

EGEA 8th Conference

Nutrition and Health: From science to practice

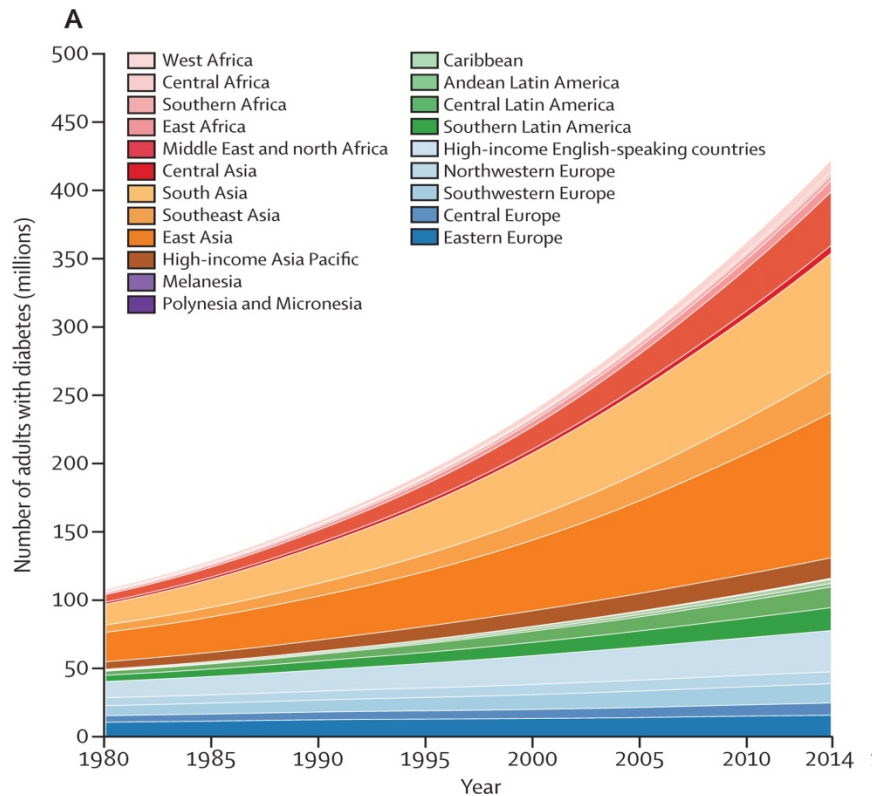
Lyon, November 7-9th, 2018

Epigenetics and pregnancy

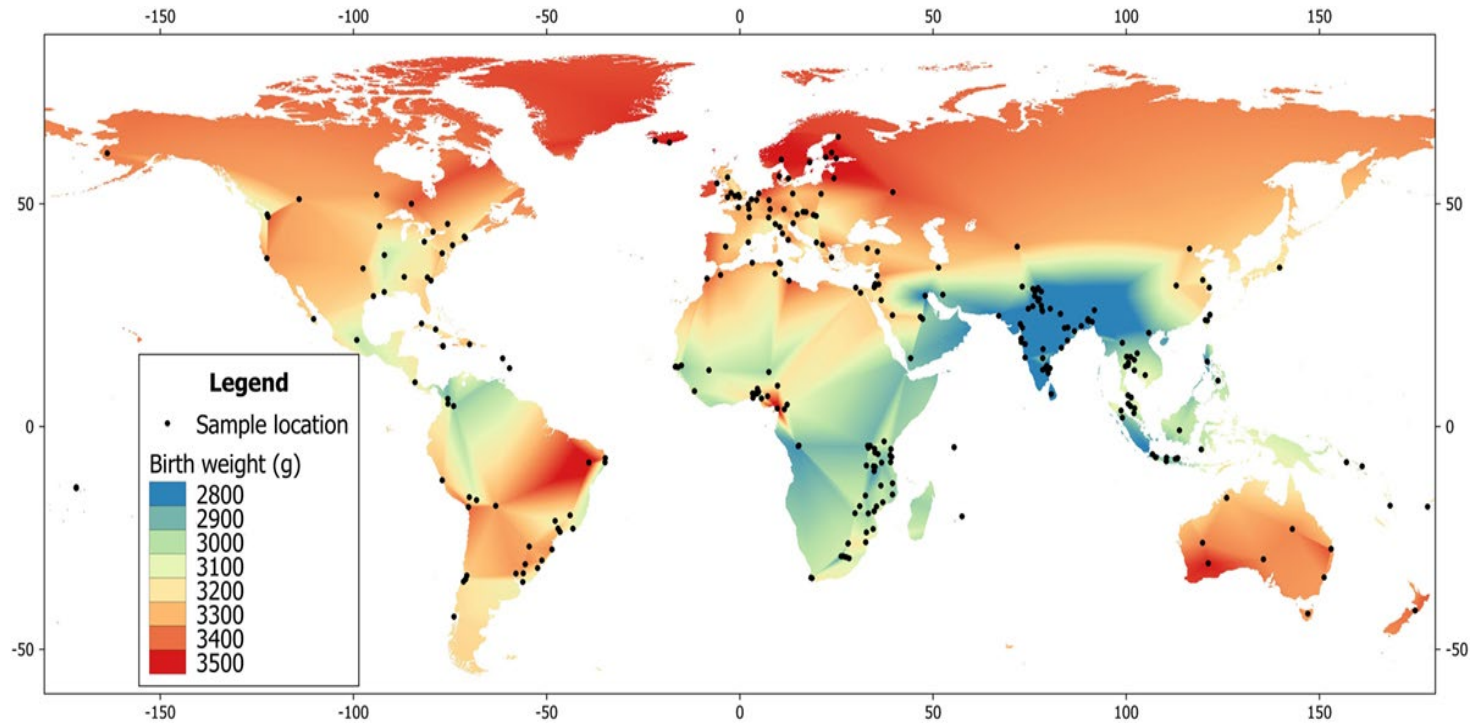


Umberto Simeoni
Division of Pediatrics & DOHaD Lab
CHUV & FBM/UNIL
Lausanne, CH

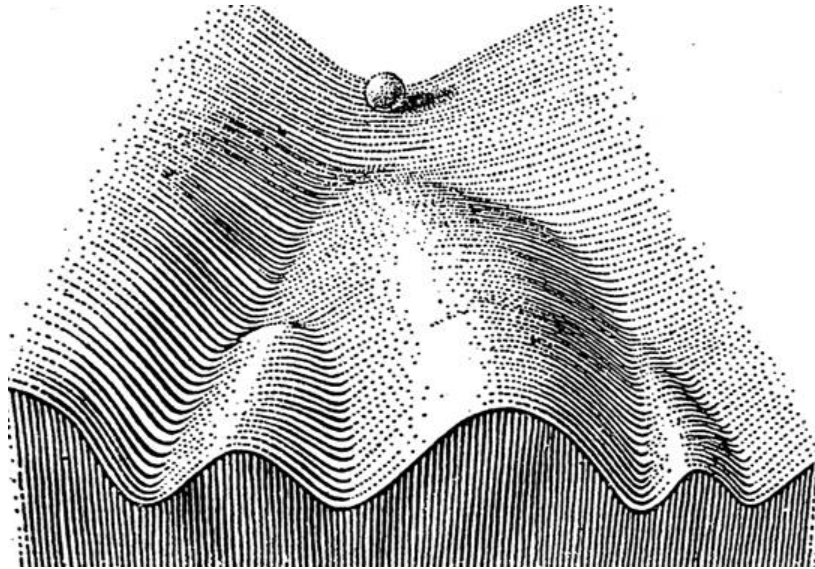
Trends in the number of adults with diabetes by region 1980-2014



Global map of mean birth weight (WHO)



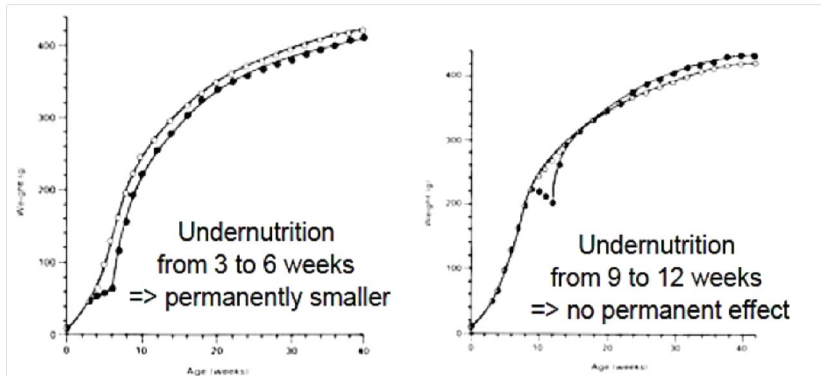
