SMA NEWS
VOLUME 40 NO.10 **OCTOBER 2008**
MICA (P) 200/01/2008

Interview with Professor Charis Eng

By Dr Toh Han Chong, Editor

Dr Charis Eng is the Chairman and founding Director of the Genomic Medicine Institute of the Cleveland Clinic Foundation, founding Director and attending clinical cancer geneticist of the institute's clinical component, the Center for Personalised Genetic Healthcare, and Professor and Vice Chairman of the Department of Genetics at Case Western Reserve University School of Medicine. She holds a joint appointment as Professor of Molecular Medicine at the Cleveland Clinic Lerner College of Medicine and is a full member of Cleveland Clinic's

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Dr Toh Han Chong: You are an American citizen, and you have established yourself as an eminent clinician-scientist. Can you let our readers know what your connection with Singapore is?

Professor Charis Eng: I was born in Singapore, and so were my parents. I took a brief one year sojourn to Bristol, England at the age of four when my father was sent there for his Honours training in Economics. I returned to Singapore, and went to the Methodist Girls School (MGS) until the age of 13, when my father was again sent on a scholarship to the University of Chicago in the US from the Institute of Education. I am an only child and so my mother and I followed him, and that is how I made it to Chicago.

The Laboratory Schools belong to the University of Chicago and is the great educationist John Dewey's original school. Therefore, you are allowed to progress at your own rate. I basically finished all of high school (8^{th}-12^{th} grade, in other words, five years) in three years. At that point, my father had finished his Ph.D. You have to understand that for the social sciences at the University of Chicago, a Ph.D takes 10 years; he took two and a half and was ready to go home. Something inside me said the education at the Laboratory Schools is second to none. I've never learnt so much in my life and the teachers are so dedicated, and you are really learning for life, not just for an exam. Thus I said I wanted to stay, so, we went to visit the Principal, Mr Geoff Jones, who said that as a minor, I could not stay without my parents, unless I entered University and that I should apply to the University of Chicago. So I did, I went for my interviews and they accepted me. My parents went home and I entered the University of Chicago at the age of 16.

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Published by the Singapore Medical Association, Level 2, Alumni Medical Centre, 2 College Road, Singapore 169850.
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URL: http://www.sma.org.sg
SMA Reg. No.: ROS 198/59 TAP

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THC: Did you know that you were keen on a career in Science at such a young age?

CE: Well, my uncle Professor Lee Yong Kiat was an inspiration since I was very little. I guess since the age of four, I've always wanted to be a doctor. In Primary Four at MGS, there was a health sciences subject and in that we learnt about medical discoveries and read about the great medical scientists such as Louis Pasteur; that was when I wanted to be a biomedical scientist too. As you know, there was no MD-Ph.D or physician-scientist training in Singapore at that time and not really even now. And so I just kept this at the back of my head.

THC: Certainly at that stage, being a clinician-scientist was quite an uncharted field because there was no such thing in Singapore. It must have been quite a courageous move to be both a medical doctor and a scientist. Why didn't you become a full time clinician like Professor Lee?

CE: Actually, you could view my uncle as a clinician-clinical investigator in the sense that he didn't work at the bench, but he certainly worked as a clinical investigator. That was well before clinician-investigators were fashionable. He was certainly my role model as I saw him making clinical discoveries. As well, I saw that he was the greatest diagnostician of all time. When you are a doctor, you help that one patient at a time. When you are a scientist, you have the probability, or at least the hopeful goal of helping thousands, if not millions of people.

THC: As Chairman and Director of the Genomic Medicine Institute at Cleveland Clinic, what would you change about the Human Genome if you had a choice?

CE: That's a very good question. Let's step back and say, when we are studying the heart or the brain, we always question why God didn't make it more robust, why didn't He make the heart have more collateral arteries, why does the brain only have a circle of Willis which often is not completely redundant, and so on.

