Finding graphical correlations between *Θ* and CD4 T-cell levels in different HIV-1 progressor groups

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BIOL 368
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Outline

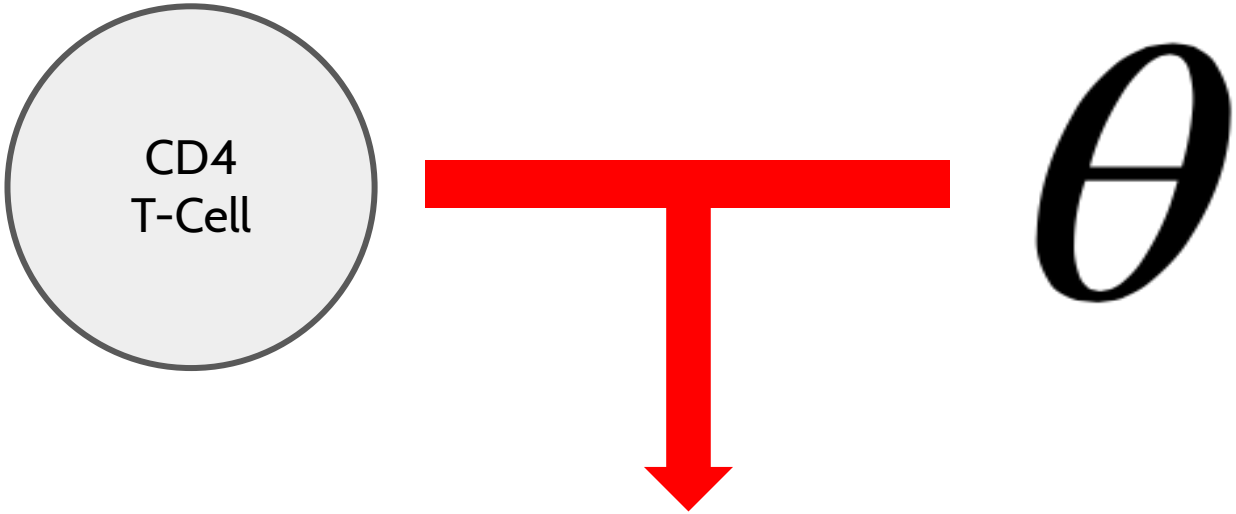
- **Markham *et. al*. (1998) found that higher levels of genetic divergence in HIV-1 variants were associated with greater declines in CD4 T-cell levels.**
- Θ and CD4 T-cell levels were plotted against each other within each progressor group.
- No groups had "strong" correlations, except Subject 14, who had a "relatively strong" correlation.
- Non-progressor group data showed a **direct** relationship, rather than an **inverse** relationship.
- The data was supported by our model, with the exception of non-progressors who show sustained CD4 T-cell levels.

Gaardbo *et. al.*, 2012

As genetic divergence increases, CD4 T-cell levels decrease.

- Those in the rapid progressor group lost, on average, 349 T-cells per year (Markham *et. al.*, 1998).
- High mutation rates allow for fast adaptation in a host, which makes the HIV-1 virus hard to "cure."
- Θ represents genetic divergence, or how clones have changed through time.
- With more genetic variability comes more immediate T-cell loss.

Ultimate Goal



Graphical correlation?

Hypotheses

- **Null**: There is not an inverse relationship between Θ vs. CD4 T-cell levels in the HIV-1 patients in the study.
- **Alternate**: There is an inverse relationship between Θ vs. CD4 T-cell levels in the HIV-1 patients in the study.
- If the p-value ≤ 0.05, we will reject the null hypothesis.

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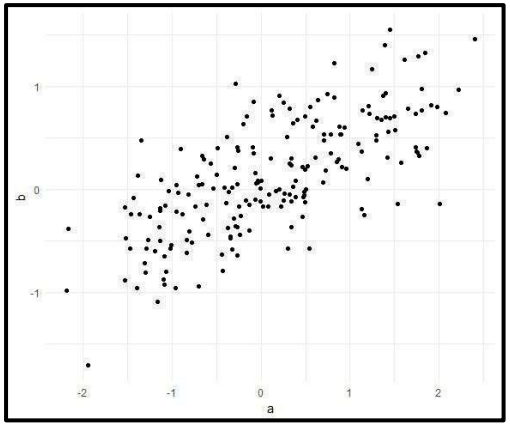
Comparing Θ and CD4 T-cell levels

- Created scatterplots of Θ vs. CD4 T-cell levels in Microsoft Excel and placed regression lines and R^2 on each graph.
- Deleted data points in which Θ values were not recorded.
- Clustered sequence alignment and phylogenetic tree created for Subject 14.
- Utilized LINEST and FDIST on Excel for statistical analyses of linear regressions.

