

# Analysis of Neutralization Escape Suggests Limited Neutralizing Antibody Specificities in Early HIV-1 Subtype C infection

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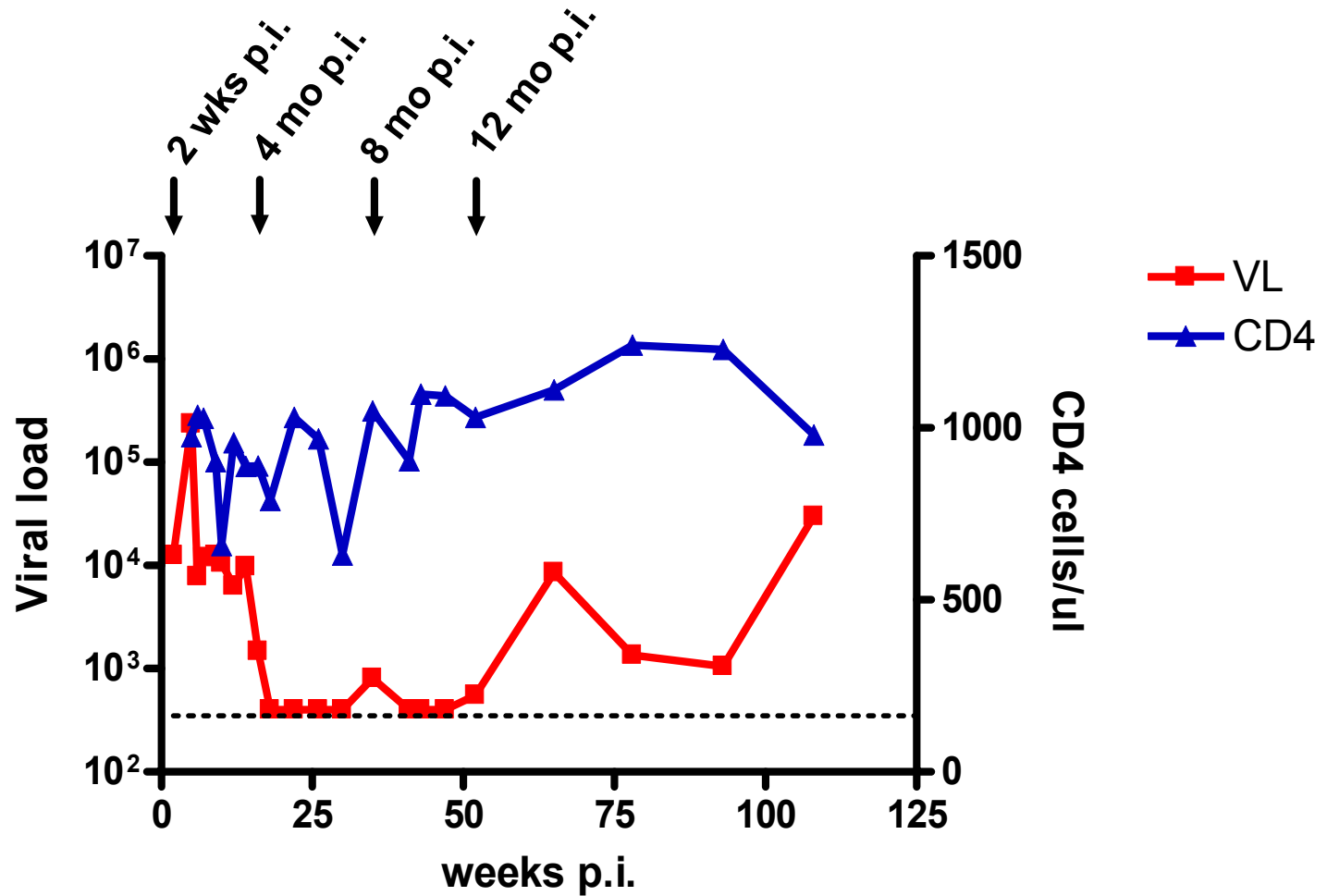


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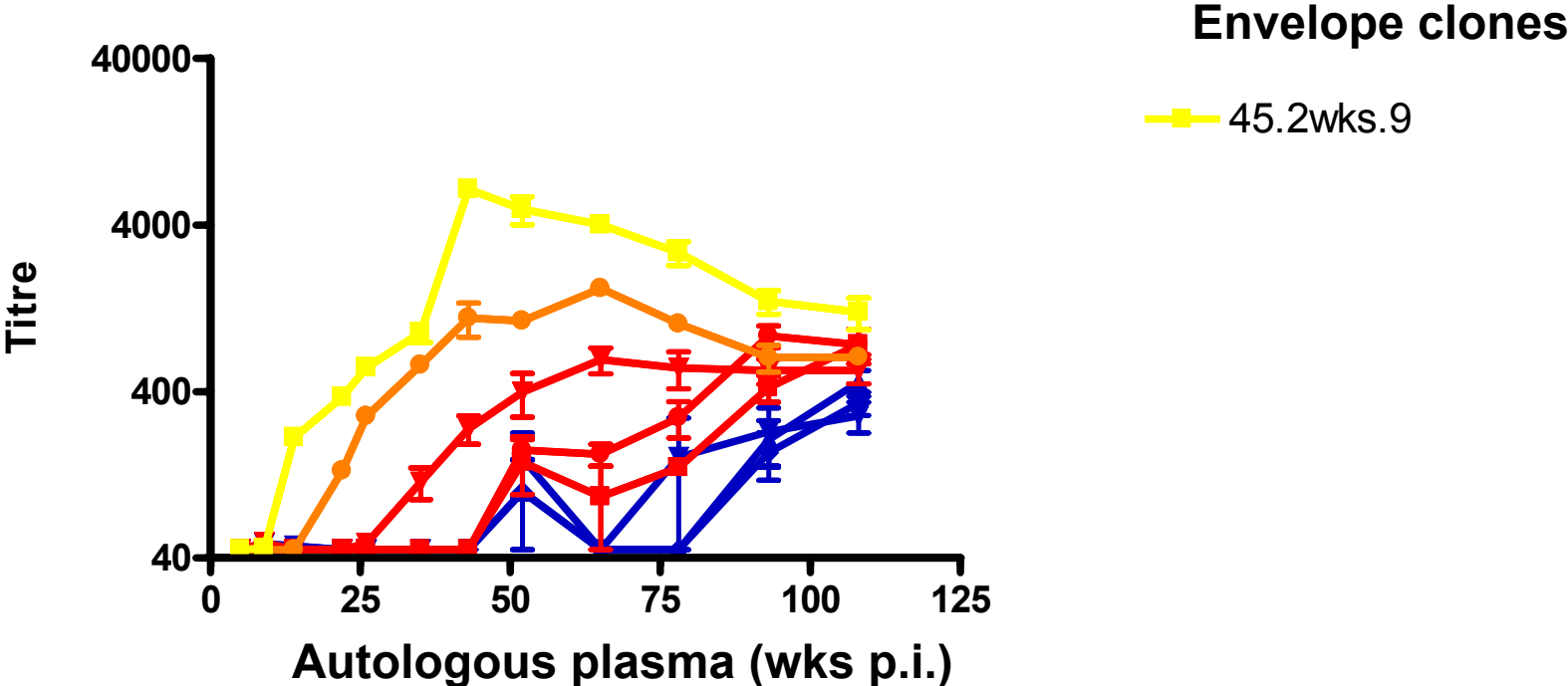
# CAP45 – controller with low genetic diversity