With the Human Genome, we can say we have to make it mutation-proof but if we do that, there will be no human variation. Without human variation, there will not be an evolutionary process that in the end, we hope, brings out physiologic strengths.

THC: If you had stayed back in Singapore and gone from MGS to a local junior college, then to University in Singapore, do you think life would have been very different?

CE: Completely different. I think I would not be in the position that I am in today. I can't tell you what I would be. I am grateful for the many serendipitous opportunities afforded me in life.

THC: Can you suggest ideas or philosophy in education that we can incorporate into Singapore's education?

CE: I think the key difference in Singapore, even in MGS, is that you were trained to pass examinations. You were trained to memorise, and in fact to regurgitate. I didn't like that but I had a great memory, and what struck me was that the Laboratory Schools and the University of Chicago encouraged you to innovate and to think analytically. Of course, you have to memorise certain content but you have to be able to do it in an analytic manner so that you are not memorising everything.

The other thing is that the Singapore school system gets their students to sub-specialise very early; streaming starts in Secondary Three. I went through the University of Chicago where undergraduates go through a liberal arts education. Thus, as a major in biology, I had to do all the courses which made one expert in biomedical sciences, physical sciences and mathematics, but there was a Common Core which includes two years of humanities, social sciences, analytical writing and so on. That has really stood me in good stead in writing scientific grants and manuscripts.

THC: Biomedical sciences is set to be the fourth pillar of Singapore's economy, and there has been a lot of support for this enterprise. What are some of your insights and advice for this initiative?

CE: I have seen very little – I have been here for only three days. I have of course spoken to many of you wise people and I would say this is a small country – so think big – and this means regionally. You have unique resources, so concentrate on diseases that are peculiar to here and other nearby regions.

Do not set up competition amongst each other because you are a small country and hence cannot afford to compete because of the country's size. In

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Taussig Cancer Center and of the CASE Comprehensive Cancer Center. Dr Eng was recently honored with the Sondra J. and Stephen P. Hardis Endowed Chair in Cancer Genomic Medicine. She continues to hold an honorary appointment at the University of Cambridge. Dr Eng's research interests may be broadly characterised as clinical cancer genetics translational research. Her work on RET testing in multiple endocrine neoplasia type 2 and the characterisation of the widening clinical spectra of PTEN gene mutations have been acknowledged as the paradigm for the practice of clinical cancer genetics.

In 2001, she was honored with the conferment of the Davis Professorship and appointed Co-Director of the Division of Human Genetics in the Department of Internal Medicine. In 2002, she was promoted to Professor and Division Director, and was conferred the Klotz Endowed Chair. She moved to the Cleveland Clinic in Sept, 2005.

Dr Eng has published over 290 peer reviewed original papers in such journals as the New England Journal of Medicine, JAMA, Lancet, Nature Genetics, Nature, Cell and Molecular Cell. She has received numerous awards and honors including election to the American Society of Clinical Investigation, to the Association of American Physicians and as Fellow of AAAS, the Doris Duke Distinguished Clinical Scientist Award and named a Local Legend from Ohio bestowed by the American Medical Women's Association in conjunction with the US Senate on women physicians who have demonstrated commitment, originality, innovation and/or creativity in their fields of medicine. Dr Eng is the 2005 recipient of the ATA Van Meter Award at the 13th International Thyroid Conference, the 2006 Ernst Oppenheimer Award of The Endocrine Society and the 2006 American Cancer Society John Peter Minton, MD, PhD Hero of Hope Research Medal of Honor. She was the North American Editor of the Journal of Medical Genetics from 1998 to 2005, is Senior Editor of Cancer Research and Associate Editor of the Journal of Clinical Endocrinology and Metabolism and of the American Journal of Human Genetics. Dr Eng has been elected to a 3-year term on the Board of Directors of the American Society of Human Genetics and is serving a 5-year term on the Board of Scientific Directors of the National Human Genome Research Institute.