Epigenetic Landscape and Biological Development:
How the environment affects genes regulation
and development



C Waddington

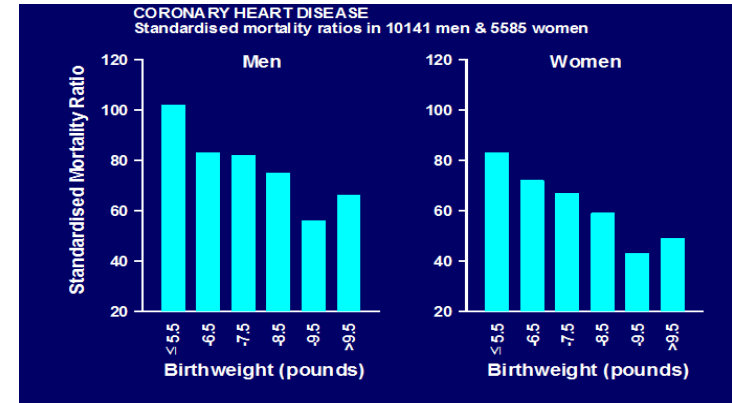
Developmental programming:

A process by which a stimulus applied during a critical period of sensitivity during development exerts not only short term, but lifelong effects



The effect of finite periods of undernutrition at different ages on the composition and the subsequent development of the rat

