Centenario de la Gripe Española de 1918. La peor pandemia en la historia contemporánea mundial: lecciones para el futuro

Centenary of the 1918 Spanish Influenza, the Worst Pandemic in the Recent History of the World: Lessons for the future

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ABSTRACT

Mechanisms and consequences of avian influenza virus polymerase adaptation to the human host

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A major barrier that prevents the emergence of influenza pandemics is the poor incompatibility of avian influenza virus with the human host. The avian influenza virus polymerase that functions very well to replicate the virus genome inside the nucleus of the cells of birds is limited in its efficiency in the mammalian nucleus. This implies there are differences in the presence or specificity of host factors that the polymerase co-opts to support its function, and/or that there are species specific restriction factors that inhibit the avian virus enzyme. All influenza viruses that circulate in humans have acquired adaptive mutations in the viral polymerase genes that overcome this host range barrier. The most well known of these is in the PB2 subunit at amino acid 627 which is glutamic acid in most avian viruses and lysine in human adapted strains. We identified a host factor, ANP32A, that differed in length and sequence between avian and mammalian species, and the requirement of unadapted avian virus polymerase for the longer avian ANP32A protein explains the low activity of avian influenza polymerase in human cells. Cells lacking ANP32 proteins are refractory to influenza replication, and this may lead to new ways to combat the virus in the future.