

Analysis of correlation between baseline diversity factors and long term adaptation

Matthew Allegretti and Isai Lopez

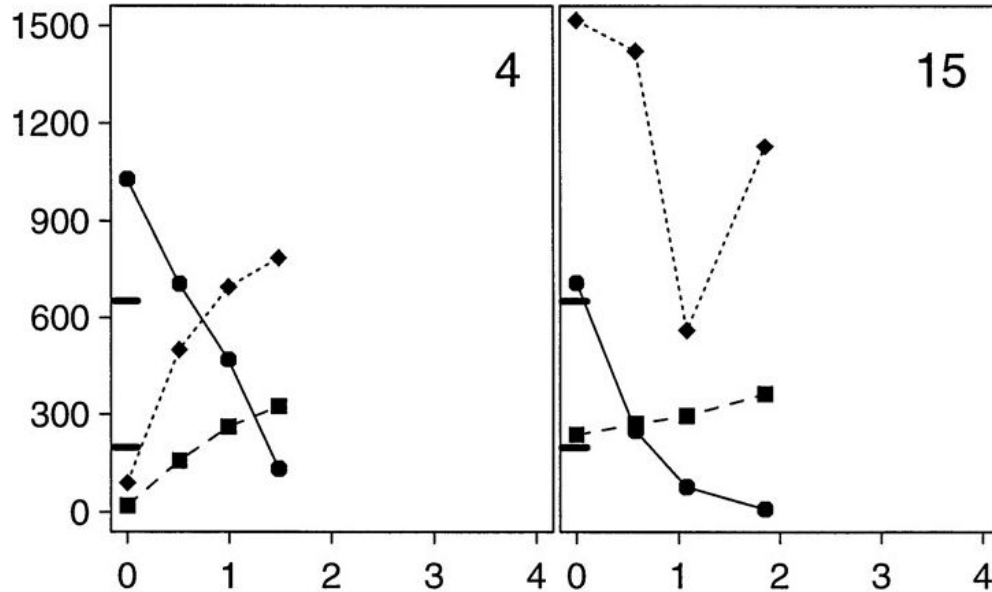
Outline

- Markham et al. suggested certain subjects failed to develop efficient immune response to HIV strains and were subsequently overwhelmed, creating a comfortable environment for the virus to replicate
- This stable environment meant little selective pressure and subsequently little reason to adapt, so strains with high initial diversity were thought to decrease in diversity over time
- The opposite seemed to occur for strains with little diversity, thus we examined trends for high and low initial diversity compared to slope of divergence
- An analysis of the data revealed no significant predictable correlation between the two values using Markham's data
- New studies show effects of outside factors on the later emergence of diversity in HIV strains

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Subjects 15 and 4 were selected as extremes for high and low diversity respectively



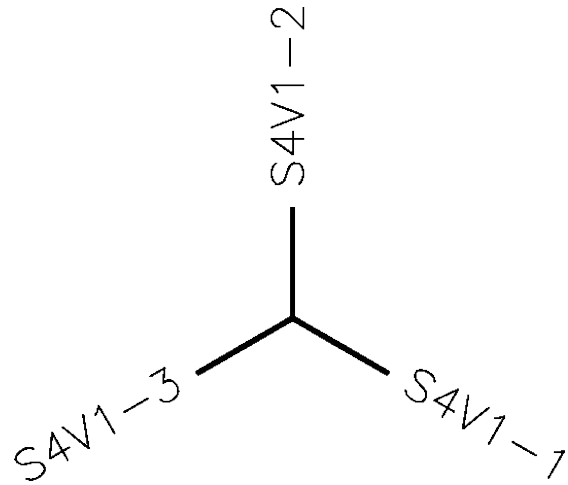
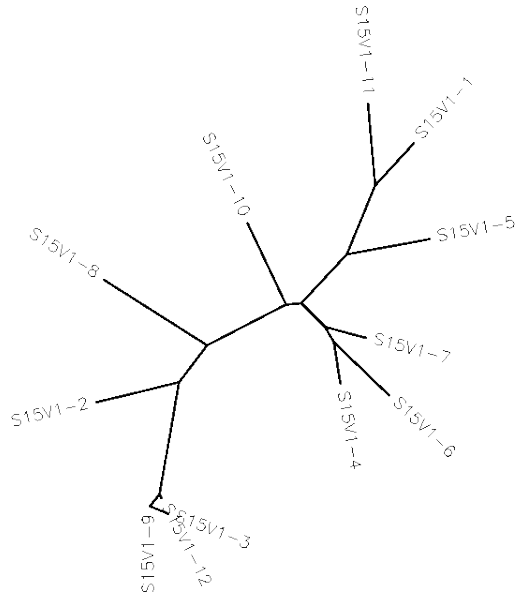
- The diversity plot for subject 4 starts low and increases over time.
- The diversity plot for subject 15 does the opposite, starting high and falling over time.

