

Researchers find simple reason why some children die despite aggressive modern therapy for brain cancer

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(Medical Xpress) -- It can be frightening enough to know that your child has brain cancer without the additional heartbreak of being told that the treatment is not working despite aggressive therapy. New research from The Hospital for Sick Children (SickKids) has now identified why some therapies for paediatric brain cancer fail – and what can be done in the future to increase cure rates.

Currently, treatment for medulloblastoma, a form of paediatric [brain cancer](#), is targeted to molecular markers formed by genetic mutations. Although in many [children](#) the disease has already spread (metastasized) at the time of diagnosis, treatment is determined only from markers found in an examination of the main tumour mass. This therapeutic strategy was based on the widely held assumption that the main tumour mass is very similar, if not identical, to the metastasized cancer cells.

However, a research team led by Dr. Michael D. Taylor, a neurosurgeon at SickKids, has found that if the cancer spreads, the metastases are genetically very similar to each other, but different from the primary tumour. The study will be published in the advance online Feb. 15 edition of *Nature*.

“This two-part genetic profile explains why some children are unaffected by treatments for their medulloblastoma,” says Taylor, who co-authored the paper with Dr. Eric Bouffet, a neuro-oncologist and Director of the

Brain Tumour Program at SickKids. "Because oncologists assumed the metastasized cancer was genetically similar to that of the primary tumour, we all thought that treatments based on testing the primary tumour would impact all of the disease sites."

However, markers identified in the primary tumour may be missing entirely from the metastatic tumours, leaving those tumours untreated. The findings imply that some children may require separate therapies for the primary tumour and the metastases.

Researchers had previously assumed that cancer spread in medulloblastoma was the result of random cell movement. However, the team discovered that metastases are the result of a small set of 'elite' cells which are able to escape the primary tumour to spread to new sites on the brain or spinal cord. Therapies that target these particularly malignant 'elite' cells might be an effective strategy to treat children with brain cancer.

Medulloblastoma is the most common malignant paediatric brain tumour. Although the survival rate is 60 per cent, many children are disabled by the harsh treatments they undergo, as radiation and high-dose chemotherapy of the developing brain and spinal cord can cause permanent damage to the nervous system.

"Now that we know we are treating a single cancer with two distinct populations, each with their own distinct genetic profiles, we can work on developing treatment plans that will kill the cancer cells in both the primary and the metastatic tumours," Taylor says. "In the future, these treatments could increase survival rates, decrease the damage done by treatment, and improve quality of life for affected children."

"These are important findings that will provide hope for children with medulloblastoma and their families," says Dr. Christine Williams, Vice

President of Research, Canadian Cancer Society, which helped fund the study. “This exciting research will lead to different directions in treatment so doctors can find more effective and less toxic ways to treat these children, so this is very promising news.”

According to the researchers, this new study suggests that when targeted therapies are used for medulloblastoma, doctors should biopsy the metastases as well as the primary tumour. Although this work is in medulloblastoma, it opens avenues for research into other cancers and how they spread.

The study was the result of an international collaboration between researchers in Canada, the United States, Germany, England and The Netherlands. It was funded in part by the Canadian Cancer Society, SickKids Foundation, Brainchild and the Pediatric Brain Tumor Foundation.

More information: [DOI: 10.1038/nature10825](https://doi.org/10.1038/nature10825)

Provided by Hospital for Sick Children

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