If you want to carry out research in Marburg, you literally have to climb mountains. It is not for nothing that the site on which the university and various research facilities are located is called "Campus Lahnberge." And so, if you want to cycle to the Max Planck Institute for Terrestrial Microbiology, you might get a little out of breath. But not Katharina Höfer – for her, it's routine.

TEXT: CATARINA PIETSCHMANN

Every morning, Katharina Höfer zips down the steep alleys of Marburg's Oberstadt on her gravel bike and then rides six kilometers through the forest, up and down hills, to the Max Planck Institute for Terrestrial Microbiology. "I have to climb 200 meters on my route. That keeps me in shape, much more than the distance itself," says the microbiologist. She also gets her best ideas while riding. As soon as she arrives at the Institute, she parks her bike in front of her desk and jumps in the shower. Clothes and up to six pairs of shoes – from comfortable to chic – are then on hand to start the day.

Höfer has been conducting research with her working group at the Max Planck Institute in Marburg since 2020. She is also associated with the Center for Synthetic Microbiology, a unique joint venture between Philipps University Marburg and the Max Planck Institute for Terrestrial Microbiology, and was recently appointed as Loewe Top Professor at Philipps University.

Höfer comes from a town of 200 near Nordhausen in northern Thuringia. She was born three years before German reunification. At the age of 18, she graduated from high school and packed her bags to study molecular biology, microbiology, and organic chemistry in Hanover. She first took up residence in a dormitory – in a small room measuring 11 square meters, with more than 20 roommates per corridor. Privacy and quiet time for studying were the exception. Six months later, she moved into a shared apartment with a fellow student. The degree program was time-consuming and demanding. Her student loan, child benefit, and some money from a part-time job gave her just enough to live on.

After graduating, she was initially unsure whether she should stay in academic research or go into industry. And so, she completed an internship at the biomedical company Miltenyi Biotec in Bergisch Gladbach. She isolated and cloned proteins there and had bacteria produce them. The proteins were then attached to magnetic particles so that certain cell types that bind to the proteins could be fished out of a solution — just like using a fishing rod. Today, the Miltenyi system is used in many immunology laboratories. "I really enjoyed putting all the theoretical knowledge from my studies into practice." After a further internship at the German Primate Center in Göttingen, she took on a master's degree in molecular biotechnology in Andres Jäschke's laboratory at the University of Hei-

