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New iontronic pump method reduces cancer cell growth in bird embryo experiments

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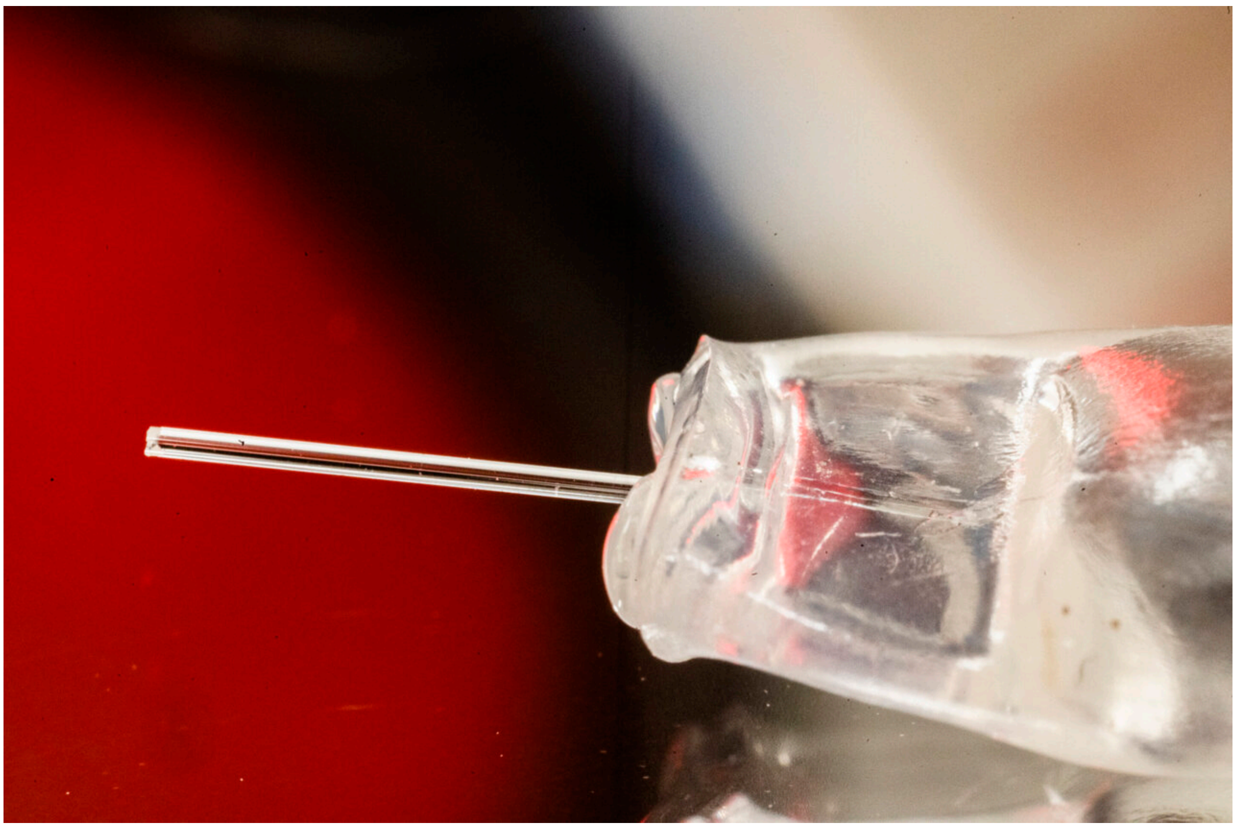

The iontronic pump could be used to locally administer drugs and inhibit cancer cell growth. Credit: Thor Balkhed

When low doses of cancer drugs are administered continuously near malignant brain tumors using so-called iontronic technology, cancer cell growth drastically decreases. Researchers at Linköping University, Sweden, and the Medical University of Graz, Austria, demonstrated this in experiments with bird embryos.

The results, published in the *Journal of Controlled Release*, is one step closer to new types of effective treatments for severe cancer forms.

Malignant brain tumors often recur despite surgery and post-treatment with chemotherapy and radiation. This is because cancer cells can "hide" deep within tissue and then regrow. The most effective drugs cannot pass through the so-called blood-brain barrier—a tight network surrounding blood vessels in the brain that prevents many substances in the blood from entering it. Consequently, there are very few available options for treating aggressive brain tumors.

In 2021, a research group from Linköping University and the Medical University of Graz demonstrated how an iontronic pump could be used to locally administer drugs and inhibit cell growth for a particularly malignant and aggressive form of brain cancer—glioblastoma. At that time, experiments were conducted on tumor cells in a petri dish.

Now, the same research group has taken the next step towards using this technology in clinical cancer treatment. By allowing glioblastoma cells to grow using undeveloped bird embryos, new treatment methods can be tested on living tumors.

The researchers showed that the growth of cancer cells decreased when low doses of strong drugs (gemcitabine) were continuously administered using an iontronic pump directly adjacent to the brain tumor.

"We have previously shown that the concept works. Now we use a model with a living tumor, and we can see that the pump administers the drug very effectively. So, even though it is a simplified model of a human, we can say with greater certainty that it works," says Daniel Simon, professor of organic electronics at Linköping University.

The concept behind a future treatment for glioblastoma involves surgically implanting an iontronic device directly into the brain, close to the tumor. This approach allows for the use of low doses of potent drugs while bypassing the blood-brain barrier. Precise dosing, both in terms of location and timing, is crucial for effective treatment. Additionally, this method can minimize side effects since the chemotherapy doesn't need to circulate throughout the entire body.

Beyond brain tumors, researchers hope that iontronics can be applied to many types of difficult-to-treat cancer forms.

"It becomes a very persistent treatment that the tumor cannot hide from. Even though the tumor and surrounding tissue try to remove the drug, the materials and control systems we use in iontronics can continuously deliver a locally high concentration of medication to the tissue adjacent to the tumor," explains Theresia Arbring Sjöström, a researcher at the Laboratory for Organic Electronics at Linköping University.

The researchers compared the continuous drug delivery of the pump with once-daily dosing, which more closely resembles how chemotherapy is administered to patients today. They observed that tumor growth decreased with the ionic treatment but not with the daily-dose approach, even though the latter was twice as strong.

These experiments were conducted using bird embryos at an early developmental stage. According to Linda Waldherr, a researcher at the Medical University of Graz and a guest researcher at LiU, this model serves as a good bridge to larger animal experiments:

"In bird embryos, certain biological systems function similarly to those in living animals, such as the formation of blood vessels. However, we don't need to surgically implant any devices in them yet. This demonstrates that the concept works, although there are still many challenges to address," she says.

The researchers believe that human trials could be feasible within the next five to ten years. The next steps involve further developing materials to allow for the surgical implantation of iontronic pumps. Subsequent experiments will also be conducted on rats and larger animals to further evaluate this treatment method.

More information: Verena Handl et al, Continuous iontronic chemotherapy reduces brain tumor growth in embryonic avian in vivo models, *Journal of Controlled Release* (2024). DOI: 10.1016/j.jconrel.2024.03.044

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