

Subject 7 Rapid Progressor Classification Does Not Change Data Interpretation

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Outline

- Subject 7 Categorized as Moderate and Not Rapid Progressor
- Research Question
- Subject 7 Moved to Rapid Progressor Group
- Diversity and Divergence Between Progressor Group Changes
- Subject 7 Does Not Significantly Impact Diversity or Divergence
- Subject 7 Differs from Moderate Progressor Trees and Resembles Rapid Progressors
- Expanding Research on Markham et al. Data
- Summary

Subject 7 Categorized as Moderate and Not Rapid Progressor

- Markham et al. 1998 progressor categorization based on CD4 T cell count within 2 years of seroconversion
 - Subject 7 CD4 T cell decline of 392/year
 - Never fell below 200 CD4 T cells

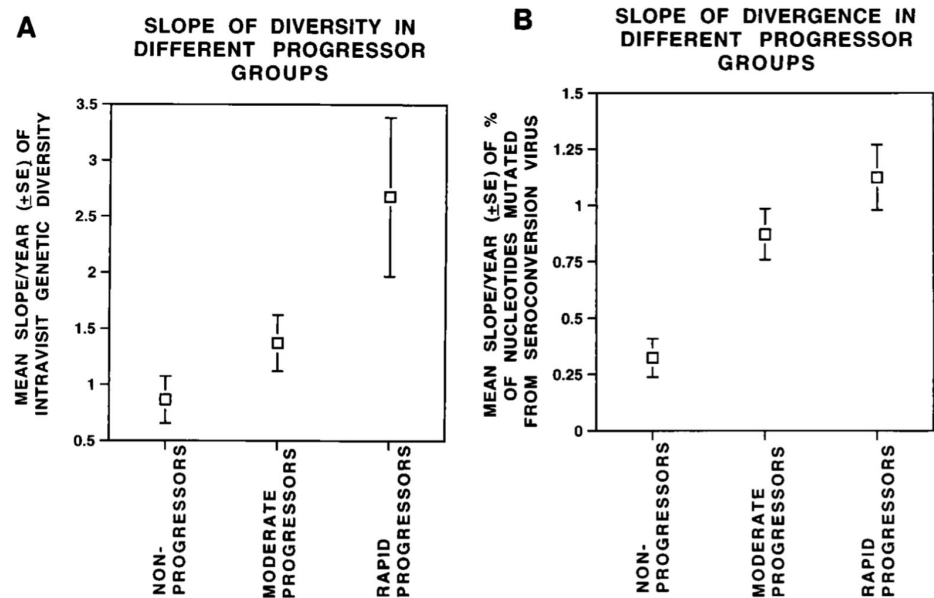
Table 1. Summary data on 15 seroconverters

Subject	No. of observations	Baseline			
		CD4	Median intravisit nucleotide differences among clones	Virus copy number (×10 ³)	Annual rate of CD4 T cell decline
Rapid Progressor					
Subject 4	4	1,028	0.90	6.8	−593
Subject 10	5	833	1.71	99.3	−363
Subject 11	4	753	2.27	62.2	−363
Subject 15	4	707	15.16	171.0	−362
Subject 3	5	819	1.82	302.5	−294
Subject 1	3	464	5.64	307.6	−117
Moderate Progressor					
Subject 7	5	1,072	2.27	317.6	−392
Subject 8	7	538	1.24	209.0	−92
Subject 14	9	523	1.00	50.9	−51
Subject 5	5	749	2.50	260.6	−41
Subject 9	8	489	9.49	265.0	−11
Subject 6	7	405	2.82	321.4	52

(Markham, 1998)

Subject 7 Categorized as Moderate and Not Rapid Progressor

- Diversity and divergence increased for all progressor groups
- Divergence- significance between:
 - Rapid and nonprogressor
- Diversity- significance between:
 - Rapid and nonprogressor
 - Moderate and nonprogressor



(Markham, 1998)

Research Question

How does the grouping of Subject 7 as a rapid progressor as compared to their original grouping as a moderate progressor change slope of diversity/divergence as well as compare to rapid progressor phylogenetic trees?



