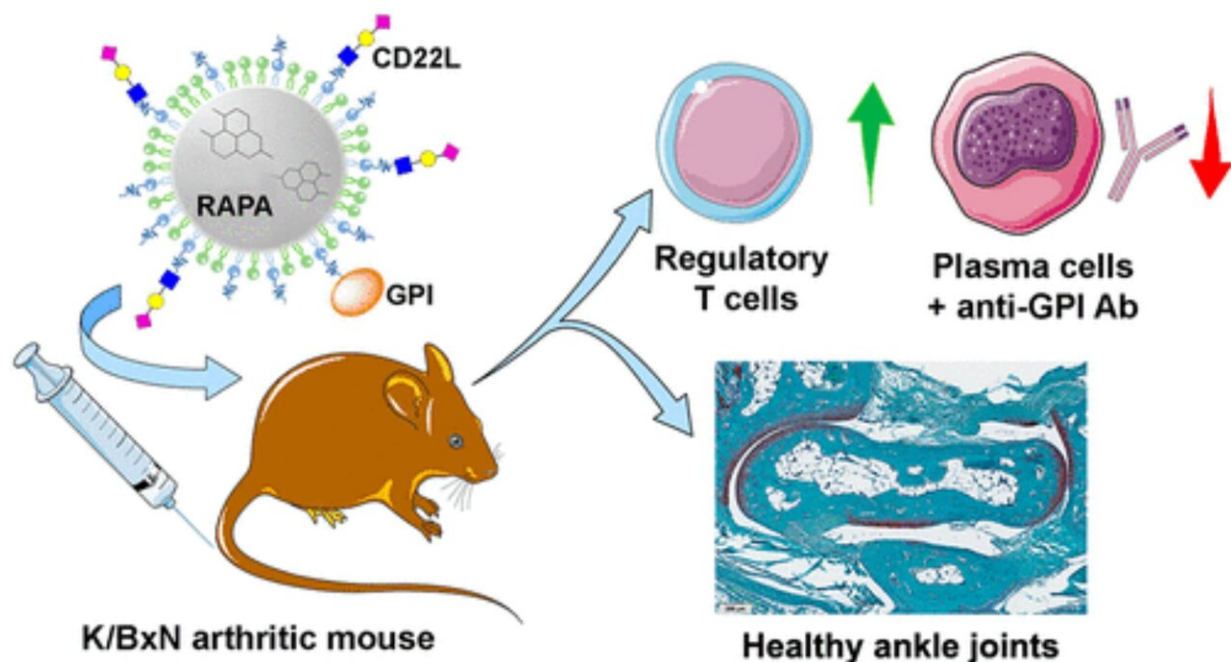


Nanotech strategy shows promise for treating autoimmune disease

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Graphical abstract. Credit: *ACS Nano* (2022). DOI: 10.1021/acsnano.2c05643

Scientists at Scripps Research have reported success in initial tests of a new, nanotech-based strategy against autoimmune diseases.

The scientists, who reported their results in *ACS Nano*, engineered cell-like "[nanoparticles](#)" that target only the [immune cells](#) driving an autoimmune reaction, leaving the rest of the immune system intact and

healthy. The nanoparticles greatly delayed, and in some animals even prevented, [severe disease](#) in a mouse model of arthritis.

"The potential advantage of this approach is that it would enable safe, long-term treatment for [autoimmune diseases](#) where the immune system attacks its own tissues or organs—using a method that won't cause broad immune suppression, as current treatments do," says study senior author James Paulson, Ph.D., Cecil H. and Ida M. Green Chair of Chemistry in the Department of Molecular Medicine at Scripps Research.

Autoimmune diseases such as [rheumatoid arthritis](#) are caused when the immune system mistakenly attacks a person's own tissues or organs. These illnesses affect an estimated 10 million people in the U.S. alone. Treatments are available and can be effective for many patients, but they tend to suppress the immune system indiscriminately, creating an enhanced susceptibility to infections and cancers—among other side effects.

Paulson and his team have taken an approach that targets the immune system more narrowly. Many autoimmune diseases are triggered or driven by immune attacks on just one protein in the patient's body, known as a "self-antigen."

The idea underlying the nanoparticle strategy is to eliminate or deactivate only the immune cells that attack that self-antigen—an approach that could be at least as effective as broad immune suppression, without the side effects. Autoimmune diseases that are dominated by immune responses to a single self-antigen include some forms of arthritis, the skin blister disease known as pemphigus and the thyroid ailment Graves' disease.

The researchers, including first author Katarzyna Brzezicka, Ph.D., a postdoctoral research associate in the Paulson lab, research assistant

Britni Arlian, and other lab members, designed nanoparticles that could deactivate two types of immune cells: B cells and T cells.

On its surface, each nanoparticle bore copies of a target self-antigen, plus a sugar-related molecule that can bind to a special "off switch" receptor on B cells called CD22. B cells, which make antibodies and are specific to different antigens, will effectively shut themselves off if they encounter both the particular antigen they target and the binding partner of CD22 at the same time.

Each nanoparticle also was laced with a powerful compound called rapamycin to stimulate the production of immune cells called regulatory T cells. T_{reg} cells, as they're also known, are responsible for suppressing other T cells needed to generate an autoimmune attack. The overall aim of the study was to effectively knock out only the B and T cells that recognize the self-antigen, leaving the rest of the B- and T-cell populations intact.

The researchers first demonstrated that their nanoparticle-based strategy could tolerize the mouse immune system to a chicken protein, ovalbumin, that would otherwise trigger a strong response. Next, they tested the strategy in a widely used mouse model of arthritis, in which the mouse [immune system](#) is genetically predisposed to attack a self-antigen called GPI.

The scientists showed that treatment of the mice with GPI-tolerizing nanoparticles at the age of three weeks greatly delayed the development of arthritis signs that would normally appear a week or two later. In fact, about a third of the mice remained arthritis-free for the maximum follow-up period of 300 days. Tests confirmed that the treatment dramatically reduced the mice's production of anti-GPI antibodies, and at the same time boosted their T_{reg} populations.

Paulson says his team plans to follow up these highly promising results with further optimization of the nanoparticle strategy.

"We were able to 'cure' a third of these animals in this early demonstration, and I think there's the potential to combine our nanoparticles with other immune modulator treatments to make it even more effective," Paulson says. "So that will our next step—as well as demonstrating our technology against other autoimmune diseases caused by unwanted immune responses to a self-antigen."

More information: Katarzyna A. Brzezicka et al, Suppression of Autoimmune Rheumatoid Arthritis with Hybrid Nanoparticles That Induce B and T Cell Tolerance to Self-Antigen, *ACS Nano* (2022). [DOI: 10.1021/acsnano.2c05643](https://doi.org/10.1021/acsnano.2c05643)

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