

# RAPAMYCIN LONGEVITY OVERVIEW

Rapamycin is the only compound that has shown very good longevity effects in multiple species and with results that are quite easy to reproduce. This is unique when it comes to longevity interventions.

## A BRIEF HISTORY OF THE COMPOUND

|                                                                                                        |                                                                                                  |
|--------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| ♂ 1965<br>Georges Nogrady collects soil samples on Easter Island (Rapa Nui)                            | ♀ 1975<br>Suren Sehgal discovers rapamycin thanks to the collected soil samples                  |
| ♀ 1978<br>Suren Sehgal discovers rapamycin's immunosuppressant properties                              | ♀ 1984<br>National Cancer Institute (NCI) discovers that rapamycin inhibits cancer cell growth   |
| ♀ 1991 - 1994<br>David Sabatini, Michael Hall and Stuart Schreiber discovers mTOR                      | ♀ 1998 - 2005<br>Suren Sehgal got colon cancer. He starts chemotherapy combined with rapamycin   |
| 📄 1999<br>Rapamycin is FDA approved for organ transplant rejection                                     | ♀ 2002<br>David Sabatini and Michael Hall discovers mTORC1 and mTORC2                            |
| ♀ 2003<br>Tibor Vellai discovers that mTOR inhibition extends lifespan in worms                        | ♀ 2004<br>Pankaj Kapahi discovers that mTOR inhibition extends lifespan in flies                 |
| ♀ 2005<br>Matt Kaerberlein discovers mTOR inhibition extends lifespan in yeast                         | ♂ 2006<br>Mikhail Blagosklonny suggests that rapamycin could be a longevity drug                 |
| 📄 2009 - 2018<br>Different FDA approvals for using rapalog for kidney cancer and other types of cancer | ♀ 2009<br>ITP study on mice showed lifespan extension on young and old mice                      |
| ♀ 2014<br>Joan Mannick shows that rapalog improves immune system & influenza vaccine response          | ♂ 2015<br>Rapamycin is FDA approved to treat lymphangioleiomyomatosis (LAM)                      |
| ♂ 2016<br>Rapamycin researcher Mikhail Blagosklonny starts taking rapamycin for longevity              | ♂ 2016<br>Physician Alan Green starts taking rapamycin for longevity                             |
| ♀ 2017<br>Rapamycin in dogs is shown safe and has positive effects on their healthspan                 | ♂ 2017<br>In the USA Alan Green starts prescribing rapamycin for longevity as a off-label drug   |
| ♂ 2018<br>Physician Peter Attia starts taking rapamycin for longevity                                  | ♂ 2018<br>Rapamycin researcher Matt Kaerberlein starts taking rapamycin                          |
| 📄 2019 - 2021<br>The website rapamycin.news and different social media rapamycin groups are started    | 📄 2021<br>The longevity PEARL trial on healthy adults who take rapamycin is crowd funded by 243% |
| ♂ 2021<br>Matt Kaerberlein start the TRIAD trial for monitoring healthspan and lifespan in dogs        | 📄 2021<br>Statistics show a big increase in people who starts taking rapamycin for longevity     |
| ♂ 2021<br>The PEARL human longevity trial is started and lead by Sajad Zalzalala                       | 📄 2022<br>FDA approves topical rapamycin gel for treatment of facial angiofibroma (skin disease) |
| 📄 2022<br>Ross Pelton publishes the first longevity book about rapamycin                               | ♂ 2022<br>Longevity researcher Pankaj Kapahi starts taking rapamycin for longevity               |
| ♀ 2022<br>ITP study on mice show positive results with combining rapamycin and acarbose                |                                                                                                  |

## THE PROMISING LONGEVITY INTERVENTIONS

|                                                | CALORIE RESTRICTION | RAPAMYCIN       | ACARBOSE           | EXERCISE     |
|------------------------------------------------|---------------------|-----------------|--------------------|--------------|
| Mechanistic longevity pathway                  | Many                | mTOR inhibition | Glucose regulation | Many         |
| Additive effect data on a already healthy life | +++                 | ++              | +++                | +++          |
| Human healthspan data                          | ++                  | ++              | ++                 | ++++         |
| Reduction of human mortality data              | ++                  | No data         | No data            | +++          |
| Best life span data in different species       | +++                 | +++             | ++                 | +            |
| Reproducible results                           | ++++                | ++++            | ++                 | +++          |
| Mice: Median life span                         | ♀ 35%<br>♂ 33%      | ♀ 26%<br>♂ 23%  | ♀ 5%<br>♂ 22%      | ♀ ?<br>♂ 17% |
| Mice: Maximum life span                        | ♀ 34%<br>♂ 36%      | ♀ 20%<br>♂ 18%  | ♀ 9%<br>♂ 12%      | ♀ ?<br>♂ 0%  |
| Works if started early in life in mice         | +++                 | ++++            | +++                | +++          |
| Works if started late in life in mice          | +                   | +++             | ++                 | ++           |
| Weight loss effect                             | ++++                | +               | ++                 | ++           |
| Easy to practice                               | +                   | ++++            | ++++               | ++           |
| Low cost to practice                           | ++++                | ++(+)           | +++                | +++          |
| Easy to acquire                                | ++++                | ++              | ++                 | +++(+)       |
| Safety                                         | +                   | ++              | +++                | +++          |
| Total clinical trials (2022)                   | 281                 | 914             | 108                | > 100k       |
| FDA approved drug since                        | N/A                 | 1999            | 1999               | N/A          |

