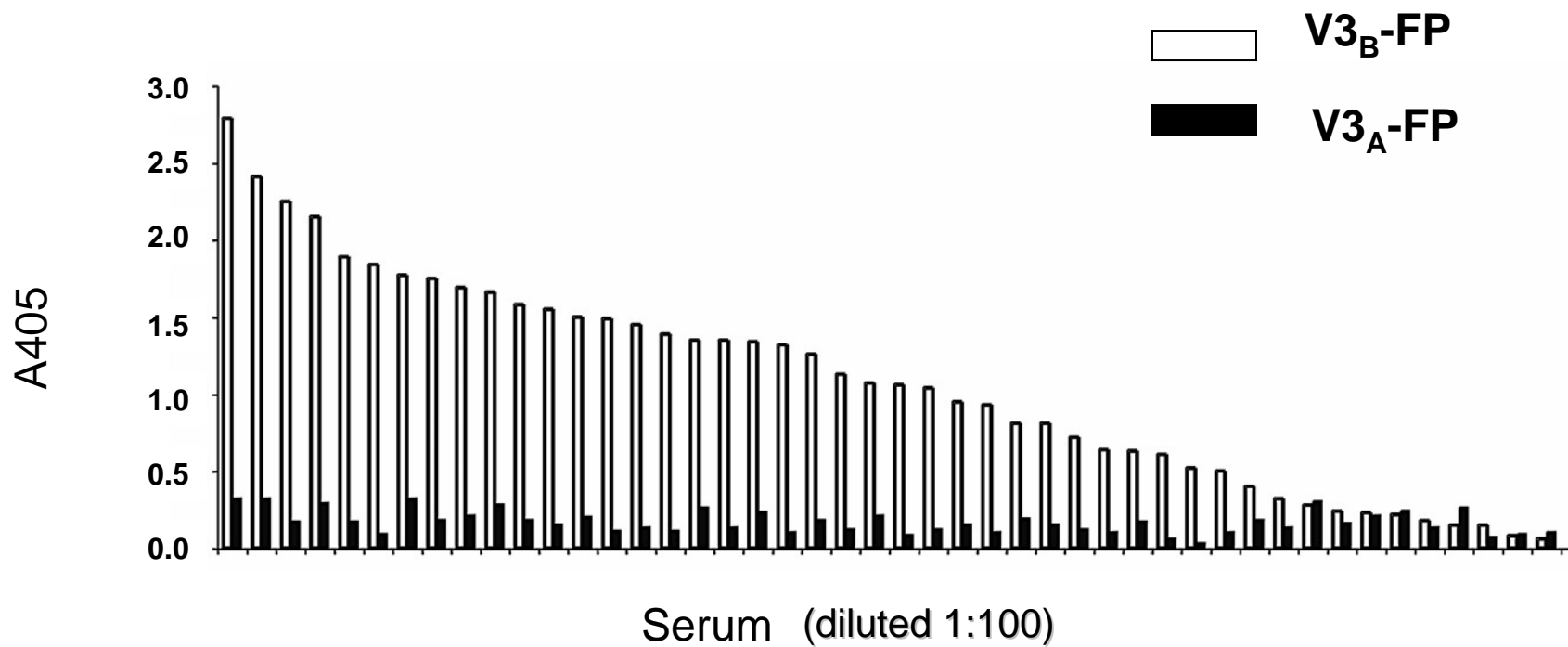


**Do specific genotypic
properties of the
infecting virus affect the
type of neutralizing Abs
that are induced?**

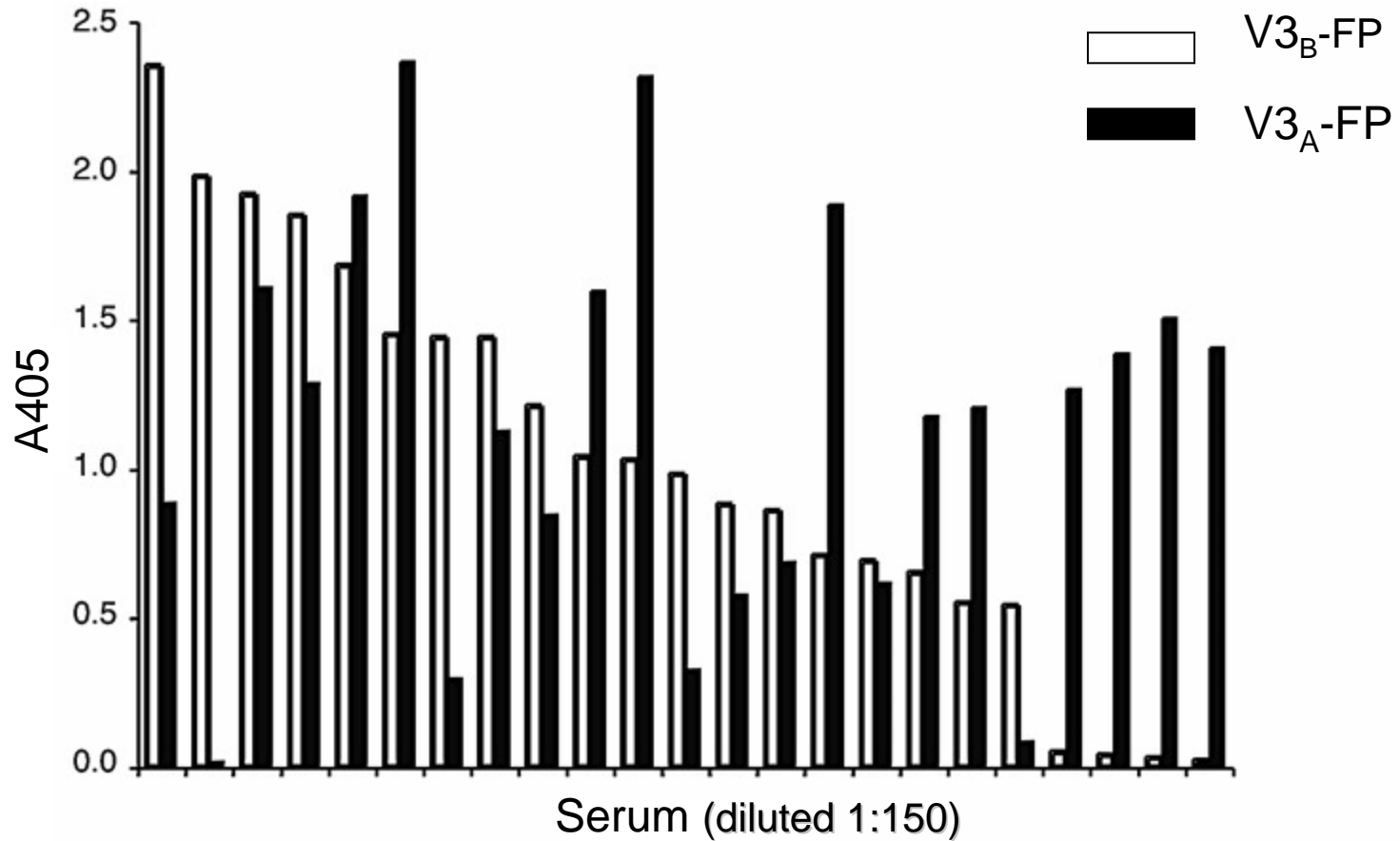
Results suggest that differences in the envelopes of viruses from different genotypes affect the breadth of neutralizing Abs

- Sera from non-B-infected individuals (from Cameroon) have more broadly-reactive serum anti-V3 Abs than do sera from clade B-infected individuals.
 - Krachmarov et al., JV, 79, 780, 2005
- Anti-V3 mAbs from non-B-infected individuals are more broadly-reactive than anti-V3 mAbs from clade B-infected individuals
 - Gorny et al., JV, 80, 6865, 2006
 - Gorny et al., poster #107363 (6-8pm, tonight)

US HIV+ serum reactivity with V3 fusion proteins



Cameroonian serum reactivity with V3 fusion proteins



Neutralizing Anti-V3 Serum Abs Are Blocked by Both Clade A and Clade B V3 Loops

Purified V3 Abs from	% Neutralization of psSF162 by Anti-V3 serum Abs	% Blocking by:	
		V3 _A -FP	V3 _B -FP
Cameroonian Patient ID			
5	79	99	116
56	90	14	56
65	78	119	118
68	100	110	108
25	95	14	111
69	100	62	110
Clade B-derived Anti-V3 mAb			
447-52D	94	12	103

