

# Customized solutions for tumors

*Dr. Hans-Georg Lerchen and his colleagues in Wuppertal, Berlin and Cologne are developing new drugs to treat cancer, the second most common cause of mortality in humans. These antibody-drug conjugates could make chemotherapy more tolerable for patients. Setbacks in his research work sometimes occur, but the dedicated sportsman Lerchen accepts them with the stoicism and calmness which some say is typical of people from the Rhineland area of Germany.*



Teamwork: Dr. Hans-Georg Lerchen (right) and his colleague Dirk Wolter are working on new antibody-drug conjugates.

Nausea, hair loss, exhaustion – chemotherapy in its current form is a grueling and stressful experience for patients. The toxins that are intended to kill the tumor cells also attack many healthy cells. “It always hits me hard when I witness or read about these people’s suffering,” says Dr. Hans-Georg Lerchen, Principal Scientist in Bayer’s Pharmaceuticals Division. According to the World Health Organization WHO, one in six deaths in 2015 were attributable to cancer, making it the second most common cause of mortality worldwide after heart disease.

“There is still plenty to do,” says Lerchen, who is conducting research into a new form of chemotherapy in his capacity as a chemist.

But the breakthrough will not come overnight. The search for new therapies demands patience, hard work and composure. The idea behind antibody-drug conjugates (ADCs for short) is based on the Trojan Horse principle. Targeted antibodies track down tumor cells, which take them up into their interior. These antibodies carry a highly toxic active substance with them. In the lysosomes –

compartments of the cells with a low pH value – enzymes split the conjugate into its component parts. Once the drug has been cleaved from the antibody, its toxic action is activated. Accordingly, ADCs only destroy the tumor cells and leave healthy tissue largely unharmed. What sounds so simple in theory is however difficult to put into practice.

To illustrate why, Lerchen sketches the structure of a conjugate: antibody – linker – drug. Each of the three components of the conjugate presents chemical and biological challenges. As lung tumor

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The work/life balance is important for the father of four: Lerchen enjoys sports in his free time (photo right) – for example, in the mountains in winter.



cells have a different surface structure than those of breast cancer cells, the researchers have to adjust their antibodies accordingly, while taking care to ensure that the payload of the linker and the active ingredient do not impair the antibody's ability to dock onto the target. So it is a complex matter. But that's not all. The linker-drug chemistry that Lerchen and his team are developing must meet two critical demands. The linker, as the el-

ement that connects the antibody and the active ingredient, must remain stable in the blood circulation, as otherwise the cell toxin could be released too soon. At the same time, however, it must be able to be cleaved later inside the lysosomes within the tumor cells so that the cell toxin can exert its action there.

It is a very fine line and the solution can be completely different in two different ADCs depending on the type of tumor

and the target in question – every new conjugate is so to speak custom-made.

Lerchen explains such complex issues vividly and patiently, which may also be a testament to his old chemistry teacher, of whom the 57-year-old has fond memories. "He was the one who inspired me to go into chemistry. And my parents always supported this path, which began when we set up a chemistry laboratory in our basement," says Lerchen. What fascinated him then and continues to fascinate him to this day? "Encountering new things. Discovering something that nobody has ever done before and that will help mankind." The conventional academic career of a university professor was something that the native of Germany's Rhineland area was reluctant to pursue. He took a deliberate decision to work in industry, "because here we work on projects that are more likely to benefit the patients in the end." The intermeshing of different disciplines and close collaboration with experts from different areas of expertise is what he likes best about his job. "I'm a keen chemist, but what I find even more fascinating is understanding the biological processes and intervening in them with chemical molecules." Lerchen has been conducting research at Bayer since 1988.

It will take some time until the most recent projects by Lerchen and his colleagues are ready to be marketed. Their ADC projects are all at different stages of development. Research in this complex field is fraught with setbacks. "A relaxed attitude, a degree of enjoyment and team spirit can make all the difference in this job," says Lerchen. His unshakable optimism – another essential asset! – is founded on the support he receives from his family and from his belief. The father of four and family man also finds relaxation in sport – he used to play handball, and now cycles and skis, and also plays in a soccer team for fun. His favorite soccer team is FC Cologne. "So I'm used to setbacks," he laughs, although his team delivered plenty of reason for optimism last season. And when things aren't going so well in the soccer stadium or the laboratory, he can always hold on to the Rhinelander's motto: "Et hätt noch emmer joot jejang," which translates roughly as "It has always worked out in the end." ■