INVISIBLE TECHNOLOGY

Cutting-edge devices are getting cheap enough for everyday use.

Lee Hood's article in this issue has given us just a glimpse of the tumult of information of science and technology that's coming into wellness. I want to explore how we can get that into the hands of the everyday person. I don't just mean First World, I mean developing world and Third World.

There is only one way to do it — and that's to miniaturise it, make it cheap and effective. People talk about point-of-care technology, I like the phrase invisible technology—invisible, automatic technology. The value-add is so high that it is worth it to make this cheap and convenient. The only way to do it is through nano-technology. I won't belabour the point, but we have seen this happening in the computer industry. We've gone from roomfuls of computing to a watch and soon we'll have little computational dust!

So if you look at what happened with Lee Hood's original invention, it's gone from $3 billion to $1000, and that's happened through nano-technology primarily. It has to get cheaper.

There are two things I want to explore here. I'd like to outline some of our clinical data and I'd like to outline two examples of some of these nano-gadgets that could potentially enable some of the things that Lee discusses.

We have a new centre at the University of Queensland; and one of the things about the Centre for Personalised NanoMedicine is that we are bringing in a lot of patients. Last year we had 300 patient samples — and funny things happen when you mix patients with technology development. This year we hope to bring in 500 and through Ravi and others we're hoping to engage more broadly across the world.

I want to outline what happened with just one patient. It is one patient that had a very deep impact on my lab, and although she has passed away she drives much of the work that we do. Patient 205 is a clear example of what we need to do to change the system and I hope that this may be one of her legacies. She was a 39-year-old woman who was diagnosed with acute myeloid leukaemia (AML). This is one of the worst blood cancers because it typically doesn't respond to treatment.

Before she came to us, in the conventional hospital system everything was thrown at her. She had two bone marrow transplants and she had four lines of chemotherapy that took her to within an inch of her life. That's the way chemotherapy works. It had no effect and the cancer was moving up exponentially and there was nothing we could do about it.

So we used the miniaturisation of some of what Lee invented all those years ago and has, within the last 12 months, become accessible so we can use it in the clinics. We sequenced her at this point. Now we did more than just the genome and it's quite remarkable that this is even possible now. I want to emphasise that this has only been available for 12 months. We did something called the genome, epi-genome, and the transcriptome. The fact that we have eyes on this now is remarkable. Humanity hasn't had eyes on this in real time in the clinic before. This is like looking at the cancer and seeing the ROM

Matt Trau is currently professor of chemistry at the University of Queensland and deputy director and co-founder of the Australian Institute for Bioengineering and Nanotechnology.

and the RAM memory of those cells. I want to acknowledge here the genius of Paul Mainwaring, who really was the key intellect behind this.

So we do something called integrated biothermatics which is basically like a bio-Google and it searches in the cancer memory to try to find out what's wrong. In patient 205's case we found something: although she had a blood cancer, the code was was very similar to a skin cancer. Who would have thought? But that's going to be the future. It's about the code, it's not about where it happens in the body.

In fact the mechanism was similar to a rare type of skin cancer, retinal cancer. A bioinformatics company in Brisbane has a register of all known drugs and it can scan to match the code with drugs that are already preapproved that you would never ordinarily use in a hospital setting. So it made a match. What lit up was that even though she had a horrible blood cancer, there is potentially a drug used for a skin cancer that could be effective. What a concept! It wouldn't have been possible without Lee Hood's initial technology.

We need cheap, accurate early detection.

She was treated with the drug, and I want to emphasise this was a tablet that was sitting in a cupboard It worked immediately, it arrested the cancer and in three days the cancer had dropped to below detectable levels. She was so ill from the chemotherapy that it took a while but eventually she went home in remission. When this happened we all fell off our chairs, we couldn't believe it. The tragedy is, and it's a lesson for all of us, she died three months later of a heart attack. The chemotherapy that wasn't effective up front is very cardio toxic and a large percentage of AML patients die of heart complications from medications.

There are three lessons here and they guide the technology that we must develop. First is early screening — we need cheap, accurate early detection. If we could have caught patient 205's cancer early, and spared her the chemotherapy treatment that caused her heart attack, she would certainly be alive today. Second, we need technologies to personalise treatment based molecular information. If we could have personalised the treatment of patient 205 before her chemotherapy treatment was given, it would have quite likely spared her life. What we did for patient 205, we should now do for all patients — and there is an urgent need to translate this fully into the hospital setting. Third, after treatment, we need to monitor to see if the treatment is effective and if it is not then we need to modify the treatment. We don't do that very much in the modern hospital system, and we need to embrace new diagnostic technologies that make this possible.

