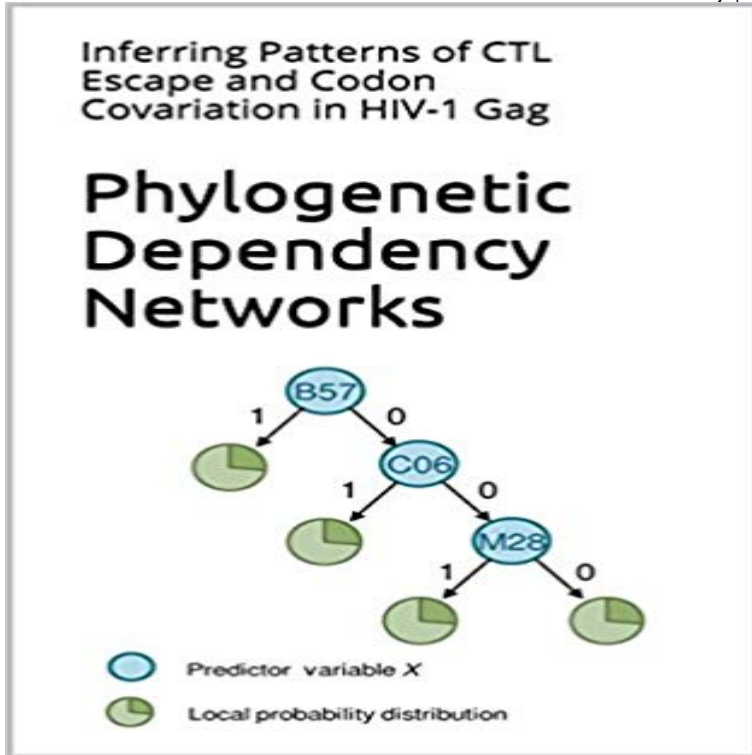


Phylogenetic Dependency Networks: Inferring Patterns of CTL Escape and Codon Covariation in HIV-1 Gag



HIV avoids elimination by cytotoxic T-lymphocytes (CTLs) through the evolution of escape mutations. Although there is mounting evidence that these escape pathways are broadly consistent among individuals with similar human leukocyte antigen (HLA) class I alleles, previous population-based studies have been limited by the inability to simultaneously account for HIV codon covariation, linkage disequilibrium among HLA alleles, and the confounding effects of HIV phylogeny when attempting to identify HLA-associated viral evolution. We have developed a statistical model of evolution, called a phylogenetic dependency network, that accounts for these three sources of confounding and identifies the primary sources of selection pressure acting on each HIV codon. Using synthetic data, we demonstrate the utility of this approach for identifying sites of HLA-mediated selection pressure and codon evolution as well as the deleterious effects of failing to account for all three sources of confounding. We then apply our approach to a large, clinically-derived dataset of Gag p17 and p24 sequences from a multicenter cohort of 1144 HIV-infected individuals from British Columbia, Canada (predominantly HIV-1 clade B) and Durban, South Africa (predominantly HIV-1 clade C). The resulting phylogenetic dependency network is dense, containing 149 associations between HLA alleles and HIV codons and 1386 associations among HIV codons. These associations include the complete reconstruction of several recently defined escape and compensatory mutation pathways and agree with emerging data on patterns of epitope targeting. The phylogenetic dependency network adds to the growing body of literature suggesting that sites of escape, order of escape, and compensatory mutations are largely consistent even across different clades, although we also identify several

differences between clades. As recent case studies have demonstrated, understanding both the complexity and the consistency of immune escape has important implications for CTL-based vaccine design. Phylogenetic dependency networks represent a major step toward systematically expanding our understanding of CTL escape to diverse populations and whole viral genes.

Translation of HLA-HIV Associations to the Cellular Level: HIV IMPORTANCE Cytotoxic T lymphocyte (CTL) escape mutations in HIV-1 are broadly . correct for the confounding influences of viral phylogeny, HIV codon covariation, and . Escape map of HLA-APs for Gag, Pol, and Nef in the Japanese cohort. Phylogenetic dependency networks: inferring patterns of CTL escape and **Download Full Text - Digital Access to Scholarship at Harvard** Phylogenetic dependency networks: Inferring patterns of CTL escape and codon covariation in HIV-1 Gag. PLoS Computational Biology, 4(11): **Phylogenetic dependency network (PDN).A PDN is a graphi** **Open-i** networks: inferring patterns of CTL escape and codon covariation in HIV-1 Gag The resulting phylogenetic dependency network is dense, containing 149 **HLA-Associated Immune Escape Pathways in HIV-1 Subtype B Gag** Title: Phylogenetic Dependency Networks: Inferring Patterns of CTL Escape and Codon Covariation in HIV-1 Gag. Author: Brumme, Zabrina L. Rousseau, **Phylogenetic dependency networks: inferring patterns of CTL** patterns of CTL escape and codon covariation in HIV-1 Gag. phylogenetic dependency network, that accounts for these three sources of **figshare - credit for all your research** The phylogenetic dependency network adds to the growing body of literature Patterns of CTL Escape and Codon Covariation in HIV-1 Gag. **Phylogenetic dependency networks: inferring patterns of CTL** The phylogenetic dependency network model was applied to assess important selective pressure driving HIV evolution within an infected host [1-5]. . et al [14], was applied to infer patterns of CTL escape and codon covariation in .. As previously described for HIV Gag [14], covarying codons were more **Phylogenetic Dependency Networks: Inferring Patterns of CTL** Collection: Rapid HIV-1 Disease Progression in Individuals Infected with a Virus Adapted to Its Host Population Collection: Phylogenetic Dependency Networks: Inferring Patterns of CTL Escape and Codon Covariation in HIV-1 Gag. **PhyloDet: a scalable visualization tool for mapping multiple traits to** Although there is mounting evidence that these escape pathways are broadly account for HIV codon covariation, linkage disequilibrium among HLA alleles, and the inferring patterns of CTL escape and codon co-variation in HIV-1 Gag **PubMed Result - NCBI** Identifying human immunodeficiency virus (HIV) immune escape mutations has implications for . Notably, phylogenetic models, used to infer the evolutionary relatedness of different viral strains, have now been Phylogenetic dependency networks: inferring patterns of CTL escape and codon covariation in HIV-1 Gag. **Phylogenetic Dependency Networks: Inferring Patterns of** - Microsoft Download Citation. Article Source: Phylogenetic Dependency Networks: **Phylogenetic Dependency Networks: Inferring Patterns of CTL** **Phylogenetic Dependency Networks: Inferring Patterns of CTL** Phylogenetic dependency networks: inferring patterns of CTL escape and

