

**Work in Progress:**  
**Does A Significant Change in CD4  
Cell Count Affect The Number of  
Amino Acid Mutations in A Subject's  
Corresponding DNA Sequence.**

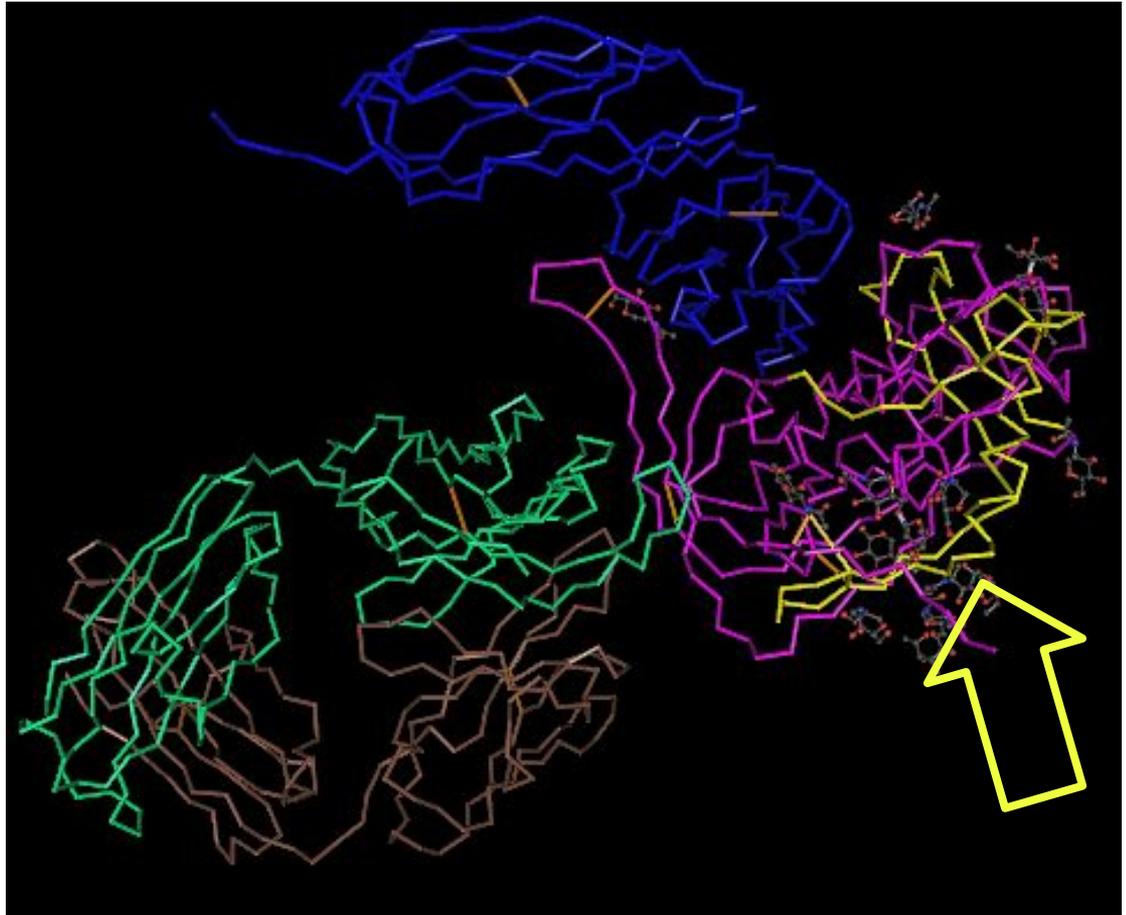
Courtney Merriam and Shivum Desai  
Biology 368: Bioinformatics  
November 8, 2016

# Outline

- Markham paper focused on a segment of DNA in the V3 region.
- This experiment was designed to show a connection between the change in a subject's CD4 cell count and their amino acid sequences.
- The results of this experiment showed little evidence of the correlation between CD4 cell count and amino acid mutations.

