Expandable nanoparticles show promise in treating lethal abdominal cavity tumors

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(PhysOrg.com) -- Too often, patients with ovarian cancer or mesothelioma develop metastases that spread within the abdominal cavity, and when that occurs, the chances of surviving beyond five years drops to less than 40%, even after surgical removal of the metastatic tumors.

In attempt to develop a new therapeutic approach to treating peritoneal metastases, a research team at Boston University has developed a novel, drug-loaded polymeric nanoparticle that responds to the acidic pH inside tumor cells by expanding, releasing the anticancer agent paclitaxel slowly over a period of 24 hours. Tests with these new nanoparticles demonstrated that they not only decreased tumor growth, but prevented new tumors from implanting themselves in the abdominal cavity.

Mark Grinstaff led the research team that published its work in the journal *Biomaterials*. Investigators from Brigham and Women's Hospital also participated in this study.

The goal of the investigator's efforts was to create a nanoparticle that would release paclitaxel only when taken up by tumors, release drug slowly to maximize the number of dividing cells exposed to the drug, and that would remain in the vicinity of the tumors while it released drug. The investigators prepared their cross-linked polymeric nanoparticles using a technique known as mini-emulsion polymerization to create a material that remains intact but swells at the low pH characteristic of tumor cells. Tests with paclitaxel-loaded nanoparticles

showed that they release about 4% of their drug load each hour for 24 hours, creating a sustained load of drug in the vicinity of the nanoparticle. When added to mesothelioma cells growing in culture, the drug-loaded nanoparticles showed substantial cell-killing activity.

Based on these initial results, the investigators treated mice that had an aggressive form of mesothelioma with their nanoparticles, free paclitaxel, or paclitaxel loaded into a similar, but not expandable, nanoparticle. Only the expandable nanoparticles produced a substantial reduction in tumor mass and disease severity scores. Moreover, only the drug-loaded expandable nanoparticles prevented the development of peritoneal tumor implants. Finally, animals treated with the drug-loaded expandable nanoparticles survived nearly twice as long as did animals treated with free paclitaxel, the current therapy of choice for peritoneal tumors. Other experiments conducted by the investigators showed that when injected into the abdominal cavity, the drug-loaded expandable nanoparticles homed to tumor sites and remained there for at least seven days.

This work is detailed in a paper titled, "The performance of expansile nanoparticles in a murine model of peritoneal carcinomatosis." An abstract of this paper is available at the journal's website.

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