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TIFR STUDY REVEALS ROLE OF GLUCOSE IN REGULATING LIVER FUNCTIONS, AGEING

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Life activities: The study paves the way to regulating this modification, which maiy help tackle lifestyle disorders and ageing related diseases. | Photo Credit: magicmine

An enzyme that goes by the name SIRT1 is known to be associated with regulation of metabolic activities and also ageing and hence has become a target of therapeutics. A study by researchers from Tata Institute of Fundamental Research, Mumbai (TIFR) shows that glucose controls the function of SIRT1 directly. A shortage or absence of this control can lead to a diabetic-like state, while excess feeding and sustained low levels of SIRT1 can lead to obesity and enhanced ageing. The study was published in the *Proceedings of the National Academy of Sciences.*

There are many diseases related to high calorie content in the body, such as metabolic disorders as shown in animal studies. Studies have shown that metabolic diseases are associated with wrong feeding regimen, even in humans. Every organism has evolved so as to feed and then alternately fast, so it becomes important to understand this cycle. This cycle, known as the feed-fast cycle is a basic pattern and the metabolism related to this is largely taken care of by the liver.

In an earlier work, published in *Cell Reports,* researchers in the lab of Ullas Kolthur-Seetharam from the Department of Biological Sciences at TIFR, found the mechanism that triggers the liver to go from one stage to another in the feed-fast cycle.

Now, working on a different angle, the group has discovered that glucose controls the functions of a protein SIRT1 which in turn maintains everyday feed-fast cycles and is also associated with longevity. “In normal healthy individuals, SIRT1 protein levels are known to increase during fasting and decrease during feed, which is essential to maintain a balance between glucose and fat metabolism,” says Prof Kolthur-Seetharam.

“Despite decades of work on the beneficial roles of SIRT1, metabolic factors that decrease its functions both during normal feed-fast cycles and in nutrient excess states (like obesity) was unknown,” explains Tandrika Chattopadhyay, who is the first author of the *PNAS* paper in an email to *The Hindu.*

“While there is active research to identify drugs that can activate SIRT1 which would be beneficial in countering ageing and metabolic diseases, the cost of uncontrolled overactivation of SIRT1 has not been investigated especially since it decreases in a healthy individual in a fed state,” says Dr. Chattopadhyay.

Glucose puts a check on the activity of SIRT1 in the fed state. In the absence of this check, SIRT1 activity increases and results in hyperglycaemia in a fasted state, mimicking diabetic state. “Constant feeding or high calorie intake that leads to sustained reduction in the levels of SIRT1 (by glucose) is associated with ageing and obesity,” she says.

“Our study shows that both over-activation and under-activation of this longevity factor could lead to diseases,” she adds.

This study paves the way to regulating this modification, which might be beneficial in tackling lifestyle disorders and ageing related diseases.

The group next seeks to investigate if glucose-dependent control can dictate gene expression during feed-fast cycles. “Also, we would like to investigate if small chemical molecules or drugs can selectively activate SIRT1 which could be used in the clinic to either increase or decrease the levels of SIRT1, as per the needs of the individual,” says Prof. Kolthur-Seetharam.

The WHO had to come up the name in line with the 2015 guidelines between the global agency, the World Organisation for Animal Health and the Food and Agriculture Organization.