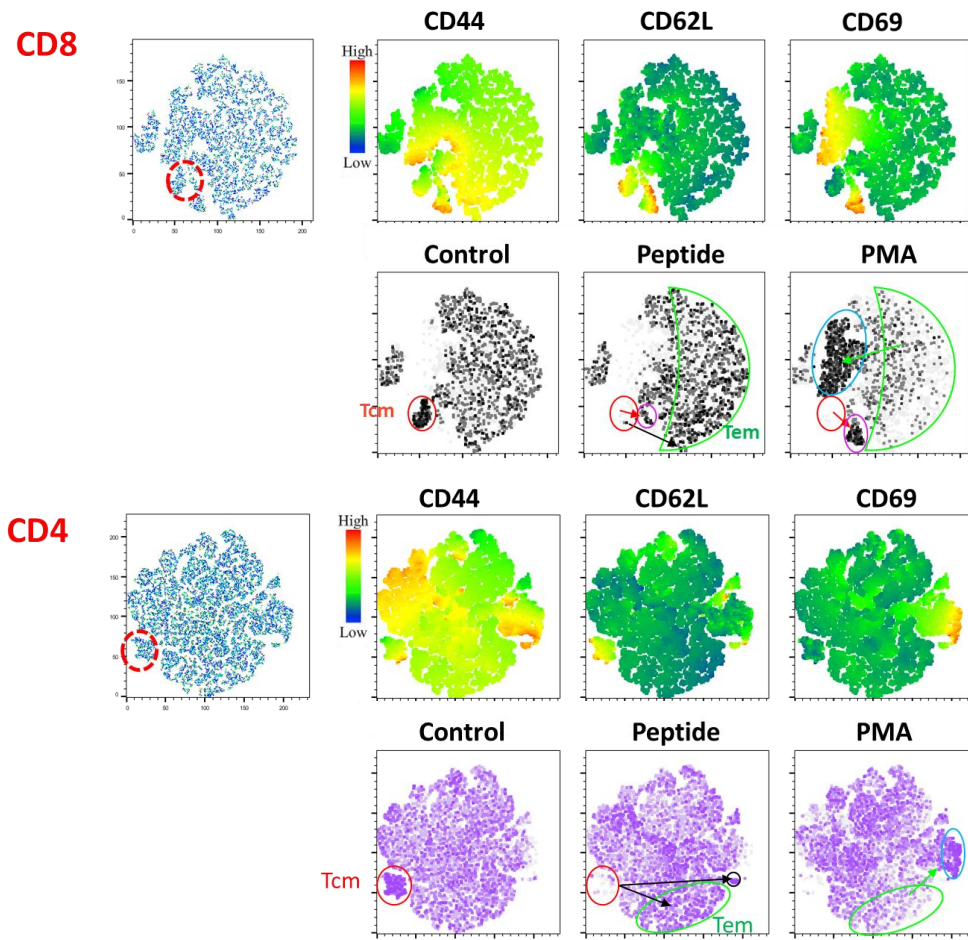
Method: Reactivation of memory T cells; T cell Phenotypic Transformation; t-SNE map of T cells from VLP vaccination

Only VLP vaccination, not DNA, elicit HIV-specific Tcm and Tscm

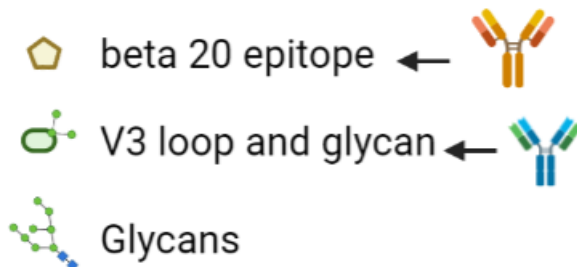
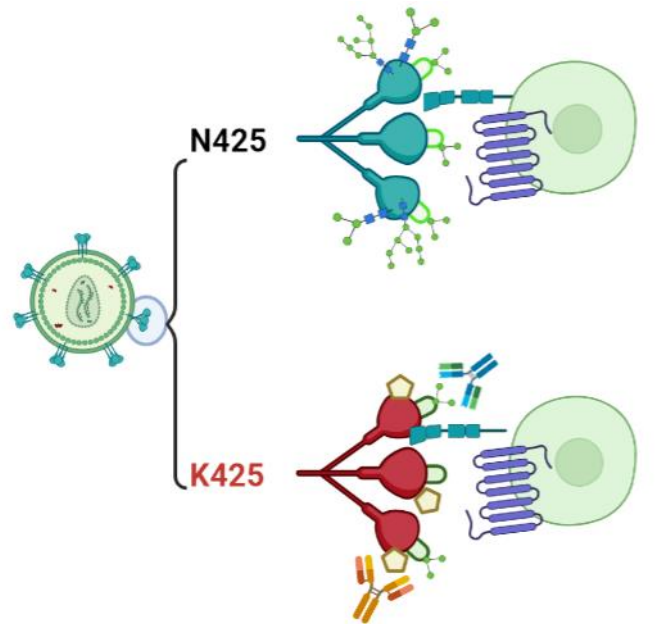
- HIV antigen recall:** HIV-specific Tcm & Tscm → Tem or activated Tcm
- PMA:** HIV-specific Tcm & Tem → CD69+ activated T cell

3. CD4/CD8 Double Positive (DP) HIV-specific stem central memory T cells (Tscm)

- Phenotype:** CD62L+, CD44-, CD69+
- HIV peptide:** great proliferation + transform to Tem
- PMA:** no response

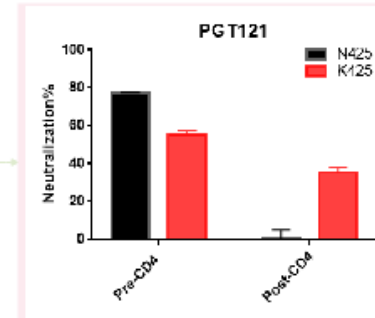


HIV-1 K425 polymorphism → better exposed CD4-induced conserved epitopes upon human CD4 interaction



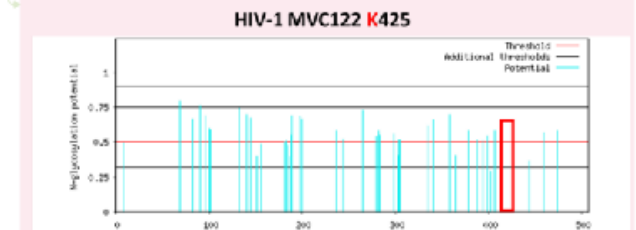
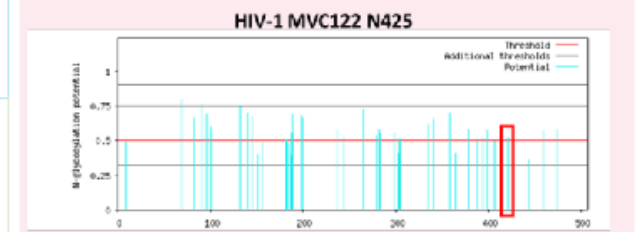
K425

Maintain Neutralizing Ab susceptibility post-CD4 engagement



Missing glycan at K425 of the beta20 epitope

CD4 supersite for neutralizing Abs
protective CD8+T cell development



High CD4 binding affinity to expose CD4-induced binding sites

