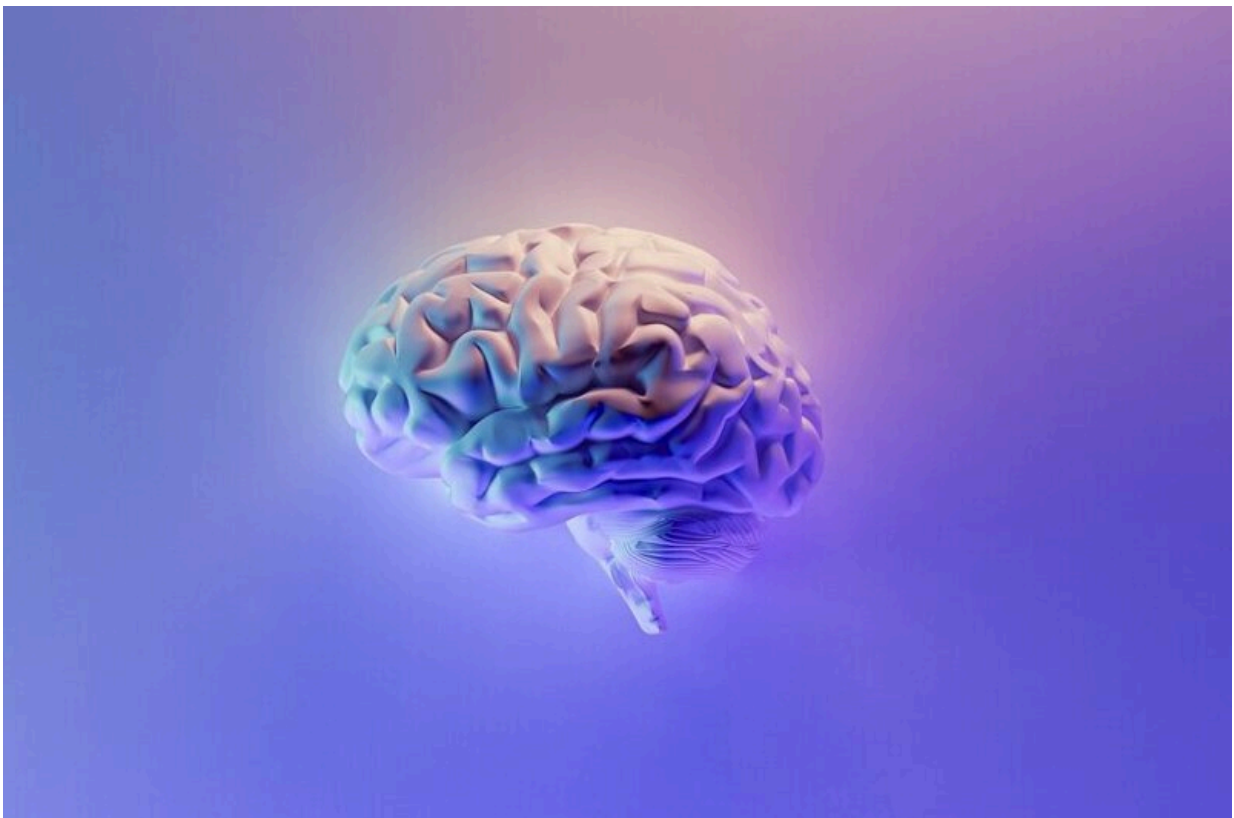


Scientists develop novel approach to enhance drug delivery for treatment of brain tumors in children

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Mount Sinai Health System and Memorial Sloan Kettering Cancer Center researchers have developed a new drug delivery approach that

uses nanoparticles to enable more effective and targeted delivery of anti-cancer drugs to treat brain tumors in children.

The technology allows for the enhanced delivery of anti-cancer drugs to the specific locations of brain tumors while sparing normal brain regions. The result is improved effectiveness and reduced toxicities of anti-cancer drugs, according to their study, published March 2, 2023, in *Nature Materials*.

"We show that we can more successfully deliver lower doses of the drug in a more effective manner to the specific sites of tumor within the brain, while sparing the bone toxicity that is seen in younger patients," says Praveen Raju, MD, Ph.D., Co-Director of the Children's Brain and Spinal Tumor Center at Mount Sinai Kravis Children's Hospital, and senior author of the study.

Medulloblastoma is the most common malignant pediatric brain tumor, accounting for about 20% of all brain tumors in children. It is highly aggressive and difficult to treat, and is considered incurable in nearly 30% of patients. Even children who are "cured" experience severe long-term disabilities and health issues, primarily due to the adverse side effects of radiation and chemotherapy. Site-directed [drug delivery](#) to the affected brain tissue is hindered by a distinct and highly regulated [blood-brain barrier](#), which normally protects the brain from infections or other harmful substances.

In this study, the researchers made use of a normal mechanism that the [immune system](#) uses to traffic white blood cells to sites of infection, inflammation, or tissue injury. Rather than randomly sending [immune cells](#) throughout the body, there is a homing mechanism on activated blood vessels that immune cells use to go where they are needed. The researchers used this unique homing feature, which is also found within brain tumor blood vessels, to target their drug-loaded nanoparticles to the

site of the disease and not the normal brain regions.

Using the new drug delivery platform in a genetically relevant mouse model of medulloblastoma, the research team was able to enhance the efficacy of an anti-cancer drug that could potentially be useful for a subset of medulloblastoma patients, but which is currently limited by the bone toxicity it secondarily creates in children.

"In addition, we showed that this targeted drug delivery approach is further enhanced with very-low-dose radiation, which is a standard therapy already used for most children and adults with primary and metastatic brain tumors," says Dr. Raju, Associate Professor of Neurology, Neuroscience, and Pediatrics at Icahn School of Medicine at Mount Sinai.

"Importantly, our blood-brain barrier drug delivery approach has the potential to improve the delivery of drugs for other pediatric [brain tumors](#) and localized diseases in the brain in both children and adults, including focal epilepsy, multiple sclerosis, stroke, and possibly neurodegenerative disorders."

"Certain proteins appear on [blood vessels](#) at sites of inflammation that help [white blood cells](#) exit the bloodstream. They work like [police officers](#) at the site of a car accident, who let in [emergency personnel](#) to help," says Daniel Heller, Ph.D., Head of the Cancer Nanomedicine Laboratory and Member in the Molecular Pharmacology Program at Memorial Sloan Kettering Cancer Center, and senior author on the study. "We sent in our own emergency personnel, in the form of drug-loaded nanoparticles, composed of certain sugar molecules that can target these same proteins."

The researchers anticipate that continued investigation and development of this method to harness and improve the transport of materials across

the blood-brain barrier and other sites will be instrumental for improving the efficacy of several classes of approved and experimental therapeutics. This drug delivery platform can be used to treat cancers in the brain and other sites of the body, as well as other inflammation-related diseases in the central nervous system and elsewhere.

More information: Praveen Raju, P-selectin-targeted nanocarriers induce active crossing of the blood–brain barrier via caveolin-1-dependent transcytosis, *Nature Materials* (2023). [DOI: 10.1038/s41563-023-01481-9](https://doi.org/10.1038/s41563-023-01481-9).
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