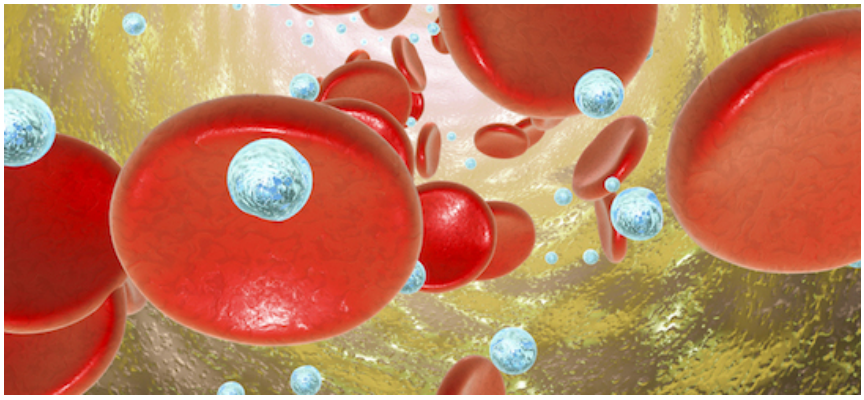
# Nanoparticles Shepherd Therapeutic Molecules Through Blood-Brain Barrier to Preserve Critical Astrocytes

From a therapeutic standpoint, the brain is a tough nut to crack. The blood-brain barrier (BBB) protects the central nervous system from pathogens and other dangers but also blocks potential treatments. But now, researchers at Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine have developed biodegradable nanoparticles that can shepherd therapeutic molecules through the BBB to brain cells called astrocytes, protecting them and the neurons they support. The findings were published in the journal *PNAS*.

“We developed a nano delivery system that can accumulate in the brain, as well as astrocytes in the brain,” said Shanta Dhar, Ph.D., assistant director of technology and innovation at Sylvester, associate professor of biochemistry and molecular biology, and senior author on the paper. “This delivery system can take therapeutics to astrocytes and make them more functional so they can protect neurons undergoing neurodegeneration.”



Nanoparticles in blood, 3D illustration. Conceptual image illustrating treatment and diagnostics with nanoparticles

The BBB acts as a protective barrier, allowing sanctioned molecules to get through while blocking the rest. Most chemotherapies, for example, cannot make it into the brain. While previous studies showed nanoparticles can cross the BBB, they did not always accumulate where they were targeted.

To overcome this, Dr. Dhar and colleagues developed biodegradable polymeric nanoparticles, which act as Trojan horses, ferrying therapeutic agents across the barrier and (in this case) into astrocytes. The nanoparticles are directed by a lipophilic positively charged ion, which helps them cross the barrier. In addition to astrocytes, this approach could be used to infiltrate cancer cells.

These minute systems have a lot on their plates. In addition to getting through the BBB, they must also target and penetrate both astrocytes and their energy-producing mitochondria. The researchers hoped reducing oxidative stress would preserve the astrocytes. In turn, these cells would continue to protect surrounding neurons.

“The particles have a complicated job but are really quite simple,” said Dr. Dhar. “They can be made

from a single polymer, in a one-step process, and can still do all these different tasks."

Using animal models of neurodegeneration, the researchers showed the nanoparticles could successfully carry $CoQ_{10}$, a natural antioxidant, and modified aspirin, a powerful anti-inflammatory, through the BBB. The cargo-carrying nanoparticles then accumulated in astrocytes, and ultimately mitochondria, particularly in the cerebral cortex and cerebellum, and had only low concentrations in the liver. There was little evidence of toxicity, and the particles did not illicit an immune reaction. Most importantly, they protected astrocytes from reactive oxygen and possible cell death.

This study is proof of concept that these nanoparticles can effectively transport therapeutics to targeted cells, opening an enormous range of applications. The Dhar lab has already begun studying how these tools could be used to treat glioblastoma, brain injury, Alzheimer's disease, Neuro HIV and other neurodegenerative conditions.

"We can reduce oxidative stress using the antioxidants in these nanoparticles," said Dr. Dhar, "but that's just the tip of the iceberg. These particles can take chemotherapeutic agents to treat brain tumors or deliver therapeutics for Parkinson's or Alzheimer's. There's so much we can do."

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