Envelope clones

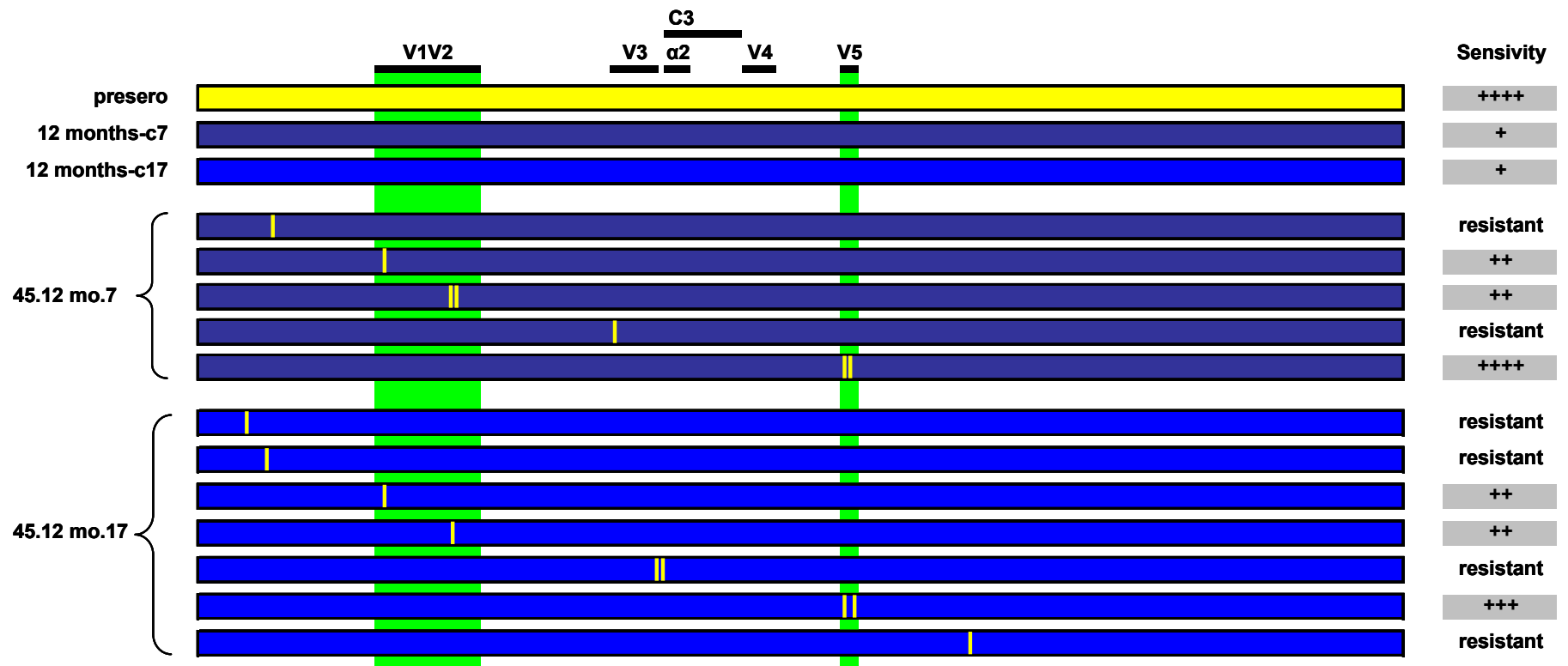


Maximum Percentage Diversity at 12 months p.i. = 0.95%

# CAP45 - Neutralization Escape

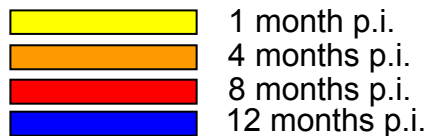
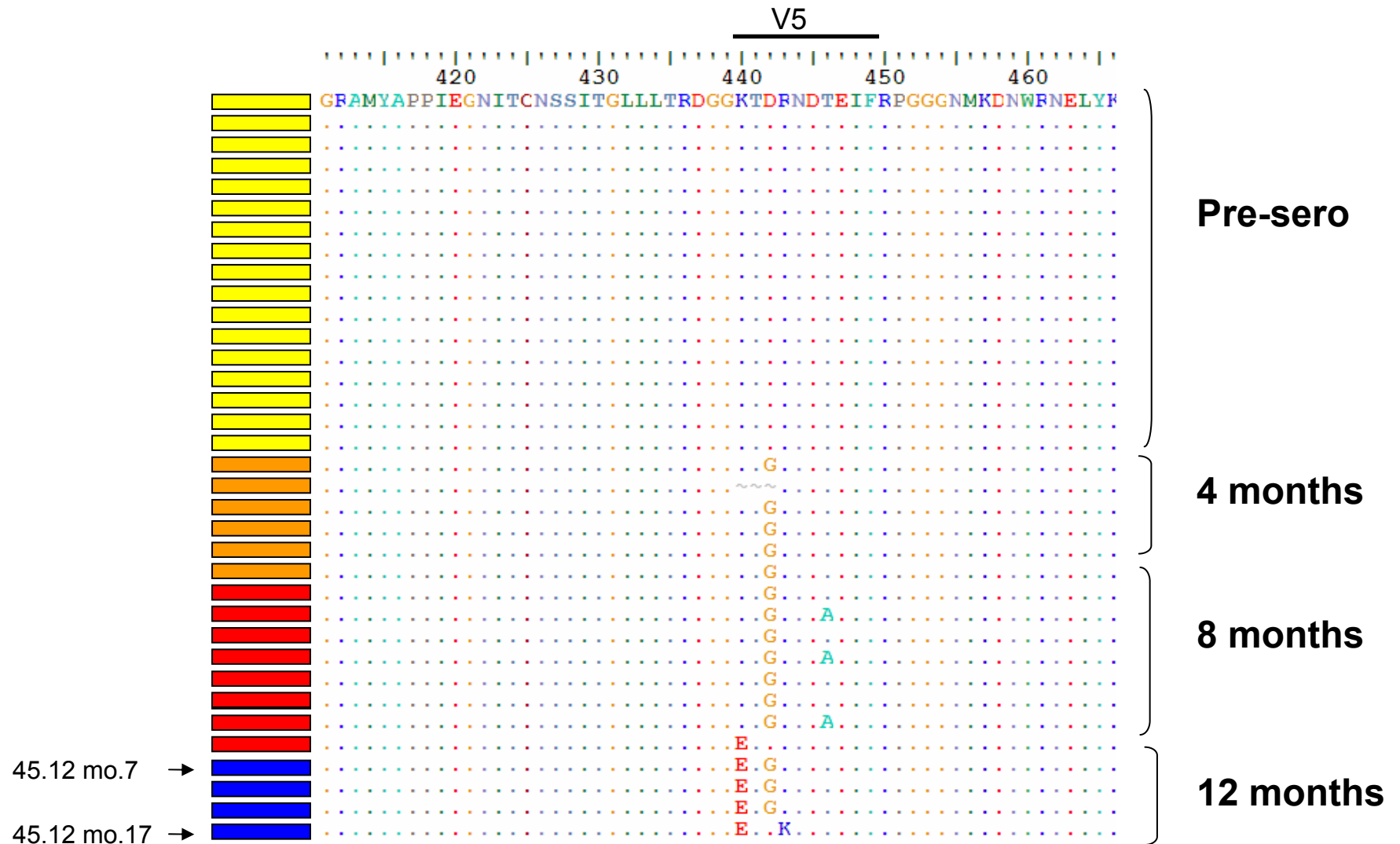


