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Tomorrow's Cure**

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RESEARCH IN THE LIMELIGHT

A NEW GENE DISCOVERY THAT CAN IMPROVE THE EFFICACY OF CHEMOTHERAPY

RESEARCHER FINDS LINK BETWEEN KLF5 GENE AND CANCER CELL DEATH

- Dr Gopal IYER

As a teen, Dr Gopal Iyer had always harboured dreams to be an Indian classical musician. But reality hit hard when, at the age of 18, his first (and only) cassette album sold less than 50 copies, most of which were probably bought by his parents. Fortunately for the medical world, he then decided to ditch his ambition of becoming a musician and studied medicine instead. Today, Dr Iyer is making important contributions in the field of medical science.

Dr Iyer, who recently returned after a year's training in Head and Neck Surgery at the Royal Prince Alfred Hospital in Sydney, is one of National Cancer Centre Singapore's (NCCS) very promising clinician-scientists. He is now an Associate Investigator at NCCS Wee Kim Wee Laboratory of Surgical Oncology and an Associate Consultant at the Department of Surgical Oncology. His latest discovery is in identifying a gene that can alter or affect how cancer cells die in response to chemotherapy.

Normal body cells have a number of important characteristics, including the ability to stop reproducing at the right time. The cells also have tumour suppressor genes (TS gene) that act as guardians of the cell and will instruct cells that are old and damaged to self-destruct. One of the best-known TS genes is p53.

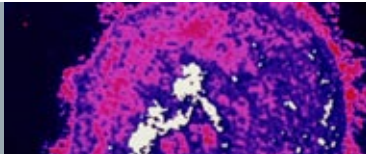
Explained Dr Iyer: "Unlike normal cells, cancer cells commonly have an abnormal or missing p53, and lose this protective mechanism allowing cancer cells to reproduce uncontrollably. Hence, many scientists are looking for a way to replace the damaged p53 with a normal one."

"Also, in instances where p53 is missing, chemo and radiotherapy will be less effective. Doctors will have to look for other alternatives to stop reproduction of cancer cells and promote apoptosis or the process of cell death", added Dr Iyer.

Thanks to funding from NCCS Cancer Research and Education Fund and the Singhealth Foundation, Dr Iyer and his team have discovered one such alternative.

A gene, known as the Kruppel-like factor 5, or KLF5, modulates apoptosis through the Pim1 gene independent of p53. KLF5 acts as an important regulator of cell function affecting cellular survival and death. If there is an increase in KLF5, cancer cells will tend to survive and proliferate. However, when KLF5 is removed from the cell, there is an increase in apoptosis through a pathway involving another gene called Pim1.

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RESEARCH IN THE LIMELIGHT

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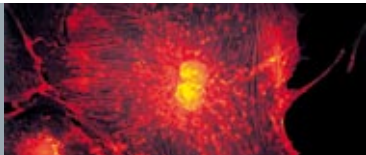
This discovery could potentially lead to the development of a new drug that can block the function of either KLF5 or Pim1 and potentially promote cell death; this would be an easier solution in cancer cells rather than trying to “put back” the normal p53 gene. It also provides valuable insight to unknown aspects of tumour biology with consequent prediction of patient outcomes and their response to chemo and/or radiotherapies.

“Research is a very trying and tedious process. It can take days, weeks, months or even years to make a discovery. Sometimes its more important to be lucky than to be smart.”

– Dr Gopal IYER

There is still some more work to be done by Dr Iyer and his team in testing possible inhibitors that can block this pathway, and this can be quite a laborious process. As he put it: “Research is a very trying and tedious process. It can take days, weeks, months or even years to make a discovery. Sometimes its more important to be lucky than to be smart.” However, it is clear that Dr Iyer enjoys doing research and claims that his best ideas seem to come when he is hiking or running at one of our national parks during the weekends (in an almost futile attempt at weight loss) or while driving home in his Mini blasting Kanye West (yes hip hop rapper Kanye West!) on his stereo system.

Unknown to many, Dr Iyer, who is a vegetarian, also helms the kitchen on Sundays to do little “research” on his own with a bit of this and a dash of that. “I love cooking and seem to have gotten pretty good at it. My greatest achievement was demystifying risotto, a dish which I now think is one of the simplest but most impressive dish to cook.” Now, how about that as food for thought?



