Plasticity, genotype-by-environment interactions, and evolution

What can we learn from animal models?

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Outline

Factors affecting ageing and health

Variation and life span; genes, environments and its interactions; evolutionary mismatch

Phenotypic plasticity, adaptation, and development

Theory and evolution; maternal fitness model; predictive adaptive response; experiments and acid tests

From observations to mechanisms: insect models

Effects of developmental environment; thrifty genotype and thrifty phenotype and interactions; physiology and gene expression
Human life expectancy has spectacularly increased over the last 150 years. Research focuses on explaining the variation in lifespan, ageing, and health in contemporary populations.

Which factors underpin variation in human populations?
Ageing and longevity are determined by genetic and environmental factors, as well as their interaction.

![Venn diagram showing the interaction between genes (G) and the environment (E)].

Selection shaped the human life history in our evolutionary environment.

- [Evolutionary environment]
- [Contemporary environment]
Two of the main environmental changes in human populations are caloric value and composition of foods.

Scarce  Optimal  Affluent

selection

curtailing of life expectancy

“Old” genes in “new” environments: diabetes and obesity
Two relevant hypotheses

**Thrifty genotype**

*Neel, 1962*

*During human evolution our genotype has been shaped to deal with feast and famine and generally adverse nutritional conditions*

**Evolutionary mismatch**

**Thrifty phenotype**

*Barker and Hales, 1992*

*Poor conditions during development produces ill-health at later ages when under favourable (affluent) nutritional conditions*

**Developmental mismatch**  maternal fitness model (MFM)  predictive adaptive response (PAR)
Variable environments: phenotypic plasticity

ENVIRONMENTAL CUE during ontogeny, X or Y

ADULT ENVIRONMENT A or B

PHENOTYPE 1 ➔ FITNESS in A

PHENOTYPE 2 ➔ FITNESS in B

Acid test!

Predictability of cue

GENOTYPE 1

development & physiology

PP NS
Critical observations

- Adaptation needs to be experimentally confirmed

- “Predictive” time window, rate of reproduction and length of life

- Interactions between mother/offspring, cooperation and conflict (IGF2 paternal/maternal imprinting)

- Acknowledging G-by-E interactions
Ageing research should expand to DEVELOPMENTAL effects because natural selection has integrated the whole of an organism’s LIFE HISTORY.
From observations to mechanisms: insect models

Effects of developmental environment; thrifty genotype and thrifty phenotype and interactions; physiology and gene expression
SR selection

Scarce	Optimal	Affluent

SR selection

Drosophila melanogaster

Bicyclus anynana

Rain
Temperature

Month

MJ AS ND F

MJ AS ND F

MJ AS ND F

MJ AS ND F
Selection for Starvation Resistance, LH traits

- Starvation Resistance

- Metabolic rate

- Body reserves

- Reproduction

Survival vs. Age (days)

0 1 2 3 4 5 6 7 8 9 10 11 12 13

Survival vs. Age (days)

0 20 40 60 80

male
female
Adaptive phenotypic plasticity and ageing

Rain
Temperature

*Bicyclus anynana*

Ad lib; ns

Restricted; *P* < 0.05

“Imprinting”
A working model

Dry Season conditions:
Low temperature

Development

RMR

Larval survival

Adult

RMR

Imprint

d

Direct

a

Resultant

e

Starvation resistance

b
Selection for Starvation Resistance, gene expression

Phenotypic plasticity

- Temperature
  - Dry season
    - long-lived energy saving
  - Wet season
    - short-lived energy expenditure

Gene expression

- Stock
  - SR
  - Wet season

Stress

- Age
- Lines

Indy → Sod2 → Catalase → H₂O + O₂

O₂ → H₂O₂
Selection for Starvation Resistance, LH traits

- **Lifespan**
- **Metabolic rate**
- **Body reserves**
- **Reproduction**

**Male**
- Lifespan: ↑
- Metabolic rate: ↔
- Body reserves: ↑
- Reproduction: ↓

**Female**
- Lifespan: ↑
- Metabolic rate: ↔
- Body reserves: ↑
- Reproduction: ↓

**Relative SR**

**Female starvation resistance at different ages**

**Generation**

0 2 4 6 8 10 12 14 16 18 20

0.8 1 1.2 1.4 1.6 1.8 2
Selection for Starvation Resistance, gene expression

<table>
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<th>Line</th>
<th>Condition</th>
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<th>S2</th>
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<td></td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Starved</td>
<td></td>
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Environment (50%) Genotype (20%) Genotype by Environment (10%)

FDR = 0.05

2 lines * 2 sexes * 2 time points * 3 food levels

Control

Starvation resistance lines

- SR
- C

Food level

Lifespan

n
Individual pathways: INS

Insulin-like receptor

Pi3K regulatory subunit

Foxo

Survival and reproduction
Barker hypothesis

Dutch hunger winter ’44-’45

Metabolic Syndrome; diabetes, heart disease, premature death

1985-1995

Interest in how events during development affect adult lifespan and ageing

“Scarring” £ ≠ IP

SDUE “Imprinting”
The genes of interest: INS positive and negative effectors, and transcription factors

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<td>2x</td>
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</table>

C and SR
day 1 and day 7
Within colours +ve correlations

Between colours -ve correlations
Within colours +ve correlations

Between colours -ve correlations
Outlook, mechanisms of G-by-E

- Discovering the mechanisms underpinning PP
- Discovering the pathways involved in G and E responses to food and temperature environments
- Relate variation in gene expression to physiology and LH traits
- Understand effects of E in pathway dependent manner
- Predict variability and regulation of genes depending on pathway topology
- Predict “undiscovered” regulation in pathways from patterns of gene expression
A potential new model: live-bearing fish

Live-bearing fish
- Comparable with *in utero* growth, easy to rear, easy to manipulate, short life span

*Heterandria formosa*
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