MedicalXpress

SIRT6 over-expression may prevent progression of diabetes, study finds

July 18 2019

Targeting obesity through exercise and calorie restriction is often the first line of approach to treat diabetes and related cardiovascular disorders, such as cardiomyopathy. A recent animal study published in *The FASEB Journal* explored an alternative sirtuin-based therapy to block the development of obesity and cardiomyopathy under conditions of excess nutrition, when diet restriction and regular exercise are not feasible.

For this study, researchers assessed the potential of SIRT6—often considered a longevity factor—to protect the heart from developing diabetic cardiomyopathy. Prior research has shown that a deficiency of nuclear sirtuin SIRT6 can lead to the development of cardiomyopathy in mice.

To conduct the experiment, researchers generated a group of whole-body SIRT6-overexpressing transgenic mice (Tg.SIRT6). The research team then observed the following groups of mice for 24 weeks: 1) control non-transgenic (N.Tg) mice fed a normal diet; 2) Tg.SIRT6 mice fed a normal diet; 3) control non-transgenic (N.Tg) mice fed a high-fat, high-sucrose (HF-HS) diet; and 4) Tg.SIRT6 mice fed a HF-HS diet.

As expected, the control N.Tg mice fed a HF-HS diet developed obesity, compared to the N.Tg and Tg.SIRT6 mice fed a normal diet. Surprisingly, however, the Tg.SIRT6 mice fed a HF-HS diet did not develop obesity. This unexpected finding demonstrated that over-expression of SIRT6 can prevent the development of obesity under the

conditions of excessive nutrition.

"We believe the information presented in this study will help us understand the pathogenesis of diabetic cardiomyopathy and its progression," said Mahesh P. Gupta, MS, Ph.D., professor and director of the University of Chicago's Cardiothoracic Surgery Research Program. "One day, a SIRT6-based therapy would be beneficial to patients who are unable to undertake regular exercise or diet restrictions to prevent the evolution of diabetes."

"These are intriguing findings," said Thoru Pederson, Ph.D., Editor-in-Chief of *The FASEB Journal*. "We have always thought of the sirtuin pathways as impinging on 'aging' in a generic sense but of course there are specific elements and this study has uncovered one that interacts with the morbidity/mortality factors of obesity and diabetes. We now might think of a 'sirtuin syndrome.'"

Provided by Federation of American Societies for Experimental Biology