Rapamycin for CFS and anti-aging

Table of Contents

Executive Summary

Background: Rapamycin a.k.a. sirolimus (brand name Rapamune among others) was discovered in soil samples from Easter Island (Rapa Nui) in the early-mid ‘70s being a compound produced by the bacteria *Streptomyces hygroscopicus.* Originally considered an antifungal, it was later found to suppress the immune system and inhibit the mammalian target of rapamycin (mTOR), a pathway that was itself discovered due to the drug. In the 1990s it was approved by the FDA for immunosuppression for renal (kidney) transplant patients and, later, as an adjunctive therapy for some cancers.

In 2009 the Intervention Testing Program (ITP) showed rapamycin increased maximal lifespan in both male (by 9%) and female (by 14%) mice when given late in life. Subsequent studies have shown even greater lifespan extension when started earlier (up to 26-29%).

Dosing: Rapamycin dosing for anti-aging is a matter of debate but according to surveys is usually in the 3-10 mg range once per week, most commonly 5 or 6 mg once per week. Immunosuppressant dosing is 2-5 mg / d.

Benefits (animals): In summary rapamycin can reduce the rate of aging, improve age-related diseases by inhibiting the mTOR pathway, and prolong lifespan and healthspan effectively.

Immune: Expands viral specific memory CD8+ T cells in addition, RAPA exposure is reported to skew the CD4+ T cell compartment, with a decrease in pro-inflammatory TH1 and TH17 subsets. This is consistent with the reported efficacy of RAPA in suppressing autoimmunity in rodents. However, it may also explain the increased susceptibility of treated mice infected with West Nile virus.

Benefits (humans): Trials on healthy adults have only been done in the elderly so far. One trial using the rapalog Everolimus (Mannick et al.) showed improved immune response to a flu vaccine and a decrease in viral illness a year afterwards, suggesting a reversal of immunosenescence. Another 8-week study showed no benefit in physical or cognitive measures but some decreases in red blood cell markers (Kraig et al.). There have been numerous studies showing a decrease in cancer, although some higher dose studies have shown the opposite.

It has been shown to suppress autoimmunity (type I diabetes, multiple sclerosis, etc.). In transplant patients fewer skin cancers, non-Hodgkin’s lymphomas, viral infections, and reduced cardiac allograft vasculopathy has been seen.

Anecdotally there are reports of rapamycin improving/resolving CFS, reducing muscle and joint pain, reducing inflammation, and improvements in strength and body composition.

Side effects: Anti-aging reports: Mouth and lip ulcers (canker sores). Other side effects include herpes simplex (HSV) reactivation and epstein-barr virus (EBV) reactivation, subcutaneous bacterial infections, glucose dysregulation (pre-diabetes/diabetes), lipid dysregulation, growth of skin tags, and headaches. In a forum poll nearly half (47%) didn’t have any noticeable side-effects

Clinical trials (lower dose: note no clinical trial uses the once per week dosing, generally they use daily dosing 1-1.5 mg): GI issues, mouth ulcers, facial acne rash, menstrual cycle disturbances, ovarian cysts, and decreased red blood cell markers (Hb, HCT, RBC, RDW, MCV, MCH).

Clinical trials all (typically higher dose): leukopenia, thrombocytopenia, hypertriglyceridemia, hypercholesterolemia, aphthous ulcers, edema, arthralgia, interstitial pneumonia, acne, delayed wound healing, sinus tachycardia, decreased renal function, gastrointestinal toxicity, rash, ovarian cyst, infections, mild oral mucositis; sinus tachycardia; elevated creatinine, transaminase; and thrombocytopenia [low blood platelets].

Peer-reviewed Research

Reviews

Zhang et al. S. (2021). The Role of Rapamycin in Healthspan Extension via the Delay of Organ Aging. [1]

