P005 Expression of GPR40 receptor family in islets

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GPR40 is a G-protein coupled receptor that responds to long-chain fatty acids (FAs) and shows 30-40% homology with GPR41 and GPR43 receptors activated by short-chain FAs. GPR40, 41 and 43 mRNAs were detected in MIN6 β-cells and in mouse and human islets by RT-PCR, and GPR43 mRNA was also identified in αTC3 cells. These mRNAs were translated into proteins of the appropriate molecular weights, as determined by Western blotting using MIN6 cells. Furthermore, immunohistochemistry indicated that GPR43 was expressed at relatively high abundance by mouse islet α-cells and, to a lesser extent, by β-cells. Short-term activation of GPR40 with a selective agonist (AZ168) resulted in potentiation of glucose-stimulated insulin secretion from MIN6 cells (20mM glucose + 40μM AZ168: 189±10% 20mM glucose-stimulated response, $P<0.01$) and increased calcium in Fura-2-loaded MIN6 cells (2mM glucose + 40μM AZ168: 70±3% of tolbutamide response, n=109 cells, 4 experiments). Our data indicate that mouse and human islets express GPR40, 41 and 43, and that GPR43 is expressed by both α- and β-cells. The use of a selective agonist indicated that GPR40 activation is coupled to an increase in calcium levels and insulin secretion. We are currently investigating the role of GPR43 in the effects of short-chain FAs on α- and β-cell function using GPR43 knockout mice.