

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

Influenza virus-host interactions

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Influenza A viruses have a remarkable host breadth, ranging from different mammalian to avian species, the latter being its natural reservoir. A high mutational rate, combined with viral gene assortment due to a segmented genome, allows the virus to adapt to new hosts, including the evasion of host-specific antiviral innate immune mechanisms. In the recent years, the viral protein NS1 has been characterized as a multi-tasking virulence factor, playing an essential role in inhibiting the type-I interferon antiviral response and enabling viral replication. However, the specific contribution of the different NS1s present in circulating influenza A virus strains in the overall replication, pathogenicity and host preference of these strains is not known. We have used a novel approach to analyze the NS1 evolutionary landscape and host tropism using a barcoded library of recombinant influenza A viruses containing a curated selection of NS1 genes representative of the NS1 sequence diversity found in nature. Relative viral fitness was analyzed through barcodebased deep sequencing, which revealed host species-driven selection events for specific NS1 genes within the viral population. Surprisingly, the results revealed diverse evolutionary pathways taken by the NS1 of influenza A viruses according to their multiple phylogenetic lineages, with some NS1s becoming very specialized for specific host species, and others promoting efficient viral replication in multiple hosts. The high evolutionary plasticity of this viral protein underscores the ability of influenza A virus to adapt to multiple hosts.