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Scientists test potential new way to treat anemia

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Treatment of anemia caused by chronic kidney disease or other diseases often requires repeated—and costly—injections or infusions of an artificial form of the hormone erythropoietin (EPO), which stimulates production of red blood cells.

Now a Vanderbilt-led research team has shown they can reverse anemia in mice by injecting a kind of white blood cell called a T-cell that has been genetically engineered to secrete EPO.

When the initial injection is followed by "booster shots" of antigens that cause the T-cells to proliferate and expand, they remain in the bloodstream for several weeks. Human T-cells grown in the laboratory also can be genetically modified to secrete EPO, the researchers reported April 10 in the journal *Nature Communications*.

While further study is necessary before this approach can be tested in patients, the findings suggest that delivery of therapeutic molecules via T-cell "trucks" may be an effective way to treat anemia and other disorders. Researchers have been trying for several years to develop alternative methods of administering hormones like EPO.

"This is an important study as it shows that T cells can be genetically modified to serve as vehicles to deliver therapeutic proteins in a live animal," said Matthew Wilson, MD, Ph.D., associate professor of Medicine at Vanderbilt and the paper's corresponding author.

"We found that we could 'boost' T-cells even 300 days after their delivery to an animal," Wilson said. "This allowed us to use EPO as a model system for therapy of a disease, in our case anemia of chronic kidney disease."

Previous studies have shown that segments of the DNA can be moved—or transposed—into T-cells to allow insertion of new genetic material. T-cells have been reprogrammed in this way to identify and destroy cancer cells in patients with leukemia or lymphoma.

The study by Wilson and his colleagues suggests that a similar "transposon system" could be used for long-term cellular delivery of therapeutic peptides. These are protein fragments that have shown promise in treating type 2 diabetes, heart disease, hormone deficiencies and other disorders.

A major limitation is that peptides are broken down and rapidly excreted by the body and they don't travel well through biological membranes. T-cells modified to produce and deliver disease-altering cargos to their target cells may be a way to solve this problem.

More information: Richard T. O'Neil et al. Transposon-modified antigen-specific T lymphocytes for sustained therapeutic protein delivery in vivo, *Nature Communications* (2018). DOI: 10.1038/s41467-018-03787-8

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