A genetic change for achieving a long and healthy life

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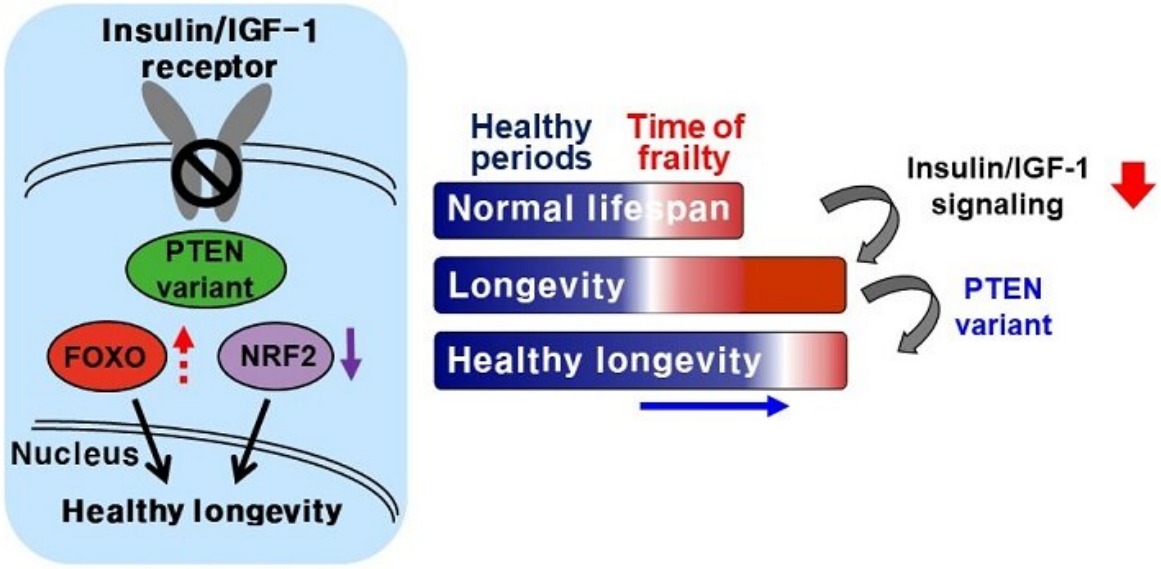

Credit: The Korea Advanced Institute of Science and Technology (KAIST)

Living a long, healthy life is everyone's wish, but it is not an easy one to achieve. Many aging studies are developing strategies to increase health spans, the period of life spent with good health, without chronic diseases and disabilities. Researchers at KAIST presented new insights for improving the health span by just regulating the activity of a protein.

A research group under Professor Seung-Jae V. Lee from the

Department of Biological Sciences identified a single amino acid change in the tumor suppressor protein phosphatase and tensin homolog (PTEN) that dramatically extends healthy periods while maintaining longevity. This study highlights the importance of the well-conserved tumor suppressor protein PTEN in health span regulation, which can be targeted to develop therapies for promoting healthy longevity in humans. The research was published in *Nature Communications* on September 24, 2021.

Insulin and insulin-like growth factor-1 (IGF-1) signaling (IIS) is one of the evolutionarily conserved aging-modulatory pathways present in life forms ranging from tiny roundworms to humans. The proper reduction of IIS leads to longevity in animals but often causes defects in multiple health parameters including impaired motility, reproduction, and growth.

The research team found that a specific amino acid change in the PTEN protein improves health status while retaining the longevity conferred by reduced IIS. They used the roundworm C. elegans, an excellent model animal that has been widely used for aging research, mainly because of its very short normal lifespan of about two to three weeks. The PTEN protein is a phosphatase that removes phosphate from lipids as well as proteins. Interestingly, the newly identified amino acid change delicately recalibrated the IIS by partially maintaining protein phosphatase activity while reducing lipid phosphatase activity.

As a result, the amino acid change in the PTEN protein maintained the activity of the longevity-promoting transcription factor Forkhead Box O (FOXO) protein while restricting the detrimental upregulation of another transcription factor, NRF2, leading to long and healthy life in animals with reduced IIS.

Professor Lee said, "Our study raises the exciting possibility of simultaneously promoting longevity and health in humans by slightly

tweaking the activity of one protein, PTEN."

More information: Hae-Eun H. Park et al, A PTEN variant uncouples longevity from impaired fitness in Caenorhabditis elegans with reduced insulin/IGF-1 signaling, *Nature Communications* (2021). DOI: 10.1038/s41467-021-25920-w

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