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Sugar sensor genes in the murine gastrointestinal tract display a cephalocaudal axis of expression and a diurnal rhythm

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Issue: The mechanisms responsible for regulating the expression of the intestinal macronutrient sensors are unknown. Many physiological processes (e.g. intestinal sugar transport) display a diurnal rhythm that is controlled by clock genes. We therefore hypothesised the GI tracts nutrient sensors also display a diurnal rhythm that is entrained by clock genes.

Aims: In rodents, determine evidence of a diurnal rhythmicity in sugar sensor (T1r2/3, SGLT3) and sugar transporter (SGLT1, GLUT2, GLUT5) and gut peptide expression levels along the length of the GI tract.

Methods: Sixteen C57BL/6J mice were fed ad libitum at the standard 12 h light/dark cycle. After six weeks the animals were sacrificed at 7 am (n=8) and 7 pm (n=8). Tongue, stomach, duodenum, jejunum & ileum were prepared for RT-qPCR. Expression levels for each gene were relatively quantified against three reference genes using the 2-ΔΔCT method.

Results: Sweet taste receptor (tas1r2/tas1r3/gnat3/gnat1) sugar transporter (slc5a1, slc2a2, slc2a5) and putative sugar sensor (slc5a4a and slc5a4b) gene expression levels were highest in tongue, proximal and distal small intestine, respectively. Clock gene (cry2/arntl) activity was detected in all regions studied. Slc5a4a and slc5a4b gene expression showed clear diurnal rhythmicity in the small intestine and stomach, respectively, although no rhythmicity was detected in SGLT3 protein expression. Tas1r2 and tas1r3, gnat3 and gcg displayed a limited rhythm in gene expression in proximal small intestine. Microarray analysis revealed a diurnal rhythm in gut peptide gene expression in tongue (7 am vs. 7 pm) and in silico promoter analysis indicated intestinal sugar sensors and transporters possessed the canonical E box elements necessary for clock gene control over gene transcription.

Conclusion: Sugar sensors, transporters and gut peptides, but not αGustducin/transducin, exhibit a diurnal pattern of gene expression in specific regions of the GI tract. Disruption in clock control of intestinal nutrient sensing may contribute to disturbances in metabolism.

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