Amino Acid Variation Found in the Immunogenic Tip of the V3 Region of the gp160 Protein From Subjects with Varying dS/dN Ratios in Makham et al. 1998

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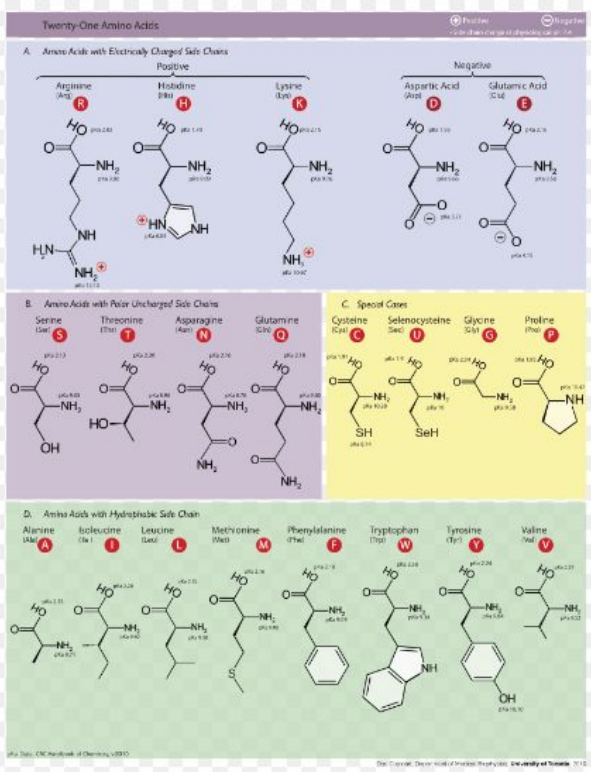
Background on HIV including information about function of places where there is variation

- HIV in general
- Information about Structure and functions of different parts of HIV from papers

dS/dN ratios from Markham et al. subjects show non-synonymous mutation rates which may have a correlation with changes in amino acid sequence

- Non synonymous mutations (dN) are nucleotide changes that lead to the coding of a different amino acid.
- Synonymous mutations (dS) are nucleotide changes that do not lead to the coding of a different amino acid.
- These ratios were formed for each consensus strain for all subjects.
- The smaller the ratio, the larger amount of non synonymous mutations, the more potential for differences in amino acid sequences

