

THE HARTWELL FOUNDATION

2014 Individual Biomedical Research Award

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**Computational Genetic Forecasting for Improved Influenza
Vaccination Antigenicity**



Influenza is a highly contagious viral infection of the respiratory passages causing fever, severe aching and often occurring in epidemics. As an infectious disease, it is the leading cause of mortality for children between the ages of 1 and 14 in the United States. It results in more than 18,000 hospitalizations and millions of excess outpatient visits, which burden the child, parents, as well as the healthcare system. It is one of the top ten overall causes of mortality for both children and adults, resulting in up to 36,000 deaths annually in the US. Excessive outpatient visits also result in many unnecessary antibiotic prescriptions, exacerbating the significant and growing problem of antibiotic resistance. Influenza would most likely be preventable if the annual flu vaccine was a closer match to the current circulating strains of the virus. It is distressing that routine vaccination is at best, only partially effective. This is due to the rapid evolution of the influenza virus and the limitations it imposes on existing approaches for annual vaccine strain selection and development where today, directed development of a new vaccine depends upon awareness of the flu virus strains circulating in the previous flu season, 8-10 months prior. To address the unmet need for how best to select the most optimum viral strain for effective flu vaccine development, Eili hypothesizes that it should be possible to develop an algorithm to predict how the influenza strains of the prior year are likely to evolve from season to season. He will do so by combining computational models of individual viruses with a biophysical model of viral evolution and antibody binding into a global-scale model that incorporates realistic infected host contact networks and individual behavioral responses to infection. He proposes to deploy a novel laboratory method for high-throughput screening that will enable millions of influenza virus strains to evolve simultaneously. Utilizing computational methods and the latest technological advances in viral genomics, he expects to relate the effects of mutations at the molecular level to their consequences at the population level. If Eili is successful, building a direct computational link between the dynamics of virus mutation and the dynamics for probability of infection will improve the likelihood of obtaining a better match between the vaccine and the strains that ultimately will circulate during flu season. A more effective influenza vaccine will increase its protective effect; reducing mortality, hospitalizations and outpatient visits for children. More visible benefits of vaccination will in turn, encourage more widespread use of vaccination; further protecting children.