Subject 7 Moved to Rapid Progressor Group

Weighted Mean



- Multiplied each subject's given slope by their number of observations
- Added up all subject's weighted slope
- Divided it by total number of observations of all subjects

Graph



- Standard error calculated in Excel
- Graphs of standard error and weighted mean generated for both slope of diversity and divergence

Phylogenetic Tree



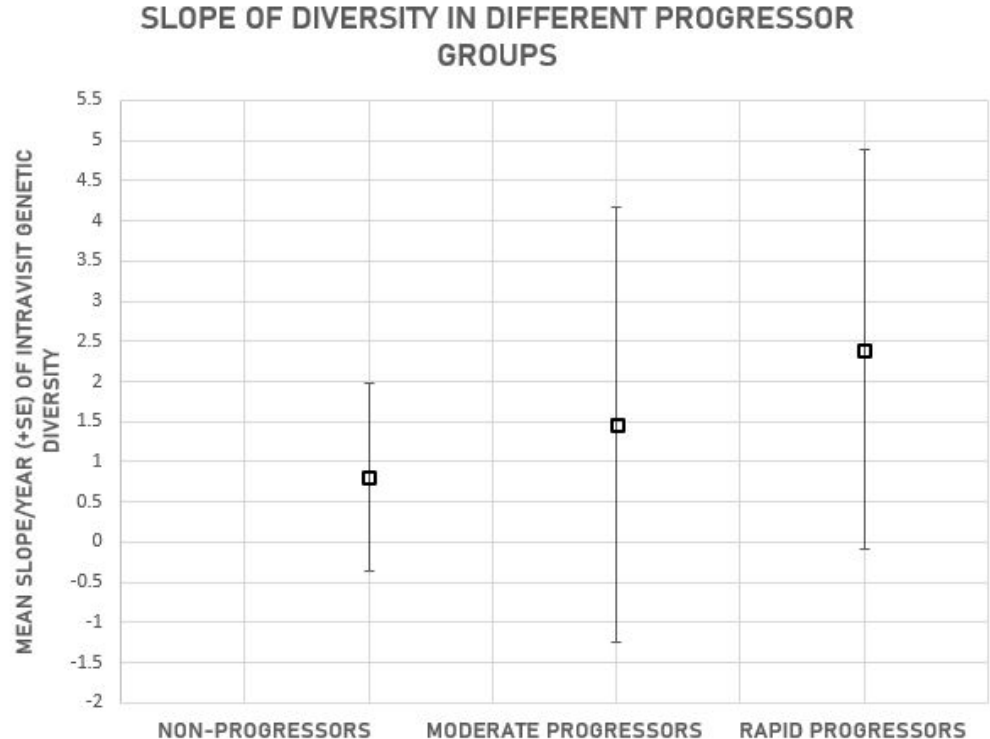
- Phylogenetic trees generated for subjects 15, 4, 10, 11, 3, 1, and 6 through Phylogeny.fr

