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Pre-clinical success for a universal flu vaccine offers hope for new third generation approach

Development of a vaccine candidate with potential to save millions worldwide will be accelerated in commercialisation deal with Blue Water Vaccines.

The antigenic evolution of influenza is thought to occur by a process of “drift”, where mutations in highly variable epitopes in the head domain of the major influenza antigen, haemagglutinin (HA), allow the virus to escape host population immunity. However, this assumption is difficult to reconcile with the observation that each influenza season is dominated by a single influenza strain. This paradox is typically resolved by imposing some form of arbitrary constraint or rate limiting factor on the mode and tempo of viral mutation. Our research group has hypothesised by contrast (and somewhat controversially) that constraints on the antigenic evolution of influenza arise primarily through strong immune selective pressure on epitopes of ‘limited variability’.

We have recently identified one of these

epitopes of limited variability in the head domain of the H1 HA protein. We have shown that children aged 6–12 years exhibit periodic historical immunity mediated by one conformation of this epitope. Mutagenesis of one epitope conformation into another removes or reduces this cross-reactivity. We have demonstrated that vaccinating with this epitope in mice induces an identical pattern of cross-reactivity to that shown by the children, and that an epitope contained in the H1N1 influenza strains circulating in either 2006 and 1977 protects mice against challenge with a strain that last circulated in 1934!

Due to the nature of these epitopes – they are highly immunogenic and limited in variability - they are also ideal vaccine targets. Vaccinating against five conformations of the epitope induces

immunity to all historical strains circulating since 1918. Our work presents, as far as we know, a unique example of where a mathematical model of the evolutionary dynamics of an infectious disease has led to the experimental identification of a novel vaccine target.

Our approach won a Royal Society Translational Award in 2017, and Dr. Craig Thompson has just won the MPLS Early Career Impact work in recognition of this achievement. Very excitingly, Oxford University, through its innovation arm Oxford University Innovation (OUI), has entered into an option agreement for a universal influenza vaccine with US-based startup Blue Water Vaccines (BWV), which is raising \$15m to support development of this universal flu vaccine.



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Sunetra Gupta
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