By the time Peter Seeberger arrives at the campus of the Freie Universität Berlin-Dahlem shortly before ten o'clock, he has already accomplished a few things – perhaps the most pleasant ones on his agenda. He has taken his daughter to elementary school, played with his son for an hour, and then driven the three-year-old to the university daycare center. These are things the 49-year-old would like to do more often than just once a week. But his job leaves him little room for maneuver.

Currently, Peter Seeberger also has to commute between two sites: His Biomolecular Systems Department was recently finally able to move into the extension of the Max Planck Institute of Colloids and Interfaces in Potsdam-Golm. Some of his staff, however, are still located in Berlin, at a university-affiliated institute where the 75-member team has been working for the past six years. But Seeberger's Berlin office is already empty, apart from a standard desk-and-chair set, making our conversation echo around the room. Better to retreat to a bench outside to enjoy the pleasant sun of another hot July day.

Peter Seeberger, dressed casually in a polo shirt and jeans, has just launched his fifth company. Vaxxilon, founded by the Max Planck Society and the Swiss-based company Actelion Ltd. in Berlin-Adlershof, will develop and market sugar-based vaccines to prevent bacterial infections.

Sugars, especially those that form long, branched chains and cover cells like a fluffy fur coat, are Seeberger's domain. Attached to proteins and lipid molecules that anchor them to cell membranes, they are a means for cells to interact with their environment – with friend and foe alike. Bacteria and viruses also carry complex sugars on their surfaces and use them to attach to human cells.

Seeberger has developed a synthesizer to automatically produce these sugar chains, which are also known as glycans (see MaxPlanckResearch 3/2013, p. 54). His team is particularly interested in the glycans found on the surfaces of parasites and bacteria that cause tropical diseases like malaria, leishman-

Photo: David Ausserhofer

A Scientist with a **Sweet Tooth**

Basic scientist, entrepreneur, citizen and family man: what **Peter Seeberger**, Director at the **Max Planck Institute of Colloids and Interfaces** in Potsdam, manages to cram into one lifetime would take others three. One of his goals is to prevent diseases that afflict particularly people in developing countries – and his weapon of choice is sugar.

TEXT **CATARINA PIETSCHMANN**

iasis and a particular form of encephalitis. The aim is to develop novel vaccines based on these glycans.

SEEBERGER IS ABLE TO INSTILL ENTHUSIASM IN OTHERS

Sugars alone are not very effective as vaccines. They need an adjuvant, an immunostimulator to enhance its activity. A novel adjuvant has been developed that – unlike conventional carrier proteins – is not a heat-sensitive protein, but a stable glycolipid, a compound consisting of a fatty acid and sugar. Immunization with such a completely synthetic vaccine is less likely to trigger allergic reactions and is also much cheaper, because the substance can be transported to the most remote villages in Africa and Asia unrefrigerated. With conventional vaccines, the refrigeration chain accounts for half the immunization costs.

Vaxxilon, however, will focus primarily on hospital-acquired infections. "We can find investors for these much more easily than for poverty-associated diseases," says Seeberger, who speaks from experience. More on that later.

When the Max Planck Director speaks, his soft Franconian accent is unmistakable. His years spent in the US, Switzerland and even multicultural Berlin have done nothing to temper it. And Peter Seeberger also speaks extremely fast, as though he doesn't want to waste time talking so as to leave enough to implement all the ideas flowing out of his brain.

But these two things are only a brief distraction, because Seeberger has a gift that few possess and that can't be learned: He can quickly put listeners under his spell and instill enthusiasm for his ideas. His candid manner certainly helps him win people over. He speaks plainly and invites his conversation partners to do the same. He is also aware that he sometimes comes across as arrogant – but the longer you listen to him, the more you realize: it's not about himself but about his research.

