PRESS RELEASE

IIT Mandi team discovers a molecule that can be used for the treatment of Type 1 and Type 2 diabetes

Researchers found that the molecule PK2 not only increases insulin release but also prevents and reverses beta cell loss, making it effective for both Type 1 and Type 2 diabetes.

Video link: https://drive.google.com/drive/folders/1-e0Z_xFryEC624RcKlxWVdO7PqH0SL6k

Mandi, 2nd May 2022: Researchers at the Indian Institute of Technology Mandi have identified a drug molecule that can be used to treat diabetes. This molecule, called PK2 is able to trigger the release of insulin by the pancreas and can potentially be used as an orally administered medicine for diabetes.

The findings of the research have been published in the Journal of Biological Chemistry. The paper has been authored by Dr. Prosenjit Mondal, Associate Professor, School of Basic Sciences, and co-authored by Prof. Subrata Ghosh, School of Basic Sciences, IIT Mandi, along with Dr. Sunil Kumar, ICAR- IASRI, PUSA, New Delhi, Dr. Budheswar Dehury, ICMR RMRC, Bhubaneswar, Dr. Khyati Girdhar, Ms. Shilpa Thakur, Dr.Abhinav Choubey, Dr. Pankaj Gaur, Ms. Surbhi Dogra, Ms. Bidisha Biswas from IIT Mandi, and Dr.Durgesh Kumar Dwivedi (Regional Ayurvedic Research Institute (RARI) Gwalior),

Explaining the rationale for their research, Dr. Prosenjit Mondal, said "Current drugs such as exenatide and liraglutide used for diabetes, are administered as injections, and they are costly and unstable after administration. We seek to find simpler drugs that are stable, cheap, and effective against both Type 1 and Type 2 diabetes."

Diabetes is associated with insufficient insulin release by the beta cells of the pancreas in response to blood glucose levels. The release of insulin entails many intricate biochemical processes. One such process involves protein structures called GLP1R present in the cells. A hormonal molecule called GLP1, released after the ingestion of a meal, binds to the GLP1R and triggers the release of insulin. Drugs such as exenatide and liraglutide mimic GLP1 and bind to GLP1R to trigger insulin release.

To find alternatives to these drugs, the multi-institutional team first used computer simulation methods to screen various small molecules that can bind with GLP1R. While PK2, PK3, and PK4 had good binding abilities with GLP1R, they subsequently chose PK2 because of its better solubility in solvents. The researchers then synthesized PK2 in the lab for further testing.

Describing the preliminary research, **Dr.Khyati Girdhar, said,** "We first tested the binding of PK2 on GLP1R proteins in human cells and found that it is

able to bind well toGLP1R proteins. This showed that PK2 can potentially trigger insulin release by the beta cells." The researchers found that PK2 was rapidly absorbed by the gastrointestinal tract, which means that it can be used as an oral medication rather than an injection. Furthermore, after two hours of administration, PK2 was found distributed in the liver, kidney, and pancreas of the mice, but there were no traces of it in the heart, lungs, and spleen. There was a small amount present in the brain, which shows that the molecule may be able to cross the blood-brain barrier. It was cleared from circulation in about 10 hours.

Dr. Prosenjit Mondal points to another critical finding in their work, "Beyond increasing insulin release, PK2 was also able to prevent and even reverse beta cell loss, a cell essential for insulin production, making it effective for both Type 1 and Type 2 diabetes."

In order to test the biological effects of PK2, the researchers administered it orally to experimental mice developing diabetes and measured glucose levels and insulin secretion. There was a six-fold increase in serum insulin levels in PK2-treated mice over the control group. These findings provide hope for inexpensive oral drugs for diabetic patients.

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About IIT Mandi

IIT Mandi has four Academic Schools and three major Research Centers. The Schools are: School of Computing and Electrical Engineering, School of Basic Sciences, School of Engineering, and School of Humanities and Social Sciences. The Centers are: Advanced Materials Research Centre (AMRC; set up with an investment of Rs. 60 crores), Centre for Design and Fabrication of Electrical Devices (C4DFED; has Rs. 50 crores worth of fabrication tools), and BioX Centre (has acquired research equipment worth Rs. 15 crores).

The unique, project-oriented B.Tech. curriculum is centred around its 4-year long Design and Innovation stream. From August 2019, IIT Mandi started 3 new and unique B. Tech. programmes in Data Science and Engineering, Engineering Physics, and Dual Degree in Bioengineering. Since the inception of the Institute, IIT Mandi faculty have been involved in over 275 Research and Development (R&D) projects worth more than Rs. 120 crore.

IIT Mandi set up the IIT Mandi iHub and HCI Foundation (iHub; a section-8 company) on its campus at Kamand with significant funding of INR 110 crores from the Department of Science and Technology (DST), Government of India. The iHub is planned to fuel research and technology development, skill development, startup and innovation, and collaborations in the HCI and allied AI/ML areas in India. IIT Mandi is the only second-generation IIT to be featured at rank no. 7 in the Atal Ranking of Institutions on Innovation Achievements of the Innovation Cell, Ministry of Education, Govt. of India.

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