Heart drug could significantly increase survival rates for children with an aggressive form of brain tumour

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Researchers at the University of Nottingham have discovered that repurposing a heart drug could significantly increase the survival rate for children with ependymoma—a type of brain tumor.

The findings, published in *Scientific Reports* and led by experts in the University's Schools of Medicine and Life Sciences, suggest that co-treatment with a drug normally used to treat cardiac hypertrophy can overcome chemotherapy resistance and increase survival in over a third of ependymoma patients.

Ependymoma are the second most common malignant brain tumors in children. They can occur across all age groups, but the outcome for children is lower than in their adult counterpart. The poorest survival is seen in infants, with the five year prognosis at just 42-55 percent.

The use of chemotherapy in children with ependymomas has had variable levels of success, leading to the frequent belief that ependymomas are chemoresistant tumors, since over half of tumors cannot be cured by chemotherapy alone.

The study was led by Dr. Beth Coyle from the University of Nottingham's School of Medicine and Dr. Ian Kerr from the School of Life Sciences. The Ph.D. student who undertook the research, Durgagauri Sabnis, was a recipient of a University of Nottingham Vice Chancellor's Research Excellence Scholarship and the British Federation of Women Graduates (BFWG) foundation grant.

Dr. Coyle said: "We are hopeful that by combining this repurposed drug with current treatments we can give new hope for long term survival to patients with these devastating brain tumors."

In this study the authors set out to determine the nature of this chemoresistance. They show that, in patients treated with chemotherapy alone, the presence of a chemotherapy drug-pumping protein called ABCB1 was associated with a significantly poorer outcome.

tumors that expressed ABCB1 were less likely to respond to chemotherapy and more likely to be locally invasive.

The authors then used a heart drug to inhibit ABCB1 function in cells taken from patient's tumors. The heart drug was able to stop ABCB1 pumping chemotherapy drugs out of the tumor cells making them more sensitive to chemotherapy and less able to migrate.

ABCB1 is expressed in over one third of patient's tumors, all of whom could potentially benefit from repurposing of this heart drug in future clinical trials.

More information: Durgagauri H. Sabnis et al. A role for ABCB1 in prognosis, invasion and drug resistance in ependymoma, *Scientific Reports* (2019). DOI: 10.1038/s41598-019-46700-z

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