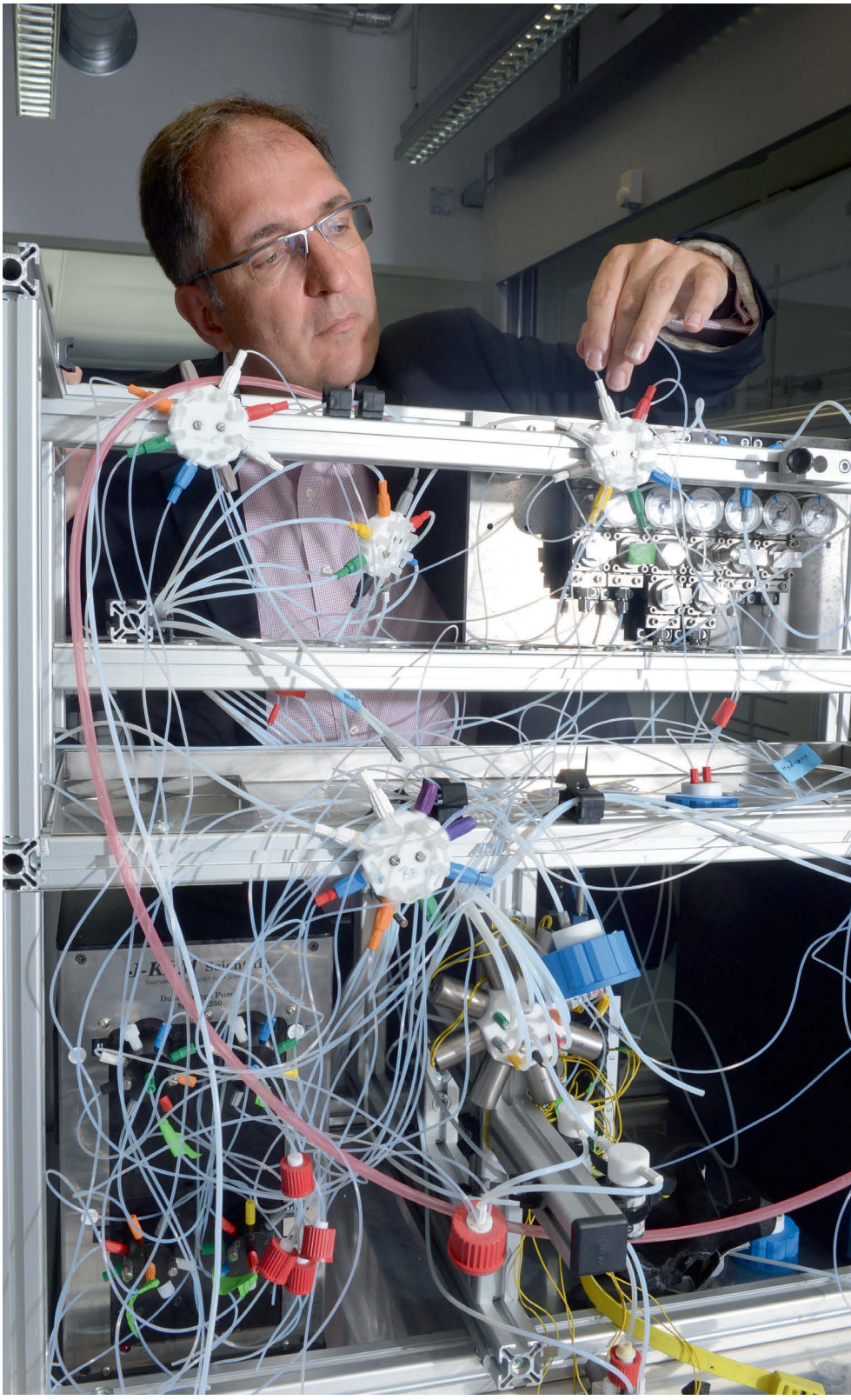
Seeberger was born in Nuremberg and grew up in a caring home. His father was trained as an auto mechanic;

his mother worked in an office. And although he was the first in his family to attend a university, he never shed his no-nonsense roots. As a boy, Peter wanted to become a garbage man, and later, a librarian. Starting in fifth grade, his goal was to become a mathematics professor. Seeberger laughs. "Well, that almost happened." He found learning easy, and his chemistry teacher at his high school in Fürth had no trouble sparking his interest in atoms and molecules. But sports, especially team handball, was often more important than his lessons. The game helped shape his character. "Handball is a team sport, and that is also fundamentally true of a research group."

