

## Neuroblastoma study identifies new subgroups with distinct prognoses and potential vulnerabilities to therapies

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Researchers have identified new variations in neuroblastoma that could lead to a more accurate prognosis and better-targeted treatments for this



devastating childhood cancer.

A <u>study</u> published in the *British Journal of Cancer* reveals three new subgroups of the most common type of <u>neuroblastoma</u>, each with different genetic traits, expected outcomes, and distinguishing features that offer clues as to which treatments may be most effective.

Dr. Yihua Wang from the University of Southampton, a senior author on the paper said, "This research represents a pivotal advancement in our understanding of MYCN non-amplified neuroblastomas. The results are striking. These kinds of neuroblastomas can be classified into three distinct subgroups, each demonstrating unique prognostic implications and varying vulnerabilities to investigational therapies."

About 100 children are diagnosed with neuroblastoma each year in the U.K., representing 6% to 10% of all childhood cancers. Neuroblastoma is a cancer that starts in a type of nerve cell called a neuroblast. It can present in the abdomen, chest neck or pelvis and can spread to other parts of the body.

The overall prognosis of the disease is poor, with just 20% of patients still alive at 5 years after diagnosis, but the likelihood of the cancer being cured varies widely, with some tumors spontaneously regressing and others proving resistant to therapy and progressing.

One of the key indicators of risk is the amplification of a gene called MYCN, where tumors have too many of this type of gene. This occurs in around 20% of cases and accounts for about 40% of high-risk neuroblastomas.

Researchers from the University of Southampton and China wanted to find out more about cases where the MYCN gene isn't amplified to better understand the diversity of outcomes within these cases. Using



advanced analytical techniques, the research team analyzed more than 1,500 biopsy samples from 16 different datasets sourced from Gene Expression Omnibus (GEO) and ArrayExpress.

The team were able to identify three distinct subtypes of these MYCN non-amplified cases based on their transcriptional signatures—patterns of gene expression that can provide valuable insights into biological processes.

The first subgroup makes up around half of MYCN non-amplified cases and has the best prognosis, with a long-term survival rate of more than 85%, despite some cases being clinically classified as high risk.

Subgroup 2, representing a quarter of MYCN non-amplified cases, had the worst outcomes with a long-term survival rate of 50%. Interestingly, this group had a similar genetic signature to cases where MYCN is amplified.

Researchers found a protein called Aurora Kinase A (AURKA) was expressed at significantly higher levels than in the other two subgroups. On further analysis, they found that AURKA mRNA levels alone could predict overall survival. This suggests that patients within the subgroup may benefit from treatment with AURKA inhibitors.

Meanwhile, Subgroup 3, which made up another quarter of MYCN nonamplified cases, is characterized by an "inflamed" gene signature, with significantly higher levels of activity in immune cells. Further analysis indicates that patients in this subgroup were predicted to respond better to immunotherapy.

Dr. Wang added, "This research opens new avenues for personalized medicine in the treatment of neuroblastomas. By leveraging transcriptional subtyping, we are now equipped to offer more precise



prognosis and tailor therapies accordingly for patients with MYCN nonamplified neuroblastomas, potentially improving outcomes and quality of life."

**More information:** Xiaoxiao Hu et al, Identification of MYCN nonamplified neuroblastoma subgroups points towards molecular signatures for precision prognosis and therapy stratification, *British Journal of Cancer* (2024). DOI: 10.1038/s41416-024-02666-y

Provided by University of Southampton

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