New â€œlongevity geneâ€• spurs hopes of long life

by Bend_Weekly_News_Sources

In studÂ-ies datÂ-ing back 70 years, mice and many othÂ-er speÂ-cies subÂ-sistÂ-ing on a near-starvation diÂ-et have conÂ-sistÂ-entÂ-ly lived as much as 40 perÂ-cent longÂ-er than norÂ-mal. But just why has been unÂ-clear.

Now, reÂ-searchÂ-ers at the Salk InÂ-stiÂ-tute for BiÂ-oÂ-logÂ-iÂ-cal StuÂ-dÂ-ies in La Jolla, Calif., reÂ-port they have cracked the ridÂ-dle, findÂ-ing the first gene that specifÂ-iÂ-cally links this â€œcaÂ-lorÂ-ic reÂ-stricÂ-tionâ€• regÂ-iÂ-men to lonÂ-gevÂ-ity. â€œWe fiÂ-nalÂ-ly have geÂ-netÂ-ic evÂ-iÂ-dence to unÂ-ravÂ-el the unÂ-derÂ-lyÂ-ing moÂ-lecÂ-uÂ-lar proÂ-gram reÂ-quired for inÂ-creased lonÂ-gevÂ-iÂ-ty in reÂ-sponse to calÂ-oÂ-rie reÂ-stricÂ-tion,â€• said the inÂ-stiÂ-tuteâ€™s AnÂ-drew DilÂ-lin, who led the study pubÂ-lished onÂ-line in the May 2 isÂ-sue of the reÂ-search jourÂ-nal NaÂ-ture. The findÂ-ing opens the door to deÂ-velÂ-opÂ-ment of drugs that mimÂ-ic calÂ-oÂ-rie reÂ-stricÂ-tionâ€™s efÂ-fects, he added. These could alÂ-low peoÂ-ple to reap health benÂ-eÂ-fits withÂ-out goÂ-ing hunÂ-gry. One comÂ-pound that may fit this deÂ-sÂ-cÂ-ripÂ-tion, resÂ-verÂ-aÂ-trol, is alÂ-ready marÂ-keted and has shown promÂ-ise in anÂ-iÂ-mal studÂ-ies. But itâ€™s not clear whethÂ-er it acts specifÂ-iÂ-cally on the biÂ-oÂ-chemÂ-iÂ-cal pathÂ-way of diÂ-etary reÂ-stricÂ-tionâ€”one of three sepÂ-aÂ-rate pathÂ-ways known to afÂ-fect lonÂ-gevÂ-iÂ-ty, DilÂ-lin said.CaÂ-lorÂ-ic reÂ-stricÂ-tion alÂ-so is the onÂ-ly stratÂ-eÂ-gy apart from diÂ-rect geÂ-netÂ-ic maÂ-niÂ-puÂ-laÂ-tion that conÂ-sistÂ-entÂ-ly proÂ-longs life in anÂ-iÂ-mals, DilÂ-lin notÂ-ed. It alÂ-so cuts the risk of canÂ-cer, diÂ-aÂ-beÂ-tes, and carÂ-diÂ-oÂ-vasÂ-cuÂ-lar disÂ-ease and staves off age-reÂ-latÂ-ed neuÂ-rodeÂ-genÂ-erÂ-aÂ-tion in labÂ-oÂ-rÂ-aÂ-toÂ-ry anÂ-iÂ-mals from mice to monÂ-keys. The price: caÂ-lorÂ-ic reÂ-stricÂ-tion requires cutÂ-ting to around 60 perÂ-cent of norÂ-mal calÂ-oÂ-rie inÂ-take while mainÂ-tainÂ-ing a healthy diÂ-et rich in viÂ-taÂ-mins, minÂ-erÂ-als, and othÂ-er nuÂ-triÂ-ents, DilÂ-lin said. AlÂ-though some peoÂ-ple live by this regÂ-iÂ-men, itâ€™s too soon to say whethÂ-er it will exÂ-tend lifeÂ-span in huÂ-mans, DilÂ-lin said.In the quest for genes inÂ-volved in the caÂ-lorÂ-ic reÂ-stricÂ-tion reÂ-sponse, gradÂ-uÂ-ate stuÂ-dent SuÂ-zanne Wolff and othÂ-ers in DilÂ-linâ€™s labÂ-oÂ-rÂ-aÂ-toÂ-ry studÂ-ied an arÂ-ray of genes reÂ-latÂ-ed