Medical Xpress

Scientists present new research on childhood neuroblastoma

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In the journal *Cell Reports* researchers at Karolinska Institutet together with international colleagues present new data on the pediatric tumor neuroblastoma. Neuroblastoma is a nerve cell cancer that affects young children and originates in the peripheral nervous system along the spine and in the adrenal glands.

"In some high-risk tumors the MYCN gene is activated and can be amplified up to 100 copies in a single cell, said Marie Arsenian-Henriksson, professor at Karolinska Institutet and the principal investigator of the study, in a comment to the publication."

The research team has found that the cortisol receptor, a hormone receptor located in the cell nucleus, is down regulated by a certain microRNA cluster, miR 17-92, which in its turn is activated by the MYCN protein.

They have then studied the effects of combining reduced MYCN protein levels followed by activation of the cortisol receptor, and found that this treatment results in neuronal maturation and decreased tumor growth in mice. The results may have implications for the treatment of neuroblastoma patients. One possibility is that dexamethasone or steroid hormones could be used for the therapy of patients who have high levels of the cortisol receptor.

"Our study also shows that cells from high-risk patients with high levels of MYCN respond with maturation when treated with a combination of

MYCN inhibitors and dexamethasone. The MYCN inhibitors both reduce MYCN levels as well as increase the cortisol receptor thus enabling the cells to respond to dexamethasone and to differentiate into nerve cells, says Marie Arsenian-Henriksson."

"We hope that this new combination therapy soon will be used in clinical trials in neuroblastoma patients," concludes Diogo Ribeiro.

More information: Diogo Ribeiro et al, Regulation of Nuclear Hormone Receptors by MYCN-Driven miRNAs Impacts Neural Differentiation and Survival in Neuroblastoma Patients, *Cell Reports* (2016). DOI: 10.1016/j.celrep.2016.06.052

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