Information/Background About Amino Acids/Changes in Amino Acids



Limitations in Subject Selection Due to Inconsistencies in Subject Visits

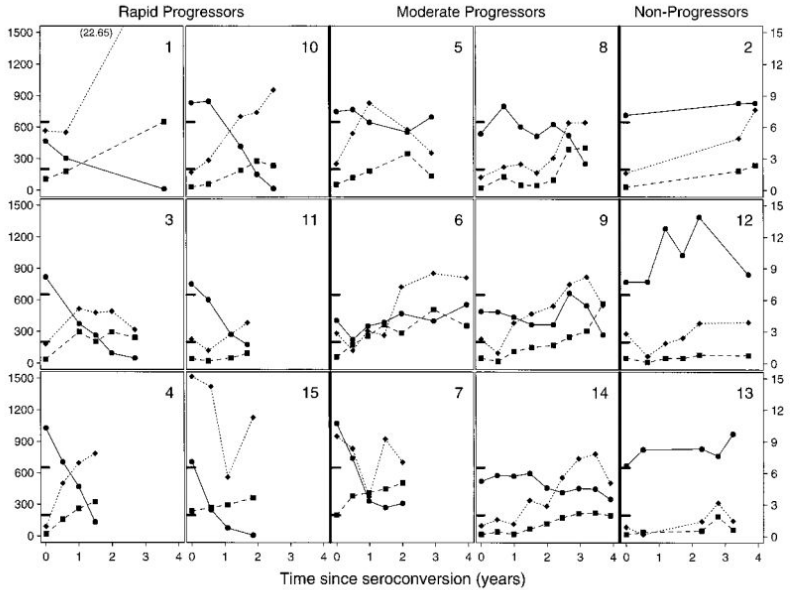


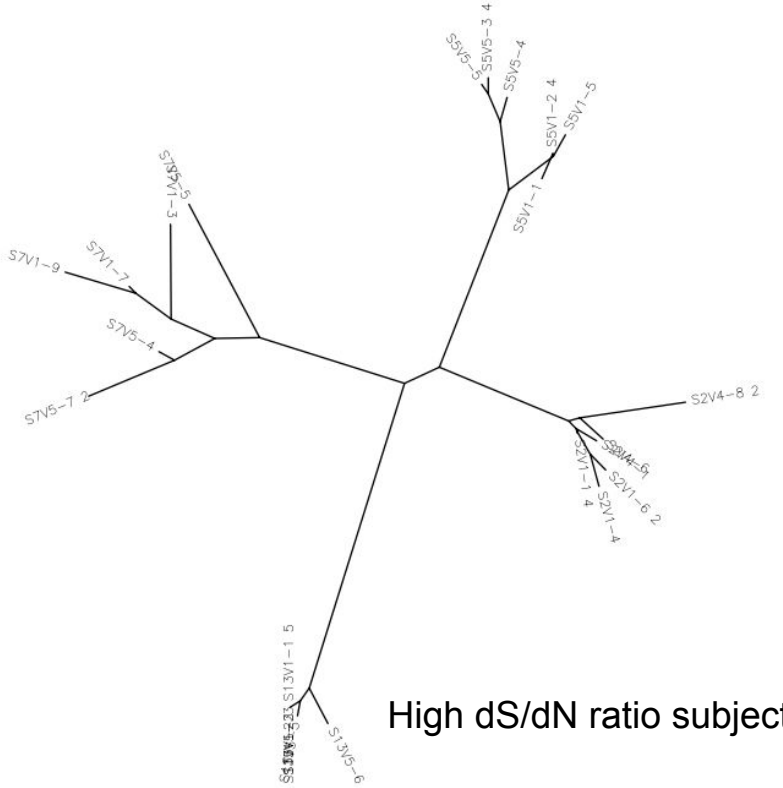
FIG. 1. CD4 T cell trajectory, diversity, and divergence over time since first seropositive visit ($t = 0$) in each of the 15 subjects. CD4 T cell counts (—●—●—) are shown on the left vertical axis. The solid dashes on the left vertical axis indicate the 200 and 650 CD4 T cell count levels that were used to distinqish the different progressor groups. Diversity (--◆--◆--) and divergence (—■—■—) values are shown on the right vertical axis. For diversity, axis values indicate the mean of the nucleotide differences between intravisit clones. For divergence, the values indicate the median percent of nucleotides per clone that diverged from the original postseroconversion consensus sequence. For Subject 1, the diversity value at 3.57 years postseroconversion was 22.65 nt differences, which is offscale. Subject identification numbers are given in the upper right corner of each graph.

Groups were formed based on subjects who demonstrated the highest and lowest non-synonymous mutation rates