- The activation of mammalian target of rapamycin (mTOR) signaling is one of the core and detrimental mechanisms related to aging; **rapamycin can reduce the rate of aging, improve age-related diseases by inhibiting the mTOR pathway, and prolong lifespan and healthspan effectively.**
- Low-dose oral rapamycin increased the risk of menstrual cycle disturbances and ovarian cysts (Braun et al., 2012, RCT, n=39, 1.5 mg/d, 18 mths).
- A human study that estimated the efficacy and adverse effects of rapamycin on refractory/relapsed acquired pure red cell aplasia indicated tolerable adverse effects that included infections; mild oral mucositis; sinus tachycardia; elevated creatinine, transaminase, triglyceride, or cholesterol; and thrombocytopenia (Long et al., 2018, open-label, n=31, 1-3 mg/day, 6-24 mths).
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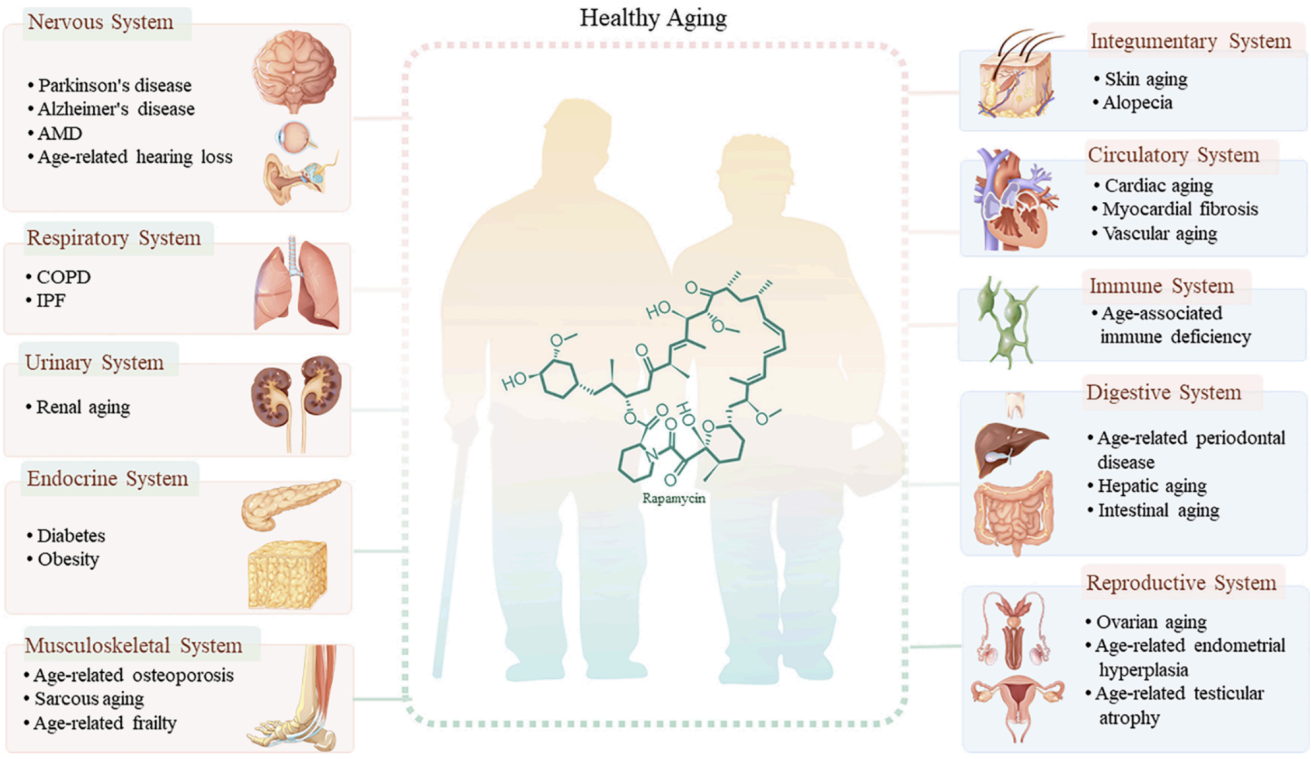

Fig. 2. The overall view of rapamycin in promoting healthy aging by attenuating aging in multiple organs.

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[1] https://sci-hub.se/10.1016/j.arr.2021.101376

Blagosklonny M. V. (2019). Rapamycin for longevity: opinion article. [2]

- 20 years ago, it was labeled an immunosuppressant and used to treat renal transplant patients. If rapamycin had been labeled an immunomodulator and anti-inflammatory drug instead, it would sound much more appealing now.
- At anti-aging doses, rapamycin "eliminates hyperimmunity rather than suppresses immunity" or, more figuratively, it "rejuvenates immunity" . This enables rapamycin and everolimus, a rapamycin analog, to act as immunostimulators, improving immunity in cancer patients and the elderly.
- For example, rapamycin reduces the risk of CMV infection in organ transplant patients, improves antipathogen and anticancer immunity in mice, prolongs lifespan in infection-prone mice and protects aged mice against pneumonia. Rapamycin also inhibits viral replication.
- As a noteworthy example, rapamycin inhibits replication of the 1918 flu virus (the deadliest flu virus in history) by 100-fold, and also protects against lethal infection with influenza virus when administered during vaccination.
- Still, as Dr. Allan Green (https://rapamycintherapy.com) advises, patients taking rapamycin should be carefully monitored for skin and subcutaneous bacterial infections, which should be treated with antibiotics.

