Kelly Chibale: An advocate of innovation

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Kelly Chibale remembers being amazed by the colourful reactions and changes from the simple chemistry experiments in his high-school classes. This appreciation led him to study organic chemistry in his home country at the University of Zambia. Says Chibale: 'Life, whether it's cells, clothing, materials or food, is all made up of molecules. Knowing that the manipulation of the molecules can change its properties made me fall in love with organic chemistry.'

Chibale recognised his need to further his education beyond a first degree. There were no postgraduate opportunities in Zambia at the time so he began applying for scholarships that would take him abroad. He made contact with Stuart Warren at the University of Cambridge in the United Kingdom, who agreed to supervise him provided he found funding. Chibale won a Cambridge Livingstone Trust scholarship and enrolled in 1989.

Chibale quickly realised how inferior his education was relative to the education his peers had received. Because of a lack of financial and human resources, undergraduates at the University of Zambia had very limited practical experience. 'There was no money for chemicals and other materials. We did modest practicals that didn't prepare me for research at Cambridge.'

Nonetheless, he found the environment there stimulating. The fact that his classmates were clearly ahead of him only served to motivate him to reach their level. 'You can moan and complain about how something hasn't been in your favour or how you've been disadvantaged, but you can also turn it around and use it as a challenge.' With the help of his supervisor, who understood Chibale's background and was prepared to work with him, and with the support of his friends, he quickly caught up and settled into the lab environment. Within three years, Chibale had finished his PhD without having done an honours or a master's degree.

Even before he finished his PhD, he recognised that there was a long road ahead. 'I started thinking about and applying for postdoctoral research opportunities in the UK, Canada and the US.' He won a fellowship that allowed him to conduct postdoctoral research at the University of Liverpool, upon completion of his PhD. Thereafter he was awarded a second postdoctoral research fellowship that took him to Scripps' Research Institute in La Jolla, California.

In his postdoctoral positions, he began to focus his interests. Chibale's PhD at Cambridge was in the field of synthetic organic chemistry. He worked particularly on synthetic methodology, developing methods for making chiral or optically active molecules. In Liverpool, he focused on developing methods for making optically active alcohols using asymmetric organolanthanide reagents in which a chiral organic molecule is modified by a lanthanide metal. At Scripps, he applied various types of methods strategically and creatively to assemble complex natural molecules from readily available building blocks, a process called the total synthesis of natural products.

His time at Scripps greatly influenced the direction of his career. He worked on a project on angiogenesis – the growth and development of new blood vessels. Although angiogenesis is a vital physiological process, it is also a process utilised by cancer cells. Tumours can induce angiogenesis by secreting various growth factors. The new blood vessels then supply the tumour cells with the nutrients they need to grow. However, there is a peptide that can block angiogenesis. As peptides are difficult to use as therapeutic agents because of their instability, Chibale and his colleagues were given the task of designing small molecules that would mimic this peptide. In order to do this, the team had to integrate synthetic aspects with other disciplines (biology, pharmacology, drug metabolism and toxicology) to design a molecule that could be used therapeutically. 'That for me was the introduction to what we call drug discovery, in a broad sense, or medicinal chemistry. That was the seed that was planted in me when I decided to come here to mount an independent research programme.'

Chibale's decision to return to Africa was largely based on the work environments he had experienced in the UK and the USA. 'When I arrived in the UK, I experienced culture shock on

a number of levels – the weather was strange, the food was strange, and the people were strange. They were not strange to me personally, but they were strange even to each other.' He found the UK culture to be conservative and overly polite. In the USA, he found people to be very aggressive. He saw that people who spoke the loudest and looked the smartest were rewarded above those who just went about their business doing what they had to do. Chibale found that his working environment was causing him to alter his personality to fit in with the unnecessary and unjustified aggression. 'I wanted to start my own thing. I resolved that I would not allow myself or my team to treat anyone with the loud aggression I'd experienced in the States.'

He decided that the place to make this new start would be Africa. Chibale contacted James Bull, then Professor of Organic Chemistry at the University of Cape Town (UCT). Bull had offered Chibale a postdoctoral position two years earlier. 'That was about 1994 and I was very nervous about the transition and the elections. I thought there was going to be a civil war. I didn't want to be caught up in that, so I decided not to come.' But, in 1996, Chibale joined Bull's department as a lecturer and quickly rose through the ranks.

Chibale celebrated his 16th year at UCT in October 2012. He and his team of researchers at the Drug Discovery and Development Centre (H3-D) made this year memorable by discovering an aminopyridine compound (MMV390048) which has the potential to become a part of a single-dose cure for malaria. MMV390048 was used successfully to cure mice infected with malaria parasites and is active against an array of resistant strains. It is the first compound researched in Africa that has made it into pre-clinical development and is scheduled to enter human clinical trials by the end of 2013. If trials go well and the compound is successfully developed, it could be launched as a drug as soon as 2018.

The local media have all embraced the discovery with enthusiasm and excitement. 'I must thank them for providing me with the opportunity and the training to communicate the kind of message that the public understands.' By contrast, Chibale has been disappointed by the coverage given to the discovery abroad. It was announced a few weeks after the shootings at the Marikana Platinum Mine, and the foreign media continues to be fixated on the violence: 'I would have preferred the media to also highlight something positive coming out of Africa.'

Although the discovery itself is very important, Chibale considers the development of the process to be far more important than the development of the molecule. 'Sure we are trying to solve malaria, but the skills and expertise we have developed in this process we can apply to other diseases as well.'

When he was first made head of H3-D, Chibale went in search of people who had experience in drug discovery. He took a sabbatical in 2008 and spent 6 months at the School of

Kelly Chibale with his rotary evaporator, which is used to remove solvents from organic solvent solutions and to isolate the molecule of interest – in this case, the drug's lead molecule (photo: Jenny Leonard).

Medicine at the University of Pennsylvania, as a US Fulbright senior scholar, and 6 months at Pfizer Inc., the world's largest research-based pharmaceutical company, learning about drug discovery. At Pfizer, he was assigned to a number of projects at different levels. Chibale attended project meetings, observed the various stages of drug discovery, and became conversant in the field. 'The whole cascade of events that leads to the discovery of a molecule that is ready to enter human trials is the process we call drug discovery. It is not something you find in a test tube.' Chibale is excited to have pioneered and established a working system for drug discovery at UCT with the help of his mentors and colleagues. 'Because of this experience, we can do it again, for malaria, or for any disease.'

Chibale would like to encourage researchers to work on programmes that integrate scientists from different disciplines and expertise, and really make a difference in South Africa. 'We need to be able to show our leaders and the powers that be that while we can do the basic science, we can also apply this knowledge to dealing with real life issues. We need to give a positive message and publicise the value of science through tangible outputs.' He's not talking about publications. 'The public doesn't care about publications in scientific journals. But they will care about how science can change their lives.' He has inspired many by his discovery, and will continue to inspire us as he designs and synthesises the tools to create more innovative drug discoveries.