Gesamter Artikel (PDF, DE): www.tum.de/faszination-forschung-30

Krebs behandeln ohne Kollateralschaden

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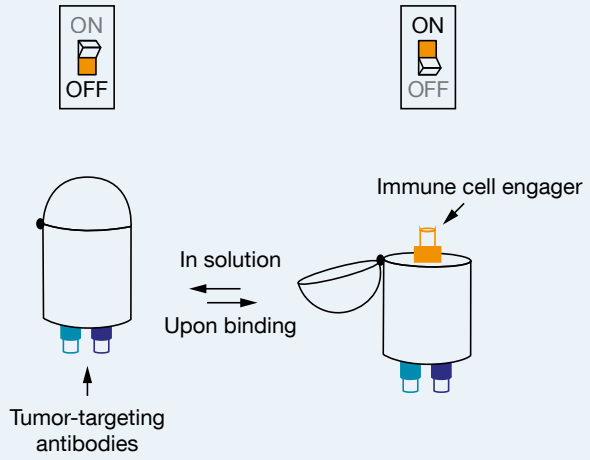
Krebszellen gezielt angreifen und gesunde Zellen intakt lassen: Das Start-up-Unternehmen Plectonic hat einen Nanoschalter aus DNA entwickelt, der gezielte Antikörper-Immuntherapien ermöglicht.

Cancer Treatment **without Collateral Damage**



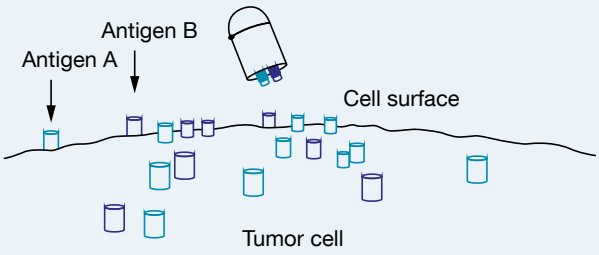
Made from DNA, the LOGIBODY nanoswitch will only turn on when an antibody binds to a target cell with two different antigens.

For many, conventional cancer treatments are lifesaving. But when healthy cells are caught in the crossfire, these same treatments can substantially decrease patients' quality of life. Enter Plectonic, a start-up with a game-changing approach: DNA nanoswitches that enable the body's own immune system to target cancer cells without harming healthy cells.

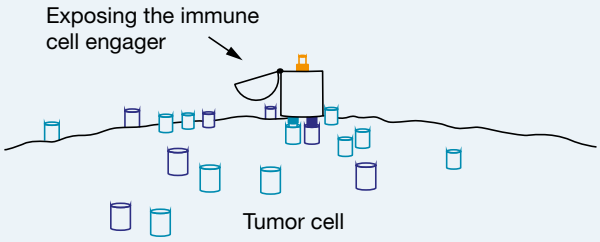
Link
www.plectonic.com

The start-up Plectonic began with a lofty goal – and a long way to go to reach it. "Revolutionizing cancer immunotherapy from a biophysics lab is like starting a Formula 1 team with nothing but a driver's license," says Dr. Klaus Wagenbauer, one of the company's co-founders. He met Dr. Jonas Funke and Dr. Benjamin Kick in Prof. Hendrik Dietz's lab at TUM where each was working on a different PhD project centered around DNA origami. An approach that exploits the ability of DNA to self-assemble, fold, and encode information, DNA origami makes it possible to build ultra-miniature molecular devices that can carry out tasks. As their doctoral work ended, the three searched for a real-world application for DNA origami. "The idea that this technology can be used therapeutically came up very quickly because DNA origami is really made for it. But which type of therapeutic application it is used for is very important. You can employ it as a drug-targeting agent, but utilizing it for targeted cancer immunotherapy, as we're doing, really gives our approach an edge over existing therapies," says Funke.

