High fat diet differentially regulates olfactory receptors in the duodenum of obesity-prone and obesity-resistant rats

**Introduction**

The gastrointestinal tract is an important factor in the regulation of food intake, nutrient sensing and nutrient absorption. Obesity-prone Osborne-Mendel (OM) rats are less sensitive to the satiating effects of a duodenal infusion of fatty acids than obesity-resistant SSB/PI (SSB) rats, suggesting that the gastrointestinal tract differentially senses the presence of fat in these two strains. Based on microarray analysis of the duodenal enterocytes, it was hypothesized that olfactory receptors present in the duodenum of OM and SSB rats were differentially regulated by the intake of a high fat in fat. OM and SSB rats were fed either a high fat diet or a low fat diet for 2 weeks, in which OM rats consumed more high fat diet than SSB rats. The mRNA levels of four olfactory receptors (OLR1744, OLR50, OLR124, OLR1507) were assessed from the duodenal enterocytes of these rats. The duodenal mRNA levels of OLR1744, OLR124 and OLR1507 were significantly elevated in OM rats fed the high fat diet, but not SSB rats. No differences in the expression of OLR50 receptor mRNA were detected. These data suggest that several olfactory receptors present in the duodenum are selectively regulated in obesity-prone OM rats fed a high fat diet. Therefore, these receptors may play a role in the sensing and regulation of dietary fat, and may be important for the individual susceptibility to obesity in these two strains.

Consumption of a High Fat Diet selectively increased expression of the olfactory receptors, Olr1744, Olr124, and Olr1507 in duodenal enterocytes of Obesity-prone Osborne-Mendel rats

**Methods**

Subjects: 8-9 week old male Osborne-Mendel and SSB/PI rats were used in these studies (PBRC breeding colony). Rats were individually housed and maintained on a 12/12h light/dark cycle. All procedures were conducted in an AAALAC accredited facility and in accordance with the PBRC IACUC committee.

Diet: OM and SSB rats were given ad libitum access to either a high fat (55% kcal from fat) or low fat (10% kcal from fat) diet for 2 weeks prior to sacrifice. Food intake and body weight were measured daily.

RNA isolation: Enterocytes from the duodenum were collected and isolated using a modified Tri-Reagent protocol and the Qiagen RNeasy Kit.

Microarray Analysis: Gene expression profiles were generated using Applied Biosystems Rat Genome Survey Microarray. Genes with a p-value of less than 0.05 and a fold-change of greater than 4 were used in these analyses. Biological function determination was based on the Panther database (www.pantherdb.org).

Real Time PCR: Reverse transcriptase was conducted using the High Capacity cDNA Reverse Transcription Kit (Applied Biosystems). Real-Time PCR was conducted using primers designed by Primer Express (Applied Biosystems). mRNA levels were normalized to cyclophilin levels prior to statistical analysis.

**Summary & Conclusions**

- The mRNA expression of several olfactory receptors examined were increased by the consumption of High Fat Diet in the duodenal enterocytes of obesity-prone Osborne-Mendel rats.
- Olfactory receptors expression in enterochromaffin cells in human gut have been linked to the influx of Ca++ and subsequent release of serotonin.
- Obesity-resistant SSB rats are more sensitive to the effects of serotoninergic drugs administered peripherally.
- Olfactory receptors are chemoreceptors and though their exact role in the GI tract is not fully understood, it is apparent from these data that these receptors are susceptible to diet manipulations.
- These receptors may play a role in the sensing and regulation of dietary fat, and may be important for the individual susceptibility to obesity in these two strains.

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