

# Change in CD4 T-Cell count and HIV Evolution from First to Last Visit in Injection Drug Users

Lizzy Urbina, Karina Vescio, Sahil Patel

# Outline

1. Analysis of Markham's research that intrigued us.
2. Proposed analysis of data from a different angle.
3. Methods and results of our experiment.
4. Analysis of the change in CD4 T-Cell count from first visit to last visit in each of the three progressor types.
5. Decline of CD4 T-cells is directly proportional to the evolution of HIV virus.

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# Markham's Research Conclusion.

- The technique and standards used to classify each subject into three categories.
- Omission of phylogenetic trees of non-progressor and rapid progressors.
- The irregularity of scale in each graph.
- Test their theory of non-progressors selection of absence of change, since evolution favors diversity.

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**Is it necessary to record and analyze the interim visits of the subjects for an accurate analysis of the CD4 T-cell decline in order to accurately map the progression of HIV evolution?**

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# Methods/Results conducted in our analysis

- Statistical Analysis of CD4 T-cells count and sequence data.
- Graph and calculate the slope in order to classify the subjects.
- Creation of the phylogenetic trees of each subject.
- Compare and contrast our classification and Markham's.

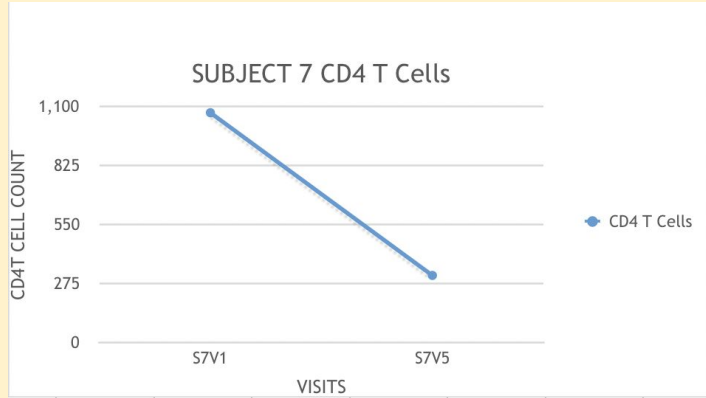


# Statistical Analysis of CD4 T-cells count and sequenced data.

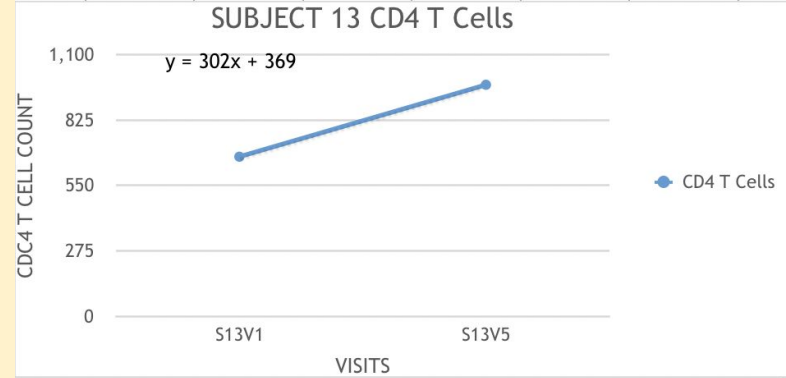
Subject	CD4 T Cells
S1V1	464
S1V5	14
Subject	CD4 T Cells
S2V1	715
S2V4	829
Subject	CD4 T Cells
S3V1	819
S3V6	47

- Some subjects had visits with CD4 T-cell counts, but no sequences.
- The data taken into consideration was the last CD4 T-cell count with corresponding sequences

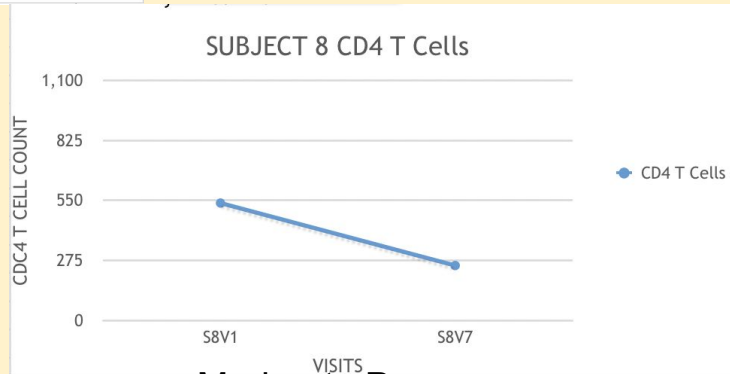
# Graph and calculate the slope in order to classify the subjects