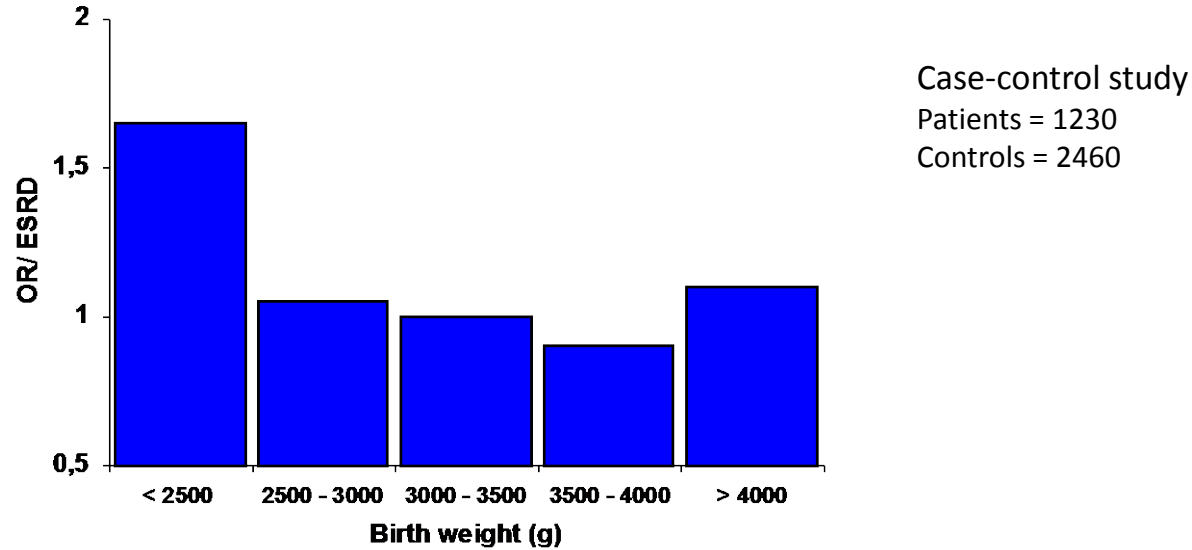
Widdowson & Mc Cance, Proc. Roy Soc London 1966



The effect of birth weight on the mortality ratio of coronary heart disease in human

