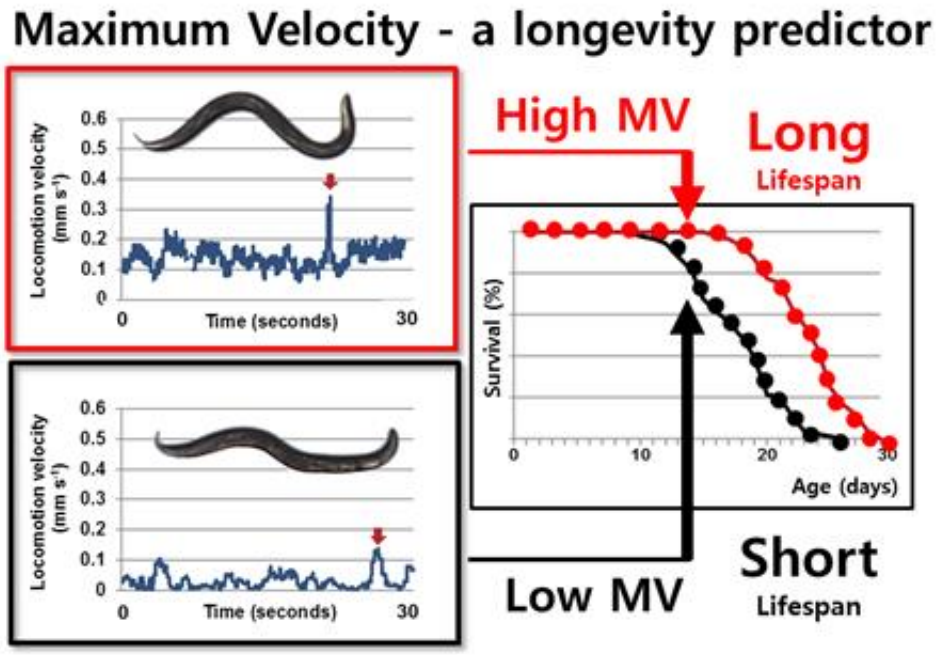
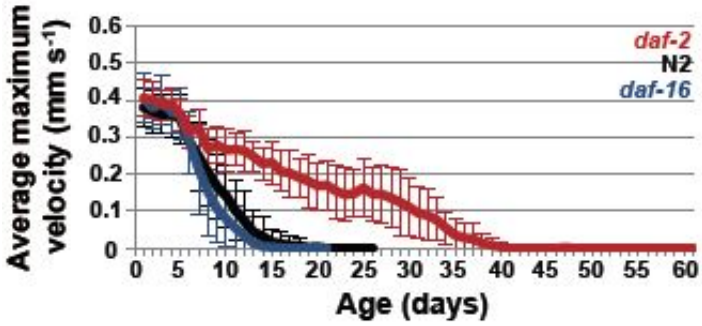
How fast you move can predict how healthy you'll be

November 20 2015



Instead of focusing on drawing out the length of life, South Korea's IBS Center for Plant Aging Research and the research group led by Coleen Murphy, a professor at Princeton University have created a tool that can be used for accurately predicting lifespan as well as assessing the current health state, and discovered the regulatory mechanism that extends "healthspan", the time in which an organism is at its optimal health.

As humans have begun to live longer it has become clear that the quality of our lives is equally as important as the duration. In the lab, a dramatic extension of lifespan isn't difficult to achieve. In previous experiments using several types of mutated Caenorhabditis elegans roundworms (C. elegans), researchers were able to significantly extend the worm's lifespan. The lengthened life that the worms experienced was not necessarily a good one, as many of the mutated varieties were less healthy than wild-type worms, especially during the segment of life that was extended beyond normal. Instead of focusing on drawing out the length of life, South Korea's IBS Center for Plant Aging Research and the research group led by Coleen Murphy, a professor at Princeton University have created a tool that can be used for accurately predicting lifespan as well as assessing the current health state, and discovered the regulatory mechanism that extends "healthspan", the time in which an organism is at its optimal health.

