

# Targeted 'click-to-release' chemotherapy gives good results in mice

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Tagworks Pharmaceuticals, based at Radboud University Medical Center, has developed a new technique for the targeted delivery of chemotherapy for tumors in difficult cases. By way of controlled 'click-to-release' of the chemotherapy drug from its tumor-binding carrier, the treatment can be activated at the right location. The company is publishing the results of studies in mice that have been treated with this method in *Nature Communications*.

Antibody [drug](#) conjugates (ADCs) are relatively new anti-cancer drugs. They consist of an antibody to which a cell-killing chemotherapy molecule is attached. Antibodies can recognize and bind to cellular receptors in a very targeted way. The antibody in an ADC is designed to adhere exclusively to receptors that are characteristic of [tumor cells](#). The drug cargo is not released until the receptor has delivered the entire structure into the cell, and then the chemotherapy drug can do its job.

ADCs are currently used for the treatment of lymphoma and [metastatic breast cancer](#). "These ADCs work very well," says Marc Robillard of Tagworks Pharmaceuticals, a company based at Radboud university medical center. "But for many other tumors, including [colon cancer](#) and [ovarian cancer](#), this method is not yet applicable. The problem is that there are not many suitable cancer-specific receptors that automatically drag such an ADC into the cell, and if the ADC gets stuck on the outside, the chemotherapy drug will not be released, and therefore can't do its job."

It is vital to ensure that the chemotherapy drug is also released if the ADC remains on the outside of the tumor cells. To achieve this objective, Tagworks has designed a smart variant of the ADCs. The ADC is injected and then binds to the receptors on the tumor cells. After a day or two, the tumor is filled with these ADCs. Robillard says, "Our innovation is that we inject a second

component that 'click-releases' the chemotherapy drug from the ADC. As a result, a large quantity of chemotherapy is released very quickly, attacking the tumor. This method will hopefully enable us to treat many more types of cancer."

The first results of this new 'click-to-release' method in mice have now been published in *Nature Communications*. Robillard says, "We studied ovarian cancer and an aggressive form of colon cancer. In both cases, we observed a pronounced anticancer effect. For control purposes, we also applied a 'traditional' ADC, i.e., without the second component that causes the chemotherapy drug to release, but this approach had no therapeutic effect in these forms of cancer."

**More information:** Raffaella Rossin et al, Chemically triggered drug release from an antibody-drug conjugate leads to potent antitumour activity in mice, *Nature Communications* (2018). [DOI: 10.1038/s41467-018-03880-y](https://doi.org/10.1038/s41467-018-03880-y)

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