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VISIT TO

KATHARINA HÖFER

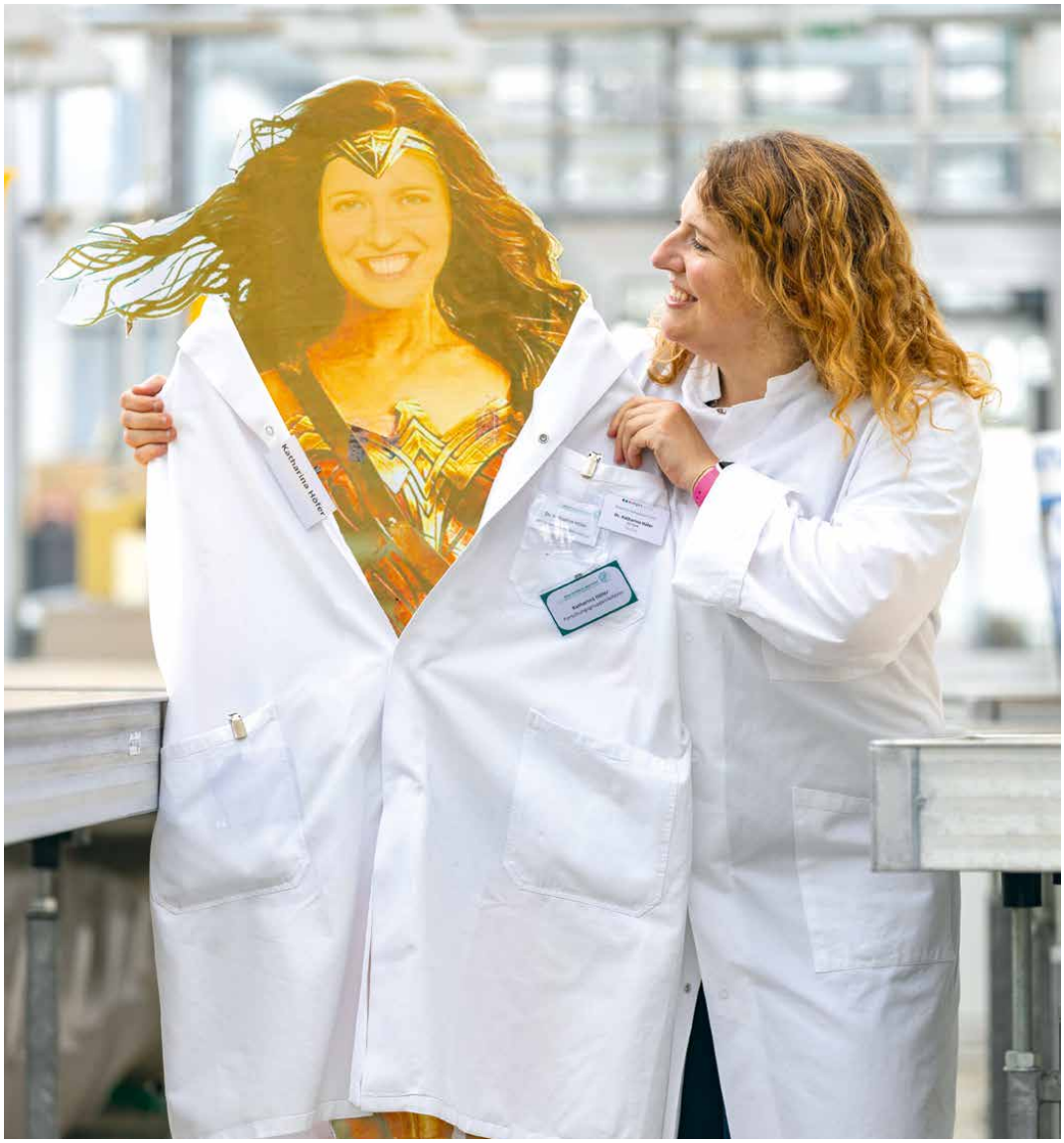


PHOTO: CHRISTOPH SEELBACH FOR MPG

Katharina Höfer with a gift from her team: her cardboard superwoman doppelganger.

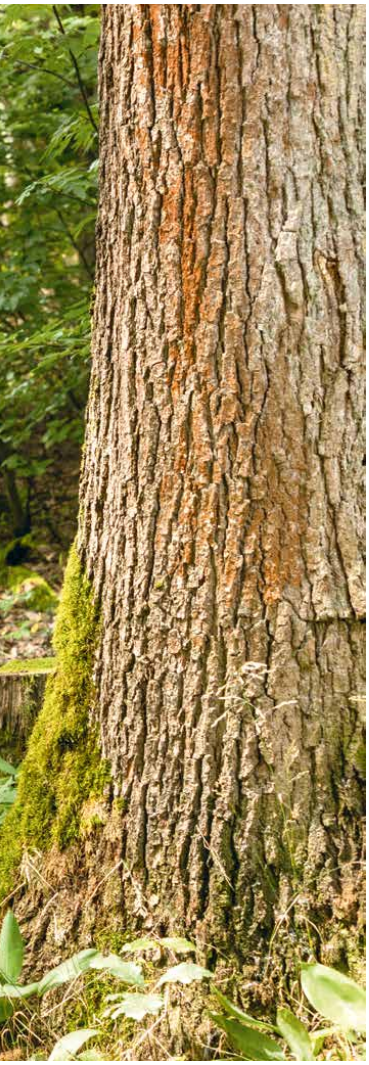
delberg. She was so fascinated by the research there that she followed up her master's degree with a doctorate, booking the "lifetime ticket," as she refers to it. The idea for the first project of her doctoral thesis, visualizing RNA formation in real time, came to her in the shower – back when she didn't have to cycle up any hills to her Institute. For her project, she used spinach RNA – an artificial RNA molecule that can make small molecules glow. The intensity of the fluorescence can be measured and used to calculate the amount of RNA formed. This method already works in living cells. Höfer was able to demonstrate that the technique also works in the test tube, outside of cells. Her research on RNA brought her into contact with BioNTech employees. BioNTech – then a small and unknown start-up, later to become one of the first developers of a coronavirus vaccine – was interested in her method and still uses it today. "This still makes me proud."