Human Clinical Studies

Mannick et al. (2018). TORC1 inhibition enhances immune function and reduces infections in the elderly. [3] Level A: RCT, n=264, > 65 YO, 6 weeks, Everolimus

- Inhibition of the mechanistic target of rapamycin (mTOR) protein kinase extends life span and ameliorates aging-related pathologies including declining immune function in model organisms.
- The objective of this phase 2a randomized, placebo-controlled clinical trial was to determine whether low-dose mTOR inhibitor therapy enhanced immune function and decreased infection rates in 264 elderly subjects given the study drugs for 6 weeks.
- A low-dose combination of a catalytic (BEZ235) plus an allosteric (RAD001) mTOR inhibitor that selectively inhibits target of rapamycin complex 1 (TORC1) downstream of mTOR **was safe and was associated with a significant** (P = 0.001) **decrease in the rate of infections reported by elderly subjects for a year after study drug initiation.**
- In addition, **we observed an up-regulation of antiviral gene expression and an improvement in the response to influenza vaccination** in this treatment group.
- Thus, selective TORC1 inhibition has the potential to improve immune function and reduce infections in the elderly.

Kraig et al. (2018). A randomized control trial to establish the feasibility and safety of rapamycin treatment in an older human cohort: Immunological, physical performance, and cognitive effects. [4] Level A: RCT, n=11 (rapamycin) n=14 (controls) (70-95 YO)
Dose: 1 mg rapamycin / day, 4 months / 8 weeks

- Side effects (rapa): acneiform facial rash (1), stomatitis [mouth ulcer] (1), GI issues (2)
- Side effects (control): stomatitis (1)
- Blood parameters (rapa): ↓ Hb, HCT, RBC, RDW, MCV, MCH
- Cognitive tests: no change
- Physical tests: no change

[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6814615/
[3] https://sci-hub.se/10.1126/scitranslmed.aaq1564
[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5869166/

- Immune parameters: largely unchanged as well, possibly due to the advanced ages of the cohort. RAPA-associated increases in a myeloid cell subset and in TREGS were detected, but changes in most other PBMC cell subsets were not statistically significant.
- Importantly, the OGTTs revealed no RAPA-induced increase in blood glucose concentration, insulin secretion, and insulin sensitivity.
- Thus, based on the results of our pilot study, it appears that **short-term RAPA treatment can be used safely in older persons who are otherwise healthy**; a larger trial with a larger samples size and longer treatment duration is warranted.

Pinchera et al. (2022). mTOR Inhibitor Use Is Associated With a Favorable Outcome of COVID-19 in Patients of Kidney Transplant: Results of a Retrospective Study. [5] Level B

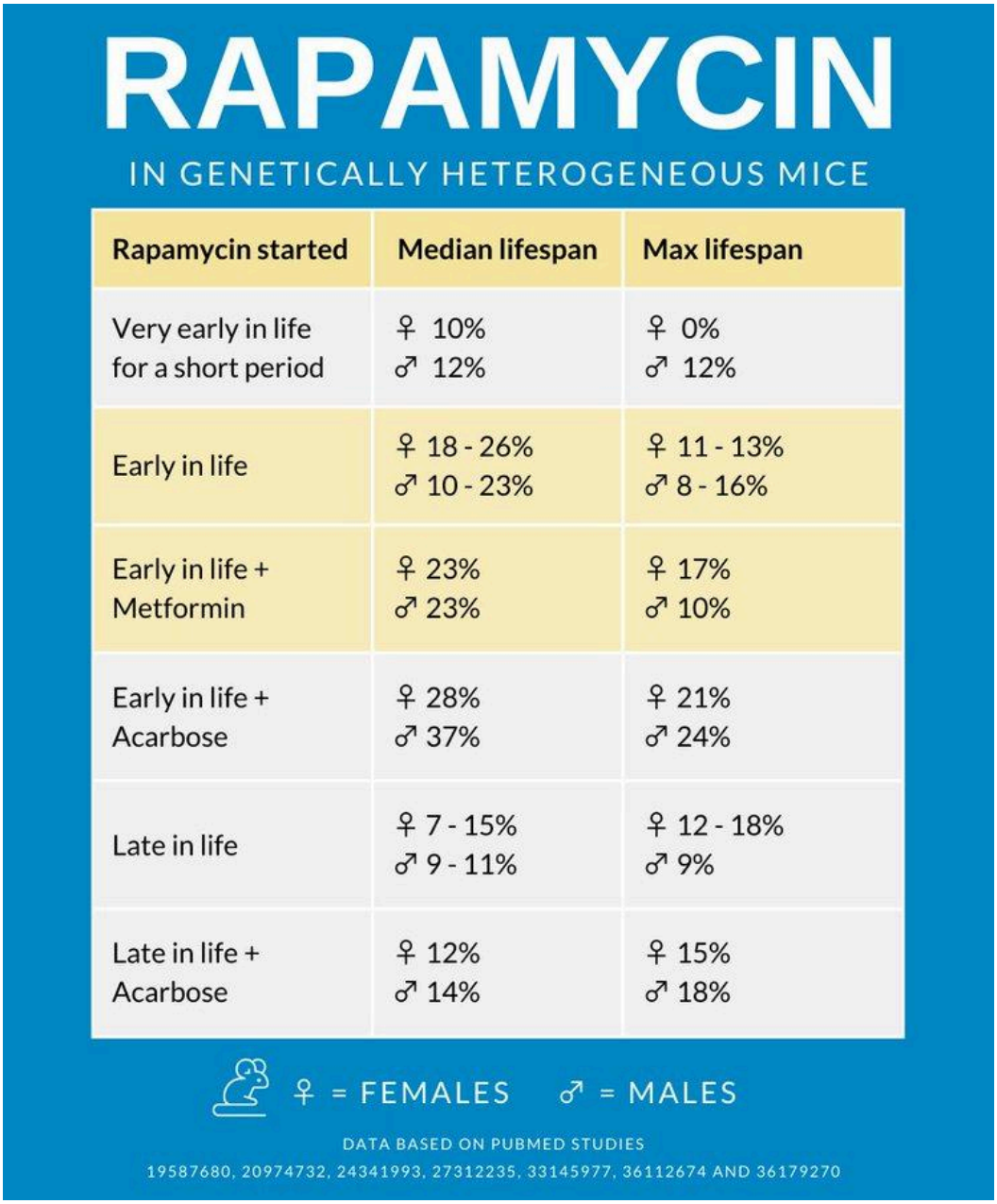
- We enrolled 371 patients, of whom 56 (15.1%) contracted SARS-CoV-2 infection during the period of the study.
- There were no differences observed among the different immunosuppressive therapies concerning the risk of acquiring SARS-CoV-2 infection.
- In contrast, the type of immunosuppressive therapy had a significant impact on the outcome of the disease.
- In detail, **patients who received mTOR inhibitors**, as part of their immunosuppressive therapy, compared to other regimens **had a lower chance of developing a moderate or severe form of the disease** (OR = 0.8, 95, CI: (0.21–0.92), P = 0.041).