# Neutralisation escape in CAP45



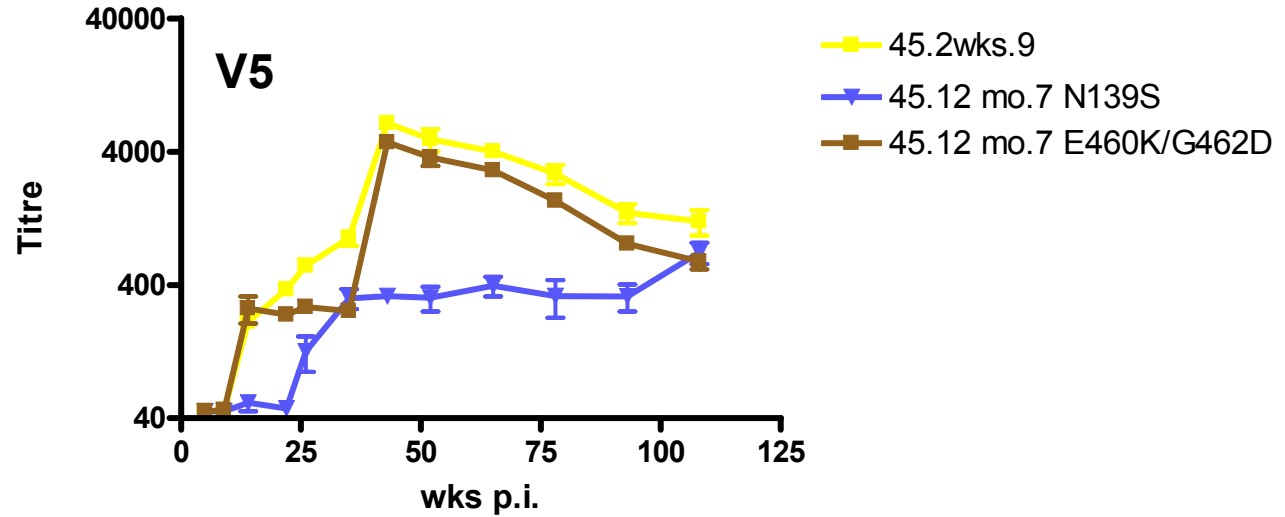
Regions involved in neutralization escape

