Breakthrough understanding of biomolecules could lead to new and better drugs

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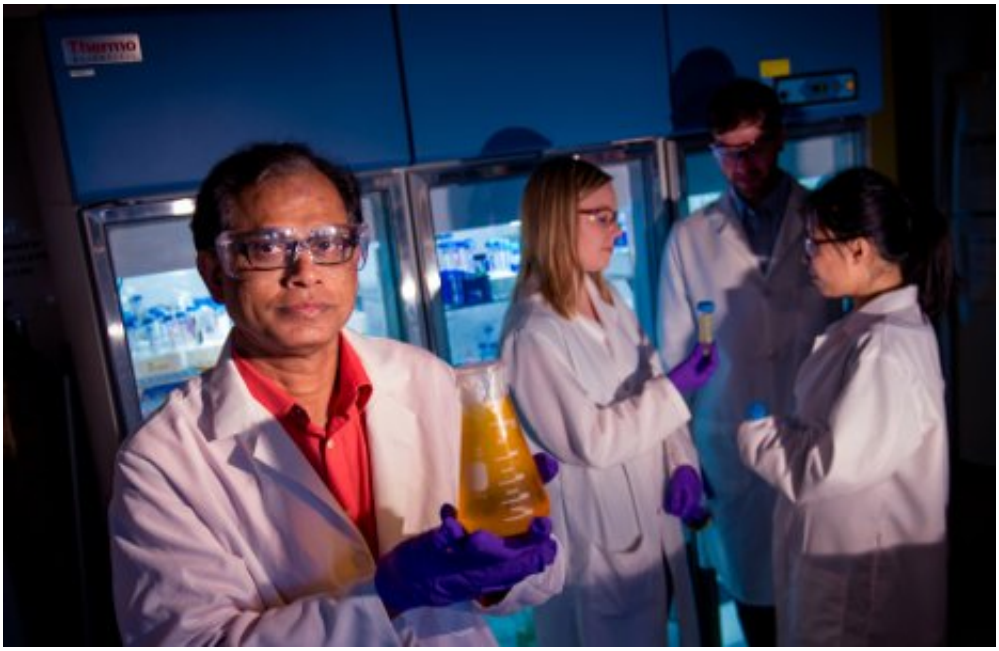


Michigan Tech biochemist Tarun Dam with a solution containing lectin, used to study how an important class of biomolecules react in the body. Credit: Sarah Bird

(Phys.org) —There's a certain type of biomolecule built like a nano-Christmas tree. Called a glycoconjugate, it's many branches are bedecked with sugary ornaments.

It's those ornaments that get all the glory. That's because, according to conventional wisdom, the glycoconjugate's lowly "tree" basically holds

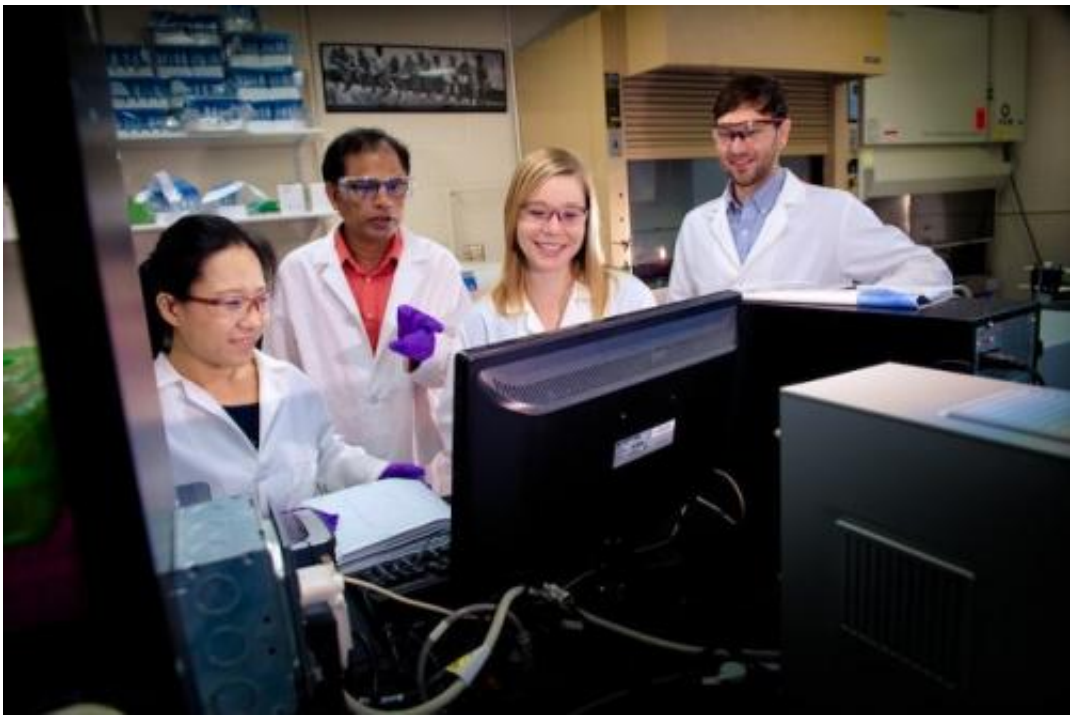
the sugars in place as they do the important work of reacting with other molecules.

Now a biochemist at Michigan Technological University has discovered that the tree itself—called the scaffold—is a good deal more than a simple prop.

"We had always thought that all the biological function resides in the sugar," said Tarun Dam, principal investigator of the Mechanistic Glycobiology Lab at Michigan Tech. "People didn't appreciate that the scaffolds were active."

The discovery opens up new avenues for research, in particular the development of more and better pharmaceuticals. Glycoconjugates are found naturally in the body, but they are also an important class of drugs that includes anything from cancer treatments to vaccines.

To determine if the scaffold had a role to play in biological reactions, Dam and his team built and tested two types of glycoconjugate molecules. They had the same sugars and virtually identical shapes but were comprised of different scaffolds, one made of protein, the other a synthetic. The scientists then tested how the different glycoconjugates reacted with biomolecules called lectins. Lectins play an important role in numerous biological processes and are a target for many glycoconjugate drugs.



Chemist Tarun Dam with his three graduate students who collaborated on the research and coauthored the paper. Left to right are Ni Fan, Dam, Melanie Talaga and Robert Brown. Credit: Sarah Bird

If the scaffolds had been inert, the reactions would have been identical. However, the sugars on the protein scaffold reacted with the lectins differently.

"If the scaffolds are different, they can cause my drug to work one way and your drug to work another way, even though they have similar epitopes [sugars]," Dam said. "Tweaking the scaffold can change the drug's function."

More information: "Significant Other Half of a Glycoconjugate: Contributions of Scaffolds to Lectin–Glycoconjugate Interactions." Melanie L. Talaga, Ni Fan, Ashli L. Fueri, Robert K. Brown, Yoann M. Chabre, Purnima Bandyopadhyay, René Roy, and Tarun K. Dam.

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