Θ	CD4
2.980	749
6.445	768
8.535	648
4.305	552
2.980	698
2.828	405
2.121	223
3.867	351
5.031	387
7.777	471
8.837	399
8.463	556
9.898	1072
8.095	740
5.302	333
7.070	273
8.484	312



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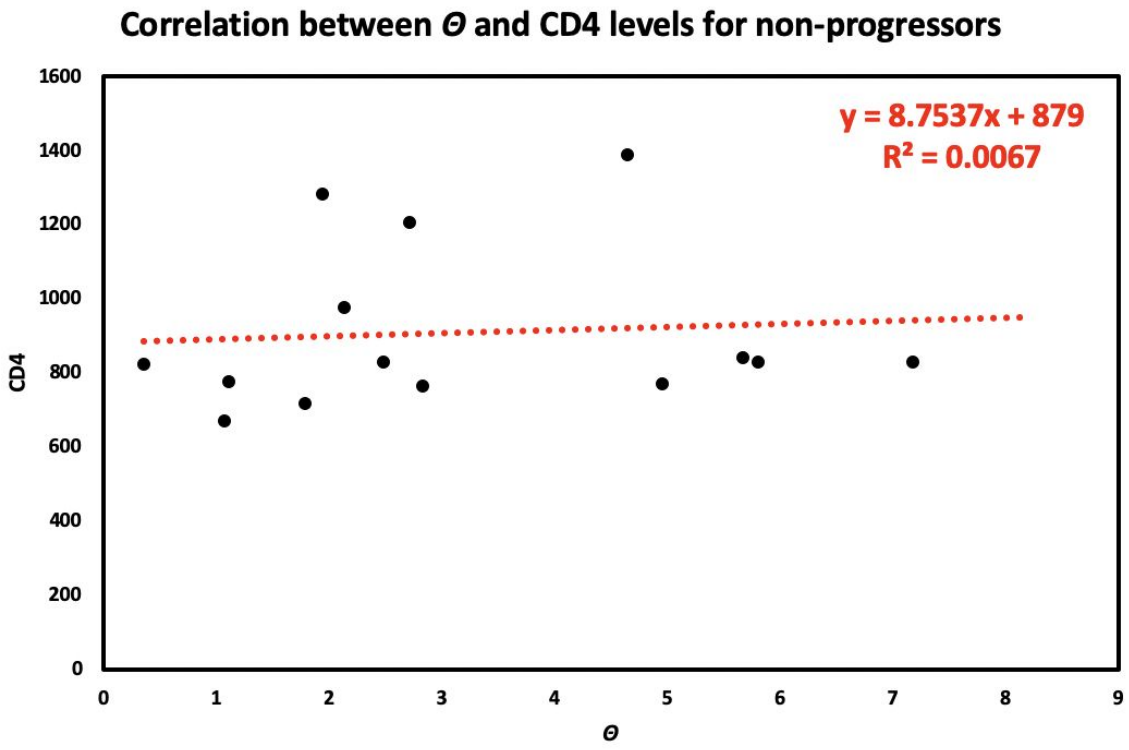
Non-progressor data indicates a slight direct relationship.

