Elucidating Influenza host-pathogen interactions through data integration and analysis utilizing the BioHealthBase BRC

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BioHealthBase BRC

Introduction

The primary mission of the BioHealthBase Bioinformatics Resource Centers (BRCs) for Biodefense and Emerging/Re-emerging Infectious Diseases is to assist Influenza virus (A, B, C), Francisella tularensis, Mycobacterium tuberculosis researchers in their development of vaccines, therapeutics, and diagnostics. The BRCs, contracted through the National Institute of Allergy and Infectious Disease's (NIAID) Division of Microbiology and Infectious Diseases (DMID), will provide both central repositories for a wide variety of scientific data on these pathogenic microorganisms and a platform for software tools that support investigator-driven data analysis. A description of the NIAID BRC program can be found at: http://www.niaid.nih.gov/dmid/genomes/brc/default.htm

Influenza Specific Features

• Sequence
• Creation of consensus sequence based on sequence multi-alignments
• Analysis
• Influenza sequence alignments and polymorphism frequencies
• Epitopes
• Immune Epitope Database (IEDB) validated epitopes
• MHC class I predicted epitope using NetCTL
• Visualization
• Concatenated (8-segment) genome display of A/Puerto Rico/8/34
• Pathways
• Influenza life cycle pathways, host-pathogen interactions in the Reactome database

Reactome Pathways and Host-Pathogen Interactions

Current Features

• Integrated data sets from NCBI, UniProt, Pfam, IEDB, etc.
• Web-based data-mining and visualization tools
• Sequence data repository for several strains
• Structural features and functional annotation
• Metabolic and signaling pathway annotation

Collaborators Welcome

We are currently seeking Influenza researchers who would like to work with our team to develop the BioHealthBase application. If you are interested in providing data for analysis, feedback on existing functionality, or recommendations for new functionality, please contact us at feedback@biohealthbase.org.

Current and Future Work

Our initial contributions to the Reactome project include the Influenza A virus life cycle stages and their subcomponents. Our immediate priority is to flesh out the Influenza pathways that directly relate to NS1, M2 ion channel inhibition and neuraminidase inhibitors. Future work includes efforts to map out host-pathogen interactions between Influenza virus and a human host. Our first host pathways, RIG-I and TLR3, have been released in the Reactome release (May 2006) with pathways directly interacting to follow in the future.

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The Reactome project is a collaboration among Cold Spring Harbor Laboratory, The European Bioinformatics Institute, and The Gene Ontology Consortium to develop a curated resource of core pathways and reactions in human biology. Working in collaboration with Influenza experts and Reactome personnel we have added the Influenza A virus life cycle foundation to the Reactome project. Additionally, we have added the Toll-like receptor 3 (TLR3) and RIG-I host response pathways to the Reactome project.

Plan:
1. Influenza Life Cycle Foundation
2. Host Response Pathways
3. Detailed Influenza Pathways
4. Connect Host and Pathogen

Figure 1. BioHealthBase BRC Influenza page.

Figure 2. Concatenated sequence view of Influenza.

Figure 3. Diagram of the Influenza A virus life cycle.

Figure 4. Influenza A virus Reactome life cycle outline.

Figure 5. Reactome detail view

Figure 6. Host immune system signaling pathways.