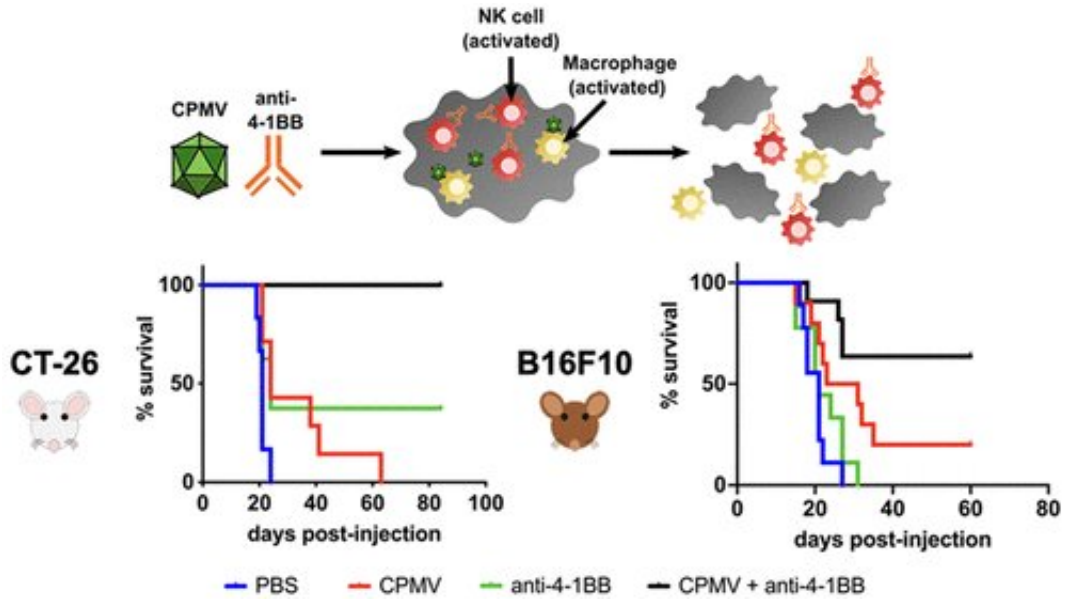
# Plant virus plus immune cell-activating antibody clear colon cancer in mice, prevent recurrence

June 22 2022




Credit: *Nano Letters* (2022). DOI: 10.1021/acs.nanolett.2c01328

A new combination therapy to combat cancer could one day consist of a plant virus and an antibody that activates the immune system's "natural killer" cells, shows a study by researchers at the University of California San Diego.

In mouse models of colon cancer, the combination therapy eliminated all tumors and prevented their recurrence, which in turn resulted in 100%

survival. The therapy also increased survival in mouse models of melanoma.

The work is reported in a paper published June 17 in *Nano Letters*.

The proof-of-concept therapy enhances the activity of cancer killing immune cells known as natural killer cells, which naturally reside in the body and in tumors. The job of natural killer cells is to target and destroy cancer cells—in doing so, they release molecules called antigens that the immune system can recognize and produce antibodies against.

The problem is that there are not enough natural killer cells in or near cancerous tumors to be effective. And those that are in the tumors cannot do their job because cancer cells can secrete molecules that bind to natural killer cells and suppress them.

The therapy overcomes these problems using two key ingredients: cowpea mosaic virus, which is a plant virus that infects legumes but is harmless to animals and humans, and an antibody called anti-4-1BB. Cowpea mosaic virus has a special ability to attract natural killer cells to the tumor microenvironment, while anti-4-1BB binds to receptors on these cells to snap them out of their immunosuppressed state. By joining forces, the plant virus and antibody not only draw a large enough crowd of natural killer cells to the tumors, but also fire them up for attack.

"With a combination therapy, we significantly improve cancer response," said study senior author Nicole Steinmetz, professor of nanoengineering and director of the Center for NanoImmunoEngineering at the UC San Diego Jacobs School of Engineering. "Cancers work by manipulating the body through multiple pathways. When we hit on multiple pathways by combining different therapeutic agents (cowpea mosaic virus and anti-4-1BB), we get better results."

"Nowadays, cancer is not treated with just one medication—it requires a multi-pronged approach. Our work takes advantage of different strategies to activate the innate immune system and destroy tumors. This can then initiate an adaptive immune response to help prevent tumor recurrence," said first author Edward (Ted) Koellhoffer, a resident physician in radiology at UC San Diego Health who is a clinician-scientist in Steinmetz's lab.

The researchers first tested their combination therapy on mouse models of colon cancer. The treatment regimen consisted of one weekly injection of cowpea mosaic virus and two weekly injections of anti-4-1BB. The injections were administered into the abdominal cavities of the mice for three weeks. All mice that were given the combination therapy experienced complete tumor elimination and survived for at least 90 days. When these mice were later rechallenged with colon cancer, any new tumors were also eliminated, and the mice all survived. The researchers also tested cowpea mosaic virus as a solo therapy and while it exhibited potency, the combination therapy demonstrated synergy and outperformed any controls.

"What's remarkable is that the treated mice gain an immunological memory, meaning that their immune systems remember the tumor cells and can attack them on their own when the cancer reappears," said Koellhoffer.

The researchers tested the same treatment regimen on mouse models of melanoma. Again, the combination therapy reduced tumor growth and protected the surviving mice from recurrence of the disease when rechallenged with melanoma.

"While the combination therapy was most impressive in the colon cancer model, improvement was also seen in the melanoma model," said Steinmetz. "Based on the data, more research is needed to understand

whether this therapy is effective against a broad range of cancers, or whether the real potential is for intraperitoneal disseminated disease."

Steinmetz's team plans to explore that further. The researchers hope that their combination therapy will lay the groundwork for an in situ cancer vaccine.

The research paper is titled "Cowpea mosaic virus and Natural Killer Cell Agonism for In Situ Cancer Vaccination."

**More information:** Edward C. Koellhoffer et al, Cowpea Mosaic Virus and Natural Killer Cell Agonism for In Situ Cancer Vaccination, *Nano Letters* (2022). DOI: 10.1021/acs.nanolett.2c01328

Provided by University of California - San Diego