2-S23-4 Symposium23

Regulation of glucagon secretion and pharmacotherapy for diabetes

Licht Miyamoto, Koichiro Tsuchiya

Dept. Medical Pharmacology, Inst. of Biomedical Sciences, Tokushima Univ.

Recent studies have suggested significance of glucagon in diabetes. Recent topics related to glucagon and pharmacotherapy of diabetes will be discussed. SGLT2 inhibitors lower blood glucose levels by preventing renal glucose reuptake, but they often cause hyperglucagonemia. Potential role of SGLT2 as a glucagon suppressor in pancreatic alpha cells was demonstrated recently, though it has been under debate. Thus, we conducted functional analyses of SGLT2 in a typical model of pancreatic alpha cell, α-TC cells to unveil roles of SGLT2 in the glucagon secretion. Glucagon secretion as well as intracellular ATP level decreased in response to glucose deprivation. SGLT2 inhibitors reduced glucose uptake, but glucagon secretion nor ATP level was affected. An inhibitor of KATP channel increased glucagon secretion without changing ATP level. Therefore, glucose starvation should not facilitate but suppress glucagon secretion possibly by raising AMP/ATP ratio which mitigates membrane potential through KATP channel. We also found SGLT2-mediated glucose uptake in α-TC cells. Nevertheless, the glucose influx is supposed to be too small to take effects on ATP level, and SGLT2 inhibitors should not directly alter glucagon secretion. Glucose starvation-induced glucagon secretion may require interaction among different types of the cells in islets.