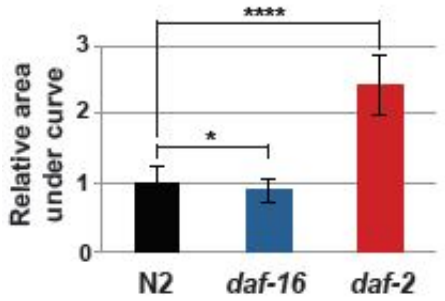


The scientists created their own health assessment for C. elegans, modeled after the Short Physical Performance Battery (SPPB), one of the most widely used tests of physical performance in elderly humans, which can accurately predict their future health. Among other things, the

SPPB measures walking speed which was the inspiration for the C. elegans version of the test. The scientists recorded the maximum velocity (MV) of wild-type C. elegans worms during timed 30 second sessions for a life time. In the experiment, the worms all showed a decrease in MV from day 6 and onwards just as the movement ability of humans starts to decline at some point of our later life and onwards. Additionally, they found that at day 9 (midlife), the median lifespan of worms in the high MV group (23 ± 3.2 days) was 35.3% longer than that of the worms in the low MV group (17 ± 3.6 days) (Fig. 1). They concluded that MV of wild-type worms at day 9 of adulthood is a reliable predictor of longevity. Another factor they observed was the state of C. elegans mitochondria. Elderly humans have weaker muscles and less strength resulted from mitochondrial defects which occur later in life. C. elegans with lower MV exhibit similar defects by midlife but there are far fewer defects in worms with higher MV at the same age. These observations indicate that MV correlates with mitochondrial health expression, suggesting that MV can be a reliable indicator of the actual physical state. The findings show that MV of C. elegans is a reliable indicator of age-related physical decline, accurately reports movement ability and if measured in mid-adulthood, is predictive of future longevity.

What sets this research apart from previous studies is that they discovered a genetic regulator that can lengthen good quality life, which was not properly appreciated by others. The research groups found overwhelming evidence which contradicts a previous study by Bansal, et al which concluded that daf-2(e1370) insulin/IGF-1 signaling (IIS) mutants are less healthy than wild-type animals, disproportionately extending their "unhealthy" lifetime. The daf-2 mutation affects the insulin/IGF-1 signaling (IIS) pathway which in turn has a direct effect on longevity through its control of the metabolism of nutrients and enhances many physiological functions with age. Tests with daf-2 mutants showed that they had a higher MV than wild-type worms with age, especially at