Chimeric pseudoviruses used to examine the cross-reactivity of V3

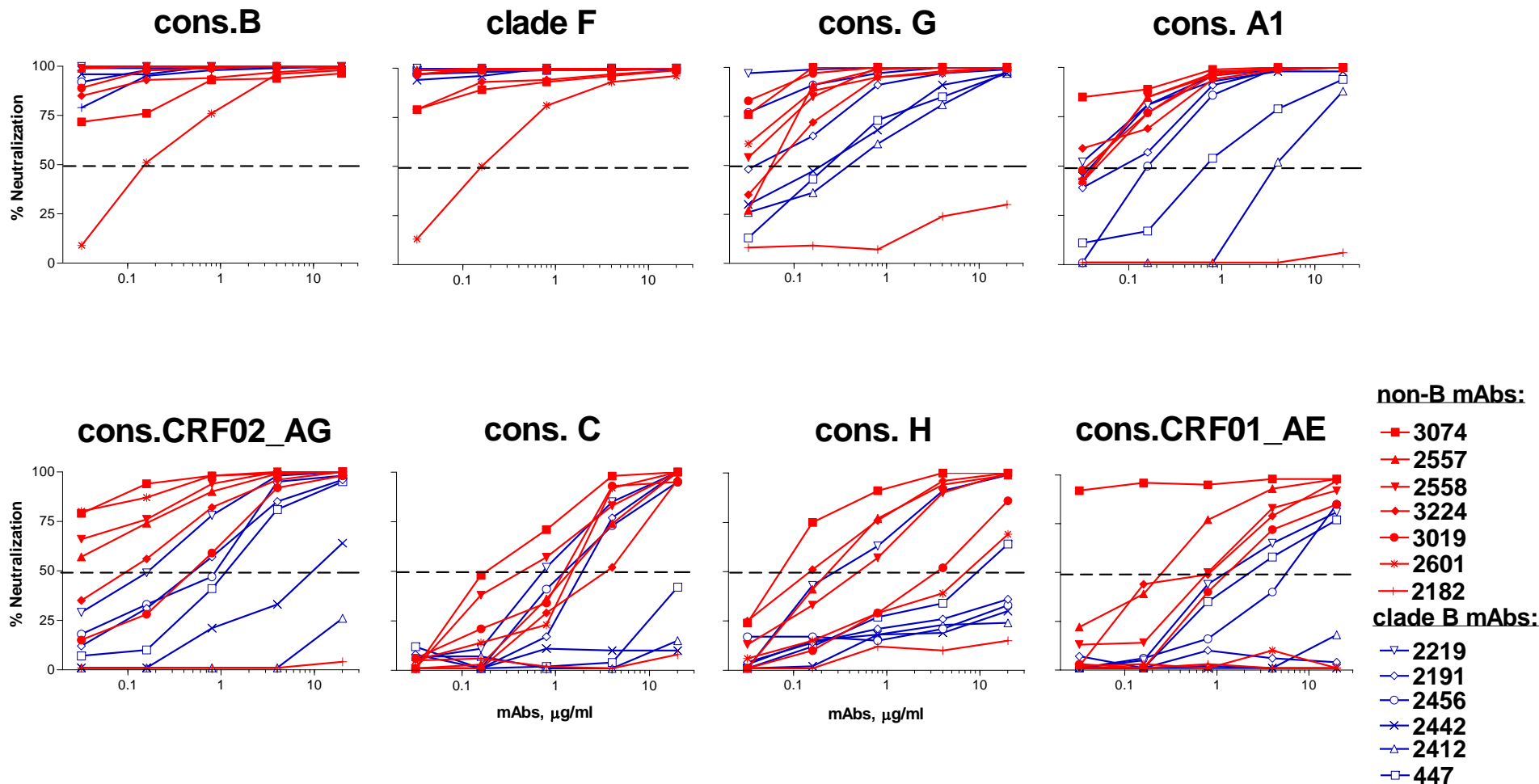
V3

gp120_{SF162}



etc.