Cancer Reduction Studies

https://www.rapamycin.news/t/rapamycin-for-cancer-prevention/1254/9

[5] *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9254357/*

Animal Studies



[6]

Ham et al. (2022). Distinct and additive effects of calorie restriction and rapamycin in aging skeletal muscle. [7]

- Preserving skeletal muscle function is essential to maintain life quality at high age.
- Calorie restriction (CR) potently extends health and lifespan, but is largely unachievable in humans, making “CR mimetics” of great interest.
- CR targets nutrient-sensing pathways centering on mTORC1. The mTORC1 inhibitor, rapamycin, is considered a potential CR mimetic and is proven to counteract age-related muscle loss.

[6] https://twitter.com/KristerKauppi/status/1576245751532777472
[7] https://www.nature.com/articles/s41467-022-29714-6

- Therefore, we tested whether rapamycin acts via similar mechanisms as CR to slow muscle aging. Here we show that long-term CR and rapamycin unexpectedly display distinct gene expression profiles in geriatric mouse skeletal muscle, despite both benefiting aging muscles.
- Furthermore, CR improves muscle integrity in mice with nutrient-insensitive, sustained muscle mTORC1 activity and rapamycin provides additive benefits to CR in naturally aging mouse muscles.
- We conclude that rapamycin and CR exert distinct, compounding effects in aging skeletal muscle, thus opening the possibility of parallel interventions to counteract muscle aging.

Selvarani et al. (2021). Effect of rapamycin on aging and age-related diseases-past and future.
Level B: Review

- The current mouse data conclusively demonstrate that rapamycin is **effective in preventing/reversing a broad range of age-related conditions, including lifespan with minimal adverse effects or toxicity.**
- However, there is always a concern as to how well discoveries in mice translate to humans.
- …Salmon's group recently reported that 9 months of rapamycin treatment had minor effects on clinical laboratory markers (e.g., plasma levels of glucose, cholesterol, triglycerides, and C-reactive protein did not change significantly) in middle-aged male or female marmosets.
- The side effects of rapamycin in humans are well established, e.g., ulcers of mouth and lips, hyperglycemia/diabetes, hyperlipidemia, and hypercholesterolemia [CR - in high doses]
- Mannick et al, 2018 (see above) found that the rapalog, RAD001, was safe when given to subjects ≥ 65 years of age for 6 weeks; the RAD001-treated group actually showed improved response to influenza vaccination and reduced infections. In a pilot study with subjects 70 to 95 years of age who were otherwise healthy
- Kraig et al.[8] found that 8 weeks of rapamycin was safely tolerated, e.g., the subjects showed no changes in cognitive or physical performance and in self-perceived health status. Importantly, **they found that rapamycin had no significant effect on glucose tolerance or plasma triglyceride levels**.
- Transplant patients receiving immunosuppressant regimes containing rapamycin have been reported to become diabetogenic and have increased blood triglyceride levels. However, as Dumas and Lamming (2019) have pointed out, when taking rapamycin to treat human conditions related to aging, the side effects and the risk-benefit trade-off need to be considered. For example, the side effects are viewed as acceptable in treating cancer and would be acceptable in treating Alzheimer's disease because there is currently no effective treatment.