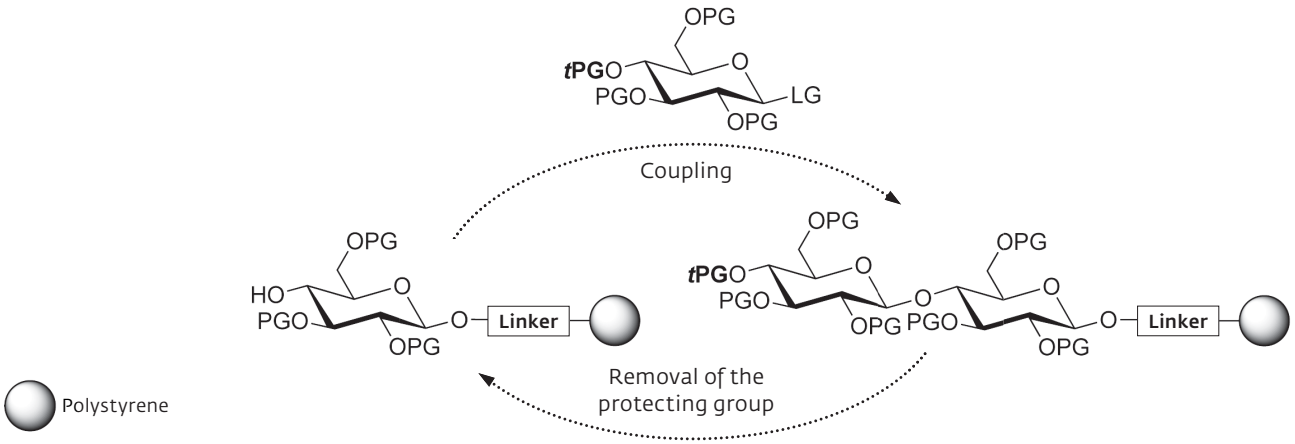
He didn't really apply himself until the final two years of high school, when there was a promise of a scholarship for gifted students. With his high school grades, he could have studied dentistry, but after completing his military service, Peter Seeberger enrolled to study chemistry and economics at Erlangen University. "In an ideal world, I would have become an archeologist, but the job prospects were pretty miserable."

PRODUCING CARBOHYDRATES AUTOMATICALLY?

After six semesters – by which time he had nearly completed all of his degree requirements – he won a Fulbright scholarship on the strength of his grades and, with his BSc diploma in his pocket, traveled to Boulder, Colorado for a year as an exchange student. It soon became apparent that the university was an incubator for outstanding biochemists. But he had studied only chemistry. "I didn't have a clue!" he says. For the first time in his life, he wasn't among the best in his class, but at the bottom, instead. And no wonder – all the classes were in English, which he had pretty much neglected in school, thinking: I'll never need it. After all, I live in Bavaria.



Custom-made sugar: Peter Seeberger developed a synthesizer that facilitates the manufacture of a wide variety of specified carbohydrates.



Building a sugar chain step by step: A sugar molecule is linked to a polystyrene carrier by means of a chemical linker. Protecting groups (PGs) mask most of the hydroxyl groups, thus shielding them from chemical reactions. During the coupling, this molecule combines with another sugar molecule precisely at the site of a leaving group (LG). The attached molecule carries a temporary protecting group (tPG) where another chain link can be attached. As soon as the tPG is removed, the cycle is repeated.

In short: the first year in Boulder was really tough. Seeberger had to hit the books hard. In the breaks between studying, he went to the mountains to ski and hike. When he completed his second semester at the top of his class, he was invited to stay on and study for a doctorate in biochemistry. So he continued in the laboratory of Marvin Caruthers, who had invented the DNA synthesizer in 1980. Although he has a sweet tooth, Seeberger was of course motivated to turn his attention to sugars for entirely different reasons. While he experimented with peptides and nucleic acids for five years, he kept asking himself: if DNA and peptides can be manufactured automatically, why not carbohydrates?

