Subtyping Sequences from *Patterns of HIV-1 evolution in individuals with differing rates of CD4 T cell decline* by Markham et al.

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Outline

- Markham et al. did not take into account the different subtypes of HIV-1, so there may be a correlation between Markham's grouping and the subtypes.
- Collinson-Streng et al. had sequences of HIV-1 from Uganda separated by subtype.
- When compared, the two groups of sequences were drastically different sequentially.
- A broader look at the different subtypes needs to be done to see if they were even grouped together sequentially.
- Performing a study similar to Markham et al. with grouping by subtype could yield interesting results.

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Markham et al. grouped subjects by CD4 T-Cell Count

- Markham et al. studied the relationship between CD4 T-Cell decline and diversity of HIV-1 sequences
- In the study the subjects were split into three groups; rapid progressors, moderate progressors, and nonprogressors
- Markham et al. did not take into account the different subtypes of HIV-1 which could lead to the different progression rates of the virus

Collinson-Streng et al. Grouped Subjects by HIV-1 Subtype

- Collinson-Streng et al. studied distribution of HIV-1 subtypes in different areas of Uganda
- While both studies were centered around diversity of HIV-1, the study by Collinson-Streng et al. grouped subjects by HIV-1 subtype while Markham et al. grouped subjects by CD4 T-Cell decline.

Grouping Markham et al. sequences by subtype

- Our question: Will the Markham et al. sequences group into the 10 different subtypes present in the Collinson-Streng et al. study?
- Hypothesis: Yes, the Markham et al. sequences will group themselves close enough to certain subtypes from the Collinson-Streng et al. sequences to determine their subtype.

Collecting Markham et al. sequences

HIV-1 subject 1 visit 1 clone 8 from USA, envelope glycoprotein V3 region (env) gene, partial cds

4. 285 bp linear DNA

Accession: AF016767.2 GI: 33187149

GenBank FASTA Graphics

HIV-1 isolate S3V6-1 from USA envelope glycoprotein (env) gene, partial cds

5. 285 bp linear DNA

Accession: AF089142.1 GI: 3916714

GenBank FASTA Graphics

- 2 clones from each of the 15 subject's first visit were randomly selected.

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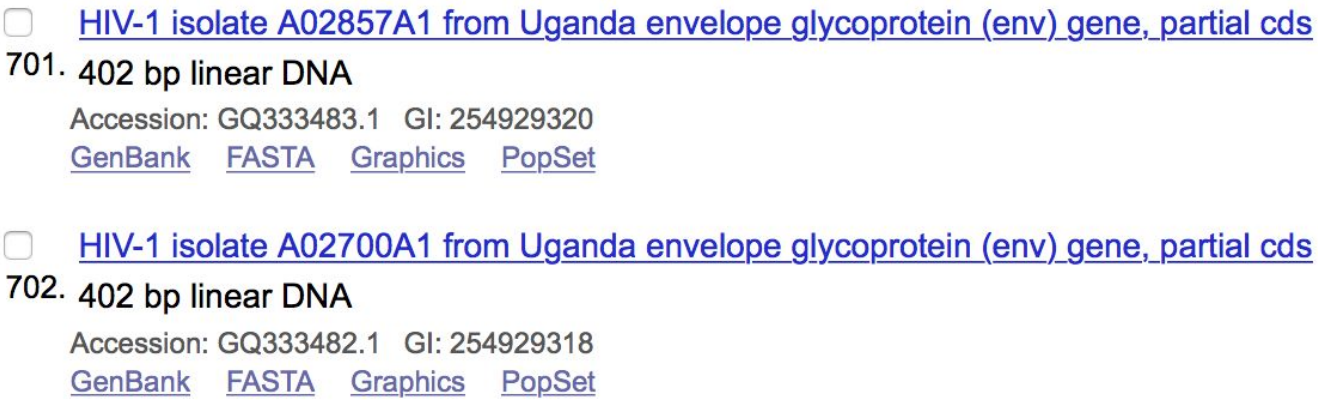
10 Different subtypes described in Collinson-Streng et al. sequences



- Around 72 sequences per subtype in this study
- 3 sequences from each of the 10 subtypes were randomly selected.

