

Functional genomics lab moves to automation

For the past two years, Dr Julie Parenteau has been focused on the yeast *Saccharomyces cerevisiae* in the Laboratoire de Génomique Fonctionnelle de l'Université de Sherbrooke, in Sherbrooke.

In this laboratory, researchers, funded in part by the Canadian Institutes of Health Research (CIHR), are evaluating the function of certain regions of 300 specific genes in *S. cerevisiae*. By removing some parts of specific genes within the yeast cells, their function can be better observed and understood. Phenotypes of mutated yeast cells are studied under various growth conditions and in the presence of different drugs to determine the role of the targeted gene.

At the onset of this project, Dr Parenteau grew each mutated yeast strain in triplicate under the outlined growth conditions. Approximately 10ml of cells were cultured in tubes, and a small amount was removed every hour to obtain an OD measurement with a standard spectrophotometer. These measurements were then used to manually plot a growth curve.

Cultures were grown in liquid media, as the drug sensitivity of yeast is better represented in liquid form rather than solid media, and subtle phenotypes of mutants can be detected even when weakly expressed. In order to better manage this massive and labour-intensive process, only WT cells were used and the testing was limited to determining the best concentration of drugs in liquid media. Although scaled back, Dr Parenteau realized that the enormity of the project was still overwhelming.

"The amount of time and labour involved would have created roadblocks; there was simply too much to do, and not



Dr Parenteau with research assistant Mathieu Durand at the Laboratoire de Génomique Fonctionnelle.

enough time to get it done," she says. "There was no time for anything else, including sleep!"

So, with funding from Genome Quebec and Genome Canada, she decided to move into a microplate format and automated instrumentation to streamline her research.

Options for automation

Faced with a multitude of options in automated microplate readers, Dr Parenteau narrowed the field with specific criteria. Shaking and incubation were essential as she wanted to grow the yeast samples in the microplate reader, thereby increasing efficiency and reducing the number of steps in the process. Additionally, sterility and evaporation

were both of concern, so it was important for the microplate reader to read microplates with covers.

To compare the growth of WT yeast cells and mutant yeast cells, and determine any dissimilarity between the strains, the desired microplate reader also needed to incorporate kinetic measurements. This measurement provided definitive data on the function of the mutated gene. Finally, as Dr Parenteau would be reading the microplates in triplicate, she required a high degree of reproducibility from the microplate reader.

The choices were narrowed to three manufacturers and their respective microplate readers. Each was brought into the Laboratoire de Génomique

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BioTek's microplate spectrophotometer

Fonctionnelle for evaluation. After rigorous testing of each unit, Dr Parenteau selected the BioTek Instruments' microplate spectrophotometer.

"We had to shake the microplates for nine minutes, and then read for one minute over the growth period," she explains. "Only BioTek could make a guarantee of performance and repeatability with their ... reader under these conditions; the other manufacturers couldn't make the same guarantee."

In addition, she notes that the software controlling the instrument enabled her to easily and quickly collect data, export to a spreadsheet, and analyze to determine various metrics of the yeast cells.

Trouble-free conversion

According to Dr Parenteau, the conversion to microplate format and use of the spectrophotometer was trouble-free.

"Thankfully, scaling our yeast cultures to microplate volumes was straightfor-

ward, and the [microplate spectrophotometer] offered just what we were looking for, including much-needed speed and simplicity," she says.

Now, 10 mutant strains can be grown and analyzed in a single microplate, substantially increasing productivity. Given that the yeast cells and microplates never leave the instrument during the experiment, sources of contamination are virtually eliminated. Additionally, growth curves and other environmental observations may be more statistically indicative of true yeast cell activity in the microplate format as the total volume per well is stable throughout the process compared to data obtained via sampling. When sampling from a larger volume, the loss of sample volume can distort final results if not properly adjusted for in calculations.

Dr Parenteau concludes that the laboratory is now equipped with over a dozen of BioTek's microplate spectrophotometers to aid in her research.

"Switching to microplate format and incorporating the ... readers has been very useful; now we can even perform 24 hour studies on the yeast cells without having to be in the laboratory the entire time," she says. "We've saved a ton of time, and we're able to gather more accurate information on how *S cerevisiae* mutated cells react under different drug conditions."

By Lenore Buehrer, product manager, BioTek Instruments