# V5 SGA sequences from CAP45 at multiple time-points

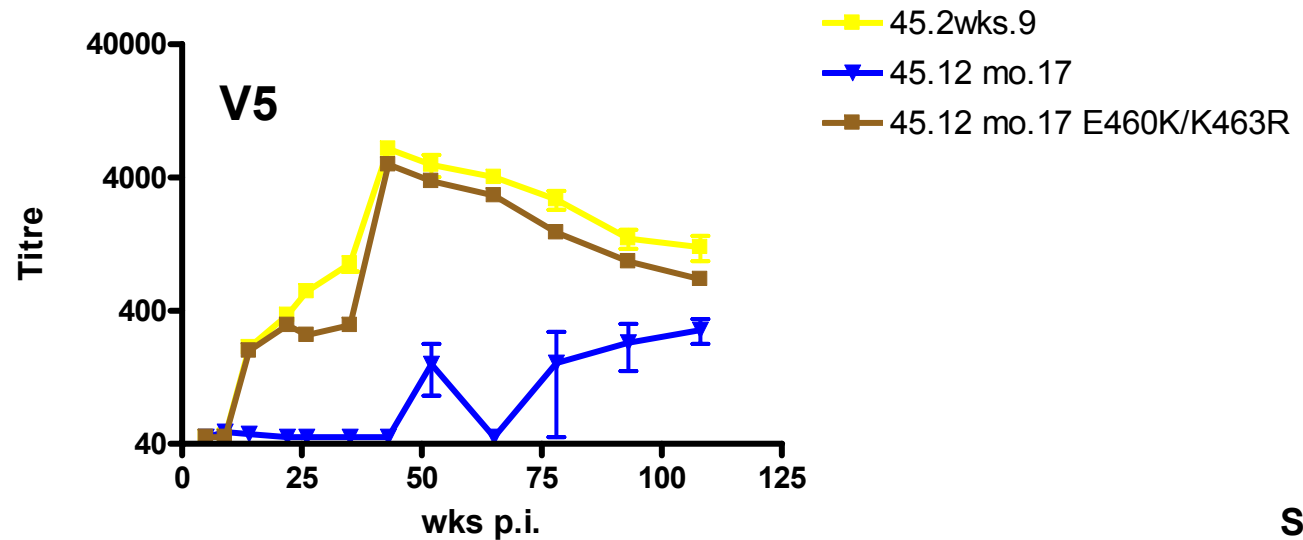


# Mutations in V5 account for complete escape

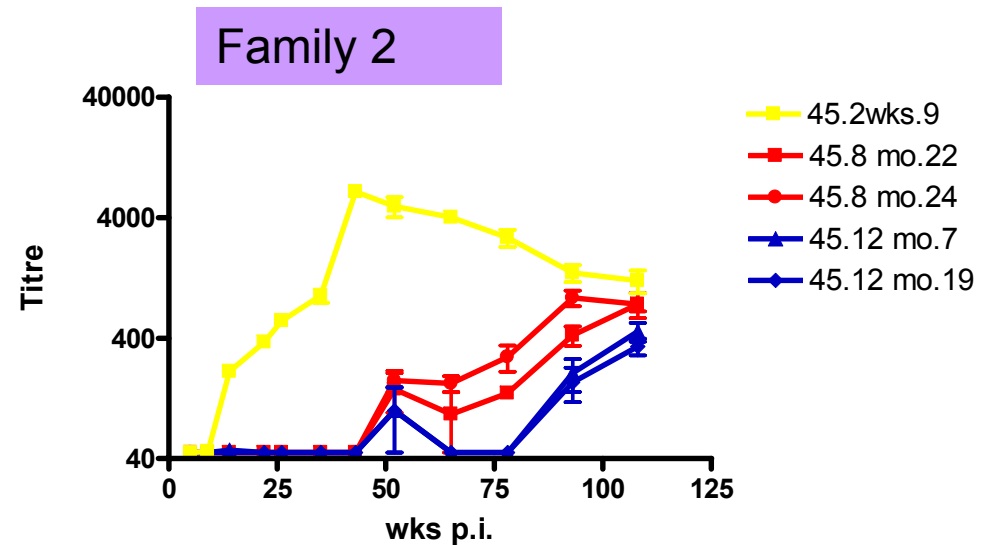
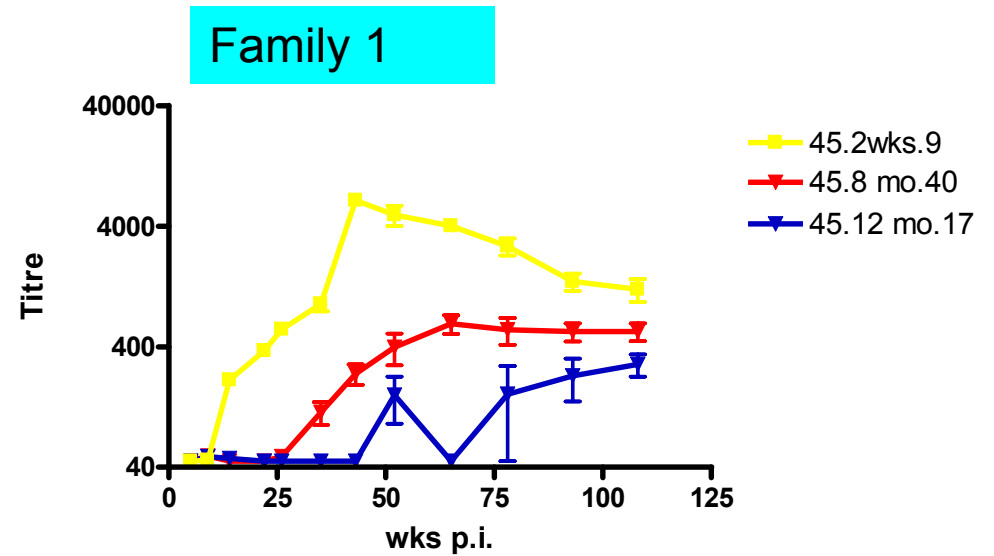
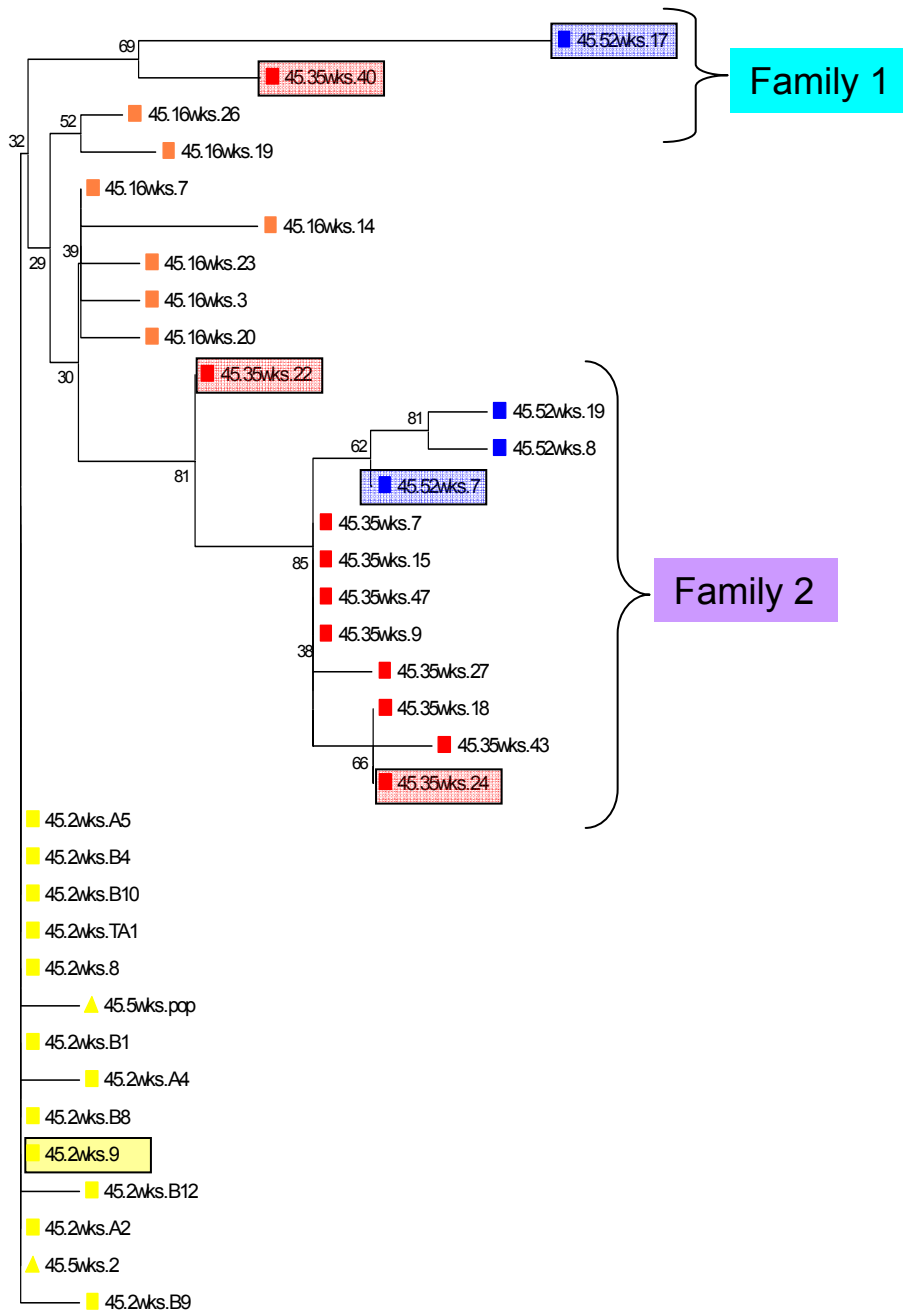
## CAP45.12 mo.7



