Modeling pathogen responses

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The search for a vaccination against HIV has been in progress since 1984, with very little success. Traditional methods used for identifying potential cellular targets can be very costly and time-consuming. The key to creating a vaccination lies in knowing which parts of the pathogen to target with which antibodies.

A new study by David Heckerman and colleagues from Massachusetts General Hospital, publishing on October 12, 2007, in PLoS *Computational Biology*, has come up with a way to match pathogens to their antibodies.

At the core of the human immune response is the train-to-kill mechanism in which specialized immune cells are sensitized to recognize small peptides from foreign pathogens (e.g., HIV). Following this sensitization, these cells are then activated to kill cells that display this same peptide. However, for sensitization and killing to occur, the pathogen peptide must be "paired up" with one of the infected person's other specialized immune molecules—an HLA (human leukocyte antigen) molecule. The way in which pathogen peptides interact with these HLA molecules defines if and how an immune response will be generated.

Heckerman's model uses ELISpot assays to identify HLA-restricted epitopes, and which HLA alleles are responsible for which reactions towards which pathogens. The data generated about the immune response to pathogens fills in missing information from previous studies, and can be used to solve a variety of similar problems. The model was

applied to data from donors with HIV, and made 12 correct predictions out of 16. This study, says David Heckerman, has “significant implications for the understanding of…vaccine development”. The statistical approach is unusual in the study of HLA molecules, and could lead the way to developing an HIV vaccine.

Source: Public Library of Science