C7

Characterization of Voltage-Sensitive Calcium Channels and Insulin Secretion and the effect of 4,4'-Dichlorobiphenyl in RINm5f cells

Ihn-Soon Lee[1], Eun-Mi Hur[1], Sungkwon Chung[2] and Kyong-Tai Kim[1]
[1]Dept. of Life Science, Pohang University of Science and Technology, Pohang
[2]Dept. of Physiology, Sungkyunkwan University School of Medicine, Suwon

Opening of Ca^{2+}-channels represents the final common pathway for insulin secretion in pancreatic beta-cells and related cell lines. We investigated voltage-sensitive calcium channels (VSCCs) and insulin secretion in RINm5F, an insulinoma cell line derived from rat pancreatic beta-cells. Several types of VSCCs were identified in RINm5f cells: dihydropyridine-sensitive L-type, ω-conotoxin GVIA-sensitive N-type, ω-agatoxin IVA-sensitive P-type channels, and ω-conotoxin MVIIC sensitive Q-type channels. We observed that nifedipine, ω-conotoxin GVIA, ω-agatoxin IVA, and ω-conotoxin MVIIC inhibited high K^+-induced calcium influx by 38 ± 5%, 9 ± 4%, 5 ± 2%, 54 ± 2%, respectively.

Non-coplanar congeners of polychlorinated biphenyls (PCBs), environmental contaminants, are known to induce release of insulin in RINm5F cells. We investigated the effect of 4,4'-DCB (dichorobiphenyl), a coplanar polycholorinated biphenyl (PCB) congener, on insulin secretion. Not only inducing insulin secretion, 50 μM of 4,4'-DCB also inhibited high K^+-evoked insulin secretion by 50%. We then investigated the effect of 4,4'-DCB on VSCCs since VSCCs are the final pathway for insulin secretion. 4,4'-DCB inhibited high K^+- induced cytosolic calcium increase in a concentration-dependent manner with a half maximal inhibitory concentration of 30 μM. Its inhibitory effect reached maximum within 1 min, suggesting that it might directly inhibit VSCCs. The presence of calcium channel blockers did not affect the extent of inhibition occurred by the treatment of 4,4'-DCB, indicating that 4'4-DCB did not have any calcium channel selectivity. Whole cell patch-clamp recordings on RINm5f cells confirmed that 4,4'-DCB inhibited VSCCs without type specificity.

Here we show that there are L-, N-, P-, and Q-type VSCCs in RINm5f cells. We also show that a coplanar congener of PCB, 4,4'-DCB, inhibits insulin secretion, and that the inhibition of insulin secretion might occur via inhibiting various types of VSCCs in RINm5f cells.