**Title:** Induction of protective T cell immunity against influenza using a novel peptide vaccine

**Body:** Influenza infection remains an important cause of global morbidity despite current vaccine strategies which generate antibody responses to surface viral proteins. Recent studies have established that naturally occurring T cells which recognise highly conserved core viral proteins and limit illness against a range of viral strains. We aimed to demonstrate that induction of T cell memory using a novel peptide vaccine (Flu-V) could limit influenza severity using a human viral challenge model. 32 seronegative healthy males were randomised to receive 500 µg of peptide vaccine or placebo. All subjects were challenged by nasal instillation of live A/Wisconsin/67/2005 (H3N2). Safety, tolerability, influenza severity and cellular immunity data were collected. The vaccine was safe and well tolerated. No pre-existing T cell responses to the novel Flu-V vaccine were seen at baseline by IFN-γ release assay. All subjects in the treatment arm demonstrated strong induction of the peptide specific cellular response (fold rise 8.2± 3.9 (Range 2.0-30.6) p=0.0005). The strength of the induction of T cell response to Flu-V inversely correlated with influenza illness severity -symptoms r=-0.786, p=0.02 and viral shedding r=-0.821, p=0.01. Furthermore the peptide vaccine induced strong cellular responses against heterologous strains including H1N1pdm in vitro. Peptide vaccination can induce cellular immunity to influenza which correlates closely with disease protection in humans. T cell responses can be induced against a range of strains and therefore this approach carries potential for the induction of broad heterologous immunity required to protect against future pandemics.