Taking the fight into the enemy's territory

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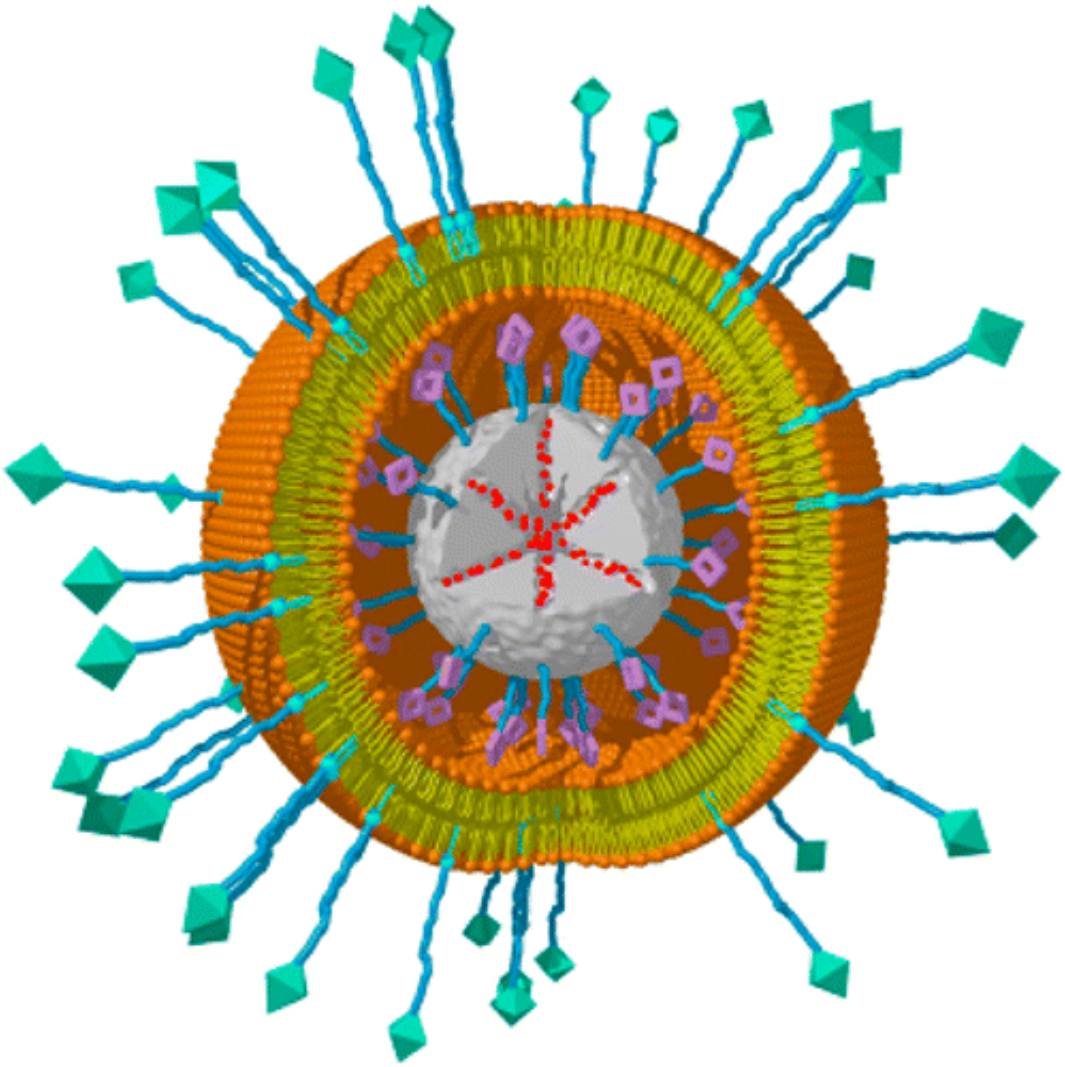

Credit: ACS

(Phys.org) —German researchers have developed a scheme for the

preparation of nanoparticles that offer a highly versatile system for targeted drug delivery directly into diverse types of tumor cells.

Nanoparticles have dimensions of a few millionths of a millimeter, and are thus small enough to conquer cells. This property opens new opportunities in the fight against cancer, which are currently the subject of intensive research. An LMU team led by Professor Christoph Bräuchle and Professor Thomas Bein has now developed a highly adaptable platform for the production of nanoparticles that can be used as "nanoferries" for the targeted delivery of a range of drug cargoes to various types of cancer cells. The system is described in a paper that has just appeared in the journal *Nano Letters*.

Above all, the new approach makes it possible to fabricate custom-designed nanoparticles for particular tasks. "The particles can be easily loaded with a variety of chemical agents and equipped with labels recognized by specific cell types. Thus, they bind specifically to certain cancer cells and release their cargo only after uptake by the cell," says Christoph Bräuchle who, like his collaborator Thomas Bein, is a member of the Nanosystems Initiative Munich (NIM), a Cluster of Excellence. The system thus provides a means of transporting anti-cancer drugs directly and specifically into tumor cells.

The use of such nanoparticles as delivery vehicles ensures that their cargo exerts its effect only inside the targeted cells. The compounds used in cancer chemotherapy are often highly toxic to many cell types, so targeting is crucial if one wants to minimize collateral damage to healthy bystander cells. Efficient targeting thus significantly lowers the risk of serious side-effects, while allowing the dose required for a meaningful clinical response to be reduced.

Intelligent freight systems

Intelligent nanoparticles capable of targeted drug delivery must fulfill a number of criteria. They must have a high capacity for cargo, and they need an envelope that is compatible with biological membranes and can present ligands that bind to specific receptors on target cells. Once the particles have entered the cell, they must be stimulated by some sort of signal to release their chemical cargo. "It is extremely difficult to design a particle that meets all these criteria at once. But we have now developed a system which, in principle, achieves this goal, and provides a generally applicable platform that is compatible with different cargos and target cells," says Thomas Bein.

The system is based on nanoparticles of mesoporous silicon dioxide, which can be safely biodegraded and whose pores offer a large storage volume for cargo. A photosensitizer is attached to the particle surface, and the drug cargo is loaded into the pores. Each particle is then enclosed in a lipid bilayer similar to the plasma membrane of a typical cell. A ligand recognized by receptors found on specific types of cancer cell is then inserted into the bilayer. In the new work, the team tested ligands specific for either hepatoma or cervical cancer cells. The activation of the photosensitizer with red light leads to a break-up of the lipid envelope and therefore a release of cargo.

"That the photosensitizer responds to red rather than the blue light used in previous experiments, is an important advance. Red light is less toxic to cells and penetrates deeper into tissues," says Veronika Weiss, whose contribution to the study will form part of her doctoral thesis. Her colleague Alexandra Schmidt adds: "Another critical point is that the photosensitizer is bound directly to the drug carrier, so that its effects are localized to the immediate vicinity of the nanoparticle itself, and do not have a destructive impact on larger regions of the cell interior."

The new study represents a further step for a highly successful long-term partnership. In 2010, the same collaboration developed the basic method

for triggering the release of cargo from nanoparticles after their uptake by target cells.

More information: pubs.acs.org/doi/abs/10.1021/nl400681f

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