Modulation of food intake by selective TAS2R stimulation in rat

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INTRODUCTION

Metabolic surgery modulates the enteroendrocrine hormone profile, which leads, among other effects, to changes in food intake.

Bitter taste receptors (TAS2Rs) have been identified in extra-oral locations such as the gastrointestinal tract, while their specific stimulation has been linked to the control of ghrelin secretion.

We hypothesize that the optimal stimulation of bitter taste receptors could help to modulate enteroendocrine secretions, thus leading to the regulation of food intake.

AIM

We aimed to evaluate the response to defined agonists for the human bitter taste receptors hTAS2R5, hTAS2R14 and hTAS2R39 on:

- Enteroendocrine secretions from rat intestinal segments
- In vivo food intake experiments with rats.

METHODS

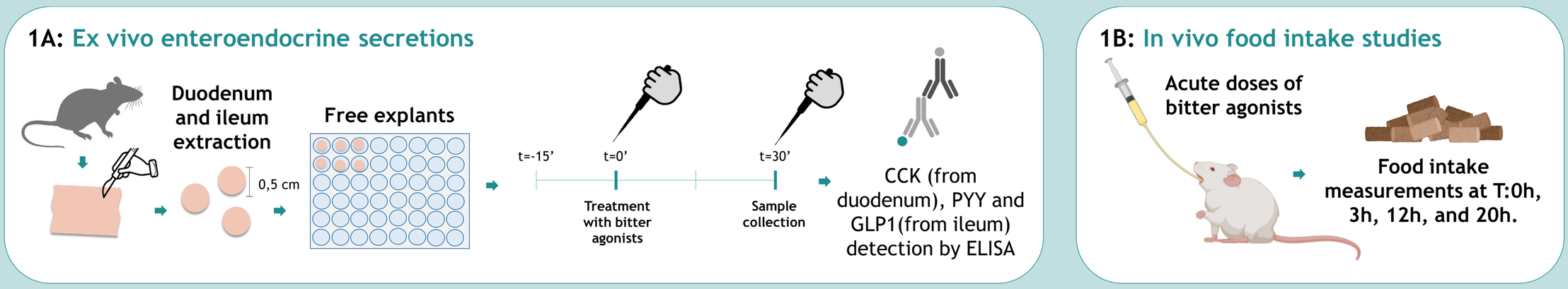

Figure 1. Graphical representation of the experimental design. (A). For ex vivo enteroendocrine secretion studies we used duodenum and ileum segments from rats and we treated them with different bitter agonists. (B) For in vivo food intake studies, we treated the rats by oral gavage with different bitter agonists and we measured their food intake at three time points: 3h, 20h and 24h.

Table1. List of bitter agonsits used and their defined receptor.

Agonists used	Bitter receptor	Agonists used	Bitter receptor
1,10-Phenantroline	hTAS2R5	EGCG	hTAS2R5 and hTAS2R39
Thiamine	hTAS2R39	Flufenamic acid	hTAS2R14
ECg	hTAS2R39	Protocatecuhic acid	hTAS2R14
Epicatechin	hTAS2R5 and hTAS2R39	Vanillic acid	hTAS2R14
B2 gallate	hTAS2R5 and hTAS2R39	Procyanidin B2	Undefined