Outline

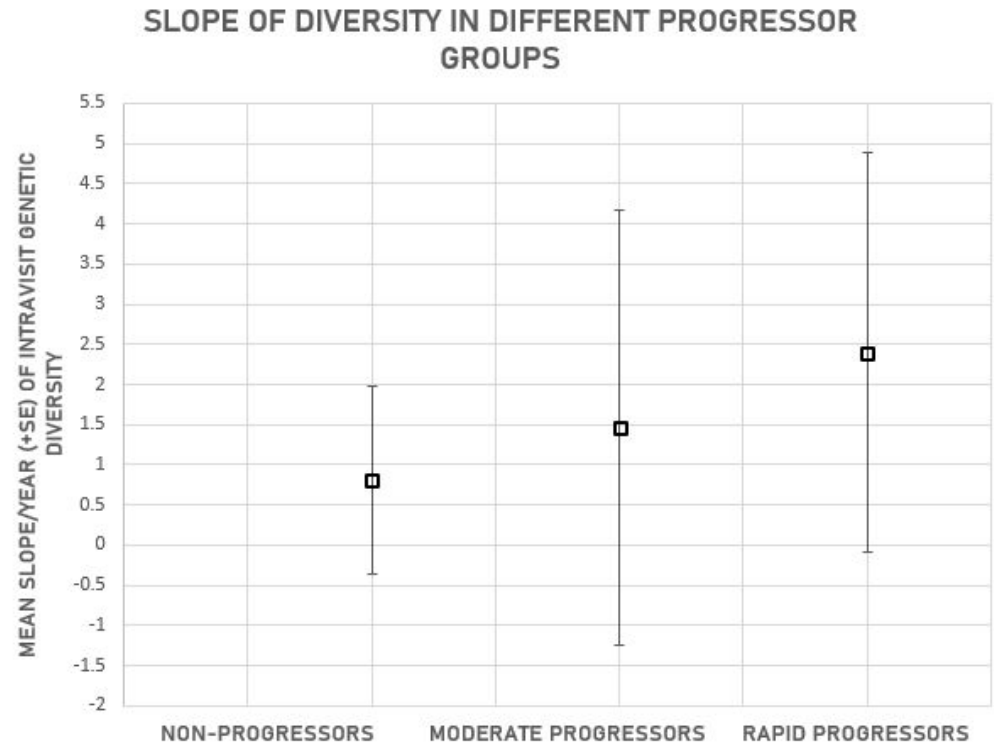
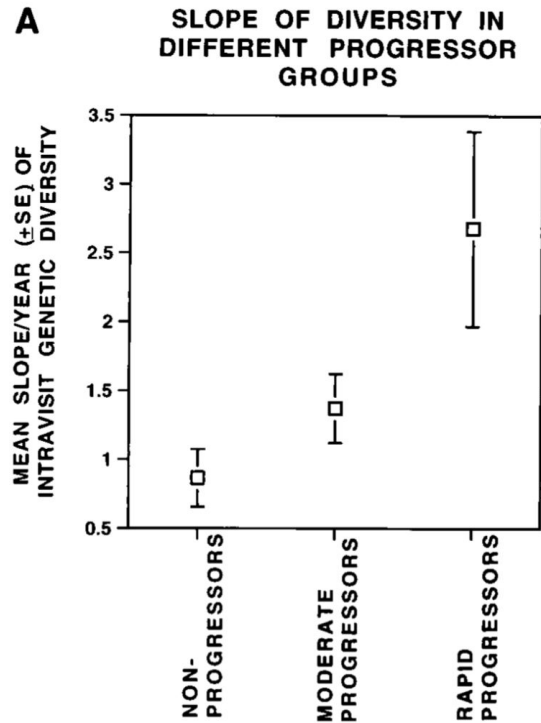
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Diversity Between Progressor Groups Changes

- Rapid progressor mean slope: 2.4
- Moderate progressor mean slope: 1.47
- Nonprogressor: remains the same

