

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

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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.

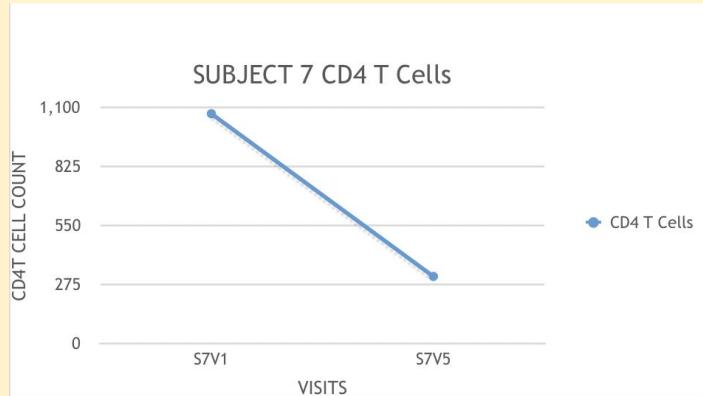
Subject	CD4 T Cells
S1V1	464
S1V5	14

Subject	CD4 T Cells
S2V1	715
S2V4	829

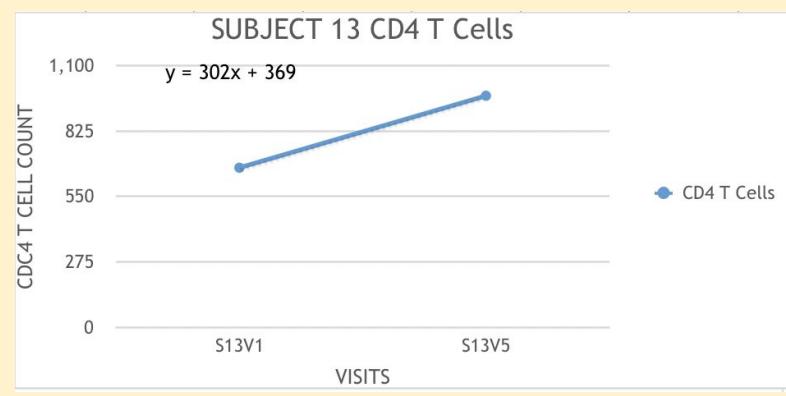
Subject	CD4 T Cells
S3V1	819
S3V6	47

- 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

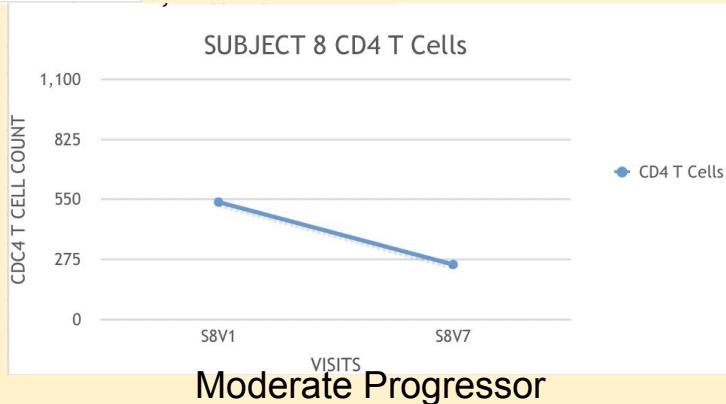
Graph and calculate the slope in order to classify the subjects



