

## MEET THE PROFESSOR

### Professor Stephen Kwok-Wing Tsui: targeting pathogen genomes

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**Figure 1.** Prof. Stephen Kwok-Wing Tsui.

The 10<sup>th</sup> Anniversary of Anti-SARS symposium, organized by the National Key Laboratory of Respiratory Disease and co-organized by *Journal of Thoracic Disease*, was successfully held on April 12<sup>th</sup>, 2013 in Guangzhou, China. In the symposium, Prof. Stephen Kwok-Wing Tsui (Professor of School of Biomedical Sciences, Figure 1) gave a wonderful speech on “Modulation of Potential Respiratory Pathogens by pH1N1 Viral Infection Revealed by Next Generation Sequencing”. “In order to have a better preparation for the pandemic, one of the areas that we should focus on is the evolutionary trend of the virus. With a better knowledge about the genome evolution, we might have the chance to forecast the mutations and thus the change in virulence and drug resistance”, said Prof. Stephen Kwok-Wing Tsui.

Prof. Stephen Kwok-Wing Tsui is now leading the Division of Genomics and Bioinformatics, and appointed as the Associate Director of CUHK-BGI Innovation Institute of Trans-omics, Director of Centre for Microbial Genomics and Proteomics and Director of Hong Kong Bioinformatics Centre in The Chinese University of Hong Kong. His expertise includes drug resistant of pathogenic bacteria, molecular virology of HIV and HBV, gene regulation in human cancers and bioinformatics.

In the following interview, Prof. Stephen Kwok-Wing Tsui will share with us his experience in combatting SARS and other infectious disease.

***JTD: Pandemic epidemics (in the recent years) seem to be in favor of targeting our respiratory tract as a lesion, what do you think is the main reason? What's your opinion in how to effectively prevent or treat the respiratory viral infection?***

Prof Tsui: This is because of the speed of viral spread. For infection of the respiratory tract, the infection could be easily spread to other individuals by cough or facial communication. This is very different from other blood borne diseases like HIV/AIDS or other sexually transmitted diseases. Encouraging people to wear masks when they have respiratory infection seems to be the most logical and efficient way, although we all know it is not easy to change the behaviors for some people.

***JTD: As an expert in respiratory pathogen research, could you give your comments on recent progress in SARS and flu virus research? What is the challenge and opportunity?***

Prof Tsui: From my experience, the genomes of the SARS-coronavirus and the influenza virus could be easily mutated so that the efficacy of drug treatment and vaccine is limited and not long-

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lasting. So, it is quite probable that our wars against these viruses will never end. In order to have a better preparation for the pandemic, one of the areas that we should focus on is the evolutionary trend of the virus. With a better knowledge about the genome evolution, we might have the chance to forecast the mutations and thus the change in virulence and drug resistance. The genome sequences of these two pathogens are accumulating very rapidly and this is the right time to start the study of their molecular evolution.

***JTD: Could you brief the clinical significance of studying composition of bacteria that lead to secondary infection?***

Prof Tsui: Because of the Human Microbiome Project, more and more scientists realized that the complex interaction among microbes inside our body plays an important role in health and diseases. For example, one of my recent published articles reported that the virus causing the swine flu can modulate the microbial community of the respiratory tract so that bacteria that can enter the lower respiratory tract are enriched. This may significantly increase the incidence of pneumonia with bacterial origins. Besides influenza, I am also studying human immunodeficiency virus (HIV) and acquired immunodeficiency syndromes (AIDS). Researchers found that the depletion of T cells is not directly caused by the HIV and recently there is a new hypothesis it is the bacteria entering the bloodstream that trigger the immune activation, which ultimately causes the T cell depletion. In fact, microbiome modulation is becoming a very popular topic in the scientific community.

***JTD: How can high-throughput sequencing method facilitate the gene sequencing of pathogenic bacteria?***

Prof Tsui: I worked on DNA sequencing when I was a graduate student 20 years ago. At that time, I could only get the sequences of around 1,000 base pairs (bp) per week. However, using the HiSeq 2000 from Illumina, now we can generate around 500 Gbp within a week. The throughput of sequencing has been increased by 500 million times! So, before the emergence of the high throughput sequencing, we can have a glimpse of the beauty of the biological world by investigating genes one by one. But now we can have a panoramic view of the genomes of all the species around us. Another important aspect of the high throughput sequencing is its primer-free nature. Some years ago, it is well known that if we want to sequence a gene, we need to design a pair of specific primers to amplify a gene using polymerase chain reaction (PCR). The necessity of primers has already limited the scope of investigation. But now we can use the genome amplification kit to amplify the DNA in hand for high throughput sequencing. That means we can sequence any DNA fragments

that can be extracted from any samples. This nature of high throughput sequencing has already enabled a lot of innovative applications of this revolutionary technology.

***JTD: SARS-CoV, like many other RNA viruses, recombines and mutates easily. Do you think SARS is likely to take another fierce attack? Are the existing precautionary measures and medicines able to counteract another outbreak of SARS?***

Prof Tsui: The virulence and infectivity of SARS-coronavirus is relatively mild when compared with other viruses causing respiratory infection. With the experience accumulated during the SARS outbreaks in 2003, I think the current precautionary measures and medicines are sufficient to counteract another SARS outbreak. The most crucial factor that controls the size of the outbreak is the awareness of medical professionals. Without such awareness, the initial number of patients of the coming outbreak may be increased to an extent that the current system is unable to handle.

***JTD: Great advances are achieved in the follow-up research on SARS. What can we learn from the experience in dealing with H7N9?***

Prof Tsui: My expertise is genome sequencing. Now, based on the sequencing of the H7N9 genomes, we can already know whether the virus can be propagated efficiently among humans. This is crucial for the implement of appropriate public health measures at the right time in the right place.

***JTD: From H1N1 to H7N9, variants of this virus family keep emerging one after another. Is the emergence of these variants a phenomenon as survive of the fittest? If yes, does this mean the H7N9 is more adaptable and invasive in the parasites than H5N1? If not, what catalyze the variation?***

Prof Tsui: Yes, this is a common phenomenon of genome evolution. H7N9 may not be very adaptable but should be very virulent to humans because the human immune system is not familiar with this strain and therefore will produce a much stronger immune response upon infection so that the lung could be severely damaged when the body tries to clear the virus.

***JTD: Would you like to share with us any stories, particular challenges, setbacks, or successes that you've encountered along the way in your research?***

Prof Tsui: When my team worked on the SARS-coronavirus genomes in 2003, we just liked fighting in the darkness because at that time scientists did not have a standard method to sequence the genome of a pathogen. Moreover, we did not have a Biosafety Level 3 (P3) cabinet at that time and therefore we

were all in danger all the time. However, it is thankful that all the members in my team were very dedicated and committed so that we finally cracked the SARS-CoV genome within half a month and our university designed the quick diagnostic test based on our work. The incorporation of quick genome sequencing and rapid real-time PCR assay has also become the standard practice when other teams later worked on outbreaks and pandemics. As a scientist in the area of biomedicine, I am so glad to have done

something that can really contribute to the whole world. My experience in SARS has also aroused my interests on the study of pathogen genomes and I will continue to work on this research area in coming years.

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