

# Just a spoonful of sugar

**Peter Seeberger** has founded nine start-ups to date. With these companies, the Director of the **Max Planck Institute of Colloids and Interfaces** in Potsdam wants to put the results of his basic research into practice. One goal is to introduce sugar-based vaccines against multi-resistant bacteria.

TEXT **CATARINA PIETSCHMANN**

**P**eter Seeberger bursts in through the door. His last meeting, dealing with his latest company, took a little longer than expected. But then he gets straight into the subject at hand without slowing down. He speaks extremely quickly since he has no time to lose. The ideas that keep bubbling out of the 53-year-old just have to be implemented.

The subject is sugar. This is not about the fine, white crystals of the ubiquitous sweetener that spring to mind. Nor is it diabetes. Actually, Peter Seeberger is interested in the biological functions of longer-chain sugar molecules, the oligosaccharides. These molecules surround every living cell like a fine fur, no matter whether human, animal, or plant.

Here they form parts of large molecules, namely glycoproteins and glycolipids, that project out from the cell surface like small antennae. Cells use these antennae to communicate with their surroundings. Messenger substances dock here, triggering cas-

ades of signals inside the cell. And, they serve as a critical checkpoint for friend-or-foe identification. Bacteria and viruses also have these antennae and use them to dock onto human cells. This is what makes these sugar chains, known as glycans, so interesting for medicine – as antigens in new vaccines or as diagnostic tools, therapeutic antibodies or drugs. Peter Seeberger, Director of the Biomolecular Systems Department at the Max Planck Institute of Colloids and Interfaces in Potsdam since 2009, is one of the pioneers of molecular glycobiology.

## A SYNTHESIZER FOR VACCINE CANDIDATES

It all started in Boulder, Colorado, where the native of Nuremberg earned his doctorate in biochemistry after studying chemistry in Erlangen, Germany. There he asked himself, why are there machines with which we can synthesize any type of DNA, but nothing comparable for glycans? First, he familiarized himself with the chemical aspects

of the question in the New York laboratory of sugar synthesis specialist Samuel Danishefsky. At the Massachusetts Institute of Technology (MIT) in Boston, he then modified an old DNA synthesizer to assemble oligosaccharides and founded his first company, Ancora Pharmaceuticals, in 2002. This company produces custom-made glycans. GlycoUniverse in Potsdam, which Seeberger founded in 2013, provides easy access to the world of glycans for scientists in academia and industry with the Glycoener 2.1, developed by his team as the first commercial synthesizer for oligosaccharides.

The synthesizer now makes it almost child's play to reproduce key sugar structures from pathogens and thereby generate candidates for vaccines that stimulate the human immune system to produce antibodies. To get closer to clinical application in the development of sugar-based vaccines than is possible at a Max Planck Institute, Seeberger founded Vaxxilon AG in 2015. This company specializes in targeting resistant hospital germs.



Chemist Peter Seeberger experienced starting companies as a completely normal act during his time at MIT. This is one reason why he is pursuing developments with several start-ups, especially in the field of glycobiology.

These include *Klebsiella pneumoniae* (triggering pneumonia and sepsis) and *Clostridium difficile* (intestinal inflammation), which are especially dangerous due to their resistance to many drugs.

#### **THE FAST TRACK TO MALARIA DRUG ARTEMISININ**

Seeberger's role models include U.S. physician and microbiologist Maurice Ralph Hillemann (1919-2005), who developed nearly 40 vaccines. These include vaccines against measles, chickenpox and hepatitis A and B. "In the end, he managed to make the world a little bit better," says Peter Seeberger. This statement also describes his own motivation: to make the world "a little bit better" through his research, especially in regions of the world that lack comprehensive medical care.

In his Department in Potsdam, Seeberger conducts basic research out of scientific curiosity. "But when we find something interesting, we continue to pursue it. And yes, I do always ask myself if there is an application." As a re-



Automated sugar synthesis: the synthesizer brings the reactants together at the right time and in the right quantity. Seeberger commercialized this method at the Ancora Pharmaceuticals and GlycoUniverse companies.

sult, nine companies have been founded as of January 2020.

With one company, ArtemiFlow GmbH, founded in 2013, the chemist has taken up the fight against malaria. This disease kills nearly 500,000 people every year – most of them children. In an effort to do something about it, a team headed by Peter Seeberger also tried and tested path of sugar-based vaccines. The researchers developed a flow synthesis device using UV light to take a critical step towards developing the malaria drug artemisinin, which enables the conversion of a substance from the sweet wormwood plant to the active ingredient within 15 minutes. ArtemiFlow uses this process to produce artemisinin on a large scale.

In the meantime, the subsidiary ArtemiFlow USA was founded. “We are now growing sweet wormwood in former tobacco fields in Kentucky,” explains the chemist. The scientists also want to investigate artemisinin as a potential active substance in fighting cancer. “There are now clinical studies that

show this substance to be effective against 114 different types of cancer as well as several autoimmune diseases.” FluxPharm, founded in 2016, is also developing commercial flow synthesis. The company also wants to use this method to produce important drugs cost-effectively – also directly in developing countries. Just recently, Peter Seeberger’s group even developed and patented a device for autonomous chemical synthesis. These are small systems that can be located anywhere and controlled from a laptop. This would make it possible to produce drugs on demand in developing countries in the future. But production in industrial nations would also be more cost-effective. “No pharmaceutical company would have to continue producing its drugs in low-wage countries like China or India. Instead, they could be produced fully automatically in Germany.”