# Markham Focused On The V3 Region

- ❖ We used the sequence of this protein to find the position of the Markham sequence that started with *EVV* ended with *HSS*
- ❖ The highlighted section is what corresponds to the Markham sequence



# Outline

- Markham paper focused on a segment of DNA in the V3 region.
- This experiment was designed to show a connection between the change in a subject's CD4 cell count and their amino acid sequences.
- The results of this experiment showed little evidence of the correlation between CD4 cell count and amino acid mutations.

# **Subject's First and Last Visits Were Compared To Observe Mutational Differences In Amino Acids.**

- The purpose of this experiment was to show a correlation between the subject's CD4 cell count and the number of mutations in their amino acid sequence.
- Clones from each subject's first and last visits were compared together.
  - Rapid progressors subjects 10 and 4
  - Nonprogressors subjects 12 and 13

# **A Decrease In CD4 Cell Count And An Increase In Amino Acid Mutations Was Suspected.**

- Hypothesis #1: It was hypothesized that the rapid progressor subjects would have a larger amount of mutations, when comparing their first and last visits, than the nonprogressor subjects.
- Hypothesis #2: A large decrease in a subject's CD4 cell count would correlate with a large amount of amino acid mutations.

# Outline

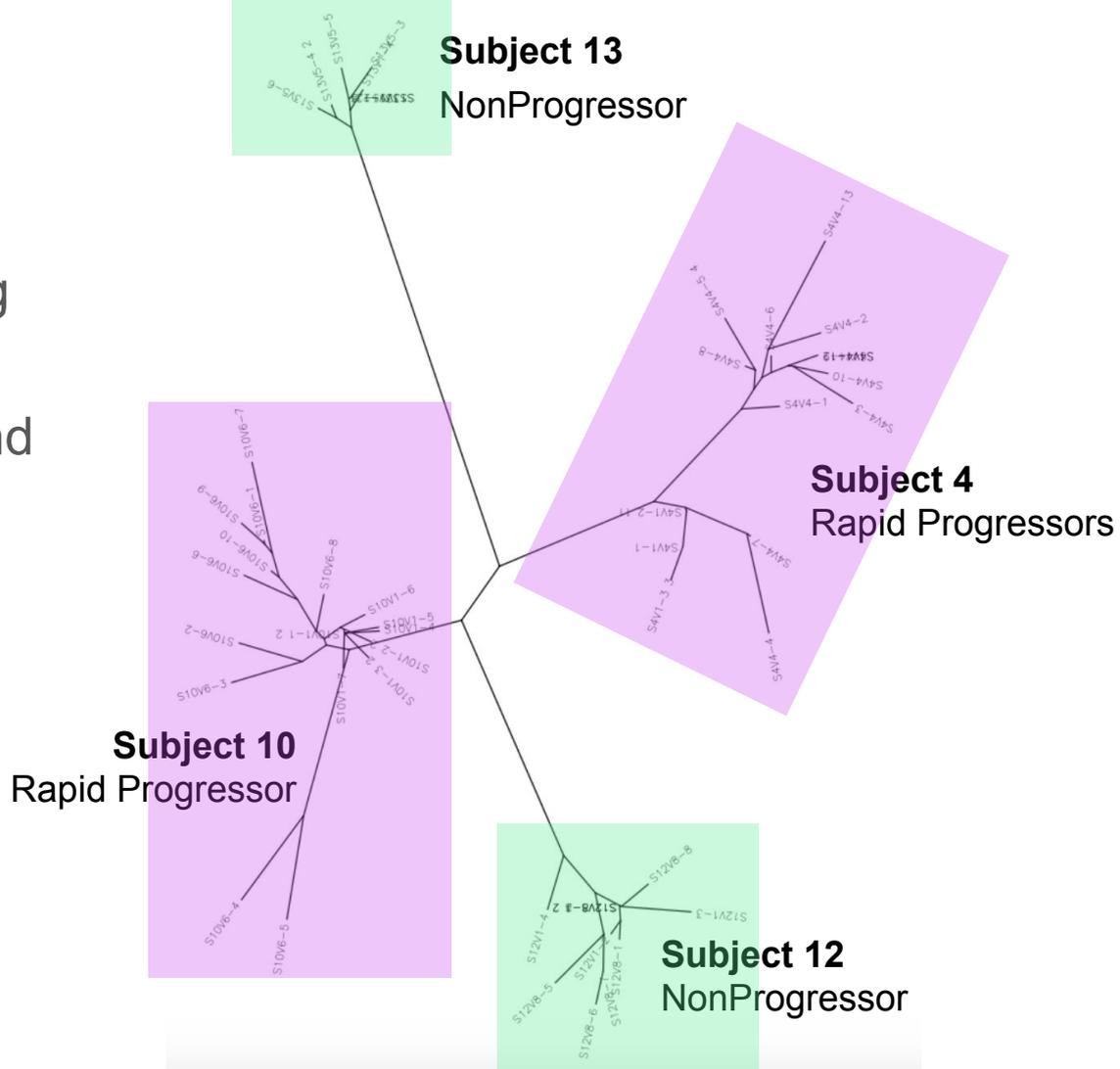
- Markham paper focused on a segment of DNA in the V3 region.
- This experiment was designed to show a connection between the change in a subject's CD4 cell count and their amino acid sequences.
- The results of this experiment showed little evidence of the correlation between CD4 cell count and amino acid mutations.

