Protein enhances lethality of influenza virus

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Often called the most devastating epidemic in the recorded history of the world, the 1918 influenza virus pandemic was responsible for more than 40 million deaths across the globe. The incredible lethality of the 1918 flu strain is not well understood, despite having been under intense scrutiny for many years.

Now, a new study published by Cell Press in the October issue of the journal Cell Host & Microbe unravels some of the mystery surrounding the devastating 1918 pandemic and provides key information that will help prepare for future pandemics.

It is relatively rare for an influenza virus to be virulent enough to cause death in healthy humans. Many deaths associated with influenza are caused by the combined influence of viral disease and the following secondary bacterial infection. Although the 1918 pandemic strain was one of the few influenza viruses capable of killing healthy victims on its own, the majority of fatal cases from the “Spanish Flu” can be attributed to secondary bacterial pathogens rather than primary viral disease. This important interaction between influenza viruses and bacteria is not well understood.

Dr. Jonathan A. McCullers from the Department of Infectious Diseases at St. Jude Children’s Research Hospital in Memphis, Tennessee and colleagues examined this interaction by studying a newly discovered influenza A virus (IAV) protein, called PB1-F2. The gene encoding PB1-F2 is present in nearly all IAVs, including highly pathogenic avian IAVs that have infected humans and the IAV associated with the 1918

pandemic. “PB1-F2 was recently shown to enhance viral pathogenicity in a mouse infection model, raising questions about its effects on the secondary bacterial infections associated with high levels of influenza morbidity and mortality,” explains Dr. McCullers.

The researchers found that expression of PB1-F2 increased the incidence of and exacerbated secondary bacterial pneumonia in a mouse model. Intranasal delivery of a synthetic peptide derived from a portion of PB1-F2 had the same effects. Further, an influenza virus engineered to express a version of PB1-F2 identical to that in the 1918 pandemic strain was more virulent in mice and led to more severe bacterial pneumonia, explaining in part both the unparalleled virulence of the 1918 strain and the high incidence of fatal pneumonia during the pandemic.

The finding that PB1-F2 promotes lung pathology in primary viral infection and secondary bacterial infection also provides critical information for the future. “Given the importance of IAV as a leading cause of virus-induced morbidity and mortality year in and year out, and its potential to kill tens of millions in the inevitable pandemic that may have its genesis in the viruses currently circulating in southeast Asia, it is imperative to understand the role of PB1-F2 in IAV pathogenicity in humans and animals,” says Dr. McCullers. “These findings also reinforce the recent suggestion of the American Society for Microbiology that nations should stockpile antibiotics for the next pandemic, since many of the deaths during this event are likely to be caused by bacterial super-infections.”

Source: Cell Press