Tiny bubbles used to treat common childhood cancer

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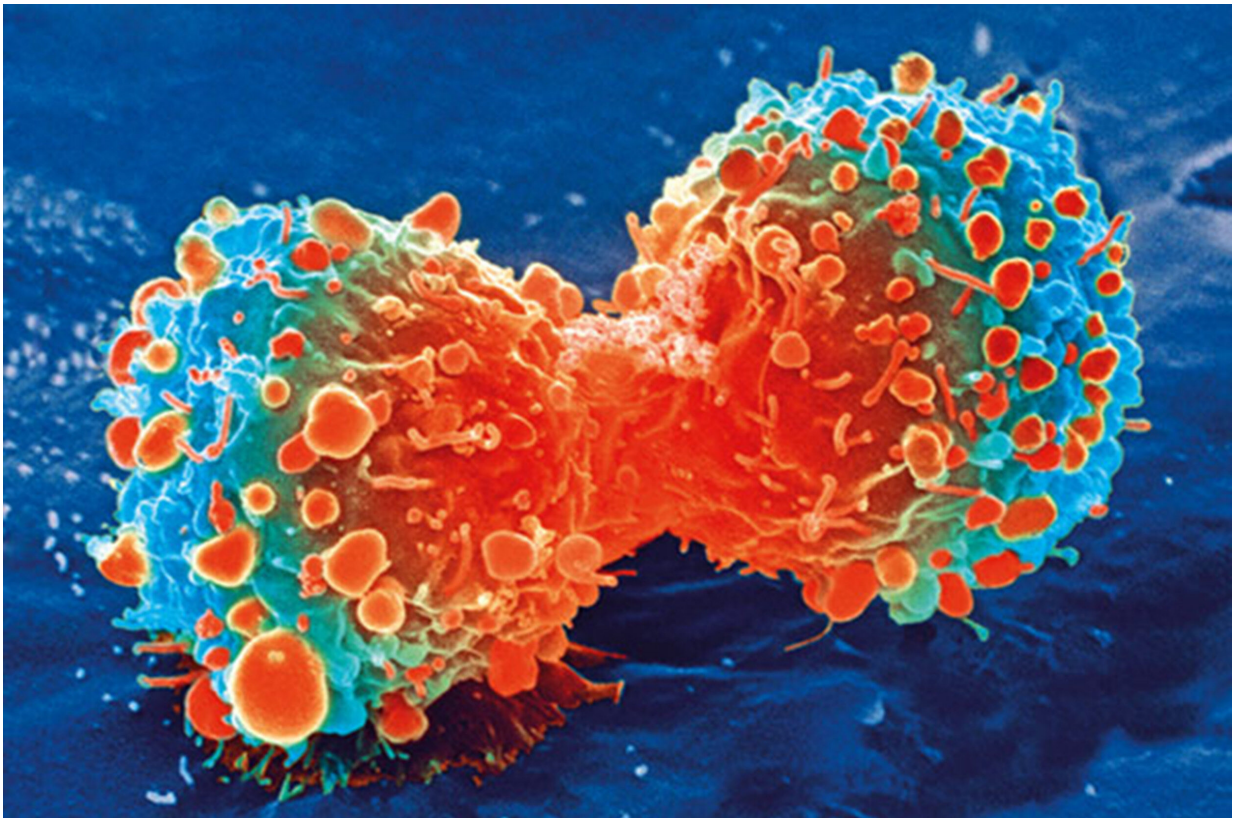

Cancer cell during cell division. Credit: National Institutes of Health

Researchers at UCL have developed a new way to deliver drugs that can shut down cancer-promoting mutations in neuroblastoma. The findings in mice, show the method, which uses tiny bubbles to deliver therapies

directly to tumor cells, reduced tumor growth and improved survival.

Neuroblastoma is the most common solid tumor found in children and accounts for about 15% of all cancer-related deaths in children. Tumors develop from certain types of nerve cells and are most commonly found in the abdomen. Children who are diagnosed above the age of one often fail to respond to treatment or relapse at a later time, meaning that there is an urgent need for new treatment options.

The research, published in *Advanced Functional Materials* and funded by Worldwide Cancer Research, now offers a new potential treatment approach. MYCN is a gene that is associated with poor prognosis and is found to be mutated or overactive in about 20% of neuroblastoma cases. The gene is usually expressed during fetal development and is involved in cell growth and development. Neuroblastoma cells continue to express too much MYCN, leading to uncontrolled cell growth and division and preventing cancer cells from dying.

Researchers at UCL Great Ormond Street Institute of Child Health have now found a way to silence MYCN by delivering a certain type of genetic material called siRNA, directly to the tumor cells. They developed nanoparticles—or tiny bubbles—that use the leaky blood vessels around the tumor and certain features that are only present on tumor cells to home in on the tumors.

The vast majority of nanoparticles, which were delivered via injection, located to the tumor and successfully shut down the MYCN gene causing the cancer. The treatment caused the tumors to grow at a slower pace and prolonged the time that the mice survived the cancer.

Senior author Professor Stephen Hart, UCL GOS ICH, said: "These findings show that this approach with MYCN siRNA delivered by a nanoparticle is a new potential therapy for neuroblastoma. The next steps

would be to develop methods of scaling up production to clinical grade, and to show that the treatment is safe. Current therapies such as surgery, radio and chemotherapy are effective at removing the primary tumor but, unfortunately, in many cases the tumor will return at other sites in the body, which is much harder to treat. We hope that this therapy might augment conventional therapies and provide a way of targeting the therapy to these new tumor sites."

Dr. Helen Rippon, chief executive at Worldwide Cancer Research said: "Each year about 100 families in the UK receive the devastating news that their child has developed neuroblastoma. Unfortunately, the cancer is often detected at a relatively late stage and intense treatment is needed.

"We are funding researchers, like Professor Hart, to start new cancer cures and this innovative research shows just how important investment in early-stage discovery research is. Using new methods, such as nanoparticles, to deliver treatment straight to the heart of cancer is an incredibly exciting area of research. These new results now offer hope to patients and their families by paving the way for effective new treatment options."

More information: Aristides D. Tagalakis et al, Integrin-Targeted, Short Interfering RNA Nanocomplexes for Neuroblastoma Tumor-Specific Delivery Achieve MYCN Silencing with Improved Survival, *Advanced Functional Materials* (2021). DOI: 10.1002/adfm.202104843

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