Working towards cancer-free childhoods

Developing cancer drugs for clinical trials involves not only identifying and evaluating suitable agents, but also observing how they interact with the cocktail of other drugs in a cancer treatment regime. For the Telethon Kids Cancer Centre in Perth, Western Australia, increasing throughput and reducing assay volumes are essential to save money and time in the race to beat cancer.

The Telethon Kids Cancer Centre (TKCC) brings together a dedicated group of researchers and clinicians from across the globe to work collaboratively towards developing more effective cures to treat childhood cancer. Brain tumors are the most common form of solid tumor in children, affecting 200 children in Australia each year, and many more worldwide. Within the TKCC, the Brain Tumour Research Program (BTRP) – headed up by Dr Nick Gottardo and Dr Raelene Endersby – is striving to improve patient survival rates and quality of life, through basic and preclinical research, with a key focus on providing the necessary evidence to help a therapy transition to clinical trials.

The TKCC is home to a diverse range of researchers from academia and industry, as well as clinical oncologists, neurosurgeons, radiologists, chemists, pharmacologists and bioinformaticians. It has a close connection with oncologists at the Princess Margaret Hospital – the only children's hospital in the state – and this relationship is key to defining the direction of its research, based on the lack of treatment options currently available to patients. The aim is to uncover more targeted, less DNA-damaging treatments to tackle the tumors.

Raelene explained: "My lab is interested in looking for agents that sensitize cancer cells to conventional treatments, such as chemo- and radiation therapy, and then evaluating them for safety and efficacy. We generate *in vitro* and *in vivo* models of pediatric brain cancer using surgical specimens or genetically modified mice, and then use those tumor cells for drug screening and preclinical testing such as drug sensitivity assays, diluting drugs from high to low concentrations to identify effective doses. What's important for us is looking at how different drugs interact with each other; if we were to put a new drug into an existing protocol, would the drug interfere with the current treatment?"

Three years ago, the team looked to develop the automation in its workflow, to help carry out the thousands of necessary drug tests. Raelene continued: "We were doing lots of dilutions, and serial dilutions, which we were carrying out either manually, or using a much slower robot. When we found out about the D300e, it was a lightbulb moment. This instrument has transformed the activities of our lab. Previously, working together with a colleague, you could generate a small number of plates working solidly for three to four hours. With automation, our throughput went through the roof and increased by four or five times; we are now able to generate faster and more consistent results. Working manually, we would often see a lot more inter-experiment variability than we now do with the D300e, where all of the data overlays beautifully. The error bars are much smaller compared with our previous data, and the increased reliability means that we don't need to repeat the experiment as many times."

Left to right: BTRP team members Tracy Seymour, Hetal Dholaria, Stacey Fazio, Brooke Strowger, Raelene Endersby, Mathew Ancliffe, Hilary Hii and Jacqueline Whitehouse

Dr Jacqueline Whitehouse, senior scientist in the BTRP, agreed: "What would take hours on our previous liquid handling robot, now takes minutes on the Tecan system. The fact that we can use small picoliter volumes also saves money, as some of the novel anticancer drugs are quite expensive and hard to synthesize. Using manual pipetting or our previous robot, we could only work with a minimum volume of about five microliters. We would be wasting a lot of drugs just by the nature of the pipettors and their accuracy, whereas we can now dispense picoliter volumes consistently. We were skeptical at first, but were pleasantly surprised when we were still seeing effects of our drugs on cells using such small volumes. The other advantage is its size, it's so small that it can easily fit inside a biosafety cabinet. This is important for both our precious cultured cells – minimizing the risk of contamination – and for the user, protecting them from exposure to potentially hazardous or toxic novel chemotherapeutics."

"It's very easy and quick to set up; you just copy and paste your data from Excel®. It's been simple to train people and there's not much people can do to break it; the leukemia group within the TKCC is also using our system and it's a good instrument to share with people knowing that it will come back in one piece. We've used it pretty heavily for the past two years and, since there are not many moving parts, it's been great," Jacqueline concluded.

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To learn more about Telethon Kids, visit
www.telethonkids.org.au