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Creation of an Influenza B Epigraph Vaccine

Leigh Jahnke
University of Nebraska-Lincoln, leigh.jahnke@huskers.unl.edu

Kristine Hoagstrom
University of Nebraska-Lincoln, khoagstrom@gmail.com

Eric A. Weaver
University of Nebraska-Lincoln, eweaver2@unl.edu

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Abstract

The CDC struggles to predict the upcoming influenza viruses resulting in an ineffective influenza vaccine. The 2019 – 2020 influenza vaccine provides an example of vaccine mismatch where the vaccine poorly matches the circulating influenza strains. We have created Influenza B Epigraph hemagglutinin (HA) immunogens that are computationally designed to select the greatest coverage of B and T cell epitopes in the natural population. Our preliminary data shows Epigraph immunogens induce superior cross-reactive antibody responses, overall T cell immunity, breadth of T cell epitopes, and protection against influenza virus. The primary goal of this study is to clone the influenza B Epigraph HA immunogens into DNA and Adenoviral mammalian expression systems. We will characterize these novel HA immunogens for the prevention of influenza B virus infections. Ultimately, we seek to develop novel universal influenza vaccines that provide a foundation of immunity which protects against all past, present, and future influenza viruses.

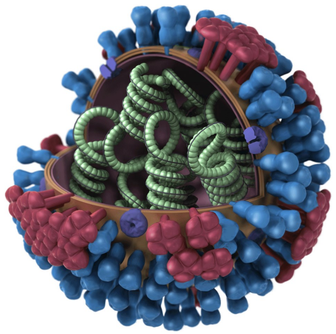

Figure 1. Model of Influenza Virus

Introduction

- There are two strains of the Influenza B virus
  - B/Yamagata/16/88
  - B/Victoria/2/87
- The 2019-2020 flu season had a significantly higher incidence of influenza B compared to past flu seasons

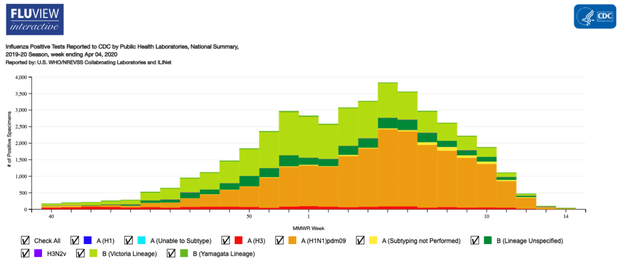

Figure 2. Positive Influenza virus cases during the 2019-2020 flu season where the Influenza B (green) was heavily prevalent.

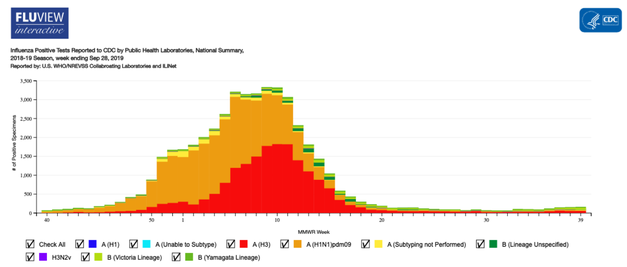

Figure 3. Positive Influenza virus cases during the 2018-2019 flu season where the Influenza B (green) was not significantly prevalent.

Methods

- Three B/Victoria/2/87 and three B/Yamagata/16/88 epigraph genes were created
- The 6 different epigraph genes were originally received in a pMA-T backbone
- Each gene was then amplified, confirmed, and ligated into the plasmid pshuttle-CMV
- This plasmid was then amplified, confirmed, and linearized with pMeI in order to co-transform each pshuttle-CMV epigraph gene and an Adenovirus plasmid (pAd-Easy-1) into E.coli cells (BJ5183s)

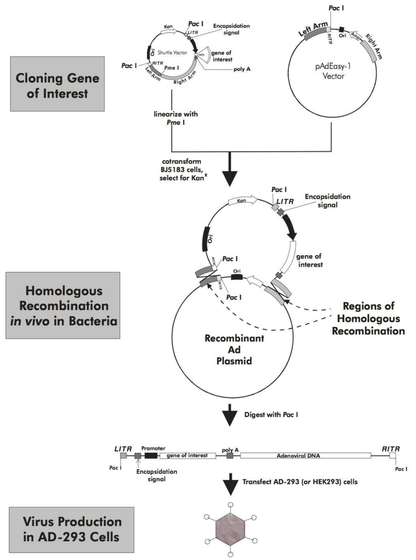

Figure 4. Cloning strategy for inserting Yamagata and Victoria strains into an Adenoviral Vector system.

Future Steps

After the cloning of pAd-Easy-Vic1, pAd-Easy-Vic2, pAd-Easy-Vic3, pAd-Easy-YAM1, pAd-Easy-YAM2, pAd-Easy-YAM3 is complete, each of the six genes will be rescued in cell culture, thus creating a mammalian expression vector. Each gene will be transfected into 293T cells, which are derived from a human embryonic kidney. This cell line will be used because of its high transfectability and its high titer production when producing retroviruses. In order to amplify the virus, consecutive infections into greater quantity of cells will be conducted. Once the virus is amplified to an adequate concentration, it will be moved to the next stage involving infection into *Mus musculus*. After that is successful, we will confirm protein expression by Western blot. Western blotting involves transferring proteins that are separated by gel electrophoresis to a membrane where the proteins are analyzed. This research project will take a considerable amount of time which is why it was not fully completed during this past academic semester.

Acknowledgements

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