

Genetic signaling pathway blocks formation of a cancer in the cerebellum

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A research team at the Krembil Research Institute has discovered that a signaling pathway which controls blood vessel development in the brain has the ability to stop brain tumor formation in animal models of medulloblastoma, the most common malignant brain tumor diagnosed in children.

The findings, published today in the journal *eLife*, are the first to show that blocking a <u>signaling</u> pathway called Norrin/Frizzled4 (Fzd4) drives changes in the support structures that surround pre-cancer cells and promotes medulloblastoma development in subjects that are genetically susceptible to the disease.

"Our study brings a new dimension to our understanding of Medulloblastoma," says Dr. Valerie Wallace, principal investigator of the study, Norrin/Frizzled4 Signaling in the Preneoplastic Niche Blocks Medulloblastoma Initiation, and Co-Director of the Donald K. Johnson Eye Institute.

"It adds another component to understanding tumour initiation, which is a longstanding question in the field."

Her team's new research found that blocking the Norrin/Fzd4 signal created more opportunities to form pre-cancerous growths and speed up tumour initiation. This work also suggests that an activated pathway may therefore block tumour formation.



The research, which was carried out in large part by Dr. Erin Bassett and Mr. Nicholas Tokarew, was initiated at the Ottawa Hospital Research Institute and continued at the Krembil Research Institute after Dr. Wallace relocated to Toronto. The discovery came from replication of a human condition called Gorlin Syndrome in lab experiments. People with Gorlin Syndrome have one copy of a tumour-suppressing gene instead of two, which makes them susceptible to medulloblastoma.

"While there is some treatment success for medulloblastoma, it is not perfect," says Dr. Wallace. "Our research reveals new observations that down the road might change what happens in the clinic."

The team's next step will be to investigate how the blood vessels impacted by Norrin/Fzd4 signaling communicate with pre-cancerous cells to make them more likely to become malignant.

"We don't think that is due to a passive supply of nutrients from the vessels," Dr. Wallace explains. "The vessels play a role in the development of this cancer and we want to understand what that role is."

Provided by University Health Network

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