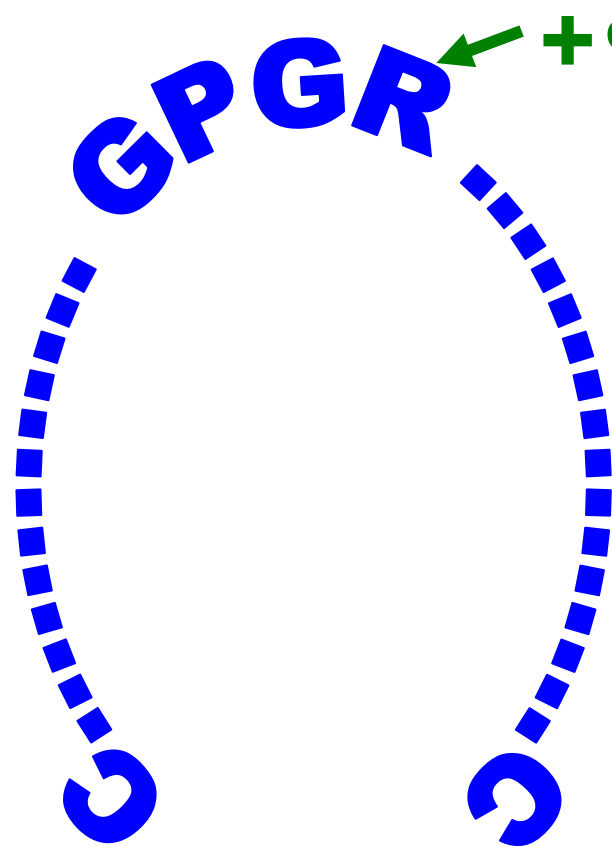
Neutralization of chimeric V3 viruses by anti-V3 mAbs derived from **clade B-infected** and **non B-infected** individuals



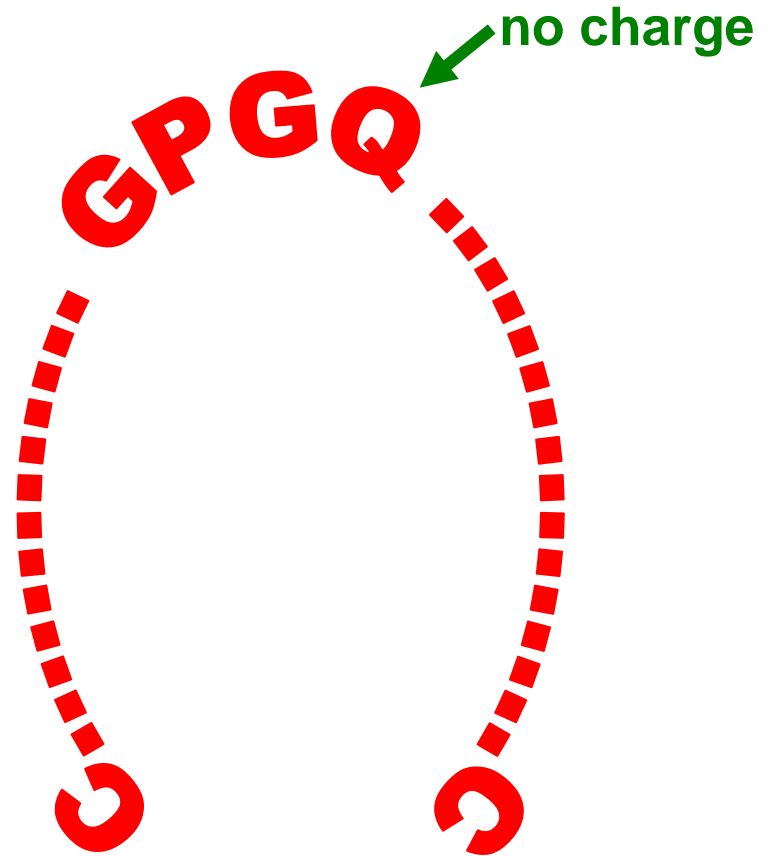
Structural Explanation

The Arg (R) in the GPGR motif at the tip of the V3 loop of most clade B viruses strongly influences and restricts the reactivity of Abs to this region.