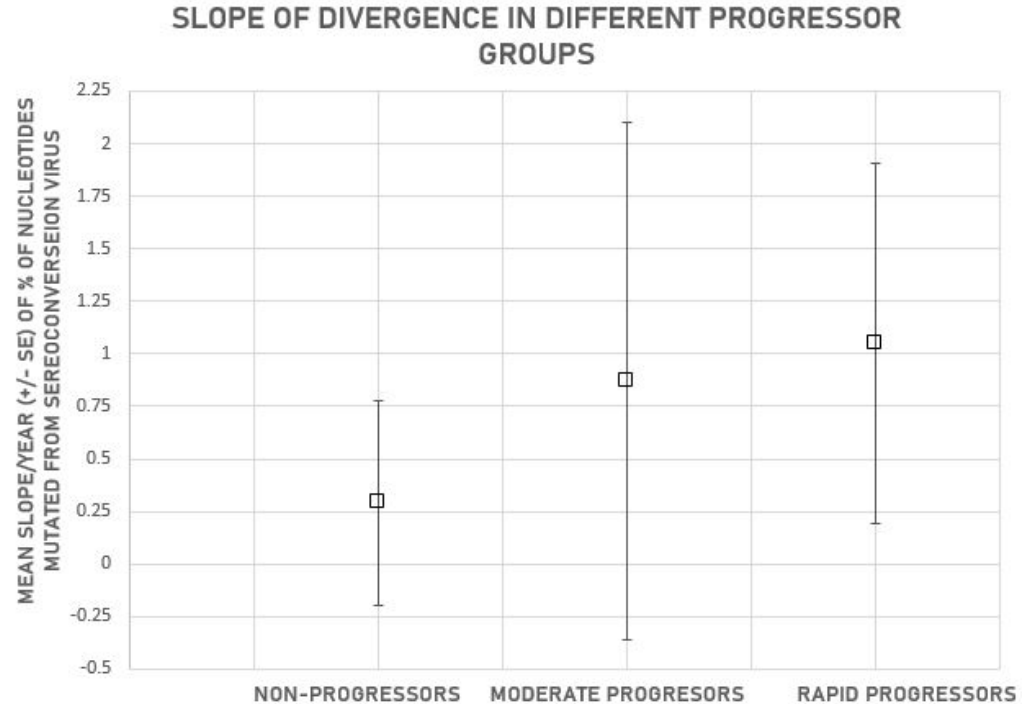


Diversity Between Progressor Groups Changes

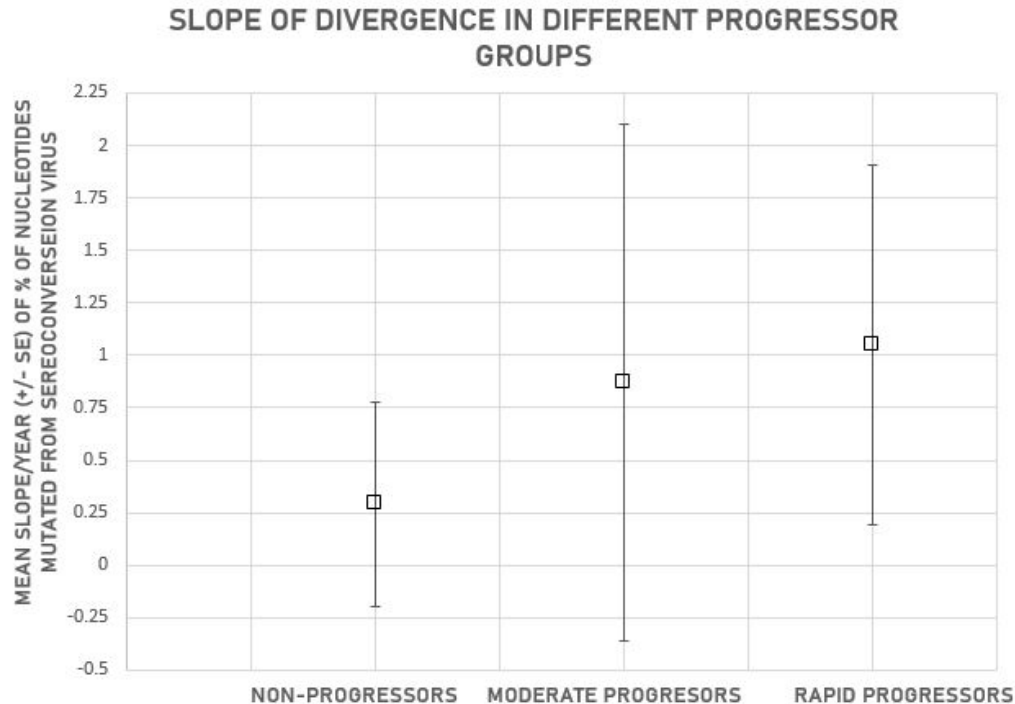
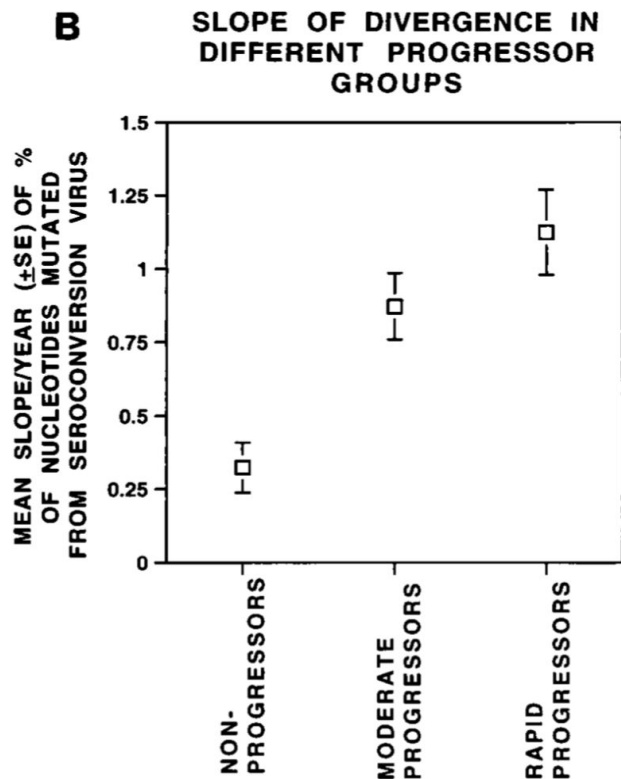


