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Gleevec could be novel therapeutic agent for type 2 diabetes

Published on March 28, 2016 at 1:34 PM

The cancer treatment drug Imatinib, otherwise known as Gleevec is approved to treat various forms of cancer, mostly notably chronic myeloid leukemia (CML). However, researchers have stumbled onto another possible use for it, curing type 2 diabetes.

The team--made up of scientists from the Scripps Research Institute in United States, South Korea-based company Hyundai Pharm Co., Ltd., the Seoul National University, and Ulsan National Institute of Science and Technology (UNIST)--has identified for the first time that, through control of PPAR γ , Gleevec lowers the level of insulin resistance, thereby reducing the risk of both hyperglycemia and obesity.

According to the team, led by Prof. Jang Hyun Choi (School of Life Sciences) of UNIST, "Although TZD-based medicines work effectively at improving glucose uptake by skeletal muscle and other peripheral tissues, due to increased risk of adverse effects they have been withdrawn from the market ." He continues, "In order to develop new type of medication that have fewer side effects, we have discovered a new compound that can maintain stable blood sugar levels."

Among insulin-sensitizing drugs, TZDs are a therapeutic class that are selective agonists for PPAR γ , which plays a central role in how the body metabolizes glucose, stores fat, and controls immune and inflammatory responses.

In the study, the team observed that the phosphorylation of PPAR γ is closely related to developing diabetes. They also discovered that the removal of phosphoric acid from PPAR γ shows anti-diabetic effects. To determine whether phosphoric acid is bound to PPAR γ , the team developed a new chemical screening procedure. Using high throughput phosphorylation screening, the team discovered that Gleevec blocks CDK5-mediated PPAR γ phosphorylation devoid of classical agonism as a PPAR γ antagonist ligand.

Prof. Choi states, "Although studies have shown that Gleevec treatment may show improved insulin sensitivity and decrease blood glucose in patients with known diabetes, the exact cause hasn't been proven yet." He continues, "Through this research, we discovered Gleevec, which is used in leukemia medications, can inhibit the phosphorylation of PPAR γ ."

Moreover, when tested with high-fat diet-fed mice, Gleevec showed improved insulin sensitivity without causing severe side effects seen with other PPAR γ -targeting drugs. The researchers note that Gleevec was also found to reduce lipogenic and gluconeogenic gene expression in liver and improved inflammation in adipose tissues. Increased browning of white adipose tissue (WAT) and energy expenditure were also seen with Gleevec.

The team notes, "Taken together, Gleevec exhibits greater beneficial effects on both glucose/lipid metabolism and energy homeostasis by blocking PPAR γ phosphorylation." They continue, "These data illustrate that Gleevec could be a novel therapeutic agent for use in insulin resistance and type 2 diabetes."

Source:

Ulsan National Institute of Science and Technology(UNIST)
