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A glycolytic target for somatostatin-mediated inhibition of glucose metabolism in pancreatic beta-cells

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Introduction The inhibition of glucose-stimulated insulin secretion from pancreatic beta-cells by somatostatin is in part due to a block of its metabolism, however, the underlying molecular process remains unknown (1). The aim of this study was to explore glycolysis as a target site for the action of this peptide hormone in the pancreatic beta-cell line MIN6.

Methods The metabolic fate of glucose by aerobic glycolysis and mitochondrial respiration were simultaneously measured by the rate of lactate production (LPR) and oxygen consumption (OCR) respectively. Experiments were performed on stirred MIN6 cells suspensions of known density at 32℃ in a closed system. LPR was measured with Sari ssa lactate electrodes (1), whereas OCR was determined with Clark oxygen electrodes (2). Electrode calibration allowed stoichiometric quantification of the metabolic fate of glucose. Data are given as mean ± SEM (n = number of determinations). Data was analysed by ANOVA with Holm-Sidak's multiple comparisons test,.

Results In the absence of exogenous substrate, LPR was negligible whereas basal OCR was 2.3±0.4 nmol O_2 10^7 $cell^{-1}$ min^{-1}. Addition of 10 mM glucose stimulated OCR by 2.3±0.1 nmol O_2 10^7 $cell^{-1}min^{-1}$ to 5±0.5 nmol O_2 10^7 $cell^{-1}$ min^{-1} ($P<0.01$, n=9); this was associated with an LPR of 6±1.2 nmol 10^7 $cell^{-1}$ min^{-1} ($P<0.01$, n=9). These values yield an oxidative/glycolytic ratio (OGR) for the metabolic fate of glucose of 1±0.2. Addition of 100 nM somatostatin-14 inhibited OCR by 36% ($P<0.001$, n=9) and LPR by 28% ($P<0.0001$, n=9) relative to the water vehicle control. Overall, however, the OGR was unaffected at 1.2±0.2.

Conclusion In pancreatic beta-cells, pyruvate produced by glycolysis undergoes two metabolic fates: oxidative respiration by the mitochondria, with the remainder lost as lactate (3). Somatostatin-14 blocked glucose-stimulated respiration and lactate production by stoichiometrically equivalent amounts suggesting that the major metabolic target for this peptide is upstream of pyruvate production at an early step of glucose utilization, either glycolysis itself or glucose uptake. Furthermore, since the LPR to OCR molar ratio for MIN6 was similar to that found for glucose in rat islet beta-cells (3), this supports the use of the MIN6 cell line as an appropriate metabolic model of native beta-cells in which to study the action of compounds that affect their metabolism.

References:

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3. Sener A. et al. (1976) Biochem. J. 156: 521-525.