UNIVERSITÉ DE GENÈVE

PRESS RELEASE

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Stimulating the immune system with sponges made of silica

Silica nanoparticles developed by a team from the UNIGE and Ludwig-Maximilian University of Munich have significantly increased the effectiveness and precision of immunotherapies.

Immunotherapies are increasingly used to fight cancer and aim to stimulate the immune system to defend itself by destroying tumour cells. While these treatments are often effective, their significant impact on the body can generate severe side effects. In order to increase their precision and limit undesirable side effects, a team from the University of Geneva (UNIGE) and the Ludwig-Maximilian University of Munich (LMU) has developed silica nanoparticles with a very precise opening mechanism that can transport a drug exactly to where it should act. These microscopic vehicles could possibly be used not just for cancer treatment, but also to deliver other drugs at the very heart of our immune system, thus paving the way for entirely new therapeutic or preventive strategies. These results can be read in the journal *ACS Nano*.

In medicine, nanoparticles are used to encapsulate a drug in order to protect it: indeed, their nanosize allows them to be taken up by dendritic cells, the body's first line of defence. "The function of dendritic cells is to phagocytose foreign elements to bring them to the lymph nodes and thus trigger the immune response", explains Carole Bourquin, professor at the UNIGE Faculties of Medicine and Science, who led this research. "We are taking advantage of this mechanism to have these cells transport a drug encapsulated into nanoparticles, which thus reaches the lymph nodes directly, where the immune response is initiated."

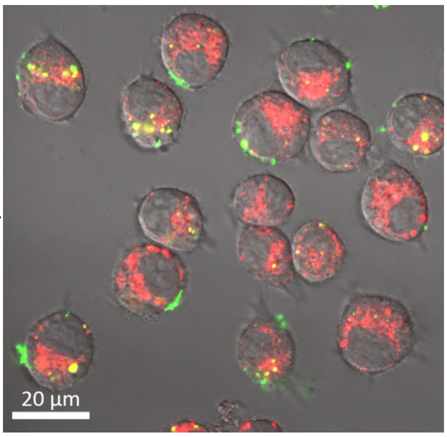
Silica, a material with multiple properties

Although nanoparticles are already used in certain treatments — the most recent example being the messenger RNA vaccines against Covid-19 — the system can still be improved. "Medical nanoparticles are generally composed of polymers or lipids", says Julia Wagner, a PhD student in Professor Bourquin's laboratory and the first author of this work. "In some cases, however, the solubility of the substance to be transported is incompatible with the characteristics of the nanoparticles. This makes it impossible to load the particles with the drug."

The scientists therefore turned to silica, a mineral that can be found naturally in the environment. "Silica nanoparticles are like little sponges with cavities that can easily be filled and whose properties can be modified to better match those of the drug", explains Julia Wagner. "The anti-tumour drug we used, for example, had already been tested with other particles, but it often leaked out too quickly."

A lid that only opens in the right place

To further improve the performance of their particles, the research team added a lid that covers the drug-laden cavities and prevents the drug from escaping during transport. "The lid reacts according to the



Confocal microscope image of immune cells (in red). In green, silica nanoparticles. The nanoparticles, once taken up by the immune cells, appear in yellow.

High resolution pictures

pH of its environment: when the particles are circulating in the blood, which has a neutralpH of around 7.40, it remains firmly in place. But once the particles are taken up by the dendritic cells, they arrive in vesicles inside the cell whose pH is acidic. Then the lid comes off and the drug is released", reports Carole Bourquin.

This technical prowess ensures the high precision of the treatment: the seal maintains the integrity of the drug, and therefore its duration of action, while preventing it from spreading in the body, thus reducing undesirable side effects. Indeed, some drugs stimulate the immune system extremely strongly, but disappear within a few hours, requiring repeated administration of high doses. "With our nanoparticles, the drug can take effect up to six times longer, which would make it possible to administer lower and better tolerated doses", say the authors. Their work provides a proof of concept of the mechanism governing these nanoparticles, which could be used against cancer as well as against other diseases, or as part of preventive or therapeutic vaccines. "Our work will now continue in order to confirm these initial results, and to reproduce their validity with a wider range of anti-tumour drugs."

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