Nanoparticles working in harmony

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For decades, researchers have been working to develop nanoparticles that deliver cancer drugs directly to tumors, minimizing the toxic side effects of chemotherapy. However, even with the best of these nanoparticles, only about one percent of the drug typically reaches its intended target. Now, a team of researchers from MIT, the Sanford-Burnham Medical Research Institute, and the University of California at San Diego (UCSD) has designed a new type of delivery system in which a first wave of nanoparticles hones in on the tumor, then calls in a much larger second wave that dispenses the cancer drug. This communication between nanoparticles, enabled by the body's own biochemistry, boosted drug delivery to tumors by more than 40-fold in a mouse study.

This new strategy could enhance the effectiveness of many drugs for cancer and other diseases, say the investigators. This multi-institutional team was led by MIT's Sangeeta Bhatia, who is also a member of the MIT-Harvard Center of Cancer Nanotechnology Excellence, part of the National Cancer Institute's Alliance for Nanotechnology in Cancer. This research is described in a paper published in the journal Nature Materials. Michael Sailor of UCSD and Erkki Ruoslahti of the Sanford Burnham Institute, both senior members of the Alliance for Nanotechnology in Cancer, also participated in this study.

Dr. Bhatia and her collaborators drew their inspiration from complex biological systems in which many components work together to achieve a common goal. For example, the immune system works through highly orchestrated cooperation between many different types of cells. In this case, the team's approach is based on the blood coagulation cascade — a

series of reactions that starts when the body detects injury to a blood vessel. Proteins in the blood known as clotting factors interact in a complex chain of steps to form strands of fibrin, which help seal the injury site and prevent blood loss.

To harness the communication power of that cascade, the researchers needed two types of nanoparticles — signaling and receiving. Signaling particles, which make up the first wave, exit the bloodstream and arrive at the tumor site via tiny holes in the leaky blood vessels that typically surround tumors (this is the same way that most targeted nanoparticles reach their destination). Once at the tumor, this first wave of particles provokes the body into believing that an injury has occurred at a tumor site, either by emitting heat or by binding to a protein that sets off the coagulation cascade.

Receiving particles are coated with proteins that bind to fibrin, which attracts them to the site of blood clotting. Those second-wave particles also carry a drug payload, which they release once they reach the tumor.

In a study of mice, one system of communicating nanoparticle systems delivered 40 times more of the widely used anticancer agent doxorubicin than did non-communicating nanoparticles. The researchers also saw a correspondingly amplified therapeutic effect on the tumors of mice treated with communicating nanoparticles.

To pave the path for potential clinical trials and regulatory approval, Dr. Bhatia and her colleagues are now exploring ways to replace components of these cooperative nanosystems with drugs already being tested in patients. For example, drugs that induce coagulation at tumor sites could replace the signaling particles tested in this study.

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