Rapid Progressor



Non-Progressor



Moderate Progressor

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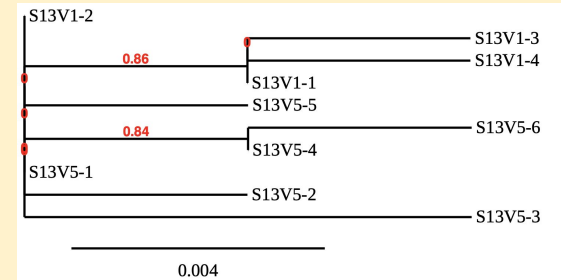
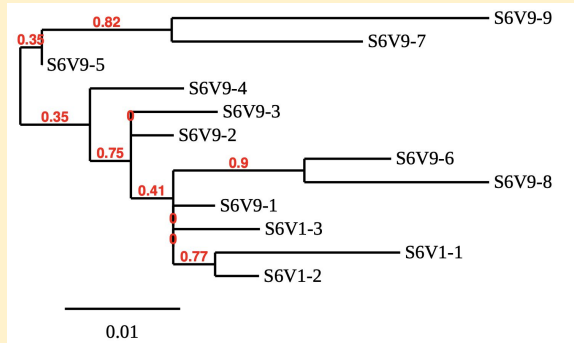
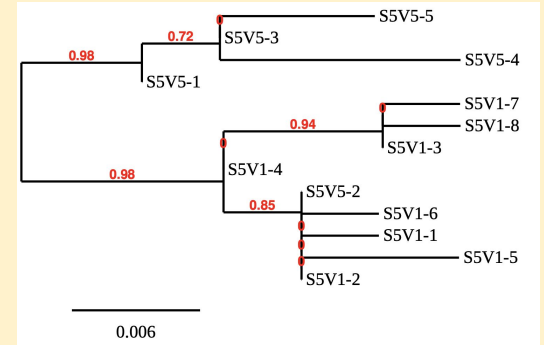
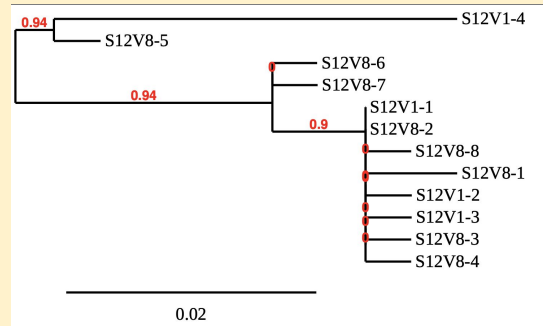
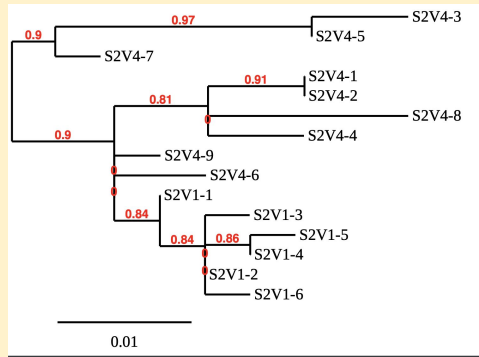
# Classification of change in CD4 T-Cell count from first to last visit in each of the Progressor Types

Rapid-Progressors		
Subject	CD 4 T Cell	Rate of Change
S1V1	464	-450
S1V5	14	
S3V1	819	-772
S3V6	47	
S4V1	1028	-895
S4V4	133	
S7V1	1072	-760
S7V5	312	
S10V1	833	-816
S10V6	17	
S11V1	753	-577
S11V4	176	
S15V1	707	-697
S15V4	10	

Moderate-Progressors		
Subject	CD 4 T Cell	Rate of Change
S8V1	538	-286
S8V7	252	
S9V1	489	-220
S9V8	269	
S14V1	523	-171
S14V9	352	

