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Scattered light rapidly detects tumor response to chemotherapy

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New technology developed by Duke University bioengineers can help clinicians more precisely detect whether specific cancer drugs are working, and should give basic researchers a powerful new tool to better understand the underlying mechanisms of cancer development.

By interpreting how beams of light scatter off of tumor cell samples, researchers can determine if cancer cells are responding to chemotherapeutic agents within a matter of hours.

Most chemotherapy drugs work by forcing cancer cells to commit cellular suicide, a process known as apoptosis. As cells undergo this process, bodies within the cell, such as the nucleus or mitochondria, go through structural changes. Using the new approach, researchers can analyze the light scattered by these bodies to detect the apoptotic changes in real time.

"The new technology allowed us to detect the tell-tale signs of apoptosis in human breast cancer cells in as little as 90 minutes," said Adam Wax, associate professor of biomedical engineering and senior member of the research team. "Currently, it can take between six and eight weeks to detect these changes clinically. It appears that this approach has the potential to be helpful in both clinical and laboratory settings."

The results of the Duke team's experiments were published in the February issue of *Cancer Research*.

The light-scattering technology is known as angle-resolved low coherence interferometry (a/LCI). In this process, light is shined into a cell sample and sensors capture and analyze the light as it is scattered back. The technique is able to provide representations of sub-cellular structure without disrupting the cells, and can be used to scan a large number of cells in a short time.

"Now, oncologists typically judge if a chemotherapeutic agent is working by looking for shrinkage in the tumor using imaging techniques, such as MRI or PET, or pathological response at time of surgery" said Julie Ostrander, Duke molecular cancer biologist, who along with Duke bioengineer Kevin Chalut were the paper's first authors.

"If we had a way to detect early on in the apoptotic process whether or not a drug was working, patients would not have to wait weeks to months to find out," Ostrander said. "The idea that you could shine a light at a tumor and use the light-scattering pattern to measure the success of drugs is a big step forward."

For their experiments, the Duke team studied a well-known cell culture line of human breast cancer. The cells were exposed to two common chemotherapy drugs, doxorubicin and paclitaxel. Using the a/LCI technology, the researchers looked for specific patterns, which indicate that structural changes have occurred.

The researchers found that when compared to control cells, the paclitaxel-treated cells began showing significant increases in a pattern called fractal dimension within 90 minutes. Doxorubicin-treated cells exhibited the same increases within three hours. Interestingly, the fractal dimensions began decreasing at six hours, only to increase again within 12 hours of treatment.

"The fact that the changes in structure appear over two distinct time

scales suggests that multiple mechanisms are involved in these early events in apoptosis," Wax said. "Further analysis showed the early changes we observed were taking place in the mitochondria, while the changes in the structure of the nucleus were responsible for the later ones."

Ostrander said that this technology will help laboratory investigators like her determine how cancer cells become resistant to apoptosis, and therefore are resistant to drugs. Before this technique can be employed for human breast cancer, further studies will be carried out in animals.

Wax and colleagues at the University of North Carolina at Chapel Hill are currently conducting a pilot clinical trial in humans using a similar technology for early detection of pre-cancerous cells in the epithelial lining of the esophagus, a condition known as Barrett's Esophagus.

Source: Duke University