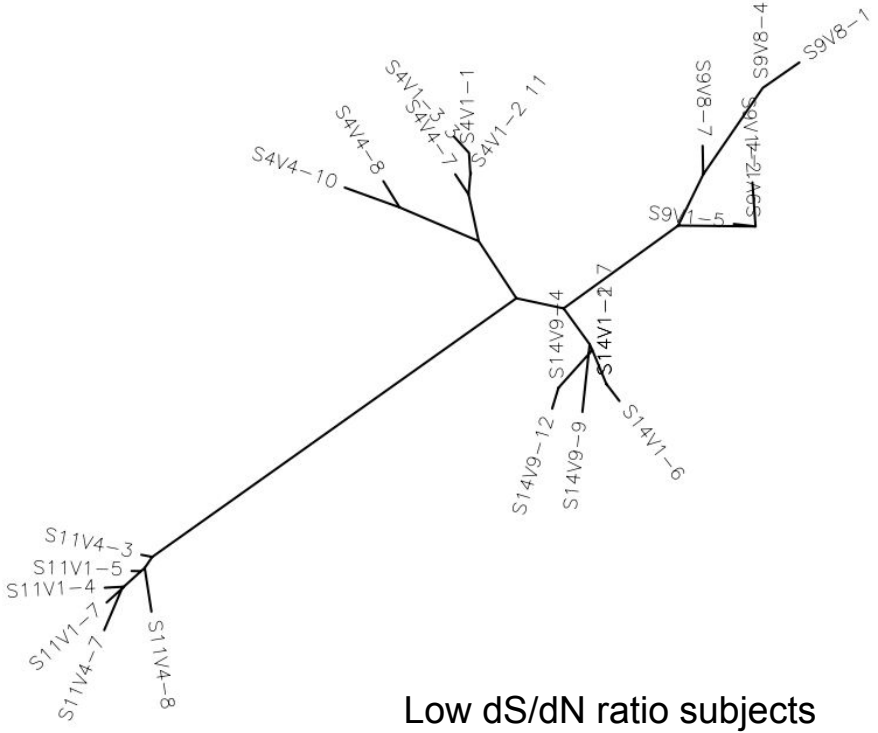
Rapid Progressor (Subject #)	Moderate Progressor (Subject #)	Non-progressor (Subject #)
4	**7**	**2**
10	8	12
11	**14**	**13**
15	**5**	
3	**9**	
1	6	

Subjects demonstrating highest dS/dN ratios	Subjects demonstrating lowest dS/dN ratios
7	4
5	9
2	11
13	14

Phylogenetic Trees Showed No Clear Difference in Variation between Low dS/dN Subjects and High dS/dN Subjects



High dS/dN ratio subjects



Low dS/dN ratio subjects

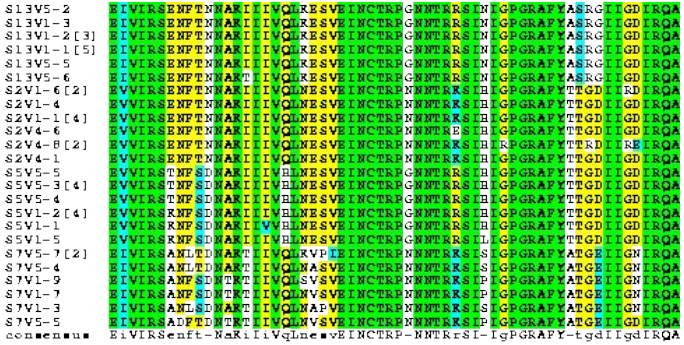
Biology Workbench: ClustalW

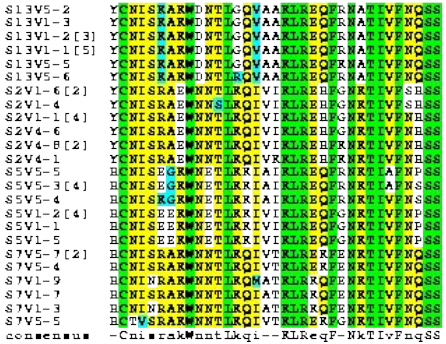
Low dS/dN Ratio Subjects Had More Non-Consensus Sites Than High dS/dN

	High dS/dN Ratio Subjects	Low dS/dN Ratio Subjects	All Subjects
Fully Conserved Residue	49	43	30
Conservation of Strong Group	22	20	23
Conservation of Weak Group	10	6	13
No Consensus	14	24	31