# Several Processes Were Used to Obtain Data In This Experiment.

- A multiple sequences alignment was conducted to observe trends in amino acid mutations.
  - Intent was to identify a trend of mutations which could be classified based on their characteristics. (i.e. polar uncharged→nonpolar)
- ClustalDist tool was used to measure the similarity between all the subjects, their visits, and clones.

# Analysis of Unrooted Tree

- Unrooted Tree presenting subjects 4, 10, 12, 13.
  - Including their first and last visits.
- Subjects 4 and 10 are **rapid progressors**
- Subjects 12 and 13 are **NonProgressors**



# Visual Examination of Multiple Sequence Analysis Showed No Trend In Amino Acid Mutations

## Amino Acid Mutations Between Subject's First and Last Visits

- Subject 4 → 1 mutation
- Subject 10 → 8 mutations
- Subject 12 → 3 mutations
- Subject 13 → 0 mutations

None of these mutations that occurred had any type of trend that showed a consistent change in the characteristics of the amino acids.

# Results From ClustDist Support Both Hypotheses

## Experimental Subjects

- Subject 13-visits 1 and 5
- Subject 12-visits 1 and 8
- Subject 10-visits 1 and 6
- Subject 4-visits 1 and 4

## ClustalDist Results

- Subject 13: 0.021
- Subject 12: 0.053
- Subject 10: 0.116
- Subject 4: 0.117

# Summary

- The Markham paper focused on a specific sequence of DNA in the V3 region of the gp120 gene.
- This experiment was designed to show a connection between the change in a subject's CD4 cell count and their amino acid sequences.
- The results of this experiment were slightly conflicting, but overall did not show any evidence of a correlation between CD4 cell count and amino acid mutations.

# Acknowledgments

We would like to thank Dr. Dahlquist and the Department of Biology at Loyola Marymount University for their help on this presentation.

# References

- Kirchherr, J. L., Hamilton, J., Lu, X., Gnanakaran, S., Muldoon, M., Daniels, M., Kasongo, W., Chalwe, V., Mulenga, C., Mwananyanda, L., Musonda, R.M., Yuan, X., Montefiori, D.C., Korber, M.T., Haynes, B.F., & Musonda, R. M. (2011). Identification of amino acid substitutions associated with neutralization phenotype in the human immunodeficiency virus type-1 subtype C gp120. *Virology*, 409(2), 163-174. DOI: 10.1016/j.virol.2010.09.031
- Markham, R.B., Wang, W.C., Weinstein, 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. Dos: 10.1073/pnas.95.21.12568