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Asymmetrical glycans synthesized in lab

Method uses core carbohydrate to build variations of ubiquitous but enigmatic biomolecules.

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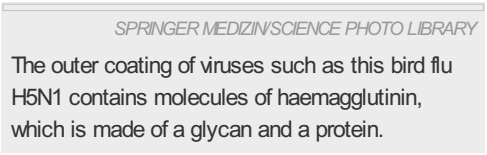
Scientists have demonstrated a new method for synthesizing glycans, a class of crucial but elusive carbohydrates. The technique opens the way to a comprehensive study of glycans, one of four key macromolecule groups in biology — along with proteins, nucleic acids and lipids — and the least studied of them. The results could also lead to a better understanding of the outer shells of viruses.



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The outer coating of viruses such as this bird flu H5N1 contains molecules of haemagglutinin, which is made of a glycan and a protein.

Glycans are made of sugar molecules, which can form simple chains or more elaborate, branching arrangements. They are ubiquitous in the living world. For instance, they form a major component of the outer membrane of all living cells. The human immune system recognizes glycans associated with specific pathogens, enabling it to respond to bacteria and viruses.

“Almost every major disease is linked to proteins and carbohydrates on the surface of cells,” says Geert-Jan Boons, a chemical biologist at the University of Georgia in Athens, who led the study, published today in *Science*[1].

But these molecules have been difficult to isolate from cells or to produce in the laboratory, except for ones with symmetrical shapes, Boons says. He has calculated that as many as 85% of glycans in nature are asymmetrical.

Boons and his team have now developed a strategy to synthesize a broad family of glycans based on a simple carbohydrate similar to one found in eukaryotic cells. This starting material is modified to enable specific sites in the carbohydrate chain to be altered independently of other locations, so that, for example, one arm keeps growing and branching out while another one does not.

A similar, but less sophisticated, synthesis technique was reported in 2005 by Yukishige Ito, a synthetic chemist at the RIKEN Advanced Science Institute in Wako, Japan, and his colleagues[2]. The latest strategy “is practical as a powerful tool in glycobiology”, he says, adding that Boons and his colleagues have demonstrated “more convincingly” a strong candidate strategy for constructing a library of complex glycans.

Boons’ study also went on to demonstrate how a glycan’s structure — and, in particular, whether it is symmetrical — affects how it binds to proteins on the surfaces of influenza viruses. Sabine Flitsch, a chemical biologist at the University of Manchester, UK, says that the methodology is “likely to be a discovery tool” in viral recognition.

“This is a major advance in the study of asymmetric glycans,” says Ajit Varki, a physician and physician-scientist at the University of California, San Diego. But he adds that it is only a start. “Many more efforts of this kind are needed before we can fully explore the functions of the vast universe of glycan complexity found in nature.”

Another issue will be to scale the technique up to produce large-enough amounts of glycans for researchers to work with, says Pauline Rudd, a glycobiologist at the National Institute for Bioprocessing Research and Training in Dublin. “The researchers have developed a very elegant methodology, but it may be difficult to apply to mass production.”

Glycoscience could help to advance not only basic biology but also fields such as biomass production for energy and polymer science. A report last year published by the US National Academy of Sciences recognized this potential, proposing a ‘glycoscience road map’ that includes focusing on advanced synthesis and creation of a comprehensive database of glycan information — an effort potentially much more challenging than the Human Genome Project.

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References

1. Wang, Z. *et al. Science* **341**, 379–383 (2013).

2. Hanashima. S., Manabe, S. & Ito, Y. *Angew. Chem. Int. Ed. Engl.* **44**, 4218–4224 (2005).