

Scientists develop 'designer protein,' opening new door in cancer research

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A major breakthrough in how to target and destroy the most malignant and aggressive brain cancer cells has been made by researchers at Wake Forest University Baptist Medical Center.

Scientists have identified a way to target and destroy Glioblastoma multiforme (GBM) cells without harming healthy cells.

The finding allows for new possibilities in cancer research previously not known to be readily feasible.

"Treatment of patients with Glioblastoma multiforme is still a major challenge, as GBM is extremely difficult to manage," said Waldemar Debinski, M.D., Ph.D., director of the Brain Tumor Center of Excellence at Wake Forest Baptist. "Over the last 30 to 40 years, with all the [cancer research](#) efforts out there, we have only been able to extend the survival rate in these patients by about one month per decade of research. People who have this kind of cancer survive for an average of 14.5 months after diagnosis, although some with this form of cancer can live longer than that average. I don't think anyone would label this satisfactory progress."

Debinski, a professor of [neurosurgery](#) and senior investigator on the study, and colleagues have thus focused their efforts on finding a way to treat these tumors - something potentially less toxic and invasive than surgery, radiation and chemotherapy - in the form of molecular targeting.

Their latest achievement, recently featured on the cover of the journal *Genes and Cancer*, is the result of years of research funded by the National Cancer Institute.

Almost 20 years ago, Debinski and colleagues developed what Debinski has dubbed a "designer protein," a single-chain protein that is able to seek out and make its way into specific cells, such as cancer cells. The challenge, and most recent focus of the researchers' work, has been finding a way to program that protein, once inside the targeted cell, to locate and accumulate at a specific subcellular compartment such as the nucleus, which houses a cell's DNA, or the [mitochondria](#), the "powerhouse" of a cell, without harming normal neighboring tissue.

Recently, the researchers were able to do just that, creating a designer protein that not only targets a specific cell type, but then invades that cell and is drawn directly to a chosen compartment.

The researchers hope their continued investigation will soon lead to a way to attach a drug to the designer protein and deliver it directly to the cell's nucleus.

"It's possible that we could design the protein in such a way that it recognizes GBM cells and then delivers a drug or some other therapy into those cells in a way that will put those active agents inside a specific subcellular compartment like the nucleus, destroying only that specific cell," Debinski said. "Some radiation, if applied to the body, will do nothing to the cancer cells because it can't penetrate far enough into the body to reach its specific site of action in the cells. However, if we deliver that same radiation specifically to the nuclei of GBM cells, it can destroy the DNA of the cancer cell, leaving the cell unable to live any longer. It dies and the neighboring healthy cells go untouched. In this way, we think we may be able to provide a therapy that is both effective and at the same time less toxic."

Debinski's study is the first to document in a direct way both a single-chain protein that can recognize GMB [cancer cells](#) and its journey from attaching to the cells' surface to reaching the cells' nuclei.

"GMB is one of the most vicious of human malignancies," Debinski said. "Very little research has been done so far along this path, so this approach is very new and our study opens the door for more investigation."

Debinski noted that the use of a designer protein to deliver therapies to specific action sites will have to go through extensive safety and animal research before it can translate to human patients.

"As a researcher, one can think and dream about many possible scenarios during the quest to find a way to treat cancer," he said. "This is one that we now know we can actually do. It's feasible - and it's fantastic. That's the best way to describe it."

Hetal Pandya, a Ph.D. student in Debinski's lab and the first author on the paper, has been instrumental in developing this project, Debinski said, as well as research associate Denise M. Gibo, BSc.

Provided by Wake Forest University Baptist Medical Center

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