GETTING TO KNOW YOU

A/Prof Caroline LEE IMPRESSION OF SILICON VALLEY, CALIFORNIA FROM AN NCCS SCIENTIST VIEWPOINT

After her attachment with Stanford University, A/Prof Caroline Lee is even more determined to lead her team to break new frontiers in medical research

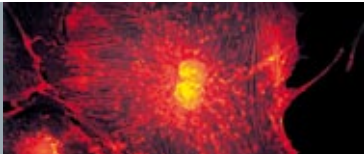


It may have been just six months that A/Prof Caroline Lee spent researching amongst the best at Stanford University, but the difference in the research and innovative culture certainly left a deep and lasting impression on her.

And, her verdict is: We can try, but it is extremely difficult to replicate the culture of Silicon Valley, California in Singapore unless there is a sea of change in our attitudes and values.

A/Prof Lee, who is doing research on pharmacogenetics and hepatocellular carcinoma or liver cancer, was on sabbatical leave in the laboratory of Dr Mostafa Ronaghi, co-inventor of pyrosequencing at the Stanford Genome Technology Center from July till December 2007.

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GETTING TO KNOW YOU

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"The research culture is so different. People are willing to explore and try new and risky ideas without much fear of failure even though some of the ideas may not be too orthodox," explained A/Prof Lee.

Indeed, so noticeable was this "out-of-the-box" approach even to life that she pointed out that it was not uncommon to see individuals along the streets riding their own unusual, one-of-a-kind contraptions with no one else batting an eyelid. In fact, this city is so environmentally conscious and friendly that there are probably more hybrid cars on the road than anywhere else in the world. It is a place where new ideas and inventions are being tested out on a regular basis. "People there do not prejudge your ideas and if your idea fails, no one will scoff at you or label you as a failure. You just pick up the pieces, try again another time and go on with life".

Even sending her 3½ to 4-year-old son to the preschool in Palo Alto was an eye-opener for A/Prof Lee. With a result-oriented Singaporean mindset, she was uncomfortable that although the preschool there was substantially more expensive, her son was not learning much in school as he was primarily left alone to do what he wanted. She later realised that their philosophy and approach to childhood education primarily focuses on "child-initiated" rather than "teacher-initiated" activities. Hence, although her son may not have learned much academically during the six months compared to his peers in his preschool in Singapore, he has learnt a lot about the intangible and hard-to-measure life-skills.

"If we ever dream of developing a Silicon Valley here in Singapore, we have to start with the very young around my son's age and provide him with the kind of culture and environment that promote creativity and innovation. Otherwise, once he starts schooling in the current Singapore schools, he'll grow up to be just another typical exam-savvy Singaporean, with all its mindset and values based on KPIs (Key Performance Indicators)," shared A/Prof Lee.

As it stands, A/Prof Lee is very happy with her experience at Stanford and she greatly values having another team of scientists among her circle of friends. "I keep in touch with them and we are collaborating on some work which hopefully will turn out good results in the future," she said.

But that is not to say that the research culture in the National Cancer Centre Singapore (NCCS) isn't up to speed, she was quick to add. "In fact the calibre of our scientists and investigators can match their counterparts in Silicon Valley. What we lack is the necessary funding support to do the things that they are able to do," she lamented.

A/Prof Lee was also quick to add that despite our modest funding situation, our scientists have published many of their findings in reputable international scientific journals attesting to their quality of work.

She pointed out that NCCS has the largest number of Singaporean and Singapore permanent resident scientists and principal investigators which speaks well of the home-grown team.

"We have very good leadership at NCCS and just like the scientists in the US, we work just as hard on our projects. However, because they have greater funding, they are able to embark on even what is seen as 'high-risk' research. In NCCS, besides some institutional funding provided kindly by the National Medical Research Council (NMRC), most of our funding is derived from individual grants through NMRC, BioMedical Research Council (BMRC), SingHealth and other funding agencies. The quantum of funding for each grant is usually quite small and one of the primary criteria that determine whether a particular grant is fundable is based on the feasibility of the project. Hence, we are compelled by our limited funds to go for the 'safer' research projects, which leave little room for creativity and risk-taking or for venturing into the unknown."