Divergence Between Progressor Groups Changes

- Rapid progressor mean slope: 1.05
- Moderate progressor mean slope: 0.87
- Nonprogressor: remains the same



Divergence Between Progressor Groups Changes



Subject 7 Changed Diversity and Divergence Slopes

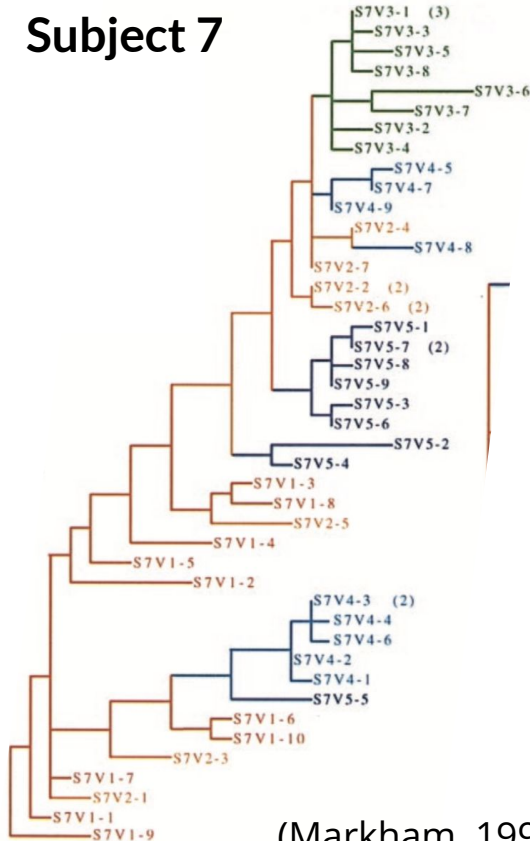
- Inclusion of Subject 7 into rapid progressor group decreased the slope of diversity
- Inclusion of Subject 7 into rapid progressor group decreased the slope of divergence
- Comparison of slopes between each progressor group are nonsignificant ($p > 0.05$)
- Indicate that the classification of subject 7 was not impactful to overall data interpretation

Outline

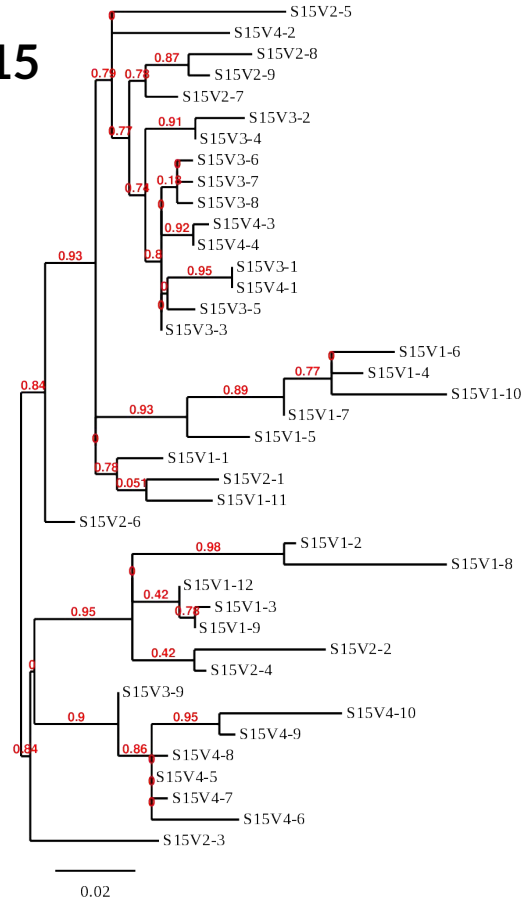
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Subject 7 Closely Resembles Subject 15