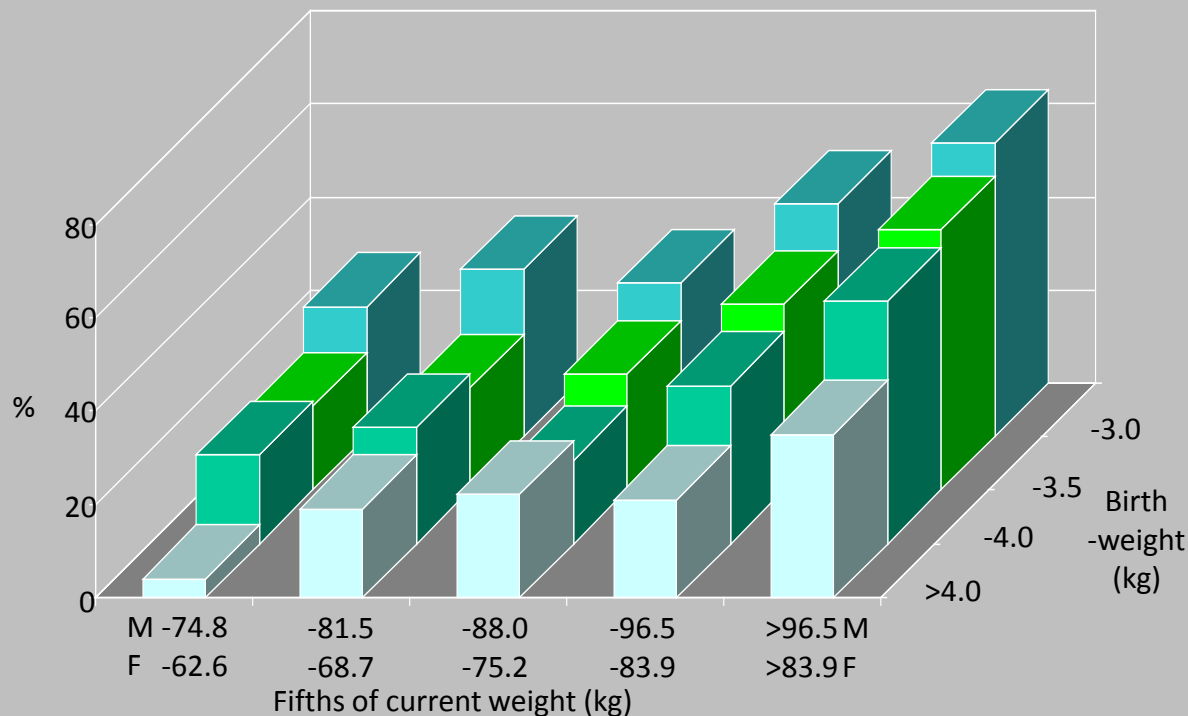
Barker et al, Lancet 1989

Birth Weight vs Chronic Renal Failure

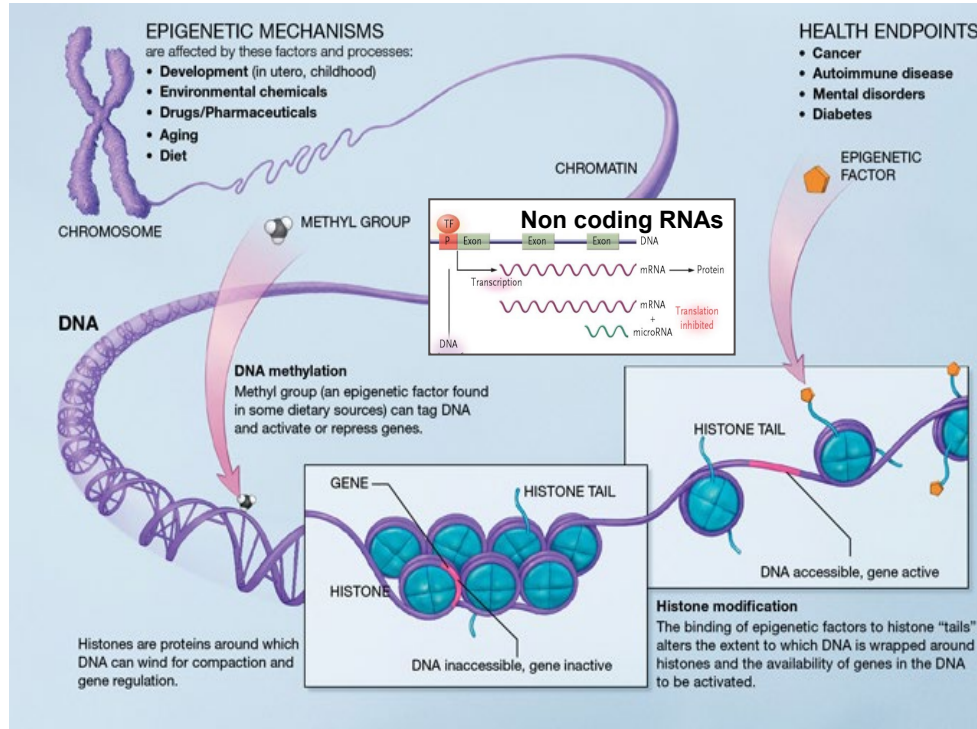


Lackland BT et al. Arch Intern Med 2000, adapted

Effect size of developmental programming: prevalence of hypertension



Epigenetics: a long lasting, heritable molecular translation of early genome-environment interactions, in the absence of gene sequence alteration

