Researchers study effect of delay in transportation of glucose into heart cell

Photograph: Dr. Samrat Chatterjee and his team at THSTI

New Delhi, July 14: You might have heard that the duration between an insulin dose and meals is significant for people with diabetes. Or the fact that people with diabetes are more at risk of getting a cardiovascular disease. Ever wondered why?

Glucose present outside a heart cell (cardiomyocyte) is transported into the cell by a set of proteins called glucose transporters (primarily GLUT4). This process of glucose transport is regulated by circulating insulin levels. A secondary messenger, calcium, continuously moves and oscillates to maintain the contraction and relaxation mechanism of the heart cells. The glucose inside the heart cells fulfills the energy requirement of a healthy heart. There is orchestration with the plasma glucose, plasma insulin, intracellular glucose, and cytoplasmic calcium inside a heart cell. A delay in transport can affect a proper maintenance of healthy cardiac function.

Dr. Samrat Chatterjee and his team at the Department of Biotechnology's Translational Health Science and Technology Institute (DBT-THSTI) studied these complex interactions through a four-dimensional delay-induced model under set conditions. The study aimed to understand the role of the delay in transport of glucose in a heart cell and explore restoration mechanisms as therapeutic targets in diabetes-like conditions.

The team developed a four-dimensional delay differential model involving plasma glucose, plasma insulin, intracellular glucose, and cytoplasmic calcium concentration in a heart cell (cardiomyocyte) as state variables. This helped to find out that the glucose input rate in the bloodstream (during diabetes) is the most sensitive parameter influencing all other state variables. They found glucose adsorption rate by non-cardiac cells, insulin production, and degradation rate as other sensitive parameters. Any perturbation in these sensitive parameters leads to the irregular oscillations of calcium in heart cells leading to heart dysfunction.

Further analysis identified that the rate of degradation of intracellular glucose is pivotal in deciding the calcium dynamics of a heart cell. In this model, mimicking the diabetic condition was achieved by changing parameters related to the uptake rate of insulin-dependent glucose and delay in glucose transport. Thus, the regulated input of glucose in blood plasma is suitable for normal oscillations of calcium in cardiomyocytes. Other ways to control calcium oscillations and glucose are to manipulate other parameters depending on time delay associated with the uptake rate of intracellular glucose.

Link to the research paper: https://link.springer.com/article/10.1007/s10867-020-09551-8#citeas

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