

Crossing the Blood-Brain Barrier to Deliver Lifesaving Drugs

Seaweed-based nanoparticles may offer a way to deliver cancer drugs directly to brain tumors.

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A major challenge in treating brain cancer is delivering drugs across the blood-brain barrier (BBB), the dense network of cells and blood vessels that prevents toxins and pathogens from entering the brain. Unfortunately, the BBB also bars entry to therapeutic molecules, leaving highly toxic radiation or chemotherapy treatment as the only recourse for many patients with brain cancer.

But at Memorial Sloan Kettering Cancer Center, former Damon Runyon Fellow Daniel A. Heller, PhD, and his colleagues may have discovered a Trojan horse that can ferry cancer drugs across the BBB and directly into brain tumors.

Nanoparticles crossing the blood-brain barrier escorted by P-selectin

Courtesy of Damon Runyon Cancer Research Foundation

P-selectin is a protein expressed in the blood vessels surrounding sites of infection, injury, or inflammation—including cancers—that directs immune cells to where they are needed. If a vessel carrying a cancer drug could somehow bind to P-selectin the way immune cells do, it could get a free ride to its target. To get across the BBB, however, the vessel would have to be very small.

Luckily, Dr. Heller's lab develops nanotechnologies, including nanomedicines, using particles a thousand times smaller than the width of a human hair. (Last spring, the team reported on a [nanosensor](#) that can detect ovarian cancer much earlier than current tests.) Now, they have constructed a "nanocarrier" that can both hold a cancer drug and attach itself to P-selectin. Their secret ingredient is a sugar molecule called fucoidan, derived from brown seaweed from the Sea of Japan, which, the team discovered, has a particular affinity for P-selectin. When this fucoidan-coated nanoparticle, loaded with a cancer drug, binds to P-selectin, it triggers a process called transcytosis, which shuttles the particle across blood vessel walls.

In a previous study, Dr. Heller's team showed that this delivery mechanism worked in lung tumors in mice. But recently, they put it to the ultimate test: delivering vismodegib, a drug approved for

the treatment of skin cancer, to mice with medulloblastoma, an aggressive pediatric brain tumor.

The results were striking. Not only could these nanocarriers, escorted by P-selectin, cross the BBB intact, but they also homed in on the tumor cells with great precision, leaving the healthy brain tissue alone. This allowed for a lower dose of vismodegib to be effective with far fewer toxic side effects.

While further research is needed before these seaweed-based nanoparticles can reach human patients, their potential is anything but small. A drug delivery mechanism that can cross the BBB without damaging the brain could be used to treat not only brain tumors but a wide range of other brain conditions, such as multiple sclerosis, stroke, and epilepsy.

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