Rapid Progressor



Non-Progressor



Moderate Progressor

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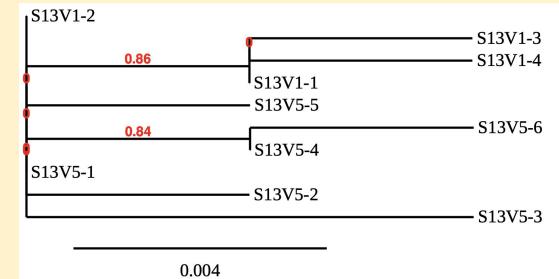
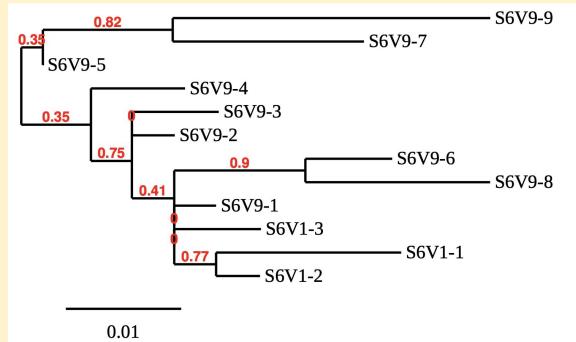
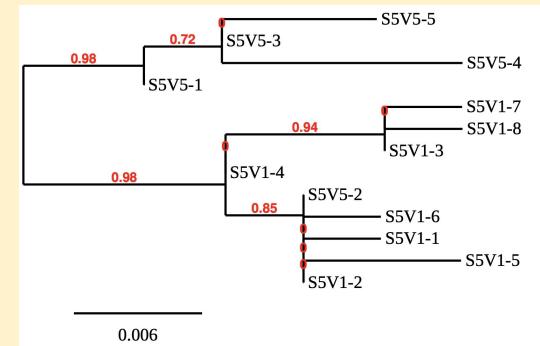
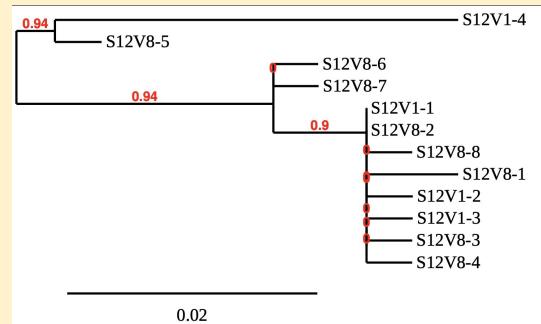
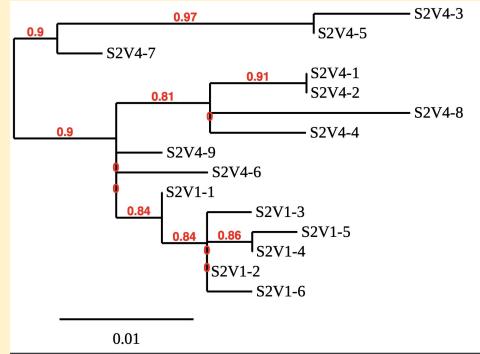
Classification of change in CD4 T-Cell count from first to last visit in each of the Progressor Types

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

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

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

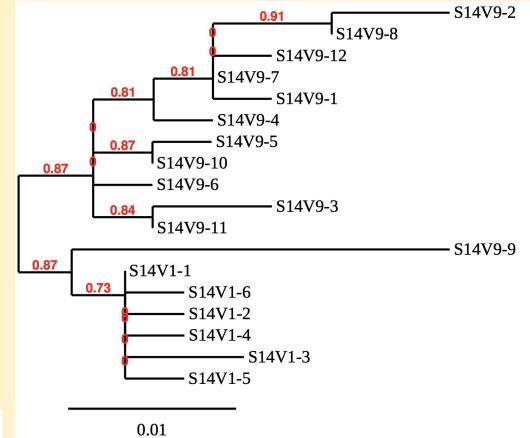
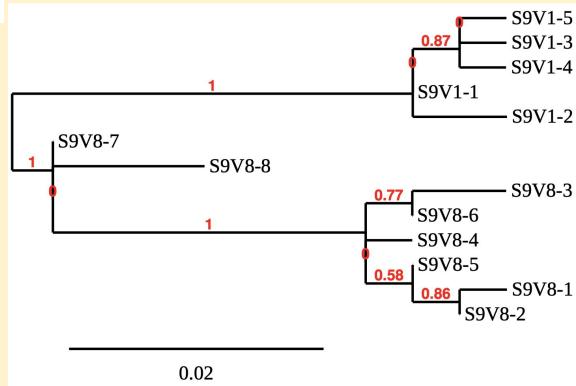
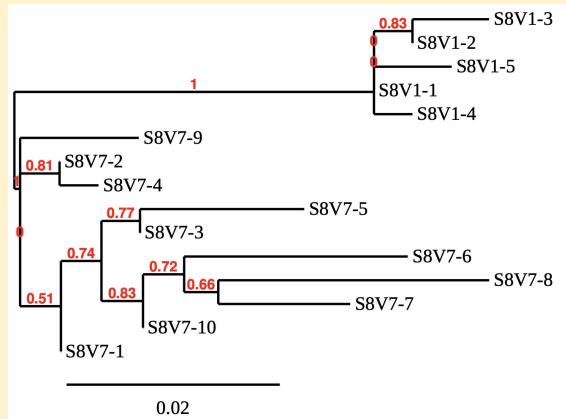
Phylogenetic Trees of Non-progressors