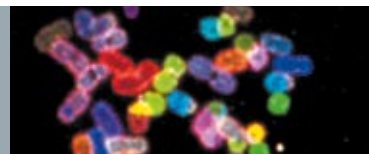
While admitting that there is a lot of "wastage" in the way research projects are carried out in the Silicon Valley, she explained that such wastage may be necessary as one explores the unknown to find the big cutting-edge discoveries that will change the lives of everyone.

For those who were at the Scientific Advisory Board meeting at NCCS in November 2007, they will recall seeing A/Prof Lee presenting her research project to the board members via video conferencing.

Now that she is back with her team at NCCS, she has resumed shuttling between her laboratory here and teaching cum administrative duties at the National University of Singapore and Duke-NUS Graduate Medical School. After seeing the work at Stanford, A/Prof Lee is even more convinced that soon it may be possible to sequence the entire human genome (which previously took 14 years to sequence and done in large genome centres) in one or two days using equipment no larger than a notebook at a cost that even individual labs can afford.

A/Prof Lee and her team are actively trying to break new frontiers in research that could benefit many cancer patients. This includes the development of a chip which could potentially be used in a clinical setting to help doctors determine the differences in genetic profiles amongst their patients for the better customisation of drug therapies.

KEEPING YOU POSTED



NCCS STAFF TAKE ON TEACHING ROLES AT DUKE-NUS

Medical and clinician scientists at the National Cancer Centre Singapore (NCCS) are taking on an additional role to impart their knowledge and expertise to the next generation of aspiring medical researchers in the various specialities.

Ten NCCS doctors have been given faculty appointments at the Duke-NUS Graduate Medical School (GMS).



A/Prof Cynthia GOH, Head of Palliative Medicine Department in NCCS, is one of the pioneers of Singapore's hospice movement since 1986. She is presently Board Member of the Singapore Hospice Council, Honorary Secretary of the Asia Pacific Hospice Palliative Care Network and Co-Chairman of the Steering Group of the Worldwide Palliative Care Alliance. Her newest appointment is Centre Director of the Lien Centre for Palliative Care of the GMS, located at NCCS. A/Prof Goh received the Galloway Memorial Lecture and Gold Medal for excellence in research in 1991 from the Academy of Medicine, Singapore, and the Public Service Medal in 1997 for her contributions to hospice care.



Dr HA Tam Cam is an epidemiologist who joined NCCS in 2005 after obtaining a PhD in epidemiology from the University of Sydney. Her research interests include investigations of factors that influence the different patterns of cancer incidence and survival in different ethnic populations. In particular, her research has focused on genetic and viral risk factors for cancers with a high incidence in Asia. She also holds a joint appointment as Course Director at Duke-NUS GMS for the Investigative Tools and Methods course, which is a combination of evidence based medicine and intuitive biostatistics.



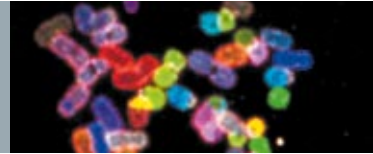
Dr KON Oi Lian is an internist with research interests in gastric cancer and cellular therapy of metabolic disorders (diabetes mellitus and hemophilia A). She has headed the Medical Sciences Division since the inception of NCCS in 1999. The Division aims to foster translational research with the objective of applying advances in basic research to clinical care, including new diagnostic and therapeutic technologies. Dr Kon also chairs the National Cancer Centre Tissue Bank Committee and co-chairs one of National Medical Research Council's Scientific Review Panels. Dr Kon graduated with an MD in 1989 from the National University of Singapore.



A/Prof KOO Wen Hsin graduated from National University of Singapore with an MBBS in 1982 and obtained his MRCP in 1987. He joined NCCS in 2000 as a Consultant in the Medical Oncology Department and became the head four years later. Prior to joining NCCS, A/Prof Koo was the Chief Executive Officer and Medical Director at the Dover Park Hospice. He holds other appointments at various institutions including Chairman of Singapore Cancer Society. A/Prof Koo and his team are also actively involved in clinical trials to enhance patients' prognosis.



