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Suppressing a gene in mice prevents heart from aging, preserves its function

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(PhysOrg.com) -- Scientists prevented age-related changes in the hearts of mice and preserved heart function by suppressing a form of the PI3K gene, in a study reported in *Circulation: Journal of the American Heart Association*.

"The study provides evidence that delaying or preventing heart failure in humans may be possible," said Tetsuo Shioi, M.D., Ph.D., senior author of the study and assistant professor of medicine at Kyoto University Graduate School of Medicine in Kyoto, Japan.

"Advanced age is a major risk factor for heart failure. One reason is that aging increases the chance of exposure to cardiovascular risk factors. However, natural changes due to aging may also compromise the cardiovascular system."

According to the American Heart Association, 5.7 million Americans have heart failure, and nearly 10 out of every 1,000 people over age 65 suffer heart failure every year.

Shioi and his colleagues studied elderly mice genetically engineered to suppress the activity of one form of the PI3K gene, which is a part of the insulin/IGF-1signaling system that helps regulate the lifespan of cells.

A variation of PI3K, known as the p110α isoform, plays an important role in tissue aging. Suppressing the isoform's activity in the roundworm C. elegans extends its life. And in fruit flies, suppression prevents the

age-dependent decline of heart function.

The Japanese researchers compared aged mice with a functional p110α to aged mice with suppressed p110α and found that mice with the suppressed gene had:

- improved cardiac function;
- less fibrosis (fibrosis causes the heart to lose flexibility);
- fewer biological markers of aging; and
- a pattern of cardiac gene expression like that of younger mice.

"This study showed that aging of the heart can be prevented by modifying the function of insulin and paves the way to preventing age-associated susceptibility to heart failure," Shioi said.

The researchers concluded that PI3K's role in cardiac aging involved regulating other points further downstream in the insulin/IGF-1signaling pathway, which resulted in changes in how insulin acted in heart cells. The biological mechanism by which suppressing the gene's activity improved the survival of the mice remains unclear.

"The heart failure epidemic in the United States and many other countries is due, in part, to our aging population," said Mariell Jessup, M.D., an American Heart Association spokesperson and professor of medicine at the University of Pennsylvania School of Medicine in Philadelphia. "Aging humans experience a slow but gradual loss of heart cells and a host of other cellular and sub-cellular abnormalities which make the remaining cells contract less efficiently. Thus, this early work in a mouse model, clarifying the role of PI3K in cardiac aging, could

ultimately allow scientists to understand if human hearts are similarly influenced."

Source: American Heart Association (news : web)