

## Invited Speaker Plenary 3: Gene-Nutrient Interactions

### **The influence of postnatal nutrition on metabolic and cardiovascular risk: insights from animal studies**

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**Background** - Population studies suggest that nutrition in early life can influence subsequent risk of obesity and high blood pressure. Childhood obesity is increasing throughout the world, and demographic data suggest that environmental influences operating early in life are involved. Importantly, childhood obesity is associated with subsequent hyperlipidemia, glucose intolerance and hypertension. Managing childhood obesity and its consequences requires an understanding of the pathophysiological changes induced by early onset overnutrition. We are investigating the impact of early over- or under-nutrition in rodents on subsequent body weight, adiposity, hormone profile, blood pressure and brain neurotransmitters implicated in feeding.

**Methods** - To examine the impact of early postnatal overnutrition on blood pressure and adipose-derived mediators, we adjusted rat litters to 3 or 12 male pups (overnutrition and control respectively) on day one of life. This intervention provides pre-weaning overnourishment, which to date has been little examined. We have also examined the impact of continuous over-nutrition from birth, induced by small litter size followed by a high fat (30% calories as fat) diet.

**Results** - Small litter animals were significantly (25%) heavier than normal litter animals by day 14, and consumed approximately 25% more milk than normal litter rats. At weaning (day 24) plasma leptin concentrations were more than doubled, and remained significantly increased at 8 weeks of age, regardless of the post-weaning diet.<sup>1</sup> By maturity (16 weeks) there was no significant effect of being raised in a small litter on plasma leptin, although consuming a high fat diet led to a doubling of leptin compared to low fat diet.<sup>1</sup> At this time the white adipose expression of 11 beta hydroxysteroid dehydrogenase 1, the enzyme that converts inactive cortisone into cortisol, was significantly increased in small litter rats, across dietary groups. This suggests long-term effects of early onset overnutrition, possibly representing a programming effect. While body weight was not significantly elevated 16 weeks after overnourishment during the pre-weaning phase, we consistently observe a 5% higher body weight in rats raised in small litters, and on a population basis, relatively small changes such as these may be relevant to disease burden. Increases in blood pressure were more likely to be associated with high fat feeding, and these appeared delayed relative to the increases in body weight and plasma leptin. Similar 10-15 mm Hg increases in blood pressure were observed in rats subjected to high fat feeding as adults.<sup>2</sup>

**Conclusions** - Adjustment of litter size, thereby influencing early feeding patterns, can influence adult blood pressure. Rats overfed from an early age developed increases in body weight, along with changes in mediators involved in the both the regulation of feeding and blood pressure. An important question under investigation presently is the site of fat deposition as in humans central obesity was recently shown to be associated with greater sympathetic activation relative to peripheral obesity, possibly linked to greater cardiovascular risk.<sup>3</sup>

#### **References**

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2. Morris MJ, Velkoska E, Cole TJ. Central and peripheral contributions to obesity associated hypertension: impact of early overnourishment. *Exp Physiol* 2005; (in press).
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