**News**

**Stopping leukaemia from recurring**

Clinician Scientist Award winner Dr Charles Chuah is looking for ways to kill hardy leukaemia stem cells

**BY TRISTAN CHAN**

Imatinib is one of the first drugs to identify and destroy leukaemia cells. However, one problem with this otherwise successful targeted therapy to treat blood cancers soon became evident: Leukaemia stem cells grow resistant to the drug, especially in patients with more advanced phases of the disease. When treatment stops, the leukaemia often recurs.

For Dr Charles Chuah, Senior Consultant, Department of Haematology, Singapore General Hospital (SGH), the problem of drug resistance has long been a fascination and a challenge. At the turn of this millennium, working as a registrar beginning to specialise in haematology, Dr Chuah witnessed “the remarkable clinical response” imatinib achieved in patients suffering from chronic myeloid leukaemia. But he also realised resistance to the drug was “a significant problem” which needed to be overcome.

As recently as a decade ago, someone diagnosed with leukaemia might have felt that he had been handed the death sentence, but advances in medicine have significantly improved their prospects.

DR CHARLES CHUAH, SENIOR CONSULTANT, DEPARTMENT OF HAEMATOLOGY, SINGAPORE GENERAL HOSPITAL

Years – and many research projects – later, Dr Chuah is leading a team of researchers from Duke-NUS Graduate Medical School and the Cancer Science Institute of Singapore to investigate how cancerous stem cells, the smallest units in the body that are capable of renewing themselves, can be eradicated in types of leukaemia such as chronic myeloid leukaemia.

“We will investigate if a combination of novel and existing targeted therapies using drugs like imatinib will be effective in killing leukaemia stem cells,” said Dr Chuah.

“One strategy is to combine drugs that are effective against different targets or pathways required for the survival of the leukaemia stem cells. This is the premise of our research.”

**Seeking that “Eureka!” moment**

Undertaking research comes from the belief that often “unexpected outcomes, good or bad” occur in trying to answer specific questions, said Dr Charles Chuah, Senior Consultant, Department of Haematology, Singapore General Hospital (SGH).

“The challenge in trying to understand these surprises and the ‘Eureka!’ moments that follow make research both exciting and rewarding. I have always liked to take the path less trodden,” he said.

In 2002, he won a research fellowship at Hammersmith Hospital, a major teaching hospital in the UK, to understand resistance to imatinib, one of the first drugs to identify and destroy leukaemia cells, and research strategies to overcome this resistance.

“During my two 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,” Dr Chuah said.

“It was especially rewarding when one of my research projects in chronic myeloid leukaemia was translated into an early phase clinical trial at Hammersmith.”

Dr Chuah has come a long way since. His investigative work on leukaemia, in particular chronic myeloid leukaemia, has been published widely in prestigious international medical and scientific journals such as Nature (“Regulation of myeloid leukaemia by the cell-fate determinant Musashi” in July/August) and The New England Journal of Medicine (“Dasatinib versus Imatinib in newly diagnosed chronic-phase chronic myeloid leukaemia” in June).

He was the principal or lead investigator in many grant-sponsored studies, including a pre-clinical programme to investigate novel compounds and strategies to target signalling pathways in chronic myeloid leukaemia for which he received a Singapore Cancer Syndicate grant of $601,000 for 2006-2009.

He also led a study targeting downstream signalling pathways to overcome resistance and improve responses in chronic myeloid leukaemia, which received a National Medical Research Council grant of $200,000 for 2007-2010.

**Starting with chronic myeloid leukaemia stem cells, Dr Chuah hopes to be able to apply the same-combination drug therapy on other types of leukaemia stem cells later.**

**To study leukaemia stem cell function, the project will use a mouse model developed by Professor Daniel Tenen, Director, Cancer Science Institute of Singapore, and that was engineered to have similar characteristics as human chronic myeloid leukaemia. The study also involves the use of cord blood cells which will be used to determine if the drug therapy spares the normal stem cells while eliminating leukaemia stem cells, said Dr Chuah, adding that the cord blood cells will be provided by Singapore Cord Blood Bank.**

A breakthrough in the findings will have wider implications. “Chronic myeloid leukaemia is a model disease for understanding cancer stem cell biology and therapeutics. If we are able to show that drug therapy eradicates chronic myeloid leukaemia stem cells through a certain pathway (or a sequence of reactions by which one substance is converted into another), we can adopt a similar strategy for other types of leukaemia stem cells which are dependent on that pathway for survival,” said Dr Chuah.

As recently as a decade ago, someone diagnosed with leukaemia might have felt that he had been handed the death sentence, but advances in medicine have significantly improved their prospects, said Dr Chuah. “I have been fortunate to witness this revolution as a haematologist, but a lot more still needs to be done for an alternative and effective treatment method to be implemented.”

Dr Chuah has long been passionate about finding a solution to drug resistance. **"Eureka!" moment**