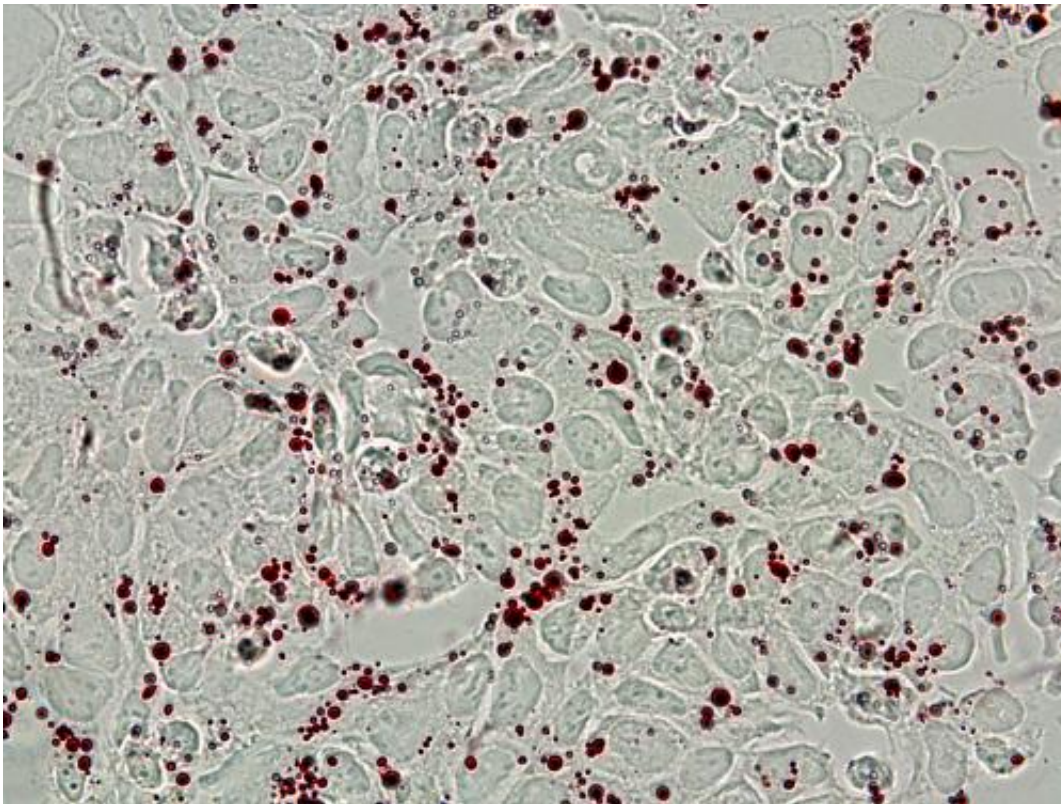


New strategy for defeating neuroblastoma found

June 3 2013



The images shows Lipid droplet accumulation (red) in neuroblastoma cells following treatment with a MYC-targeting molecule. Credit: Anna Frenzel, Karolinska Institutet

Researchers at Karolinska Institutet in Sweden have found a promising strategy for defeating neuroblastoma – a malignant form of cancer in children – that focuses on the so-called MYCN protein. A specific

chemical molecule helps to break down MYCN, which either kills the cancer cell or makes it mature into a harmless neuron. The discovery, which is published in the scientific journal *PNAS*, raises hopes for new and more effective treatments in the future.

Neuroblastoma is the third most common form of cancer in children. It usually develops before the age of two and affects around two dozen children per year in Sweden and around 800 in the US. The tumours are normally located in the [peripheral nervous system](#), but in very young infants they can sometimes spread over the entire body. Current therapies are tough and have serious side effects, and for many of the patients the prognosis is poor. In its most aggressive form only a minority survive, which makes finding [alternative treatments](#) particularly urgent.

In the case of neuroblastoma, extra copies of the gene that encodes the MYCN protein are normally found in the cancer cell. This in turn is a clear indication of a [poor prognosis](#), as it has long been known that the incorrect activation of the MYCN and similar MYC genes causes cancer. The strategy of the research group for defeating the disease was therefore to identify substances that prevent MYC-triggered cell division or that kill [cancer cells](#) in an MYC-specific manner.

"We have found that a small chemical molecule, that is known from previous studies to inhibit the activity of the c-MYC-protein, also inhibits the activity of MYCN," says Principal Investigator Marie Arsenian Henriksson, Professor of molecular tumour biology at Karolinska Institutet. "The substance disrupts the binding between MYCN and another protein called Max, which results in the degradation of MYCN and subsequently either to [cell death](#) in [neuroblastoma cells](#) with [extra copies](#) of the MYCN gene, or to their development into [neurons](#), at which point their malignity disappears. Small chemical molecules that knock out MYCN are therefore a possible therapy option

for children with neuroblastoma as well as for other MYC-driven tumours."

The molecule used by the researchers is no drug candidate; instead the finding is to be seen as a model that can inspire future cancer therapies. However, the researchers did find that the survival rate increased when they applied test treatments on mice with neuroblastoma. The study also led to a new discovery on what happens inside the cancer cell, where the treatment caused an accumulation of fat droplets, suggesting that the MYC proteins affect tumour cell metabolism and the normal breakdown of fatty acids.

"This is an original finding," says Professor Arsenian Henriksson. "It has not previously been observed that the inhibition of MYC affects tumour cells in this way. This does not only open new avenues for novel therapies for certain forms of cancer, but may also have implications for metabolic diseases, such as diabetes."

More information: 'MYC inhibition induces metabolic changes leading to accumulation of lipid droplets in tumor cells', Hanna Zirath, Anna Frenzel, Ganna Oliynyk, Lova Segerström, Ulrica K. Westermarck, Karin Larsson, Matilda Munksgaard Person, Kjell Hultenby, Janne Lehtiö, Christer Einvik, Sven Pålman, Per Kogner, Per-Johan Jakobsson, and Marie Arsenian Henriksson, *PNAS* online 3-7 June 2013. www.pnas.org/cgi/doi/10.1073/pnas.1222404110

Provided by Karolinska Institutet

Citation: New strategy for defeating neuroblastoma found (2013, June 3) retrieved 4 May 2024 from <https://medicalxpress.com/news/2013-06-strategy-defeating-neuroblastoma.html>

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