Early origins of adipose tissue

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Adipocyte cell number is established early and is greater in obese individuals.

Knittle et al 1979; Spalding et al 2008
Adipose tissue composition

Brown adipose tissue

White adipose tissue
Mitochondria and heat production

- regulation of ROS production
- apoptosis?
- uncoupling?
- heat production in BAT

UCP 1
- mobile component of electron transport chain

UCP 2
- regulation of ROS production
- apoptosis?
- uncoupling?

VDAC
- supply of ADP for energy production
- apoptosis?

cyt c

inner mitochondrial membrane

outer mitochondrial membrane
Ontogeny of brown adipose tissue

UCP1
Revised origin of Brown Adipose Tissue

PRDM16: the interconvertible adipo-myocyte switch, Trends in Cell Biology, Volume 19, Issue 4, 141-146, 13 March 2009
Large animal models

Born with a mature hypothalamic-pituitary-adrenal axis after long gestation

Comparable:

- birth weight and offspring number
- organogenesis
- adipose tissue development
- offspring not confined within a restricted environment
A non-invasive measure of thermogenesis
Thermal supraclavicular areas co-locate to areas of brown adipose tissue.
Supraclavicular thermal area and temperature increase with hand cooling.

- Before cool challenge
- 1 min
- 2 min
- 5 min

- 36.5 – 37°C
- 36.0 – 36.49°C
- 35.5 – 35.99°C
Supraclavicular temperature and thermal area with immersion of one hand into cool water

Before cool challenge 5 min

6 years

13 years

58 years
Activity is the fat controller (deposition)?
The life-style environment and physical activity - a programmed response?
Lean  Obese
Experimental models of maternal nutrition during fetal and postnatal development

- **Maternal Nutrition**
  - 100%
  - 50%
  - 100%

- **Offspring Nutrition**
  - ad libitum feed/inactive

Phases:
- **Juvenile**
- **Adolescence**
- **Weaning**

Graph shows weight gain over gestation (%): Fetus, Placenta, and Offspring nutrition.
Outcomes of juvenile obesity

Sebert et al. 2009 Endocrinology 150: 634-641
Ectopic lipid accumulation – a primary marker of the metabolic syndrome is enhanced by the early in utero diet following adolescent obesity.
Adipose tissue inflammation is amplified when obesity follows maternal undernutrition in early gestation.

Sharkey et al. 2009 FASEB J
Potential adipocyte specific epigenetic adaptations to early in utero dietary restriction – at 1 week of life
Maternal nutrient restriction during early adipocyte development

- Pre-adipocyte differentiation
  - DNMT-1 ↑

- Adipocyte hypertrophy & hypoxia
  - ↑Inflammatory markers:
    - iNOS/
    - Cytokines

- Adipose tissue remodelling
  - ↓VEGF-A & ↑DNMT-1

- Transiently improved vascularisation

- Further expansion of adipocytes

- Obesity

- Inflammation
  - Insulin resistance
  - Liver
  - Heart
  - Kidney

- Lipid overflow to external organs

- Crown-like structures & ↑TRL-4
Past activity on Nutrition of infants with overweight and obese mothers

A roundtable workshop was organised in Sept. 2009

Objective:

• Produce a review of the evidence from a series of parameters on long term health outcomes in the offspring born to obese and overweight mothers

Outcomes:

• Obesity in Pregnancy: Implications for the Mother and Lifelong Health of the Child. L. Poston, L. Harthoorn, and E.M. van der Beek. *Pediatric Research* 2011;69 (No. 2)
ILSI Europe’s Task Force on Metabolic Imprinting

Current activity on Maternal obesity, diet, and developmental programming -Aligning mother-child studies

A workshop held in October 2011

Objective:
• To identify the key outstanding questions in the area of ‘Early life nutritional determinants of offspring obesity and its metabolic complications’
• To define the optimal methodological approaches to answer these questions

Focus on different methodological aspects:
• Maternal dietary habits / status
• Maternal body weight, composition, and lifestyle
• Infant growth, body weight regulation and early risk factors
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