Subject 7



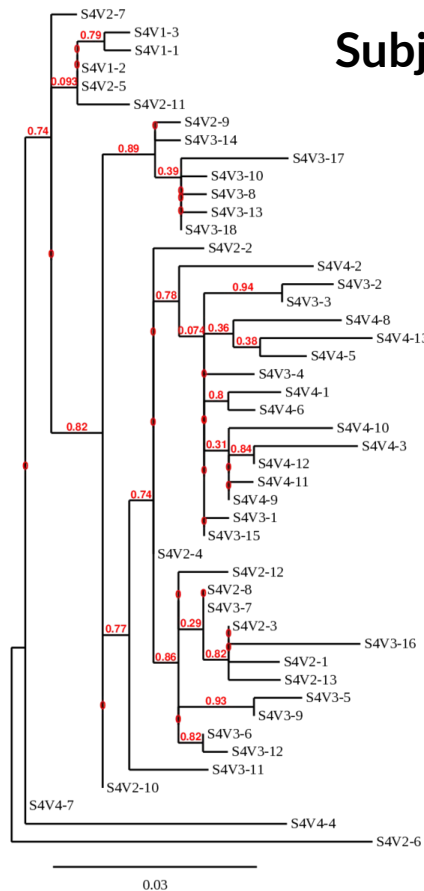
Subject 15



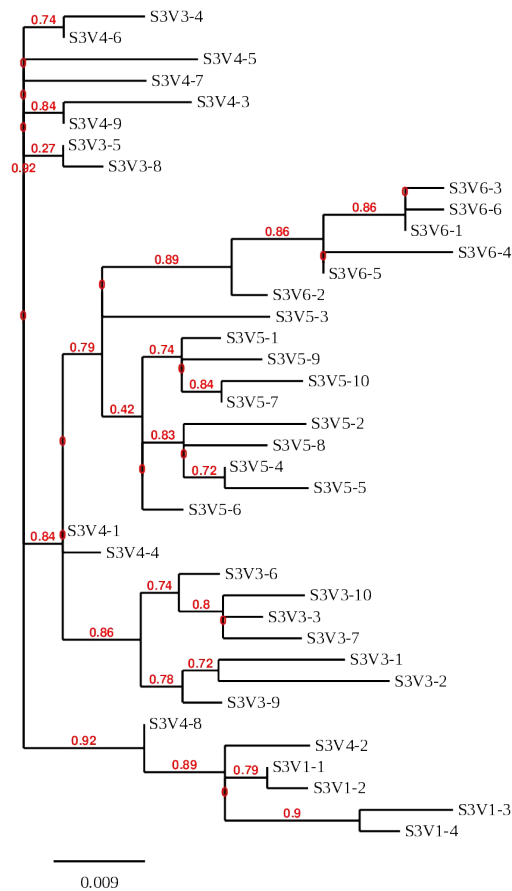
(Markham, 1998)