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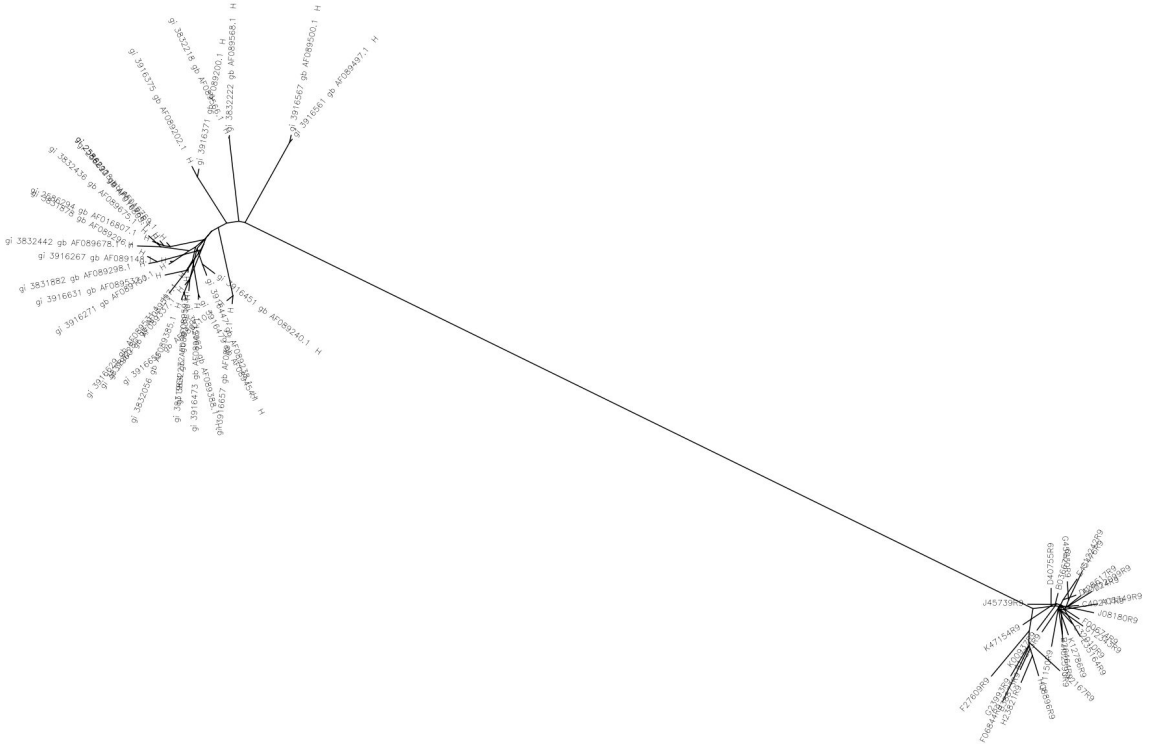
Comparing the two groups of sequences: Methods

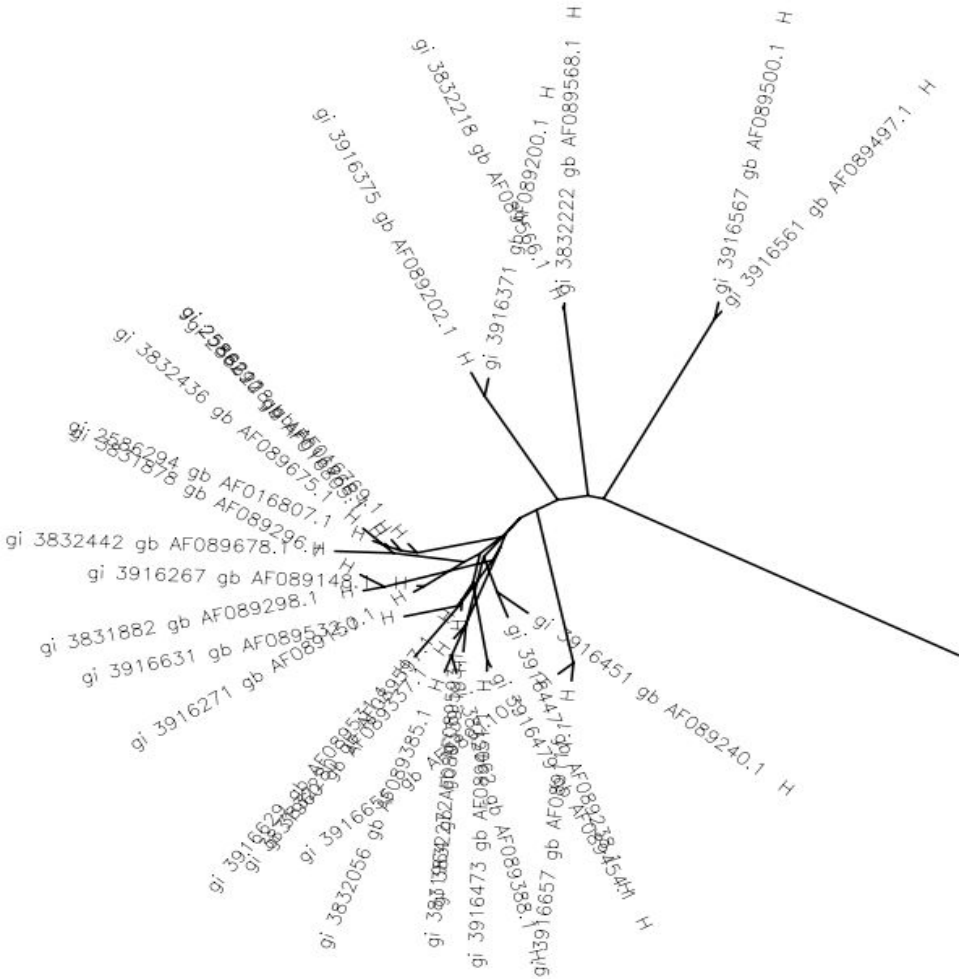
- Each of the Ugandan sequences had to be cut due to their length.
- The two groups were compared together in the multiple sequence alignment function of Biology Workbench
  - Postulated an unrooted tree and data for the values of S and theta.
- The sequences were then ran in the Clustaldist function
  - Gave us the table used for minimum and maximum

