Dissecting Genetics of Host-Pathogen Interactions

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Methods in computational and molecular biology generally study the genetic processes of one model organism at a time. In reality, life is anything but a pure culture. Pathosystems extend the single-species paradigm across multiple replicating organisms and present new problems, because infected cells house both host and pathogen. Examples from three distinct pathosystems highlight scientific questions and computational solutions developed in concert with collaborators. The first pathosystem involves the plant pathogen *Phytophthora sojae* interacting with its host, *Glycine max* (soybean).

Comparative lexical analysis enables determining the "species of origin" for gene transcripts isolated from infected plant roots with greater accuracy than comparative sequence similarity searching. The second and third pathosystems investigations study variation in cell-mediated immunity to identify significant immunogenetic associations with response to chronic viral infection by HCV and HIV.

For HCV, analyzing contingency tables of immunogenetic data from 22,038 US liver-transplant recipients identified a protective advantage among carriers of heterozygous HLA-DRB1 alleles, i.e., "heterozygote advantage". In treating HIV infections, the setpoint, or quasi-stationary viral titer during the chronic phase, is a known predictor of the duration of infection, with high setpoints corresponding to rapid progression in the absence of antiretroviral therapy. Description lengths of setpoint distributions calculated with consideration of human leukocyte antigen (HLA) genotypes identified a protective advantage among carriers of rare HLA-B alleles. In each pathosystem, quantitative methods were able to deconvolve genetic components of host-pathogen interactions.