## CAP45.12 mo.17

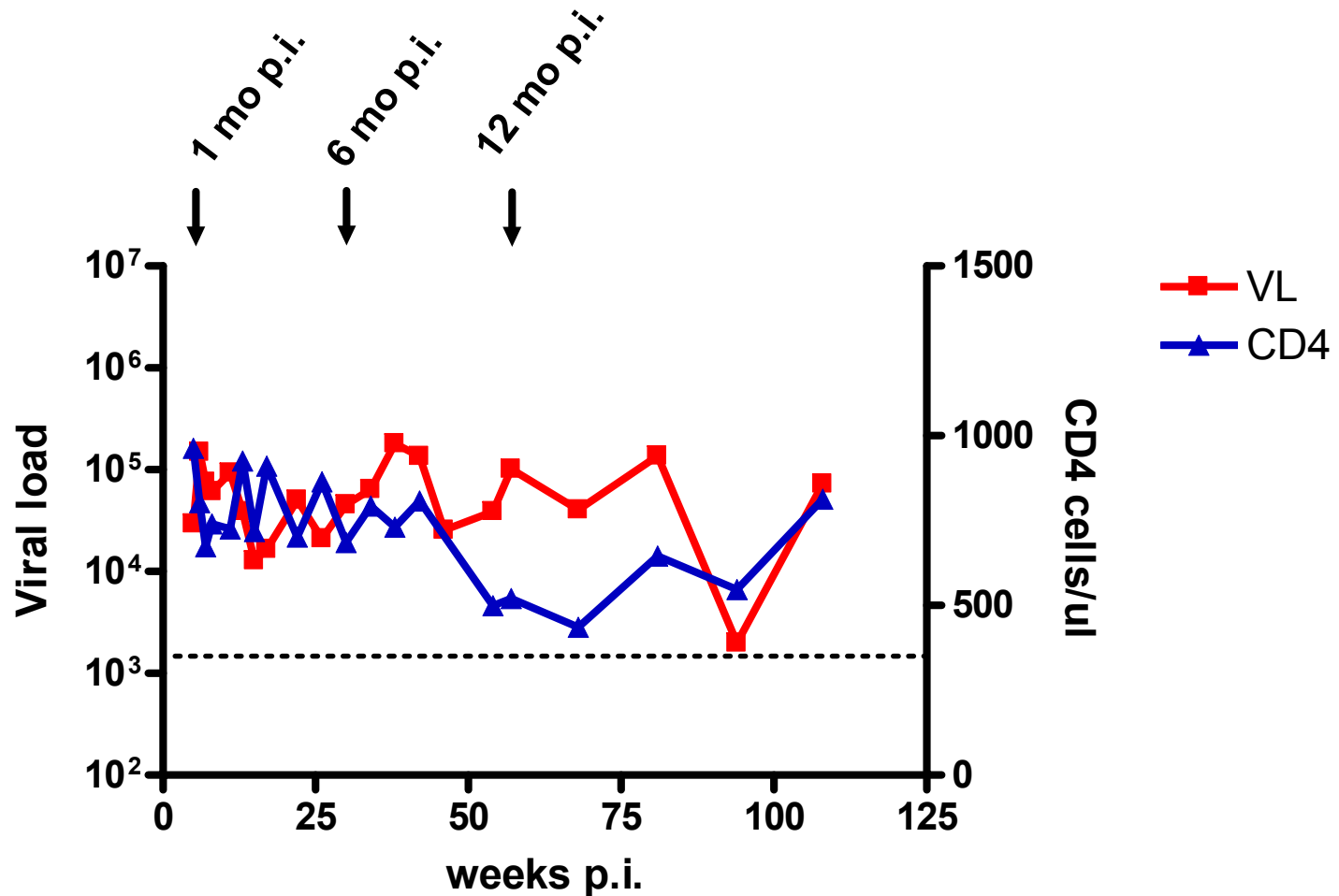


# Different routes, same result...



# CAP88 – intermediate progressor with moderate genetic diversity

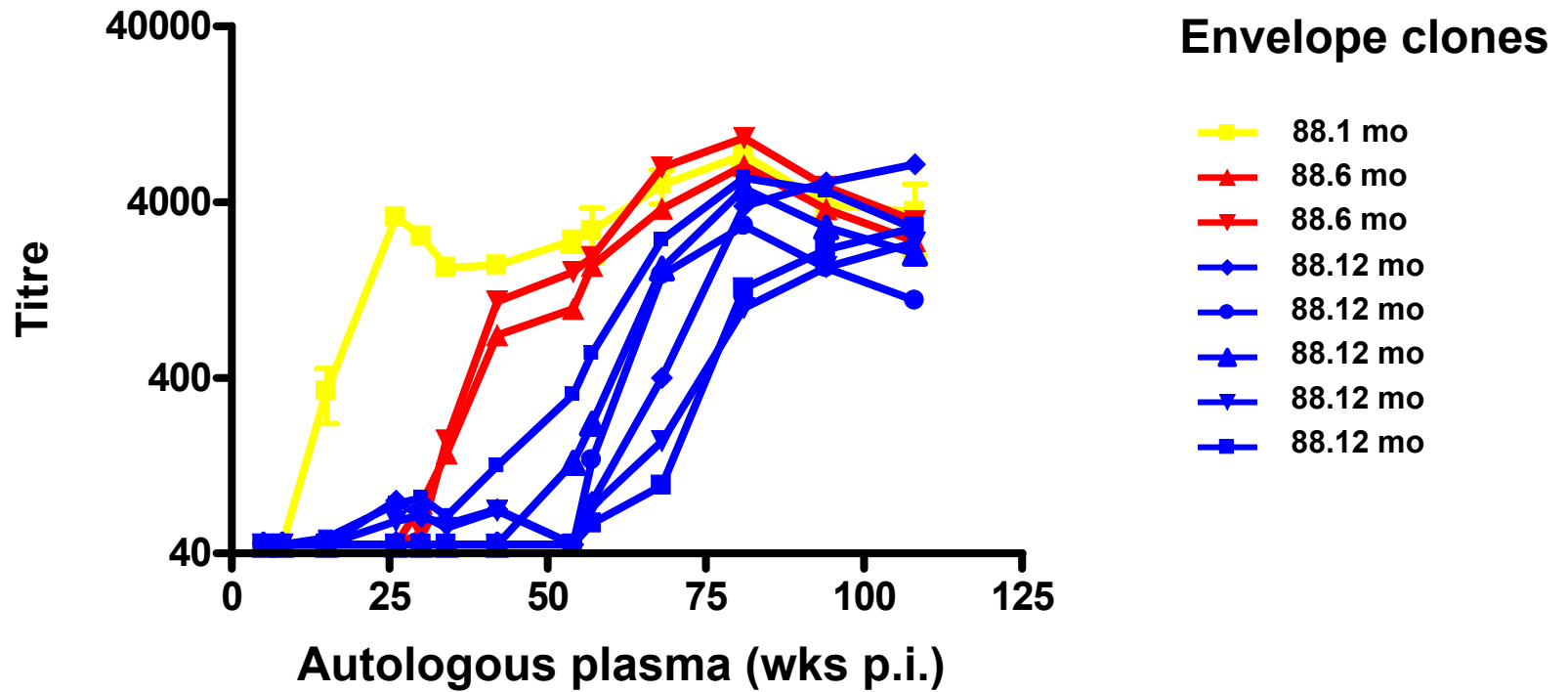
Envelope clones



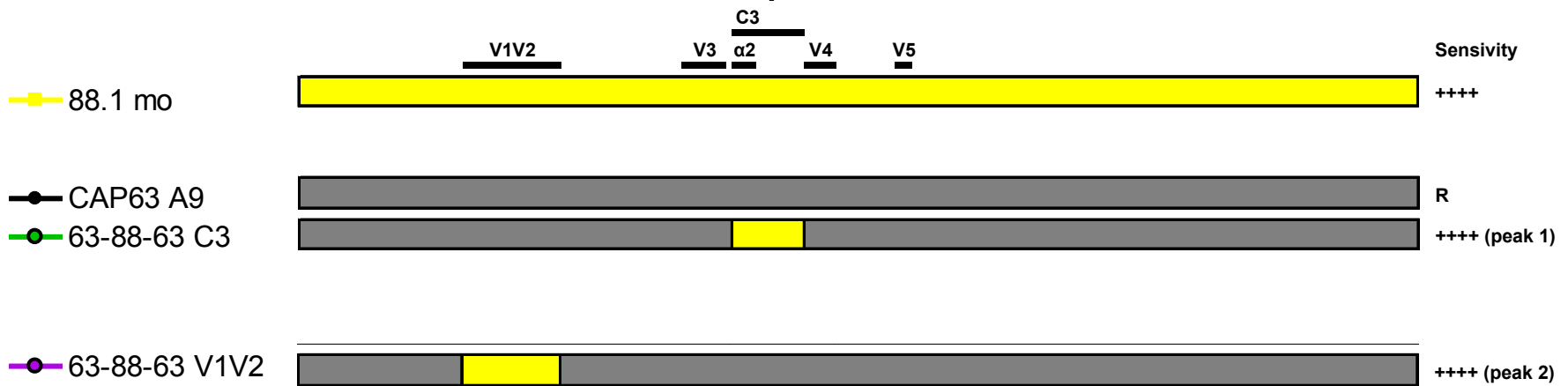
