Year 1 MBChB
Lecture 14
Gut communication with its environment - Nutrient sensing & uptake

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Learning outcomes

Lecture 14: Gut communication with its environment - Nutrient sensing & uptake

- Describe the taste receptors including the different types and taste modalities
- Explain nutrient sensing in the GI tract and the “Gustotopic” map of the tongue.
- Describe the taste receptors in the gut (stomach, gallbladder, small intestine, colon) and relevant nutrient transport mechanisms
- Nutrient sensing and the potential for future medicines?
The tongue and taste

- Taste receptors in the tongue send information via VII and IX cranial nerves to reach the nucleus of the solitary tract (NTS) in brain stem.

- Initiate visceral reflexes to gut to prepare for incoming meal (Cephalic response)

Taste buds/cells - Chemosensitive receptors

Gustatory afferent neurons

Efferents VII, IX and X

Thought, sight, smell, taste

Chemosensitive receptors

VII and IX cranial nerves

Nasal Cavity - Oral Cavity - Larynx opening into pharynx

Tongue

Rasch Cavity - Oral Cavity - Larynx opening into pharynx

Taste cells - Foliate papillae - Circumvallate papillae

Fovea papillae

Gastric acid output

Time after feeding (hours)
Taste, olfaction and gustatory responses

- The nucleus of the solitary tract projects to a specific gustatory nucleus in the thalamus, and from there to the insular cortex.

- A great deal of what we call taste is based on olfactory signals. During a nasal infection the olfactory receptors are injured or blocked, we lose ~90% of our ability to appreciate flavours.

Visceral responses
- Salivary secretion
- Gastric juice
- Pancreatic secretion
- Gallbladder contraction

Main olfactory pathway
- runs from the olfactory bulb to the primary olfactory cortex (piriform cortex) on the underside of the temporal lobe
Taste in the mouth – the gustotopic map

Old model

New model

Lingual Epithelium **Taste Receptors**

**Taste Receptor 1** (T1R) has three members. T1R1, T1R2 and T1R3

- **Combination** of T1R1+T1R3 = taste of L-amino acids (*umami*), taste of monosodium glutamate.

- **Combination** of T1R2+T1R3 = **Sweet taste**.

**Taste receptor 2** family or T2Rs (~30 separate genes encode members of T2R family) = **bitter taste**.

- These receptors are **G protein** (guanine nucleotide binding protein) coupled receptors (GPCRs).
- G-protein that couples to these receptors is called **Gustducin**, belonging to the Transducin family of GPCRs.
Other Lingual Epithelium Taste Receptors

**ENaC** – epithelial Sodium (Na\(^+\)) channel is also found in taste receptors, where it plays an important role in **saltiness perception**.

**PKD2L1** - reported to be a candidate receptor for **sour taste** based on molecular biological and functional studies.
In much the same way as the tongue, the gut also tastes what we eat.

**TASTE CIRCUITS**

Cells with taste receptors are found throughout the body (shown in green). Along the digestive tract, their presence is probably related to food. But in bile ducts — that carry only secretions produced by the body — their purpose is more enigmatic.
Gut enteroendocrine cells (EECs) - nutrient sensors

- Nerve endings that enter the villi do not reach the luminal content. Hence EECs are central to the chemosensing pathway of the intestinal tract.

- There are at least 12 different EEC populations of the GI tract producing >20 hormones.
- Nutrient sensing GPCRs are expressed on the luminal membrane of EECs.
- Nutrient sensing through these receptors leads to secretion of key regulatory gut hormones.
Taste receptors on gut endocrine cells control the release of hormones in response to nutrients.

**Region** | **Cell** | **Hormone/Nutrient/Taste receptors** | **Action**
---|---|---|---
Stomach | G cell | gastrin: regulation of acid and pepsinogen secretion | peptides: GPR92 AA: CaSR, GPRC6A
 | P/D1 cell | ghrelin: control of hunger | sugars, AA: TAS1R3 bitter: TAS2R
Duodenum | I cell | CCK: control of satiation and motility | LCFA: GPR120, FFAR1 peptides: GPR92 AA: CaSR, TAS1R1-TAS1R3 bitter: TAS2R
Jejunum | Enterocyte | GLP-1: regulation of glucose levels, satiation, motility | sugars: TAS1R2-TAS1R3
 | ileum | GLP-1: regulation of glucose levels, satiation, motility | sugars: TAS1R2-TAS1R3 LCFA: GPR120, FFAR1 AA: GPRC6A bitter: TAS2R
 | Colon | L-cell | PYY, GLP-1: regulation of satiation, ion secretion and motility | SCFA: FFAR2, FFAR3

CaSR, calcium sensing receptor; FFAR1, free fatty acid receptor 1; FFAR2, free fatty acid receptor 2; FFAR3, fatty acid receptor 3; GPR92, G-protein coupled receptor 92; GPRC6A, G-protein coupled receptor family C group 6 member A; LCFA, long-chain fatty acids; TAS1R1, taste receptor type 1 member 1; TAS1R2, taste receptor type 1 member 2; TAS1R3, taste receptor type 1 member 3; TAS2R, taste receptor type 2.
Nutrient sensing & the cholecystokinin (CCK) I cell

- Long chain fatty acids
- Protein/AAs
- Bitter

Small intestine lumen

Apical

basolateral

Cease food intake
Reduce gastric emptying

CCK CELL

CNS

pancreas

gallbladder

Nodose ganglion

CCK receptors

Vagus nerve

Circulation
Sweet sensing & regulation of glucose absorption

**SGLT1** - major route for the absorption of dietary sugars from intestinal lumen into enterocytes.

Glucose also stimulates gut hormone secretion (GLP-1) – stimulates pancreas insulin release, increasing glucose uptake to tissues (and enhancing enterocyte glucose uptake via increasing expression of SGLT1 and GLUT2 in enterocytes.

**Glucagon-like-peptide 1** - An incretin

**INSULIN**

**Enterocyte GLP-1R**

**SGLT-1**

**glucose**

**Na⁺**

**H₂O**

**Cl⁻**

**Glucose**

**Na⁺**

**K⁺**

**Na.K. ATPase**

**ATP → ADP + Pᵢ**
Taste receptor targeting to prevent and treat obesity and diabetes

- In disease, disturbances or adaptations in the expression or sensitivity of taste receptors and their signalling pathways may affect digestive behaviour and metabolism

**Future clinical potential?**

- Compounds that block activation of the gut’s taste receptors might serve as appetite suppressants – e.g. Bitter agonists

- Selective targeting of taste receptors on cells in the gut to release hormones that signal a feeling of fullness, thereby mimicking the physiological effects of a meal and fooling the body into thinking that it has eaten, could replacement bariatric surgery approaches to cause profound weight loss

- Diabetes might be treated by activating the taste receptors on gut L cells so that they release GLP-1 to augment insulin release.