

# New form of interleukin-2 could be fine-tuned to fight disease

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Scientists are reporting development of a new way to modify interleukin-2 (IL-2), a substance known as a cytokine that plays key roles in regulating immune system responses, in order to fine-tune its actions. Harnessing the action of IL-2 in a controllable fashion is of clinical interest with potential benefit in a range of situations, including transplantation and autoimmune disease. The modified IL-2 molecules inhibited the actions of endogenous IL-2, potentially more effectively than existing agents, as well as inhibited the actions of another interleukin, IL-15, with additional therapeutic potential.

The research is published in the journal *Immunity*.

The principal research teams include scientists from the National Heart, Lung, and Blood Institute (NHLBI), Stanford University, and the Howard Hughes Medical Institute, with contributions from other scientists at the National Cancer Institute, and the National Institute of Allergy and Infectious Diseases. Co-senior authors of the paper were Warren J. Leonard, M.D., chief of the Laboratory of Molecular Immunology and director of the Immunology Center at NHLBI, and K. Christopher Garcia, Ph.D., professor, Stanford University School of Medicine, and investigator, Howard Hughes Medical Institute

The scientists developed altered forms of IL-2 where activity can be tuned to either boost or block immune responses depending on the desired therapeutic application. In laboratory studies, treatment with one type of modified IL-2 prolonged survival in a mouse model of graft-

versus-host disease and blocked the growth in vitro of T-cells from a patient with chronic/smoldering adult T-cell leukemia, a rare form of cancer, they note. A similar approach could potentially be used to engineer other immune-system cytokines to generate new molecules with therapeutic potential, the scientists say. The research was funded in part through NIH grant numbers R01AI051321 and F30DK094541.

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