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Molecular characterization of the hemagglutinin receptor-binding specificity of avian influenza viruses: Predicting the jump across the species barrier

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Influenza is a constant global burden to human health. Seasonal influenza results in significant infections and death, cycling through both hemispheres. On occasion, a novel avian influenza virus crosses the species barrier from birds to humans resulting in an influenza pandemic. The threat of pandemic avian influenza continues with H5N1 and H7N9 consistently infecting humans. In order to evolve from its avian form and gain the pandemic potential for increased transmissibility between humans, the hemagglutinin (HA) of avian influenza viruses will need to undergo mutations in its receptor binding site (RBS) that bring about an avian to human receptor preference switch. In order to understand the major determinants of virus transmissibility and the pandemic potential of the novel avian influenza viruses we have determined the crystallographic structure of the novel avian influenza H10N7 A/Turkey/MN/3/79 to 1.96 Å and mapped the RBS. The amino acid residues responsible for conferring receptor selectivity were identified by site-direct mutagenesis of recombinant H10 HA proteins. The receptor-binding selectivity of the HAs was determined using sialyl glycan binding assays. Docking models were constructed of the H10 HA in complex with α 2, 6-sialic acid (human) and α 2, 3-sialic acid (avian) pentasaccharide receptor analogs to ascertain the correlation between the binding assay data and the interactions within the receptor binding pocket. The presented findings provide a structure-recognition perspective for the receptor binding properties of the novel avian H10 influenza HA.

Biography

Tony Velkov completed his PhD in 2000 from Monash University. His anti-infective discovery research is at the leading edge globally. He was awarded a NHMRC Research Fellowships in 2006, 2011 and 2014. The quality and impact of his independent research was recognized by the NHMRC with an Excellence Award in 2011. He has published over 50 papers in high-caliber journals, 3 book chapters and 15 conference presentations. The dynamic team he leads consists of 3 Post doctorate, 3 RAs and 9 PhD students. Over the last 6 years, he has obtained >\$9M funding from the NIH, NHMRC and foundations.

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