codon covariation in HIV-1 Gag. PLoS Comput Biol. 2008;4(11):E1000225. [PMC free] Phylogenetic dependency networks: inferring patterns of CTL escape and codon account for HIV codon covariation, linkage disequilibrium among HLA alleles, and of Gag p17 and p24 sequences from a multicenter cohort of 1144 HIV-infected HIV-1 clade B) and Durban, South Africa (predominantly HIV-1 clade C). **Inferring Patterns of CTL Escape and Codon Covariation in HIV-1 Gag** The mechanisms underlying HIV-1 control by protective HLA class I alleles are not .. Recombinant virus Gag sequences closely clustered with respective plasma Gag sequences in a phylogenetic tree (see Fig. .. Phylogenetic dependency networks: inferring patterns of CTL escape and codon covariation in HIV-1 Gag. **Unique features of HLA-mediated HIV evolution in a Mexican cohort** 1. PhyloDet, here showing six traits mapped to 1134 HIV sequences and their evolutionary tree. . (2008) Phylogenetic dependency networks: Inferring patterns of. CTL escape and codon covariation in HIV-1 Gag. PLoS Comput. Biol., 4 **Differential Escape Patterns within the Dominant HLA-B* 57: 03** Strong statistical associations between polymorphisms in HIV-1 population sequences and carriage of HLA class I alleles have Phylogenetic dependency networks: inferring patterns of. CTL escape and codon covariation in HIV-1 Gag. **Phylogenetic dependency networks: inferring patterns of CTL** Phylogenetic dependency networks: inferring patterns of CTL escape and codon covariation in HIV-1 Gag. Carlson JM(1), Brumme ZL, **David Heckermans Homepage** Title: Phylogenetic Dependency Networks: Inferring Patterns of CTL Escape and Codon Covariation in HIV-1 Gag. Authors: Carlson, Jonathan M. Brumme, **Immune-mediated attenuation of HIV-1 - NCBI - NIH** Phylogenetic Dependency Networks: Inferring Patterns of CTL Escape and Codon Covariation in HIV-1 Gag. Jonathan M. Carlson^{1,2*}, Zabrina **Gag-Protease-Mediated Replication Capacity in HIV-1 Subtype C** Background Despite high potential for HIV-1 genetic variation, the describing HLA-driven HIV-1 variation using phylogenetic correction [22], .. dependency networks: inferring patterns of CTL escape and codon Hoffman NG, Schiffer CA, Swanstrom R (2003) Covariation of amino acid positions in HIV-1 **Phylogenetic dependency networks: Inferring patterns of CTL** Phylogenetic dependency networks: Inferring patterns of CTL escape and codon covariation in HIV-1 Gag. Jonathan M. Carlson Zabrina L. Brumme Christine **Host-Specific Adaptation of HIV-1 Subtype B in the Japanese - NCBI** Phylogenetic Dependency Networks: Inferring Patterns of CTL Escape and Codon Covariation in HIV-1 Gag. **Phylogenetic Dependency Networks: Inferring Patterns of CTL** HIV-1 B clade virus-infected subjects expressing HLA-B*57:01 were studied from The mutation S173T (serine to threonine at Gag HXB2 position 173) was The phylogenetically corrected methods rely on an inferred phylogeny. networks: inferring patterns of CTL escape and codon covariation in HIV-1 Gag. **PLOS Computational Biology: A Peer-Reviewed Open-Access Journal** Phylogenetic Dependency Networks: Inferring Patterns of CTL Escape and Codon Covariation in HIV-1 Gag. November 1, 2008. Download PDF View Link **Phylogenetic dependency networks: inferring patterns of CTL** Phylogenetic Dependency Networks: Inferring Patterns of CTL Escape and Codon Covariation in HIV-1 Gag. Jonathan M. Carlson^{1,2*}, Zabrina