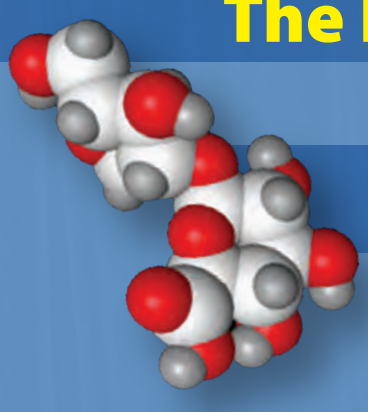
A Simpler, Safer Synthetic Heparin

A team of researchers at the University of North Carolina at Chapel Hill and the Rensselaer Polytechnic Institute has created a simplified version of heparin, a widely used anticoagulent. The new version of heparin requires drastically fewer steps to produce than the only synthetic heparin currently on the market.

The Process



Starting disaccharide

Researchers start with a two-sugar molecule extracted from bacteria.

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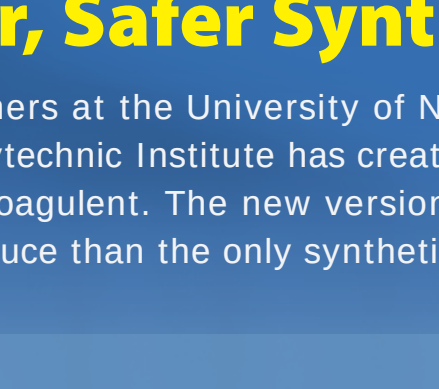
Cofactors

Cofactors are “helper molecules.” They are nonprotein chemical compounds that assist enzymes in biochemical transformations. In this case, three cofactors help transform the starting disaccharide into heparin molecules:



Enzymes

Enzymes use molecules from the cofactors to elongate the starting disaccharide and add sulfates.

UDP-GlcNTFA

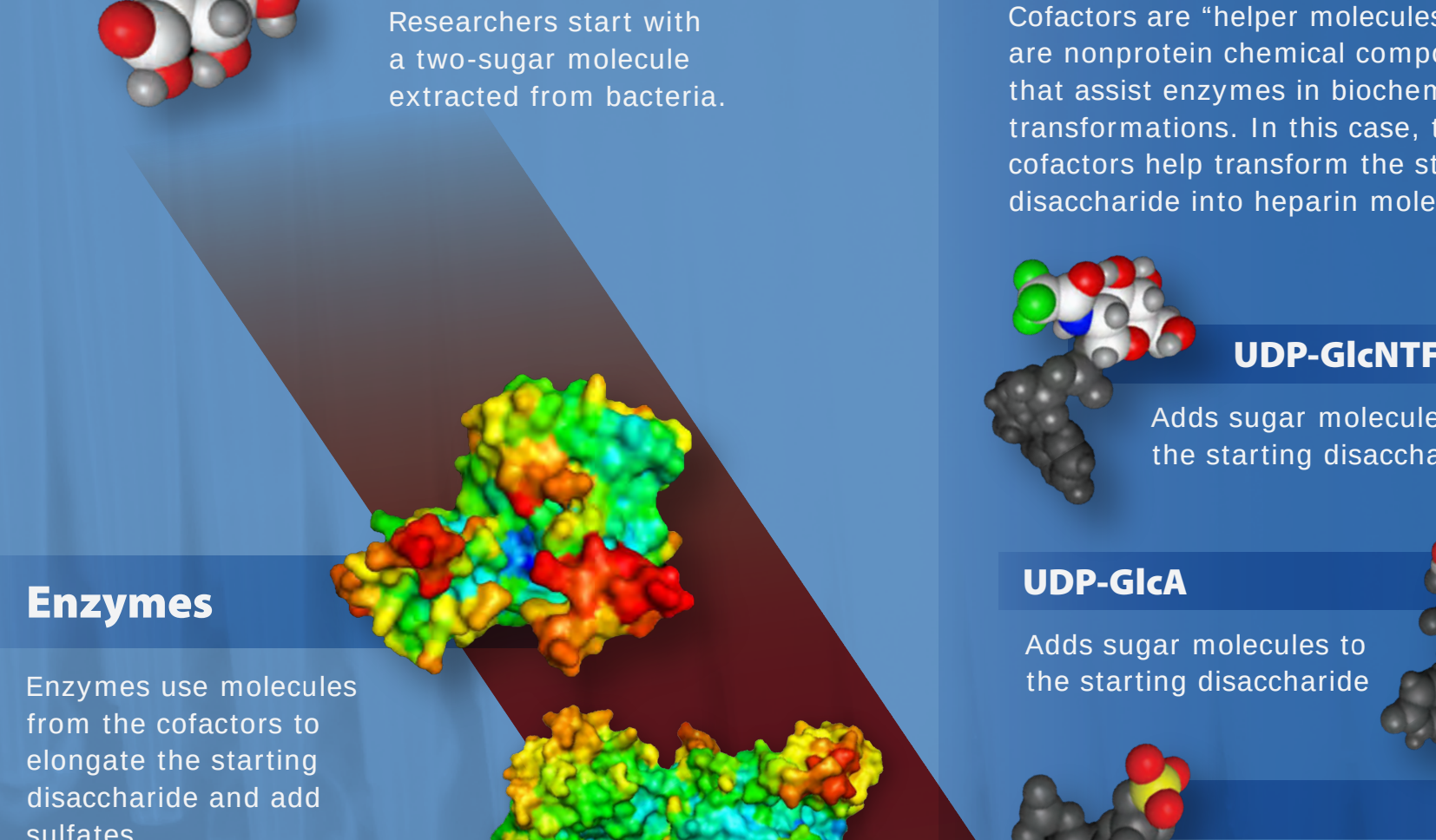
Adds sugar molecules to the starting disaccharide

