Medical Xpress

'Shotgun' method allows scientists to dissect cells' sugar coatings

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Sugar molecules coat every cell in our bodies and play critical roles in development and disease, yet the components of these "glycans" have been difficult for scientists to study, because of their complexity.

Researchers at Emory University School of Medicine have adapted gene chip microarray technology to the study of glycans, with an approach they call "shotgun glycomics." The Emory team has developed a new chemical method for attaching a fluorescent dye to glycans purified from cells. The individual glycans are separated into tiny spots fixed to glass slides.

The approach is described in an article published this week in the journal Nature Methods.

"These slides separate and display all the glycans in the cell, so that we can test what sticks to them," says senior author David Smith, PhD, professor of biochemistry and director of the Glycomics Center at Emory University School of Medicine. "However, the structures of the glycans are unknown. This is why we use the word 'shotgun' to describe our quasi-random approach of studying them."

The research team was led by Smith, first author Xuezheng Song, PhD, assistant professor of biochemistry, and Richard Cummings, PhD, chair of the Department of Biochemistry and co-director of the Glycomics Center.

As a demonstration of the technique's utility, the team used it to identify a molecule recognized by self-reactive antibodies present in the blood of most patients with Lyme disease. Lyme disease is caused by infection with Borrelia bacteria after a tick bite, but severe cases have features of an autoimmune response, triggered by the immune system's reaction to the bacteria.

"Being able to analyze glycans in this way may lead to new diagnostics for human autoimmune disorders, and perhaps, therapies to cleanse the body of self-reactive antibodies or inhibit their pathological attack on cells," Cummings says.

Completely dissecting glycans' structures is more difficult, compared with proteins or DNA, because glycans form branched structures in which not every link is chemically the same. Scientists have estimated that cells contain hundreds or thousands of different glycans, which can be attached to proteins or lipids. When using the shotgun approach, if scientists find that proteins from the body -- antibodies or toxins, for example -- bind to one particular glycan spot, they can then go back to that spot and determine its entire sequence, sifting out important glycans from the thousands on the slide.

"The sugars present on glycoproteins and glycolipids can contribute decisively to these molecules' functions," says Pamela Marino, PhD, who oversees glycobiology grants at the National Institutes of Health's National Institute of General Medical Sciences (NIGMS). "Understanding what information is encoded in these sugars and how they facilitate interactions with other proteins has been a major road block in deciphering the molecular language of glycans. This study, which is funded through the NIGMS EUREKA program for high risk research, has now provided proof of principle for an extremely novel 'shotgun' approach to interpreting this glycan code, and allows for examination of the role of glycans in infection and immunity."

The Emory team applied shotgun glycomics to red blood cells, tumor cells and brain-derived lipids. Cummings says the technique could be used to look for distinct sugar molecules displayed by cancer cells, for example. Identifying cancer-specific glycans could similarly lead to diagnostic tools or therapies, he says.

"A slide displaying glycans from a given cell type can be thought of as a book in the library, with the entire library constituting the human glycome," he says.

More information: X. Song, Y. Lasanajak, B. Xia, J. Heimburg-Molinaro, J.M. Rhea, H. Ju, C. Zhao, R.J. Molinaro, R.D. Cummings and D.F. Smith. Shotgun glycomics: a microarray strategy for functional glycomics. *Nature Methods* (2010)

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