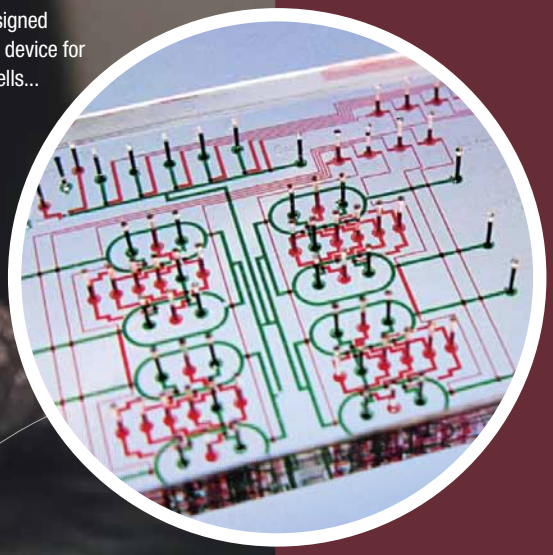
The single-cell detective

Prof Angela Ruohao Wu is hunting down the cells that cause cancer using novel bioengineering techniques that can profile individual cells with greater accuracy and sensitivity

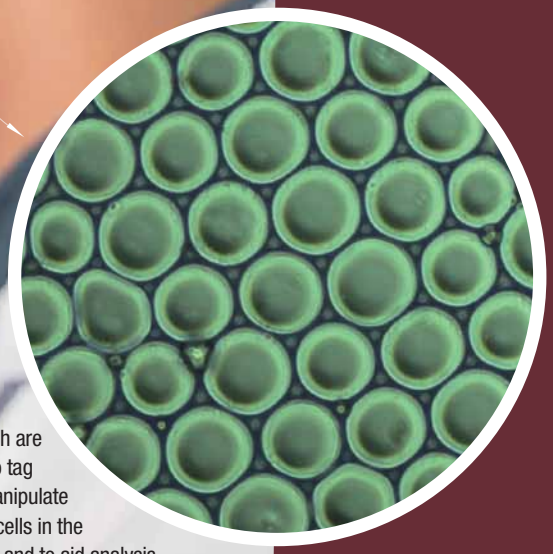
Wu Lab-designed microfluidic device for capturing cells...



Prof Angela Wu is seeking to bridge the gaps between biology and engineering.

...and generating hydrogel beads...

... which are used to tag and manipulate single cells in the device, and to aid analysis.



Rising academic star Prof Angela Ruohao Wu, Chemical and Biological Engineering, and her research into tumor initiation reveal her passion for engineering that makes a difference.

Where she is making that difference is in the cutting-edge emerging field of single-cell genomics and the design of microfluidic devices ("lab-on-a-chip") that can isolate individual cells, enabling single-cell analysis of their genome and uncovering errors, including mutations. "Just as different people have different characteristics and play diverse roles in society, different cells have their own unique identities and functions in an organ. Traditionally, researchers take millions of cells from an organ and study their average genomic profile, which doesn't say much about an individual cell," she noted. Her work helps to provide the techniques to enable each cell to be located and identified to provide a "human cell atlas", rather like a Google map.

"What motivates me every day is the joy of working with my team to invent new technologies, and make discoveries about biology to help us fight diseases such as cancer"

"Even when the cells 'go rogue' and become pathological, for example in cancer, the diversity of cell types in tumors remains important at the individual cell level. To give us the location, function, and role of each individual cell, I design microfluidic devices to isolate individual cells," she said. "We can then read and analyze their genome individually at the single-cell level and discover mistakes, such as mutations."

Understanding cancer

While most one-cell researchers to date have explored DNA and RNA separately, Prof Wu and her team are seeking to make a unique contribution by studying them together, using a new technique that will provide a more complete set of information about a cell. What this technique could offer is the potential to learn more about the origins of the disease, for example, the fundamental reason – "big bang event" – that initiates a cancer tumor.

The Wu Lab team: one-cell researchers using novel technologies to study DNA and RNA together.

Prof Wu's findings should be generally applicable to many cancer types. "Currently, people who study cancer from the DNA mutation perspective have found evidence that cancer is a disease caused by these mutations. Those who study cancers and their growth have evidence that there may be a so-called cancer stem cell giving rise to the rest of the cancer. So far there is no way to directly connect these two phenomena," she said.

Bioengineering pioneer

Prof Wu was born in China and raised in the Mainland, Hong Kong, and Australia. She initially took up biology because her "tiger parents" thought it was a promising direction for a career. Before long, she had become utterly fascinated, leading her to the "eureka" moment during her first single-cell experiment where she saw individual cells being caught in each chamber inside a microfluidic biochip. "Wow, I'm one of the very first people to do this," she recalled thinking. "It was really exciting."

She studied for her bachelor degree in bioengineering at the University of California, Berkeley and for her master's and doctoral degrees in the same field at Stanford University. At Stanford she was supervised by Prof Stephen Quake, a leading figure in genomics, biophysics and bioengineering technologies that facilitate rapid analysis of the human genome and microfluidic automation. She was awarded the Bio-X Bowes Graduate Student Fellowship for interdisciplinary research and the Siebel Scholarship for top bioengineering graduates. As a postdoctoral fellow in the Quake lab, she was one of the first to come up with a framework for analyzing complex single-cell datasets.

Prof Wu joined HKUST in December 2015 as a faculty member. During interviews with Asian institutions, she found HKUST to have the most open and independent academic culture. She was also drawn to the international atmosphere, culturally diverse and productive faculty, dynamic students, and the University's spectacular campus.

Practical applications

With an ultimate goal of bridging gaps between biology and engineering, Prof Wu is not only working on basic research but also on practical ways to benefit healthcare. Her research team is developing DNA-based diagnostics for intensive care units together with Prince of Wales Hospital in Hong Kong and the Chinese University of Hong Kong. In addition, as the co-founder of Agenovir Corporation, a US start-up established in 2014, she is driving forward the use of genome editing technology to target and delete disease- and cancer-causing viruses inside the genome. In targeting destruction of viral DNA, the biomedical firm aims to remove viruses from the cell to make the cure permanent.

Prof Wu's contributions to the field of single-cell analysis technologies and her work at Agenovir were recognized internationally when she was named one of *MIT Technology Review*'s Top 10 Innovators Under 35 in Asia in 2017. Her research has also been published in prestigious journals including *Nature*, *Nature Methods*, and *PLoS Genetics*.

With her passion for solving problems, Prof Wu finds engineering both rewarding and empowering. "When I am presented with challenges, it feels extra-good to overcome them," she said. "I hope more women will consider engineering as a career to change the status quo and to say, 'I can do it too'."

Team spirit and novel technologies

Prof Angela Wu considers the 2014 founding of Agenovir Corporation, together with her Stanford University PhD advisor Prof Stephen Quake and two other Stanford University affiliates, to be a milestone in her learning curve, providing insight into the importance of good communication, team spirit, respect for different perspectives and partners with complementary skill sets. Prof Wu still harbors a passion for bringing useful technologies to market to help patients, and her experience at Agenovir helped her explore how to translate academic concepts into a commercial setting. She hopes to continue her entrepreneurial pursuits in her career at HKUST.