Comprehensive molecular and clinical databases and repositories of influenza

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ABSTRACT

A member of Orthomyxoviridae, influenza virus is the causative agent of respiratory tract illness and is prevalently seasonal. Influenza is contagious illness affecting the nose, throat, and lungs. There are four types of influenza viruses: A, B, C and D. Furthermore, type A is subdivided based on two surface proteins of the virus: the hemagglutinin (H) and the neuraminidase (N). There are 18 different hemagglutinin subtypes and 11 different neuraminidase subtypes. There are several questions related to antigenic type, origin, year of isolation and virulence that need to be answered to better understand the evolution and infection of the influenza virus. Various databases are available, which compiles the research work by virologist and medicos. The paper summarizes about the different primary secondary and tertiary databases and resources available related to influenza. Repositories disseminating knowledge about the prophylaxis and therapeutic protocols available are discussed in detail. The paper will be a valuable resource for influenza researchers and medicos to select and apply the appropriate knowledge.

Keywords: - Virus, Antigen, Virulence, Database, Prophylaxis.

INTRODUCTION

Influenza virus is one of the main causes of prevalent epidemics and pandemic in the world [1-2]. Although pandemics do not happen often, they are major reason of widespread mortality.

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With such widespread data pertaining to the virus [3-7], many repositories have been established. Maintenance of accurate data for influenza may form a key resource for efficient emergency management protocols. Databases can be classified on the basis of type of information it hosts. Primary databases contain experimentally derived data such as nucleotide sequences, protein sequences and three dimensional structures. Secondary databases are constituted by

the analysis of primary data. Tertiary databases combine information from various primary databases and amalgates the data for the benefit of researchers [8]

Lately, cutting edge deep-sequencing projects for influenza virus genomes (Fig 1) has generated immense data and the databases have collected and presented it with clinical characteristics to understand evolutionary trends with public health significance. In this mini review, we discuss some of the public databases which are designed to create awareness and may be accessed by general public with ease.

Influenza info for health professionals

University of Auckland has created an information portal, Influenza info for Health Professionals (http://www.influenza.org.nz/antivirals) whereby, it details about the different immunization procedure and drugs available. The immunization for adults and children are different and hence dosage variation is evident. Additionally, influenza vaccination recommendations vary between countries. The United States (U.S.) recommends annual vaccination for all persons from 6 months of age. The site updates the vaccines available as per seasonal strains in US.

For example, it was clarified that vaccine available in 2017 (InfluVac) will offer protection against A(H1N1): an A/Michigan/45/2015 (H1N1) - like virus (new strain), A (H3N2): an A/Hong Kong/4801/2014 (H3N2) - like virus and B/Brisbane/60/2008 - like virus and another quadrivalent vaccine available will be effective against B/Phuket/3073/2013-like virus. The efficacy and effectiveness of influenza vaccines has also been discussed in the site. New Zealand data from the SHIVERS study have shown that the influenza vaccine used during the 2014 influenza season was around 53% effective (95% confidence intervals, 28–70%) at preventing influenza-related presentations to general practice and 52% effective (27%–68%) preventing hospitalisations overall. In the 2015 season the influenza vaccine was around 36% effective (95% confidence interval, 11–54%) at preventing influenza-related presentations to general practice and 50% effective (20%–68%) preventing influenzarelated hospitalisations overall.

As antiviral medications are effective only for the treatment and prevention of influenza but cannot replace influenza vaccination which is suggested stratagem for the control of epidemic. The neuraminidase inhibitors are the preferred class of antivirals approved for use in New Zealand. They include TAMIFLU® (oseltamivir) and RELENZA® (zanamivir) which are active against influenza A and B viruses. The website details about the chemoprophylaxis protocol, it also gives information regarding precautions and

hazards during pandemics at medicos and non medicos at home and hospital [10-13].

FluID

A comprehensive database named FluID (http://www.who.int/influenza/surveillance_monitoring/fluid/en/) presents regional influenza epidemiological data into and connects everything in a single global database. FLUID associates existing data and databases and may additionally be used to upload data via national focal points through a web-based interface. Both qualitative and quantitative data monitoring global trends, spread, intensity, and impact of influenza may be explored in this platform (Fig II).

The Global Influenza Programme of WHO provides a global platform for influenza surveillance information reporting, analysis and presentation. The information is shared through FluNet and FluID by the Global Influenza Surveillance and Response System (GISRS) and national epidemiological institutions [14-15].

The data is freely accessible to health policy makers and facilitate establishment of informed decisions regarding the management of influenza. Data is represented in the forms of graphs maps and tables (Fig.III).

Influenza Research Database (IRD)

The Influenza Research Database (IRD) (https://www.fludb.org/brc/home) is a freely available, National Institute of Allergy and Infectious Diseases (NIAID) funded resource. IRD works in collaboration with centres of excellence for influenza research and surveillance (CEIRS), J.Craig Venter Institute, Immune Epitope Database and Analysis Resource (IEDB), SDI and Cold Spring Harbor Laboratory, the European Bioinformatics Institute, and the Gene Ontology Consortium (Reactome) for data generation and storage.