P-value = 0.936

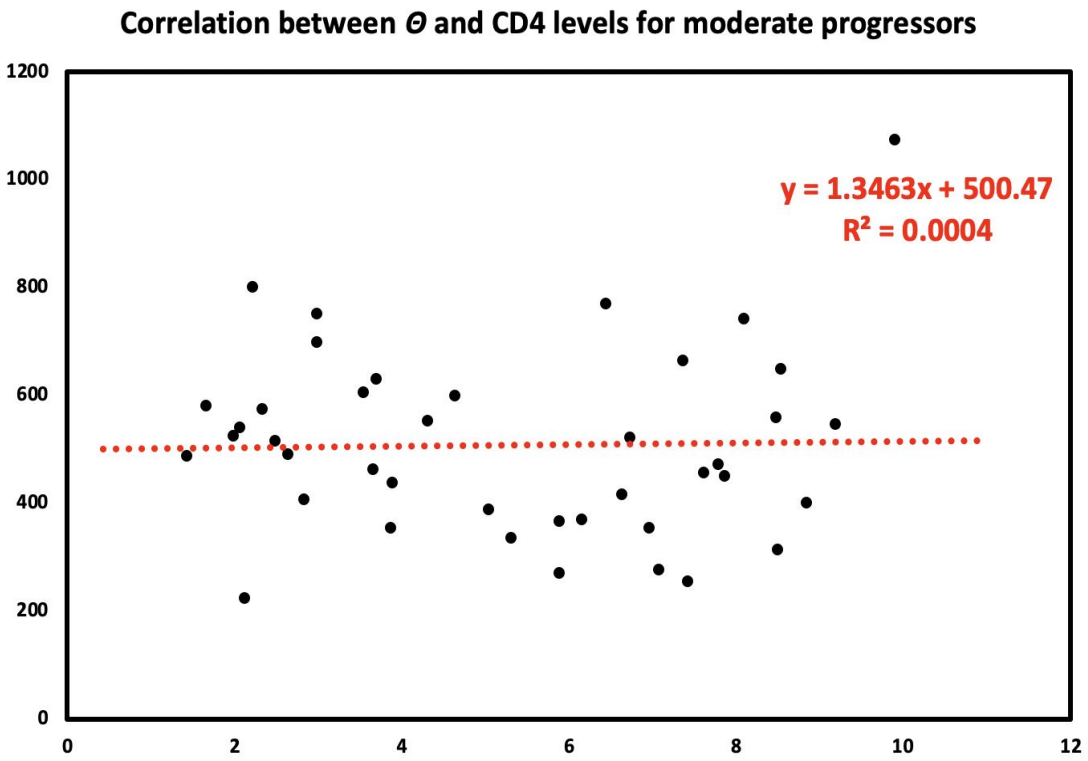
P>0.05, so we fail to reject the null. There is not significant statistical evidence to say that there is an inverse relationship.



Moderate progressors show no correlation between variables.

P-value = 0.903

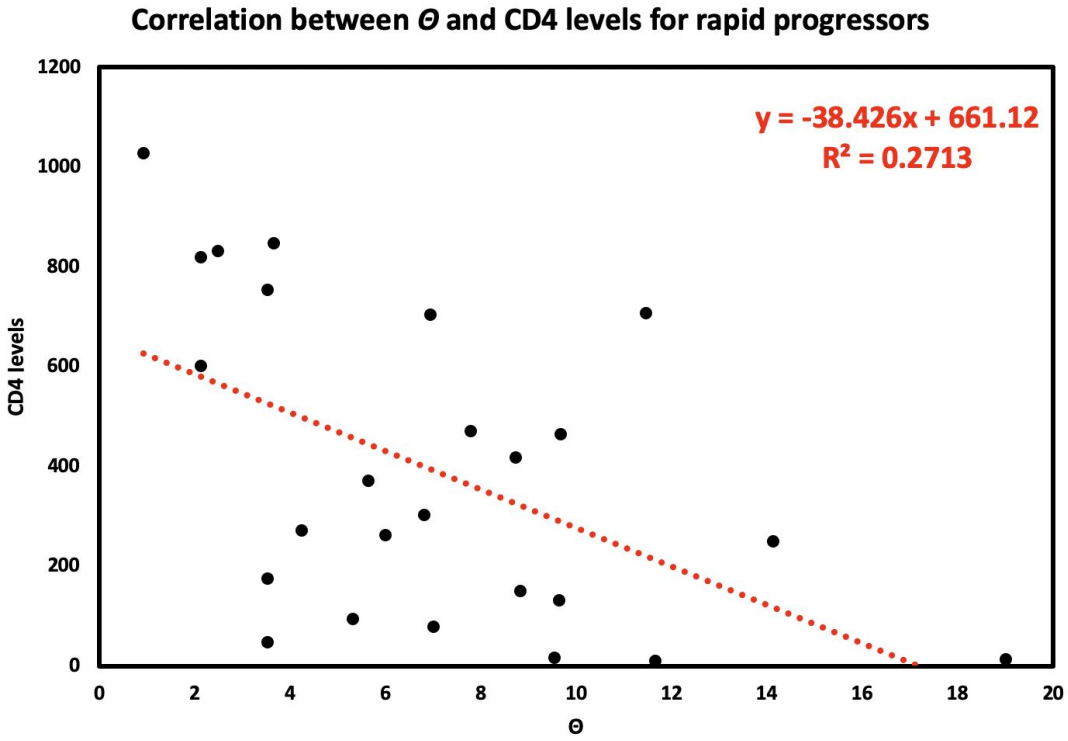
P>0.05, so we fail to reject the null. There is not significant statistical evidence to say that there is an inverse relationship.