Sugar synthesis was the specialization of Samuel Danishefsky in New York. He accepted Seeberger as a postdoc at the Sloan Kettering Cancer Center, where Seeberger synthesized complex carbohydrates. He worked 16-, sometimes 18-hour days. "But we always had a bit of fun afterwards," he recalls. The team used to go out together, and many a friendship was forged in this period. After all, everyone was in the same situation. And he made time to go to the opera at the Met.

Seeberger actually wanted to teach in Germany, but Danishefsky had other plans for him: Why not take up a post as assistant professor at MIT? When the invitation from the Massachusetts Institute of Technology came, Seeberger moved to Boston. He was only 30 when he became a professor. He built up his research group from its initial 4 members to 35, and published articles in Science about automatic sugar synthesis. He was offered tenure after just three and a half years.

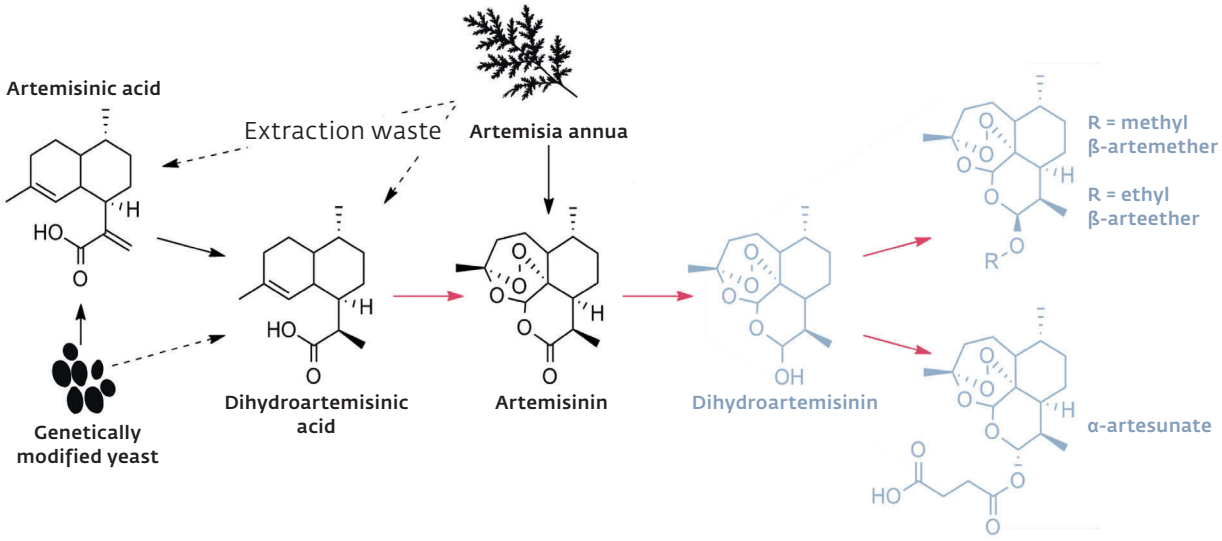
SWITZERLAND – A CULTURE SHOCK AFTER 13 YEARS IN THE US

His work days didn't become any shorter, and his private life was as good as non-existent. Relationships culminated in the reproach: "There's no point. You're never there anyway!" Seeberger, who wanted to have a family at some point, realized with dismay that few of his colleagues at MIT managed to reconcile work with family life. Things seemed easier in Germany, so he was thrilled to receive an offer for an eminent professorship in organic chemistry in Munich. But this soon proved a disappointment. The two sides were unable to agree on terms, and Seeberger turned down the post.

A short time later, the renowned German organic chemist Dieter Seebach from ETH Zurich held a lecture at MIT. After the two discussed chemistry for three hours one Saturday morning, Seebach asked Seeberger to send him his CV. The invitation from ETH came a few months later. "I knew that if I also turned down Zurich after rejecting Munich, I would probably never have been able to return to Europe. The only hope would then be Max Planck." But that seemed to be in an entirely different league. Nevertheless, the interview at ETH went much better than the one in Munich, and Seeberger, now 36, moved to Switzerland in 2003. After 13 years in the US, it was a real culture shock, he says.