The SMA News was kindly invited to interview Professor Eng as she lunched at Iggy's.

the private industry, you compete because there is fitness in competition, and it is healthy. If you fight amongst yourselves in scientific endeavours, you will achieve nothing. You need to unite, collaborate and break down the silos. Your competition is outside Singapore, so band together.

Resources wise, I am very impressed that the resources here for biomedical research are huge, as compared to the US, which is going absolutely the wrong way. But I also understand from many of you that the resources are unevenly allocated, so you should think about asking your leadership to consider allocating resources more widely.

THC: As a woman in science and having reached a pinnacle of success, what are your insights to some of the struggles or challenges of being a woman in science? Is it an equal playing field, even in the lands of opportunities?

CE: No, it is definitely not. We have to be much better than the next guy for every endeavour, whether it's for scientific recognition or leadership roles. It is and remains extremely difficult although it is the 21st century.

THC: Do you have any role models in science whom you look up to?

CE: I have. I guess the Number One role model whom I look up to is my uncle Yong Kiat. I told him that yesterday, and I told him that I would dedicate my talk to him tomorrow. I also asked for his permission, may I dedicate it, because he is a very private person and he may very well have said no. *(Laughs)*

For the other role models, one of them is Ed Garber, he was my Professor of Genetics when I was at the University and I did undergraduate research with him, on the genetics of crop fungi and he has been my lifelong mentor until his death in October 2004. The funny part is that I have never had a mentor within my own institution ever since I became an independent member of faculty. That's ironic. I've had external mentors, Bob Gorlin (of Gorlin's Syndrome) has been a wonderful mentor as well as collaborator, until his death two years ago. It was a really sad day.

There's David Ginsberg as well (HHMI Investigator at the University of Michigan, Ann Arbor). And of

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course at the University of Chicago, as a female role model, there's Janet Rowley. She is still going strong; she is a real lady in addition to a wonderful scientist.

THC: A look into British science and American science – what are your own personal experiences and insights, having been in both places?

CE: I would say the undergraduate experience is certainly much stronger in the University of Chicago because of the liberal arts aspects. The medical school in the American system, as you now know, is a post-graduate system and science is always intertwined. I happened to do an MD-Ph.D and I did internal medicine at the Beth Israel Hospital and medical oncology at the Dana Farber Cancer Institute (both Harvard hospitals) in Boston. I then went to University of Cambridge in the UK to be Senior Registrar in Clinical Cancer Genetics and I trained as a postdoctoral fellow in human cancer genetics at the bench with Professor Bruce Ponder.

There was no formal Clinical Cancer Genetics programme in the US. How it worked was when I was at Dana Farber, the Chiefs then had always been interested in cancer genetics and they thought that the field was going to be burgeoning, and so they should send one of the fellows. They picked me above the other fellows, who were all men by the way. They asked me if I wanted to go to Utah, Johns Hopkins or Cambridge, and without thinking, I said Cambridge. They asked if I had to consider the options and I said no. I have been thinking about this all my life and they asked why. I replied that Cambridge has both bench and bedside training that are equally strong. Hopkins is strong at the bench but there's nothing at the bedside to the same level and it is the same with Utah. It's almost all bench and there is no integration.

THC: How did you know the programmes in these places before actually being there?

CE: Well, cancer genetics is a small world so even as a trainee you do know.

THC: What were your fondest memories of Cambridge University?

CE: I think my three years in Cambridge are amongst the happiest in my life. There was wonderful training – great training at the bench and it was not just working with Bruce Ponder, it was working with the people whom he was training. It was good training, and to receive unique training in clinical cancer genetics was something that I dreamt about since I was a child. As you know, I thought of putting cancer and genetics together when I was at the Lab School. It was really amazing and being in College, sitting at high table as a Fellow was the best time to learn about wine, and the rest is history. And also, I still hold an honorary appointment at the Cancer Research UK and Emmanuel College in Cambridge.

THC: Do you think that personalised medicine is going to be a reality?

