AN INTERVIEW WITH PROFESSOR LAP-CHEE TSUI

Professor Tsui is the fourteenth Vice-Chancellor of the University of Hong Kong. Prior to his present appointment in September 2002, Professor Tsui was Geneticist-in-Chief and Head of the Genetics and Genomic Biology Program of the Research Institute, at The Hospital for Sick Children in Toronto. He was also the holder of the H.E. Sellers Chair in Cystic Fibrosis and University Professor at the University of Toronto. He received international acclaim in 1989 when he identified the defective gene that causes cystic fibrosis, which is a major breakthrough in human genetics. He has also made significant contributions to the study of the human genome, especially the characterisation of chromosome 7, and, identification of additional disease genes. His works have been cited more than 35,000 times; he has 300 peer-reviewed scientific publications and 65 invited book chapters and papers.
1. Could you please share with us briefly about your key research areas?

I am a molecular biologist by training, so my interest is to use molecular biology to solve problems in human genetics. Human diseases are one of the several things I was looking into at the time I started my own research. I picked cystic fibrosis as my subject of study, because it is a genetic disease and is very clear from previous studies. In addition, since DNA markers were available and basic principles were formed, we could apply the classic human genetic principles using modern molecular biology techniques. Long and behold, we found the gene for cystic fibrosis. Since then, I continue to study the basic defect of the disease and other mutations of the gene. I’m also interested in gene therapy and understanding the interaction of this gene with other genes in the patients or body and try to help to treat the disease. This is my basic direction of research.

2. How did you become involved in this research, were there any challenges encountered along the way and what motivates you to continue in these areas of research?

Of course there were difficulties. I remembered when we first tried to use this particular technology, later coined by Francis Collins as positional cloning. It was the first time we used this approach to identify disease gene so there were lots of unknowns and lots of concepts that we had to try out. Often, the experiments did not really tell us anything or did not work. And it was very tedious because the Human Genome Project had not started yet. In fact, the cloning of the cystic fibrosis gene was used as an argument that we should have the human genome sequenced because we spent so much time trying to decipher whether there is a gene or not in a piece of chromosome we isolated. Now, thanks to the Human Genome Project, we have all the genes in front of us, so to find a disease gene today is so much easier than when we were doing our work at that time.

TR: Definitely, but that sounds that it will do a lot of good for the community and I suppose that is the reason why you find it motivating to continue and find a disease gene and help people in that sense.

Yes, that is correct. That is the reason of motivation. In fact, a lot of other groups were trying to find the gene too and there were some competition among different groups. Interesting that we knew we had a job to do – to find the gene to help the patients. So while we competed, we also collaborated. And we collaborated by sharing information about the regions of chromosome 7 which were being worked on and compare notes with each other at meetings and conferences. So the atmosphere at that time was very competitive yet there was a friendly element.

3. Why do you think your research papers have been highly cited?

Well, I think obviously it was a piece of classic and pioneering work – it was the first time that we managed to demonstrate the principle that one could identify a disease gene without any chromosome abnormalities to point the location and without any biochemical clue. From our work, it became possible to dissect a very complicated disease with multi-organ abnormalities to gain a fundamental understanding of the basic defect in cystic fibrosis. Second, cystic fibrosis is a rather prevalent genetic disease in the Caucasian population, affecting 1 in 2,500 to 3,000 at the time. Finding the gene gave an important clue of the disease whereby better treatment and new drugs could be developed. Sometimes we joke that even though there is still no magic drug for the disease, a better understanding of the disease has already brought significant benefit and hope to the patients – they live much longer comparing with 20 years ago. In addition, because cystic fibrosis is a rather interesting disease but a challenging problem to work on, there are more scientists working on the disease than there are patients. For example, the molecule in which the defect occurs is a very interesting molecule itself, so a lot of biologists study it as a biological molecule. Of course, they eventually also contribute to the understanding of the disease. So, for all these reasons, scientists cite our original work in 1989.

4. Do they usually describe a new discovery, methodology, or synthesis of knowledge? Could you summarize the significance of your papers in layman’s terms?

Refer answer for Question 3

5. What outcomes or impact on society do you hope to see as a result of your research? Where do you see your research heading in the future?

Our work was important because it provided an important clue to solving a very important human genetic disease. Second, it was the first time that this particular approach or methodology was used to identify a human disease gene; the same might be applied to many other diseases. And, because of the amount of time we’ve spent on this work and the labour involved, it then made sense that the world should come together and get the Human Genome Project done, so that the information could help all disease research. As I’ve said earlier, it is now easy to find a disease gene as long as you have the patient materials for the disease you wish to study. Patient materials mean the DNA; one can get the DNA from different tissue samples now – not just from blood anymore. From any body tissue, including buckle swab, you get sufficient cells and DNA from there and perform the genetic studies like what we did before, but of course much simpler due to the availability of the human gene map and sequences. So you can say that our work had really changed the field of disease gene research.

The future is really now. Cystic fibrosis is a simple disease. It is due to mutation of a single gene. Since scientists have a good handle for most of the single gene diseases, they are now moving towards understanding complex diseases. These are the common diseases, like diabetes and coronary heart diseases, which affect major fractions of the world population. In addition, there are more and more mental illnesses being delineated and their respective genetic contributions are being deciphered. These are the so-called genetic dispositions; when we have such combination of genetic factors, which may not be gene mutations at all, we become susceptible to these diseases; they can be different variations of such susceptibility genes or different combinations of these variations, making us develop a tendency of having the disease. Research for these common diseases proves to be very difficult because the contribution of individual genes to the so-called disease susceptible state could be very minor. Although the work may be very challenging, the payoff would be very significant. Simply put, you may discover from genetic analysis that you have a genetic tendency to develop diabetes, but then you can avoid developing diabetes by choosing to live a proper life style and watch your diet, so that you may never develop diabetes. Therefore, understanding the genetic contributions to these diseases will be very helpful to preventing and treating them, thereby providing health to individuals and the entire population.