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Conserved epitope regions (cer) - Elucidation of stable, immunologically active regions of human H1N1 influenza viruses

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The first pandemic of the 21st century arose in March of 2009 but it was not until December of that yearthat a vaccine for the pandemic strain was available to the general public. The nine-month time frame for vaccine production is not restricted to pandemic outbreaks. In fact, every year a new vaccine must be produced for seasonal flu infection, which takes the same length of time to prepare. The influenza vaccine has to be reproduced each year due to the virus mutating in an effort to evade host immune response, a process known as antigenic drift. A significant challenge is to predict which influenza strains will be prevalent in the human population when the vaccine is ready.

In an effort to create a vaccine that minimizes or eliminates the effect of antigenic drift, we have developed a method to elucidate conserved epitope regions (CER) within eachflu protein. CERs are regions with minimal polymorphic activity that also possess strong epitope activity in the form of T-cell and B-cell activity.

Utilizing the pre-computed polymorphism analysis data from the Influenza Research Database (IRD) (www.fludb.org), we determined the rate of polymorphism across all 10 proteins of human H1N1 subtype influenza viruses. The polymorphism score was calculated using a sliding 5-mer window to obtain an average polymorphism score for the region. Epitope coverage for each amino acid position was computed using custom scripts and experimentally determined epitopes from the Immune Epitope database (IEDB) (www.immuneepitope.org).

The two datasets were then plotted along the length of each protein and CERs were selected that represented minimal polymorphism scores with increased epitope coverage. Comparing CERs to experimentally determined cross-reactive epitopes validated the CERs. Specifically, experimentally determined antibody binding regions are covered by one or more CERs. Finally, the CERs for HA also include all four highly cross-reactive predicted epitopes and are found to be conserved in both seasonal H1N1 and the pandemic H1N1 2009 viruses.