Medical Xpress

New technique quickly detects cancer indicator

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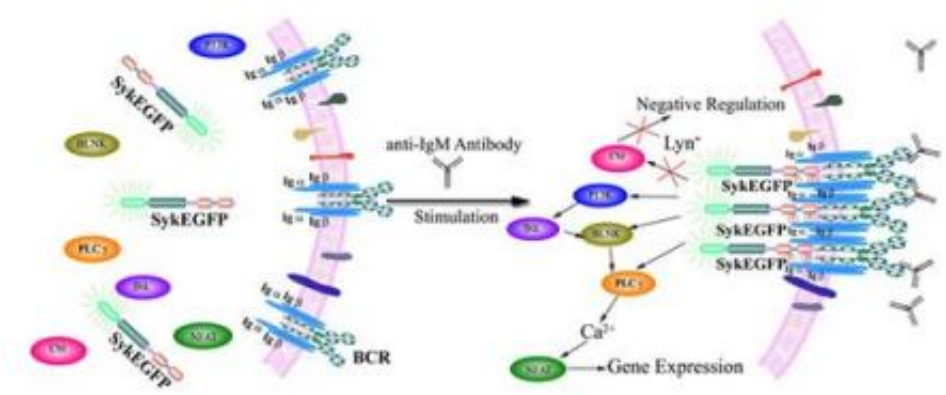

Proteins, labeled SykEGFP, are shown moving from the cell interior to the interior of the plasma membrane. Such movement, or translocation, is involved in cancer development and other important processes. (Purdue image/Chang Lu)

Researchers have developed a new way to detect protein movements inside cells, which signal a variety of cellular changes such as those in cancer cell development. The method could help diagnose cancer in the future.

By combining two distinct techniques, the technology can examine large numbers of cells individually, a feat not previously possible, said Chang Lu, a Purdue University assistant professor of agricultural and biological engineering.

"We really have bridged the gap between different technologies, allowing us to do science on a whole new level," he said.

In a study published this month in *Analytical Chemistry*, Lu demonstrated that the technique can detect a handful of protein movements, or translocations, within entire populations of cells.

These movements are important to detect because they are involved in many disease processes, such as oncogenesis, wherein a normal cell becomes malignant, said Robert Geahlen, a study co-author and researcher in the Department of Medicinal Chemistry and Molecular Pharmacology.

"Protein translocations are involved in the activation of tumor cells," he said. "Detecting these movements could help diagnose the type and stage of cancer in the future."

Lu's method uses two existing technologies: electroporation - used to determine protein location - and flow cytometry, a technique capable of rapidly examining individual cells but blind to intracellular protein locations on its own.

The Purdue technique, called "electroporative flow cytometry," harnesses the discerning power of the first method with the speed of the second, Geahlen said.

The method involves cells being sent through tiny channels within a microchip and undergoing electroporation, wherein electrical pulses open pores in cell membranes and protein is released from inside. Then, sensors measure protein concentrations. Since a protein's subcellular location can directly influence the amount of protein leaving the cell, as Lu and Geahlen have shown, this method is capable of indirectly determining location, Geahlen said.

If proteins are in their original position, floating freely in the cell's interior, or cytoplasm, a large percentage of them will flow out of the cell upon electroporation, Lu said. If translocation has occurred, in which proteins migrate from the cytoplasm to tightly bind to the interior of the cell membrane, few will be able to leave.

Previous technologies detect either protein movement in a few individual cells via slow imaging techniques or take average measurements from larger groups of cells, data usually irrelevant to protein location in individual cells, Lu said.

"When looking at a few cells, you see the trees but not the forest," he said. "When you take average measurements from large groups, you see the forest but not the trees. Our method allows us to know something about each tree in the forest."

The technology has the potential to be scaled up significantly, Lu said. In the study, 100-200 cells were processed per second, but that rate could potentially increase to speeds typical of flow cytometry, which goes through 10,000 cells per second. Speed increases can be achieved by optimizing the technology he said.

The study examines the movement of a certain type of protein called kinases. Kinases and their translocations are important for activating and deactivating cells and sending signals to one another, Geahlen said.

"There are many important kinases, enzymes and other proteins that become activated by translocation to the plasma membrane, and we've shown that we can detect one type of translocation," he said. "It's a first step."

Lu has filed a provisional patent for the technique and said that he could see it being used in a clinical setting in five to 10 years.

Study co-authors include graduate students Jun Wang, Leela Paris, Hsiang-Yu Wang, and postdoctoral researcher Ning Bao.

Source: Purdue University