Together with partners in Denmark, Seeberger founded Draupnir Bio ApS in 2017 for the preclinical development of new sugar-based agents to lower chole-

sterol. Stimulated by an inquiry from a Danish colleague, Seeberger’s team, with its comprehensive glycan library, launched the search for a sugar that binds effectively to PCSK9. This enzyme plays a very important role in lipid metabolism. “It is important to inhibit this in people with high cholesterol levels to prevent potential heart attacks. Unfortunately, statins, the classic cholesterol reducers, do not work in one out of five patients.” Seeberger identified a sugar that blocks PCSK9 by a different mechanism from that of statins and which can be taken orally.

A very recent addition is Tacalys GmbH, founded in Berlin in 2019. With this company, Seeberger wants to take on a heavyweight opponent: cancer. Even malignant tumors have glycan structures on their cell surfaces. Could it be possible to vaccinate against cancer by using sugar structures from tumor cells to provoke an immune response in humans?

As a postdoc, Seeberger learned about a candidate vaccine that was

then tested 20 years later in Asia. It protected 50 percent of the test subjects from cancer because their immune system generated antibodies against cancer cells. The other half of the study participants did not respond to these sugars. Tacalyx is now developing monoclonal antibodies against sugars on the surface of cancer cells to specifically target them.

### CLOTHING FROM CRUSTACEAN SHELLS AND RICE STRAW

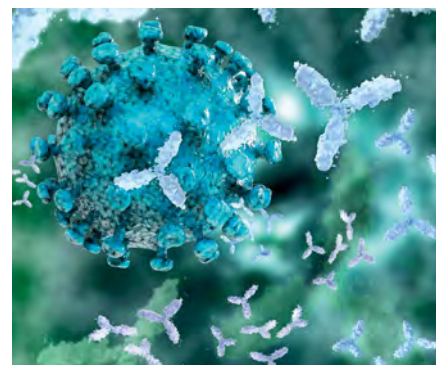
Peter Seeberger's repeated implementation of results from promising basic research in start-ups is due in part to the attitudes of established companies towards these developments: "We usually develop something completely new that is associated with a paradigm shift," the chemist explains. "Industry often has difficulty handling this." In addition, it comes naturally to him to combine research and entrepreneurship. This also has to do with his past experience. Early in his career, he was a professor at MIT in Cambridge, Massachusetts. "Starting up companies is an everyday event there."

Seeberger's wide-ranging experience with start-ups has also highlighted the biggest hurdles: "Finding the right people for management and, of course, obtaining solid financing." Now, he knows many people and knows who, and in which position, can move something forward. The work of Max Planck Innovation has also been very helpful. Seeberger greatly appreciates their support in matters such as selecting appropriate licensing models or in financing companies. More than that, however, he appreciates the freedom that the Max Planck Society generally provides him in his research.

The search for sugar-based vaccines could have just simply continued. But Seeberger's research took a new turn after the working group relocated from its temporary quarters on the campus of the Free University of Berlin to a building expansion at the Max Planck Institute in Potsdam in 2015. There, his focus shifted to carbohydrate-based materials. This area of interest essentially imposed itself upon him since the biomaterials experts are right next door in Potsdam. "I had hardly looked at structural aspects before, only the biological function," he says. "80 percent of biomass on Earth is made of sugars – and most of these sugars have structural functions! Typical examples are cellulose in wood or chitin in crustaceans."

So could cotton, which requires large land areas and large quantities of water to grow, be replaced by a fabric made from crustacean shells? "We are also considering how we could combine chitin with cellulose. Both are flexible and both form fibrils." This would yield unconventional, sustainable hybrid materials: T-shirts, clothing and bed linen that simply lands on the compost pile and turn into humus once they are worn out.

Today, crustacean shells from shrimp farming are simply thrown back into the sea. And in Vietnam alone, 170 mil-



Sweet defense: Peter Seeberger and his team are searching for sugar-based vaccines that stimulate the immune system to produce antibodies with specialized targets, such as the glycoproteins of pathogens.

lion tons of rice straw, which also consists largely of cellulose, are burned annually. What a resource! "Our vision is to develop a completely new recycling economy based on renewable raw materials, away from oil and towards producing everything based on sugars. And all of this from ordinary animal and vegetable wastes!" Peter Seeberger is just getting started in this field. There is therefore a good chance that one, two or three more start-ups will result based on these resources over the next few years. ◀

### GLOSSARY

**Flow synthesis** is a chemical process whereby the reaction medium is routed through an apparatus in which the conversion takes place. Since the reaction products can be separated out relatively easily at the end of the process, the chemical industry prefers this type of process over one in which the reaction takes place in a closed container.

**Glycan:** A polysaccharide comprising a chain of simple sugars, such as glucose or fructose. An example is cellulose. Polysaccharides also occur in signal molecules on the surfaces of cells in connection with proteins in the form of glycoproteins or in combination with fat molecules as glycolipids.