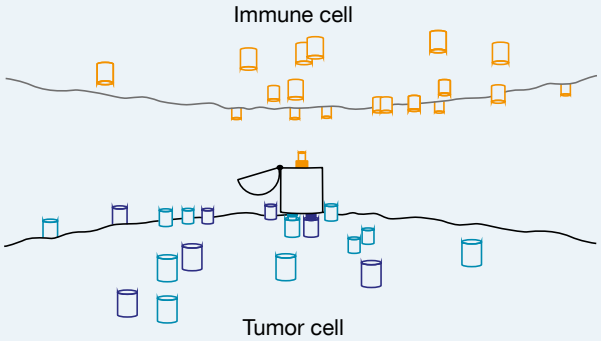
A major problem with some existing immunotherapeutic approaches is that they rely on identifying tumor cells by only one antigen. When healthy cells also have that same antigen, as is often the case, the treatment results in the destruction of both tumor cells and healthy cells. This is



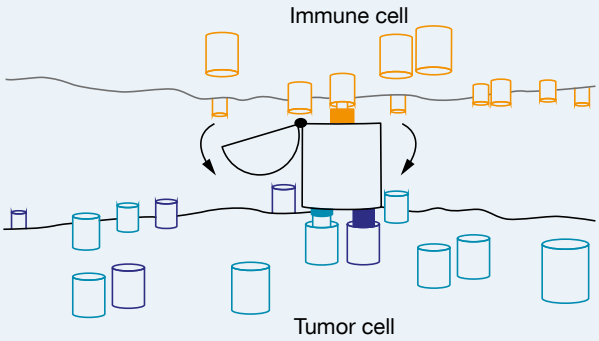
1. Binding to a tumor-specific antigen pattern



2. The switch turns on and changes its shape



3. Immune cell engaging



4. Tumor cell killing

what is so innovative about the LOGIBODY technology developed by co-founders Wagenbauer, Funke and Kick with support from their mentor and co-founder Dietz. Made from DNA, a LOGIBODY nanoswitch will only turn on when an antibody binds to a target cell with two different antigens. “We call it a switch because like switching on a light, you want to switch on – or activate – a drug at the tumor site,” says Kick.

Making two antigens the target rather than just one makes all the difference – this way, the two antigens serve as a tumor cell’s unique fingerprint. If a tumor-targeting antibody binds to a cell with only one of the two necessary antigens, the switch remains off. If, however, the antibody binds to a cell with both kinds of antigen, the switch turns on and changes its shape. This change exposes the antibody’s immune cell engager, which directs killer T cells – the body’s immune cells – to bind to the cell in question so that they can destroy it. Thanks to a LOGIBODY switch, tumor cells previously flying under the immune system’s radar become detectable so they can be killed, while healthy cells remain out of the crossfire.

Armed with funding from the German Federal Ministry of Education and Research’s (BMBF) GO-Bio initiative, the Else Kröner-Fresenius Foundation, and their winnings from the Bavarian Ministry of Economic Affairs, Regional Development and Energy’s m4 Award, the team has already passed a number of important milestones. They have ensured that their origami structures bind to antibodies on tumor cells and built T cell engagers that recruit T cells to tumor cells, both of which were done in cell culture. They then checked that these successes translate to studies on living mice, and were happy to discover that they do. “We are very grateful to Hendrik Dietz, who, besides being a great co-founder, gave us the opportunity to use his lab. This lab is part of the Munich Institute for Biomedical Engineering (MIBE), one of TUM’s Integrative Research Institutes, so we are also grateful to Bernhard Gleich, the MIBE General Manager, who has been very supportive,” says Funke. Now, the team has big plans for the future of the company, currently fifteen employees strong, which they will carry out thanks to funding from the Federal Agency for Disruptive Innovation SPRIND. The founders have what they call a very promising lead candidate for treating one type of blood cancer, a manufacturing process for their LOGIBODY technology, and intend to submit an Investigational New Drug Application to the United States Food and Drug Administration. From there, they hope to use their technology to treat solid tumors. “Sounds easy!” says Kick, with a smile. ■

Sarah Puschmann

Graphics: ediundsepp (source: TUM)