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Protein involved in nerve-cell migration implicated in spread of brain cancer

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The invasion of brain-tumor cells into surrounding tissue requires the same protein molecule that neurons need to migrate into position as they differentiate and mature, according to new research from the University of Illinois at Chicago College of Medicine and published August 7 in the online journal *PLOS ONE.*

The researchers investigated similarities between the transition of neural stem cells into neurons and the process whereby cancer cells invade surrounding tissues.

"Both processes involve the mobilization of cells," says Anjen Chenn, director of clinical pathology and molecular diagnostics at UIC. "During embryonic development, stem cells that go on to become neurons must migrate long distances to other parts of the brain before they mature into adult neurons. We thought that this type of cell migration might have similarities with cancer cells that spread from tumors."

Chenn and colleagues analyzed the proteins expressed by embryonic mouse neural stem cells as they began their migration.

They found that one protein, cadherin11, was found in especially high concentrations in these transitioning cells.

Chenn said the protein "regulates how the cells stick to each other and is also important in helping cells pull themselves along certain pathways as they travel to their final destinations."

When the researchers caused the protein to be overexpressed in embryonic mice, the neural stem cells began their migration prematurely.

"This confirmed that cadherin11 was involved in the initiation of migration," said Chen.

To determine whether the protein was involved in the invasion of cancer cells into healthy tissues, the researchers looked at its function in glioblastoma, the most common and aggressive type of adult brain cancer. They examined survival data from patients with glioblastoma and noticed that patients whose tumors expressed elevated levels of the cadherin11 gene had the worst survival rates.

"We also saw that in our tissue samples, the tumor cells with high expression of cadherin11 tended to be located near blood vessels, suggesting that the protein could be involved in encouraging blood vessels to enervate tumors," Chenn said.

When Chenn and his colleagues mixed cells from blood vessel walls with human glioblastoma cells, the glioblastoma cells increased their expression of cadherin11.

"We have long known that tumors recruit their own blood supply, but this finding was particularly interesting because it suggests that blood vessels might actually be stimulating tumor cells to come to them," Chenn said. "Our results together indicate that cadherin11 is critical in inducing cell migration in cancer, and could be an important therapeutic target for preventing its spread."

Provided by University of Illinois at Chicago