IRD facilitates an understanding of the influenza virus and its interactions with different hosts. This resource contains the surveillance data for different host organisms, human clinical data associated with specimen information, and associated genomic and proteomic data for influenza viruses. It also links host surveillance and clinical data to sequence and phenotypic data for all well characterized influenza virus strains. The IRD also supplements a suite of bioinformatic analysis tools and workbench so that researchers may store lists of important data selected from that available on IRD. The suites encompasses functions like phylogenetic analysis, point mutations identification, alignment and annotation of proteins and peptide fragments classifications, metadata analysis and risk assessment [16].

FluWeb

FluWeb Influenza Historical Resources Database (http://influenza.sph.unimelb.edu.au/) was developed with the aid of a research grant from

the National Health and Medical Research Council (NHMRC) of Australia and is hosted by the School of Population Health, University of Melbourne. It details number of rare and valuable sources of data regarding past influenza outbreaks.

Resources available in this database are of two categories:

1. Content from rare historical sources that are no longer copyrighted.
2. Widely available/contemporary resources with bibliographic reference

The primary resource has been presented in form of fully downloadable version specifying influenza history in Great Britain and Ireland with statistics, bacteriology, clinical features, prophylaxis and epidemiology of the outbreak and outbreaks in Africa, Asia , Europe and USA in 1918-19 [17]

The database may also be searched for specific data based on data type, population type and size, recording methods,spatial type, country and time frame (Fig IV). It is an easy to use interface and the output is presented in table containing data downloadable format.

FLUomics Database

FluOMICS (http://www.fluomics.org/news.html) is a tertiary database developed by US investigators for prediction of influenza virus pathogenesis. A systems biology based approach was employed to identify the key host genes and networks that are involved in the early stages of influenza virus infection and influence viral pathogenicity. Specifically, the platform serves as a repository of data on changes to the transcriptome, epigenome, proteome (including post-translational modifications) and the metabolome along with functional genomics (RNAi and cDNA) The methodology additionally employed identification of biomarkers for predicting pathogenic potential of new strains, prediction of populations may prone to disease based on genetic variability and exploration of therapeutic interventions. The laboratories involved in updating information for this site are, Icanhn school of medicine , Mount Sinai, Salk institute of biological sciences, Northwestern university, University of California and Oregon state university [18]

EpiFlu™ Database

Under the aegis of GISAID initiative, a knowledge sharing platform , FpiFlu database was developed by Max-Planck-Institute. It is the one of the most comprehensive and exhaustive collection in terms of influenza metadata, both clinical and epidemiological. Its functionality continues to be tailored to the needs of influenza researchers from both the human and the veterinary fields. Within the first year of its operation, thousands of users have made EpiFlu^TM database their primary source for novel data that contains a complete collection of all data

from other public sources as well as unique data not found elsewhere [19-20].

Influenza viruses database (IVDB)

The Beijing Institute of Genomics (BIG), Chinese Academy of Sciences (CAS) is the key institute in generation of IVDB(http://influenza.big.ac.cn/). It currently contains 43,874 influenza virus nucleotide sequences, 53,983 CDS sequences and 53,983 protein sequences IVDB has created a knowledge and analysis platform for genetic, genomic, and phylogenetic studies of the virus. A searching system is developed for users to retrieve a combination of different data types by setting various search options. It has enabled investigation of the transmission and evolution of viral strains globally.

IV Sequence Distribution Tool (IVDT) has been employed to study geographic distribution of the viral genotypes and to correlate it with epidemiological data (Fig V) [21-22].

Another resource for primary information is the Influenza virus resource (https://www.ncbi.nlm.nih.gov/genome/viruses/variation/flu/). It encompasses genome sequencing information from NIAID and Genbank. It also features annotation tools for unknown viral sequences [23-24]. Analysis tool for influenza virus surveillance (ATIVS) is a server which enables surveillance on the basis of genotypes and antigenic shifts in influenza strains. ATIVS

can analyze both serology and sequence inputs [25].

CONCLUSION

Influenza databases and resources have enabled us to access data to both scientists and medicos alike. It has provided much needed information from where the scientist may utilize the knowledge for drug design and development whereby the medicos may further it for clinical trials. The accumulation of vast data in databases has given the researchers a template to start their research and is highly beneficial.