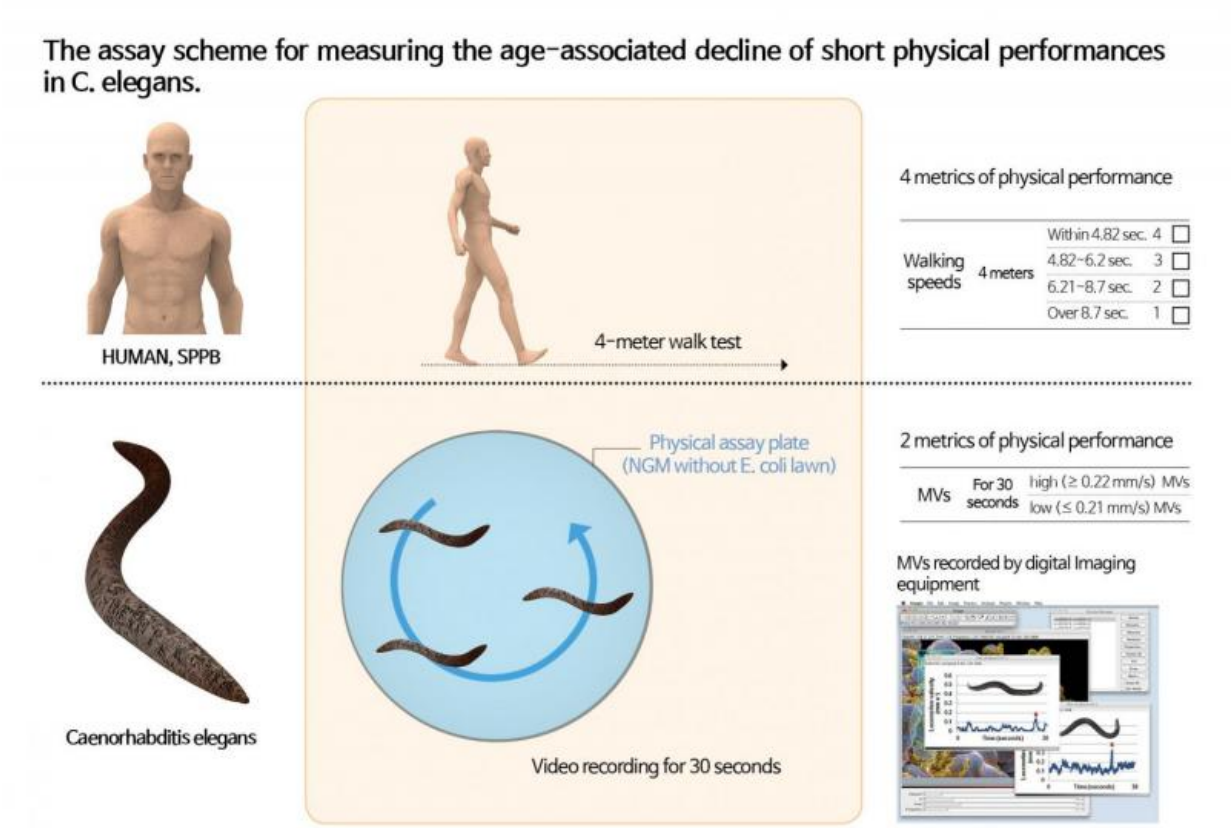
day 10 and after. Even after all the wild-type worms had died at day 26 of adulthood, the daf-2 mutants still maintained on average 36% of MV (Fig. 2). Fig. 3 shows the area under the MV curve which serves as an indicator of overall physical performance., daf-2 mutants showed a 2.4-fold increase over wild type in overall physical performance. The researchers showed that daf-2(e1370) mutation extends both lifespan and healthspan, without proportionally extending the unhealthy part of life, in contrast to Bansal, et al.'s conclusions.



As part of their efforts to explain the discrepancies with the previous research, the research groups recorded movement of daf-2 mutants across an unseeded surface, contrary to the previous research that used the seeded plates full of food, assuming that the food source actually may get in the way of the worm's desire to explore. They found that daf-2 mutants have an inherently higher preference for food than exploration, presumably because its high levels of the odr-10 odor receptor cause daf-2 mutants to prefer food over exploration, slowing its movement on bacteria. Corresponding author and IBS director of the Center for Plant Aging Research Hong Gil Nam explains that "because this type of movement is not limited by ability, but rather by preference,

it may be difficult to draw conclusions regarding healthspan from on-food motility assays." From these results the researchers concluded that the only way to accurately measure worm motility is to conduct the trials on a bacteria-free surface, so the worms didn't get preoccupied by their ingrained food-seeking behavior.

The IBS Center for Plant Aging Research, which was originally designed to gain insight into cell-death processes of plants, has recently expanded its focus to animal longevity and senescence. Despite the challenge of embarking on a new area of research, the group has made some important breakthroughs. According to Hong Gil Nam, "our analysis takes into account the length of time an individual can expect to live, and how healthy that individual can expect to be with age." Many parts of the insulin/IGF-1 signaling (IIS) pathway that enable these functions have been identified, and many of these genes and the underlying mechanisms are conserved in mammals, which mean that the extended abilities that insulin/IGF-1 signaling (IIS) exhibits could offer therapeutic target possibilities for humans in the future. The IBS Center isn't just looking at push the limits for long life; instead they are unraveling the mechanisms in our cells to maximize our health as we age.



The assay scheme for measuring the age-associated decline of short pH

More information: Jeong-Hoon Hahm et al. C. elegans maximum velocity correlates with healthspan and is maintained in worms with an insulin receptor mutation, *Nature Communications* (2015). DOI: 10.1038/NCOMMS9919

Provided by Institute for Basic Science