New clue to Huntington’s disease

Insulin signalling could slow the disease’s progression

A study by researchers at the Department of Genetics, Delhi University, South Campus, has shown that it is possible to restrict the progression of Huntington’s disease by increasing insulin signalling in the brain’s neuronal cells.

The study, which was conducted in fruit flies (Drosophila), found that increasing the level of insulin signalling enriches the cellular pool of proteins that are essential for cellular functioning and survival. This in turn restores the cellular transcription machinery, which typically collapses due to the disease, and thus stops the disease from progressing.

Dr. Surajit Sarkar, who led the study, said “The study was a follow up to investigations which had revealed that the insulin signalling pathway, which is a critical controller of cellular metabolism and energy homeostasis, was severely compromised in Huntington’s and other polyglutamine disorders like SCA3.”

Still without a cure

There is no treatment or cure for Huntington’s at present. Afflicted individuals lose their ability to walk, talk, think and reason. This disease begins between ages 30 and 45, and every individual with the gene for the disease will eventually develop the disease. It is an autosomal dominant genetic disorder, which means that even if one parent carries the defective Huntington’s gene, their offspring has a 50:50 chance of inheriting the disease.

When experiments were conducted to check whether it would help if the level of insulin signalling was increased by up-regulating the insulin receptor in the disease affected neuronal cells, researchers found that it worked.

They then tried to unravel the molecular mechanism. They found that improving the insulin signalling pathway resulted in a significant reduction in the cellular level of neurotoxic protein aggregates or inclusion bodies, with a remarkable decrease in the neuronal cell death.

“It appears that enhanced level of insulin signalling rejuvenates the neuronal cells which are otherwise stressed during disease condition. Our findings strongly suggest that anti-diabetic drugs could be efficiently utilised to restrict the pathogenesis of polyglutamine disorders,” the study says.

Commenting on the work, Dr. Krishnananda Chattopadhyay, Head of the Structural Biology and Bioinformatics Division at the Indian Institute of Chemical Biology, Kolkata, who was not involved in the study, said, “The study has immense potential application. Subsequent investigations by including higher organisms and anti-diabetic drugs would provide a novel approach to combat the devastating human polyglutamine disorders.”

The study by Dr. Sarkar and Dr. Kritika Raj has been published in the journal, Molecular Neurobiology. The work was supported by research grants from the Department of Biotechnology. – India Science Wire