

The Observable Amino Acid Divergence in Late Visit Clones (and the impact of those changes).

**Loyola Marymount University
Department of Biology
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Will Fuchs & Matt Oki

Outline

- Scope of the project
- Subject 10 gives the most amount of data points with the most drastic drop in CD4-T cell count.
- Multiple sequence alignment of amino acid and nucleotide sequences reveals disproportionate values for S, theta, min, and max.
- Clones of later visits showed an increased amount of divergence as compared to the original sequence.

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Research Direction

Question: Will there be a visible protein sequence change that correlates with a decline in CD4-T cell count?

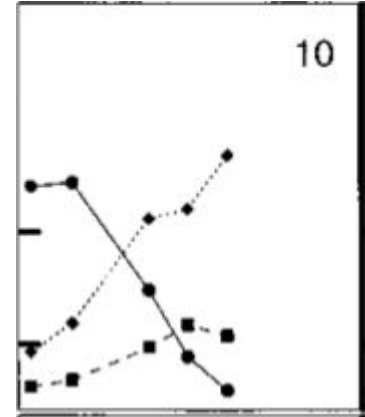
Hypothesis: Given that the amino acids of the clones of subject 10 are changing simultaneously there will be an observable drop in CD4-T cell count in response to the ongoing changes in the clones' proteins.

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Subject 10 shows a drastic drop in CD4-T cell count with a large increase in diversity

- Subject 10 recorded 6 visits with a total of 49 clones.
- The change in condition in the subject suggests an amino acid composition change.



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A Change in DNA Sequence Doesn't Ensure Amino Acid Sequence Change

