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*Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.*

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#### C10 and PC20

### **A mismatched pre- and post-weaning diet has window of exposure- and sex-specific effects on energy homeostasis, adiposity and cardiovascular function in mice**

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Maternal diet during pregnancy and/or lactation plays a role in inducing the offspring metabolic phenotype. We examined the phenotypic outcome in offspring if they were fed a diet mismatched between pre- and postnatal life.

Pregnant MF-1 mice were assigned to either control (C, 18% casein) or protein-restricted (PR, 9% casein) diet. PR dams were further sub-divided into those fed the PR diet throughout pregnancy (PRP) or both pregnancy and lactation (PRPL). Weaned offspring were then fed a high fat (HF, 45% Kcal fat) diet or standard chow (C, 21% Kcal fat) to adulthood. This generated six experimental groups based on dam/offspring dietary consumption: C/C, C/HF, PRP/C, PRP/HF, PRPL/C and PRPL/HF. Food intake and body weight were monitored and blood pressure was recorded by tail cuff plethysmography before animals were sacrificed. Hypothalamic tissues and fat depots were then collected for gene expression analysis by real time-PCR. Body weight and food intake was analyzed by mixed model analysis. All other data was analyzed by ANOVA with the appropriate post hoc test.

HF offspring were heavier vs. C animals, regardless of maternal diet during pregnancy. However, PRPL/HF males were lighter vs. C/HF group, but were significantly fatter ( $p<0.001$ ). The increased adiposity observed in PRPL/HF males was not evident in the PRP/HF group. Daily energy intake was similar for all groups except for the PRP/HF males, whose intake was reduced by 20% vs. the PRP/C or C/HF groups ( $p<0.001$ ). PRP/HF males had reduced hypothalamic mRNA levels of genes involved in appetite regulation, namely neuropeptide Y (NPY) and the leptin receptor Ob-Rb, vs. PRP/C animals ( $p<0.001$  and  $p<0.05$ , respectively). These PRP/HF males also had reduced expression of genes involved in thermogenesis, namely beta-3 adrenergic receptor and uncoupling protein 1, in the interscapular brown adipose tissue vs. PRP/C animals ( $p<0.05$ ). These changes in gene expression were not observed in PRPL offspring. Systolic blood pressure in all PR offspring was greater by 16% and 10% in males and females, respectively,

vs. C offspring ( $p<0.05$ ), and increased further ( $p<0.05$ ) by 15% and 7% in the HF male and female offspring, respectively. Our study shows that maternal protein restriction during pregnancy leads to sex-specific adaptive responses in male offspring, resulting in altered energy homeostasis following post-weaning HF-feeding. Extending maternal protein restriction to include the lactation period resulted in greater adiposity in the HF-fed male offspring. Nevertheless post-weaning HF-feeding exacerbated cardiovascular dysfunction in both male and female offspring, regardless of whether maternal protein restriction was imposed during pregnancy or both pregnancy and lactation.

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#### C11 and PC21

### **Plasma cysteine and total body fat mass in humans**

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#### **Background**

Cysteine is a non-essential sulfur aminoacid, synthesized from methionine and homocysteine by the two sequential enzymes: cystathionine beta synthase (CBS) and cystathionase. Plasma total cysteine (tCys) concentrations are positively associated with body mass index (BMI) in the general population [1], but the direction of causality is unknown.

#### **Aim**

To investigate whether the association of tCys with BMI is mediated through body lean mass or fat mass, and to search the literature for underlying mechanisms.

#### **Methods**

The study included 5179 Norwegians (aged 46-73 y), recruited from the general population in the Hordaland Homocysteine Study [2], who underwent two assessments 6 y apart. Dual-energy X-ray absorptiometry was performed at follow-up. Linear regression models and concentration-response curves were used to investigate cross-sectional associations of tCys with lean mass and fat mass with adjustments for potential confounders. We also investigated associations of baseline tCys and change in tCys over 6 y with body composition at follow up

#### **Results**

tCys was not associated with lean mass, but showed a strong positive association with fat mass (partial  $r=0.25$ ,  $P<0.001$ ),