Short Communication

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Bacteriology and Infectious Diseases 2018 - Bioinformatics in influenza surveillance: From sequence to structure to molecular mechanisms with the FluSurver

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Bioinformatics can play an important role in infectious disease surveillance and research from epidemiological data processing with geographic and temporal visualization to comparing genome phylogenies and structural modeling of mutations. As a classical example, interest in new influenza outbreaks as well as regular surveillance of circulating seasonal strains produce a constant flow of influenza genome sequences that need to be analyzed and interpreted for epidemiological and phenotypic features. Several steps in typical influenza sequence analysis can be automated and we have been actively developing the free online analysis pipeline FluSurver over the last 6 years to facilitate identification and interpretation of mutations in influenza sequences and link them with possible phenotypic consequences. The tool has already been instrumental in the discovery of new influenza strain variants with altered antiviral susceptibility, host specificity, glycosylation and antigenic properties and is being used by researchers, National Influenza Centres, WHO Collaborating Centres and the GISAID initiative. With the help from the greater infectious disease community, it is feasible to extend this tool for the monitoring and surveillance of other pathogens. The Influenza Research Database is an integrative and comprehensive publicly available database and analysis resource to search, analyze, visualize, save and share data for influenza virus research. IRD is one of the five Bioinformatics Resource Centers (BRC) funded by the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), which is an agency of the United States Department of Health and Human Services. Bioinformatics can play an important role in infectious disease surveillance and research from epidemiological data processing with geographic and temporal visualization to comparing genome phylogenies and structural modelling of mutations. As a classical example, interest in new influenza outbreaks as well as regular surveillance of circulating seasonal strains produce a constant flow of influenza genome sequences that need to be analysed and interpreted for epidemiological and phenotypic features. Several steps in typical influenza sequence analysis can be automated and we have been actively developing the free online analysis pipeline FluSurver over the last 6 years to facilitate identification and interpretation of mutations in influenza sequences and link them with possible phenotypic consequences. The tool has already been instrumental in the discovery of new influenza strain variants with altered antiviral susceptibility, host specificity, glycosylation and antigenic properties and is being used by researchers, National Influenza Centres, WHO Collaborating Centres and the GISAID initiative. Following an introduction of the tool and example application successes by Dr. Sebastian Maurer-Stroh, a walkthrough demo will be presented by FluSurver key developer Raphael Tze Chuen Lee. Coming from Austria, via Belgium to Singapore, Dr. Sebastian Maurer-Stroh leads a group of experts in computational sequence and structure analysis as senior principal investigator in the A*STAR Bioinformatics Institute (BII) since 2007. With more than 100 publications in the field, he is known for leading the team developing the currently most comprehensive influenza mutation analysis tool, the FluSurver, which is used by researchers, National Influenza Centres, WHO Collaborating Centres and the GISAID initiative. He also initiated a cross-division programme at BII combining groups from dif-

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ferent backgrounds to extend the range of methods applied to battle Human Infectious Diseases. Mr Raphael Tze Chuen Lee received his MSc in Bioinformatics in 2004. Since joining Dr Maurer-Stroh's lab in 2008, he has published more than 20 infectious disease related publications with him. The Global Influenza Surveillance and Response System (GISRS; formerly known as the Global Influenza Surveillance Network) evolved as an integrated scientific and technical global collaboration to fulfil the objectives and activities of the Global Influenza Programme (GIP), initiated in 1947 as one of the initial programmes of the newly established World Health Organisation (WHO). Seventy years on it is as relevant today, with an estimated one billion cases of influenza annually, of which 3-5 million are severe, causing between 290 000 and 650 000 deaths,3 and even more so given the constant pandemic threat from recent novel zoonotic influenza infections. While the principal objectives remain little changed, its modus operandi has adapted to the changing intellectual, technical and political environment. Following introduction of the first influenza vaccines in 1942 and an appreciation of a need for vaccine components to reflect changes in the circulating viruses, the establishment of the WHO Global Influenza Surveillance Network in 1952 recognised the need to monitor changes in the viruses in relation to the impact of disease. Thus from the outset the global network encompassed surveillance of the epidemiology and impact of influenza, sharing of viruses isolated by WHO designated National Influenza Centres (NICs) with WHO Collaborating Centres on influenza (WHO CCs) for antigenic characterisation of the viruses and selection of suitable vaccine viruses, in relation to the manufacture, regulation and administration/distribution of influenza vaccines. Initiated at a time when there was relatively little detailed knowledge about the viruses, their structure and mechanisms of infection, their ecology or the inter-relationships among the influenza viruses infecting humans and animals, research was a high priority, not only of methods for virus detection and analysis of their antigenic properties, but also of the fundamental virological properties of the virus. Many of the advances in our understanding of influenza were made in close association with the network—the "free" sharing of viruses and information providing a vital resource for the research community. Thus, revelation of the protein composition of the virus, the segmented nature of the virus genome and the structural (sequence) relationships between segments 5 in relation to genetic reassortment, and the antigenic relationships between animal and human influenza viruses, as the basis of pandemics were closely associated with the work of members of the WHO network and the WHO CCs in particular. Elucidation of the crystal structure of the haemagglutinin (HA) provided the first clear understanding at the molecular level of antigenic drift,9 of different receptor specificities between human and animal viruses in relation to host range restriction10 and the mechanism of virus entry into a cell, and more generally the mechanism of membrane fusion. Other notable spin-offs from research on resistance and immunity to infection were the discovery of interferon12 and the uncovering of the peptide basis of cell-mediated immunity.

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