Self-assembling nanofilaments enhance drug delivery

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(Phys.org)—While most nanoparticles under development as drug delivery vehicles are spheres, a growing body of research suggests that cylindrical nanoparticles would perform even better at the twin goal of surviving in the blood stream long enough to reach their intended target and penetrating the cell wall to deliver their therapeutic payload inside of tumor cells where it is most needed. A team of investigators at the Northwestern University Center of Cancer Nanotechnology Excellence (Northwestern CCNE) has invented a cylindrical nanofilament structure that significantly reduces tumor growth in an animal model of breast cancer.

A team led by Vincent Cryns, who recently moved from Northwestern to the University of Wisconsin School of Medicine and Public Health, and Samuel Stupp, developed the self-assembling nanofibers. The investigators report their findings in the journal *ACS Nano*.

To create their tumor-inhibiting cylinders, the investigators turned to a family of molecules known as peptide amphiphiles. When put into water, these molecules, which can be made using automated peptide synthesizers, which spontaneously self-assemble into long, thin filaments. Depending on the choice of starting materials, these filaments can display large number of biologically active peptides on their surfaces that enable the fibers to serve as both drugs and drug deliver agents simultaneously without the need to further encapsulate anticancer agents within the nanostructure.

In earlier work, the Northwestern CCNE team had shown that one such nanofiber was more toxic to cancer cells than non-malignant cells, but this nanofiber was degraded rapidly in the blood stream. To improve the pharmacokinetic properties of their nanofiber, the investigators created a second peptide amphiphile, this one linked to poly(ethylene glycol) (PEG), a polymer widely used to increase the survival of nanoparticles in the blood stream. When the researchers mixed the peptide amphiphile with the PEGylated amphiphile, the two molecules together self-assembled into nanofilaments. By adding the PEGylated peptide amphiphile to the mix the investigators increased by eight-fold the amount of intact nanofiber that survived degradation by the enzyme trypsin compared to the original nanofiber.

To see if this nanofiber showed promise in a live animal studies, the investigators administered it to mice with human breast tumors. After dosing the animals twice weekly for three weeks, the researchers observed that the tumors in the treated animals grew much slower than in control animals. They also noted that the animals showed no signs of drug-related toxicities.

More information: "Coassembled cytotoxic and pegylated peptide amphiphiles form filamentous nanostructures with potent antitumor activity in models of breast cancer," *ACS Nano*. dx.doi.org/10.1021/nn302503s

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