RANTES (CCL5) reduces glucose-dependent secretion of glucagon-like peptides 1 and 2 and impairs glucose-induced insulin secretion in mice.

Abstract:

Type 2 diabetes is associated with elevated circulating levels of the chemokine RANTES and with decreased plasma levels of the incretin hormone glucagon-like peptide 1 (GLP-1). GLP-1 is a peptide secreted from intestinal L-cells upon nutrient ingestion. It enhances insulin secretion from pancreatic β-cells and protects from β-cell loss but also promotes satiety and weight loss. In search of chemokines that may reduce GLP-1 secretion we identified RANTES and show that it reduces glucose-stimulated GLP-1 secretion in the human enteroendocrine cell line NCI-H716, blocked by the antagonist Met-RANTES, and in vivo in mice. RANTES exposure to mouse intestinal tissues lowers transport function of the intestinal glucose transporter SGLT1, and administration in mice reduces plasma GLP-1 and GLP-2 levels after an oral glucose load and thereby impairs insulin secretion. These data show that RANTES is involved in altered secretion of glucagon-like peptide hormones most probably acting through SGLT1, and our study identifies the RANTES-receptor CCR1 as a potential target in diabetes therapy.

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