Comparing the two groups of sequences: Unrooted Tree



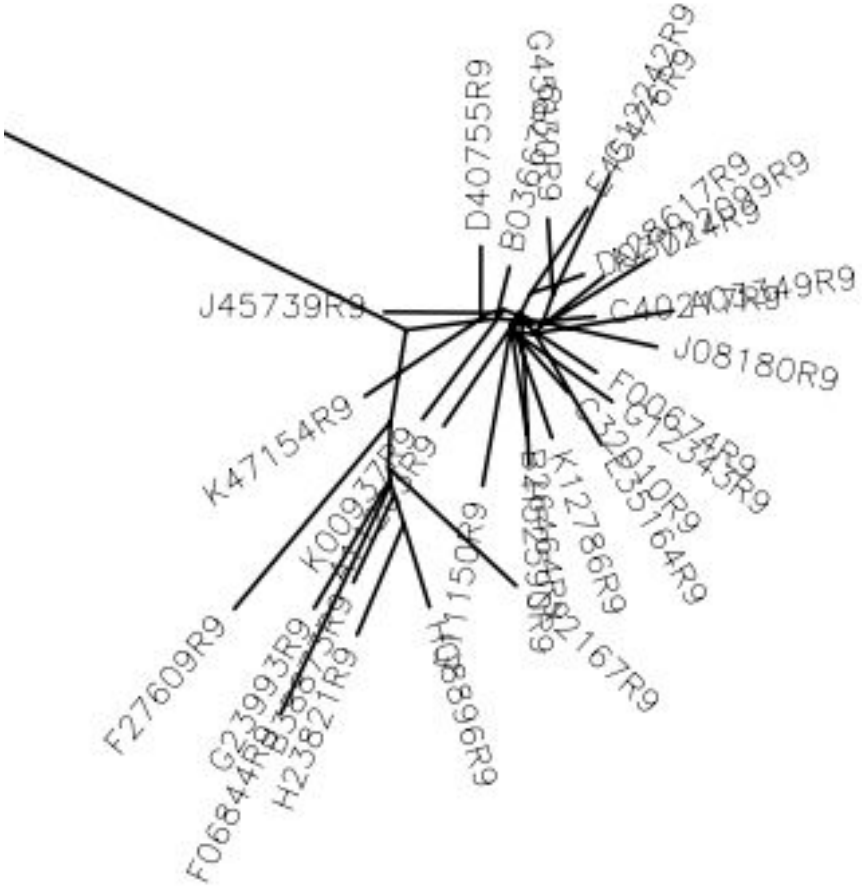
Comparing the two groups of sequences continued

Markham et al. sequences



Comparing the two groups of sequences continued

Collinson-Streng et al. sequences



Comparing the two groups of sequences: Diversity Values

	# of Clones	S	θ-Value	Min. Difference	Max. Difference
Markham et al. vs Collinson-Streng et al.	260	260	55.76	2	174
Markham et al.	144	144	36.36	0	59
Collinson-Streng et al.	109	109	27.52	8	47

Overview of Results and Reasons

- The two groups of sequences were genetically very different
  - The Markham study's sequences were much more diverse than Collinson-Streng's sequences.
- This was most likely due to the differences in time and place where the two studies took place
- More shockingly, there was genetic diversity amongst subjects from the same subtype from the study by Collinson-Streng et al.

Hemelaar, Joris, et al. 2004

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Comparing the HIV-1 subtypes in more depth

- The different subtypes we used showed no correlation between each other.
  - We expected at least the same subtypes to group together.
- In order to prove that there was no correlation between the subtypes, we would have to expand our comparison to a lot more sequences from each subtype

Using Markham's methods to correlate progressors to subtypes

- Grouping sequences by subtypes and running the same types of tests as the Markham et al.
- Using the results of this future study, we would be able to correlate the subtypes with the different types of progressors in Markham.

References

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Acknowledgements

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