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Conversations

The origins of viral infection sleuth

The events of the past year have underscored the serious and rapid threat that emerging viruses pose to global health. However, much of the rapid progress in understanding and combating SARS-CoV-2 was made possible because of the decades of important groundwork laid from researchers studying other emergent infectious diseases. The 2021 John Dirks Canada Gairdner Global Health award recognizes the contributions of Joseph Sriyal Malik Peiris and Yi Guan toward understanding the origins and options for control of newly emerging infectious disease outbreaks in Asia, notably zoonotic influenza and severe acute respiratory syndrome (SARS). Cell's Nicole Neuman corresponded with Yi Guan about his path to becoming a viral infection sleuth and the challenges of understanding emerging pathogens and their origins. Excerpts of their exchange are included here.



Yi Guan, The University of Hong Kong and Shantou University Medical College

Nicole Neuman: What brought you to the field of virology? What is the motivation to study different viruses throughout your career?

Yi Guan: My PhD training brought me to the field of virology. Before this, I had practiced for 10 years as a pediatrician specializing in respiratory infectious diseases. Almost every day this made me think about, and try to understand, the etiological basis for the diagnoses of my patients.

In my career, the trigger point to study different viruses was the SARS outbreak. This event clearly demonstrated that many viruses can have pandemic potential, not just the well-known influenza A virus. The major research direction of my team is “pandemic preparedness in Asia.” While SARS and MERS have provided the best recent examples, a few influenza A virus lineages (H5Nx, H9N2, H7N9, and swine viruses) have been enzootic in different types of animals in China for decades, and we must watch them carefully.

NN: What is the biggest challenge you have overcome during your research of unknown viruses, for example your studies of SARS around 20 years ago?

YG: I think that the biggest challenge I had to overcome during my studies to trace emerging viruses was the field work. This forced me to create opportunities to access different types of animals and to get large enough sample sizes. Apart from sampling, I had to understand which types of animals were the most likely candidate hosts for different viruses. This meant I had to have different hypotheses in mind before starting my sampling. An example is my work on SARS, where my major contribution was to successfully identify the direct source of human infections in the 2003 and 2004 outbreaks. I had to have relevant, clear thoughts in mind about which types of wild animals in the wet markets might be candidates to carry SARS-like viruses before visiting sampling sites. I had to decide the likely infection sites in the animals that we would need to sample and the different types of samples we needed to obtain. Whenever we did this type of work, my colleagues and I were forced to expose ourselves to many risks, even though we took standard biosafety measures. On the occasion that I was able to recognize the dromedary camel as the intermediate host for human infections with the MERS virus in the Middle East, my

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colleagues and I had to sample more than 1,300 camels, which took 9 months to accomplish.

NN: You have accomplished many achievements in the influenza field. What do you think is the biggest challenge in this field?

YG: My achievements in influenza research are based on my long-term efforts and persistence in building the largest influenza surveillance network in China. This work has been conducted for more than 20 years, and over one million samples have been collected. We have systematically and regularly sampled different types of poultry, swine, and humans over that entire period of time. This gave our laboratory the chance to not only understand the nature of evolution in the different virus lineages but also to discover the different events leading to the reassortment and interspecies transmission of viruses, the common pathways by which pandemic influenza virus strains emerge. Thus, the biggest challenge to accomplish my work is how to constantly and systematically maintain a surveillance system.

NN: Last year must have been very difficult. How has the research in your lab changed during the pandemic?

YG: In 2020, our world experienced the first coronavirus pandemic in history. The whole world lacked preparedness, drugs, and vaccines. Our first work was, and still is, trying to identify the source of the SARS-CoV-2 virus. Even though we have a lot of experience in this type of work, and discovered that pangolins also carried SARS-CoV-2-related coronaviruses, the biggest challenge was to have the opportunity to check different types of animals in Wuhan. Our research direction has changed to try to understand the evolution of the SARS-CoV-2 virus in humans, along with helping to select the right vaccine candidates. This will be important to improve the performance of human vaccines and the development of antiviral drugs.

NN: How have your experiences in different viruses helped with your work on SARS-CoV-2?

YG: As our team had successfully identified the direct source of human infections, the intermediate hosts, for both the SARS- and MERS-CoVs, it made sense that we should also try to find something relevant to the pathway on which the SARS-CoV-2 virus emerged. We examined many different types of wild animals in adjacent regions at different wet markets; however, no relevant viruses were found.

NN: Working on infectious viruses during a viral pandemic must be very stressful. Can you give us some advice on how to keep your passion and deal with the high pressure at work?

YG: Just keep thinking about how you could save more human lives and make our world safer.

NN: How do you balance your life and the research?

YG: Honestly, I don't have too much of a family life or many hobbies. I spend most of my time working to organize different research activities in three different institutes in Hong Kong and south China.