Subjects 3 and 4 Present Similar Trees

Subject 4

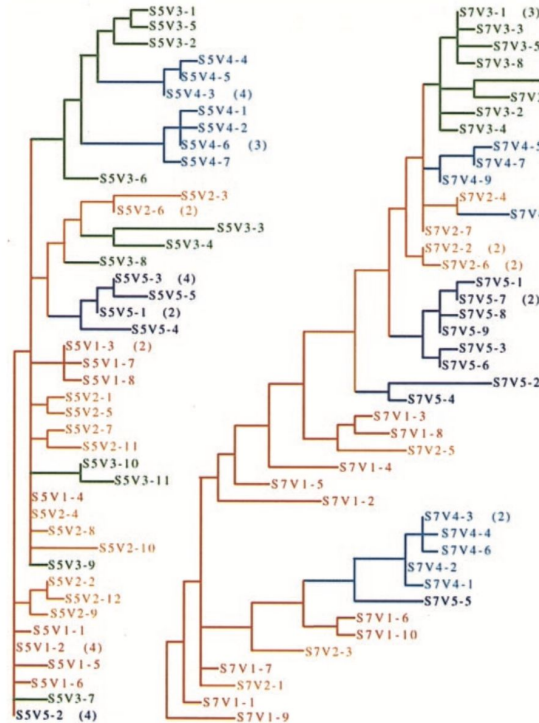


Subject 3

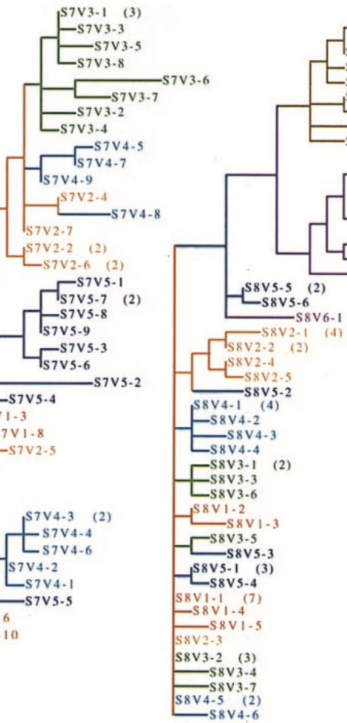


Subject 7 Differs from Moderate Progressor Phylogenetic Trees

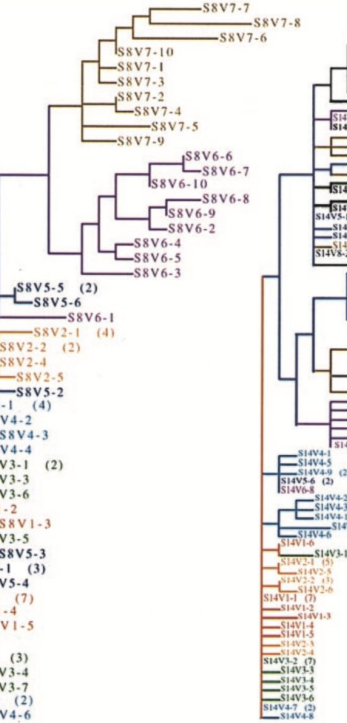
Subject 5



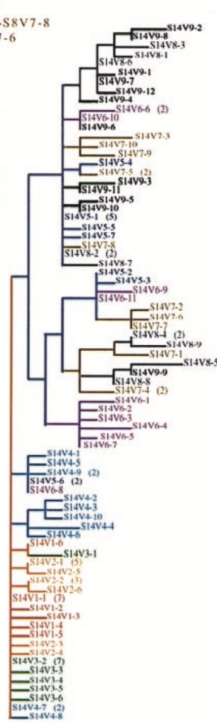
Subject 7



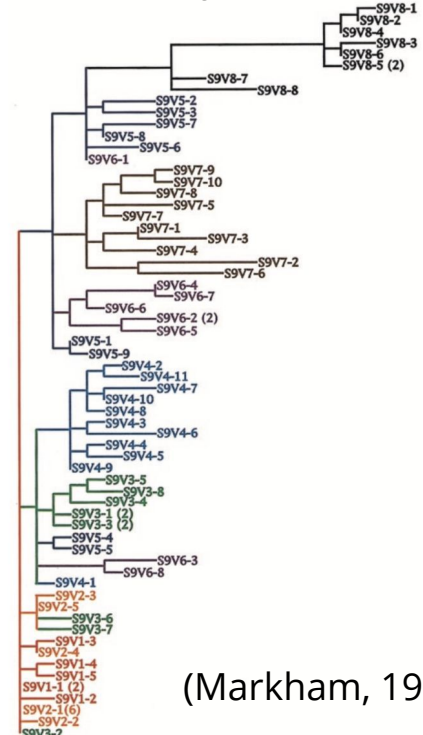
Subject 8



Subject 14



Subject 9



(Markham, 1998)

Subject 7 Tree Closely Resembles Rapid Progressor Trees

- Indicates that evolution of clones of subject 7 is more similar to rapid progressors
- No evidence that Subject 7 was miscategorized
 - Did not significantly impact slopes for moderate and rapid progressors

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Expanding Research on Markham et. al Data

- Study differences in between first and last visits since each subject had a different number of observations
- Fully examine non progressor trees as well to see if patterns of evolution present differently
- Change the criteria for different progressor groups

Summary

- Diversity and divergence between progressor group changes
- Subject 7 did not significantly impact diversity or divergence
- Rapid progressor trees showed similarity
- Subject 7 differed from moderate progressor trees and resembled rapid progressors
- Subject 7 progressor classification did not change data interpretation
- Potential for progressor categorization to yield more similarities between phylogenetic trees

