RAPAMYCIN

The Science of Longevity · mTOR Inhibition · Healthspan Extension

Discovered in the soil of Easter Island. Validated across decades of research.
Now at the forefront of the science of healthy aging.

36%
lifespan increase
in male mice
(NIA ITP)

1972
year of discovery
Isolated from Streptomyces

60+
clinical trials
across multiple indications

~5mg
weekly dose
Common longevity protocol

mTOR INHIBITION

Rapamycin selectively inhibits mTORC1, the master regulator of cell growth, protein synthesis, and autophagy — the cellular recycling process central to aging.

IMMUNE MODULATION

At low doses, rapamycin reshapes immune function, improving vaccine responses in older adults and reducing markers of immunosenescence.

AUTOPHAGY ACTIVATION

By suppressing mTOR, rapamycin powerfully induces autophagy — clearing damaged proteins and organelles, a hallmark of cellular rejuvenation.

> "Rapamycin is the most robust intervention ever discovered to extend lifespan in mammals."
>
> — Dr. David Sabatini, Whitehead Institute / MIT, pioneer of mTOR biology

ORIGIN: RAPA NUI

In 1972, Canadian biochemist Suren Sehgal isolated a remarkable compound from *Streptomyces hygroscopicus* bacteria found in soil samples collected on Easter Island (Rapa Nui). Initially studied as an antifungal agent, rapamycin was later found to possess potent immunosuppressive and antiproliferative properties — and ultimately, extraordinary longevity-extending effects in every organism tested.

1972 — Isolated from Easter Island soil

1999 — FDA approval (transplant)

2009 — ITP: +9–14% lifespan in mice

2020 — Human longevity trials begin

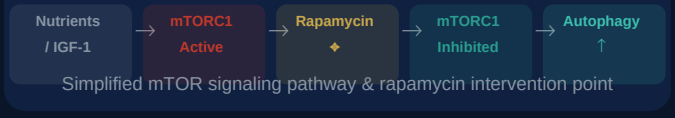
2025 — Expanding clinical evidence

Mechanism, Evidence & Application

HOW IT WORKS: THE mTOR PATHWAY

mTOR (mechanistic Target Of Rapamycin) is a serine/threonine kinase that serves as a master controller of cell metabolism, growth, and survival. Overactivation of mTOR — driven by nutrient excess, insulin signaling, and aging itself — accelerates the hallmarks of aging including cellular senescence, loss of proteostasis, and mitochondrial dysfunction.

Rapamycin binds to FKBP12, forming a complex that directly inhibits mTORC1 activity. This brake on mTOR suppresses anabolic processes and powerfully activates **autophagy** — the cell's self-cleaning program — enabling clearance of damaged proteins, aggregates, and dysfunctional organelles.



Simplified mTOR signaling pathway & rapamycin intervention point

KEY DOCUMENTED EFFECTS

- **Lifespan Extension:** Up to 36% in male mice when started late in life (NIA ITP, 2016).
- **Immune Rejuvenation:** 20% improvement in influenza vaccine response in elderly humans (Mannick et al., 2014).
- **Cardiac Protection:** Reversal of age-related cardiac hypertrophy and restored function in mice.
- **Cognitive Preservation:** Improved memory and reduced amyloid burden in Alzheimer's models.
- **Cancer Prevention:** Reduced tumor incidence across multiple animal model studies.
- **Metabolic Benefits:** Improved insulin sensitivity and reduced visceral adiposity in some models.

SAFETY CONSIDERATIONS

At immunosuppressive doses (transplant medicine), rapamycin carries meaningful side effect risks. However, at the much lower intermittent doses explored in longevity protocols — typically 5–6 mg once weekly — the adverse effect profile appears substantially more favorable. Reported concerns at low doses include: mouth sores (aphthous ulcers), mild lipid changes, and potential effects

LANDMARK CLINICAL EVIDENCE

TAME Trial (2024–)

NIH-funded landmark trial targeting aging biology directly. Tests metformin as first aging drug, with rapamycin trials closely following the framework.

Mannick et al. (2014)

Novartis study: RAD001 (everolimus, rapamycin analog) improved vaccine response in adults 65+, providing first human evidence of immune rejuvenation.

NIA ITP Studies

Independent testing program confirmed lifespan extension across genetically diverse mouse strains — even when rapamycin was started at 20 months (equivalent to ~60 human years).

PEARL Trial (2024)

First dedicated human longevity trial of rapamycin in healthy older adults, measuring biomarkers of aging, immune function, and physical performance.

AI-RAPA Study

Ongoing investigation of rapamycin in age-related macular degeneration — another indication leveraging its anti-inflammatory and autophagy-promoting properties.

COMMON LONGEVITY DOSING PROTOCOLS

5–6 mg	10 mg	Variable
Weekly Pulse	**Biweekly**	**Physician-Guided**
Once per week oral	Every two weeks	Personalized based on bloodwork

WHO IS EXPLORING RAPAMYCIN?

A growing cohort of longevity-focused physicians, researchers, and health-optimizing individuals are exploring low-dose rapamycin as an off-label intervention. Notable figures include **Dr. Peter Attia** (author of *Outlive*), **Dr. Matt Kaeberlein** (University of Washington aging researcher), and **Dr. Alan Green** — who has prescribed rapamycin to hundreds of patients in an observational longevity practice since 2013. The **Dog Aging Project** also conducted the first placebo-controlled trial of rapamycin in companion dogs, showing improved cardiac function with minimal adverse effects.

Work with a longevity-informed physician to evaluate rapamycin for your protocol.

Biomarker testing · Risk stratification · Ongoing monitoring · Personalized dosing