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Scientists identified T372R mutation as potential target for diagnosis and treatment of insulinoma

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Chinese researchers from Rui-Jin Hospital, Shanghai Jiao-Tong University School of Medicine, BGI and other institutes identified the recurrent T372R mutation in the transcription factor YY1 (Yin Yang 1) are related with insulinoma oncogenesis, implicating a potential marker for the diagnosis and treatment of functional pancreatic neuroendocrine tumors (PNETs). The latest study was published online in *Nature Communications*.

Pancreatic neuroendocrine tumors are classified into functional and nonfunctional tumors by hormone secretion and clinical symptoms. Functional PNETs are mainly represented by insulinoma, which secrete insulin independent of glucose and cause hypoglycemia. The major genetic alterations in insulinomas are still unknown.

In this study, researchers identified T372R mutation in YY1 by whole exome sequencing of 10 sporadic insulinomas samples. It is noteworthy that the T372R mutation was the first reported in public available databases such as 1,000 Genomes and dbSNP database. YY1 is a multifunctional protein, which takes part in regulating normal physiological progress such as development, differentiation, replication and cell proliferation. It also plays an important role in regulating insulin and insulin-like growth factor (IGF) signaling that is crucial for pancreatic β-cell survival and insulin secretion.

Subsequently, researchers validated T372R mutation in 103 additional insulinomas samples. The results showed that 31 in 103 cases had the T372R mutation, providing evidence to support that T372R mutation is a pathogenic factor of insulinoma. In addition, they found T372R mutation could enhance the transcriptional activity of YY1. The mTOR inhibitor which has been approved to use for cancer treatment also can regulate the transcriptional activity of YY1.

Lin Li, Project Manager from BGI, said: "In this study, we conducted whole exome sequencing on sporadic insulinomas, and found the hotspot mutations of T372R in 30% insulinomas. The findings not only contribute new diagnostic and medical therapies of PNETs, but also provide new insights into diabetes studies."

Provided by BGI Shenzhen

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