Nano-Dwarves Turn Tumor Assassins

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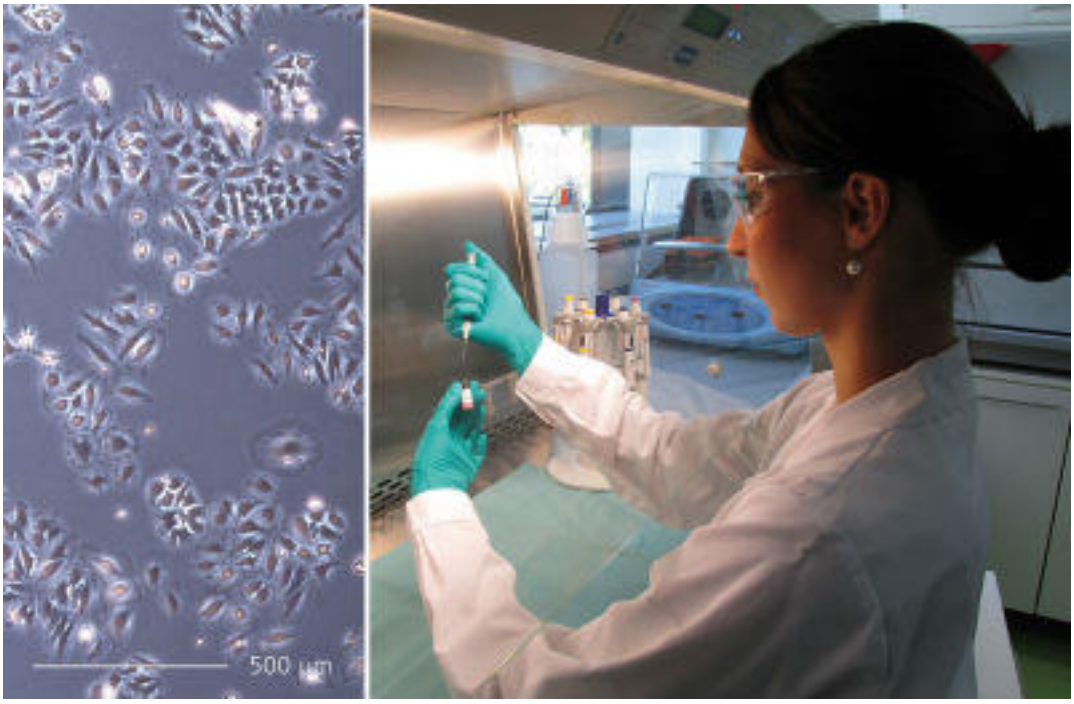
Chemotherapy is often preferred for fighting cancer, but its side effects can be considerable. A new technique may reduce these in future: nanoparticle-encapsulated substances could kill off tumor cells selectively. This will be easier on patients.



Hair loss, nausea, vomiting, fatigue, loss of appetite, loss of eye lashes and eye brows, susceptibility to infection – the list of possible side effects from chemotherapy is lengthy. Many cancer patients suffer from the intense effects that accompany the treatment. High dosages of cytostatic agents are injected subcutaneously or administered intravenously to halt the growth of tumors and also to destroy resistant cells. The more frequently that cells divide, the more effective the active agent is. This applies especially to malignant tumors. However, healthy mucosal tissue and hair cells divide very rapidly as well. They are therefore attacked as well. Scientists have searched long and hard for a therapy that selectively kills off the tumor cells without damaging healthy tissue. Using a new methodology, researchers from the Fraunhofer Institute for Applied Polymer Research (IAP) in Potsdam, Germany, hope to break the vicious circle by utilizing nanoparticles as vehicles for the anti-cancer agents. Since the particles resemble cells on account of their structure, they are suited to steering pharmaceutical substances to the tumor selectively, docking there, and efficiently eliminating the malignant cells.

The researchers have decided to use hydrophobic, water-insoluble lipid vesicles as the tiny, 200-250 nanometer pharmaceutical carriers. They are biologically degradable and disintegrate in the body after deployment. Polymers are used to

stabilize the nano-envelope, which is furnished with molecules highly specific to and recognized by tumor cells. The envelope of the nanoparticle – experts call it the vesicles – is constructed similarly that of a cell. The scientists load these carriers with doxorubicin, one of the anti-cancer agents frequently used in chemotherapy. Sodium tetradecyl sulfate (STS), a surfactant, helps the active agent to be absorbed better.

The researchers have already been able to prove the efficacy of their approach in laboratory tests. “We utilized both a cervical cancer strain (HeLa) and cancer of the large intestine (HCT116) for our in-vitro tests. They each react very differently to doxorubicin. HCT116 cells are sensitive to the substance, in contrast to HeLa cells. We ran the experiments with pharmacologically relevant dosages, used by clinicians. The doxorubicin was added to the cell cultures both directly and encapsulated in the nano-carriers,” explains Dr. Joachim Storsberg. He developed the new therapy jointly with Dr. Christian Schmidt and Nurdan Dogangüzel from IAP in close collaboration with colleagues from the pharmaceutical sciences, Prof. Mont Kumpugdee-Vollrath and Dr. J. P. Krause from Beuth University of Applied Sciences in Berlin.

Making Chemotherapy More Tolerable

The results from the laboratory tests: after three days, 43.3 percent of the HeLa cells survived a dose of unencapsulated, 1 micromolar (µM) doxorubicin. When the active agent was introduced via encapsulated vesicles, only 8.3 percent of the malignant HeLa cells survived. “The pharmaceutical substance in the nano-envelopes was fives times more effective,” says Storsberg. This could also be observed in the tests with the intestinal cancer cells: in this experiment, 46.5 percent of the HCT116 cells survived a dose of 0.1 µM doxorubicin after two days, while only 13.3 percent of the malignant tumor cells failed to be eliminated by administering the active agent in encapsulated form. “With nanoparticles as carriers, a more effective and simultaneously lower dosage is possible. This way, and with a targeted delivery of the active agent, the healthy cells are are likely to be spared and the side effects will be minimized,” says Storsberg. An additional test result: the encapsulation material is only effective when combined with the active agent. The unloaded nano-carrier does not attack the sensitive HCT116 cells. Using their methodology, Storsberg and his team can investigate how effectively an encapsulated pharmaceutical substance acts, as well as how ‘toxic’ the actual nanomaterial is. “That has not been feasible to date,” emphasized the chemist.

The researchers will be presenting their results at Nanotech Dubai, 28-30 October 2013. However, a series of clinical tests with cancer patients will only be set up if these observations are confirmed in in-vivo experiments.