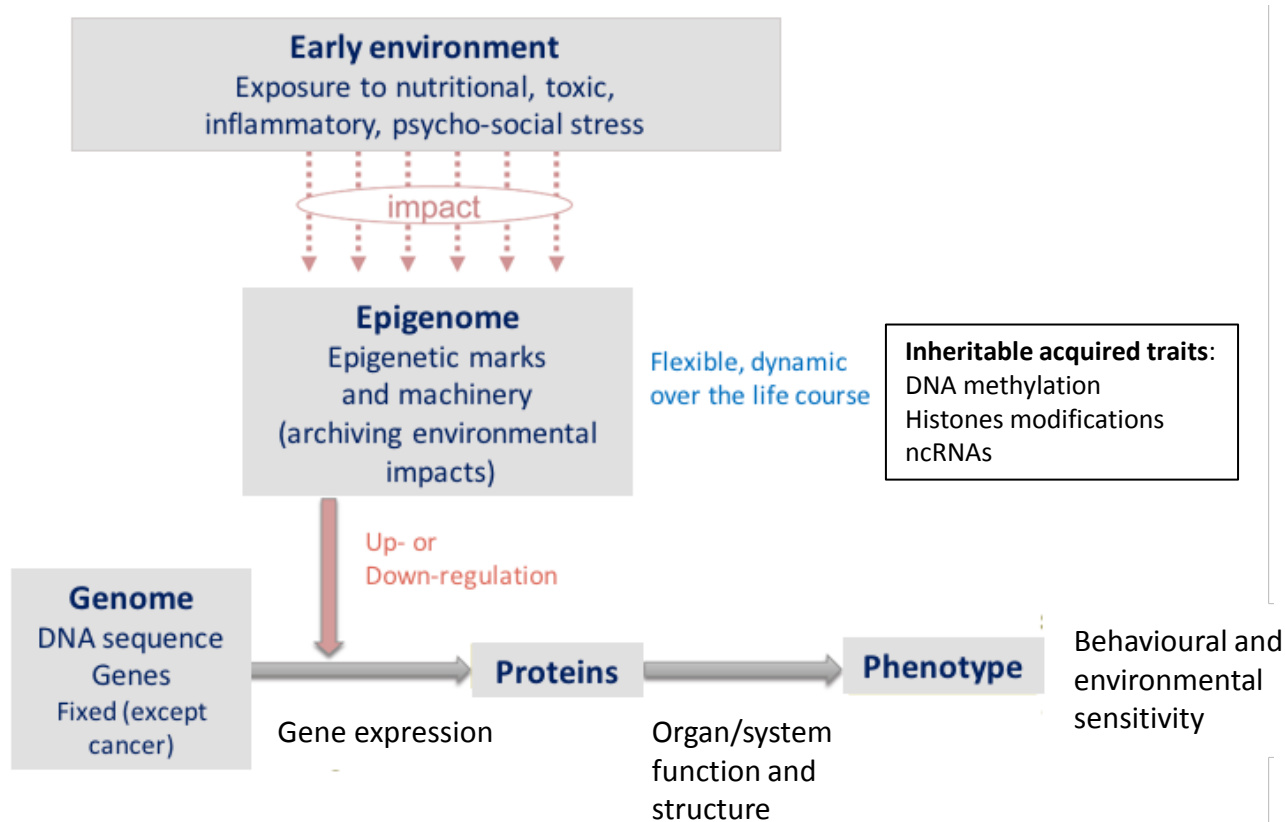


Royal jelly fed bees

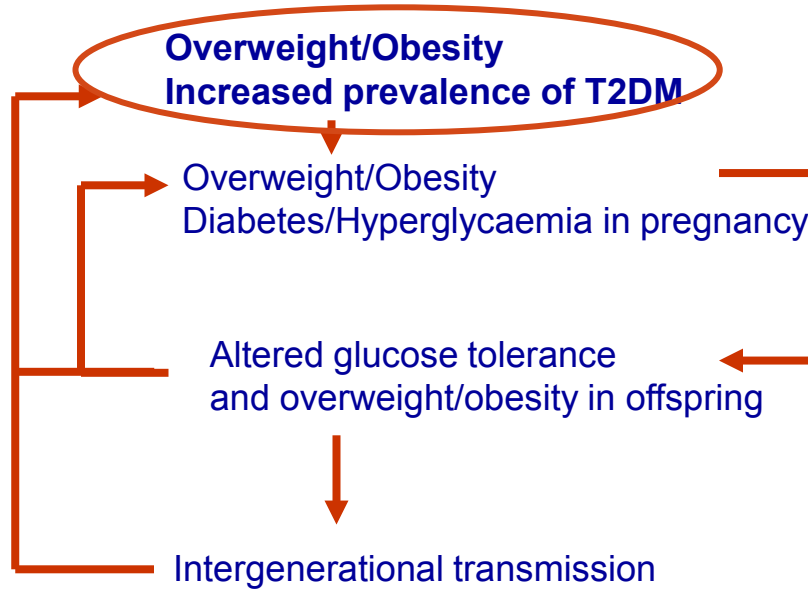


become bigger,
live longer
and are fertile.

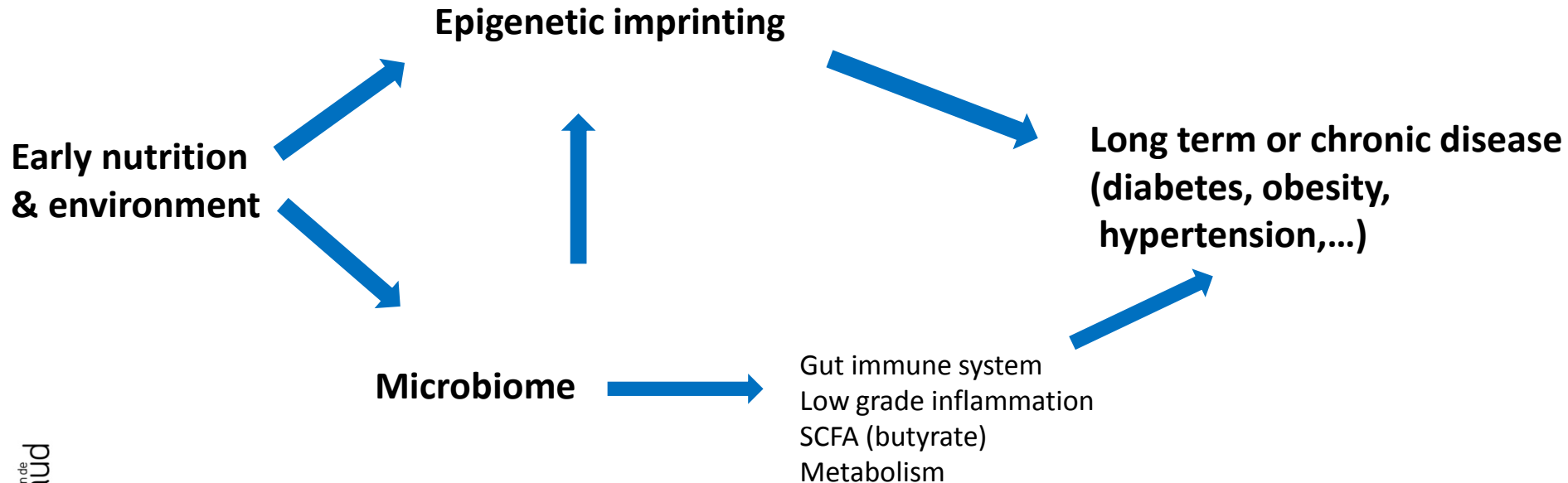
The Developmental Origins of Health and Disease (DOHaD)



