developed several compounds designed to modulate SIRT1 that are structurally distinct from resveratrol. The lead candidate, SRT2104, has been tested in a phase 1 trial and seems to be safe[8]. Whether it will also prove effective in people still remains to be seen.

Rapamycin on trial

Although resveratrol failed to have an effect in normal mice, another immune-suppressing drug called rapamycin emerged victorious from the ITP. "To everyone's delight, it had a big effect, the biggest effect of any of the compounds we've tested so far," Harrison says. Administering rapamycin to mice in their food starting at nine months of age increased median survival by at least two months on average in males and about twice that in females[7]. Similar age extensions were seen in mice exposed to rapamycin from 20 months of age[9]. If rapamycin worked as well in humans as it did in these mice, "it would give us about ten more years of healthy lifespan," Harrison says.

However, the effects weren't all positive. The mice that received rapamycin had more severe cataracts and greater testicular damage than the control mice[10]. The drug, which is currently approved to prevent rejection in organ transplant recipients, also tends to increase the risk of infectious diseases and diabetes in people. So, physicians are reluctant to give rapamycin or any of its many mimics, known as rapalogs, to otherwise healthy individuals.

A study published last year by Joseph Baur, of the University of Pennsylvania Perelman School of Medicine in Philadelphia, and David Sabatini, of the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, suggests there may be a way to separate the good effects from some of the bad. Rapamycin inhibits the protein mTOR, short for mammalian target of rapamycin, which exists as part of two separate complexes, mTORC1 and mTORC2. Rapamycin's beneficial effects appear to be due to inhibition of mTORC1. However, Baur's and Sabatini's research suggests that the drug also disrupts mTORC2, and that this disruption may explain the insulin resistance seen in mice[11]. A compound that targets only mTORC1 might have fewer side effects.

New leases on life

Aging researchers continue to test other potential life-extending compounds with demonstrated safety profiles. For example, Harrison and his ITP colleagues recently gave mice green tea extract, a component of the spice turmeric, a triglyceride commonly found in coconut oil and other health supplements with purported longevity benefits that are known to be safe in people, but they didn't see any effect on life span in the animals[12]. Now on the researchers' plate is metformin, a drug used to treat type 2 diabetes. At an aging conference in San Antonio last year, Rafael de Cabo and his colleagues from the NIA reported that a low dose of metformin extended the lifespan of mice. A high dose, however, was toxic.

Developing an antiaging pill with absolutely no side effects may simply be unrealistic, notes Matt Kaeberlein, an aging researcher at the University of Washington in Seattle. "There are reasons why these mutations that slow aging are generally not selected for in nature," he says. "They have costs associated with them." How hefty those costs might be and whether society will be willing to pay them remains a question for the ages.

Cassandra Willyard

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Living labs open door to retirees who want to join studies

Despite the fact that the elderly account for the greatest proportion of patients for certain ailments, they are often underrepresented in medical research. In addition to explicit exclusion criteria included in many trials, scientists and drug companies are often loath to include senior citizens in their studies because of the myriad logistical challenges that old age presents. Elderly individuals might not have the mobility to travel to investigational sites, and they're often less willing to switch physicians from the ones they've come to know and trust.

To encourage more participation in research among the over-65 crowd, an independent living facility at the Mayo Clinic in Rochester, Minnesota, is now trying to rethink what a study site has to look like.

On the fourth floor of a 21-story residential building, Mayo researchers have built a 'living lab' that spans 51,000 square feet and includes two mock-up apartments and rooms for convening focus groups. A small section on the floor above houses treadmills, electrocardiographs and other devices to measure physiology. Beyond simply bringing health studies closer to the elderly residents of the building, the research space has substantial built-in video recording infrastructure, allowing improved observation of how certain products and test ideas fare.

The combined space, known as the Healthy Aging and Independent Living (HAIL) lab, was established in 2011 at a retirement home called Charter House, which is affiliated with—and physically connected to—Mayo. In the past couple years, the HAIL lab has partnered with companies such as General Mills, United Healthcare and Best Buy to look at, for example, the acceptance of technology by the elderly. For now, the endeavor is concentrated on projects that are simple or observational, such as user feedback on products and exploring how video game participation might influence health in the elderly. However, "in the next five years, clinical trials with pharmacological agents might be forthcoming," says Nicholas LaRusso, director of the Mayo Clinic Center for Innovation.

The vision of providing improved health research for the elderly is shared by another HAIL partner, the Good Samaritan Society, the largest nonprofit provider of senior care and services in the US. In an ongoing independent 1,200-person study at 5 of its 240 senior care facilities, the Good Samaritan Society is looking at the benefit of motion sensor technology. It has thus far found that the technology can detect repeat trips to the bathroom, which could indicate a urinary tract infection.

Kelly Soyland, director of innovation at the Sioux Falls, South Dakota–based society, says that his team has started exploring the idea of more traditional clinical research at some of their facilities at some point down the road: "We're building the organizational capacity to work in that formal research space."

Roxanne Khamsi