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Existence of selective pressure may be apparent in the shape of a strains' phylogenetic tree

- “In this model the main assumption is that a single founder virus evolves under neutral evolution, generating a star-like phylogeny” (Tully et al., 2016).



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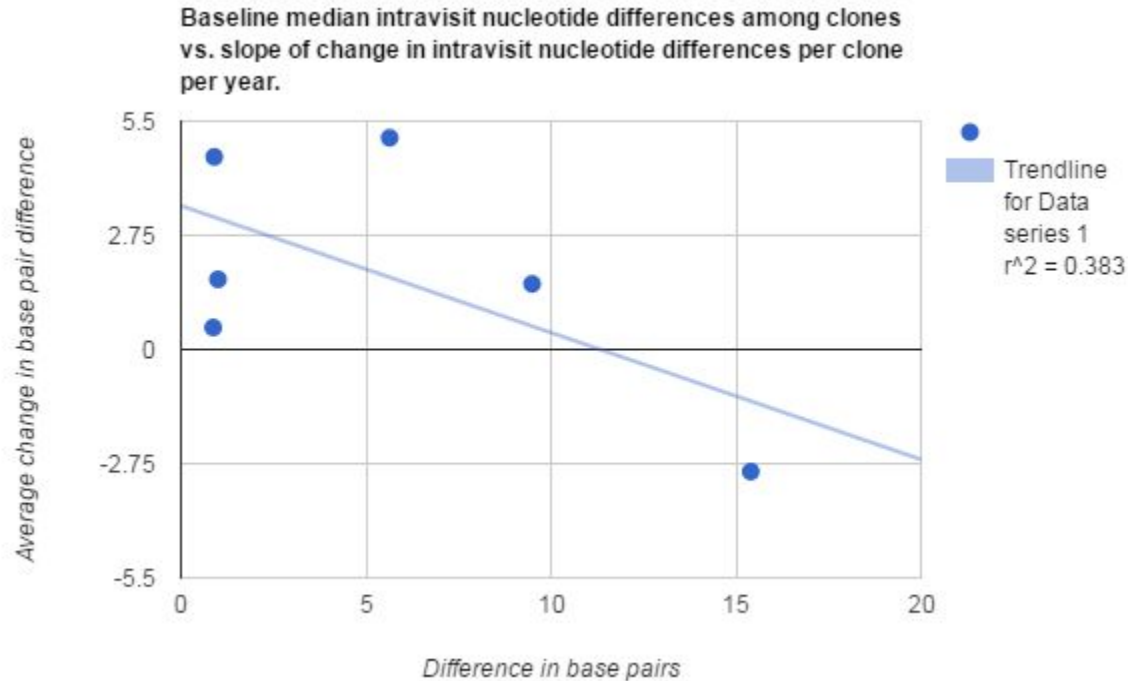
If this trend persists, subjects with high initial diversity should decrease and vice versa

- Subjects 1, 15, and 9 were selected as subjects with the highest initial diversity
- Subjects 4, 13, and 14 were selected as subjects with the lowest initial diversity
- Values for minimum and maximum distances between initial clone sequence were calculated using ClustalDist
- Unrooted trees were generated for each of the six subjects
- Scatter plots were created and an analysis done on the correlation between various data