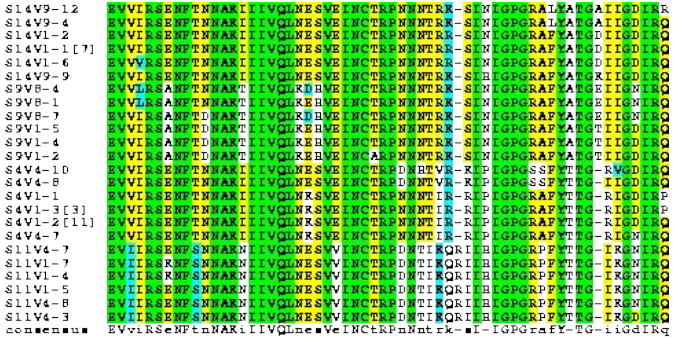
Possible Significance Test for Non Consensus

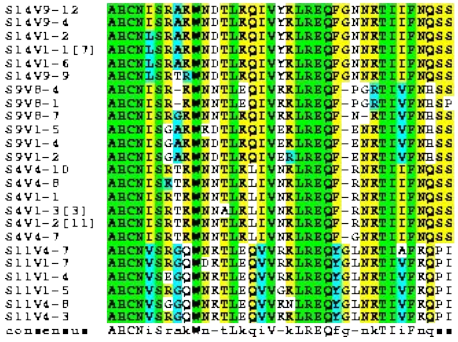
The BoxShade program on Biology Workbench highlights a higher frequency of non-consensus regions between subjects from the low dS/dN group