Predominant Motifs at the Tip of the V3 Loop

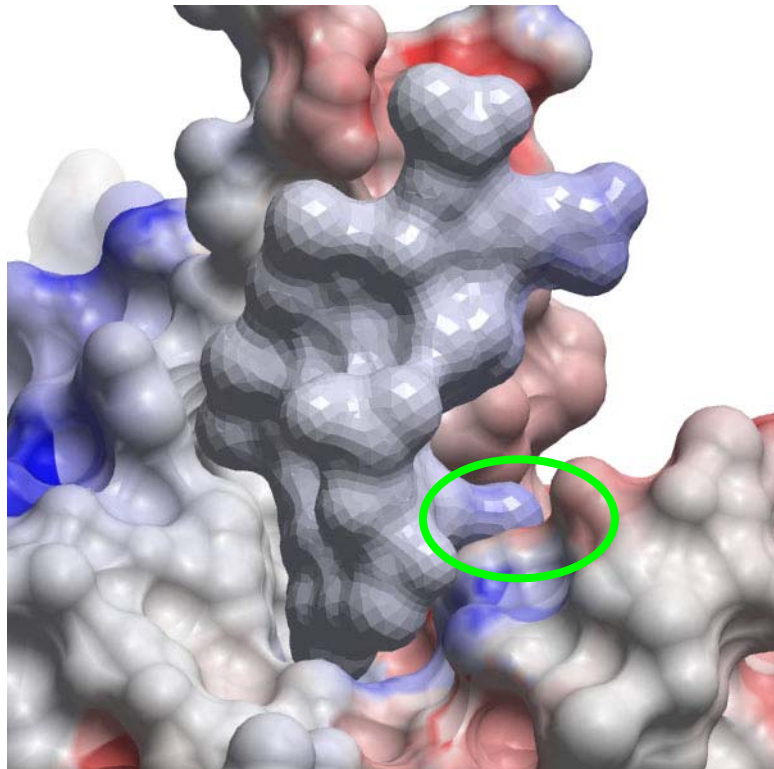


Mostly clade B

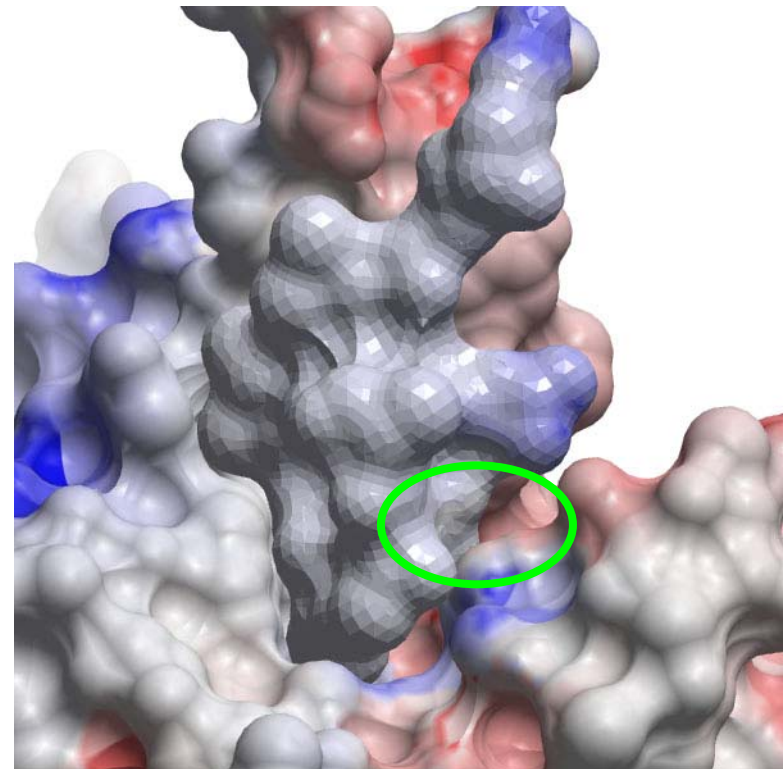


Mostly non-B clade

Crystals of mAb 447 with V3 peptides carrying the GPGR or GPGQ motifs



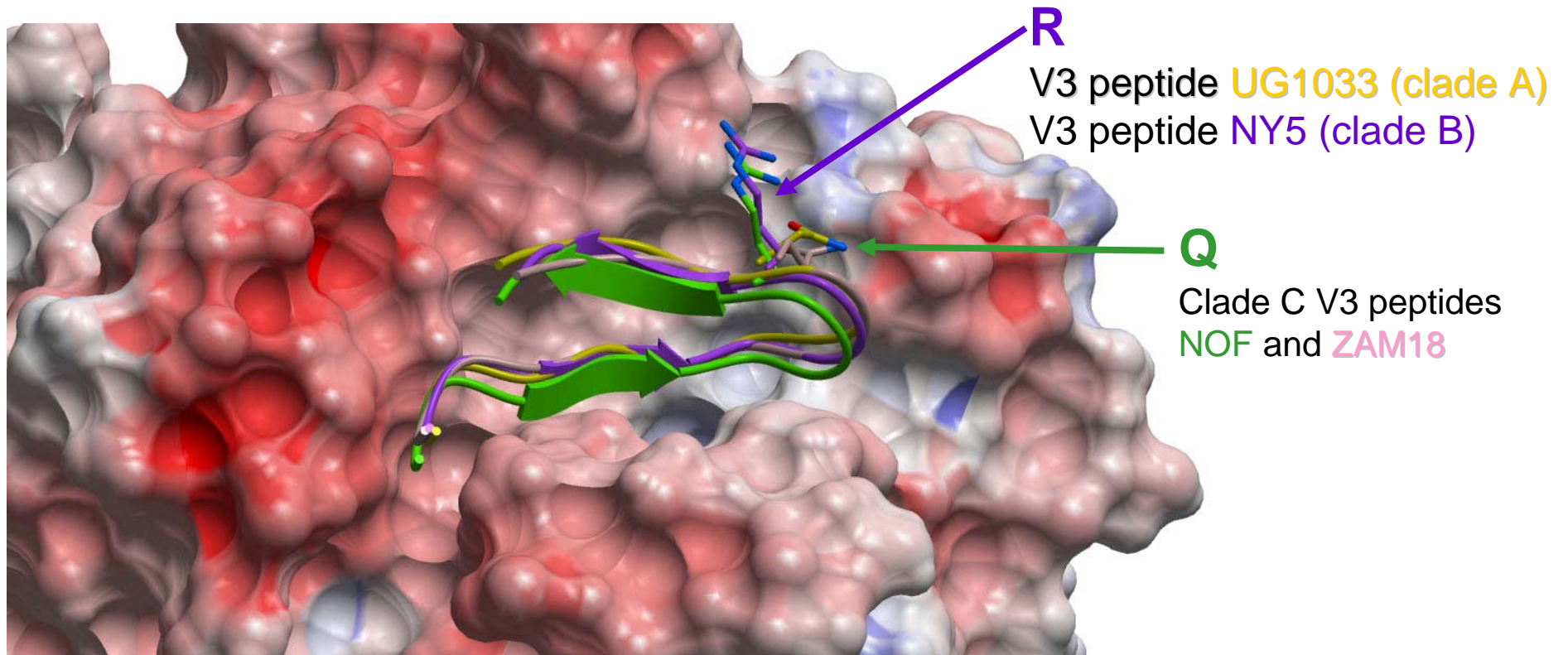
GPGR



GPGQ

“R-dependent” anti-V3 mAb

Crystals of mAb 2557 with V3 peptides carrying the GPG**Q** or GPG**R** motifs



“Q/R-independent” anti-V3 mAb

Implications for Vaccine Development

- The particular Env used for immunization will dictate the pattern of neutralizing Abs induced.
- In the case of V3 Abs, Env carrying the GPG**Q** motif appear to induce the broadest neutralizing Abs.
- The selection of the Env used as an immunogen is critical to the Ab response elicited.

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