He had set up his first start-up in Boston the year before, Ancora Pharmaceuticals, as well as a second laboratory in southern California. Zurich, Boston, San Diego and back – the frequent flyer card was rarely out of use. The work at ETH went exceedingly well. And life in Zurich? A dream! "The only way I'll leave here is feet first," Seeberger thought at the time. But as the old

Photo: David Ausserhofer; graphic: Peter Seeberger/MPI of Colloids and Interfaces



A new approach to a malaria drug: Until recently, artemisinin was obtained only from sweet wormwood (*Artemisia annua*). In the process, however, the artemisinic acid and dihydroartemisinic acid were discarded as waste products. Peter Seeberger's group developed an efficient method to synthesize artemisinin and the currently used active agents (blue) from these substances, which can also be produced in genetically modified yeast.

saying goes: if you want to make God laugh, tell him about your plans …

In 2004, the Society of German Chemists invited Seeberger to Leipzig. For the first time he had to present a lecture in German. "Sure I could still speak German! But I had only ever thought about sugars in English. I didn't know which terms to translate and which not. To be safe, he translated every word, and the audience was very amused. "That was incredibly embarrassing!"

HAVING THE SAME PROFESSION HAS ITS UPS AND DOWNS

But the remarkable thing about this event was something altogether different. Before Seeberger set foot in the auditorium, a few meetings had been arranged with colleagues, including Beate Koksch. They chatted animatedly. She had just received two job offers and asked his opinion: the US or Berlin? "Without thinking, I said: Berlin! It's much better!" Talk about arrogant, thought Koksch.

When Seeberger received the Otto Klung Weberbank Prize a few months later, they met again in Berlin – where Beate Koksch had since moved. "It took a while for us to get together." But the chemistry between them was simply too good – even professionally! So Seeberger added the German capital to his flight plan. When their daughter was born in late 2006, it became clear that their professional situation would have to be adjusted.

A year later the Max Planck Society asked Seeberger to become Director at the Max Planck Institute for Medical Research in Heidelberg. However, for several reasons, Berlin was the better option for him. "The Max Planck Society was extremely accommodating and appointed me to a post at the institute in Potsdam." And because the Max Planck Institute there was already too small and needed a new building, Peter Seeberger pursued research from 2009 on the Freie Universität campus in Dahlem, just a few hundred yards from his wife's research group.

Is it good or bad for a couple to have the same profession? "Both," says Seeberger. "We understand exactly what the other is doing and can always talk shop." That's also a disadvantage. "You have to be careful not to neglect your personal life." When they argue, it's about all the traveling that goes with the job. "Coordinating it is incredibly difficult." Otherwise, everything is well organized. Once the children are in bed, each goes to their respective office and answers e-mails, writes articles or deals with other matters until midnight or even later. Saturdays and Sundays are reserved for the family.

COMPOSITE MATERIALS FROM CELLULOSE AND CHITIN?

Seeberger didn't plan his career; it just happened – thanks to jobs that were usually brought to his attention. "Moving away from a location was always a difficult decision," he says in retrospect. "You never know what lies ahead. But each time I was able to expand my field of research." Whereas Boston was still about sugar chemistry pure and simple, biology and animal experiments for vaccines were added in Zurich. In Berlin he perfected automated synthesis, which another startup, Gly-

