

Cow immune system inspires potential new therapies

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To help people with hormone deficiencies, scientists at The Scripps Research Institute (TSRI) have developed a potential new therapy based on an unlikely model: immune molecules from cows.

Their research, published recently in the journal *Proceedings of the National Academy of Sciences*, shows that human hormones and antibodies can be fused together—mimicking long, stalk-like cow [antibodies](#).

The new study, whose senior authors were Peter Schultz, the Scripps Family Chair Professor at TSRI, and Feng Wang, a principal investigator at the California Institute for Biomedical Research (Calibr), could also provide the foundation for treatments for a range of other diseases.

"We were inspired by this unique structure found in nature, and we assembled an antibody that might one day benefit humans," said TSRI Research Associate Tao Liu, co-first author of the new study with Yong Zhang at Calibr.

Many people need injections of [human growth hormone](#) (hGH) to combat conditions such as Turner syndrome (which causes short stature in females), low birth weight and other [hormone](#) deficiencies. Unfortunately, the body degrades hGH quickly, sometimes within 30 minutes.

"This means people need to inject themselves every day," explained Liu.

"For a kid, that's really painful—and for a drug, that's really bad."

Antibodies, however, can last for weeks in the body. In the new study, the researchers drew inspiration from a bovine antibody study published by TSRI scientists in 2013. The bovine antibody has an unusual structure—a round base with a long amino-acid "stalk" pointing out. On the top of the stalk is a "knob region" that presumably binds to pathogens.

The researchers wondered whether they could switch the knob region with DNA from a human hormone, such as hGH. To test this theory, they used recombinant DNA technology to fuse hGH to a coiled version of the bovine antibody's stalks.

This fusion was stable and maintained the function of hGH, so they next tried making an antibody-hormone molecule without any cow DNA, so that the [molecules](#) might someday be applied in human therapy. They used the humanized anti-cancer antibody Herceptin as the antibody base in the new treatment.

The researchers then tested their antibody-hGH molecule in rat models. They found that hGH-deficient rats that received the treatment grew normally. In fact, the treated rats only needed injections two times a week to grow, compared with daily injections for rats given hGH without the antibody base.

"It acts just like the normal growth hormone," said Liu. "This means the treatment might only need to be injected once a week or even once a month in humans. It would be so much easier for patients."

To further test their method, the researchers attached Herceptin to leptin, a hormone that regulates body weight. They showed that the antibody-leptin molecule was just as effective in mice as natural

leptin—and it didn't have to be injected as often. Subsequent experiments showed no harmful side effects from the treatments.

The research team is working to optimize the treatment for potential use in humans, and Liu hopes the method could someday deliver longer-lasting doses of hGH—or maybe even insulin to treat type 2 diabetes—to patients in need.

More information: Liu, Zhang, Schultz, Wang et al "Functional human antibody CDR fusions as long-acting therapeutic endocrine agonists," *Proceedings of the National Academy of Sciences*, vol. 112 no. 5, 1356–1361, [DOI: 10.1073/pnas.1423668112](https://doi.org/10.1073/pnas.1423668112)

Provided by The Scripps Research Institute

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