Worldwide Type 2 Diabetes Epidemic: the amplifying effect of the cycle of reproduction



The long term memory of early environmental cues



Intra-uterine Growth Restriction, Preterm birth, or Antenatal exposure to Hyperglycaemia in pregnancy

*Common long term complications in offspring
and common programming mechanisms*

- **Hypertension & cardio-vascular disease**

Reduced nephron endowment

Altered endothelial function

- Impaired angiogenesis
- Altered endothelium-dependent vasodilating capacity (IUGR, DIP)
- Arterial stiffness, Intima-media thickness



- **Impaired Glucose Tolerance, Type 2 Diabetes Mellitus,**

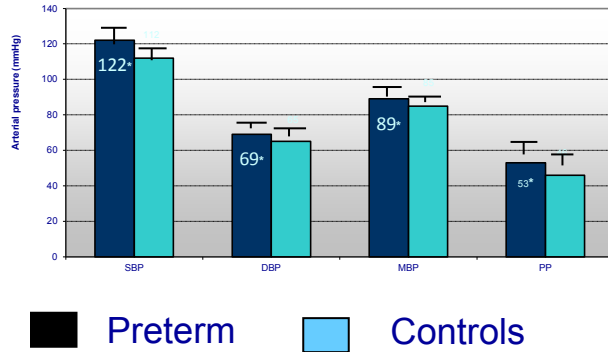
Reduced insulin sensitivity

Insufficient insulin production

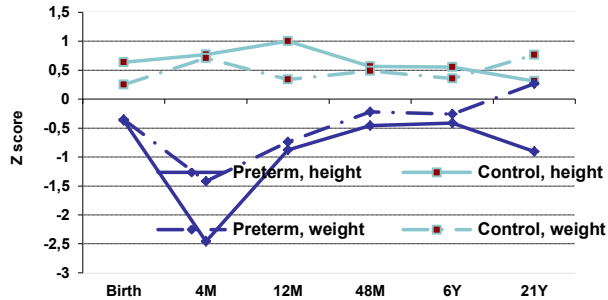
Obesity (IUGR, DIP)



Arterial Blood Pressure in Young Adults Born Preterm vs Postnatal Growth



Growth

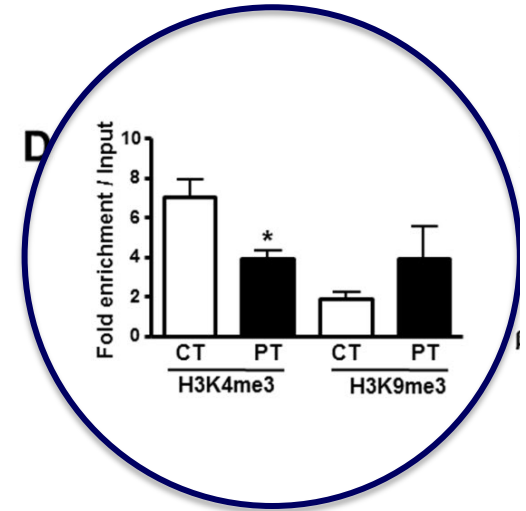
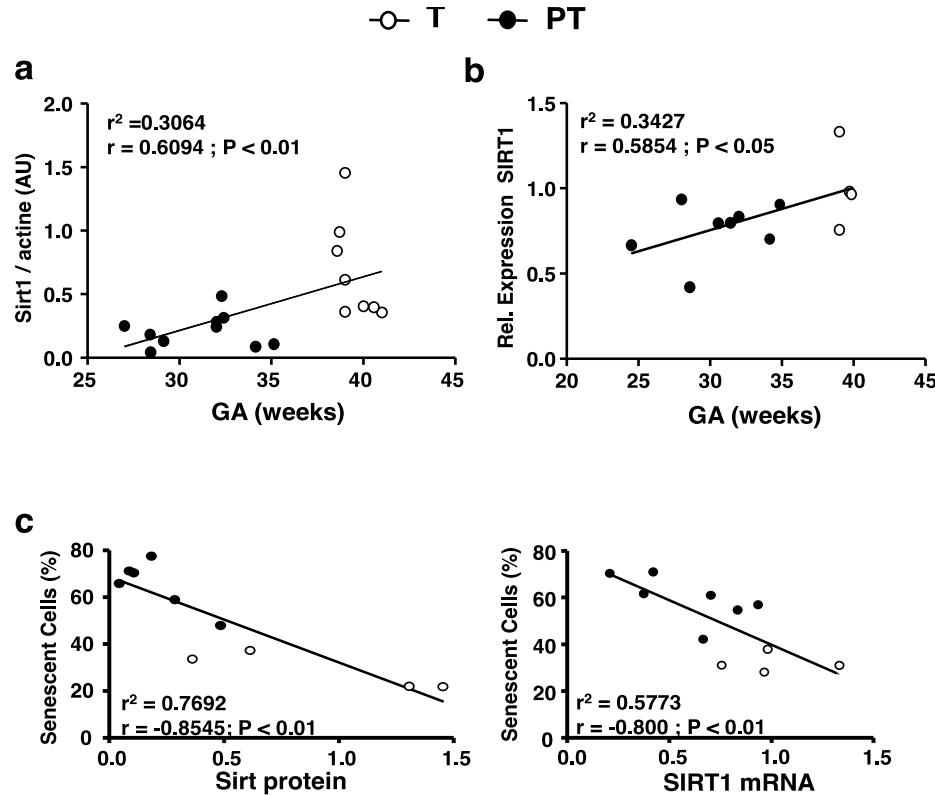


