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# P09-01. Mutation of the gp120 alpha2 helix in early subtype C HIV-1 infection fails to alter neutralization sensitivity or efficiency of *in vitro* replication

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## Background

Understanding of the autologous neutralizing antibody (Nab) targets during HIV-1 infection remains fragmentary and warrants further investigation in order to be incorporated during development of a successfully protective vaccine. In subtype C infection, the eighteen amino acid amphipathic alpha2 helix, encoded immediately downstream of gp120's V3 domain, undergoes strong positive selection where mutations track with the neutralization resistant phenotype; such characteristics would seem to make the alpha2 helix an attractive potential site for Nab targeting and escape.

## Methods

Utilizing longitudinal samples from subtype C-infected Zambian patients, we identified autologous Nab escape variants. In one patient, the alpha2 helix first mutated five months post-infection. We thus compared a sensitive 0-month viral envelope against a resistant 5-month viral envelope to determine whether the alpha2 helix contained direct Nab targets or whether escape variants depended on alpha2 helix sequence changes to maintain replicative capacity *in vitro*.

## Results

Residues responsible for conferring neutralization resistance were mapped to two amino acids in the V5 region, one of which contributed to the CD4 binding site. Alpha2 helix mutations did not alter viral neutralization sensitivity; these mutations, when introduced in either the presence or absence of identified V5 escape mutations, failed to modify *in vitro* viral replication efficiency.

## Conclusion

These studies prompt the acknowledgement that gp120's alpha2 helix, though positively selected and linked with escape, does not directly contribute to neutralization resistance in all patients. Furthermore, if mutation in this region affects the ability of HIV-1 to replicate, such impact is subtle enough so as to appear undetectable under *in vitro* conditions. Ultimately, the alpha2 helix offers a notable but incompletely defined contribution to viral immune evasion.