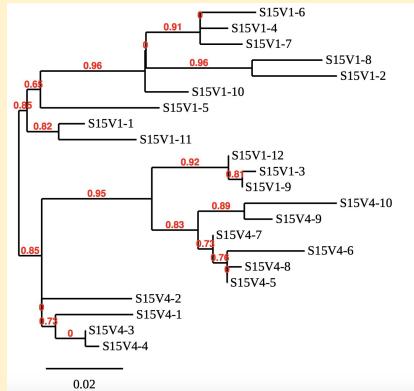
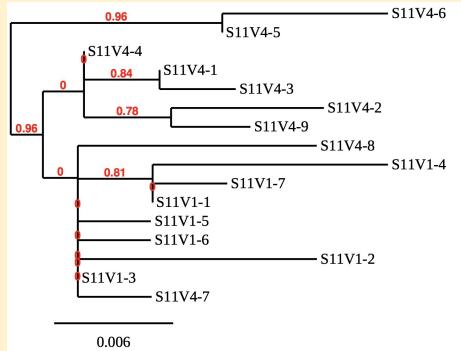
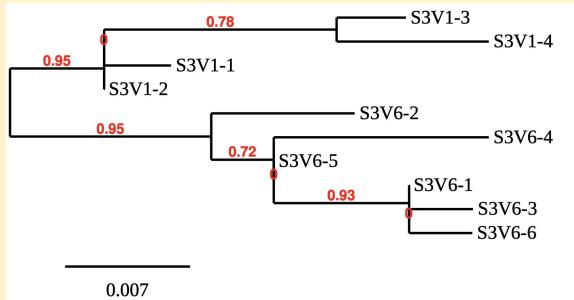
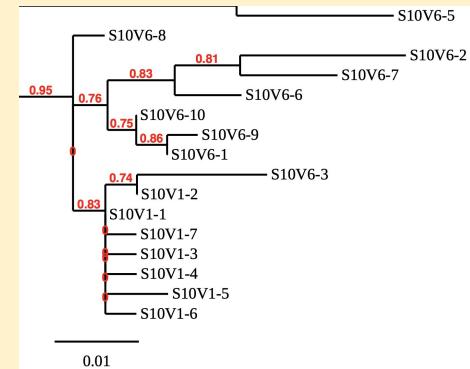
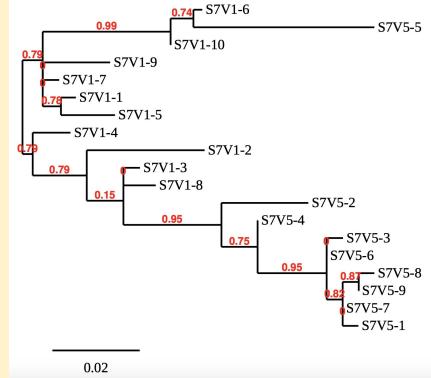
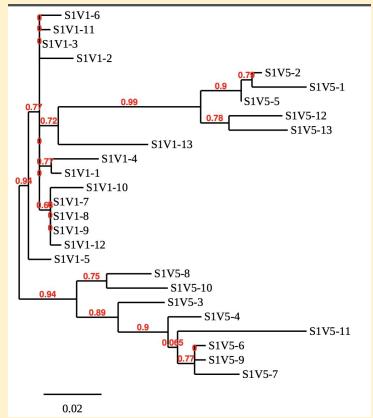
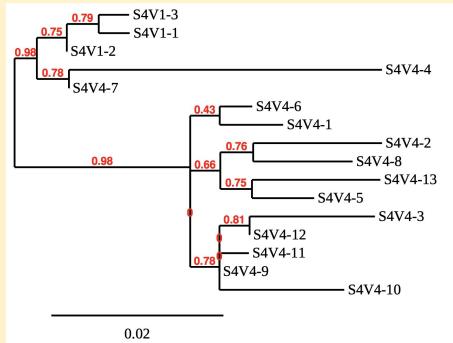
Interpretation of Non-Progressor Phylogenetic Trees

- 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.
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