CE: Absolutely. In fact, I like to give the example of ABO blood typing as an example of personalised medicine. Why the hype and excitement now, I think the Human Genome Project has captured the imagination of everyone – the public, caregivers, the whole world. I think that technology has caught up with us, that we are actually getting good and replicable data. Because of the interactions between physicians and scientists, we are putting clinical context together with content, ever so slowly, but it's coming, and we can actually do personalised healthcare.

Certainly, in my field of cancer genetics, we have been practicing personalised genetics-based healthcare for some time now, because if you have a mutation in one gene versus the other, it tells you which organ to put on surveillance or not to survey, or to conduct prophylactic surgery or not.

THC: What is the dream scenario of bedside personalised medicine that will impact on the lives of patients?

CE: I think the basic core of what we all do as physicians will not go away and certainly the history will continue to be important; the family history will take on more prominence, and may well be more vital than the physical examination. I think the routine laboratories and pathology will remain. The objectives of genetics and the -omics data will be wonderfully useful diagnostic and prognostic adjuncts, and will help us pick out – I would not say treat because management is sometimes not the same as treatment – the course that we would recommend the patient to follow, but in a manner

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where it will be 99% successful and less than 0.5% having a toxic side-effect. Not that it takes the guess work out of what we do, but it takes away the practising on the law of averages.

THC: I think there is still some way to go in cancer therapeutics. We still see a majority of patients who do not respond to these new targeted treatments.

CE: Yes, and to understand why they suddenly become resistant. Currently, we are still using single agend molecular-targeted therapy. I suspect that multi-agent targeted therapies in an integrated manner will be much more successful.

THC: Do you have advice for the young doctors of today?

CE: Continue in your field only if you feel passionate about it. If your parents asked you to do it but you want to do something else, go do something else. This is a very difficult road, this is a calling and you have to really believe in it. Also, you must learn your genetics and genomic medicine because it will dictate how all of medicine will be practiced within the next 5 to10 years – psychiatry, radiology, anesthesia, everything.

THC: How do you do it all – clinical work, research, administration, grant writing and lobbying for your Institute? How do you combine all that into 24 hours of a day?

CE: I think importantly, there has to be the passion for it that gives you energy. And of course, I am a highly organised and efficient person. A part of it is genetic, there is no doubt about that; you can teach someone to a certain level but you are innately limited by something, so we will call that genetic.

The other thing I have to say is that I was an athlete since I was very small; I was a State swimmer and I also did karate. I had to balance work and athletes know how to prioritise. Finally, I have to say that Singapore has taught me discipline; Singaporeans are extremely disciplined. So I am disciplined, organised, efficient and I know how to delegate as well as hold people accountable.

I sleep eight hours a day and that is important, you must always have your rest.

THC: Did you aspire to be a scientific leader from the start?

CE: People who aspire to be leaders for the sake of power are doing it for absolutely the wrong reasons. I never wanted to be a leader, but I figured from Day One of being a junior faculty member and working under a series of poor bosses, it struck home that the only way of creating a wonderful environment for everyone is to be a leader myself. I became a leader so I can help my faculty and help people well.

THC: What were some of the things that you wanted to implement to make the Institute environment a much more conducive one for science?

CE: Often, the poor leaders are the ones who are leaders for the sake of power. They actually want to take advantage of the people who are under them instead of helping them. They will keep taking from these people without regards for or nurturing the faculty, so that's wrong.

As a leader, what you want to do is to have a very conducive environment where you are sacrificing your own well being, academic right and so on to ensure that your junior faculty will succeed because their success is your success. And as I always say, what is good for my entire faculty is also good for me, and that is what leaders must remember.

THC: There must have been a long string of mentees under your charge. Is it very rewarding for you to see your laboratory people succeed?

CE: Absolutely, I have mentored and am probably mentoring over 50 people ranging from undergraduate level all the way to post-doctoral and clinical fellows. My first mentee Deborah Marsh, who was a post-doctoral fellow who completed her training in 1999, is now the Head of Cancer Genomics and an Associate Professor at the University of Sydney. I am very proud of her.

