

"Sweet Taste Receptors Modulate Glucose Absorption"

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Taste Receptors are nutrient chemosensors beyond the tongue





Sweet Taste Receptor sensing: Same machinery, different context



STRs regulate plasma glucose homeostasis in response to "oral" glucose delivery

intra-gastric glucose tolerance test (IG.GTT)

Glucose (1.0g/kg)







Smith et al, Mol Metab. 2018

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Peripheral glucose disposal

Gut microbiota



T1R2 intestines have reduced rate of 3-OMG flux

3-OMG (10 or 30mM) ¹⁴C 3-O-methylglucose HO H₃CO lactisole Baso-3 Apical lateral OCH₃ ł side side HC OH **T1R2 T1R3** OH mucosa \rightarrow serosa human intestinal explants wт T1R2 3-OMG (30mM) Flux (nmol/min/cm²) p = 0.002Flux (nmol.cm ⁻².min⁻¹) 60-** 157 Flux (nmol/min/cm²) 607 50 *** 40 10 40 30 20 5 20 10. wт -0 M G 3 -O M G <u>T1R2</u> 0 + ٥ 60 120 30 90 0 10 30 Veh Lac ĉ 3-OMG (mM) time(min) 3-OMG (30mM)

`O⁻ Na⁺

The role of the gut sweet taste receptor in regulating GLP-1, PYY, and CCK release in humans

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Intragastric infusion







Inhibition of sweet chemosensory receptors alters insulin responses during glucose ingestion in healthy adults: a randomized crossover interventional study^{1,2}

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Oral bolus

Glucose transport in the small intestine





(G. Kellett, E. Brot-Laroche, Diabetes, 2005)

Blood

T1R2 mice have reduced rate of GLUT2 translocation in response to an ig glucose load



Smith et al, Mol Metab. 2018

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Intestinal perfusion with sucralose potentiates GLUT2 translocation in rats





GLUT2 immunoreactivity

J Physiol 582.1 (2007) pp 379-392

Potential mechanisms for the reduced rate of GLUT2 translocation in T1R2 intestines



Mechanism for the reduced rate of GLUT2 translocation in T1R2 intestine







Ex vivo Glucose flux



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Smith et al, Mol Metab. 2018

The GLP2 analogue, teduglutide, restores plasma glucose response during an igGTT in T1R2 mice





Is T1R2-mediated nutrient chemosensing relevant to the development of metabolic disease?

Functional adaptations of intestinal STRs in response to dietary sugars



Overnight high sucrose diet (HSD) downregulates intestinal STR expression



GLUT2 Accumulation in Enterocyte Apical and Intracellular Membranes

A Study in Morbidly Obese Human Subjects and ob/ob and High Fat—Fed Mice

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Deletion of T1R2 decreases glucose excursions during an IG.GTT in Ob/Ob mice



unpublished

Unanswered questions





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