A weak correlation between Θ and CD4 T-cell values exists in rapid progressors.

P-value = 0.007

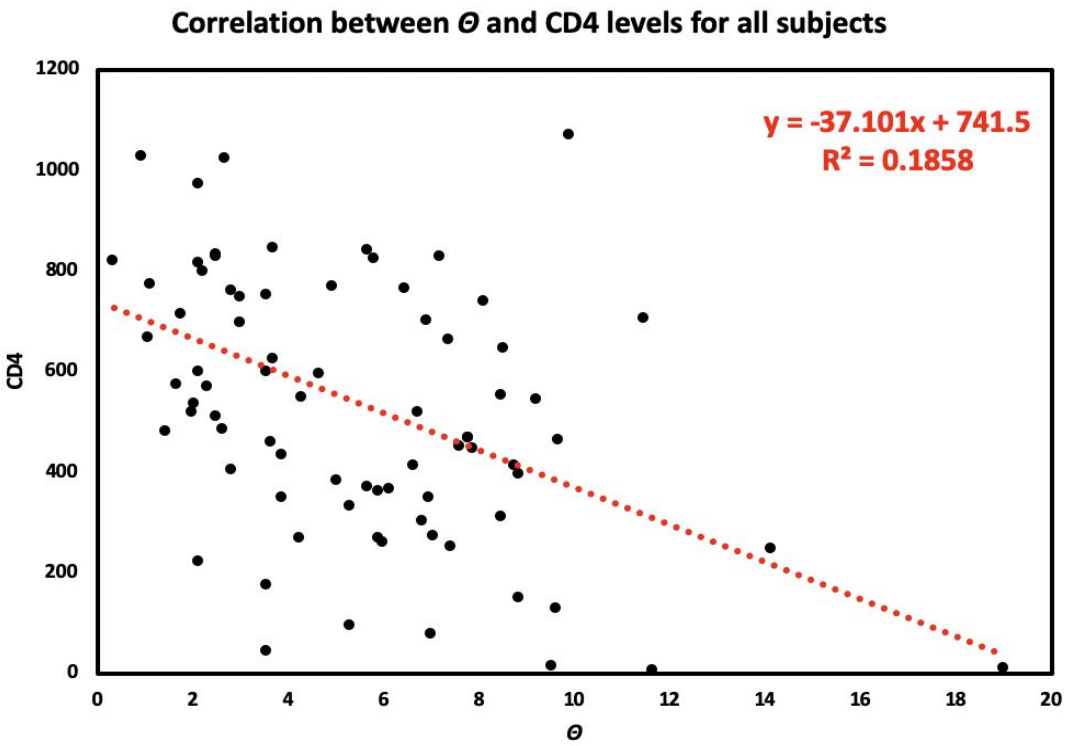
P<0.05, so we reject the null and accept the alternate.
There is significant statistical evidence to say that there is an inverse relationship.



Though, for all subjects and their data, there is a weak correlation and an inverse relationship.

P-value = 6.57×10^{-5}

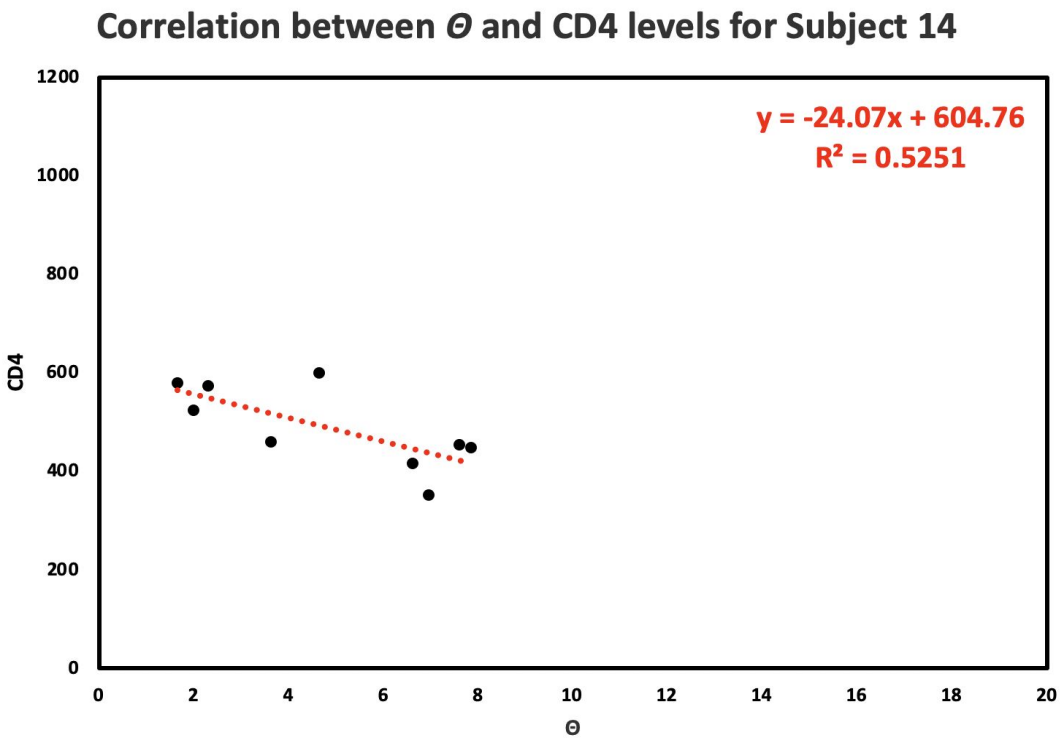
P<0.05, so we reject the null and accept the alternate.
There is significant statistical evidence to say that there is an inverse relationship.



