Immunogenic Peptides from an Unusual H1N2 Human Variant Comparison against Historical Sequences

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Background/Objective
Current seasonal influenza vaccines require regular updates due to antigenic drift causing loss of effectiveness and provide limited (or no) protection against novel influenza A subtypes. Novel vaccines based on cross-protective immunity attributed partially to CD8+ T cell (CTL) responses may offer a long term alternative strategy. However, measuring levels of induced and existing CTL cross-protection in human populations is challenging due to diversity of prior infections. This study describes variation in immunogenic nucleoprotein (NP) peptides of influenza viruses isolated from humans over the past century by comparing a historical dataset to reference NP peptides from H1N2 viruses that circulated in humans during 2000-2003. These were the first H1N2 to persist over several years possibly attributable to novel CTL NP epitopes partially explaining H1N2 viral survival.

Method
Reference peptides of the H1N2-NP gene were compared to H1N1, H2N2, and H3N2 viruses circulating from 1918-2003. The number and percentage of peptide sequences with 100% match and the non-matching variants to the reference data were reported by subtype.

Result
: Reference H1N2 NP peptide sequences were compared to those from H1N1, H2N2 and H3N2 viruses from 1918-2003. We found a range of highly conserved to highly variable peptides. No unique NP peptide sequences were noted in the H1N2 virus. However the virus had inherited the NP from a recently emerged H3N2 variant containing a novel peptide.

Conclusion
The H1N2 reassortant's success may be partly attributable to inheritance of H3N2 NP gene with novel mutations, an advantage subsequently lost with emergence of a newer H3N2 variant. Published functional studies found this mutation completely nullified recognition of NP383-391 restricted by haplotype HLA-B*2705 expressed in approximately 8% of Caucasians. Our approach provides insight into the population context in which influenza viruses emerge. This has the potential to inform immunogenic peptide selection for CTL-inducing influenza vaccines.