Tateda et al. (2017). Rapamycin suppresses microglial activation and reduces the development of neuropathic pain after spinal cord injury. [9]

- The rapamycin treatment significantly improved not only locomotor function, but also mechanical and thermal hypersensitivity in the hindpaws after spinal cord injury (SCI).
- These results indicated rapamycin administration in acute phase to reduce secondary neural tissue damage can contribute to the suppression of the microglial activation in the lumbar spinal cord and attenuate the development of neuropathic pain after SCI.
- **The present study first demonstrated that rapamycin has significant therapeutic potential to reduce the development of neuropathic pain following SCI.**

[8] *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5869166/*
[9] https://pubmed.ncbi.nlm.nih.gov/27279283/

An et al. (2020). Rapamycin rejuvenates oral health in aging mice.

- The FDA-approved drug rapamycin slows aging and extends lifespan in multiple organisms, including mice.
- Here, we demonstrate that short-term treatment with rapamycin rejuvenates the aged oral cavity of elderly mice, including regeneration of periodontal bone, attenuation of gingival and periodontal bone inflammation, and revertive shift of the oral microbiome toward a more youthful composition.
- This provides a geroscience strategy to potentially rejuvenate oral health and reverse periodontal disease in the elderly.

Harrison et al. (2009). Rapamycin fed late in life extends lifespan in genetically heterogeneous mice. [10]

- Inhibition of the TOR signalling pathway by genetic or pharmacological intervention extends lifespan in invertebrates, including yeast, nematodes and fruit flies.
- However, whether inhibition of mTOR signalling can extend life in a mammalian species was unknown.We report here that rapamycin, an inhibitor of the mTOR pathway, extends median and maximal lifespan of both male and female mice when fed beginning at 600 days of age.
- Based on age at 90% mortality, rapamycin led to an increase of 14% for females and 9% for males.
- **Rapamycin may extend lifespan by postponing death from cancer, by retarding mechanisms of ageing, or both.**

Castillo-Quan et al. (2019). A triple drug combination targeting components of the nutrient-sensing network maximizes longevity. [11] Level C: Animal study (flies)

- We show that the mitogen-activated protein kinase kinase (MEK) inhibitor trametinib, the mTOR complex 1 (mTORC1) inhibitor rapamycin, and the glycogen synthase kinase-3 (GSK-3) inhibitor lithium act additively to increase longevity in Drosophila.
- **Remarkably, the triple drug combination increased lifespan by 48%.**
- Furthermore, the **combination of lithium with rapamycin cancelled the latter's effects on lipid metabolism.**
- In conclusion, a polypharmacology approach of combining established, prolongevity drug inhibitors of specific nodes may be the most effective way to target the nutrient-sensing network to improve late-life health.

