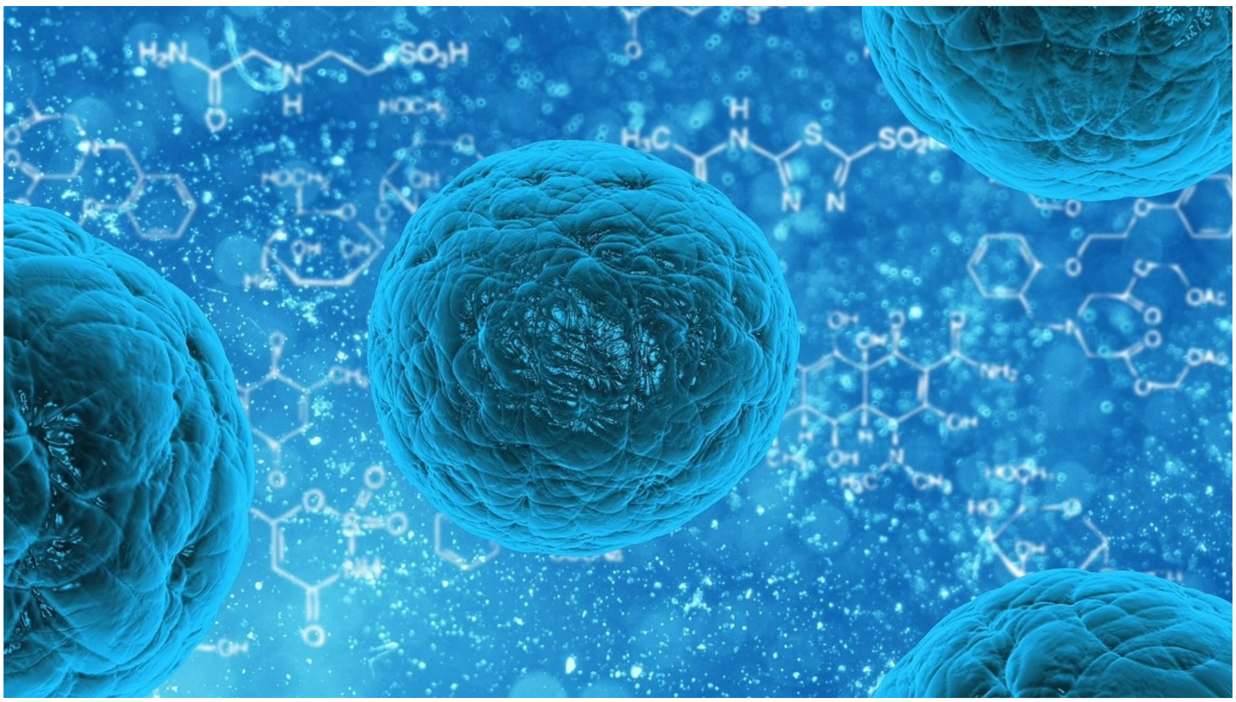
Cells use sugars to communicate at the molecular level (Update)

March 1 2019



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The human body is made up of 30 to 40 trillion cells, a large and complex network of blood cells, neurons, and specialized cells that make up organs and tissues. Until now, figuring out which mechanisms control communication between them has proven a significant challenge for the field of cell biology.

Research led by Virgil Percec in Penn's Department of Chemistry, in collaboration with the University's departments of cell and developmental biology and biology, and with Temple and Aachen Universities, provides a new tool to study synthetic cells in incredible detail. Percec and his group demonstrated the value of their method by looking at how a cell's structure dictates its ability to communicate and interact with other cells and proteins. They found that sugar molecules play a key role in cellular communication, serving as the "channels" that cells and proteins use to talk to one another. They published their findings this week in the journal *Proceedings of the National Academy of Sciences*.

"Ultimately, this research is about understanding how cell membranes function," says Percec. "People try to understand how human cells function, but it is very difficult to do. Everything in the cell is liquid-like, and that makes it difficult to analyze it by routine methods."

Cell biologists have historically used diffraction to study cells. This involves breaking them apart and taking atomic-level pictures of individual parts, such as proteins. The problem with this approach, however, is that it doesn't allow for study of the cell as a whole. Newer methods like fluorescence microscopy allow researchers to study entire cells, but these tools are complicated and don't provide the high-resolution view that diffraction can.

Using engineered synthetic cells as a model system, lead author Cesar Rodriguez-Emmenegger, a former member of Percec's group, now at Aachen, discovered a way to directly study cell membranes using a method called atomic force microscopy. This approach generates extremely high-resolution scans that reveal shapes and structures at a scale of less than a nanometer, nearly 10,000 times smaller than the width of a human hair. Percec's group then built a model that computes how the structural images relate to the cell's function.

The study is the first example of a diffraction-like method that can be done on whole synthetic cells. Using this new method, Percec's group discovered that a lower concentration of sugars on a cell membrane's surface led to increased reactivity with proteins on the membranes of other cells.

One of Percec's goals is to figure out how to control cell-to-cell communication and cell function, which is linked with his group's ongoing work in creating hybrid cells made up of parts of human and bacterial cells. While his group has been studying cell membrane mimics and engineered systems since 2010, the discovery of this new diffraction-like method was, as Percec describes, a "lucky accident."

"We approach problems that other people say there is no solution for. You cannot make a big breakthrough overnight,"Percec says. "All these people on our team are gifted and have the machinery needed to solve the various problems along the way that bring the story together."

More information: Cesar Rodriguez-Emmenegger et al, Encoding biological recognition in a bicomponent cell-membrane mimic, *Proceedings of the National Academy of Sciences* (2019). DOI: 10.1073/pnas.1821924116

Provided by University of Pennsylvania