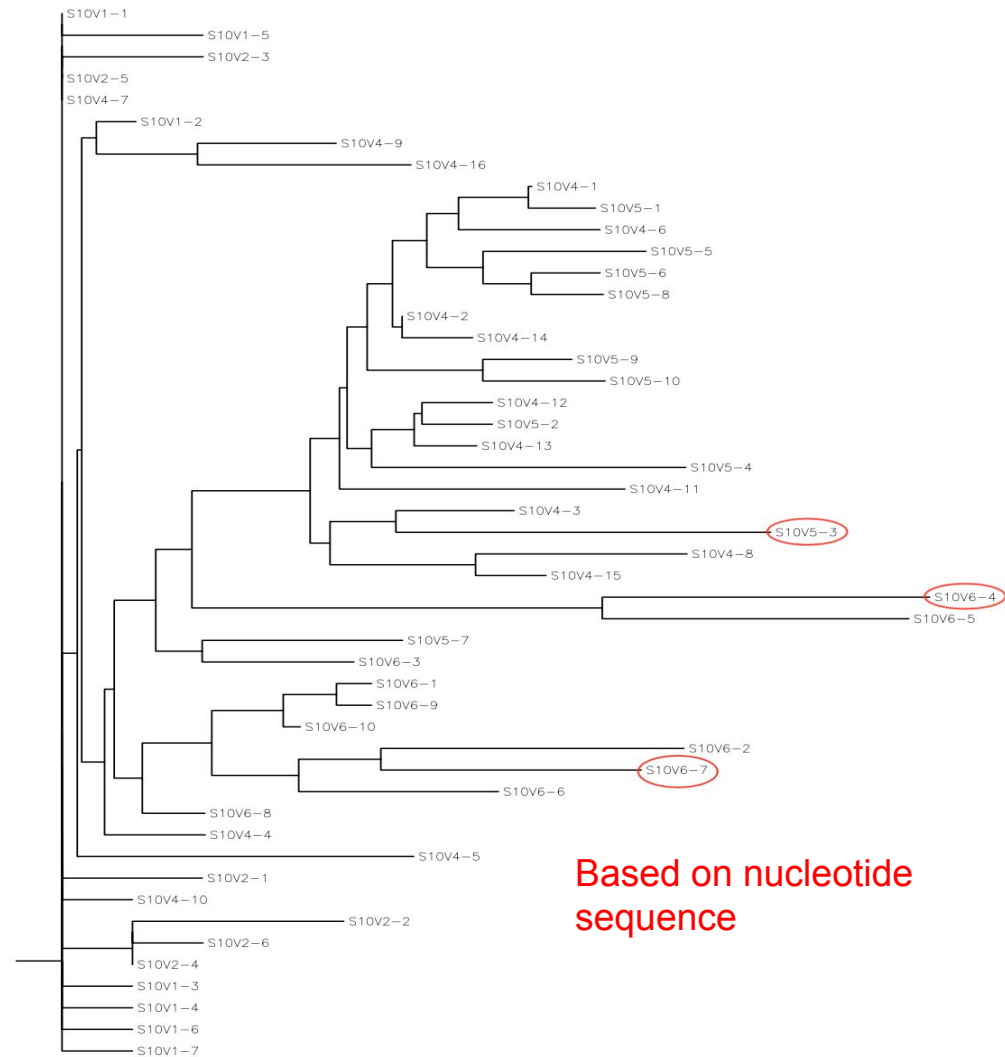
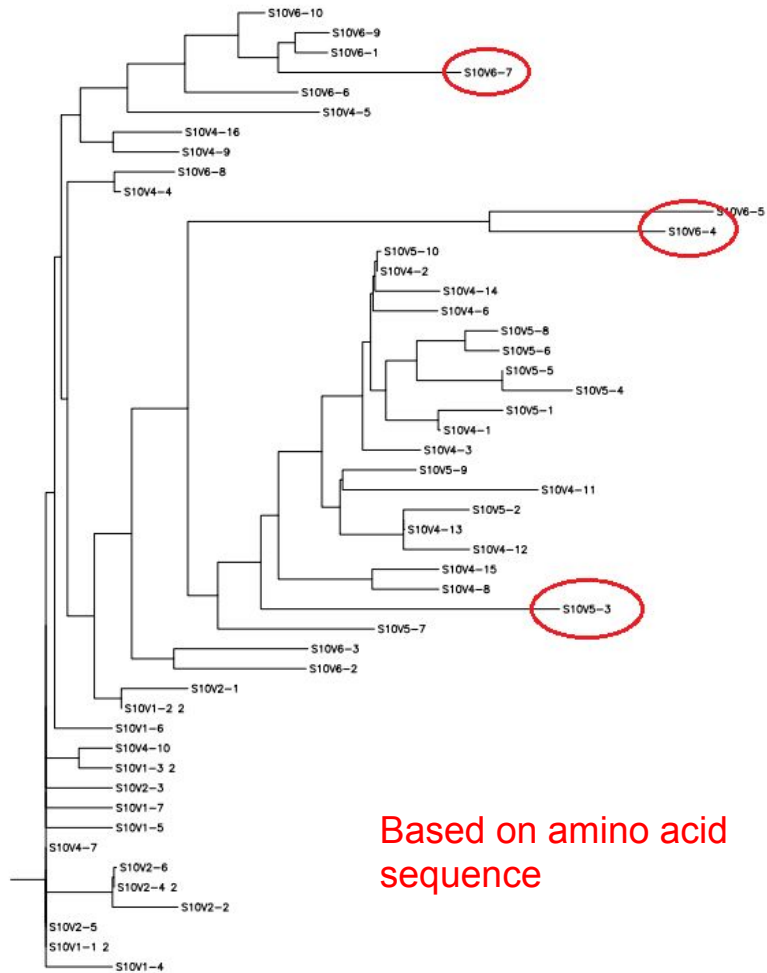
	Subject	# Clones	S	θ	Min	Max
Amino Acid	10	50	13	8.55	1	15
Nucleic Acid	10	50	74	48.65	1	21

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S10V5-3, S10V6-4, and S10V6-7 showed the highest divergence.

- When compared to the original strain these select samples showed the highest changes in their amino acid sequences.
- This was discovered through the CLUSTALDIST program highlighting where the intersections of individuals showed the most divergence.



Continued work

- We hope to further investigate the clones of interest and to discern which amino acid changes were made and predict how those significant amino acid changes would affect the greater protein.
- Potentially compare the regions of change to the 3D model of the V3 region given by the Huang et al. (2005) data.
- Are these divergent samples the reason that subject 10 became a constituent of the “rapid progressor” data set of the Markham et al. (1998) paper.

Acknowledgments

- Dr. Kam Dahlquist
- LMU Department of Biology
- Classes of 2017 and 2018



References

- Huang, C. C., Tang, M., Zhang, M. Y., Majeed, S., Montabana, E., Stanfield, R. L., ... & Wyatt, R. (2005). Structure of a V3-containing HIV-1 gp120 core. *Science*, 310(5750), 1025-1028. doi: 10.1126/science.1118398
- Markham, R.B., Wang, W.C., Weisstein, A.E., Wang, Z., Munoz, A., Templeton, A., Margolick, J., Vlahov, D., Quinn, T., Farzadegan, H., & Yu, X.F. (1998). Patterns of HIV-1 evolution in individuals with differing rates of CD4 T cell decline. *Proc Natl Acad Sci U S A*. 95, 12568-12573. doi: 10.1073/pnas.95.21.12568.