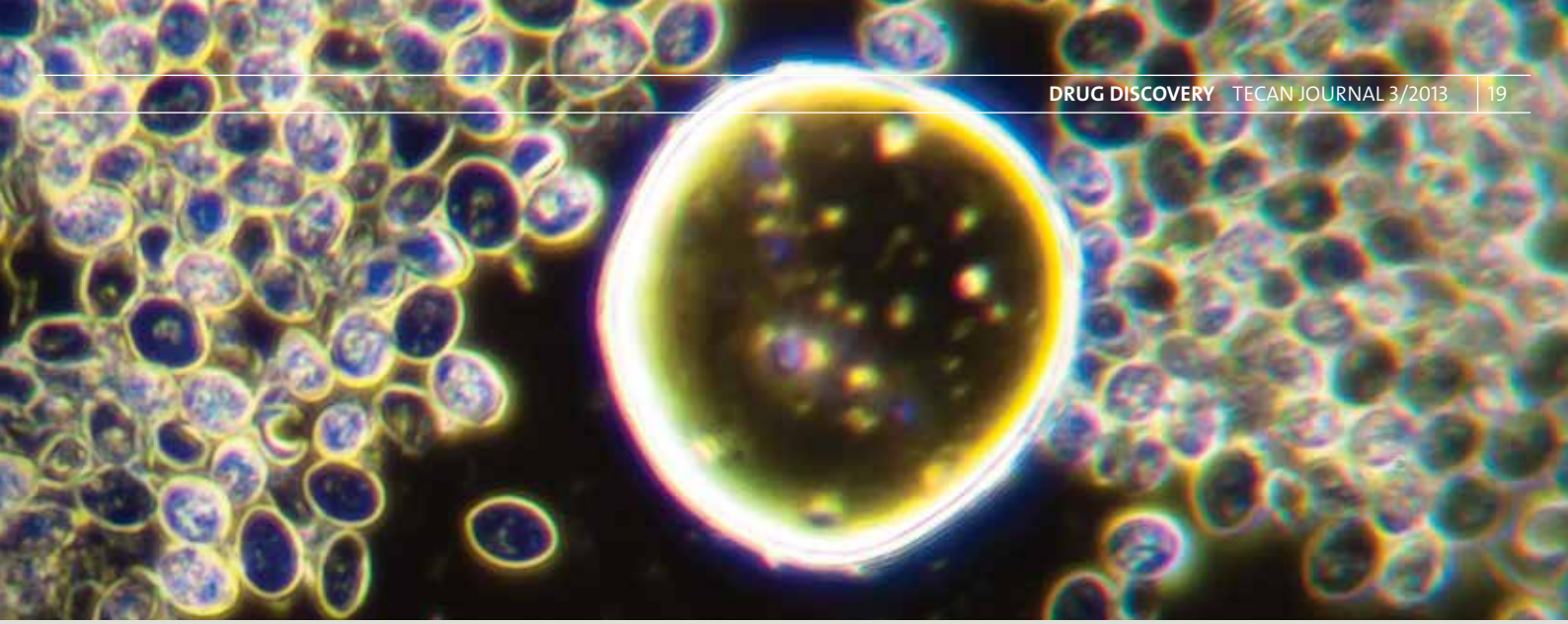
Removing the constraints of manual dose-response assays

The Stanford Genome Technology Center has invested in an HP D300 Digital Dispenser to study the effects of small molecule chemical inhibitors in yeast, enabling more experiments to be carried out more easily, and in less time.

The Stanford Genome Technology Center (SGTC) in Palo Alto, California, USA, focuses on developing genomic technologies and innovative techniques to address important biological questions. Performing yeast functional genomics studies allows the Center to investigate the effects of small molecule chemical inhibitors, as Bob St. Onge, a Senior Research Scientist at SGTC, explained: "Our goals include the identification of new chemical inhibitors that may be useful tools for studying cell biology or have the potential to be developed into a drug, as well as new druggable targets – proteins within the cell that are amenable to inhibition by small molecules. Yeast is very easy to culture and grows quite rapidly, making it ideal for our investigations; a lot of experiments can be performed that would take considerably more time to carry out in a human cell system, and many pathways – especially those related to cellular metabolism – are conserved. For example, some cancer drugs, which target specific proteins in tumor cells, target the same proteins in yeast cells. There are also experimental tools that are available in yeast, but not in other systems. We have a knock-out strain for each and every gene in yeast, and the effects of small molecules on all of these strains can be examined. The strains can be assayed individually, or collectively as a pool of knock-out strains in a single culture.

Research Assistant Sundari Suresh using the SGTC's HP D300



Instead of looking at individual targets or processes, we can essentially look at all potential targets simultaneously, getting a better idea of what is really going on. This is particularly important when small molecules are studied, as even the most specific compounds often have multiple effects on the cell."

"Yeast has a short doubling time, and we can do many experiments very quickly, testing large numbers of chemical inhibitors against many strains by performing growth assays in suspension cultures in 48-, 96- and 384-well plates. To help with this work, we recently purchased an HP D300 Digital Dispenser, which enables us to take full advantage of the yeast system. It is perfect for our experiments, allowing us to dispense compounds directly into yeast culture plates, which are then assayed in microplate readers. We have several Tecan Sunrise™ and GENios™ readers, and these play an important role in our studies, acting as yeast incubators and enabling us to monitor growth in real time over the course of one or two days, measuring and quantifying the effects of candidate compounds very precisely."

Bob continued: "The HP D300 removes the technical burdens and constraints involved in manually setting up dose-response assays, making it very simple to plan and dispense the exact drug concentrations required, which really opens up new experimental options. It is easy enough to manually test a particular drug at a certain concentration range, but looking at ten different drugs and a variety of different strains is a pretty big investment in experimental planning and pipetting, especially when studying drug combinations. Every laboratory is limited to some degree by staffing levels, time and cost, and an instrument like the HP D300 lets you perform experiments so much more rapidly; we can set up ten 384-well assay plates and obtain the results the next day, freeing up time to do other things. As the experiments are now much easier to do, we do a lot more of them, looking at the effects of specific drugs and strains either individually or in combination. I can say with certainty that we have performed experiments that we wouldn't otherwise have done, and that those experiments have actually led to some very interesting results."

"The HP D300 is also very intuitive; we were shown how to use it one day, and were setting up our own experiments the next; very little training was needed as the software is so user friendly. The instrument is in use almost every day now and, in fact, the main challenge for us is to build the informatics tools needed to keep track of, and analyze, all the new data we have generated," concluded Bob.

To find out more about Tecan's HP D300 Digital Dispenser, visit **www.tecan.com/digitaltitration**

To find out more about the Stanford Genome Technology Center, visit **www.med.stanford.edu/sgtc**

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