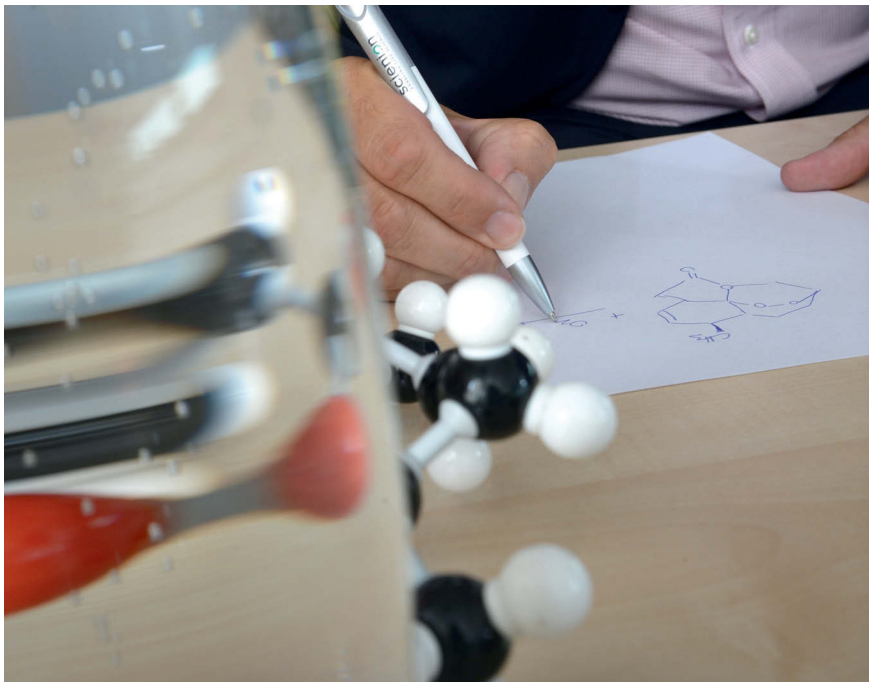
Graphic: Peter Seeberger/MPI of Colloids and Interfaces

coUniverse, has been marketing globally since 2013, complete with sugar building blocks. He also developed flow synthesis methods for some drugs there to simplify their manufacture and make them less expensive.

His colleagues in Potsdam, whose research into biomaterials and interfaces is, at first glance, a far cry from Seeberger's sugars, have given his work fresh impetus. Thanks to the possibility of building chains of up to 50 sugar links, the jump was made from oligosaccharides to polysaccharides – giant molecules that are used in nature as versatile structural materials in the form of cellulose and chitin.

"I had never previously considered structural aspects," Seeberger says enthusiastically. The option of being able to reconstruct these natural materials from scratch raises new questions: Why are carbohydrate molecules branched? What forces are at work? "How do single sugar polymers behave when we throw them on a surface? Do they tangle up? Do they fold? We simply don't know." Chitin and cellulose might be combined to form new composite materials, Seeberger continues. Another research field to be explored. "I see great potential there in the next 20 years." Projects are already under way with his Potsdam-based colleagues Peter Fratzl, Markus Antonietti and Reinhard Lipowsky.

To cover the broad range of Seeberger's research, a group is needed that isn't organized hierarchically but in small complementary teams that can nevertheless work on an interdisciplin-



New office: Many members of Peter Seeberger's group only recently moved into the new building at the Max Planck Institute of Colloids and Interfaces. At his desk, the scientist sketches new reactions on paper – an essential part of chemical research.

Photos: David Ausserhofer

ary basis. “Basically, I hire people who can do something that I can’t.” Besides chemists and biochemists, they include medical doctors, parasitologists, engineers and, most recently, a crystallographer for structural analyses. The team includes 18 nationalities, and that is as it should be, Seeberger emphasizes. “I’m completely intolerant of intolerance. And anyone who doesn’t accept that has to go.”

Does he ever think about what he will do when he retires? Rarely. One thing is certain, however. He doesn’t want to be one of those who can’t stop, who after retirement flies off to conferences or haunts institutes, giving their successors advice. “At some point you have to stop, no matter how hard it may be.”

In any case, he can already look back on an impressive career. His development of synthesis machines, for instance, has made the field of biologically relevant sugars accessible to science. After genomes and proteomes, now also glycomes have become a subject of vigorous basic research. Seeberger’s influence is also evident from what has become of his people: 47 of his more than 200 alumni are professors today, and most of them continue to push the boundaries of sugar chemistry with their ideas. Next year, for his 50th birthday, they will gather from all corners of the world at a symposium in Harnack House.

IT’S ABOUT IMPROVING THE WORLD

Of course Seeberger will continue to follow their work after retiring. But from a distance, because he believes that there should be a life after one’s career. Assuming he is still in good health, he could well imagine being more active in developing countries. For the past 11 years he has been involved in the Swiss Tesfa-Ilg Foundation, which he was instrumental in setting up. The foundation built a plant in Ethiopia in which 300 women now produce insecticide-impregnated mosquito nets.

