Introduction to the DOHaD paradigm
or
“What happens in the womb lasts a lifetime”

Associate Professor Jeffrey Craig
Melbourne Childrens

Have you heard of…?
• ‘DOHaD’?
• ‘The first 1000 days of life’?
• ‘You are what you eat’?
• ‘You are what your mother ate’?
• ‘You are what your grandmother ate’?
• ‘You can change your genes’
What happens in the womb lasts a lifetime: bit.ly/1xvrC0s

Developmental Origins of Health and Disease

Which disease? Many chronic diseases
- cardiovascular disease
- obesity
- diabetes
- asthma and chronic respiratory disease
- allergies and autoimmunity
- some cancers
- chronic liver and renal disease
- arthritis
- osteoporosis
- mental ill-health
- neurological and neurodegenerative disorders

Which factors contribute to health and disease?

The main concepts of DOHaD
- There is rarely genetic predestination
- …or environmental predestination
- A large proportion of the environmental influence on chronic disease happens in the womb
- Environment at any time of life is modifiable
The main concepts of DOHaD

**The main DOHaD research questions**
- Environments
- When?
- What?
- How?

Epigenetics: an old idea given new life

- Aristotle: 'epigenesis' the simple becomes complex during development
- Waddington (1942): epigenetics: 'the interactions of genes with their environment, which bring the phenotype into being'
- 1990-2014: epigenetics defined in molecular terms

Waddington's ‘Epigenetic Landscape’

Genes underneath

instruments = genes
musicians = epigenetics
We have thousands of genes in each of our cell types, all playing different symphonies.

Epigenetics, DNA and chromosomes: an open and shut case

Epigenetics is needed for development

Epigenetics changes the activity of genes in responds to environment

Epigenetics changes the activity of genes in responds to environment: The well-groomed Canadian rats

- Increased risk of heart disease, diabetes, cancer & mental illness as adults
- “Epigenetic legacy” found 60 years later

Dutch “Hunger Winter” in WW2

Queen

Worker
Epigenetics can be reversed by diet or drugs

Environment: what are we working against?
- Western diets
- Stress
- Endocrine disruptors
- Carcinogens
- Most act through up-regulation of epigenetic regulators
- Drugs developed to inhibit these regulators

How can we counteract ‘bad’ environments?

Knowing all this about epigenetics & DOHaD, what do we aim to do?
- Detect adverse environments in early childhood
- Detect those at risk for chronic disease in childhood
- Intervene/prevent in utero, in childhood & beyond

What have we discovered?
- Origins of chronic diseases keep getting earlier (e.g. cardiometabolic disease)
- Age of effective interventions getting younger
- But very few early biomarkers

Emerging epigenetic biomarkers
- Replicated environmental biomarkers: smoking and stress; many others in development
- Data emerging on predictive biomarkers
  - The placenta as the ‘book of pregnancy’
  - Childhood obesity
  - Response to weight loss
  - Suicide risk
How far back can environmental effects go?

- Prenatal environment
- Preconceptional environment: future mothers and fathers
- Grandparents
- Beyond?

Did they know it all along?

- Lamarck: ‘Inheritance of acquired traits’
- Darwin: ‘Gemmules’ ‘thrown off’ by cells, influenced by environment & passed through germ cells to subsequent generations

Thank You

“The doctor of the future will give no medicine, but will interest her or his patients in the care of the human frame, in a proper diet, and in the cause and prevention of disease”.

- Thomas Edison, US inventor (1847-1931)

Further information: bit.ly/UdFwVu