A/Prof KOONG Heng Nung has a subspecialty interest in cancer of the breast, lung, thorax and esophageal conditions. Prior to joining NCCS in 2000, he was a Thoracic Service Senior Registrar at Memorial Sloan-Kettering Cancer Center in the US. A/Prof Koong obtained his MBBS from National University of Singapore in 1989 and was a Fellow of the Royal College of Surgeons (Edinburg) and Academy of Medicine, Singapore. Currently, he is the Acting Head and Senior Consultant in NCCS Surgical Oncology Department. For his exceptional care and commitments to his patients, he was awarded the Excellent Service Award (Gold) organised by SPRING Singapore in 2005.



Asst Prof Simon ONG, winner of the 2003 Courage Medal for fighting SARS, is a medical oncologist who specialises in the treatment of colorectal, hepatobiliary and upper gastrointestinal tract cancers. He is also the Director of the Health Professional and Undergraduate Education Unit in NCCS where his efforts had garnered him awards such as the GCEO Excellence Award 2008 – Open Category (Education) and Medical Mentor Award in 2005 and 2006, both from SingHealth, as well as Dean's Award for Teaching Excellence in 2007. Asst Prof Ong has participated in numerous trials as a Principal Investigator. He graduated with MBBS from the National University of Singapore in 1990 and obtained MRCP from the Royal College of Physicians (UK) and MMed Internal Medicine (Singapore) seven years later.



Prof London Lucien OOI, Deputy Director, NCCS and Senior Consultant, of the Surgical Oncology Department of NCCS, graduated with MBBS from the National University of Singapore and was awarded numerous scholarships and prizes. His sub-specialty interest is in hepatobiliary and pancreatic surgery. He has trained surgeons from the region including the Philippines, Malaysia, Maldives, Nepal, Pakistan, and India. Prof Ooi is also the Chairman of Division of Surgery, Singapore General Hospital overseeing 14 clinical surgical subspecialty departments. He sits on the panel of many illustrious international advisory boards and committees including those in the Ministry of Health. Prof Ooi obtained his doctorate (MD) from NUS in 2001 for research on liver cancer.



Prof Kanaga SABAPATHY and his team work on understanding the role of tumour-suppressor genes p53 and p73. They have made several significant discoveries, including elucidating p73's role in cancer growth, which was published in the prestigious Nature Cell Biology journal in May 2007. He now shuttles between two labs in NCCS and SingHealth where he is the Principal Investigator. Prof Kanaga graduated in 1990 with a Bachelor of Science with Honours in Zoology from the National University of Singapore and also pursued his PhD in Molecular Immunology from the Institute of Molecular and Cell Biology. After spending five years at the prestigious Institute for Molecular Pathology in Vienna, Austria, he joined NCCS. Since then, he has 10 grants, four patents and numerous awards and publications to his name.



Adjunct A/Prof THNG Choon Hua, Deputy Head and Senior Consultant of the Oncologic Imaging Department, joined NCCS in 2000 and has a research interest in DCE MRI, prostate MR spectroscopy and hepatobiliary imaging. He is the Principal Investigator for a S\$0.49 million grant from the Singapore Cancer Syndicate on the use of DCE MRI as a biomarker for cancer angiogenesis. He has 46 journal publications and was a Body Imaging Fellow at the Memorial Sloan-Kettering Cancer Center, USA in 1999. Some of his recent awards include Best Conference Paper at the IEEE International Conference on Robotics and Automation in 2005.



Adjunct Asst Prof TOH Han Chong is a senior consultant medical oncologist at the NCCS. He qualified from the University of Cambridge School of Clinical Medicine, UK in 1990, and received his medical oncology fellowship training at the SGH Department of Medical Oncology, Massachusetts General Hospital Cancer Center and the Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, Texas. He was awarded Fellowship from the Royal College of Physicians, Edinburgh (FRCP) in 2003. He is an Associate Investigator at the Laboratory of Cell Therapy and Cancer Vaccine, where he has interests in translational research, especially in cell and immunotherapy and new drug development, mainly in gastrointestinal cancers.

RESEARCH WINS CHINESE GOVERNMENT AWARD

It is not just the clinician scientists and investigators who are winning awards at the National Cancer Centre Singapore (NCCS). Also getting recognition is a Chinese national who did his research at NCCS.

Wang Zihua who is a researcher in the Liver Cancer Functional Genomics Lab, Division of Medical Sciences, has won the Chinese Government award for Outstanding Self-financed Students abroad, one of 301 awardees in 2007 for Chinese students throughout the world.