From then on, Höfer never let go of RNA. She wanted to develop a method with which she could isolate RNA molecules from cells that have the building block NAD (nicotinamide adenine dinucleotide). Together with her colleagues in Jäschke's team, she searched for such NAD-RNA molecules. In 2015, the researchers published a study in the renowned journal Nature, demonstrating that NAD in bacteria can act like a protective cap, shielding molecules from degradation. She also succeeded in finding the

PHOTO: CHRISTOPH SEELBACH FOR MPG

enzymes that cleave NAD. After completing her dissertation, she received postdoctoral scholarships from the Carl Zeiss Foundation and the Baden-Württemberg Foundation. She investigated whether the NAD molecule can link RNA with proteins. She and her research group later succeeded in proving and discovering the mechanisms for this at the Max Planck Institute in Marburg. This process is known today as RNAylation. It is an enzymatic reaction occurring in bacteria that are infected with viruses, known as bacteriophages. In the process, RNA molecules are firmly linked with proteins, creating entirely new biomolecules. Höfer and her group in Marburg are now researching what functions these have. What's particularly striking here is that the protein factories of bacterial cells, the ribosomes, are being connected with RNA. It is possible that bacteriophages can regulate the production of their own proteins during an infection.

But back to Höfer's scientific career: after her postdoc, she wanted to climb to the next level in academia and set up her own research group. She weighed several offers before choosing the Max Planck Free-Floater Research Group Program: this presented the opportunity for her and her team to move to a Max Planck Institute of her choice after the start-up phase. She opted for Marburg and has since concentrated on researching bacteriophages. Having received little attention for many years, these viruses have once again become the focus of research in recent years because they are effective killers. Some can kill a bacterial cell within 30 minutes – an ability that makes them increasingly interesting for medicine in times of rampant antibiotic resistance. At the Max Planck Institute, Höfer wants to find out how gene transcription and protein production change after a phage infection. "Phages have fascinating properties," she says. "These could help us in the fight against bacterial infections. But there is still a long way to go before they can be used for medical purposes."



Katharina Höfer prefers to get around by bike – whether on vacation or on her way to work. On her gravel bike, she can also tackle bumpy forest paths in the Marburg area.

"Cycling tours give me a real sense of freedom."

She has been researching RNA since 2009. "A really long relationship," she says with a smile. Her first doctoral researchers have already been awarded their doctorates. The biggest challenge will be to find out what the almost 200 known RNA modifications actually do in a cell. This will probably keep a whole generation of scientists busy. "We won't know for at least ten years whether they can trigger diseases, for example. If so, we'll found a start-up for sure!" Then she would no longer be torn between academic and applied research: she would simply do both!

As a group leader, she is constantly on the go attending lectures and conferences and is busy providing 15 employees with new ideas and supporting them with her experience. She also has to keep an eye on the specialist literature so as not to miss any devel-

