

Diabetes mellitus is one of the most serious chronic diseases of the 21st century, affecting over 10% of all adults worldwide. The primary cause of diabetes is the progressive decline in the function of pancreatic β -cells – cells that are responsible for producing insulin, the hormone that regulates blood glucose levels. Although current therapies can manage blood sugar levels, they do not address the actual damage happening inside the body that leads to β -cell dysfunction and eventual failure.

This project explores important molecular mechanism involved in insulin signaling and β -cell damage in diabetes. Scientists have recently discovered that the protein DYRK1A plays an important role in this process by targeting another essential protein called IRS2. DYRK1A-mediated phosphorylation of IRS2 causes its degradation, which impairs insulin signaling and contributes to β -cell death. The planned research involves the use of advanced structural biology techniques, including cryo-electron microscopy to explore this mechanism in detail.

This research was chosen in response to the urgent need for new therapeutic strategies that go beyond treating only the symptoms of diabetes. By understanding how DYRK1A disrupts insulin signaling via IRS2 degradation, the project opens the door to the development of novel therapeutic approaches. For example, small-molecule DYRK1A inhibitors, drugs that block its activity and could keep IRS2 active, may preserve β -cell function and slow disease progression.

In results, this research will study exactly how DYRK1A interacts with IRS2, by obtaining a detailed 3D model of both proteins working together. These results will not only advance our understanding of diabetes at the molecular level but may also be relevant to other diseases involving DYRK1A, including various types of cancer and neurodegenerative disorders such as Alzheimer's disease. By combining cutting-edge experimental techniques with a clinically urgent research question, this project holds promise to drive the development of innovative, mechanism-based therapies for diabetes and related diseases of civilization.