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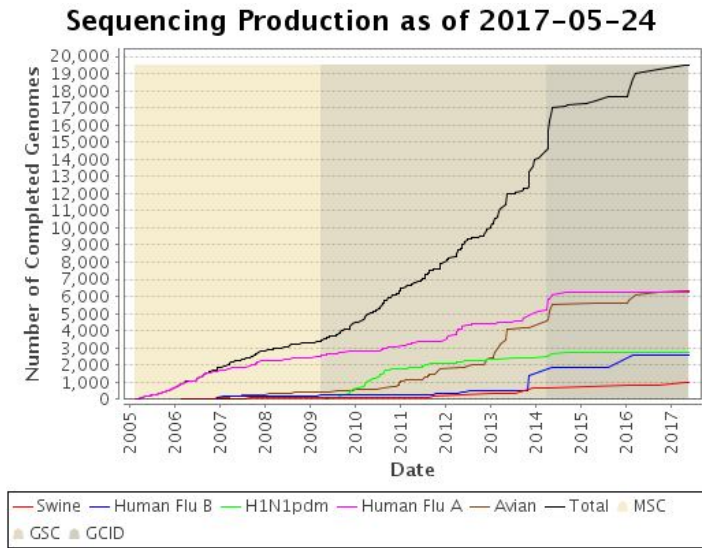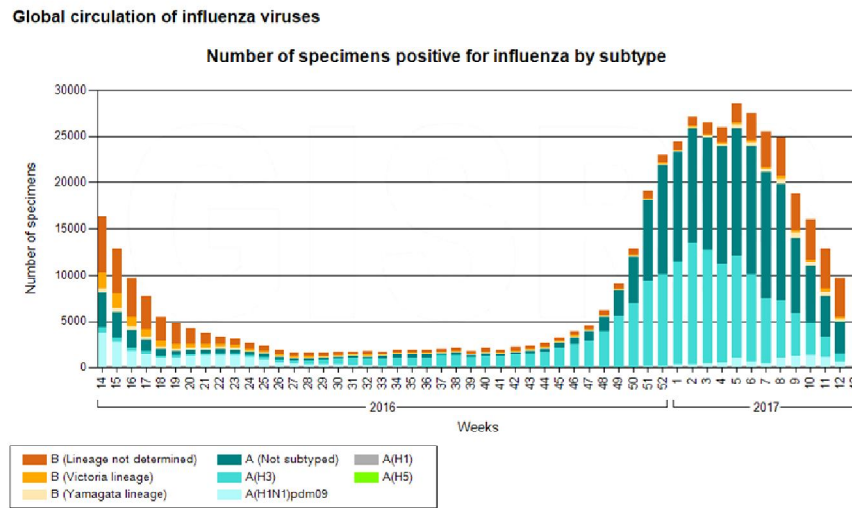
Fig I: Numebr of influenza viral genomes sequenced in different species.

http://gcid.jcvi.org/projects/msc/influenza/
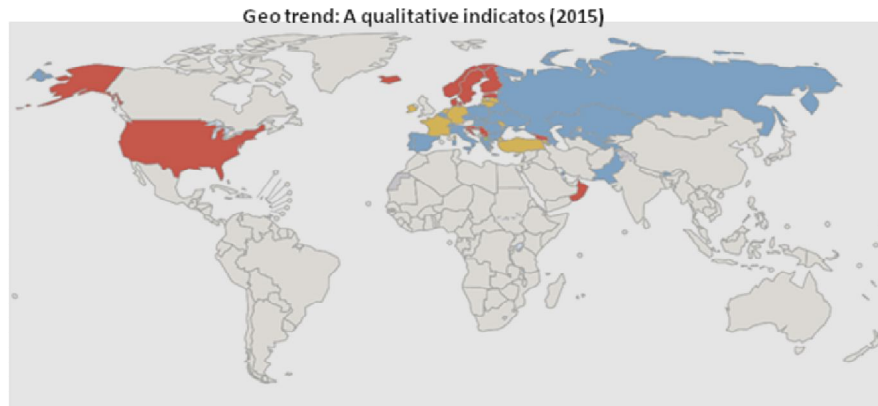
Fig II: Representation generated on the basis of query placed on geographical trends in FluID
(http://www.who.int/influenza/surveillance_monitoring/fluid/en/)

Fig III: Representation generated on the basis of query placed on influenza subtypes in 2016-17 in FluID

(http://www.who.int/influenza/surveillance_monitoring/fluid/en/)

Fig IV: An interface available on FluWeb for acquiring requisite information
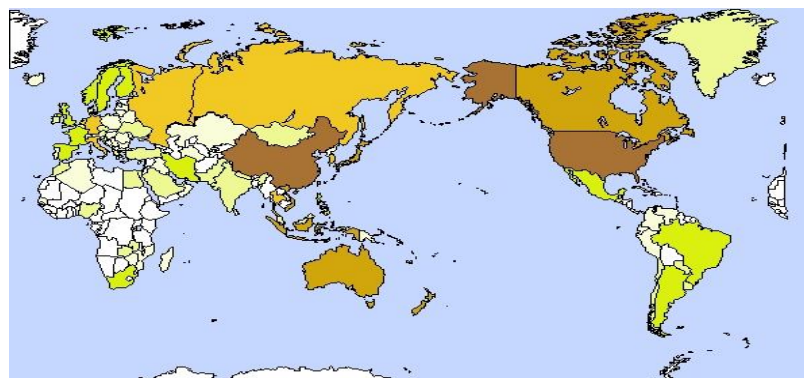
Fig V: Influenza virus sequence distribution based on epidemiological data (http://influenza.big.ac.cn)