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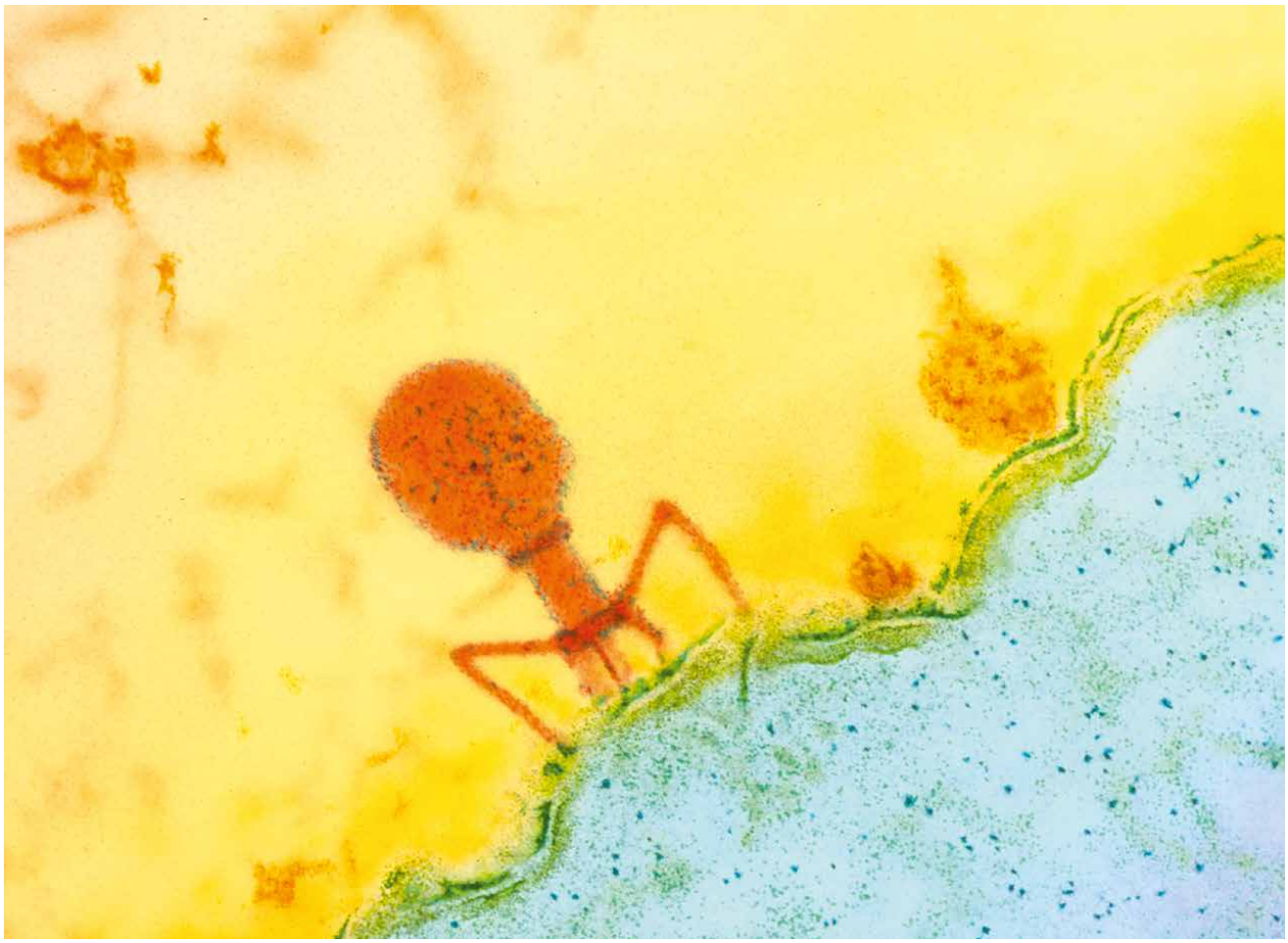

IMAGE: SCIENCE PHOTO LIBRARY / BIOZENTRUM / UNIVERSITY OF BASEL

Electron micrograph of a T4 bacteriophage (orange). Bacteriophages are viruses that infect bacteria. T4 exclusively infects Escherichia coli (blue). Its angular head part consists of proteins and contains a DNA molecule; other proteins form the tail part. The virus attaches itself to the bacterial cell with stilt-shaped proteins and injects its DNA. This no longer produces only its own proteins, but also viral proteins. After 30 minutes, countless new viruses are released, and the bacterium dies.

opments in this rapidly evolving field of research. To make her happy, one shouldn't give her a book, but rather invite her on a hike or bike ride, or to a barbecue. "When I hear the word barbecue, my Thuringian heart immediately beats faster. Of course, I get the sausages sent to me from home."

She has also always been an "outdoor child." Walking through the forest with her grandpa and sister, sorting potatoes by size – that was more her thing than poring over books. "I was at home in mud! I already needed a change of clothes before breakfast had even begun." In summer, she got up at 6:00 AM and let the chickens out of the coop. Being close to nature is still important to her today. She has crossed the Alps on foot several times. This summer, she completed the 300 kilometers and 3000 vertical meters of the Salzkammergut cycle route. "I really enjoy tours like this, they give me a real sense of freedom. And the steep alleyways of Marburg's old town are the best training for this!"

"In ten years' time, we will know whether changes in RNA can trigger diseases."