

## EM-05 The effect of dietary caloric density on neuropeptide response in mice

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**Introduction :** Hypothalamic neuropeptides, such as pro-opiomelanocortin (POMC), an anorectic peptide and neuropeptide Y (NPY), an orexigenic peptide, play key roles in the regulation of energy balance. The regulation of their expressions may be important in determining susceptibility to diet-induced obesity.

**Methods :** Three strains of mice (C57BL/6J, 129/Sv and A/J) known to have different susceptibilities to diet-induced obesity were used. They were fed a 23.6% fat, w/w, high fat diet (HF) or a 4.3% low fat control diet for two days. In the second experiment, four groups of each strain of mice were placed on diets with different fat contents and caloric densities for a period of six weeks. In both experiments, neuropeptide mRNA expression was measured using real-time quantitative reverse transcription polymerase chain reaction (RT-PCR).

**Results :** The weight gain of the mice over 6 weeks correlated with the caloric density rather than the fat content of the diets. A differential weight gain was observed between strains with C57BL/6J having the lowest threshold in developing obesity, suggesting an influence of susceptibility genes. On acute exposure to a high caloric density diet, C57BL/6J had a paradoxical rise in hypothalamic NPY expression ( $p < 0.01$ ) despite a trend to higher caloric intake. After six weeks on diets with increasing caloric density, both C57BL/6J and 129/Sv developed significant suppression in POMC expression compared to those on control diets ( $p < 0.05$ ) despite the presence of hyperleptinaemia. In contrast, the least obesity-prone A/J mice mounted a rise in POMC expression on acute exposure to a high caloric density diet ( $p < 0.05$ ) and maintained POMC expression even after prolonged exposure.

**Conclusions :** It is proposed that an acute rise in POMC expression in response to a high fat challenge may be a predictor of low susceptibility to adiposity. The dysregulation of POMC neurons in response to high caloric intake may be important in mediating diet-induced obesity.

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## EM-06 The clinical genetics of multiple endocrine neoplasia type 1 in Chinese

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**Introduction :** Multiple endocrine neoplasia type 1 (MEN 1) is characterized by a triad of neoplasia affecting the parathyroid glands, enteropancreatic endocrine tissue and the anterior pituitary gland.

**Methods :** In order to define the prevalence of MEN 1 germ-line mutations in Southern Chinese patients with MEN 1 syndrome, we performed direct sequencing of the entire open reading frame of the MEN1 gene for twelve index patients and their first degree relatives.

**Results :** Six patients had familial MEN 1 syndrome and six had sporadic disease. Nine different germ-line mutations at the MEN1 gene were identified, including three novel mutations (248-249delTT in exon 2, K559X (AAG→TAG) in exon 10 and IVS 2nt+2(G→T) in intron 2). All patients with familial MEN 1 syndrome were heterozygous carriers of a germ-line mutation and MEN 1-related disorders were only evident in their first-degree relatives who also carried the mutation. All patients with enteropancreatic lesion were mutation carriers and the absence of mutation in three apparently sporadic MEN 1 patients with only hyperparathyroidism and pituitary microadenoma might represent the presence of MEN1 phenocopy.

**Conclusions :** The finding of MEN1 germ-line mutation in all patients with familial MEN 1 syndrome suggests that genetic screening should be useful in our population to identify affected individuals within a kindred and allow early detection of MEN1-related tumours.

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