Can tumors simply be switched off? Biochemist Dr. Anette Sommer wants to find new drug candidates for aggressive forms of cancer. Although drug research is laborious and setbacks are common, she never loses her optimism.

Photos: Dominik Butzmann/Bayer AG (5), private (1)

PORTRAIT: DR. ANETTE SOMMER DEVELOPS ANTIBODY-DRUG CONJUGATES

Searching for new cancer drugs

Roughly one in three people will be affected by cancer during their lifetime; half of them will die as a result. The range of available, effective cancer drugs is still very limited. Biochemist Dr. Anette Sommer is therefore searching for compounds that could be used in new drug products. One promising approach is antibody-drug conjugates.

A tumor that cannot be treated with drug therapy? That is a topic that makes Dr. Anette Sommer listen attentively. Sommer is Principal Scientist in Oncology Research at Bayer's Pharmaceuticals Division in Berlin. She has set herself the task of "developing cancer drugs that are efficacious and well tolerated at the same time. Every tumor is different, and accordingly each one has to be treated differently," she explains. This is something that spurs her on, and has done so for the more than 20 years that she has been working in cancer research. "There's nothing else I'd rather do," says the 48-year-old biochemist, explaining what motivates her. "Most cancer drugs available on the market today are efficacious and prolong the survival of patients with cancer – but they rarely improve their quality of life." Patients can suffer from fatigue, severe digestion problems, neuralgia and hair loss. The Bayer researcher therefore wants to develop active substances that cause as few side effects as possible while nonetheless efficaciously combating the tumor.

Sporty scientist: Dr. Anette Sommer balances out the stress of her daily lab work with exercise. She cycles to work every day.

An optimum substance attacks only the tumor

Sommer is particularly interested in tumors where there is a high unmet medical need – aggressive forms of cancer for which at present there are no effective treatment options available, such as some forms of breast cancer, stomach cancer or pancreatic cancer. She is developing therapeutic substances that are designed to only attack the tumor and leave healthy tissue unscathed. To do this, she and her team utilize a trick. "We attach the highly effective active substances to an antibody which can specifically recognize certain proteins on the tumor cells, dock only there and transport the active ingredient to the cancer cells," she explains. Sommer grabs a pen and starts drawing: antibody, tumor cells, docking sites. "Scientists call these hybrid molecules antibody-drug conjugates, or ADCs for short," she explains. "You could say they're a kind of Trojan horse." The basic structure is an antibody, which is designed to bind to specific proteins on the tumor cell. These

Joint objective: teamwork is a vital element in Dr. Anette Sommer's lab. She and her co-workers and colleagues Rukiye Tamm (photo above right), and Linda Caparusagi and Dr. Jörg Willuda (photo below left) are looking for new ways to efficaciously target tumors – involving both work at the computer in the office (photo above left) and in the laboratory.

tumor markers are either exclusive to cancer cells or are present in much greater numbers on tumor cells than on healthy body cells. "And this is what makes the ADC concept so clever," enthuses Sommer. The ADC carries an active ingredient that is fatal for the tumor cells; the two elements are connected to one another by a linker. As soon as the conjugate has docked and been absorbed, it discharges its freight inside the cancer cell. The drug product starts working and the cancer cell dies. "In theory at least – since unfortunately, in reality it's not quite that simple," says Sommer.

What is it that makes working with the hybrid molecules so difficult? "ADCs combine molecules from two worlds," explains Sommer. "The active ingredient is the chemical part. The antibody – a protein – is the biological component." Numerous laboratory tests are therefore essential to verify the action of ADCs.

A persevering scientist, in the best possible way

"Drug research is an experimental science," says Sommer. That is what makes it so exciting, but at times also extremely labor-intensive. Her motivation? "I want to develop substance candidates that have the chance to be tested in clinical use and later achieve regulatory approval."