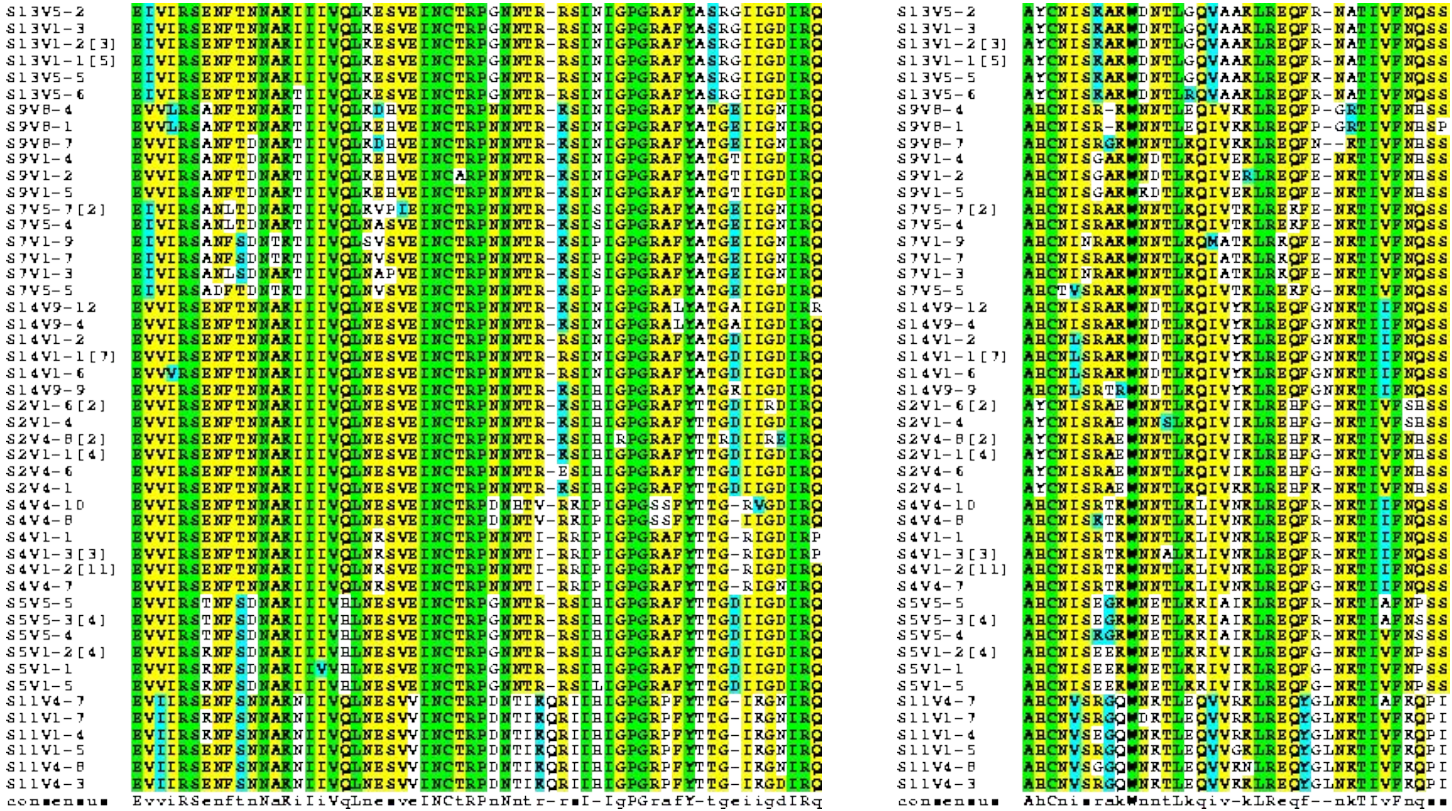
High dS/dN ratio subjects



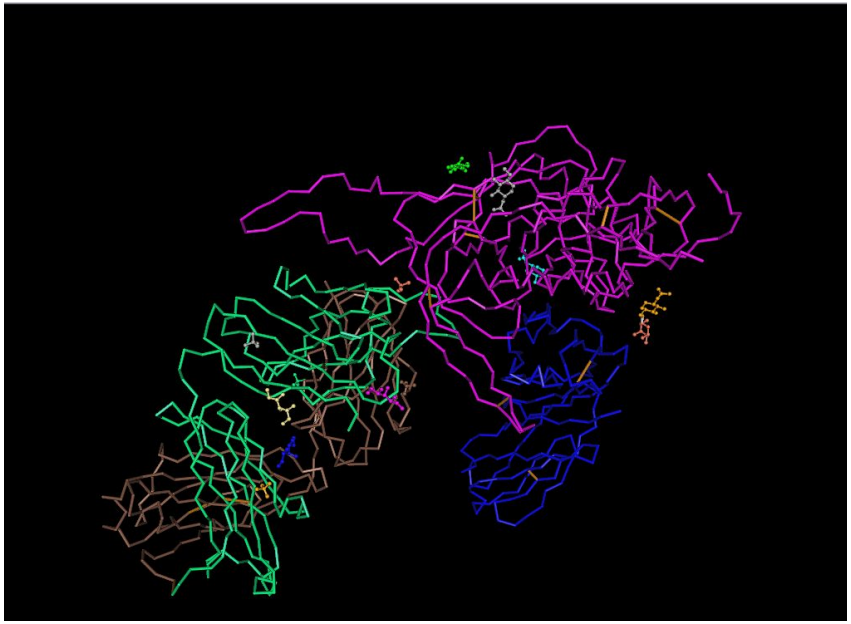


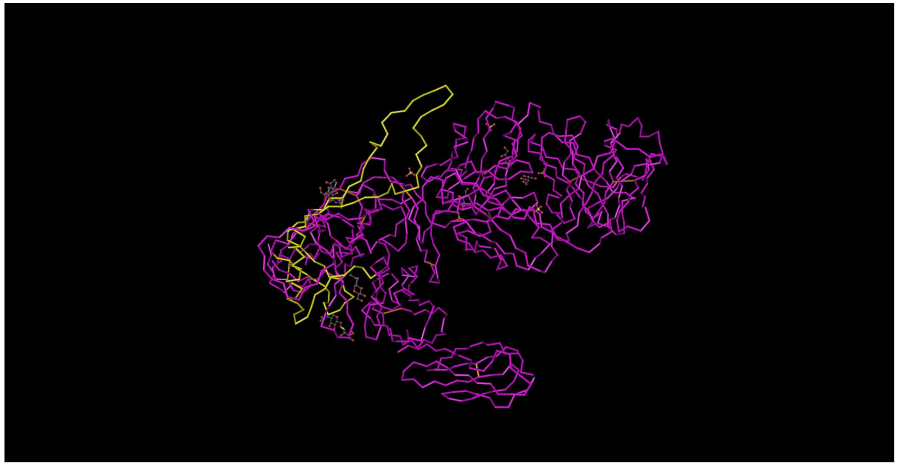
Low dS/dN ratio subjects

BoxShade identified six sites as “non-consensus” after all amino acid sequences were processed

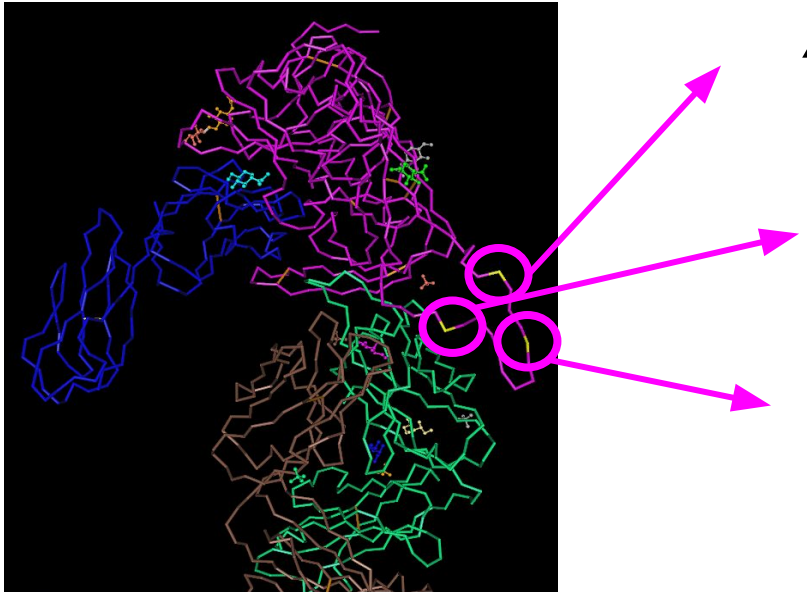


Visual settings within the Cn3D macromolecular structure viewer highlighted the V3 region of the gp160 quaternary protein structure





Three nonconsensus amino acids along the immunogenic tip of the V3 region show consistent variability with previous studies: *Kwong* and *Andrinov*



2B4C_G	vqcthgirpvvstqlllngslaeeevvirsdnftnnaktiivqlkesveinctrpnqntrksihigpgrafyttgeiigdirqahcnisrakwndtlkqiviklreqfenktivfnhssggdpeivmhsfncggeffycnsaqlfr
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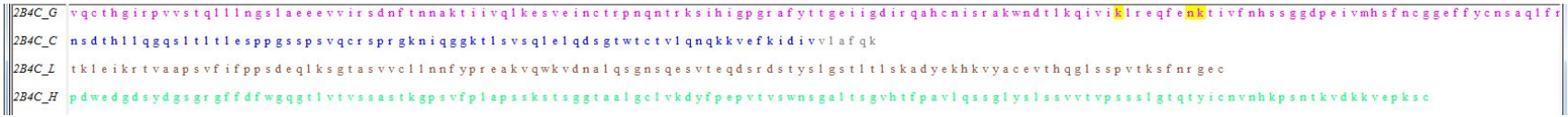
Three nonconsensus amino acids along the immunogenic tip of the V3 region show inconsistent variability with previous studies: *Kwong* and *Andrinov*



Acknowledgements

Dr. Dahlquist

Department of Biology at Loyola Marymount University

References