



## The sweet side of drug discovery: How sugars can help shape the future of medicines

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### ABOUT THE LECTURE

Sugars are more than sweeteners: These molecules also determine how drugs behave in our bodies. In this Front Row lecture, Scripps Research assistant professor Yuzhong Liu shared how her lab is using synthetic biology to overcome the limitations of natural product sourcing and chemical synthesis. By engineering microbes to produce complex sugar-containing medicines, Liu's work is transforming drug discovery and manufacturing—helping to make essential therapies more accessible, sustainable and affordable.

### TOP TAKEAWAY POINTS

- Many of today's most important medicines (including antibiotics like vancomycin, cancer treatments like paclitaxel and immunosuppressants like rapamycin) are sourced from plants and microbes found in nature. But this supply chain is increasingly fragile. Climate change, limited geographic availability, geopolitical instability and inefficient extraction processes make it difficult to meet growing global demand, leading to drug shortages and inequitable access to life-saving treatments.
- Sugars attached to drug molecules are far more than structural decoration—they control where drugs go in the body, how long they last and how well they work. Similarly, the surfaces of our cells are coated in complex sugars called glycans that govern how antibodies, immune cells and viruses interact with the body. Even small changes to a single sugar can lead to significant biological consequences, including diseases like cancer, making sugars a critical frontier in drug design.
- QS-21, a sugar-rich molecule used as a potent adjuvant in shingles, malaria, RSV and COVID-19 vaccines, illustrates the severity of the supply challenge. QS-21 is harvested from a tree in Chile that must grow for more than 30 years before producing the molecule. This unsustainable process has driven the price above \$400 million per kilogram, and chemical synthesis requires 76 steps that are not industrially viable. Meanwhile, global demand continues to rise, with the shingles vaccine market alone expected to more than double by 2028.
- Liu and collaborators used synthetic biology to achieve the complete biosynthesis of QS-21 in engineered yeast, producing the molecule through simple fermentation in a matter of days rather than decades. This approach offers dramatic improvements in production speed and cost, while decoupling the supply of this critical vaccine ingredient from geographic and climate constraints.
- Liu's lab at Scripps Research is now going beyond reproducing nature's molecules to actively evolving them. By selectively swapping enzymes and engineering new sugar patterns, the team can create "new-to-nature" molecular variants to explore structure-activity relationships, fine-tune potency and reduce toxicity. The goal is a closed-loop discovery platform that generates safer, more effective drug candidates through a sustainable and scalable process that could make advanced therapies more affordable.

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