


 A portrait of Dr Charles Chuah, a man with short dark hair and glasses, wearing a light pink striped shirt and a patterned tie. He is smiling slightly and looking towards the camera. The background is a blurred green foliage.

Bedside to Bench, and Back Again

DR CHARLES CHUAH is currently a Consultant at the Department of Haematology, Singapore General Hospital; Clinical Teacher at the Yong Loo Lin School of Medicine, National University of Singapore; and Instructor at the Duke-NUS Graduate Medical School, Singapore. He is also an Executive Committee Member of the Singapore Society of Haematology, a member of the Asia-Pacific CML Advisory Board, as well as a journal reviewer of *Singapore Medical Journal*, *Cancer Letters* and *International Journal of Haematology*. Dr Chuah was recently awarded the BMRC-NMRC Clinician Scientist Investigator Award (Category B). He is currently holding research grants from the Singapore Cancer Syndicate, National Medical Research Council and Singhealth Foundation and is a principal investigator in five multicentre clinical trials.

SMA News: How did you become involved in research? What were your formative research experiences?

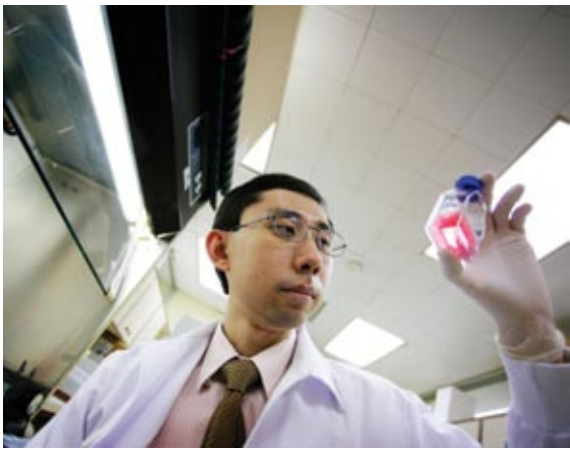
Dr Chuah: I started my haematology training in September 1999 and four months later, STI571 (imatinib or Glivec, as it was to be known later) was introduced to the haematology community at a scientific meeting in New Orleans. It was the first small molecule that fulfilled the promises of targeted therapy and was a significant ‘bench-to-bedside’

success. As a young registrar, I was fascinated with the science behind this magic bullet and was equally impressed with its clinical efficacy in the treatment of chronic myeloid leukaemia (CML). In 2000, I was fortunate to be involved as a co-investigator in clinical trials with imatinib at the Singapore General Hospital and was able to experience firsthand the remarkable clinical responses it achieved in our CML patients. However, despite the impressive responses, resistance to imatinib was a significant problem, especially in patients in the more advanced phases. It was obvious that more needed to be done to overcome or prevent imatinib resistance.

In 2002, I traded in my stethoscope for a pipette and embarked on a research fellowship and a scientific journey at the Hammersmith Hospital to understand more about imatinib resistance and the strategies to overcome this resistance. Although I was a ‘scientific novice’ in the laboratory, I was given the opportunity to work and flourish under the supervision of Professor Junia Melo. During my two memorable years in the laboratory, the values of scientific rigour and critical thinking were instilled and the knowledge and experience gained provided me with a strong foundation for the appreciation and practice of science. It was especially rewarding when one of my research projects in CML was translated into an early phase clinical trial at the Hammersmith.



Dr Charles Chuah and fellow members of the 'JVM' (Professor Junia V Melo) laboratory.



Dr Charles Chuah in his laboratory in Singapore.



Dr Charles Chuah with his wife, Linda and daughters Maria, Christina and Lydia at the Royal Albert Hall, London.

SMA News: Who are your role models and “heroes”, in clinical practice and research respectively?