♀ = FEMALES ♂ = MALES N/A = NOT APPLICABLE

## THE BEST ITP LONGEVITY RESULTS

| Intervention                                                       | Median lifespan | Max lifespan   |
|--------------------------------------------------------------------|-----------------|----------------|
| Rapamycin: 14.7 ppm + Acarbose: 1000 ppm<br>Age initiated 9 month  | ♀ 28%<br>♂ 37%  | ♀ 21%<br>♂ 24% |
| Rapamycin: 14 ppm<br>Age initiated 9 month                         | ♀ 22%<br>♂ 10%  | ♀ 21%<br>♂ 8%  |
| Rapamycin: 42 ppm<br>Age initiated 9 month                         | ♀ 28%<br>♂ 22%  | ♀ 20%<br>♂ 8%  |
| Rapamycin: 14.7 ppm + Acarbose: 1000 ppm<br>Age initiated 16 month | ♀ 12%<br>♂ 14%  | ♀ 15%<br>♂ 18% |
| Rapamycin: 14 ppm + Metformin: 1000 ppm<br>Age initiated 9 month   | ♀ 24%<br>♂ 21%  | ♀ 17%<br>♂ 14% |
| Rapamycin: 14 ppm<br>Age initiated 9 month                         | ♀ 17%<br>♂ 8%   | ♀ 16%<br>♂ 11% |
| 17-a-estradiol: 14 ppm<br>Age initiated 10 month                   | ♀ 2%<br>♂ 17%   | ♀ 0%<br>♂ 15%  |
| Rapamycin: 4.7 ppm<br>Age initiated 9 month                        | ♀ 17%<br>♂ 3%   | ♀ 14%<br>♂ 6%  |
| Rapamycin: 14 ppm<br>Age initiated 20 month                        | ♀ 13%<br>♂ 9%   | ♀ 14%<br>♂ 9%  |
| Rapamycin: 42 ppm<br>Age initiated 20 month                        | ♀ 15%<br>♂ 11%  | ♀ 12%<br>♂ 9%  |
| Acarbose: 1000 ppm<br>Age initiated 16 month                       | ♀ 3%<br>♂ 7%    | ♀ 6%<br>♂ 12%  |
| Acarbose: 1000 ppm<br>Age initiated 4 month                        | ♀ 4%<br>♂ 22%   | ♀ 8%<br>♂ 11%  |
| Acarbose: 1000 ppm<br>Age initiated 8 month                        | ♀ 5%<br>♂ 17%   | ♀ 3%<br>♂ 11%  |
| Acarbose: 400 ppm<br>Age initiated 8 month                         | ♀ 0%<br>♂ 11%   | ♀ 2%<br>♂ 11%  |
| Rapamycin: 42 ppm<br>Age initiated 20 month (every other month)    | ♀ 8%<br>♂ 9%    | ♀ 10%<br>♂ 9%  |
| Canagliflozin: 180 ppm<br>Age initiated 7 month                    | ♀ 1%<br>♂ 14%   | ♀ 3%<br>♂ 10%  |
| Captopril: 180 ppm<br>Age initiated 5 month                        | ♀ 5%<br>♂ 14%   | ♀ 8%<br>♂ 7%   |
| Acarbose: 2500 ppm<br>Age initiated 8 month                        | ♀ 4%<br>♂ 16%   | ♀ 3%<br>♂ 8%   |

ITP = Intervention Testing Program. The list is sorted by maximum lifespan

## RESEARCH STUDIES AND TRIALS

| Research study or trial                                                                               | Dose regime/s                                                                     |
|-------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| UW Rapamycin survey study<br>Status: Completed in May 2023. Pubmed: 37191826                          | 6 mg/weekly was the most common dose regime                                       |
| RAPACAT: Hypertrophic cardiomyopathy in cats<br>Status: Completed in September 2023. Pubmed: 37495229 | 0.3 mg/kg on weekly basis<br>0.6 mg/kg on weekly basis                            |
| ITP: Intervention testing program<br>Status: Ongoing (Yearly results)                                 | Testing different dose regimes and combinations                                   |
| PEARL: Safety and efficacy in reducing aging measures<br>Status: Ongoing                              | 5 mg/weekly<br>10 mg/weekly                                                       |
| TRIAD: Helthspan efficacy in dogs<br>Status: Ongoing                                                  | 0.1 mg/kg on weekly basis                                                         |
| Lifespan study in common marmosets<br>Status: Ongoing                                                 | 1 mg/kg on daily basis                                                            |
| RMR: Combine four promising longevity interventions in mice<br>Status: Ongoing                        | 42 ppm/daily and different combinations of senolytics, gene and stem cell therapy |
| REACH: Effect on Alzheimer's and cognitive health<br>Status: Ongoing                                  | 1 mg/daily                                                                        |
| EVERLAST: Everolimus aging study<br>Status: Ongoing                                                   | 0.5 mg/daily of Everolimus<br>5 mg/weekly of Everolimus                           |
| VIBRANT: Effect of Rapamycin in ovarian aging<br>Status: Ongoing                                      | 5 mg/weekly                                                                       |
| RAP-PROTECT: Safety and efficacy of Rapamycin as a geroprotector<br>Status: Ongoing                   | People at any dose can participate                                                |
| RAP PAC: Dose escalation safety study of Rapamycin and Everolimus<br>Status: Starts in 2023           | 5 mg/weekly<br>10 mg/weekly<br>15 mg/weekly                                       |
| LONGER: Healthy longevity with Rapamycin<br>Status: Submitted for ethics approval                     | 6 mg/weekly                                                                       |
| Effect on muscle performance in older adults<br>Status: Funding                                       | 6 mg/weekly                                                                       |
| Effects on periodontal disease<br>Status: Submitted for ethics approval?                              | ?                                                                                 |

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