Introduction of Professor Dennis Lo Yuk-ming

written by Professor Nick Rawlins

Universities are large, complex – and increasingly scrutinised – institutions despite having aims that are at heart rather straightforward. We might agree that we seek to generate, promulgate, and conserve knowledge and understanding, but we won't so readily agree on exactly how to do it. Those who take on the onerous task of leading a university face many difficult choices in which competing interests, constraints, and opportunities must all be borne in mind and yet, from these separate components, overall policies must nonetheless be formulated and agreed – and enacted. How does one take all those fragments of information, duly respect their individual contents, and then assemble them into a coherent whole? The problem can be even more complex in a university like The Chinese University of Hong Kong (CUHK) with its individual colleges adding further dimensions to the mix. The challenges are more obvious than the guaranteed solutions, yet today we are in the fortunate position of celebrating the installation of a Vice-Chancellor who has famously identified, analysed, and solved exactly this kind of problem. Here is part of his story.

Professor Dennis Lo Yuk-ming was born in 1963 in Hong Kong, and – perhaps like many here today – went to St. Joseph's College, a place notable not only for the quality of its education but also for the academic freedom that flourished there. The resulting breadth put the young Master Lo into the enviable position of choosing between Electrical Engineering (at Stanford) or Medicine (with offers from the University of Hong Kong and from Cambridge).

Cambridge won. Crick and Watson had famously determined the structure of DNA there, and Dennis Lo was inspired by a photograph of the pair of them standing in front of King's College Chapel – perhaps the most iconic building from English Gothic architecture's hallmark perpendicular period: two extraordinary achievements represented in one, memorable picture. That made pre-clinical medicine at Emmanuel College utterly enticing. But what came next?

Both of England's ancient universities had taught medicine since medieval times, yet despite offering excellent pre-clinical training both were slow to establish their clinical medical schools. When Dennis Lo completed his first degree in 1986, the Cambridge clinical school had only been established for seven years, whereas Oxford had almost 40 years more experience. This was part of the reason why he moved to Oxford for the next stage of his training. His Oxford College, Christ Church, might have had an even grander chapel than King's College, Cambridge, if Henry VIII had not lost patience with Cardinal Wolsey in 1529, leaving Wolsey's vision incomplete. But that itself left an opportunity for Sir Christopher Wren, who re-designed the College's frontage in a form that added aesthetic appeal there, too. That move to Oxford ultimately proved life-changing both for Dennis Lo, who met his wife there and whose research originated there, but also for many tens of millions of anxious parents and their children.

The discoveries that underpin this striking sentence arose from the medical lecture course early in his time in Oxford, in which he encountered both a new technique and a question that it might resolve. The technique was PCR – the polymerase chain reaction – which is a method for generating potentially unlimited amounts of DNA faithfully copied even from miniscule initial samples. This means that an initially undetectable signal can be rendered detectable. The question concerned an unusual set of patients whose livers had been damaged by exposure to a widely used – and generally trouble-free – anaesthetic called halothane. Had the anaesthetic directly damaged the livers of people unlucky enough to be hypersensitive in some way? Or could it instead have reactivated a latent virus in the liver which was what actually caused the damage? Despite investigations, no one had found a virus. But perhaps that could be because there was so little to be found. And, if so, might PCR help, by amplifying virus DNA which could offer an alternative way to infer the presence of the virus from which it must come?

My friend Dr Kenneth Fleming from the University of Oxford, who is here today and had raised the question, describes this lecture of his as, "very boring and dull", and yet, "at the end of the lecture, two students - one of whom was Dennis - came down to ask about all of this." He said if they were interested, he would like to try it out – and they could help. So they came to his laboratory in the evenings and on weekends – no wonder students from Hong Kong are so welcome in the UK – and, astonishingly, the first five or six cases of liver disease, while negative for hepatitis virus itself, were positive for liver virus DNA! But was that too good to be true?

The most direct way to discover whether experimental gold is in truth lead is to run a negative control: do the PCR without having included any actual liver tissue. Then you know there was no virus to start with. Yet the negative control also yielded a positive result; it had been fool's gold after all. The laboratory itself was a source of hepatitis virus DNA.

Another Fleming, Alexander, famously failed to grow bacteria in a Petri dish. That led to the discovery of penicillin. What must have initially felt like failure here led to a 1988 *Lancet* letter, identifying and offering a solution for the problem of contamination in PCR. Its three authors are all here today. Dennis Lo was first author because "[he] was absolutely crucial to all this not just in doing the experiments but thinking through the issues and solving them. We then developed lots of applications of the PCR in clinical material including the detection of fetal DNA in maternal blood, first published in 1989. All this as a medical student..."

Dennis Lo stayed in Oxford until his return to Hong Kong in 1997. During this period, he was supported by a doctoral studentship, followed by a Junior Research Fellowship at Hertford College, and then a Faculty position with a Fellowship at Green-Templeton College – his fourth Oxbridge college experience. Just under ten years later, in another *Lancet* publication, Dennis Lo and his co-workers reported that they could reliably detect fetal DNA in maternal blood plasma and serum. This game-changing discovery showed, in principle, that there could be a non-invasive method to probe the genetic make-up of a baby – something that hitherto had typically required the withdrawal of fluid from the amniotic sac that surrounds the fetus. That testing procedure conferred a risk of causing a miscarriage or early delivery. Development, validation, and clinical deployment of the non-invasive alternative took many more years of painstaking experiments, whose course was sometimes changed by moments of insight and inspiration that came not only from science but also from imagery in art and film. But those tests have now been deployed over 100 million times, averting perhaps half a million miscarriages or early births. That makes 200 million-plus parents who decided that they should take a test but didn't need to be scared of what the test procedure itself might do; parents who didn't have to watch and wait in case their need to know triggered the end of a pregnancy, pre-empting consideration of what the test result might have meant.

But Dennis Lo did not stop there. From circulating fetal DNA, he had moved on to discover the presence of circulating DNA released by a transplanted organ into the blood stream of a transplantation recipient. This has led to non-invasive tests for transplant rejection. Seeing the similarity between a fetus growing in a pregnant mother to a tumour growing in a patient, he has pioneered the development of circulating DNA-based blood tests that can detect multiple types of cancer, now called multi-cancer early detection (MCED) tests. Such tests are a Holy Grail for oncology. This is not just a metaphor for a University leader: it is the work of a forward-looking, creative, constructive and problem-solving mind – and a mind attuned to the workings of three collegiate universities, two in the form of Oxford and Cambridge, and the third one being our very own CUHK. He takes up his post after 28 years of working at CUHK: home-grown yet nationally and internationally experienced and respected, and garlanded with honours including election to five academies of sciences and prizes including a Lasker Award and a Breakthrough Prize. Welcome, Professor Dennis Lo: we salute you.