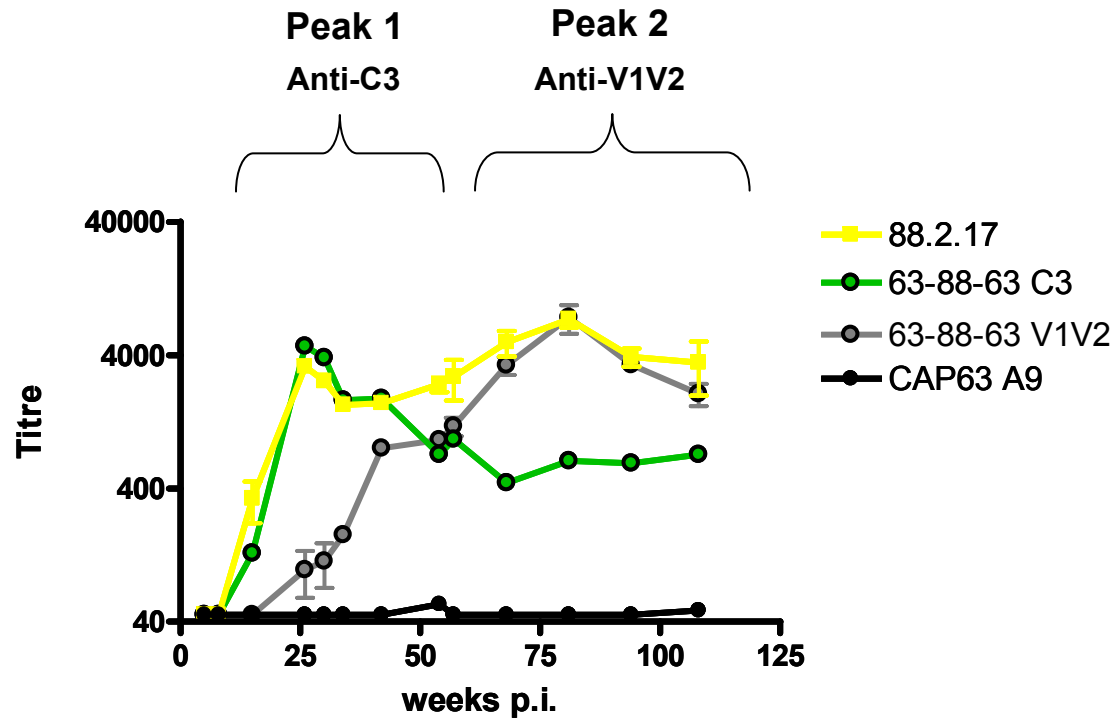
Maximum Percentage Diversity at 12 months p.i. = 2.1%



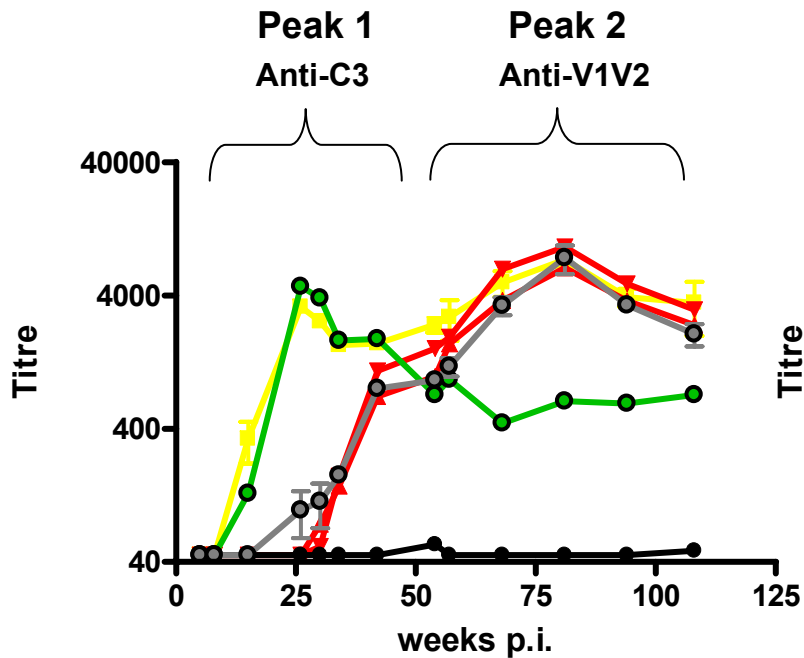
# CAP88 - Neutralization Escape



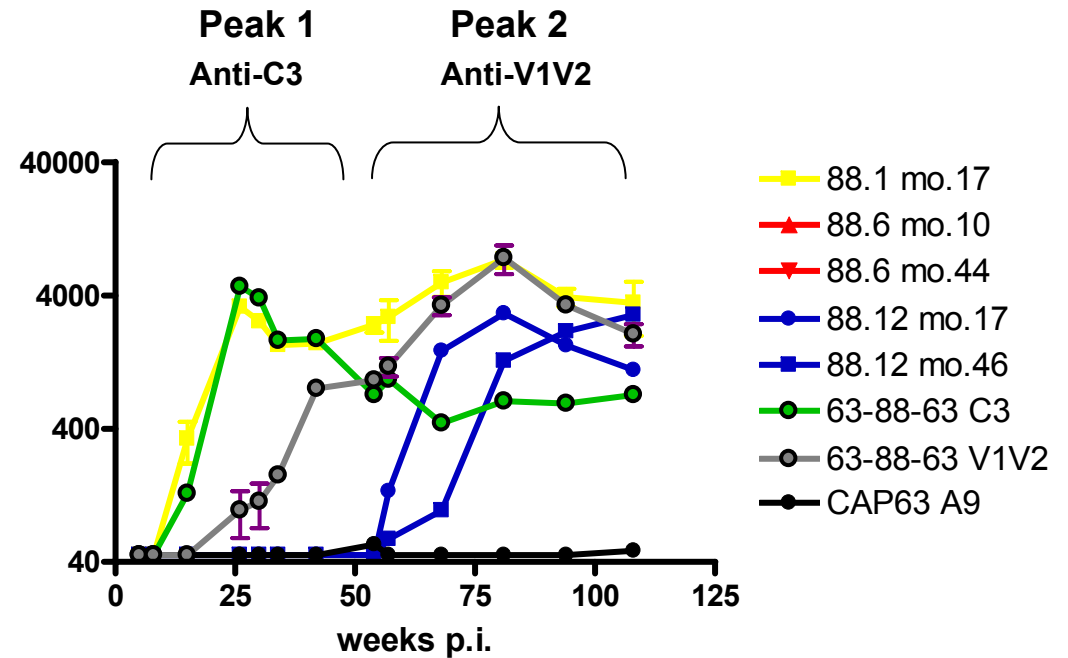
# Multiple specificities?



