# A novel influenza vaccine targeting protective epitopes of limited variability

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The antigenic evolution of influenza is often assumed to occur by 'antigenic drift' where new strains arise through the incremental addition of mutations in surface glycoproteins. However, the antigenic drift model can only explain the epidemiology and limited genetic diversity observed among influenza virus populations by imposing constraints on the mode and tempo of mutation. We have demonstrated that an alternative model known as 'antigenic thrift' successfully models the epidemiology and genetic diversity of human influenza by assuming that the antigenic evolution of the virus population is primarily driven by naturally acquired immunity against epitopes of limited structural variability [Recker et al 2007 PNAS]. We have already performed serological studies using human subjects which show that recognition of historical isolates follows a pattern consistent with the recycling of epitopes of limited variability as predicted by this model. We have further identified and characterised at least one epitope of limited variability that is under strong immune selection (Fig 1) in the major influenza antigen, haemagglutinin (HA), by using a structural bioinformatics approach in combination with our serological analyses. Mutagenesis of this epitope removes neutralisation of historical isolates among children aged between 6 to 11 years sampled in 2006/2007. Based on these results, we propose to develop a novel influenza vaccine that protects against all influenza strains of the H1 subtype by targeting this epitope of limited variability. We believe our methodology can be applied to produce vaccines against all subtypes of influenza thereby providing the opportunity to develop not only a more effective vaccine against endemic influenza, with lower healthcare costs due to the requirement for a single vaccine and/or fewer vaccine doses, but also better protection against potential influenza pandemics. The same strategy can also be used to produce vaccines for swine and avian influenza which will have significant economic consequences, particularly in developing countries, and the control of which will reduce the probability of new lineages emerging with pandemic potential.