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**Two-way Bayesian Hierarchical Phylogenetic Models: an  
Application to gp120 and gp41 Evolution during Partial  
Treatment Interruption of Enfuvirtide**

**Abstract**

Enfuvirtide (ENF) is a fusion inhibitor that prevents the entry of HIV virions into human cells and represents a new class of therapeutic agents in the treatment of HIV disease. Studying the characteristics of viral evolution during partial treatment interruptions (PTIs) lends insight into the development of drug resistance, mechanisms of viral persistence and, perhaps, whether to continue a non-suppressive regimen when no other alternative options exist. Previous work suggests that during PTI of ENF the envelope gene product gp41 continues to evolve and the loss of drug resistance-associated mutations is due to back mutation instead of the recall of archived strains. It is unknown how ENF therapy affects the selective pressure of other gene regions involved in viral entry such as gp120. To aid in understanding the evolution of both gene regions we extend our Bayesian hierarchical phylogenetic model (HPM) to allow for the simultaneous estimation of both gene regions and to test the hypothesis of independent evolution between regions through the Bayesian log linear model suggested by Albert 96. HPMs permit the simultaneous estimation of overall trends across multiple patients and genes and for pooling of information. Pooling is especially useful if one of the gene regions is poorly estimated due to small number of sites sampled (sequence length) or lack of phylogenetic information (variation). Examination of more than one gene region simultaneously provides improved precision and better insights into intra patient-evolution. This is especially important when data are expensive to obtain or rare and thus large sample sizes are not available. In seven patients undergoing PTI, examination of both gene region yields a Bayes Factor of 1427 in favor of the continued evolution hypothesis over the re-emergence of archived strains. Analysis of only the gp41 gene region yields a Bayes Factor of 30.2 suggesting that pooling did indeed improve estimation and thus provide overwhelming support of the hypothesis. We also did not find any evidence of gene region interaction. Insights into evolution and drug resistance during treatment is critical to the successful utilization of this new class of therapeutics.