

# Lifespan-extending drug given late in life reverses age-related heart disease in mice

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Elderly mice suffering from age-related heart disease saw a significant improvement in cardiac function after being treated with the FDA-approved drug rapamycin for just three months. The research, led by a team of scientists at the Buck Institute for Research on Aging, shows how rapamycin impacts mammalian tissues, providing functional insights and possible benefits for a drug that has been shown to extend the lifespan of mice as much as 14 percent. There are implications for human health in the research appearing online in *Aging Cell*: heart disease is the leading cause of death in the U.S., claiming nearly 600,000 lives per year.

Researchers at the [Mayo Clinic](#) are currently recruiting seniors with cardiac artery disease for a clinical trial involving low dose treatment with [rapamycin](#).

Rapamycin is an immunosuppressant drug which can be used to help prevent [organ rejection](#) after transplantation. It is also included in [treatment regimens](#) for some cancers. In this study, rapamycin was added to the diets of mice that were 24 months old – the human equivalent of 70 to 75 years of age. Similar to humans, the aged mice exhibited enlarged hearts, a general thickening of the heart wall and a reduced efficiency in the hearts ability to pump blood.

The mice were examined with ultrasound [echocardiography](#) before and after the three-month treatment period - using metrics closely paralleling those used in humans. Buck Institute faculty Simon Melov, PhD, the

senior author of the study, said age-related [cardiac dysfunction](#) was either slowed or reversed in the treated mice. "When we measured the efficiency of how the heart pumps blood, the treated mice showed a remarkable improvement from where they started. In contrast, the untreated mice saw a general decline in pumping efficiency at the end of the same three month period," he said. "This study provides the first evidence that age-related heart dysfunction can be improved even in late life via appropriate drug treatment," added Melov, who said the treated mice saw a reduction in heart size, reduced stress signaling in heart tissues and a reduction in inflammation.

Buck researchers, utilizing genome analysis tools, uncovered suites of related genes which rapamycin modulates in the heart. "Rapamycin affected the expression of genes involved in calcium regulation, mitochondrial metabolism, hypertrophy and inflammation," said Melov. "We also carried out behavioral assessments which showed the treated mice spent more time on running wheels than the mice who aged without intervention."

"Little has been known about the functional ramifications of rapamycin in mammalian tissues," said Buck Institute President and CEO Brian Kennedy, PhD, a co-author of the paper. "These findings are significant because we have no interest in simply extending lifespan without an accompanying improvement in the health and quality of life." He added, "It is particularly encouraging that, in this case, an already-approved drug that extends lifespan also improved function late in life."

Chronic treatment with rapamycin has been problematic in both humans and [mice](#); the drug has the potential to cause deleterious metabolic side effects including weight gain and glucose insensitivity. Melov said in this study, the drug had only mild transient metabolic effects. Future studies will focus on better understanding the molecular targets that drive age-related heart dysfunction, and why rapamycin treatment is so beneficial

to the aging hearts.

**More information:** [www.clinicaltrials.gov/ct2/show/study?term=Rapamycin&rank=11](http://www.clinicaltrials.gov/ct2/show/study?term=Rapamycin&rank=11)

Provided by Buck Institute for Age Research

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