to ones preÂ-viÂ-ously linked to anÂ-ti-agÂ-ing pathÂ-ways. They found that onÂ-ly one gene, called pha-4, specifÂ-iÂ-cally afÂ-fected the caÂ-lorÂ-ic reÂ-stricÂ-tion reÂ-sponse. In roundÂ-worms, they reÂ-ported that loss of the gene, and the proÂ-tein molÂ-eÂ-cule whose proÂ-dÂ-ucÂ-tion it enÂ-codes, neÂ-gated caÂ-lorÂ-ic reÂ-stricÂ-tionâ€™s life-exÂ-tending efÂ-fect. StimÂ-uÂ-latÂ-ing it enÂ-hanced the efÂ-fect.DilÂ-lin specÂ-uÂ-latÂ-ed that the lonÂ-gevÂ-iÂ-ty benÂ-eÂ-fits of near-starvation may have evolved as a sysÂ-tem to help anÂ-iÂ-mals live through stressÂ-ful times. Pha-4 â€œmay be the priÂ-morÂ-diÂ-al gene that regÂ-uÂ-lates nuÂ-triÂ-ent sensÂ-ing and helps anÂ-iÂ-mals live a long time through stress and diÂ-etary reÂ-stricÂ-tion,â€• he added.One othÂ-er gene, called sir-2, has been imÂ-pliÂ-catÂ-ed in the life- and health-prolonging reÂ-sponse to calÂ-oÂ-rie reÂ-stricÂ-tion, DilÂ-lin said. But while loss of sir-2 disÂ-rupts the calÂ-oÂ-rie reÂ-stricÂ-tion reÂ-sponse onÂ-ly in yeast, it has no efÂ-fect on othÂ-er orÂ-ganÂ-isms, such as worms, DilÂ-lin added. ResÂ-verÂ-aÂ-trol is proÂ-posed to stimÂ-uÂ-late sir-2.BeÂ-sides caÂ-lorÂ-ic reÂ-stricÂ-tion, the two othÂ-er moÂ-lecÂ-uÂ-lar pathÂ-ways afÂ-fecting lonÂ-gevÂ-iÂ-ty are called the inÂ-sulin/IGF sigÂ-nalÂ-ing and the miÂ-toÂ-chonÂ-driÂ-al elecÂ-tron transÂ-port chain pathÂ-ways, DilÂ-lin said. â€œIt is still not clear where sir-2 fits in. It seems to medÂ-dle with more than one pathÂ-way,â€• he added. â€œPHA-4 is speÂ-cifÂ-ic for calÂ-oÂ-rie reÂ-stricÂ-tion as it does not afÂ-fect the othÂ-er pathÂ-ways.â€•HuÂ-mans have three genes very siÂ-mÂ-iÂ-lar to worm pha-4; they all beÂ-long to a famÂ-iÂ-ly of genes called Foxa, DilÂ-lin conÂ-tinÂ-ued. All three play roles in deÂ-velÂ-opÂ-ment and latÂ-er in the regÂ-uÂ-laÂ-tion of glucagons, a panÂ-creÂ-atÂ-ic horÂ-mone that unÂ-like inÂ-suÂ-lin boosts blood sugÂ-ar leÂ-vels and mainÂ-tains enÂ-erÂ-gy balÂ-ance, esÂ-peÂ-cialÂ-ly durÂ-ing fastÂ-ing. SciÂ-enÂ-tists might be able to exÂ-ploit the findÂ-ings to creÂ-ate anti-agÂ-ing treatÂ-mentsâ€”speÂ-cifÂ-icÂ-ally, by findÂ-ing ways to stimÂ-uÂ-late Foxa acÂ-tivÂ-iÂ-ties, reÂ-searchÂ-ers said. â€œThose are exÂ-perÂ-iÂ-ments weâ€™re acÂ-tiveÂ-ly colÂ-labÂ-oÂ-ratÂ-ing on,â€• said SiÂ-ler PanÂ-owÂ-ski, a gradÂ-uÂ-ate stuÂ-dent in DilÂ-linâ€™s labÂ-oÂ-raÂ-tory.

Courtesy Salk Institute and World Science staff

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