Medical Xpress

Insulin regulates the secretion of the antiaging hormome Klotho

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Dr. Carmela Abraham, a professor of biochemistry and medicine at Boston University School of Medicine (BUSM), reports this week in the *Proceedings of the National Academy of Sciences* new findings on Klotho, an anti-aging gene that is associated with life span extension in rodents and humans. Dr. Abraham's interest in Klotho stems from her studies comparing the expression of genes in young and old brains.

Dr. Abraham and her colleagues observed that the levels of Klotho in the brain showed a striking decrease with aging. The association between Klotho and aging prompted Abraham's group to investigate the regulation of Klotho further. These studies lead to the observation that secretion of Klotho is regulated by insulin.

The Klotho protein sits in the membrane of certain cells but is also found circulating in serum and cerebrospinal fluid, which indicates that it is secreted. The fact that Klotho is secreted suggested that enzymes that act like scissors must be involved in the liberation of Klotho from the cell membrane.

Dr. Ci-Di Chen, an assistant professor working in Dr. Abraham's group, then sought to identify the enzymes responsible for Klotho release and also investigated other factors that may affect the release of active Klotho.

To their surprise, they found that insulin, a hormone usually associated with diabetes, increases significantly the levels of secreted Klotho. The

reason this finding is important is because excess insulin has been previously implicated in a biochemical pathway that is associated with a decreased life span and elevated oxidative stress.

In addition, this observation provides a potentially pivotal link between Klotho and sugar metabolism, and raises an intriguing relationship between Klotho and type II diabetes, commonly known as late onset diabetes. The authors are proposing a novel mechanism of action for Klotho whereby insulin increases Klotho secretion, i.e., activity, and in turn, the secreted Klotho inhibits insulin's actions in the cell, which are known to be detrimental when insulin is in excess.

Sonia Podvin, Earl Gillespie and Dr. Susan Leeman, all from Boston University School of Medicine, also participated in the study.

Following these findings, the Abraham laboratory is now studying various ways to increase the level of Klotho to those levels found in young individuals. "The findings reported here may lead to new research designed to regulate the aging process, in other words, compounds that would increase Klotho could become the next "fountain of youth," said Abraham.

Source: Boston University

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