

Adipose-derived Wnt Activators Contribute towards Adaptation of Pancreatic Beta Cells to Systemic Insulin Resistance

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Adipose tissue secretes number of adipokines - specific lipid molecules and protein factors in order to communicate with organ system in the body. Wnt activators, which are lipidated proteins, have recently been identified as the novel adipose-derived factors.

The aim of the present study was to determine whether adipose-derived Wnt activators contribute to pancreatic beta cell adaptation towards systemic insulin resistance. The experiments were performed on the INS-1E cells, an insulinoma beta cell line, treated with fat cell conditioned medium from insulin-sensitive and insulin-resistant 3T3-L1 adipocytes. Protein levels of active beta-catenin, the major element of Wnt signaling, were significantly increased in INS-1E cells incubated in conditioned medium from both, insulin-sensitive and insulin-resistant adipocytes. Luciferase reporter assay confirmed activation of Wnt transcriptional activity in INS-1E cells incubated in adipose-derived medium. These changes were more evident in INS-1E cells incubated in medium from insulin-resistant adipocytes, suggesting that these cells release more Wnt activators than insulin-sensitive adipocytes. Moreover, Real Time-PCR analysis showed that expression of *beta-catenin* and of two Wnt target genes, *cmyc* and *cyclinD1*, was enhanced in beta-cells incubated in medium derived from insulin-resistant adipocytes. Furthermore, proliferation of INS-1E cells and the rate of insulin secretion were significantly increased upon adipose-conditioned medium treatments. To check whether these changes are associated with increased activation of Wnt pathway, we inhibited Wnt signaling by using sFRP – a specific Wnt inhibitor. Reduction of Wnt activity by using sFRP decreased significantly both, insulin secretion and proliferation rate of INS-1E cells. Results presented herein suggest that Wnt signaling is an important component of the crosstalk between adipose tissue and pancreas and that adipose-derived Wnt activators might be involved in triggering adaptation of beta cells to the systemic insulin resistance.

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