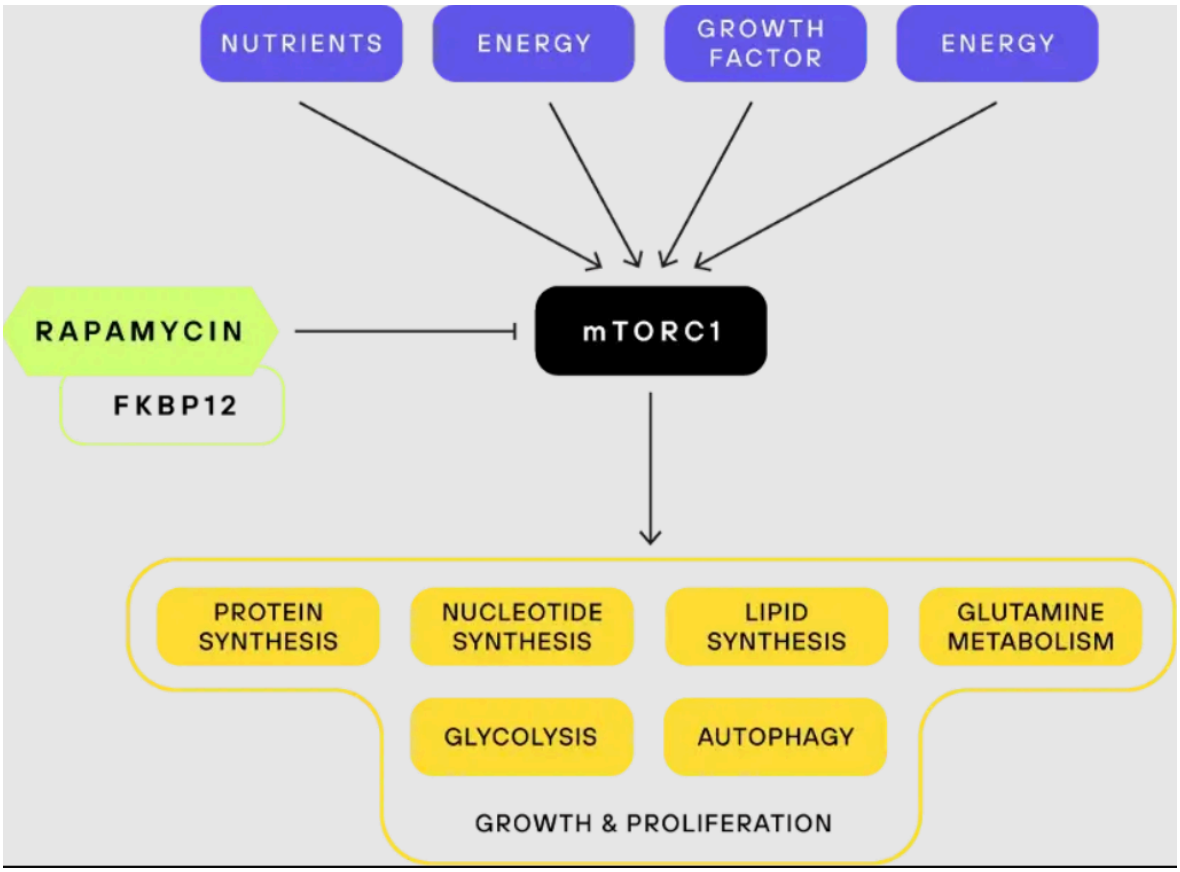
[10] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2786175/
[11] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6800352/

Blogs, Forums and Social Media

Medium

Rapamycin is the most promising aging intervention we currently have. [12]

A good article on the mechanism and effects of rapamycin.



Rapamycin News

- **The Case for Starting Rapamycin Earlier in Life (e.g. late 20s) vs middle age (e.g. 50s)**. [13]
    - One of the leading researchers in the rapamycin area, Dr. Blagosklonny, suggests people should start rapamycin at 25:
        - Blagosklonny: Thank you. But their conclusion is completely opposite to mine. I wrote you cannot wait for clinical trial because its participants will outlive you, and you will die first without rapamycin. For us time is now, actually even too late for many (**rapamycin should be started at 25**)
    - In animal studies, rapamycin has been shown to be effective at increasing healthy lifespan when usage is started either in early adulthood (e.g. equivalent to about 30 years in human terms) or middle age (equivalent to about 60 in human terms), but the longest lifespans achieved in studies so far are when rapamycin is started in earlier adulthood.

[12] https://vitadao.medium.com/rapamycin-is-the-most-promising-aging-intervention-we-currently-have-81b6e49690e0
[13] https://www.rapamycin.news/t/the-case-for-starting-rapamycin-earlier-in-life-e-g-late-20s-vs-middle-age-e-g-50s/297

    - In the National Institute on Aging's ITP studies, the longest lifespan improvements 11 have been in young adult mice (who started taking rapamycin at age 9 months, equivalent to about age 30 in people) where they saw a 23% (male) and 26% (female) median lifespan improvement. This compares the study where they did not start giving rapamycin to the mice until middle-age (20 month old, equivalent to about 60 in human terms) and the study saw a median lifespan improvement of only 11% (m) and 15% (f) using the same dose (source 4).
    - Some researchers are suggesting with optimized dosing schedules determined through rigorous rapamycin clinical studies may be able to increase human lifespan by 30 years. In fact, new 2022 results recently announced in an interview with Richard Miller 8 of the National Institutes on Aging, Interventions Testing Program showed the longest lifespan extension ever achieved in their tests; a 29% lifespan increase for male mice that are fed rapamycin and Acarbose [diabetes drug] starting in early adulthood.

- **User report (M 47, W 50, dog)** [14]
    - Working up to 5-6 mg / wk
    - Benefits
        - M: Less joint and muscle pain
        - F: Less joint and muscle pain
        - Dog: more energy, more social
    - Side-effects
        - M: mouth ulcer, acne flare

- **User report** [15]
    - 3 months
    - Levine phenotype calculator: 41.1 -> 35.7 years
    - Side effects: Glucose dysregulation/diabetes (HbA1C: 6.6)
- **User report (desertshores)** (81 YO, 1-2 years of use) [16]
    - Essentially cured my actinic keratosis. Reduced muscle and joint to the point that I am essentially pain free.

