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

Life-threatening influenza: a genetic disease

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Life-threatening pulmonary influenza can be caused by inborn errors of type I and III IFN immunity. We report a 5 year-old child with severe pulmonary influenza at 2 years. She is homozygous for a loss-of-function IRF9 allele. Her cells activate gamma-activated factor (GAF) STAT1 homodimers but not interferon-stimulated gene factor 3 (ISGF3) trimers (STAT1/STAT2/IRF9) in response to IFN-a2b. The transcriptome induced by IFNa2b in the patient's cells is much narrower than that of control cells; however, induction of a subset of interferon-stimulated gene transcripts remains detectable. In vitro, the patient's cells do not control three respiratory viruses, influenza A virus (IAV), parainfluenza virus, and respiratory syncytial virus. These phenotypes are rescued by wild-type IRF9, whereas silencing IRF9 expression in control cells increases viral replication. However, the child has controlled various common viruses in vivo, including respiratory viruses other than IAV. Our findings show that human IRF9- and ISGF3-dependent type I and III IFN responsive pathways are essential for controlling IAV.