RESULTS

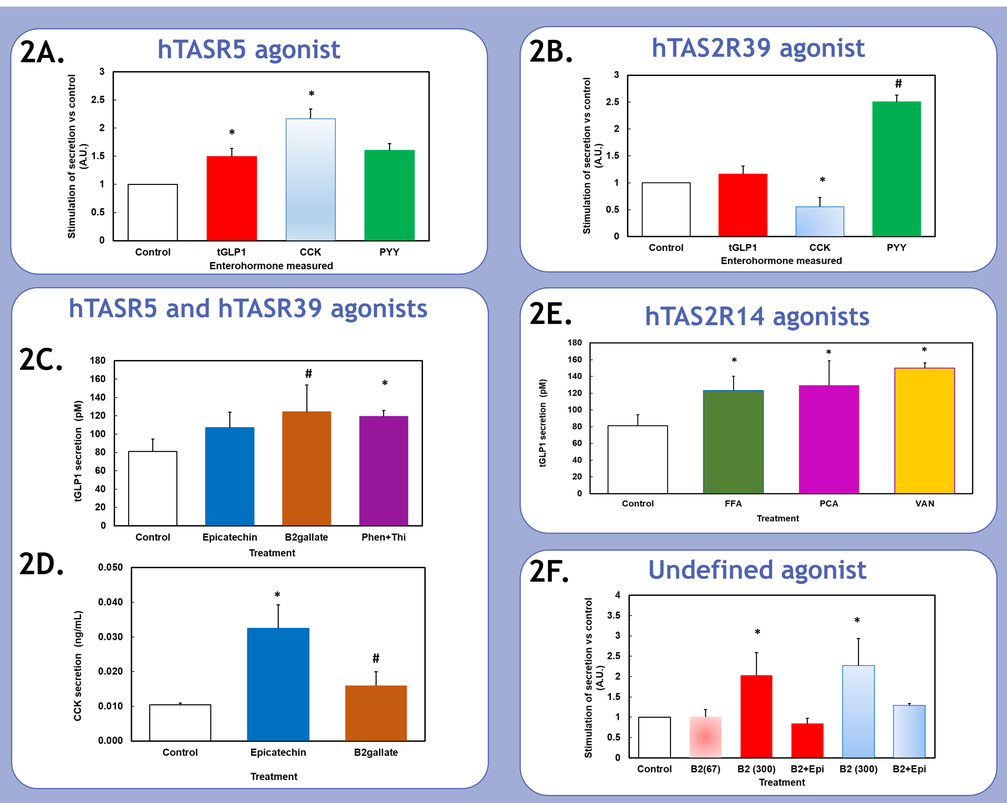

Figure 2. Enteroendocrine secretions. (A) Enterohormones released in response to 1,10-Phenantroline 150 µM. (B) Enterohormones released in response to Thiamine 1mM. (C) GLP1 released in response to Epicatechin 1mM, B2gallate 20 mM, 1,10-Phenantroline 150 mM + Thiamine 1 mM . (D) CCK released in response to Epicatechin 1mM, B2gallate 20 mM. (E) GLP1 released in response to Flufenamic acid 50 µM, protocatechuic acid 300 µM, Vanillic acid 300 µM. (F) GLP1 (red columns) and CCK (blue columns) relased in response to B2 67 or 300 µM, or B2 300 µM + epicatechin 1 mM.

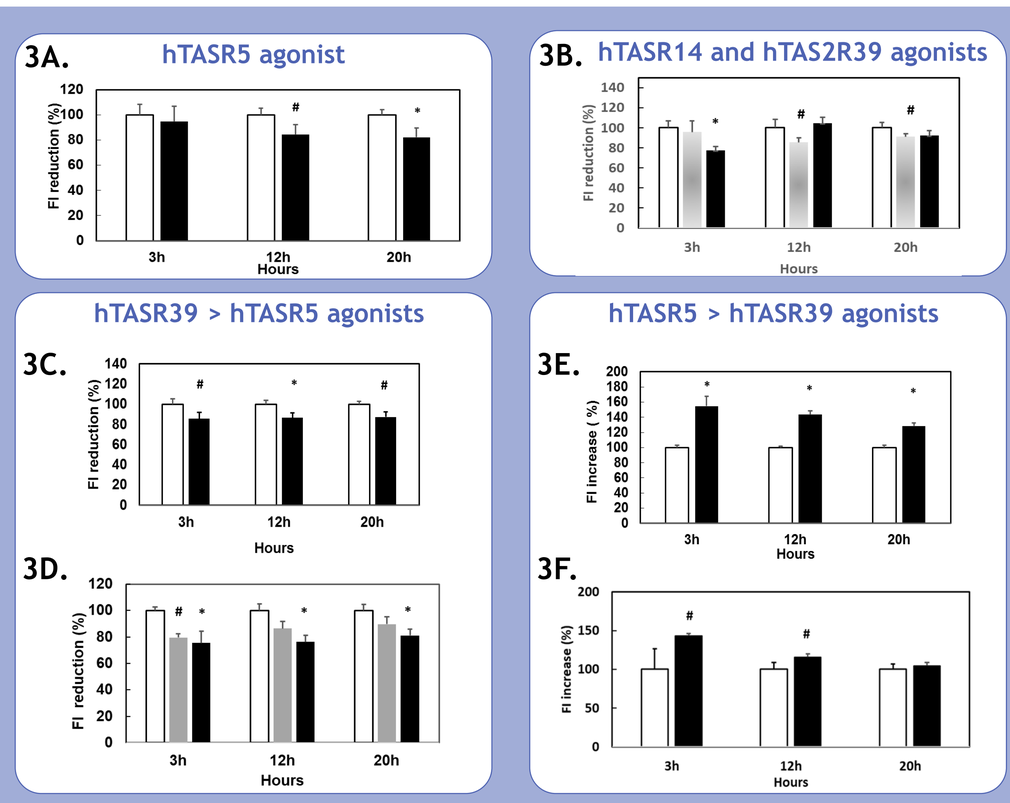

Figure 3. Food intake modulation. In all graphics, white columns are food intake in reposnse to vehicle (tap water). Darker columns are food intake in response to acute doses of: (A) 1,10-Phenantroline 200 mg/kg. (B) Vanillic acid 252 mg/kg (grey columns) and Vanillic acid + Epicatechin (252+244 mg/kg) (black columns). (C) Epicatechin+B2+ECg (200+62+18 mg/kg). (D) Epicatechin 244 mg/kg (grey) and 300 mg/kg (black). (E) Epicatechin + ECg (234+14 mg/kg). (F) Epicatechin+B2 (213+62 mg/kg).

CONCLUSION

We conclude that bitter taste receptors can be stimulated with various agonists to activate differential enteroendocrine secretions that modulate food intake.

This work has been supported by AGL2017-83477-R from the Spanish Ministerio de Ciencia Innovación y Universidades and R2B2018/03co-funded by the FEDER programme of the Generalitat de Catalunya and the URV.