# Anti-C3 and anti-V1V2 antibodies drive sequential escape at 6 months and 12 months p.i.

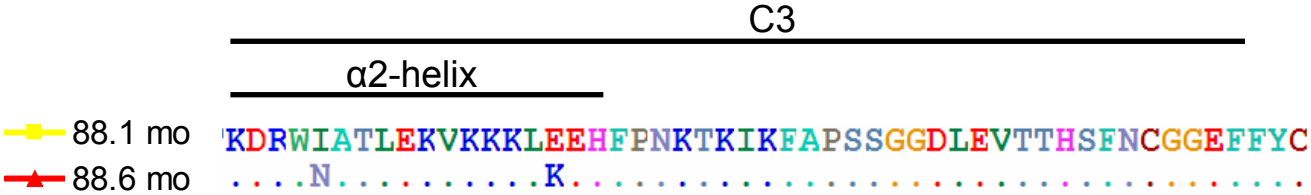
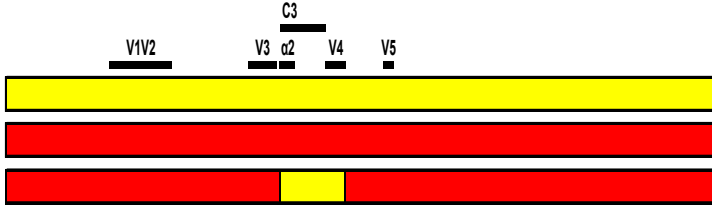
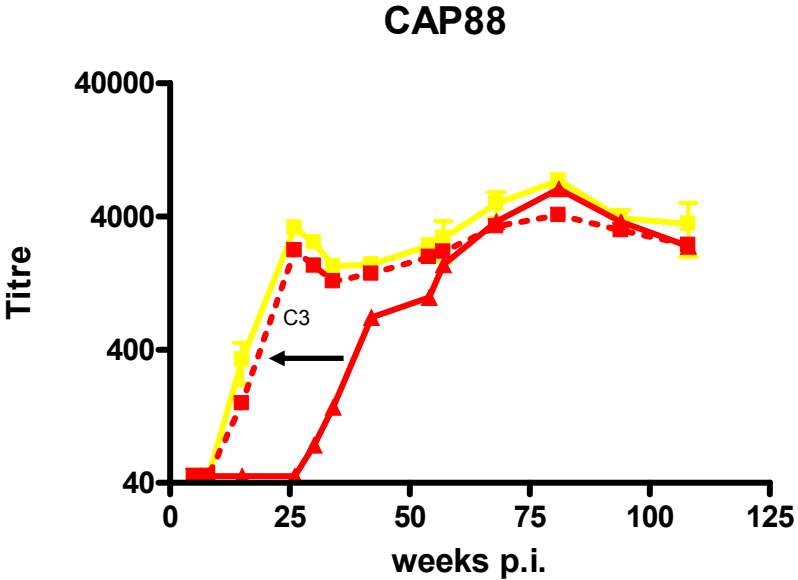


Suggests 6 month clone has escaped anti-C3 response.



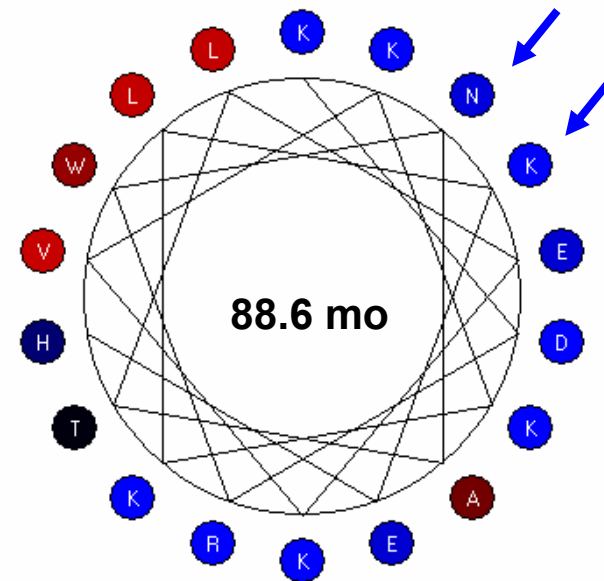
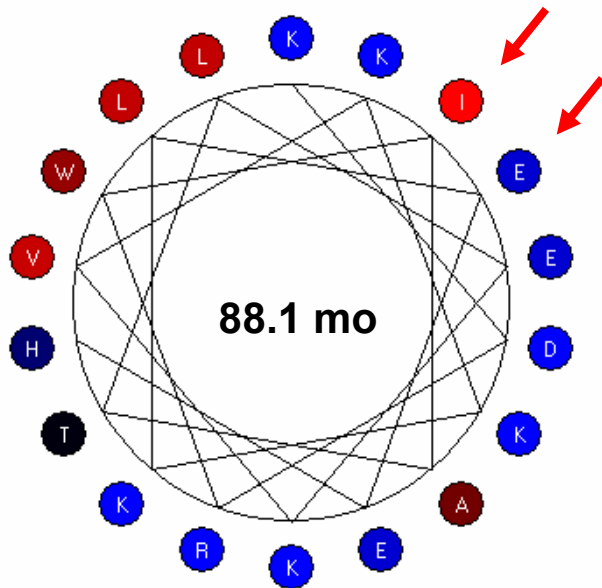
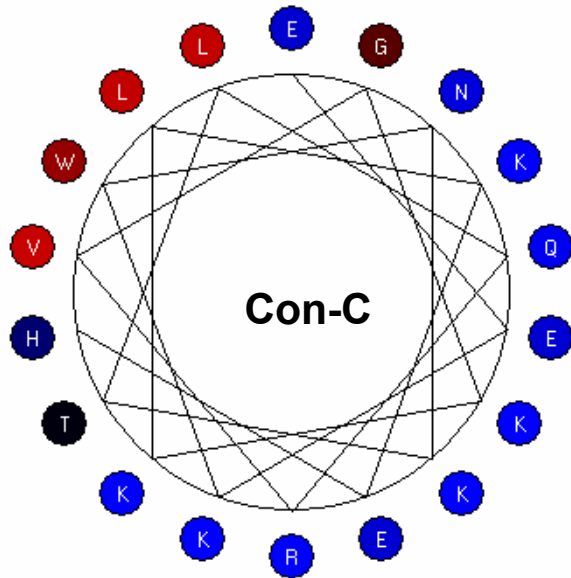
Suggests 12 month clones have escaped anti-V1V2 and anti-C3 response....

