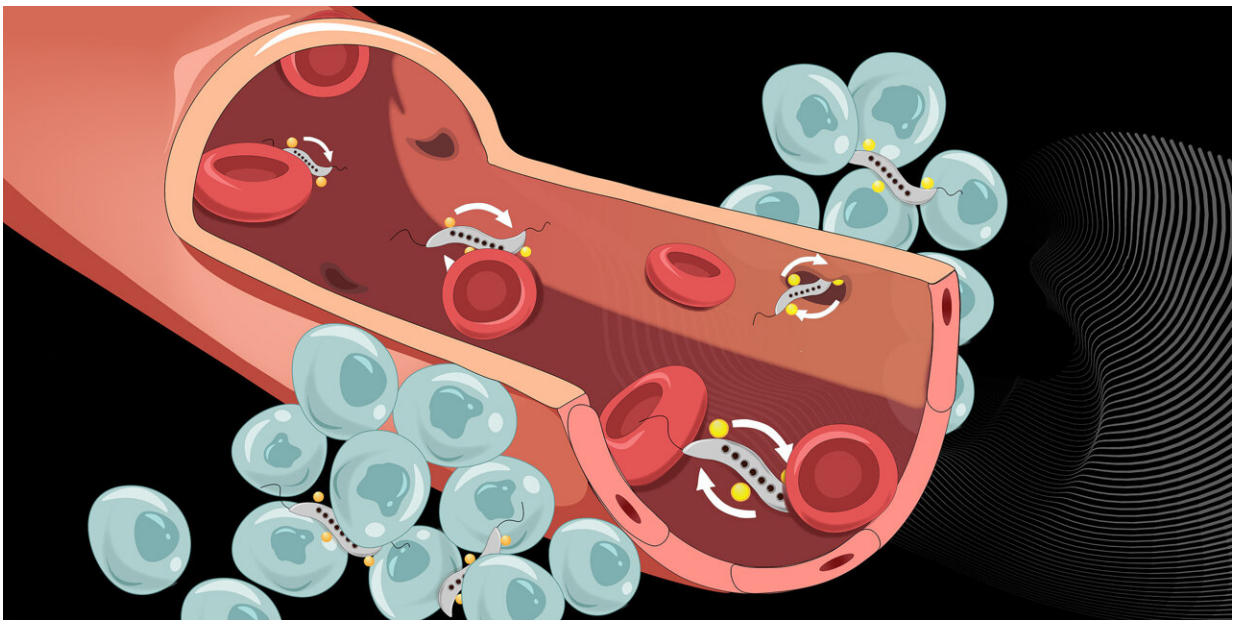


Researchers investigate fighting tumors with magnetic bacteria

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Magnetic bacteria (gray) can squeeze through narrow intercellular spaces to cross the blood vessel wall and infiltrate tumors. Credit: Yimo Yan / ETH Zurich

Scientists around the world are researching how anti-cancer drugs can most efficiently reach the tumors they target. One possibility is to use modified bacteria as "ferries" to carry the drugs through the bloodstream to the tumors. Researchers at ETH Zurich have now succeeded in controlling certain bacteria so that they can effectively cross the blood vessel wall and infiltrate tumor tissue.

Led by Simone Schürle, Professor of Responsive Biomedical Systems, the ETH Zurich researchers chose to work with bacteria that are naturally magnetic due to iron oxide particles they contain. These bacteria of the genus *Magnetospirillum* respond to magnetic fields and can be controlled by magnets from outside the body.

Exploiting temporary gaps

In [cell cultures](#) and in mice, Schürle and her team have now shown that a rotating magnetic field applied at the tumor improves the bacteria's ability to cross the [vascular wall](#) near the cancerous growth. At the vascular wall, the rotating magnetic field propels the bacteria forward in a circular motion.

To better understand how the mechanism to cross the vessel wall works, a detailed look is necessary: The blood vessel wall consists of a layer of cells and serves as a barrier between the bloodstream and the tumor tissue, which is permeated by many small blood vessels. Narrow spaces between these cells allow certain molecules from the to pass through the vessel wall. How large these intercellular spaces are is regulated by the cells of the vessel wall, and they can become temporarily wide enough to allow even bacteria to pass through the vessel wall.

Strong propulsion and high probability

With the help of experiments and computer simulations, the ETH Zurich researchers were able to show that propelling the bacteria using a rotating magnetic field is effective for three reasons. First, propulsion via a rotating magnetic field is ten times more powerful than propulsion via a static magnetic field. The latter merely sets the direction and the bacteria have to move under their own power.

The second and most critical reason is that bacteria driven by the rotating magnetic field are constantly in motion, traveling along the vascular wall. This makes them more likely to encounter the gaps that briefly open between vessel wall cells compared to other propulsion types, in which the bacteria's motion is less explorative. And third, unlike other methods, the bacteria do not need to be tracked via imaging. Once the magnetic field is positioned over the tumor, it does not need to be readjusted.

'Cargo' accumulates in tumor tissue

"We make use of the bacteria's natural and autonomous locomotion as well," Schürle explains. "Once the bacteria have passed through the blood [vessel](#) wall and are in the tumor, they can independently migrate deep into its interior." For this reason, the scientists use the propulsion via the external magnetic field for just one hour—long enough for the bacteria to efficiently pass through the vascular wall and reach the tumor.

Such bacteria could carry anti-cancer drugs in the future. In their cell culture studies, the ETH Zurich researchers simulated this application by attaching liposomes (nanospheres of fat-like substances) to the bacteria. They tagged these liposomes with a fluorescent dye, which allowed them to demonstrate in the Petri dish that the bacteria had indeed delivered their "cargo" inside the cancerous tissue, where it accumulated. In a future medical application, the liposomes would be filled with a drug.

Bacterial cancer therapy

Using bacteria as ferries for drugs is one of two ways that bacteria can help in the fight against cancer. The other approach is over a hundred years old and currently experiencing a revival: using the natural

propensity of certain species of bacteria to damage tumor cells. This may involve several mechanisms. In any case, it is known that the bacteria stimulate certain cells of the immune system, which then eliminate the tumor.

Multiple research projects are currently investigating the efficacy of using *E. coli* bacteria against tumors. Today, it is possible to modify bacteria using [synthetic biology](#) to optimize their therapeutic effect, reduce side effects and make them safer.

Making non-magnetic bacteria magnetic

Yet to use the inherent properties of bacteria in cancer therapy, the question of how these bacteria can reach the [tumor](#) efficiently still remains. While it is possible to inject the bacteria directly into tumors near the surface of the body, this is not possible for tumors deep inside the body. That is where Professor Schürle's microrobotic control comes in. "We believe we can use our engineering approach to increase the efficacy of bacterial cancer therapy," she says.

E. coli used in the cancer studies is not magnetic and thus cannot be propelled and controlled by a magnetic field. In general, magnetic responsiveness is a very rare phenomenon among bacteria.

Magnetospirillum is one of the few genera of bacteria that have this property.

Schürle therefore wants to make *E. coli* bacteria magnetic as well. This could one day make it possible to use a magnetic field to control clinically used therapeutic [bacteria](#) that have no natural magnetism.

More information: T. Gwisai et al, Magnetic torque–driven living microrobots for increased tumor infiltration, *Science Robotics* (2022). [DOI: 10.1126/scirobotics.abo0665](https://doi.org/10.1126/scirobotics.abo0665).

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Provided by ETH Zurich

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