Oestrogen causes neuroblastoma cells to mature into neurons

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The female sex hormone oestrogen can perform an important role in neuroblastoma, a form of cancer mainly affecting young children. In laboratory experiments, researchers at Karolinska Institutet in Sweden demonstrate that oestrogen treatment and overexpression of the oestrogen receptor cause malignant neuroblastoma cells to mature into neuron-like cells. The study, which is published in *PNAS*, gives hope of new treatment possibilities.

Neuroblastoma forms in the peripheral nervous system and is one of the most common forms of solid cancer in young children. The disease mainly affects babies and young children, and while in some cases the tumours can disappear of their own accord, the majority are aggressive, metastasising cancer tumours that are resistant to modern combinations of surgery, radiotherapy and intensive chemotherapy.

The most aggressive forms of neuroblastoma are often associated with a more active MYCN gene, which drives tumour cell growth and spread and inhibits the maturation of the cells.

"Our research focuses particularly on the activity of this gene and how it relates to neuroblastoma," says Professor Marie Arsenian-Henriksson at the Department of Microbiology, Tumour and Cell Biology, Karolinska Institutet. "MYCN is often seen only as a marker for a poor prognosis, but it's critical to the disease and is a possible target for new drugs."

In a previous study, her group discovered that activation of MYCN results in the formation of specific microRNAs, which are relatively small RNA molecules that regulate proteins. Some of these microRNAs disable the oestrogen receptor ERalpha. The present study shows that the inhibition of these microRNA molecules or oestrogen therapy in combination with an overexpression of the oestrogen receptor can cause aggressive neuroblastoma cells with MYCN activation to mature into neuron-like cells which behave more like normal cells.

The researchers studied tumour tissue from patients, cultivated human tumour cells and tumours in mouse models for neuroblastoma. In the mice, the neuron-like cells did not grow as quickly as the original cancer cells, and analyses of the tumour tissue from patients show that those with a high level of the oestrogen receptor have a better survival rate that those with a low.

"Our data suggests that oestrogen could be a therapeutic method for patients who express high levels of the oestrogen receptor," continues Professor Arsenian-Henriksson. "Another possible therapy could involve deregulating MYCN or upregulating the oestrogen receptor and then treating with oestrogen. We have previously shown that the deregulation of MYCN leads to a high expression of the oestrogen receptor."

More information: Johanna Dzieran et al, MYCN-amplified neuroblastoma maintains an aggressive and undifferentiated phenotype by deregulation of estrogen and NGF signaling, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1710901115

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