Undergrad has sweet success with invention of artificial Golgi

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An undergraduate student at Rensselaer Polytechnic Institute has learned very quickly that a spoonful of sugar really does help the medicine go down. In fact, with his invention, the sugar may actually be the medicine.

Among the most important and complex molecules in the human body, sugars control not just metabolism but also how cells communicate with one another. Graduating senior Jeffery Martin has put his basic knowledge of sugars to exceptional use by creating a lab-on-a-chip device that builds complex, highly specialized sugar molecules, mimicking one of the most important cellular structures in the human body — the Golgi Apparatus.

“Almost completely independently he has been able to come closer than researchers with decades more experience to creating an artificial Golgi,” said Robert Linhardt, the Ann and John H. Broadbent Jr. ’59 Senior Constellation Professor of Biocatalysis and Metabolic Engineering at Rensselaer and Martin’s adviser. “He saw a problem in the drug discovery process and almost instantly devised a way to solve it.”

Cells build sugars in a cellular organelle known as the Golgi Apparatus. Under a microscope, the Golgi looks similar to a stack of pancakes. The strange-looking organelle finishes the process of protein synthesis by decorating the proteins with highly specialized arrangements of sugars. The final sugar-coated molecule is then sent out into the cell to aid in cell communication and to help determine the cell’s function in the body.

Martin's artificial Golgi functions in a surprisingly similar way to the natural Golgi, but he gives the ancient organelle a very high-tech makeover. His chip looks similar to a miniature checker board where sugars, enzymes, and other basic cell materials are suspended in water and can be transported and mixed by applying electric currents to the destination squares on the checker board. Through this process sugars can be built in an automated fashion where they are exposed to a variety of enzymes found in the natural Golgi. The resulting sugars can then be tested on living cells either on the chip or in the lab to determine their effects. With the chip's ability to process many combinations of sugars and enzymes, it could help researchers quickly uncover new sugar-based drugs, according to Martin.

Scientists have known for years that certain sugars can serve as extremely beneficial therapeutics for humans. One well-known example is heparin, which is among the most widely used drugs in the world. Heparin is formed naturally in the Golgi organelle in cells of the human body as well as in other animals like pigs. Heparin acts as an anticoagulant preventing blood clots, which makes it a good therapeutic for heart, stroke, and dialysis patients.

The main source of heparin is currently the intestines of foreign livestock and, as recent news reports highlight, the risk of contamination from such sources is high. So researchers are working around the clock to develop a safer, man-made alternative to the drug that will prevent outside contamination. A synthetic alternative would build the sugar from scratch, helping eliminate the possibility of contamination he explained.

"I am very grateful to have the privilege of working with Dr. Linhardt who has discovered the recipe to make fully synthetic heparin," Martin said. "Because we know the recipe, I am going to use it as a model to test the device. If our artificial Golgi can build fully functional heparin, we

can then use the artificial organelle to produce many different sugar variants by altering the combination of enzymes used to synthesize them. Another great thing about these devices is that they are of microscale size, so that if needed we could fill an entire room with them to increase throughput for drug discovery."

There are millions of possible sugar combinations that can be formed and scientists currently only know the function of very few of them like heparin. "Since it is known that these types of sugars play a part in many important biological processes such as cell growth, cell differentiation, blood coagulation, and viral defense mechanisms, we feel that that this artificial Golgi will help our team to develop a next generation of sugar-based drugs, known as glycotheraputics," Martin said. "We are going to start making new combinations and we simply don't know what we are going to find. We could find a sugar whose signal blocks the spread of cancer cells or initiates the differentiation of stem cells. We just don't know."

Source: Rensselaer Polytechnic Institute