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Spotting Many Different Proteins On Single Cells

Analytical Biochemistry: DNA-based sensing of multiple proteins could aid personalized medicine

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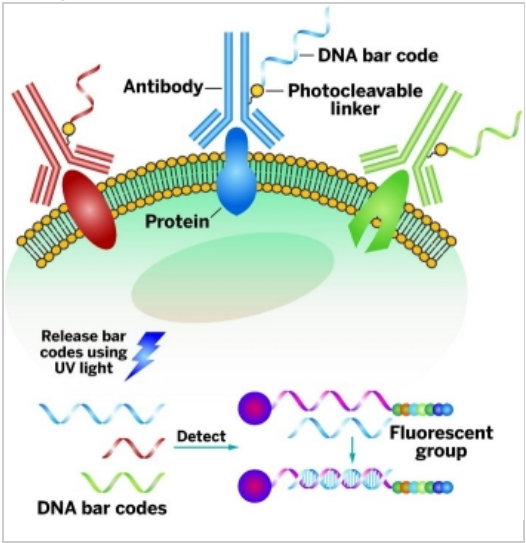

Technique uses antibody/DNA-bar-code conjugates to target specific cell-surface proteins. UV-induced bar code release, followed by hybridization with complementary DNA, enables the DNA bar codes, and the proteins they represent, to be identified fluorescently.

Using antibodies and little pieces of DNA, a new technique detects hundreds of different proteins on individual cells. It could be used to study protein variations—on different cells in the same tumor, for example—analyze responses to drugs, and diagnose diseases.

Ralph Weissleder of Massachusetts General Hospital (MGH) and coworkers developed the technique and demonstrated its ability to identify proteins on cells from patients with lung or skin cancer (*Sci. Transl. Med.* 2014, DOI: 10.1126/scitranslmed.3007361).

Weissleder notes that mass spectrometry "can do something similar, but it is not commonly used" in clinical applications because it is expensive.

The work is "a major step forward" in scientists' efforts to detect simultaneously many different proteins on the same cell, write Yesim Gökmen-Polar and Sunil Badve of Indiana University School of Medicine, Indianapolis, in a commentary about the work.

In the technique, target proteins must be determined in advance and high-quality antibodies must be available or developed for them. The antibodies are linked to single-stranded DNA "bar codes" via a photocleavable linker developed earlier by Weissleder's group. When mixed with lysed cells, the antibodies bind to specific proteins. Ultraviolet light releases the DNA bar codes from the antibody-protein complexes. The DNA bar codes, and the proteins they represent, are then identified through their sequence-specific binding to complementary DNA strands tagged with fluorescent groups.

The technique achieved simultaneous analysis of hundreds of protein markers from patients' cells. "Instead of trying to procure more tissue to study, we shrank the analysis process so that it could now be performed on a few cells," says team member Cesar M. Castro, an MGH oncologist. Those cells are obtained with minimal invasiveness, such as by using fine needles to aspirate sample fluids from patients.

The study revealed divergences in protein expression among different tumor samples. It also identified proteins that distinguish cancer patients who respond well to drug treatment from those who don't.

The method "could be very important for early detection of disease and for monitoring the effectiveness of treatments," comments Piotr Grodzinski, director of cancer nanotechnology programs at the National Cancer Institute.

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