Nanoporous Particles Deliver Novel Molecular Therapies to Tumors

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(PhysOrg.com) -- Using nanoporous silicon particles, two teams of investigators have created drug delivery vehicles capable of ferrying labile molecular therapies deep into the body. Both groups believe their new drug delivery vehicles create new opportunities for developing innovative anticancer therapies.

Mauro Ferrari, of the University of Texas Health Sciences Center at Houston, led a research team aiming to develop new methods of delivering therapeutic small interfering RNA (siRNA) molecules to tumors. He and his colleagues published their results of their studies in the journal Cancer Research. Karl Erik Hellstrom, of the University of Washington, and Jun Liu and Chenghong Lei, both of the Pacific Northwest National Laboratory (PNNL), led the research group developing methods for delivering therapeutic antibodies to tumors. Their research was published in the Journal of the American Chemical Society. Dr. Ferrari is the principal investigator of one of the National Cancer Institute's (NCI) Physical Sciences in Oncology Centers, and he played a seminal role in establishing the NCI's Alliance for Nanotechnology in Cancer.

siRNA is promising approach to anticancer therapy, and one anticancer siRNA molecule is now in clinical trials in humans (click here for a recent story). However, siRNA molecules are rapidly degraded in the body, so delivering them to tumors requires help.

Dr. Ferrari's team approached this problem by first encapsulating siRNA

molecules in lipid-based nanoparticles. Earlier work by his team had already demonstrated that these lipid nanoparticles could deliver siRNA molecules to tumors, but achieving a therapeutic effect in tumor-bearing mice required twice-weekly injections for many weeks. To reduce the number of injections needed, Dr. Ferrari and his colleagues decided to load their nanoparticle-siRNA construct into the pores of biocompatible nanoporous silicon particles.They then injected their drug delivery vehicle into mice with human ovarian tumors.

When the researchers examined the mice three weeks later, the researchers found that tumors had shrunken markedly and that the siRNA agent was still exerting its biological effect. The investigators also found that toxicities were minimal or non-existent.

Meanwhile, the University of Washington-PNNL team used nanoporous silicon to entrap large numbers of monoclonal antibodies that target a specific tumor-associated protein known as CTLA-4. Monoclonal antibodies targeting CTLA-4 have been shown to produce marked antitumor effects in human clinical trials, but therapeutic levels of this antibody can trigger unwanted autoimmune reactions and other severe side effects. Drs. Hellstrom, Liu, and Lei and their collaborators reasoned that nanoporous silicon particles could act as a reservoir that would maintain therapeutic levels of antibody right at the tumor site while reducing the overall amount of antibody circulating freely in the body.

To test their hypothesis, the investigators injected their construct directly into melanomas growing in mice. As a control, a second set of mice received CTLA-4 monoclonal antibodies injected into the peritoneal cavity. Results of this experiment showed that CTLA-4 monoclonal antibodies delivered using nanoporous silicon produced a month-long suppression of tumor growth with no toxicity, while CTLA-4 antibodies alone had little effect on tumor growth. The first group of animals also

lived far longer than the second group.

This work on siRNA is detailed in a paper titled, “Sustained Small Interfering RNA Delivery by Mesoporous Silicon Particles.” Investigators from the University of Texas M.D. Anderson Cancer Center, Rice University, Baylor College of Medicine, University of Texas at Austin, and the University of Puerto Rico Comprehensive Cancer Center also participated in this study. An abstract of this paper is available at the journal’s Web site.

This work with antibodies is detailed in a paper titled, “Local Release of Highly Loaded Antibodies from Functionalized Nanoporous Support for Cancer Immunotherapy.” An abstract of this paper is available at the journal’s Web site.

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