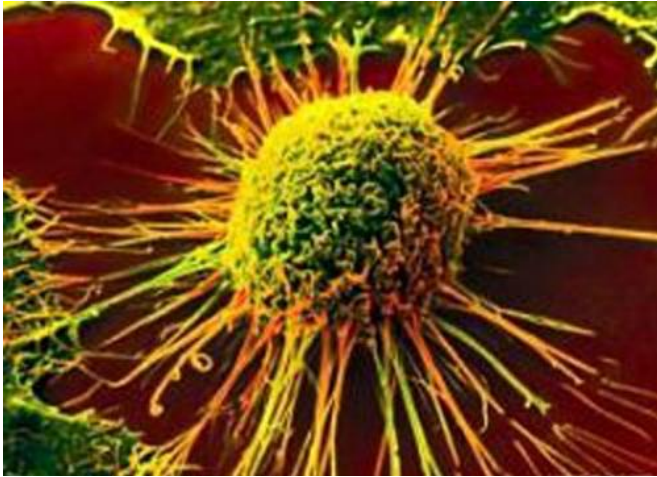


Biomarker of aggressive childhood cancer discovered

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Johns Hopkins researchers have discovered a new diagnostic marker that distinguishes a fast-growing type of the pediatric brain cancer medulloblastoma from a less aggressive type. The researchers hope that this biomarker may lead to the development of more effective therapies.

The new study, led by Ranjan J. Perera, Ph.D., director of the Center for RNA Biology at Johns Hopkins All Children's Hospital, uncovered that this biomarker differentiates aggressive group 3 medulloblastoma from the more treatment-responsive group 4 medulloblastoma. The two types look identical under the microscope and are currently classified as group 3/4 and treated the same, explains Perera, the study's senior author, who is also a senior scientist at the Johns Hopkins All Children's Cancer & Blood Disorders Institute and the Johns Hopkins All Children's Institute for Fundamental Biomedical Research, an associate professor of oncology at the Johns Hopkins University School of Medicine and a Johns Hopkins Kimmel Cancer Center member.

"There is currently no radiographic or microscopic way to distinguish group 3 from group 4," says George Jallo, M.D., pediatric neurosurgeon at Johns Hopkins All Children's Hospital, medical director of its Institute for Brain Protection Sciences, professor of neurosurgery, pediatrics and oncology at the Johns Hopkins University School of Medicine, and a collaborator on the study. "Children with group 3 medulloblastoma do not respond well to treatment and almost always relapse and die. We currently have no treatment options for this treatment-resistant group other than experimental therapies."

In an effort to identify features that differentiate group 3 from group 4 and shed light on the cause of its aggressive nature, Perera's group and collaborators reviewed a public database of 175 medulloblastoma patients' RNA sequencing data. They found that non-coding RNA—an RNA molecule that is not expressed as a protein but can nonetheless regulate gene expression through other biochemical processes—varied among the four subgroups of medulloblastoma.

When they took a closer look, exploring non-coding RNA in human cell lines of medulloblastoma, they found that the non-coding RNA Inc-HLX-2-7 was highly upregulated in group 3 medulloblastoma compared with the other three subgroups. In mouse tumor models, called xenografts, implanted into the brain with Inc-HLX-2-7-depleted medulloblastoma cells, tumors were smaller, grew more slowly, and cancer cell death increased compared with xenografts with functioning Inc-HLX-2-7.

The findings were published Dec. 1 in the *Journal of Neuro-Oncology*. "This study tells us that Inc-HLX-2-7 drives the growth of medulloblastoma and is a promising molecular marker and potential therapeutic target for group 3 medulloblastoma," says Charles G. Eberhart, M.D., Ph.D., Charlotte Wilson and Margaret Whitener Professor of Ophthalmology, professor of pathology, oncology

and ophthalmology at the Johns Hopkins University School of Medicine, a Johns Hopkins Kimmel Cancer Center member and collaborator on the study.

Medulloblastoma is a type of brain cancer that predominantly affects children. It is separated into four major molecular subgroups. About 10% of cases are classified as WNT-activated, and are associated with a very good prognosis. SHH-activated accounts for 30% of medulloblastomas and has a fair to good prognosis. They are so named for genetic characteristics that distinguish them from the other types and can serve as treatment targets. Group 4 [medulloblastoma](#) is associated with about 35% of cases and also has a fair to good prognosis. About 25% of patients have group 3, which has a poor prognosis.

More information: Karisa C. Schreck et al. Incidence and clinicopathologic features of H3 K27M mutations in adults with radiographically-determined midline gliomas, *Journal of Neuro-Oncology* (2019). [DOI: 10.1007/s11060-019-03134-x](#)

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