Stimulating production of enzyme in roundworms found to increase lifespan

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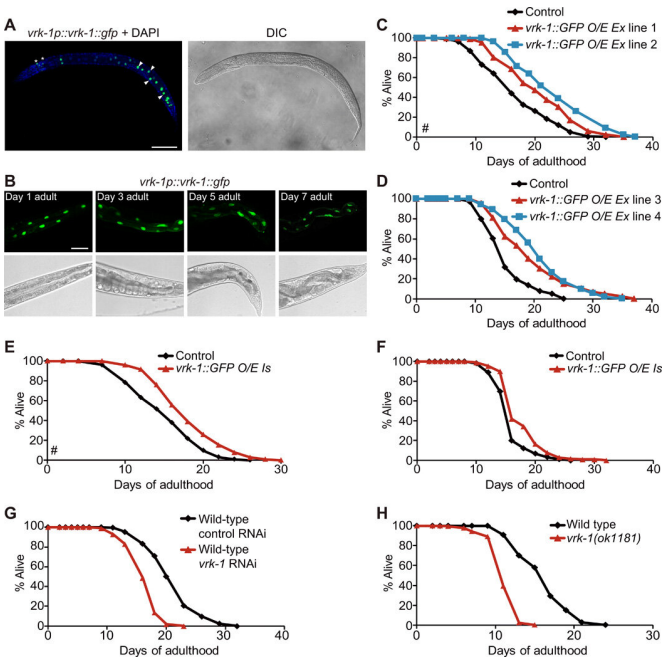

VRK-1 is a nuclear protein that increases worm life span. (A) VRK-1::GFP was localized in the cellular nuclei of multiple tissues including neurons (asterisks), intestine (arrowheads), and hypodermis (fig. S1B, arrows) at L2 larval stage. Nuclear DNA was stained with 4?,6-diamidino-2-phenylindole (DAPI; blue). See also fig. S1 (A and B) for magnified images of VRK-1::GFP and cellular nuclei for specific tissues. DIC, differential interference contrast. Photo credit: Sangsoon Park, Pohang University of Science and Technology, South Korea. (B) VRK-1::GFP was expressed in somatic tissues of days 1, 3, 5, and 7 adult worms. Scale bars, 50 ?m. Photo credit: Murat Artan, MRC Laboratory of Molecular Biology, UK. (C and D) Four independent lines of extrachromosomal vrk-1::GFP-transgenic worms (vrk-1::GFP O/E Ex) displayed increased life span with [(C), fig. S2A, transgenic lines 1 to 4] or without (D, transgenic lines 3 and 4) 5-fluoro-2?-deoxyuridine (FUDR) treatment. odr-1p::RFP (C) and rol-6D (D) were used as coinjection markers, and odr-1p::RFP (C) and rol-6D (D) transgenic worms were used as controls, respectively. We found that germline-specific transgenic expression of pie-1p::GFP::vrk-1 (16) had no effect on life span (fig. S2, C and D). VRK-1 tagged with GFP appears to be functional because previous reports have shown that GFP::VRK-1 transgenes rescued the sterility, uterine and uterine seam cell developmental defects, and protruding vulva phenotypes of vrk-1 mutants (16–18). (E and F) An integrated vrk-1::GFP transgenic line (vrk-1::GFP Is) extended life span with [(E), four of five trials] or without [(F), three of three trials] FUDR treatment. Control indicates wild-type N2. (G) vrk-1 RNAi significantly shortened life span. See also fig. S2E for life-span results of vrk-1(RNAi) animals treated with FUDR. (H) vrk-1(ok1181) mutation substantially shortened life span without FUDR treatment. In contrast, hypomorphic vrk-1(x1) mutants had a life span similar to that of wild-type worms (fig. S2, H and I). # indicates life-span results that were obtained with FUDR treatment to prevent progeny from hatching. Credit: *Science Advances* (2020). DOI: 10.1126/sciadv.aaw7824

A team of researchers affiliated with several institutions in South Korea has found that stimulating production of a certain enzyme in roundworms can increase their lifespan. In their paper published in the journal *Science Advances*, the group describes their study of the protein VRK-1 and what they learned about its impact on the longevity of roundworms.

Prior research has shown that one way to increase longevity in some species is to use techniques that slow down mitochondrial respiration. In this new effort, the researchers were looking to better understand why slowing energy use in mitochondria has an impact on aging. As part of their effort, they looked at an energy sensor in mitochondria called adenosine 5'-monophosphate-activated protein kinase (AMPK), known to play a role in controlling how much energy is used in cells in roundworms. Prior research had suggested its level of activity is controlled by the protein VRK-1. To learn more about its impact on aging, the researchers genetically engineered two lines of roundworms to force them to produce more VRK-1 and two lines of roundworms to force them to produce less VRK-1. They then monitored the

roundworms to see how long they lived.

The researchers found those roundworms expressing more than the normal amount of VRK-1 tended to live longer than average, while those expressing less than average amounts of VRK-1 had shorter lifespans. More specifically, control worms representing the normal lifespan of a roundworm lived on average 16.9 days. In their experiments, one of the lines expressing more VRK-1 lived on average 20.8 days, while the other lived on average 23.7 days. And one of the lines producing less VRK-1 lived on average just 12.7 days and the other just 15.9 days. The researchers suggest this finding indicates that VRK-1 has a direct impact on roundworm longevity.

The researchers next tried activating AMPK in human cells using the human equivalent of VRK-1 and found that AMPK was activated similarly to the ways it was activated in roundworms. They suggest it is possible that this discovery could increase the human lifespan. They note that much more testing is required, starting with other mammals, before it can be determined if therapies to force more production of VRK-1 might be used to extend human lifespans.

More information: Sangsoon Park et al. VRK-1 extends life span by activation of AMPK via phosphorylation, *Science Advances* (2020). DOI: 10.1126/sciadv.aaw7824