Health Rising

- **A Rapamycin Resurgence: An MD Moves the Needle on his ME/CFS. 2022.** [17]
    - 79 YO physician diagnosed with ME/CFS 10 years ago
    - It was triggered by an upper respiratory infection
    - Dec '21 began rapamycin 6 mg once weekly (via Dr Alan Green)
    - **Noticed improvement in 3 weeks and by 6 weeks was in remission**
    - Seven months after first trying rapamycin no longer housebound, can do household chores, engage in a full day's activity, and is regularly increasing exercise.
    - Side effect: a two-day canker sore on my tongue three weeks after starting rapamycin – a common side effect. Note that there has been a warning about increased bacterial infections because of immune suppression, but this was not his experience.
    - Comments
        - Melissa: There's virtual doctors online that will prescribe this to you. I got mine through one and am slowly healing. **I noticed an improvement after 3 weeks too** but I can't

[14] https://www.rapamycin.news/t/my-dog-my-partner-and-me-a-week-by-week-rapalogue/4252
[15] https://www.patreon.com/posts/november-2022-75669692
[16] https://www.rapamycin.news/u/desertshores
[17] https://www.healthrising.org/blog/2022/07/06/apamycin-resurgence-doctor-chronic-fatigue-syndrome/

even take the full 5-6 mg without getting stomach pain and diarrhea. I take 3mg just fine once every 5days.

- Marcia Adelman: **I indeed did have a remarkable but temporary reprieve from all of my symptoms, most strikingly – PEM and severe fatigue and cognition.** I was taking 2mg daily for around 6 months and then reduced to 2mg every other day. The dosage change did not immediately seem to affect my extreme progress – but after a month I gradually moved back down in functionality. Increased dosage again but did not improve and ultimately stopped the rapamycin altogether as I was back down to baseline functionality and insurance change made it unaffordable. That was in 2017. Now in 2022 at 68 years old, I want to try this drug again. My functional medicine GP is not inclined to prescribe off label so I will pursue other avenues, including Dr. Green. Thanks for this story and I look forward to hearing from others who have tried Rapamycin.
- Learner: I was on low dose rapamycin for about 9 months. I kept having HSV2 outbreaks and then, an EBV reactivation. **We concluded that even at a low dose, twice weekly, it was suppressing my immune system.**
- Robert Lawson: I have been on Rapamycin since December 2021. I am age 70 and my treatment goal was improving CFS symptoms. I started at 6 mg once a week and after about 4 months, I went to 10 mg once a week and now I'm at 12mg every 10 days.

  Energy levels are a little higher. My BPH has gone away. I suspect my insulin resistance is better based on how I feel. I'm getting labs soon
  My mast cell activation syndrome symptoms have been gone for months.
  There is still some fatigue which I suspect is from deconditioning.
  I also have an HSV2 outbreak. This is my third one with the first at age 69.

Reddit

- https://www.reddit.com/r/Rapamycin/

Rapamycin and Women. 2022. [18]

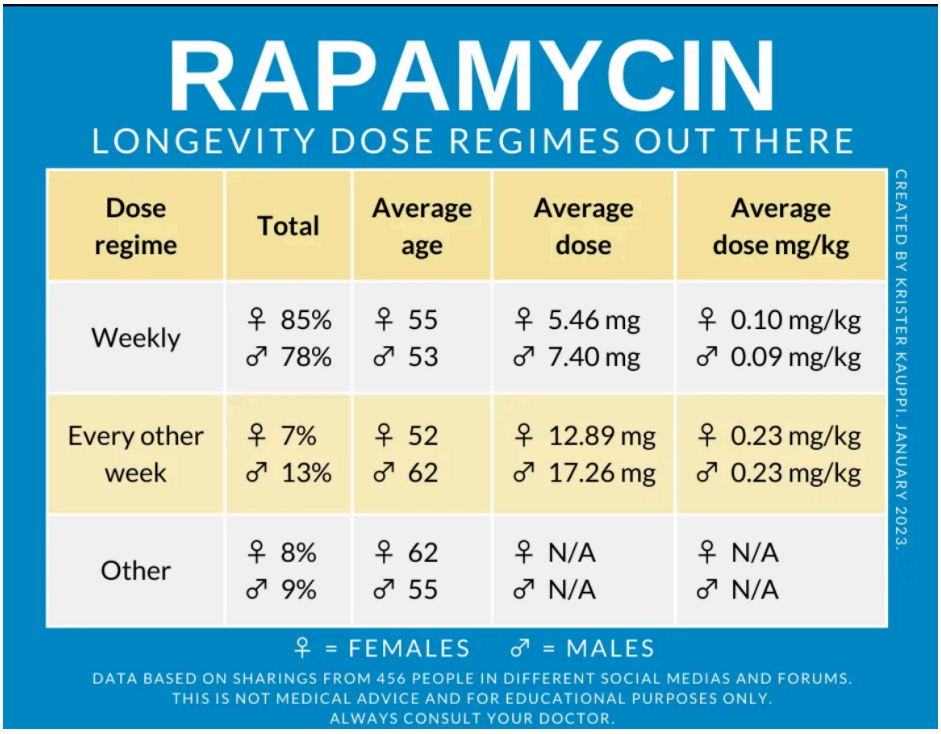
- 48-year-old female athlete interested in taking Serolimus/Rapa.
- Husband (a longevity-obsessed 53-year-old bodybuilder) has had some interesting results after taking it once a week for 3 months, **including increased strength, noticeably reduced body fat, and improved joint mobility**. His lifting routine and diet are strict so he is pretty confident it's the effects of sirolimus.
- 10 months
  - #1. **Inflammation reduction**. I have 2 torn labrums that were causing enough pain for me to look into surgery. Obviously, there's no coming back from a complete tear but for whatever reason, I no longer have the pain I used to. Before it was hard to even put on a seatbelt but now I can box again, do clapping push-ups, etc. So, either I have wolverine DNA or the rapa is helping.
  - #2. It jump-starts my period. I'm usually pretty regular but when I do a dose of rapa my period starts early (sometimes the next day) and it goes HARD. Do any other women notice this?
  - Better body composition (less fat, more muscle)

