Decades-old immunosuppressant drug rapamycin could extend life

In the 1990s, pharmacologist <u>Dave Sharp</u> of the University of Texas's Barshop Institute for Longevity and Aging Studies in San Antonio was studying mice with pituitary dwarfism—a condition in which the pituitary gland fails to make enough growth hormone for normal development. The puzzle, Sharp explains, was that research had shown that these hormone-deficient dwarf mice lived longer than normal mice. "I wondered, why is being small connected with longer life?" he says.

Yeast research led by molecular biologist Michael Hall at the University of Basel in Switzerland was to provide Sharp with an unexpected lead. In 1996, a team led by Hall (who would go on to win a Lasker award in 2017 for the work) revealed a new intracellular signaling pathway, mediated by the protein targets of a compound called rapamycin.

Rapamycin, a compound first identified in the 1970s in a soil sample from Easter Island, has been used for decades to suppress the immune system in transplant patients; it seemed counterintuitive that it could prolong life, [pharmacologist Dave] Sharp notes. "Nobody would read my proposals," he says. "They'd just laugh. You know, 'An immunosuppressant extending lifespan?" But research since then has lent support to Sharp's theory.

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