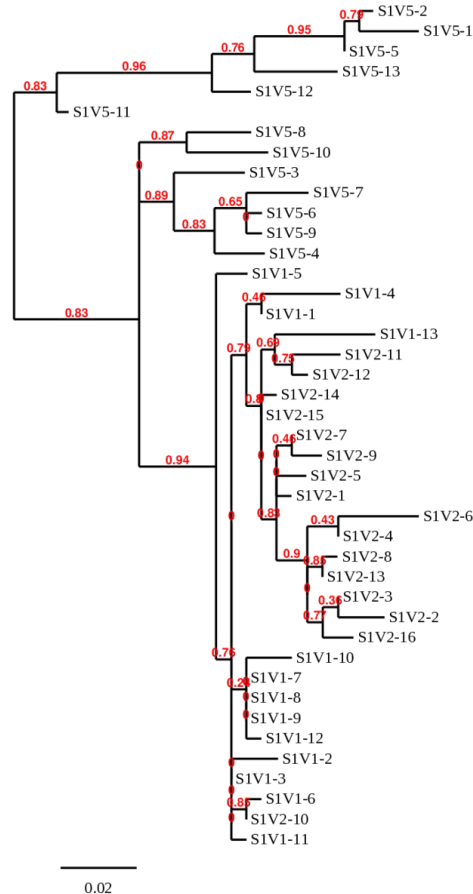
References

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 (PubMed ID: 9770526)

Thank you to the LMU Biology
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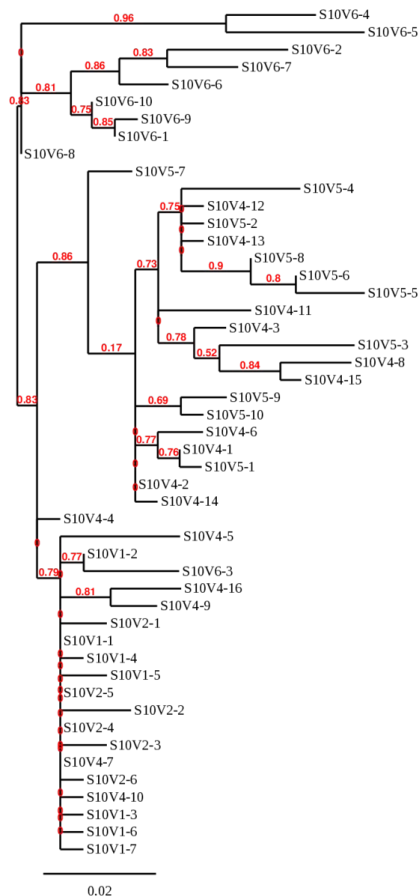
Subject 1 does not resemble other trees

BACKSLIDE

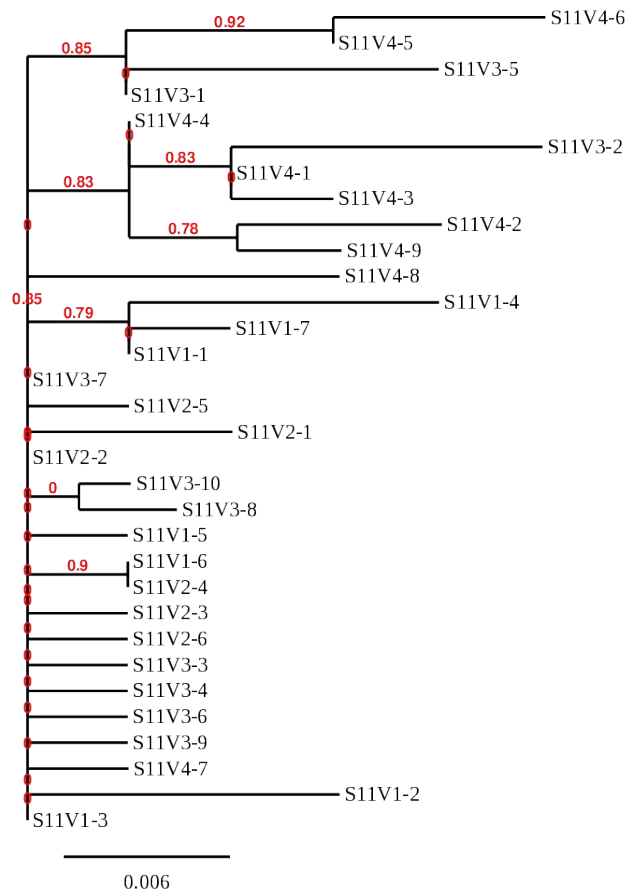


Subjects 10 and 11 Present Similar Trees

Subject 10



Subject 11



BACKSLIDE