# C3, including the $\alpha$ 2-helix, as a target of nAbs

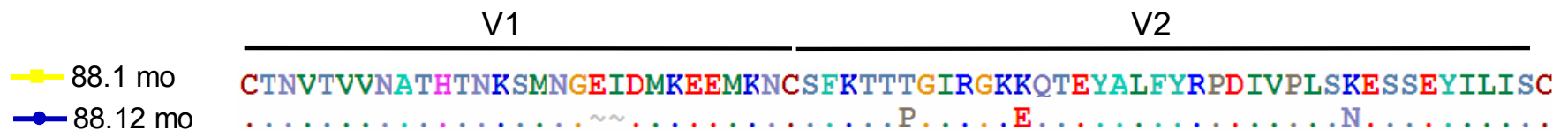
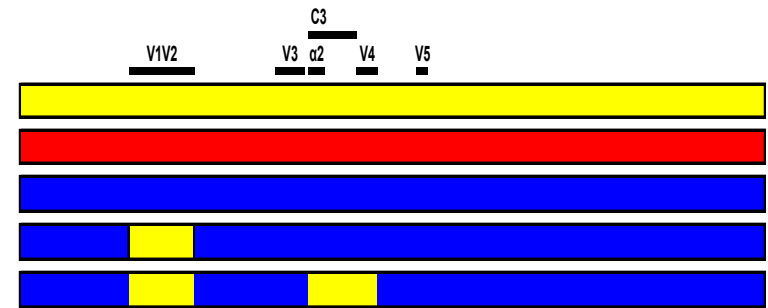
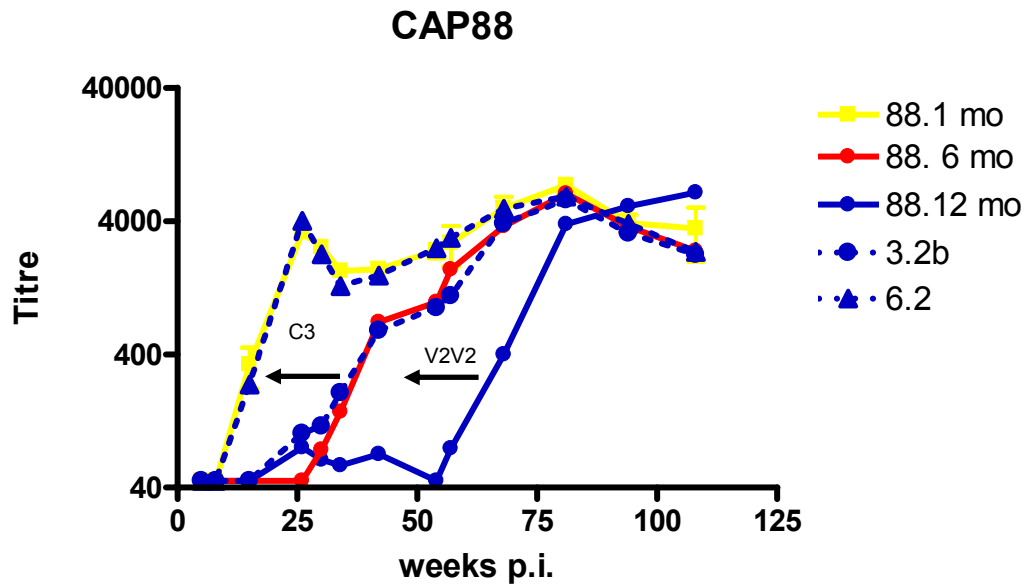


# Amphipathicity of the $\alpha 2$ -helix in C3 in HIV-1 C

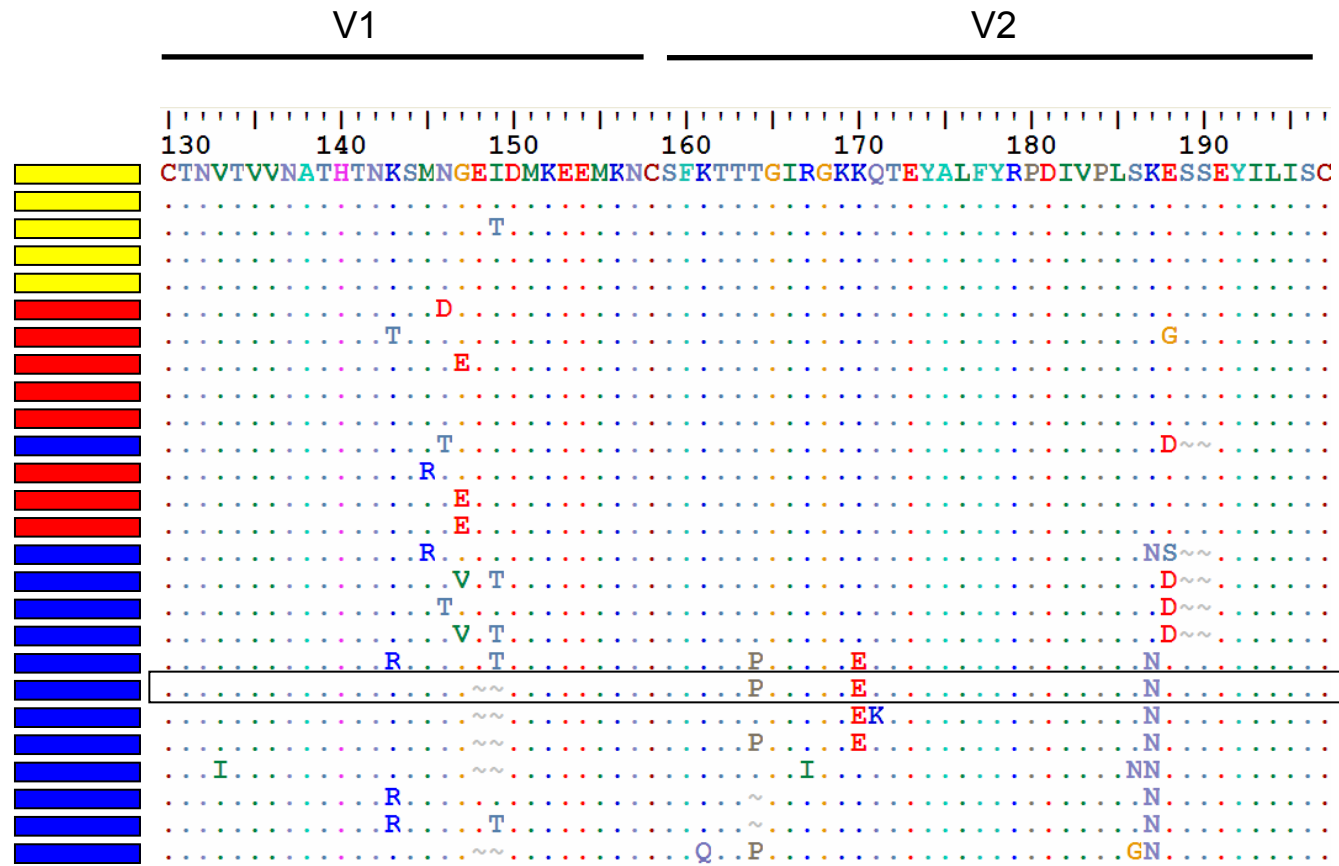
- Hydrophilic residues
- Hydrophobic residues



# V1V2 as a target of nAbs



# V1/V2 SGA sequences from CAP88 at multiple time-points



- 1 month p.i.
- 6 months p.i.
- 12 months p.i.

# Summary

- Studies in 2 HIV subtype C infected individuals suggest that limited antibody specificities in the first year of infection drive neutralisation escape
  - CAP45: Antibody specificities are not clear. 2 amino acids in V5 mediated neutralization escape but the antibody epitope is unknown.
  - CAP88: Antibodies to the C3 region developed early followed by antibodies to the V1/V2 region. The C3 region is likely to be a direct antibody target with changes in the  $\alpha$ -2 helix mediating escape
- Antibodies with single specificities show temporal fluctuations as escape occurs
- Multiple pathways to neutralisation escape from single antibody specificities



# Acknowledgements

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CAPRISA 002 study team

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