THC: Regarding the Human Genome Project, we have heard a lot about the HapMap and now about high throughput sequencing. When can we come to the day where we can explain to our patients before they get a stroke or heart disease about prediction?

CE: Hopefully today. For certain things, obviously today, so for example in our field of cancer

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genetics, we can predict for quite a few syndromes – the various breast, thyroid and colon cancer syndromes and many more. What I think you are alluding to are the common disorders and variations. That is of course difficult, because there are many common variations. Right now, we have gone with the hypothesis that common variations cause common diseases. It turns out that research has now shown that the common variations cause very little of the common diseases, probably only 2%. What I and many other scientists are afraid of is that it will turn out that multiple private variations add up to cause common diseases. It is a challenge to understand how these variations "talk" to each other, and how they "talk" to the high penetrance genes to result in a clinical disorder. The relative risk of these common variations are very small, it can be a relative risk of 1.1.

Just to give an example, say the population risk of a certain type of heart disease is 0.5% in a lifetime, a 1.1 relative risk translates to 0.55% chance of heart disease occurring instead of the 0.5% in the general population. Do you advise your patient to stop eating foie gras? I say no.

THC: You have published in some of the top journals, you are editor of some of the major journals in cancer and genetics and you are running an Institute. Where do you see yourself ten years from now and what do you think you will be doing then?

CE: I don't know, that is a good question. I hope I will be doing something that will contribute much more to the greater good; in other words, I always hope that I will be doing something with lasting and broad impact. I mean, ten years before, I was still a third year Assistant Professor and I never dreamt that I would be in this position.

THC: How did your interest in opera come about?

CE: My mother is very musical, and I think half of the Lee family is, and half of them think they are. *(Laughs)*

I think I was in Primary Three when my mother put on a tape of Madame Butterfly and it was awful, it sounded like screeching. Then she put it on again and again, and it grew on me and I grew to love the Puccini and Verdi operas and so on.

THC: When you visit cities to give talks and attend meetings, do you attend the opera?

CE: I do, and here's a secret. When I write grants – I cannot stand writing grants; I love writing manuscripts but not grants, particularly when they are onerous – I put on Pavarotti or a nice Puccini opera. Pavarotti has helped me get many grants. *(Laughs)*

THC: Have you actually listened to Pavarotti performing at La Scala?

CE: Yes, and he came to visit at Columbus, so that was a great privilege but then, his voice didn't sound right and I said to myself: "Mr Pavarotti is sick" and a couple of years later he announced that he had pancreatic cancer.

THC: Your uncle has been a major influence on your life, and are there any influential books or personalities that also played a big role in shaping your life and thinking?

CE: I used to read many books and I love the classics like the Illiad and the Odyssey. Once I learnt French in Chicago, I even read Marcel Proust and so on in French. I love reading good cartoons like Asterix and Obelix because it has a lesson for every age. You enjoy it as a child and when you re-read it as an adult, it's totally different – it's about leadership, mass reactions

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Iggy's Burger

Cauliflower mousse, sea urchin and shiso jelly

and it teaches you about how your employees react. It's all in Asterix and Obelix; the enemy or who is considered the enemy and so on.

I also keep up with my French – I can speak French, I wouldn't say that I am fluent, I actually am often called upon to be the external examiner of French doctoral theses and review grants written in French from Quebec. I can certainly order a meal and wines in French. That's what is important. I read wine books and magazines, that brings together literature and my love of oenology.

THC: From what you have seen of the strengths and weaknesses of Singapore's healthcare, do you have any advice for us?

CE: I would say the major strength is that there is health care for all and that isn't true in the supposed first world countries. I think the weakness is probably the fact that there isn't a research base locally to guide personalised healthcare.

THC: What would constitute a fabulous final meal and what wines would you pair it with?