[18] *https://www.reddit.com/r/Rapamycin/comments/tx8jey/rapamycin_and_women/*

Dosing

Anti-aging [19]

- 3-10 mg once per week.
- 5-6 mg once per week seems to be the most common dose
- Titration: start with 1mg/week and titrate up to ending dose
- Ideally take it with a meal that contains fat



[20]

Immunosuppressant [21]

- In renal transplant patients at low-to moderate-immunologic risk:
  - Rapamune and CsA Combination Therapy: One loading dose of 6 mg on day 1, followed by daily maintenance doses of 2 mg.
  - Rapamune Following CsA Withdrawal: 2–4 months post-transplantation, withdraw CsA over 4–8 weeks.
- In renal transplant patients at high-immunologic risk:
  - Rapamune and CsA Combination Therapy (for the first 12 months post-transplantation): One loading dose of up to 15 mg on day 1, followed by daily maintenance doses of 5 mg.
- Lymphangioleiomyomatosis Patients
  - Administer once daily by mouth, consistently with or without food.
  - Recommended initial Rapamune dose is 2 mg/day.
  - Adjust the Rapamune dose to achieve sirolimus trough concentrations between 5–15 ng/mL.
  - Hepatic impairment: Reduce maintenance dose in patients with hepatic impairment

[19] https://www.rapamycin.news/t/what-is-the-rapamycin-dose-dosage-for-anti-aging-or-longevity/102
[20] https://www.reddit.com/r/Rapamycin/comments/104ockj/biggest_data_summary_of_rapamycin_usage_for/
[21] https://labeling.pfizer.com/showlabeling.aspx?id=139

Doctors and Pharmacies

Individual Doctors

- US Doctor list [22]
- Dr Alan S Green
    - Patients report that Dr. Green's first visit is usually $350, and the prescription for rapamycin is included in that visit.
    - Some commenters complain that he is hard to get a hold of

Telemedicine (US) [23]

Healthspan - Online Clinic for Rapamycin

Website: https://gethealthspan.com

- Forum member says:
    - Cost was $80 / month membership fee and $40 for 12 (1mg) rapamycin pills.
- Another says:
    - I was able to get prescribed a weekly dose of rapamycin of 5mg from Healthspan. It will cost $155 per month for the visit and for monthly medication to be sent to my house. They opted for the larger starting dose instead of the 3mg per week for $125 as was advertised. I assume this may be based on my weight. 238lbs is my current weight.

Push Health

Website: PushHealth.com

Full discussion thread on PushHealth prescribing experiences [24].

- it goes through my insurance and my own pharmacy. I get 60 2mg pills for about $160 which includes the price of the pills at the pharmacy and the $67 fee I pay for each refill from the online medical service.
- They recommended 2mg 3 times a week, with one week off in between weeks, they prescribed 12 pills to start with

Worldwide Pharmacies

- Buy Rapamycin Online - List of Reliable Pharmacies [25]
- Importing Rapamycin to Save Money (pt 2) [26]

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[22] https://www.rapamycin.news/t/rapamycin-prescription-doctors-that-prescribe-it/69
[23] https://www.rapamycin.news/t/rapamycin-prescription-doctors-that-prescribe-it/69
[24] https://www.rapamycin.news/t/push-health-prescribing-experience/3802
[25] https://www.rapamycin.news/t/buy-rapamycin-online-list-of-reliable-pharmacies/437
[26] https://www.rapamycin.news/t/importing-rapamycin-to-save-money-pt-2/82