

AGING AGING AGING

My friends, if there were a Guinness world records that were dedicated to a high-achieving rodent, Mouse UT2598, would most definitely deserve a mention, why? The average life span for a mouse is 2.3 years-so having lived 1,259, days, or about 3.45 years, before her death in 2010, little Missy had an improbably long life. In fact, this little mouse had a real shot at beating the record for the longest-lived, which as of today stands at about 4. Translating that to a human life span, she hovered around the centennial mark. However, on the outside, little Missy looked no different from her much younger brethren.



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Her fur was glossy black, she was very lean, and a bit on the small side, she was no doubt scrappy and surprisingly active as she explored, always sniffed and poked around her cage that was at the University of Texas Health Science Center at San Antonio (UTHSCSA). What gave her the edge was a compound that is called rapamycin, which seems to slow the aging process and the damage that comes with it, at least to certain cells. Mouse UT2598 liver and heart functioned as if they were much younger, and her tendons had more flexibility and spring than they should have had at her age. There was also less evidence of tumors in little Missy organs than is considered normal, so she was definitely spared the effects of cancer longer. When she was placed alongside other mice that was her age, the contrast was without a doubt unmistakable.



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Mouse UT2598 is only one example of the kind of research into aging that is producing remarkable new findings-and raising a lot of new questions as each day goes by. Around the world, researchers in labs are testing all sorts of agents, some of which already exist as drugs to treat some human conditions (rapamycin is given to transplant patients to prevent any organ rejection after the surgery) and some that are purely experimental. Scientists are now also toying around with ways to manipulate the genes and pluck out aging cells, all in a mouth-watering race to find a way to extend longevity to its unfamiliar outer limits.

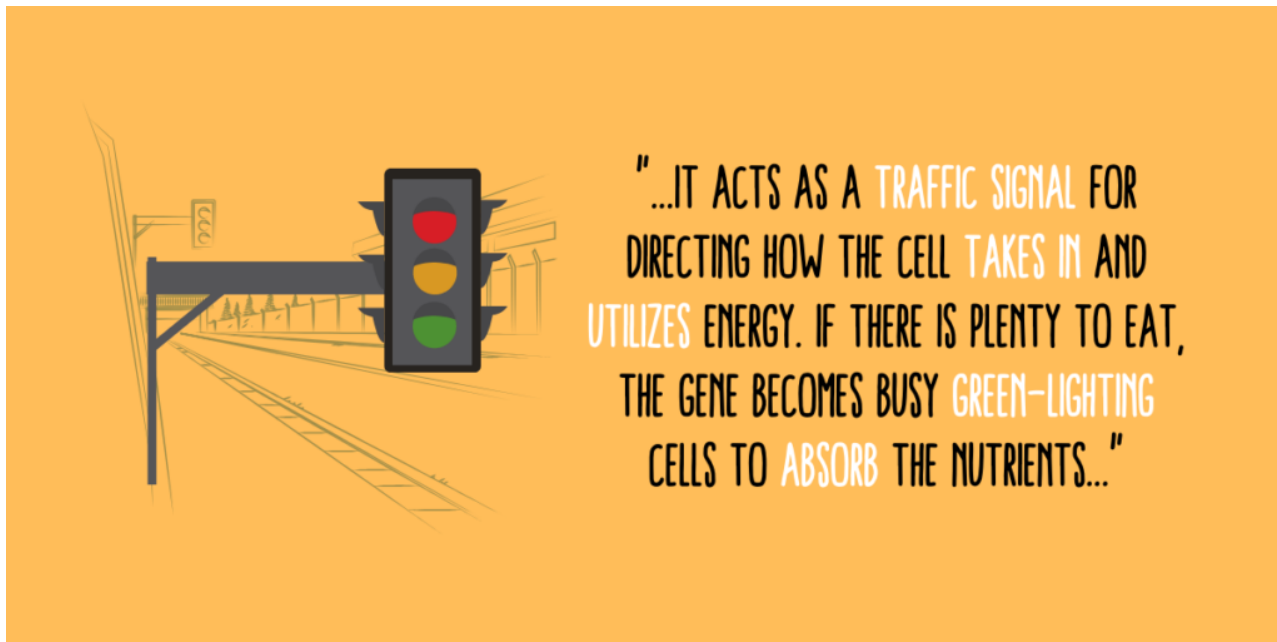
These efforts mark a unique push to examine the basic mechanisms of aging and find ways to counteract or cure them. And they are true, anything but fringe. Longevity research is now being conducted by some of the most respected scientists, with sound reasons for staking their successful careers on the hubristic notion that it is possible to slow down the process and maybe even reverse aging.

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"When I got into this field, the very notion that we could actually do anything about the aging process was only viewed as a crackpot idea", Mr Richard Miller says, who is the director of the Glenn Center for the Biology of Aging at the University of Michigan. The argument that we can slow aging, and the diseases of aging along with it, used to be only fantasy, however, now we see it as a real scientific strategy.

No one is talking about trying to live forever, however, as these experts see it, aging is the single most powerful factor in all the diseases that are most likely to cut our lives short: cancer, immune disorders, heart problems and degenerative brain conditions like that terrible Alzheimer's. "Everybody knows well that the main risk factors for heart disease are in fact high cholesterol, high blood pressure and obesity", Felipe Sierra says, who is the director of the division of aging biology at the National Institute on Aging (NIA).



But ever stronger than those factors is being 70 years old. And that is why staving off aging-or at the very least slowing it-has become such an important focus of research. We're going towards aging it-self, David Sinclair says, who is a geneticist at the Havard Medical School. We might take somebody who is showing some signs of aging and be equipped and able to do something about it, to treat aging as a disease. And that is something I never expected to see in my lifetime.

It turns out that rapamycin interrupts the function of a gene called mTOR, which is found in both man and mouse, it acts as a traffic signal for directing how the cell takes in and utilizes energy. If there is plenty to eat, the gene becomes busy green-lighting cells to absorb the nutrients and grow and grow. When food becomes scarce, the gene than become quiet, halting the cell-growing machinery until it is time for feeding again. While mTOR may explain, in some part, this phenomenon of calorie restriction and its ability to prolong life-in the 1930s, the studies in mice showed by cutting back on their daily diet could add all-most a year to their lives there is also some evidence that it taps into other energy-

related pathways to a longer life as well.



A pilot study published in 2018 examined the safety and tolerability of a short-term rapamycin treatment in generally healthy older adults, which was not previously demonstrated. This study showed that short-term rapamycin treatment can be used safely in older men and women who are considered otherwise being healthy. However, a larger-size trial and longer treatment duration are warranted.

Are rapamycin-fed mice living longer only because their cells are actually functioning like the younger ones or because they're simply delaying aging conditions like heart disease and cancer? And while we are learning more every day about the real role telomeres play in the process of aging, is the true answer as simple as finding the ways to safely lengthen them through drugs? These are not very easy questions to answer, however, the aging experts welcome them. It is because what's happening in the labs is not all about extending a life indefinitely but rather extending a healthy life for a little longer.

It may all sound a little like science fiction, however, we are really walking through the door of a new era of prolonging life for the human species. May you be always in good health, humbly yours Paul Earl.

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