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The Implications of Subtype Diversity of HIV-1 for Vaccine Development

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HIV's ability to infect a host and grow without killing the host allows the virus to accumulate genetic diversity. Over time, HIV has diverged into a number of subtypes, differing up to 30% in their nucleic acids (2). For this reason, one of the greatest problems with vaccine development is that different subtypes express different protein variants (3). With the increase of HIV recombination and human travel, geographical patterns subtypes are becoming mixed, thus allowing the virus to explore new genetic variants and evade vaccine effectiveness (5).

Different geographic areas exhibit different evolutionary subtype phenomena. In Thailand, the shift from subtype B' to a recombinant form, A/E, shows differing selection pressure within a population. It has been report that in Sweden, all subtypes have surfaced. Sequences in the Republic of Congo have shown a high rate of genetic diversity. United States viruses are the most widely studied subtype B in vaccine development.

The countries of Sweden, Thailand, USA and the Republic of Congo each provide a different environment for HIV to evolve. By comparing the neutralizing epitopes in each of these different countries, we can calculate the effectiveness of vaccines to cross-neutralize between subtypes. Characterizing the evolution of the current global isolates is the first step in developing an effective vaccine candidate. It is the goal of this research is to measure the divergence between these different subtypes, geographically, to predict the effectiveness of different vaccine candidates for various populations.

Each isolate claded in their respective subtype group. However, when the sequences of DNA were cut to the V3 region, certain isolates, especially those from the Congo, showed to clade in other subtypes. Congo shows the greatest diversity in both inter and intra-subtype relationships. Both theta and pi show that the Congo has the highest amount of genetic diversity out of all four countries. With the increase of subtype diversity Congo viruses have the opportunity to recombine from a rich reservoir of genetic variants.

Subtype B continues to be the prevalent subtype of infection in the United States. Yet, from the maximum likelihood tree we can see a new clades forming within subtypes. The estimation of genetic diversity (theta and pi) shows that USA has a low estimate of genetic diversity. We do not see the same distribution of subtypes in this country and yet, there are new clades forming. Sweden shows a relatively small estimate of genetic evolution over time but show pi value equal to that of the Congo. Thus, has the same amount of genetic diversity but Sweden has not had the same amount of time to evolve.

HIV in Sweden has been under heavy influence from the African countries. The presence of all subtypes may be attributed to the vast majority of immigrants naturalizing to the country. Overall, these sequences show a combination of evolutionary characteristics between Congo

and the United States. Sweden, in a sense, is the middle ground to the future evolutionary patterns. The recombination rates (ρ) are similar to that of USA but show genetic distances closely following Congo's.

By following the patterns beginning to form in Sweden, we may predict the future evolutionary trends in HIV in America. Sweden shows promising evolutionary change that may be the source of cross reactive vaccine bases. Of course, there are many other evolutionary pressures, such as cultural influence, transmission, random mutations and anti-viral drug use, but an increased observance in recombination and subtype diversity needs to be made a priority in order to stay ahead of the virus. By studying the Swedish population of HIV-1 infected individuals, scientists may find a good model of vaccine resistance patterns between several different subtypes.

Producing a synthetic protein that will work as an effective vaccine base will be like predicting the candidates for the flu shot. By using evolutionary analysis as a basis for the prediction, scientists will be able to hit the mark in vaccine development.

The results and conclusions were summarized in a poster that I presented at the 2003 annual Evolution conference in Chico California. At this conference I was the only virus project presented in poster format. My future goals with this project are to use it as my Honors thesis and to revise it into a publishable journal article in a scientific journal.. I am currently in the revision process with my mentor of this paper and will continue to revise until a publishable document can be written. I am very grateful for the door that this research project has given me. The grant was used to further my education and give me the opportunity to focus on my research.

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