UDP-GlcA

Adds sugar molecules to the starting disaccharide

PAPS

Adds sulfate groups to the final heparin molecule



Heparin molecule

Unlike natural heparin, which has very large molecules, this synthetic heparin contains only the fragment that provides the anticoagulent properties.

Graphics not to scale

Design: John Zhu / UNC Eshelman School of Pharmacy

The Advantages

Efficiency

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Safety

Synthetic heparin has traditionally been difficult to produce in large amounts, resulting in expensive therapies that are not widely used. While the actual manufacturing cost of this new heparin is not yet known, its simpler structure means it can be produced in significantly fewer steps than Fondaparinux, the only synthetic heparin currently on the market.

10 < **50**

Number of steps to produce the synthetic heparin created by the team at UNC and RPI

Number of steps to produce the only version of synthetic heparin currently on the market

Natural heparin is extracted from the tissues of cows or pigs, a process susceptible to contamination. In 2008, a batch of contaminated heparin caused at least eighty deaths and hundreds of other adverse reactions, leading to a recall of the drug. The cause was traced to a contaminant in the raw natural heparin extracted from pig intestines in China.

Synthetic heparin is less susceptible to contamination during production. Also, the simplified version of heparin created at UNC and RPI does not contain the parts of the molecule that can cause dangerous side effects.

Heparin: A Primer

Commonly Used to

- Prevent or treat certain blood vessel, heart, and lung conditions
- Prevent blood clotting during open-heart surgery, bypass surgery, kidney dialysis, and blood transfusions
- Prevent the formation of blood clots in certain patients

Discovered in

1916

Making it one of the oldest drugs currently in widespread clinical use

Cost for a 30-to-40 milligram dose

$25-$35

For low molecular weight heparin, a more refined version of natural heparin

$50-$60

For Fondaparinux, the only synthetic heparin on the market

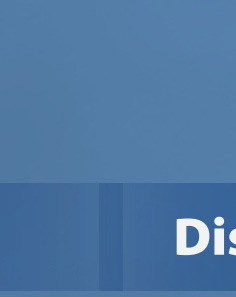
Estimated Annual Sales

$4,000,000,000

Sources: UNC Eshelman School of Pharmacy, FDA.gov, Wikipedia

The Scientists

The research team that created the new synthetic heparin is led by Jian Liu, Ph.D., a professor at the UNC Eshelman School of Pharmacy, and Robert J. Lindhardt, the Ann and John H. Broadbent Jr. ’59 Senior Constellation Professor at the Rensselaer Polytechnic Institute. The other authors of the study from the UNC Eshelman School of Pharmacy are postdoctoral research associates Yongmei Xu, Ph.D., and Renpeng Liu, Ph.D.; Haoming Xu, a UNC sophomore majoring in biochemistry; and first-year pharmacy student Juliana Jing. Additional authors are Sayaka Masuko of RPI and Madje Takieddin and Shaker Mousa, Ph.D., M.B.A., of the Albany College of Pharmacy and Health Sciences.



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Lindhardt

UNC ESHELMAN SCHOOL OF PHARMACY

More Information

http://pharmacy.unc.edu/heparin2011