Dr Chuah: There are many and it would be an injustice if I named some and not others. However, all of them have one thing in common, and that is, approachability. Many of them are the top clinicians or researchers in their fields but are never too aloof to engage in a discussion or to answer a question, whether in person or by e-mail. This is a laudable trait which is an inspiration to fledgling researchers

like myself, probably as inspiring as many of their achievements.

SMA News: What do you think of the existing system of training MOs and registrars? Does it adequately recognise research?

Dr Chuah: The existing system places a lot of emphasis on clinical training. This may not necessarily be a bad thing, as we are medical doctors after all! Furthermore, to be a competent clinician investigator or researcher, clinical acumen is an important tool. However a possible way of weaving research into this training is to, perhaps, have a dedicated research posting, either at the MO or Registrar level. This can be in the form of clinical research or time spent in the laboratory. While it may not be possible to complete a research project within three or even six months, especially a laboratory-based one, this exposure will give the junior doctor a taste of research and hopefully a foundation upon which he/she can build.

SMA News: What advice would you give to a junior doctor aspiring to become a clinician investigator?

Dr Chuah: Passion in your area of research is obviously very important. However, ‘ability is of little account without opportunity’ (Napoleon Bonaparte, 1769-1821). Opportunities for research now abound in Singapore and the onus is on the aspiring clinician researcher/investigator to seize these opportunities.

SMA News: What do you see as the big research topics in haematology, over the next 10 to 20 years?

Dr Chuah: Molecular targeted therapy will be, and in fact, is already the next big thing in haematology research and therapy. Imatinib and similar small molecules have been the major players in this paradigm shift. Understanding the mechanism of action of these drugs, and more importantly, the mechanisms of resistance at the molecular level will allow rational clinical decision making and a ‘one size fits all’ approach will be a thing of the past.

Immunotherapy will also be a very important area for research. Most, if not all, haematologic malignancies are stem cell disorders and an immunological approach may be required to eliminate the stem cells, in particular, the quiescent, non-cycling stem cells, which have been shown to be resistant to the anti-proliferative effects of the existing small molecules.

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SMA News: How has the practice of haematology changed over the years? How do you see it changing in time to come?

Dr Chuah: In my relatively short time practising as a haematologist (just over seven years), the progress made in diagnostic, therapeutic and prognostic technologies in haematology has been astounding. What is also remarkable is that much of this progress has been made based on solid scientific and clinical evidence. I believe that evidenced-based medicine will be the foundation of the practice of haematology, and the whole of medicine, for that matter, in the future.

SMA News: Tell us about an interesting book you have read.

Dr Chuah: I am not an avid reader but I did chance upon an interesting book at the NUS Medical Library a few months ago. It was the *Medical Casebook of Doctor Arthur Conan Doyle: From Practitioner to Sherlock Holmes and Beyond* by Alvin Rodin and Jack Key. This book was the first, and probably, the only one which describes Arthur Conan Doyle's life as a medical student,

medical practitioner and medical writer. Conan Doyle studied medicine at the University of Edinburgh. A year before graduation, in 1880, he spent seven months as a ship's surgeon on an Arctic whaler. Definitely not your typical medical student elective! After graduation, he practised briefly in Birmingham and that was where he wrote a letter to the *Lancet* on 'notes on a case of leucocythaemia'. Leucocythaemia was the term used then for CML and Conan Doyle's case was treated first with iron and quinine without any result and then with arsenic 'in large doses, in combination with the iodide and chlorate of potash', which 'combined with a liberal diet, and strict attention to the state of the bowels, has been remarkably efficacious' (Conan Doyle, *Lancet*, 1882). Not quite your molecular targeted therapy but probably the closest one could get at that time! He later trained in ophthalmology in Vienna and started a practice in London in 1891 but abandoned it, and his whole medical career, for full-time writing. Rodin and Key suggested 'that Conan Doyle might have been a 'great' physician if circumstances and motivation had been right'. However, as we now know, the medical world's loss was the literary world's gain. *Elementary, my dear Watson* would have otherwise never seen the light of day! ■