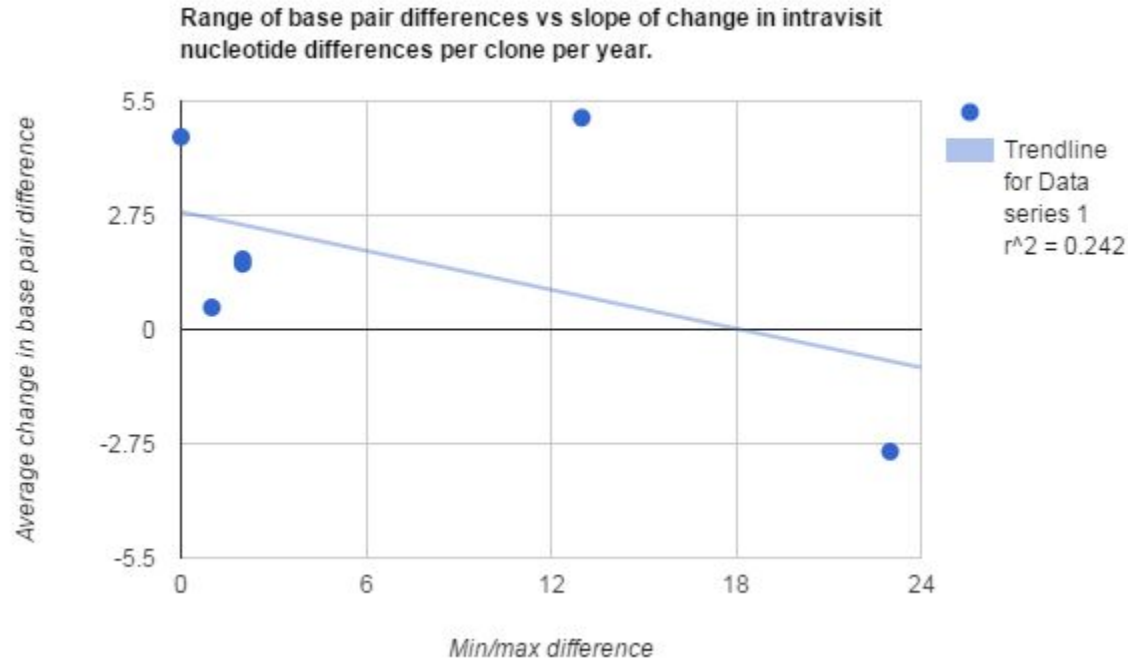
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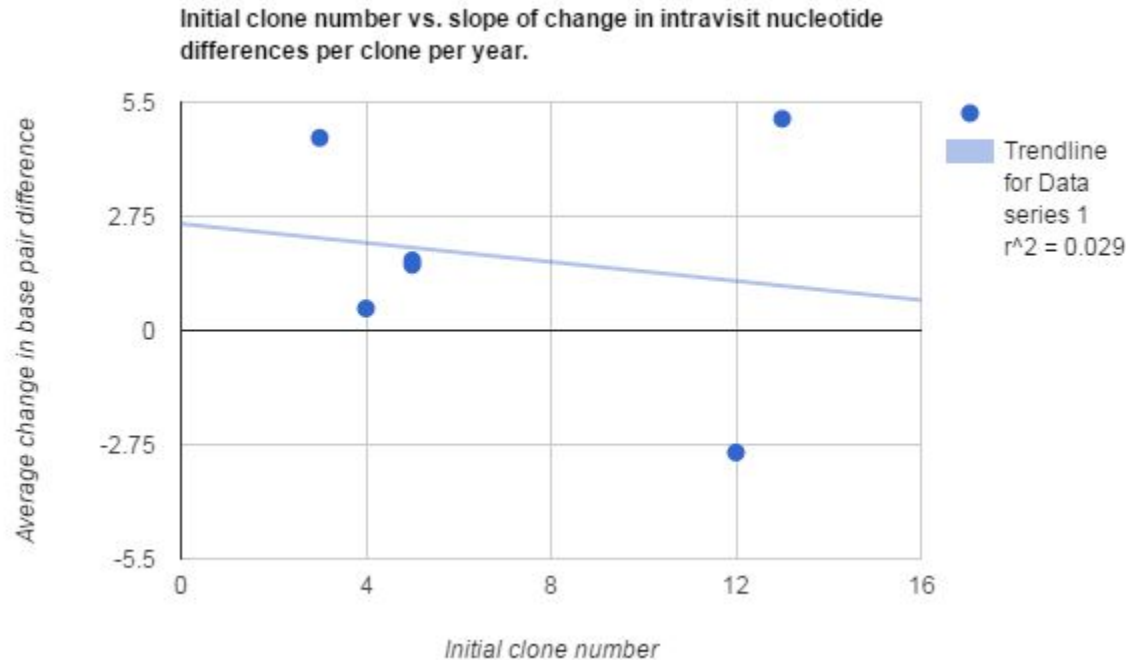
Poor correlation found between baseline nucleotide difference and slope of change in intravisit nucleotide difference per clone



Poor correlation found between the range of nucleotide difference and slope of change in intravisit nucleotide difference per clone



No correlation found between initial clone number and slope of change in intravisit nucleotide difference per clone



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Little to no correlation was found between baseline diversity and end slope change in nucleotide differences

- Lack of correlation possibly linked to presence of more important determinant factors for disease progression
 - “We speculate that in the presence of viremia some effects of active injection may be masked by the effects of untreated HIV-1 infection.” (Mehandru et al., 2015)
- Large variance in number of initial clones may have contributed to the amount of data we had for examination, equal numbers may yield a different result

Main cause of progression may not have been measured in Markham et al., 1998

- Recent studies suggest correlation between injection drug habits and disease progression.
 - “We speculate that in the presence of viremia some effects of active injection may be masked by the effects of untreated HIV-1 infection.” (Mehandru et al., 2015)

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. Proceedings of the National Academy of Sciences USA, 95(21), 12568-12573. DOI: 10.1073/pnas.95.21.12568

Tully, D. C., Ogilvie, C. B., Batorsky, R. E., Bean, D. J., Power, K. A., Ghebremichael, M., et al. (2016) Differences in the Selection Bottleneck between Modes of Sexual Transmission Influence the Genetic Composition of the HIV-1 Founder Virus. PLoS Pathog 12(5): e1005619. doi:10.1371/journal.ppat.1005619

Mehandru, S., Deren, S., Kang, S. Y., Banfield, A., Garg, A., Garmon, D., et al. (2015) Behavioural, Mucosal and Systemic Immune Parameters in HIV-infected and Uninfected Injection Drug Users. Journal of addiction research & therapy, 6(4), 1. doi:10.4172/2155-6105.1000257

Acknowledgments

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