Like mother, like offspring
Does maternal overweight predict health outcomes?

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**EARLY PROGRAMMING OF DISEASE**

**FETAL PROGRAMMING**

“a stimulus in utero establishes a permanent response in the fetus that impacts functions later in life”

**NUMBERS = IMPACT**

Maternal overweight and obesity during pregnancy are highly prevalent (~30-50%) (European perinatal health report 2010)

**NEW RISK FACTORS = NEW POSSIBILITIES TO PREVENT**

<table>
<thead>
<tr>
<th>Chronic diseases related to fetal programming</th>
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</thead>
<tbody>
<tr>
<td>• Obesity &amp; type 2 diabetes</td>
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<tr>
<td>• Heart failure &amp; cardiovascular disease</td>
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<tr>
<td>• Cognitive decline &amp; dementia</td>
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no early risk-screening policy
no primary prevention solution
no effective therapy
SPECIFIC TARGETS

Early feeding
Obesity / Diabetes

Brain development
Cognitive dysfunction

Cell senescence
Telomere length

Cardiac development
Cardiac disease
PISA, ITALY
N=91 Families (children born 2011-2014)

CHARACTERIZATION
- Cord blood (inflammatory, metabolic, hormonal)
- Body growth (weight, height)
- Breastfeeding / formula
- Dietary information (complementary)
- Cardiac development (echocardiography)
- Neurodevelopment (Griffith Mental Scale)
- Eating behaviour (Montreal Children Scale)

Gut colonisation
Late pregnancy BMI: stronger predictor than early pregnancy BMI of an obesogenic nutrition/behavior

Sanguinetti et al submitted
An increase in late pregnancy BMI led to

- A proportional increase in BMI and body fat % in the adult offspring
- Increase in diabetes risk, especially in women (10 % for each one BMI unit = 2 kg)

OBESITY & DIABETES

Helsinki Birth Cohort Study (70-80 years)
LED BY JOHAN ERIKSSON (FINLAND)
Helsinki Birth Cohort Study (70-80 years)  
LED BY JOHAN ERIKSSON (FINLAND)

An increase in late pregnancy BMI led to
• Shorter telomeres (biological aging marker) in the adult offspring, especially in women
• Shorter telomeres were expectedly associated with cardiovascular disease and diabetes

HEART DISEASE & DIABETES
LATE PREGANCY BMI PREDICTS HEART DISEASE

Eriksson J Ann Med 2014
Heart in the first year
- Thicker, heavier, more dilated, higher contractility

Heart in adults
- Higher contractility, hyperdynamic function

Preclinical models
- Congruent data in a longitudinal fashion
- Mechanistic insights on metabolic pathways
  (excess glucose exposure, insulin resistance, low glucose oxidation)

Vulnerability to ischemic damage & heart failure
Late pregnancy BMI: stronger predictor than early pregnancy BMI

Guzzardi et al J Am Coll Cardiol – Cardiovasc Imaging, in press
Animal data confirm cognition is high at weaning and low in adults. It goes with brain metabolism and insulin action (high vs low). Insulin regulates cell growth, appetite, glucose metabolism.

- word list task
- copying figure task
- delayed memory task

**MATERNAL BMI & OFFSPRING COGNITION**

**MATERNAL BMI (n=780 OFFSPRING)**

- Lower cognitive function at 70 yrs

- 
  - word list task
  - copying figure task
  - delayed memory task

**REDUCED WHITE MATTER DENSITY**

*Bucci et al submitted*
Resistance training exercise intervention


Exercise training effective but should not be discontinued

Reduced white matter density / Cognition pattern

Turku PET Centre
University of Turku, Finland
LED BY PIRJO NUUTILA


Diabetologia 2016. Resistance training improves skeletal muscle insulin sensitivity in elderly offspring of overweight and obese mothers.
WHAT TO TARGET AT AN EARLY STAGE?

The profile of gut bacteria is different in children with a lean or obese mother & correlates with cardiac size, or with cognition.

GUT BACTERIA INFLUENCE
• BEHAVIOUR

2011-2014
3-5 years

Age (months)  0  3  6  12  18  24  36  60

Foecal collection

Gut colonisation & development
Prove efficacy & effectiveness, time-window need for personalized strategies

Now we know that maternal overweight especially in late pregnancy

- Impacts early nutrition, eating behaviour, cardiac development, cognitive development,
- Predicts obesity, diabetes, cardiovascular disease, cognitive decline, death / shorter life
- Mechanisms include insulin resistance, oxidative stress, telomere shortening, gut dysbiosis
- Effects are reversible by exercise training in older people

More research needed in primary prevention

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<th>Does reversal of maternal obesity reverse consequences?</th>
<th>Is the gut microbiota a promising target for both mother &amp; offspring?</th>
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<tr>
<td>• Reduce calories? Change composition?</td>
<td>• Existing probiotics do not correct the dysbiosis</td>
</tr>
<tr>
<td>• From before conception? Very difficult</td>
<td>• Dysbiosis not the same for e.g. brain and heart</td>
</tr>
<tr>
<td>• Mainly in the last trimester? Easier</td>
<td>• Personalized microbiota-based prevention</td>
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Where would you see further needs for policy support?
Research is lost in translation, more face-to-face interaction
Developmental ORIgins of healthy and unhealthy AgeiNg
The role of maternal obesity