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P12-02. Cell-surface display and panning of HIV-1 derived envelope proteins

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Background
Available display systems allow screening of proteins out of millions of candidates and are the method of choice to identify optimized antigen-antibody binding. While phage display libraries are used for polypeptides like scFv antibodies, eukaryotic display platforms were developed to overcome the limitations of prokaryotic expression and presentation. We established a mammalian cell-surface display to present HIV-1 envelope derivatives in a natural, trimeric, membrane bound environment to generate affinity enhanced envelope derivatives against broad neutralizing antibodies (bNAb), with the objective of selecting potent envelope (Env) based vaccine candidates.

Methods
HEK 293T cells were infected with a pseudotyped HIV-1 Env library, providing different envelope derivatives. Enrichment of cells displaying envelopes, with high affinity to bNAb was achieved by cell separation. After elution of affinity enriched cells, the envelope genes were amplified and cloned back into a lentiviral vector to enter a new round of selection. Best binders were enriched by iterative rounds of selection.

Results
A specific enrichment of envelopes with higher affinities to the applied antibody was achieved as measured by FACS analysis and DNA sequencing of the selected clones. Screening clones after every panning cycle reflects the progress of the enrichment process.

Conclusion
With the method described we show that mammalian cell-surface display of HIV-1 envelopes is feasible to enrich envelope derivatives with higher affinity to the applied antibody. By using bNAbs for selection of envelopes out of different libraries new candidates for the potential use in HIV vaccine trials can be identified.