

UMass Amherst Researchers Create Nanoparticle Vaccine That Prevents Cancer in Mice

Vaccine formulation activated T cells, priming them to recognize and attack cancer.

October 13, 2025 By University of Massachusetts Amherst

A study led by University of Massachusetts Amherst researchers demonstrates that their nanoparticle-based vaccine can effectively prevent melanoma, pancreatic and triple-negative breast cancer in mice. Not only did up to 88% of the vaccinated mice remain tumor-free (depending on the cancer), but the vaccine reduced—and in some cases completely prevented—the cancer’s spread.

“By engineering these nanoparticles to activate the immune system via multi-pathway activation that combines with cancer-specific antigens, we can prevent tumor growth with remarkable survival rates,” says [Prabhani Atukorale](#), assistant professor of biomedical engineering in the Riccio College of Engineering at UMass Amherst and corresponding author on the paper.

Atukorale’s [previous research](#) showed that her novel nanoparticle-based drug design can shrink and clear cancer tumors in mice. Now, she’s demonstrated that it can also work preventively.

The first test paired her nanoparticle system with well-characterized melanoma peptides (called an antigen, similar to how a flu shot typically contains parts of the inactivated flu virus). The formulation activated immune cells called T cells, priming them to recognize and attack this type of cancer. Three weeks later, the mice were exposed to melanoma cells.

Eighty percent of these “super adjuvant” vaccinated mice remained tumor-free and survived until the completion of the study (250 days). In comparison, all of the mice vaccinated with traditional vaccine systems, non-nanoparticle formulations or unvaccinated mice developed tumors; none survived longer than 35 days.

The vaccine also protected against the spread of cancer to the lungs. When exposed to melanoma cells systemically, which mimics how cancer metastasizes, none of the nanoparticle-vaccinated mice developed lung tumors, while all of the other mice did.

“Metastases across the board is the highest hurdle for cancer,” says Atukorale. “The vast majority of tumor mortality is still due to metastases, and it almost trumps us working in difficult-to-reach cancers, such as melanoma and pancreatic cancer.”

Atukorale describes this as “memory immunity.” “That is a real advantage of immunotherapy, because memory is not only sustained locally,” she says. “We have memory systemically, which is very important. The immune system spans the entire geography of the body.”

This first test was conducted using a vaccine with well-characterized antigens that matched the type of cancer. However, developing antigens tailored to different cancers requires whole-genome sequencing or complex bioinformatics screening. So, for the second part of the study, the researchers used killed cancer cells derived directly from the tumor mass, called tumor lysate. After vaccination with the nanoparticle lysate vaccine, the mice were then exposed to melanoma, pancreatic ductal adenocarcinoma or triple-negative breast cancer cells.

The tumor rejection rates were striking: 88% of mice for pancreatic cancer, 75% of mice for breast cancer and 69% of mice for melanoma rejected tumors. Of these tumor-free, nanoparticle-vaccinated mice, all of them remained tumor-free when the researchers tested if the cancer would metastasize, given systemic exposure.

“The tumor-specific T-cell responses that we are able to generate—that is really the key behind the survival benefit,” says Griffin Kane, postdoctoral research associate at UMass Amherst and first author on the paper. “There is really intense immune activation when you treat innate immune cells with this formulation, which triggers these cells to present antigens and prime tumor-killing T cells.”

This robust T-cell response is possible because of the particular nanoparticle design of the vaccine.

Vaccines—regardless the target disease—contain two primary components: The antigen and the adjuvant. The antigen is the piece of the disease-causing pathogen (in this study, cancer cells) that the immune system can be trained to target. The adjuvant is a substance that activates the immune system to recognize the antigen, treat it as a foreign intruder and eliminate it.

The Atukorale Lab draws inspiration from how pathogens naturally stimulate the immune system. To mount a strong immune response, the body requires multiple “danger” signals triggered through different pathways. “In recent years, we have come to understand how important the selection of the adjuvant is because it drives the second signal that is needed for the correct priming of T and B cells,” says Atukorale.

However, just like oil and water, many of the most promising adjuvants for cancer immunotherapy do not mix well at the molecular level. To overcome this, the Atukorale Lab has engineered a lipid nanoparticle-based “super adjuvant” capable of stably encapsulating and co-delivering two distinct immune adjuvants that activate immunity in a coordinated, synergistic way.

The researchers say that their design offers a platform approach that could be used across

multiple cancer types.

The researchers envision that this platform can be applied to create both therapeutic and preventative regimens, particularly for individuals at high risk for cancer. This is an idea that Atukorale and Kane have turned into a startup called NanoVax Therapeutics.

“The real core technology that our company has been founded on is this nanoparticle and this treatment approach,” says Kane. “This is a platform that Prabhani developed. The startup lets us pursue these translational efforts with the ultimate goal of improving patients’ lives.”

Next, Atukorale and Kane plan to extend this technology to a therapeutic vaccine and have already taken the initial de-risking steps in translation.

Atukorale and Kane credit the Biomedical Engineering department and the Institute for Applied Life Sciences at UMass Amherst, UMass Chan Medical School, and funding from the [National Institutes of Health](#) for their support.

The study was published in the October 9 edition of [Cell Reports Medicine](#).

This [news release](#) was published by the University of Massachusetts Amherst on October 9, 2025.

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