CE: I think the meal by itself doesn't matter; it just has to be outstanding. Now as for the wine, it absolutely does matter. *(Laughs)*

As you know, just like today, a multi-class meal has to go with multi-class wines and we should always start with champagne. Perhaps we should have a 1926 Dom Pérignon Rosé and then perhaps a fabulous white wine from Burgundy. Maybe a Faiveley or William Fèvre, perhaps Puligny-Montrachet from a wonderful vintage.

Naturally, we would like some Bordeux with the main course. It has to be either a Mouton Rothschild, a Lafite Rothschild, a Pétrus or a Latour; one of the great vintages, I'm sure. One of the more recent great vintages could be the 1982 or the 1985. If we want an older vintage, perhaps we could have the 1963 or the 1926.

Finally the dessert wine, we have to have the Château d'Yquem. And to go with the cheese course, we should have a lovely port. It can be a Taylor Fladgate or Croft or maybe the 1890 Croft port. There are many good port vintages, some from 1960, 1966, 1970 and 1977. Those are the more recent vintages.

THC: At which restaurant have you had a memorable dining experience?

CE: In 1996, I was a first year Assistant Professor and was invited to Paris to give a plenary talk in the Journees Internationales HP Klotz for Endocrine Neoplasia and I gave my RET-MEN 2 talk. Unlike now, where I know that you have to book months in advance to dine at top restaurants, then I did not. It was Saturday night and I was asked where I was going for dinner. I replied that I did not know, and someone suggested calling for me, and got me in, with apologies, at Maxim's de Paris which is very glitzy and touristy. It might not have been good but I took the metro and alighted. When I got there, the doors opened as if I was the queen and they literally carried me to the table. I was speaking French and had some champagne and had a lovely meal.

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Because I spoke French and I also showed interest in their wines, I was wowed because they had half bottles verticals of Bordeux. I had a half bottle of Les Ormes de Pez 1982 St Esteph. St Esteph's are supposed to be the bargain basement of Bordeaux, and I remarked that this was certainly not from a bargain basement.

Dessert came, and I ordered a mousse au chocolat and the waiters mentioned that the order would take twenty minutes. I asked if I could see their cellar so they brought me down with great aplomb and delight, and the cellar was wonderful. There were all these Bordeux and ancient wines from 1926 and the 1800's, and the waiters were amazed because they had never seen a non-French person appreciate French food and French wine as I did. It was time for dessert so I wondered what dessert wine I should order, and the waiters told me "Don't worry, Madame, we will take care of you." They came out with this cute little bottle covered in dust and dusted it off, presenting the 1894 Croft port. I was wondering if I could even afford an 1894 port: I was just a poor Assistant Professor. They could actually uncork it, but usually the old corks are crumbly and I thought that it had to be a bluff. When it was poured out, however, it was a muddy brown like how old port looked, and so I really became worried about the cost. The waiters then told me "Madame, it is on the house because we have never seen a foreigner appreciate our food and wine like that." It was fantastic, and I will never forget that. I wish I took a photograph, but those were the days before cellphone cameras; that memory is in my mind forever.

THC: Finally, do you need to have a superior olfactory system to be a wine connoisseur?

CE: I think so, because people say that one drinks or tastes through the nose. Unfortunately I do have allergies, and so naturally, my sense of taste could have been much better

THC: Thank you very much. ■

Professor Charis Eng's lunch selection at Iggy's, Singapore

STARTER
Sea Urchin
Cauliflower mousse, sea urchin and shiso jelly

APPETIZER
Foie Gras
Classic terrine of foie gras, French toast, carmelised peach and mango mesclun

Paired with Champagne Jacquesson Rose 1997

MAIN COURSE
Iggy's Burger
Home-made wagyu beef burger, white truffle sabayon

Paired with Torbreck, The Steading 2005

DESSERT
French Toast
Chocolate cylinder, French toast, home-made maple ice-cream