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Genetic Epidemiology with MiSeq®: Tracking Influenza H7N9 in China

Emergence of a Respiratory Pathogen

- In winter of 2013, patients in eastern China were hospitalized with severe lower respiratory tract infections associated with an avian strain of influenza A virus (H7N9).

- By mid-April, 60 cases were confirmed in five Chinese provinces, rising to 130 in May. The viral transmission route was not clear, but the strain was found in chickens, implicating spread through live animal markets.

- June reports show infections continue in ten provinces, with a mortality rate of ~20%, no cases outside of China, and no confirmed human-to-human events.

- Simultaneous infection with several influenza strains raises concerns about the rapid emergence of genetic adaptations that could lead to a human pandemic.

A CDC scientist harvests H7N9 for research purposes. www.cdc.gov

Experimental Validation with MiSeq

Jiangsu Provincial Center for Disease Control and Prevention (CDC) used sequence data from the MiSeq sequencer to confirm H7N9 cases, examine strain relatedness, and to shed light on the possible transmission route of the virus. Three studies using next-generation sequencing revealed:

- Positive identification of H7N9 and phylogenetic analysis of animal and human samples show close relationships, confirming the likelihood of H7N9 transmission from chickens to humans.

- Full-genome sequencing of a patient viral isolate and an environmental one confirmed H7N9 that was 98.9% identical. Both H7N9 isolates contained variants potentially affecting the way the viral glycoprotein receptor hemagglutinin (HA) might bind to host cells, a critical step in animal-to-human transmission.

- Using RNA extracted from infected cells showed co-infection of a patient with two influenza A strains, H7N9 and H3N2. Detection of simultaneous strains within a sample is critical for understanding the mechanisms of viral reassortment from which new strains emerge.

Conclusions

- For genetic epidemiology, rapid and accurate next-generation sequencing technology provides high resolution data for the identification, classification, and transmission path investigation of viruses or any other microbial pathogen capable of producing the next pandemic.

- The successes of the dedicated Chinese researchers at the Jiangsu CDC demonstrate the effectiveness of next-generation sequencing as tool for infectious disease surveillance.

References

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2. Bao C-J, Cui L-B, Zhou M-H, Hong L, Gao GF, et al. (2013) Live-animal markets and influenza A (H7N9) virus infection. *N Engl J Med* (368) 2337–2339.

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