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OUTFOXING

MUTATED GENES

FOCUS: Genetically modified T cells to treat autoimmune disorders.

Regulatory T cells (Tregs) are key regulators of the immune response, and defects in their numbers or function are tied to several autoimmune diseases. Dr. Bacchetta and her team are developing a novel method wherein a patient's T cells turn into functional Tregs by gene addition, which could become a landmark approach to controlling many immune-mediated diseases. To prove this concept, their work is focused on a Treg cell therapeutic for IPEX syndrome, a rare disease inherited in males.

IPEX manifestations include severe diarrhea, eczema, enlargement of lymph nodes, and type 1 diabetes. Untreated, the disease is usually fatal during the first year of life. Bone marrow transplantation can be curative but is not always available; pharmacological immune suppression can prolong life and decrease some symptoms, but current treatments usually have unsatisfactory outcomes.

IPEX is caused by mutations of FOXP3, a key gene involved in immune regulation. IPEX patients' Tregs cannot properly control the immune system responses and lose the ability to distinguish what is or is not worth fighting for to maintain health.

"The idea is to provide the functional Tregs IPEX patients are missing by inserting a normal FOXP3 gene into their T cells, then infusing them back into the patient," Dr. Bacchetta says. "This work will also provide data which could broaden this Treg cell therapy to more common immune-mediated diseases, where patients have Treg cell defects not caused by FOXP3 mutations."

"Our Harrington team has provided crucial support, such as helping us complete the preclinical work and providing precious regulatory and strategic advice to define the clinical protocol."

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