Developmental determinants of Ageing and Longevity

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presented by Dr. Ingrid Meulenbelt

Integrated research on Developmental determinants of Ageing and Longevity
IDEAL

FP7-health-2010 collaborative project.
(8 EU countries, 14 groups, 2 SMEs, 12 million)
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C0-PI Bas Zwaan Wageningen University

Which early life conditions lead to late life effects on health and longevity.
Introduction

Human Life expectancy has increased BUT

Life years with disability EU 27: Men 16 years
Women 20 years

<table>
<thead>
<tr>
<th>EU 27</th>
<th>Male</th>
<th>Female</th>
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</thead>
<tbody>
<tr>
<td>Healthy life years at birth EU</td>
<td>60.9</td>
<td>62.0</td>
</tr>
<tr>
<td>Netherlands</td>
<td>61.4</td>
<td>59.8</td>
</tr>
<tr>
<td>Life expectancy at birth EU</td>
<td>76.4</td>
<td>82.4</td>
</tr>
<tr>
<td>Netherlands</td>
<td>78.7</td>
<td>82.9</td>
</tr>
<tr>
<td>% Life expectancy Without disability EU</td>
<td>79.7</td>
<td>75.2</td>
</tr>
<tr>
<td>Netherlands</td>
<td>78.0</td>
<td>72.2</td>
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http://ec.europa.eu/health/indicators
How does genetic background AND exposure to environment from early development onwards influence healthy ageing

Two examples

The Leiden Longevity Study
GEHA study
These long lived families must have:
• beneficial genetic make ups
• beneficial early environment

Early exposure to Hunger Winter with late effects

The Dutch Hunger Winter
• Rations <1000 kcal (down to 500 kcal in April)
• Clear exposure period:
  December 1944 – April 1945

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<thead>
<tr>
<th></th>
<th>Exposed</th>
<th>Sibling controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals (N)</td>
<td>122</td>
<td>122</td>
</tr>
<tr>
<td>Age (sd)</td>
<td>58.1 (0.4)</td>
<td>57.1 (5.5)</td>
</tr>
</tbody>
</table>
EPIGENIC MODIFICATIONS

- Selective activation and silencing of genes during cell differentiation other than by DNA sequences
- Allow cells to respond to changes in environment

Working concept in IDEAL
Development
Prenatal
Postnatal
Puberty
Setpoints of epigenetic control,
Adult phenotype
Loss of homeostasis and epigenetic control,
Disease, comorbidity, lifespan

Exposures:
Infection
Nutrition (CR)
Temperature
SES, Lifestyle (smoking)
Parental age
ART

WP5 Loss and maintenance of epigenetic control
WP6 Longevity genes + biomarkers of healthy ageing

WP4 Phenotypic Plasticity

IDEAL
Early life programming
Epigenetic Control?

WP1 Growth and metabolism
WP2 Immunology
WP3 Reproduction

Life Phase 1
Life Phase 2
Life Phase 3
Main expected results (advances of the IDEAL project):

1. The role of epigenetic regulation in the response to developmental conditions
   Animals ➔ translation to human conditions
   Humans ➔ translation to animal models, interventions

2. Reference libraries of gene expression and epigenetic changes as a function of chronological age.


4. Monitoring tools of epigenetic effects following developmental conditions. For example all genes affected by early malnutrition, genes affected by assisted reproductive technology.

5. Biomarkers of ageing. Monitoring tools of epigenetic and metabolic control during aging (biomarkers of disease)


7. Pathways determining human health and longevity by influencing developmental processes.

8. Impact for general public, health care and industry. We are embedded and in close contact especially with pediatric, obstetric, gynaecology and geriatric clinical departments and all the elderly subjects in our studies with whom IDEAL groups perform many lifestyle interventions to stimulate healthy and active ageing.
IDEAL and its coordinator Eline Slagboom send their warm regards to Tokyo
Thank you for your attention.