High throughput imaging speeds analysis of hormone receptors

November 1 2008

A new high throughput microscopy technique enabled researchers at Baylor College of Medicine in Houston to analyze thousands of individual cells expressing androgen receptor, a finding that could herald new ways of evaluating the effect of drugs or other treatments on cells with normal or aberrant hormone receptors.

In a report in the current issue of Public Library of Science One (*PLoS One*), Dr. Michael Mancini and his collaborators reported a new, next generation high throughput image-based assay that helps determine the level and location of androgen receptor and its transcriptional activity on a cell-by-cell basis.

"This has application to personalized medicine," said Mancini, associate professor of molecular and cellular biology at BCM and director of its Integrated Microscopy Core. "For example, we could use the high throughput microscope and robust image analysis to determine which drug might be best to turn off or repair a mutated cell that is causing disease."

In this case, he and his colleagues analyzed the androgen receptor, a molecule that binds the hormones testosterone or dihydrotestosterone and is responsible for regulating genes that give an organism or animal male characteristics.

"As our ability to image cells using high throughput microscopy got going faster and faster, we began to collect enormous amounts of

functional data that was usually only accessible by separate (and slow) biochemical experiments. Our customized software approaches then allowed us two assemble the results into a more systems-level appreciation of the biology, linking together several functional characteristics of the androgen receptor," he said

The high throughput technique, often called high content analysis, enables researchers to analyze effects on a cell-by-cell basis, taking into account the heterogeneity of the cells, he said. Before the development of new microscopes, he said, taking a few images an hour was a feat.

"Now we routinely take thousands of pictures a day," said Mancini.

Not only that, but scientists such as Adam Szafran, the M.D./Ph.D. student who is first author of this report, can essentially look at several elements of cellular response at the same time.

"We can study issues dealing with the cell cycle as it goes through its life," said Szafran. Previously, scientists had to manipulate cells to capture them at different points in their lives. The new imaging technology enables them to study the cell in a more natural form.

In the PLoS study, Szafran, Mancini and their colleagues were able to study the response of a particular androgen mutation to different ligands (molecules that can trigger binding to a particular protein).

"We could show how the receptor was defective in respect to the endogenous (or normally present) ligand. When we used a different ligand, we could rescue aspects of the receptor's function," said Szafran.

The technique could have application in personalizing medicine, said Mancini. Physicians could take the individual cells of a patient diagnosed with a disease and use the high throughput microscope to see

how different drugs affect the mutated cells. The high speed approaches for androgen receptor studies are also being used to investigate basic science and personalized medicine possibilities in several other projects, including breast and prostate cancers, and adipose (fat cell) biology.

Source: Baylor College of Medicine