Anybody meeting the Bayer researcher may soon believe that she will manage it one day, too. Sommer is stubborn, in the best sense of the word. "Once you've decided in favor of something in research, you have to stick to it," she says. This stamina is something she also needs for her hobby – running. She trains for 5 and 10 kilometer runs and regularly competes both individually and as part of a team. She has taken part in the 5x5 kilometer

relay race in the Berlin Tiergarten almost every year since 2005. This year her team called itself - what else could it be? – "The Flying Antibodies". "Our mascot was an antibody with wings, of course," reports Sommer. She spends a large proportion of her free time training. "It's a lot of fun, and a good way of getting some exercise to balance out my work." She has exhibited similar perseverance throughout her research career, despite several setbacks. Sommer's professional progress has followed the early stages of pharmaceutical research in drug development incredibly closely.

Sommer chose oncology while still at university

Drug research starts with identification of the target – the search for a site in the body which a new active ingredient can aim at. "If we know that there is no suitable drug for a specific form of cancer available, we take a closer look at the tumor in question," says Sommer. "For example, we look for receptors that are frequently overexpressed on the tumor cells and which a drug could target." Sommer started working in this area straight after her doctoral thesis at Hannover Medical School, focusing primarily on hormone-resistant breast and prostate cancer.

The second step on the road to a new drug candidate is target validation. This is an area that Sommer has been intensively involved in since 2004, when she transferred to the Enabling Technologies department. The researchers investigate tumor sections, for example, to determine whether the predefined target really does offer an opportunity for therapy. If the target is confirmed, work can begin on manufacturing a compound that binds precisely to this target. This lead structure, the lead antibody, is then examined more closely by the scientists. They optimize and perfect all of the substance's properties, such as its binding characteristics. "ADC development is a collaborative effort between experts from many different disciplines, like antibody specialists, medicinal chemists, pharmacokinetics experts, toxicologists and pharmacologists," explains Sommer. "Countless experiments ultimately lead us to the final drug candidates." The results of all the tests go to her. Sommer has been the "Coordinator for the ADC Portfolio in Early Research" since January 2015. In addition to her project work, she is also responsible for international collaborations with academic partners, such as at present with Cancer Research UK and various institutions in Singapore.

Looking back, Sommer is very happy that she started "with the basics of drug research." It taught her an understanding of the relevance of target identification and validation for the drug discovery research programs that build on them – and also made her aware of the stress levels that exist in the research-driven departments. Her own stress levels are something she counters with exercise. Every morning, she cycles from Prenzlauer Berg to the Wedding district of Berlin and back home again in the evening. "I need my sport to be able to switch off." When cycling and running are not enough, she likes to go to the fitness center on Bayer's premises or do yoga. "That's a good way of balancing out all the hassle that we sometimes have in the lab." She likes being part of a team, and also working across borders. "Lots of people from different countries work here – all with the same objective: to help cancer patients."

Sommer's father was her professional role model

Sommer has inherited her empathy and concern for her patients from her father, who worked as an internist and gerontologist specializing in pacemakers, and is a real role model for her. "Back then, I thought that the way he takes care of his patients was really very special." That's why she studied biochemistry instead of medicine like he did. Her enthusiasm for genetics and biochemical molecules was something she discovered back in school. She wanted to use her talents to help patients, like her father before her – but not as a clinician at a hospital bed, but rather as a researcher in drug development. Her team only tests the most efficacious and best tolerated of hundreds of potentially active drug candidates. "Our focus here is mainly on analyzing active compounds' interactions in the organism," explains Sommer. "Only the best compounds that meet a long list of criteria are selected as clinical development candidates to be tested in tumor patients." This is the earliest stage at which the researchers know whether a substance has potential as anti-tumor agent or not. "No matter what we do – the patient must never be harmed," says Sommer.

A fondness for science: while working on her doctoral thesis at Hannover Medical School in 1997, Sommer spent a lot of time at the microscope. Already then, oncology was her main research topic.

One of Sommer's drug candidates has already made it through to the first phase of clinical testing. "But then we had to stop development because the compound did not work as we had expected." These turning points are a constant feature of research life. "It was a disappointment, but without doubt the right decision," says Sommer. "After all, our aim is to develop drugs that are safe and efficacious." She is well aware that more than 90 percent of all new approaches in clinical testing are rejected at some point, for example because the compound isn't an ideal fit or causes unacceptable side effects. "But if other novel drugs can save lives, then all the work will have been worthwhile." ■