P016 GLUT2 initiates a sugar signal targeting the transcription of glucose-sensitive genes in enterocytes

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Dietary sugars stimulate the expression of genes involved in glucose metabolism suggesting that a sugar sensing mechanism enables intestinal adaptation to diet. In liver cells, GLUT2 initiates a signalling pathway targeting glucose-activated transcription in cooperation with metabolism. We postulated that in the intestine, despite the presence of other sugar transporters, GLUT2 might similarly contribute to the sensing of dietary sugars.

We show that metabolisable sugars activate GLUT2 and sucrase-isomaltase promoters mounted upstream a luciferase reporter gene in human Caco-2/TC7 enterocytes. This regulation was obtained in cells grown on transwell™ filters, but not on solid support. Expression of the GLUT2-intracellular loop (TM6-7) but not of the −COOH-terminal domain of the protein inhibits the sugar dependent response of the GLUT2 promoter and of the corresponding endogenous mRNA. Thus the GLUT2-loop exerts a dominant negative effect on the glucose-signalling pathway.

In vivo, the role of GLUT2 as a glucose sensor was assessed in GLUT2-null mice. Those mice loose the upregulation by dietary sugars of two sugar sensitive genes, pyruvate-kinase and sucrase-isomaltase.

Altogether, these results indicate that GLUT2 is part of a sensing pathway for dietary sugars to modulate the transcription of sugar-sensitive genes in enterocytes.v