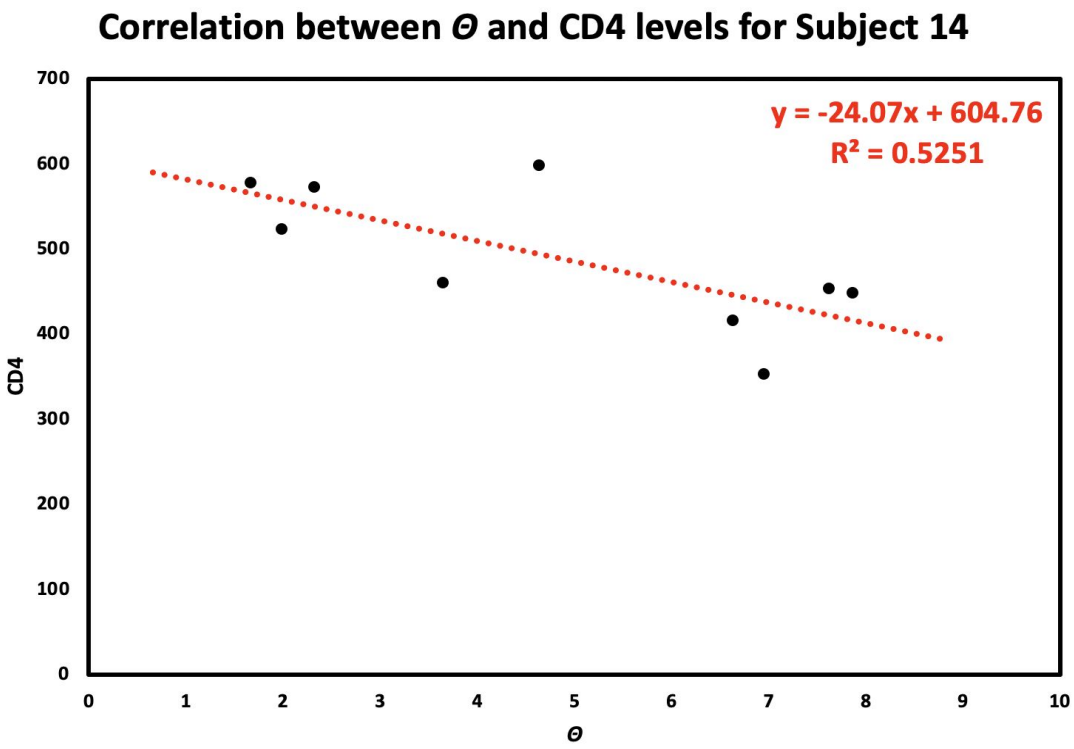
Subject 14's data showed the strongest correlation between Θ and CD4 T-cell levels...

P-value = 0.027

P<0.05, so we reject the null and accept the alternate.
There is significant statistical evidence to say that there is an inverse relationship.



...but it is best represented visually when scaled down.



