Title: Influenza A Virus and *Streptococcus pyogenes* superinfection in a mouse model[1]

Objective: The influenza virus has been attributed to facilitate post bacterial complications, also called superinfections, to infected hosts. These infections are accountable to more cases of mortality than the virus alone in previous influenza pandemics. The aim of this research is to investigate the relative mechanism of an influenza A virus (IAV) infected host with different strains of *Streptococcus pyogenes* (GAS) and how these strains vary in terms of morbidity, mortality, pathogen titers and immune response.

Rationale and Significance: The purpose of the study is to investigate the bacterial contributions to these superinfections using *Streptococcus pyogenes* since the bacteria alone are the executioners in these fatal cases. A better understanding of the virulence factors that make bacterial superinfections severe and life threatening may help in the identification of improved and successful targets for treatment of these superinfection diseases. Using a GAS isolate, MGAS 315, that is known to cause fatal superinfections, the focus of my research was on the gene *emm3,* which encodes for the virulence factor protein M3. The research described and compared the performance of the unmutated M3 bacteria to the mutated M3 bacteria of the MGAS 315 isolate so as to investigate the contribution of the M3 protein as a virulent factor towards death in a superinfection model.

Research Design and Methods : The research was conducted at the University of South Dakota, Vermillion under the direct supervision of Dr. Michael Chaussee and Dr. Victor Huber. The study began in mid May 2015 and lasted for eleven weeks of experimenting and data collection.
IAV-GAS Superinfection model. A previously characterized influenza A virus was used in this superinfection project. This reassortant virus was engineered to express the glycoproteins Hemagglutinin (HA) and Neuraminidase (NA) from the A/Hong Kong/1/68 (H3N2) sample on the background of the A/Puerto Rico/8/34 (H1N1). The *Streptococcus pyogenes* strain used was the MGAS 315 bacteria with serotypes wild type (emm3) ,mutant strain (emm3-) and complimented strain (emm3-/+) at different calculated log dilutions from 10^6 to 10^3 CFUs of bacteria. The virus and bacteria were diluted in phosphate buffered saline (PBS) prior to intranasally inoculating the mice with a volume of 100ul. Groups of the female Balb/c mice were intranasally inoculated with a sublethal dose of the HK/HK virus (0.1 LD_{50}) on day 0, and after 7 days the mice were intranasally inoculated with a 10^6 Colony Forming Units (CFU) dilution of Group A streptococcus.

Conclusion : The results obtained from all the four phases of the experiment supports the connotation that the virulent M3 protein continued to invade the infected host despite a change in its location and composition . Regardless of enclosing the M3 protein in an extracellular plasmid, the bacteria alongside the virus were found in substantial levels inside the infected host.

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