## "Long before it's in the papers"

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## Already-approved drug tied to longer, healthy life in mice

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The first drug to successfully extend the lifespan of normal lab mice also does so in a way that prolongs their healthy existence, according to a new study.

Researchers hope the drug, rapamycin, may also serve to prolong life and ward off aging-related diseases in people, especially as it's already tested and approved for another human use: to prevent transplant rejection.



A popular strain of lab mice known as C57BL/6, used in the new study by Yiqiang Zhang and colleagues at the University of Texas Health Science Center at San Antonio. (Image courtesy FDA)

But obstacles remain before any human use of rapamycin as a longevity booster. It's unclear what dosages and regimens might be required for such a purpose. Concerns about side effects linger. And mouse studies have used a special encapsulation method that's not currently used in human consumption of the drug.

A biotech firm has sprung up in San Antonio, Texas in hopes of exploiting new commercial possibilities for rapamycin, and its officials have said that clinical trials are expected soon.

In the new study, mice were fed rapamycin as part of their diet starting when they were 19 months —the equivalent of about 60 human years—old. The measured lifespan increases were more modest than in some previous studies. Compared to untreated mice, the lifespan of the treated rodents went up by about 3 percent on average, although the difference rose to 7 percent for mice who made it to older ages to begin with.

Previous studies had yielded more dramatic results.

A study in the July 2009 issue of *Nature*, using a similar methodology but different mouse strains, had found increases as high as about 10.5 percent for older mice on rapamycin compared to untreated. Another piece of research found that if treatment was started when the mice were

about half as old, then the average survival increase jumped to about 14 percent. That study appeared in the February 2011 issue of *The Journals of Gerontology: Biological Sciences.* 

The new study, in the May 16 online edition of the same journal, focused on the health effects in addition to the lifespan effects. "Whether the life-extending effects of rapamycin treatment are reflected in extended health has not yet been extensively investigated," wrote the authors, researchers with the University of Texas Health Science Center at San Antonio.

The authors included scientists who have licensed rapamycin-related technologies to the biotech company, Rapamycin Holdings Inc.

They also wrote that they investigated the health effects in greater detail because "increasing life span without simultaneously increasing health span is a fool's errand." They found that treated mice enjoyed health benefits including increased stride length and better results on a test of endurance.

Rapamycin's lifespan benefits to mice have tended to be greater for females, which received lifespan boosts up to 80 percent greater than the males depending on the study.

The investigators in the new study used rapamycin that had been "microencapsulated" by a special method in order to resist degradation when mixed with the rodent chow. This isn't the same way rapamycin, a prescription drug, is normally taken in human clinical use, although it is taken orally.

Rapamycin is thought to exert its effects on lifespan by suppressing the activity of a chemical pathway in the body known as mTOR, which helps to govern growth and survival responses in cells.

Rapamycin also helps prevent transplant rejection by blocking certain immune system cells, leading to concerns of harmful immune-suppressing side effects. But these have not proved problematic in the mouse studies, according to scientists.

Very few substances have been found to reliably prolong lifespan in lab animals. Before rapamycin, the one considered perhaps most promising was resveratrol, found to extend lifespan in roundworms, yeast and certain fish. But such benefits in lab mice, seen as an important stepping-stone toward human studies, were reported only for mice that were obese.

Rapamycin is so named because it was discovered coming from soil bacteria at Easter Island, also known as Rapa Nui.