Where does the urge come from to devote himself – professionally and privately – more to the problems of developing countries than those of industrialized countries? “I’ve always traveled a lot, even as a child with my parents, and I saw very early on that not everyone has it as good as we do.”

He doesn’t see himself as a do-gooder, but his aim is “at the end of the day to make the world a slightly better place.” And he can’t stand it when bureaucratic obstacles and financial interests of corporations make it difficult to produce drugs and vac-

Photo: David Ausserhofer

That's not the whole story by any means: Around 75 people work in Peters Seeberger's group at the Max Planck Institute of Colloids and Interfaces and the Freie Universität Berlin. Less than half of them are gathered here in the new premises in Potsdam.

cines for poverty-associated diseases such as malaria and HIV more quickly and less expensively. Patience isn't his strong suit, he says.

"On the one hand you see people dying of diseases that should no longer exist, because they can't get the drugs, or they get only counterfeit drugs," he says, his anger clearly audible. "For one thing, the drugs could be manufactured cheaply. But in the process of creating value, a lot of people earn a lot of money, and in the end the drugs are so expensive that patients in developing countries are unable to afford them!"

A SUGAR-BASED VACCINE BEFORE RETIREMENT

To remedy this situation, Seeberger has offered pharmaceutical companies his patent for the flow synthesis of artemisinin free of charge – with the proviso that they supply the malaria drug cheaply. The response? None whatsoever.

But thanks to a healthy portion of stubbornness and pragmatism, Seeberger isn't easily discouraged. "I draw energy from resistance," he says grinning. There must be another way! In 2013 he set up ArtemiFlow GmbH, which developed the method to market maturity. And now an alumnus is implementing the artemisinin project with a company in Vietnam. "Malaria is under control in the country itself, but drugs for other developing countries can be inexpensively manufactured there."

Won't artemisinin soon be superfluous, since GlaxoSmithKline plans to apply for approval of the malaria vaccine RTS,S, which the company developed with a 400 million dollar financial injection from the Bill & Melinda Gates Foundation? "In my opinion, that's only a small step in the right direction, because the efficacy of RTS,S in young children is below 10 percent."

From 2001 to 2008 Seeberger teamed up with a company to develop a sugar-based malaria vaccine. In animal experiments it had an initial 75 percent response rate and nearly 100 percent after further development work. But the project was put on ice before the first study with humans. The expected profit was too low, it was said. He was in discussions with the Bill & Melinda Gates Foundation at the time. "But I had to learn that the best technology doesn't always get the money. Contacts and political and commercial aspects are also very important." Because of a secrecy clause, Seeberger was not allowed to talk about the vaccine or even continue to research it for a long time. At least his team is now working on the substance again.

Given his personal ambitions, it's no surprise that he holds the German inventors of the 19th century in high regard. "Because they put their ideas into practice and developed things that improved people's lives. That's what I want to do." Seeberger's research always seems application related, but that was never planned, he emphasizes. It just happened. "I'm interested in basic research. But it's very satisfying if it leads to more than a paper or two." After all, most money for research comes from taxpayers, and they should see that the results are useful.

What does he plan to do in the second half of his career up to the age of 67? "My aim is for us to establish sugars everywhere: in medicine, nutrition and material sciences. There's still a lot to do." Before he retires, he would like to have at least one sugar-based vaccine approved. And it would be nice if his name were one day associated with the term sugar synthesis as firmly as the name Emil Fischer a century before. Seeberger laughs. "Okay, I'm not entirely free of vanity," he says. But you have to set the bar high. "Science is like sports: you should never be satisfied, because more is always possible! And I'm never satisfied." ◀

GLOSSARY

Glycans are carbohydrates that consist of a sometimes branched chain of various simple sugars, such as glucose and fructose. Glycans perform various functions in biology. They not only supply energy but also have a supportive function in plants in the form of cellulose or hemicellulose and enable cells to communicate with their surroundings.

Glycome: The term was inspired by the words genome and proteome. It denotes the entirety of all simple and compound sugars in an organism.