Non-Progressors		
Subject	CD 4 T Cell	Rate of Change
S2V1	715	114
S2V4	829	
S5V1	772	-74
S5V5	698	
S6V1	405	171
S6V9	556	
S12V1	772	70
S12V8	842	
S13V1	671	302
S13V5	973	

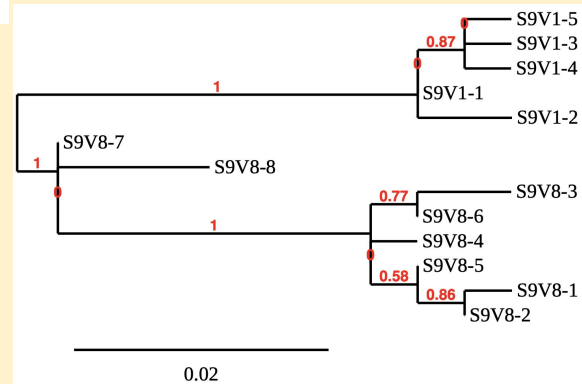
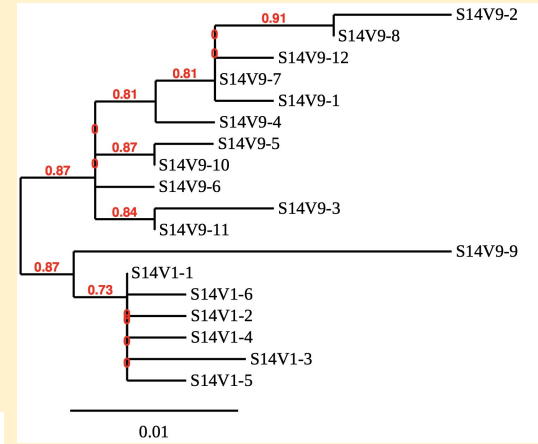
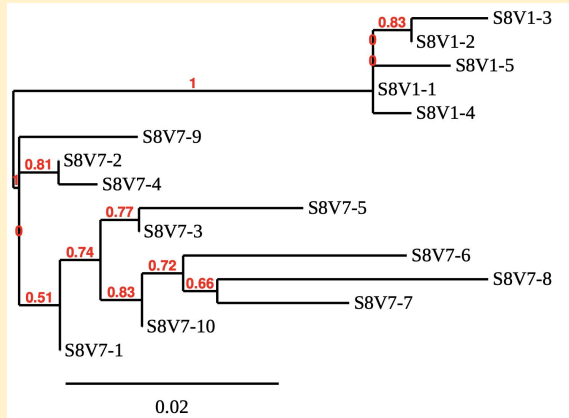
# Phylogenetic Trees of Non-progressors



