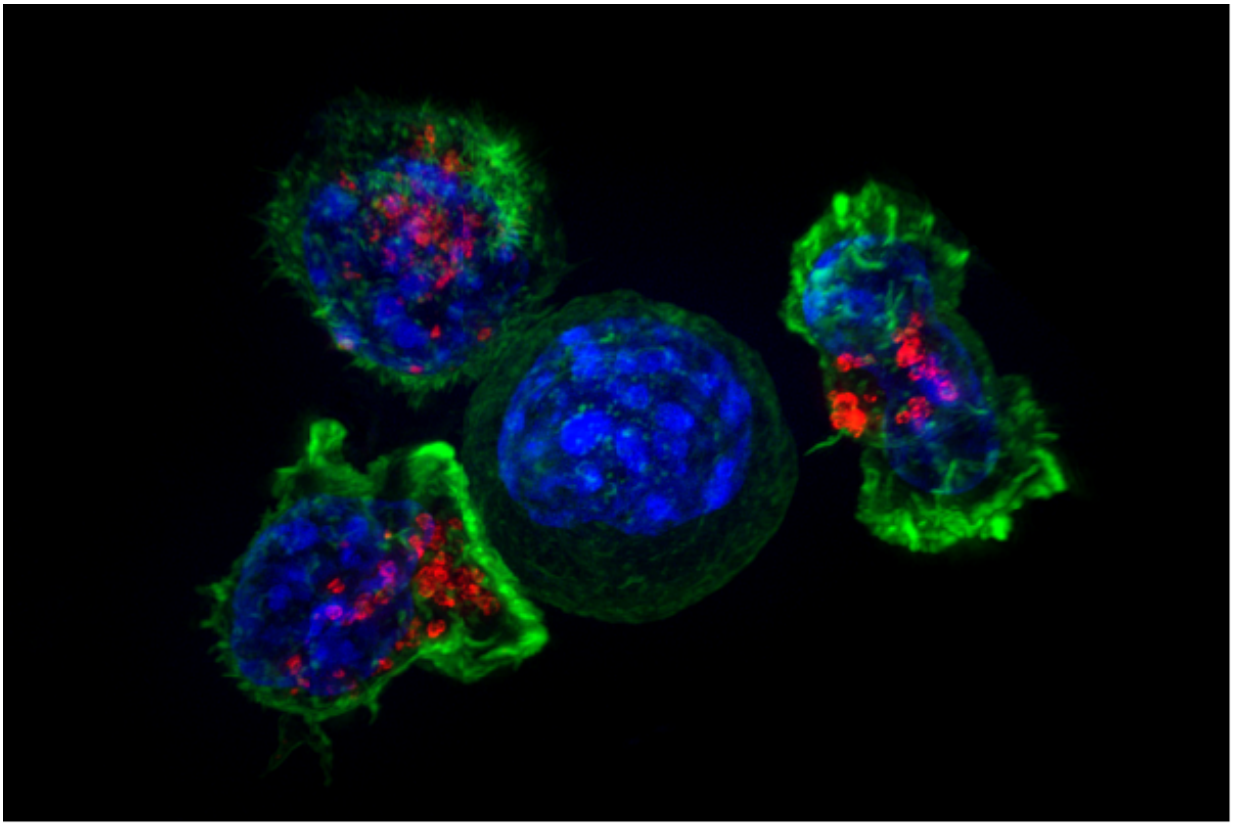
Nanomedicine opens door to precision medicine for brain tumors

July 12 2017



Killer T cells surround a cancer cell. Credit: NIH

Early phase Northwestern Medicine research has demonstrated a potential new therapeutic strategy for treating deadly glioblastoma brain tumors.

The strategy involves using lipid polymer based nanoparticles to deliver molecules to the tumors, where the molecules shut down key cancer drivers called brain tumor initiating cells (BTICs).

"BTICs are malignant brain tumor populations that underlie the therapy resistance, recurrence and unstoppable invasion commonly encountered by glioblastoma patients after the standard treatment regimen of surgical resection, radiation and chemotherapy," explained the study's first author, Dr. Dou Yu, research assistant professor of neurological surgery at Northwestern University Feinberg School of Medicine.

The findings were published in the journal *Proceedings of the National Academy of Sciences*.

Using mouse models of brain tumors implanted with BTICs derived from human patients, the scientists injected nanoparticles containing small interfering RNA (siRNA)—short sequences of RNA molecules that reduce the expression of specific cancer promoting proteins—directly into the tumor. In the new study, the strategy stopped tumor growth and extended survival when the therapy was administered continuously through an implanted drug infusion pump.

"This major progress, although still at a conceptual stage, underscores a new direction in the pursuit of a cure for one of the most devastating medical conditions known to mankind," said Yu, who collaborated on the research with principal investigator Dr. Maciej Lesniak, Michael J. Marchese Professor of Neurosurgery and chair of neurological surgery.

Glioblastoma is particularly difficult to treat because its genetic makeup varies from patient to patient. This new therapeutic approach would make it possible to deliver siRNAs to target multiple cancer-causing gene products simultaneously in a particular patient's tumor.

In this study, the scientists tested siRNAs that target four transcription factors highly expressed in many glioblastoma tissues—but not all. The therapy worked against classes of glioblastoma BTICs with high levels of those transcription factors, while other classes of the cancer did not respond.

"This paints a picture for personalized glioblastoma therapy regimens based on tumor profiling," Yu said. "Customized nanomedicine could target the unique genetic signatures in any specific patient and potentially lead to greater therapeutic benefits."

The strategy could also apply to other medical conditions related to the central nervous system—not just brain tumors.

"Degenerative neurological diseases or even psychiatric conditions could potentially be the therapeutic candidates for this multiplexed delivery platform," Yu said.

Before scientists can translate this proof-of-concept research to humans, they will need to continue refining the nanomedicine platform and evaluating its long-term safety. Still, the findings from this new research provide insight for further investigation.

"Nanomedicine provides a unique opportunity to advance a therapeutic strategy for a disease without a cure. By effectively targeting brain tumor initiating stem cells responsible for cancer recurrence, this approach opens up novel translational approaches to malignant brain cancer," Lesniak summed up.

More information: Dou Yu et al, Multiplexed RNAi therapy against brain tumor-initiating cells via lipopolymeric nanoparticle infusion delays glioblastoma progression, *Proceedings of the National Academy of Sciences* (2017). DOI: 10.1073/pnas.1701911114