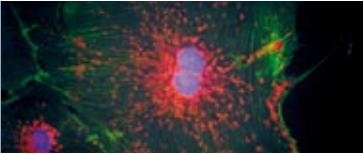
Out of 2000 eligible students from NTU and NUS, only eight won the award.

The award is given out each year to recognise outstanding Chinese PhD students under the age of 40, who are studying abroad with no financial support from the Chinese government.

There is a cash award of US\$5000 given to each awardee.

The Hebei native began his stint in NCCS in 2003 when he was a PhD student with the National University of Singapore, to research on pharmacogenetics, the study of how genetic factors in individuals affect their responses to different drugs. After completing his thesis in February this year, the 32-year-old went on to work full time with NCCS so that he could complete his research.

He attributed his success to A/Prof Caroline Lee, who supervised his thesis. "Because of the new techniques involved in my research, I would get negative results most of the time. A/Prof Lee would always encourage and advise me when I get frustrated. She really understands what I feel."



A/Prof Cynthia GOH
**BRINGING ACCEPTANCE AND SOLACE TO
LIFE'S END JOURNEY...**

Lien Foundation, a local philanthropic organisation, has collaborated with Duke-NUS Graduate Medical School (Duke-NUS) with a \$7.5 million gift over five years to set up the Lien Centre for Palliative Care.

The Singapore government has also pledged to match dollar-for-dollar, bringing the total sum to \$15 million.

On this strong note, Singapore will host Asia's first centre focusing on end-of-life and palliative care research which will have an emphasis on local and regional issues.



The Centre will also develop education programmes in palliative care for healthcare professionals, building on programmes currently run by the National Cancer Centre Singapore (NCCS) and the Asia-Pacific Hospice Palliative Care Network.

Heading the team as Centre Director is A/Prof Cynthia Goh, a veteran in palliative care. She is the current Head of the Department of Palliative Medicine at NCCS, and holds teaching appointments at both the Duke-NUS Medical School and the Yong Loo Lin Medical School at the National University of Singapore.

It was timely for A/Prof Goh when the Lien Foundation sought her views on Singapore's palliative care needs two years ago. She has been working tirelessly to build up a talent pool of doctors to be trained in this field.

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Dr KON Oi Lian & Prof SOO Khee Chee

MEMBERS

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Explained A/Prof Goh, "Palliative care services in Singapore, in both the community and in government hospitals, are reasonably well established, but there is a need to improve service standards. The only way to do that is to do the relevant research and to pass this knowledge on in order to improve services."

The Centre will be managed by Duke-NUS. Also supporting the Centre are NCCS and SingHealth, which will contribute \$2 million and \$50,000, respectively, for research funding, in addition to space and administrative support. A/Prof Goh will be recruiting a nurse educator, an administrator, and research fellows from different backgrounds, including doctors, social workers and statistician for the Centre.

The Centre's research will draw on the synergy between the clinical expertise available at the NCCS and the research capabilities of the Duke-NUS Graduate Medical School. One of its flagship programmes is to study how and where patients die in Singapore. The range of questions will include looking at how families are coping, communication issues between care givers and the patients, and the services available to patients at the end of their lives.

The Centre will complement its research work with the training and education for doctors and nurses through clinical fellowships and graduate certificate in palliative care. An estimate of over 100 professionals will be going through the Centre for training each year.

"Training is a very important aspect of our work as we are producing the future palliative care workforce. How good the services are depends a lot on the quality of the training," added A/Prof Goh.

It has certainly been a long, challenging journey for A/Prof Goh. Palliative care was recognised as a sub-specialty by the Singapore Academy of Medicine and the Specialists Accreditation Board only in 2006, 20 years after the first palliative care services were started in Singapore.

When asked why she chose to go into palliative care, a road less travelled, A/Prof Goh revealed that throughout her training from the day she walked into medical school, she was taught to look after the whole person – mind, body and spirit. "The only three specialties that will allow me to practise this whole person medicine are paediatric, geriatric and, of course, palliative medicine. But palliative medicine holds a special attraction for me. I always get a kick out of being able to communicate at a deep level with patients on issues that really matter to them, and this we have to do every day in palliative care."