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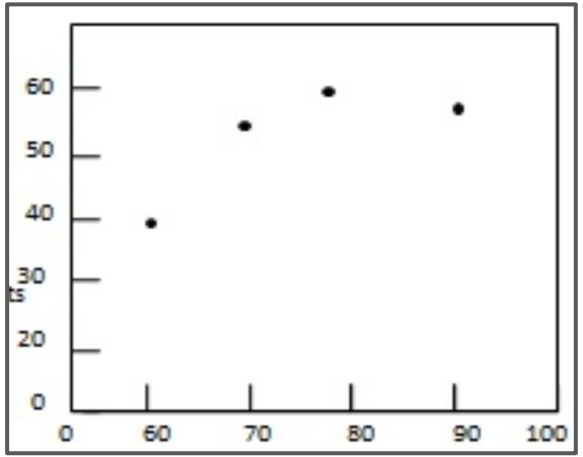
Non-progressors do not necessarily need to show a decrease in CD4 T-cell levels.

- The graphs for non-progressors and moderate progressors revealed slight positive slopes for the best fit line between variables.
  - Need virus replication for genetic diversity and divergence (Gaardbo *et. al.*, 2012)
- Our data supports the model proposed by both Markham *et. al.* (1998) and Nowak *et. al.* (1991) for the relationship between Θ and T-cell depletion in all subjects.
  - ↑ divergence → ↓ CD4 T-cell levels
- While statistically insignificant, data for all progressor groups followed predicted trends.

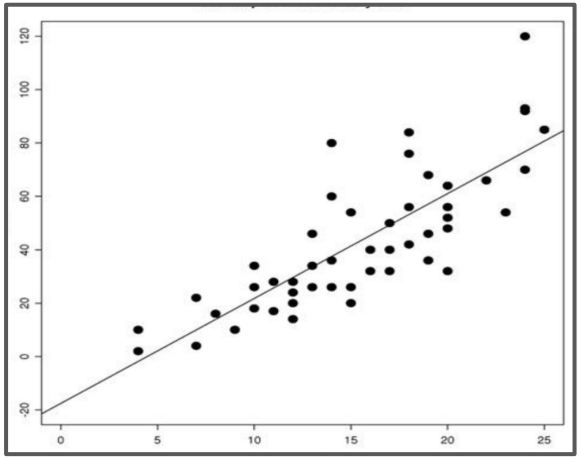
Gaardbo *et. al.*, (2012);
Markham *et. al.*, (1998);
Nowak *et. al.*, (1991)

What can be improved?

- Repeat experiment, but make sure to sequence DNA at every visit
  - More data points, more correlation if there is one



VS.



- Now that we know there is a correlation, we can develop a drug that can be used to target a wider range of genetic divergence → more effective treatment plans

Acknowledgments

- We would like to thank...
    - Professor Dr. Dahlquist,
    - TA Alice Finton,
    - our fellow BIOL 368 classmates,
    - Markham *et. al.* (1998),
    - and the Loyola Marymount University Biology department!

LMU
Seaver

References

- BEDROCK Nucleotide Sequences. (2015). Subject 14 all visits. Retrieved February 25, 2020, from http://bioquest.org/bedrock/problem_spaces/hiv/hiv_data/dna/Subject_14.txt.
- Gaardbo, J. C., Hartling, H. J., Gerstoft, J., & Nielsen, S. D. (2012). Thirty years with HIV infection—nonprogression is still puzzling: lessons to be learned from controllers and long-term nonprogressors. AIDS research and treatment, 2012.
- Markham, R. B., Wang, W. C., Weisstein, A. E., Wang, Z., Munoz, A., Templeton, A., ... & Yu, X. F. (1998). Patterns of HIV-1 evolution in individuals with differing rates of CD4 T cell decline. Proceedings of the National Academy of Sciences, 95(21), 12568-12573. doi: 10.1073/pnas.95.21.12568.
- Minitab (2013). Regression Analysis: How Do I Interpret R-squared and Assess the Goodness-of-Fit? Retrieved February 25, 2020, from https://blog.minitab.com/blog/adventures-in-statistics-2/regression-analysis-how-do-i-interpret-r-squared-and-assess-the-goodness-of-fit.
- OpenWetWare. (2020). BIOL368/S20:Week 6. Retrieved February 25, 2020, from https://openwetware.org/wiki/BIOL368/S20:Week_6.
- Phylogeny.fr. (2020) Phylogeny.fr:Home. Retrieved February 25, 2020, from http://www.phylogeny.fr/.
- Wikipedia. (2010). Wikipedia:Manual of Style/Superscripts and subscripts. Retrieved February 25, 2020, from https://en.wikipedia.org/wiki/Wikipedia:Manual_of_Style/Superscripts_and_subscripts.

Thank you for listening!

Questions? Comments?