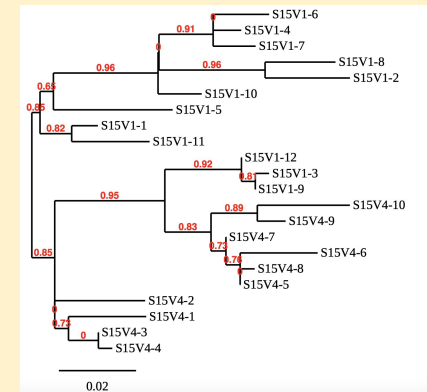
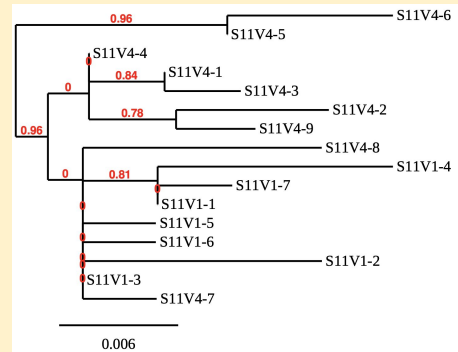
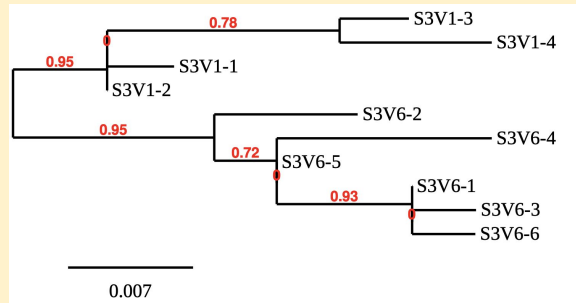
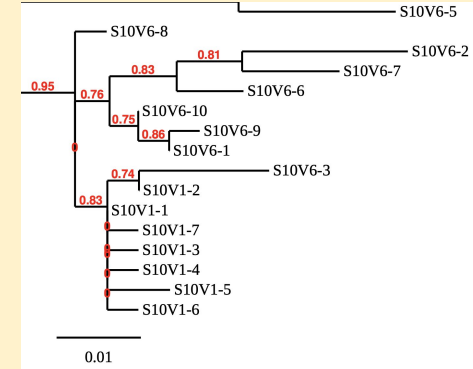
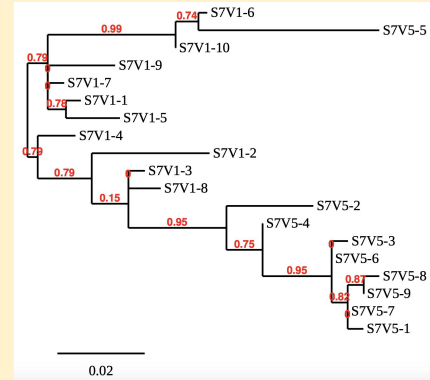
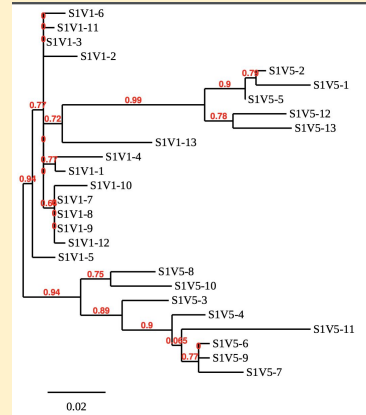
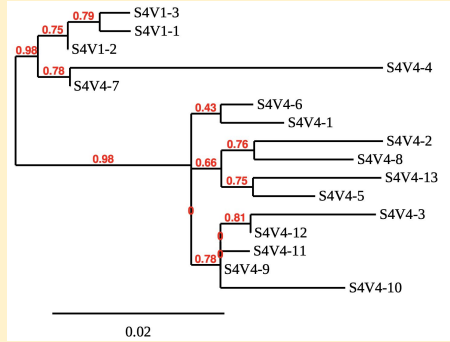
# Interpretation of Non-Progressor Phylogenetic Trees

- Non-Progressor showed less divergence and less diversity than progressor subjects.
- Non-Progressor showed possible selection against sequence change, shifted back to a previous strain of the virus.
- Non-progressors expressed the same characteristics in our analysis as Markham's conclusion.

# Phylogenetic Trees of Moderate progressors



# Phylogenetic Trees of Rapid Progressors





# Interpretation of Progressor Phylogenetic Trees

- Both moderate and rapid progressors showed an increase in diversity and divergence.
  - This supports the idea that mutation of the virus is directly proportional to the decline of CD4 T-cells.
- Progressors expressed the same characteristics in Markham's analysis.

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# CD4 T-cells and HIV Evolution.

- CD4 T-cell decline is directly proportional to the evolution of HIV.
- Non-Progressors favored absence of change, maintaining stable CD4 T-cell counts.
  - Non-Progressors showed less divergence and diversity in trees.
- Progressors favored against absence of change, revealing a relationship between mutation and decline in CD4 T-cell counts.
  - Moderate and Rapid Progressors showed increase in diversity and divergence in trees.
- The exclusion of analysis of interim visits did not affect the results of overall CD4 T-cell decline.

# Future Research

- Complete data should include the CD4 T-cell count and sequence of each visit.
- Inform when subject leaves study.
- Study the response of the immune system between the non-progressors and the rapid-progressors.

# References

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](https://doi.org/10.1073/pnas.95.21.12568) (PubMed ID: 98445411)

# Acknowledgements

- Phylogeny.fr was used to elaborate each of the phylogenetic tree.
- GenBank was used to get all the sequences of each visit.
- Dr. Dahlquist guidance throughout the research analysis.
- Markham's research data.
- BIOL 398-04 journal club.