Universität Basel

Research Project

High-throughput experiments to guide influenza vaccine strain selection

Third-party funded project

Project title High-throughput experiments to guide influenza vaccine strain selection
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Project start 01.09.2017
Probable end 31.08.2021
Status Completed

Every year, seasonal influenza infects 5-15% of the human population, resulting in over 250,000 deaths worldwide. The annual influenza vaccine is the primary public-health intervention against these epidemics. The strains in the vaccine must be selected before the influenza season. Unfortunately, the selected strains sometimes fail to closely match those that end up actually circulating in the human population; such strain mismatches reduce vaccine efficacy. Methods for better selecting vaccine strains are therefore of paramount importance to public health.

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We will use innovative new experimental and computational techniques to guide better vaccine-strain selection. Two key properties determine which influenza strains dominate a season: successful strains have high inherent fitness (manifested by a low load of deleterious mutations) and an abundance of antigenic mutations in the epitopes recognized by human immunity. We will measure how each of these properties is affected by every possible amino-acid mutation to the viral surface protein hemagglutinin. To make these high-throughput measurements, we will generate pools of viruses carrying all possible codon mutations to hemagglutinin, and then passage these mutant viruses in the presence and absence of human serum. We will then use ultra-accurate deep sequencing to count the frequency of every mutation pre- and post-selection, enabling us to quantify how each mutation affects both deleterious load and antigenic recognition by serum from a cross-section of the human population.

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To improve vaccine-strain selection, we will use a real-time web platform to overlay our measurements of deleterious mutational load and the antigenic change onto an influenza phylogeny. This platform will enable decision makers to intuitively visualize the “Big Data” generated by our experiments as they weigh all sources of evidence during the strain-selection process. In addition, we will make our data and computer code readily available, so that others can leverage our work for their own efforts to better predict influenza strain dynamics.

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This work has direct relevance to public health in that it will help guide better vaccine-strain selection at a fraction of the cost of current approaches, and thereby improve seasonal influenza vaccine effectiveness.

Financed by
Foreign Governmental Research Agencies

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