I'm going to outline two examples of technologies that we have developed to try to attack those three problems. And again they have to be simple, cheap, and accurate. The current method of pathology soaks a lot of money out of our health care system. You get a blood sample for example out of Paul Mainwaring's clinic, it's shipped somewhere and then there's something I call palaver, which is Australian slang that fits perfectly this situation. Anyway, what happens is you need, equipment, people, and technicians. You have to send the sample and then you might get the data back, all this is time and expense — palaver! For DNA there are three key steps that happen, you have to extract the DNA, then you need to amplify the DNA, and then you need to display it on a machine like the one Lee Hood invented. That's what happens in the pathology lab. There is a massive need to reduce the cost of all the stuff I've talked about.

The first technology I'd like to outline is one that we have invented and recently published about. The challenge is to invent a technology using nanotechnology to miniaturise all of this and put it in a single drop. It sounds ridiculous but it works. Basically, what we have done is put in those three key steps that I've described, with molecular machinery, sophisticated enzymatic machinery, and nanoparticles.

Each of those three steps happen automatically inside the droplet on-site. The test has comprehensive DNA and RNA analysis within a single drop. Now you don't need extensive equipment and you don't need training. You need one drop of fluid and 55 minutes. It's so simple that I can do this. It's very

similar to a pool test. This is a pathology lab in a drop, so if you've ever measured the pH or chlorine in your pool then you can do this.

The magic is that it's got single molecule sensitivity. It's as sensitive as a laboratory. It can detect one molecule of DNA. It's adaptable to all pathogens; fungi, bacteria, viruses and cancer markers. We've shown in the research paper that it can be used for HIV, tuberculosis, flu, even cattle herpes and the Panama virus in bananas. A farmer can do this on-site if he chooses to.

The other great thing about it is that you can program it to do multiple tests simultaneously within the droplet, so we can test for three different variants of the flu in one single droplet, and in the future we would like to expand that further. We think it's ideal for point-of-care. So you basically do a little bit of micro-palaver, let it sit for 45 minutes, and then within 13-14 seconds you get a readout. It's individually programmable for DNA and RNA. It can also do epi-genetic readouts—we see this as a platform, so what you saw in patient 205 was DNA genetics, epi-genetics, and transcriptomics. This technology can do it in a single droplet of fluid. We see this as one example of something that could be disruptive.

The second technology I'd like to outline addresses a big issue in cancer. What happens with cancer is that it starts with one cell and the primary tumour forms. We can treat the primary tumour to 98% effectiveness. The trouble is that every now then a little cell breaks off and goes into the bloodstream like a terrorist, and it travels through the blood and can colonise other sites (metastatic sites). So the primary tumour isn't dangerous, the dangerous part is that secondary metastatic site. The trouble is that, in the hospitals, we don't have eyes on this process. So when clinicians treat cancer they don't know if it's metastasised or not. To be able know if there are terrorists in the city is a big deal, but you also want to catch them and interrogate them so you can treat effectively. The typical blood for a cancer patient if its metastasising is 50–100 cells to 10 million healthy cells. How do you find that needle in a haystack?

When you look at our new technology, it's just a chip. You put a drop of blood in and apply an AC voltage signal — which can come from a laptop or an iPhone. When it's applied, the blood moves and when you turn off the voltage it stops. All you need is that chip and a phone. We've shown that if we spike 1ml of blood with 100 cancer cells and 10 million healthy cells this chip will find 90 of those cells each and every time. So again we see this as another potentially disruptive technology. Imagine if we could get something like that — which is cheap and effective and guides treatment — into the hospital system.

There will be an app for wellness and disease management. It'll be enabled by a series of nano-sensors.

My own personal opinion about what will happen with wellness and disease management in the future is that Lee Hood has pioneered this and opened the door for so many of us. In the future key diagnostic technologies will miniaturise, via the application of nanotechnology, become much more powerful, and get much faster. There will be an app for wellness and disease management. It'll be enabled by a series of nano-sensors. Some of them may be implanted but there are complications there. The data will be automatically uploaded into your smartwatch and it will be the way of maintaining wellness and avoiding advanced disease.