Systolic blood pressure

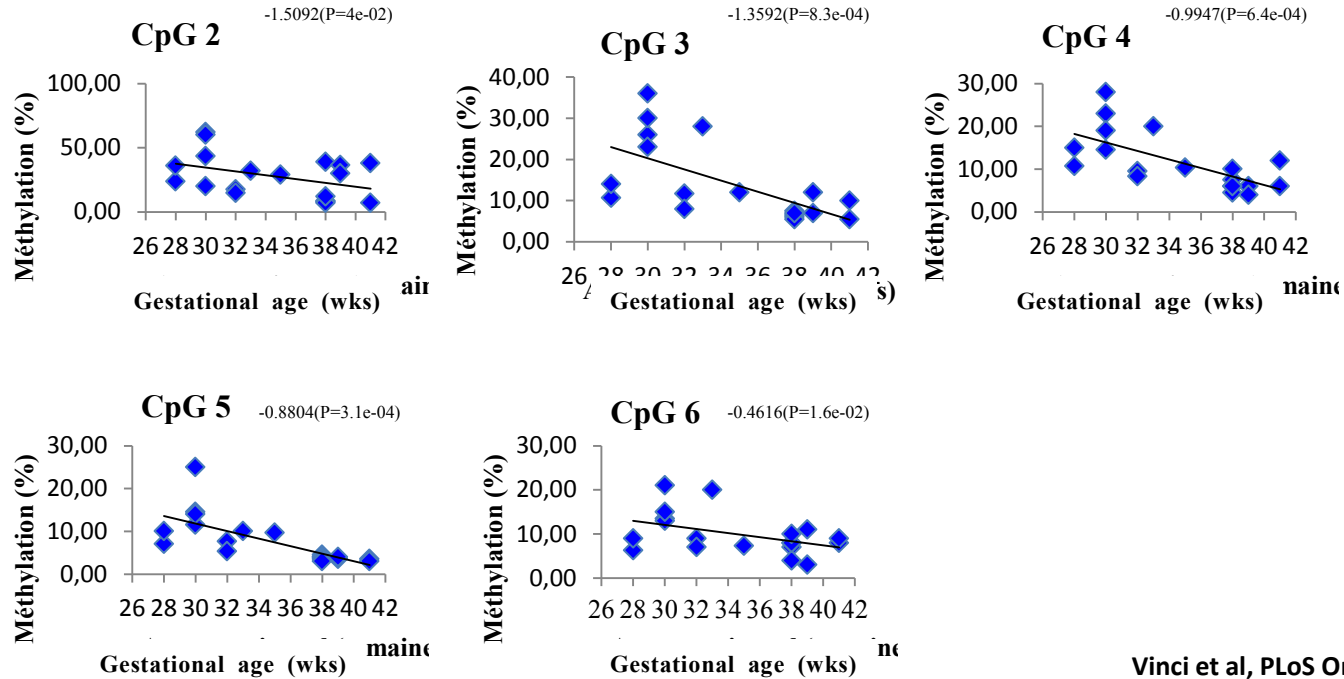
Systolic blood pressure correlations	r	p
Change in Z-score for weight (4-12 months)	0.426	0.048
Weight gain : 6-21 years (absolute)	0.419	0.03
Weight gain : 6-21 years (relative)	0.582	0.001
Change in Z-score for weight (6-21 years)	0.381	0.05
Change in BMI (6-21 years)	0.489	0.011

Altered angiogenesis in preterm infants:

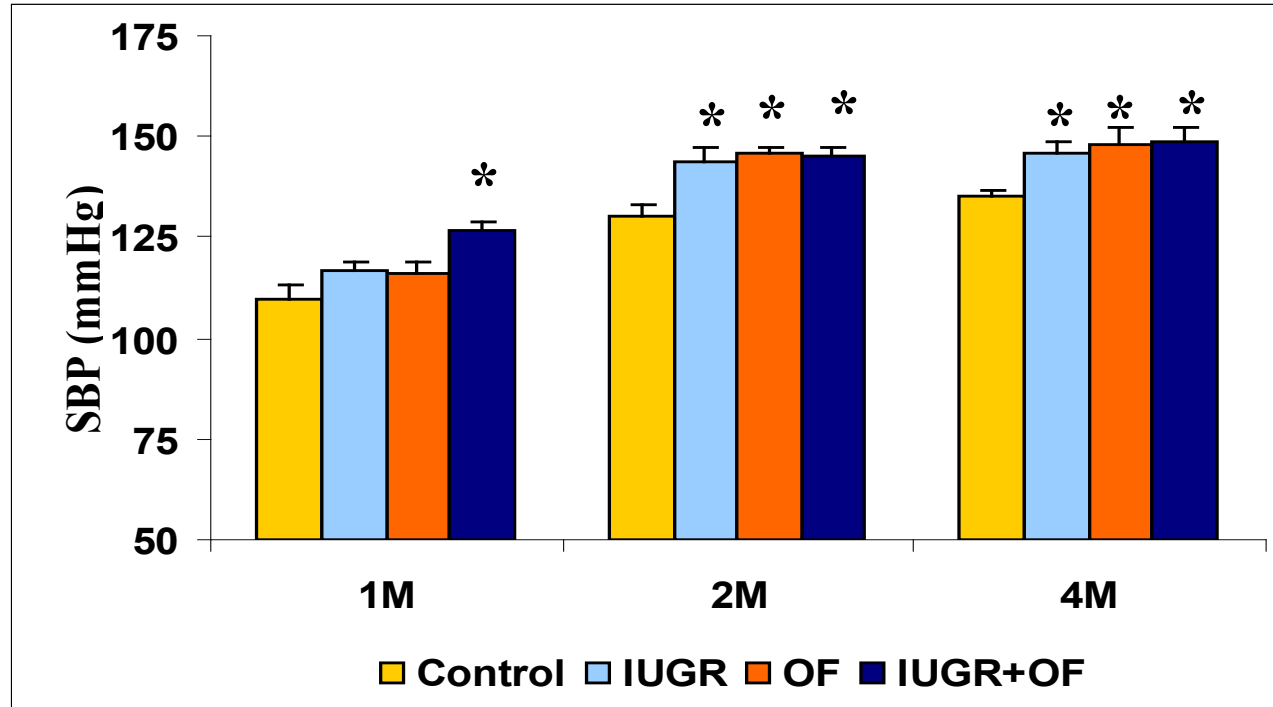
SIRT1 decrease correlates with accelerated senescence in Endothelial Colony Forming Cells (ECFCs)



Human Cord Blood Endothelial Progenitor Cells Angiogenic Capacity: Maturation of AMOT gene methylation rate



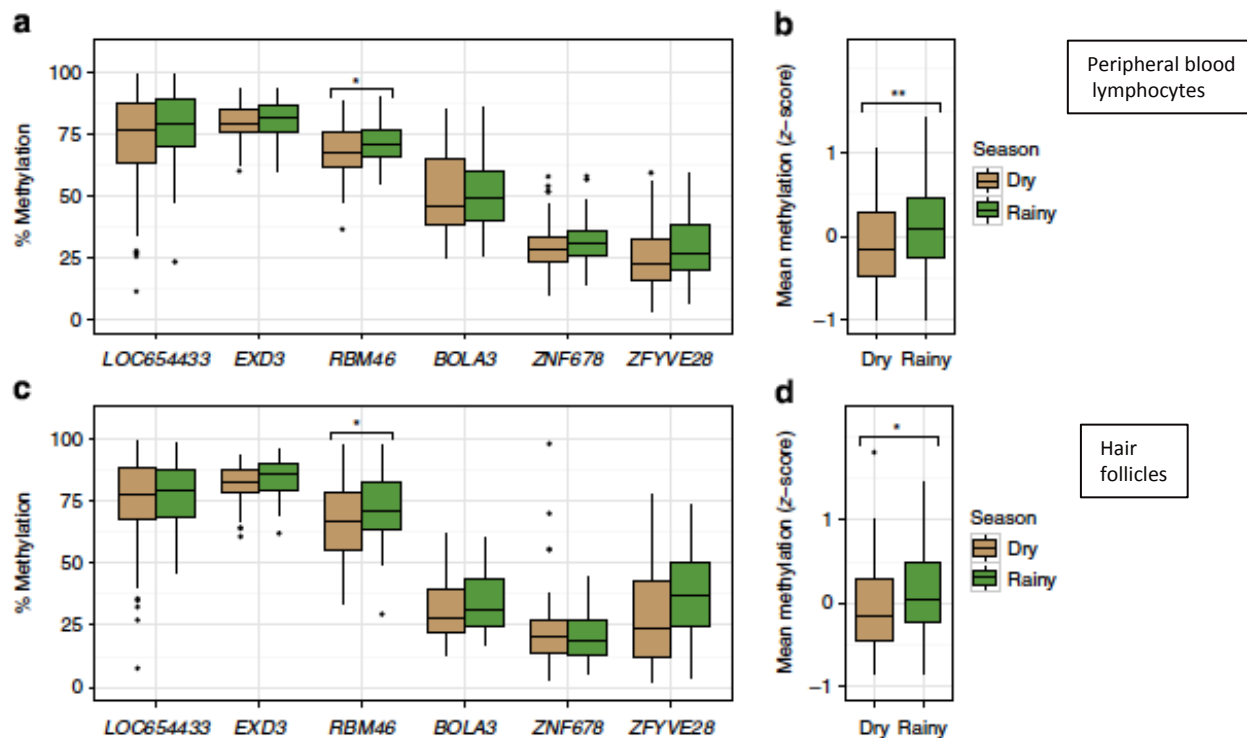
Maternal Low Protein Diet during Gestation (IUGR) ± Postnatal Overfeeding during Lactation (OF): Offspring Systolic Blood Pressure (SBP)



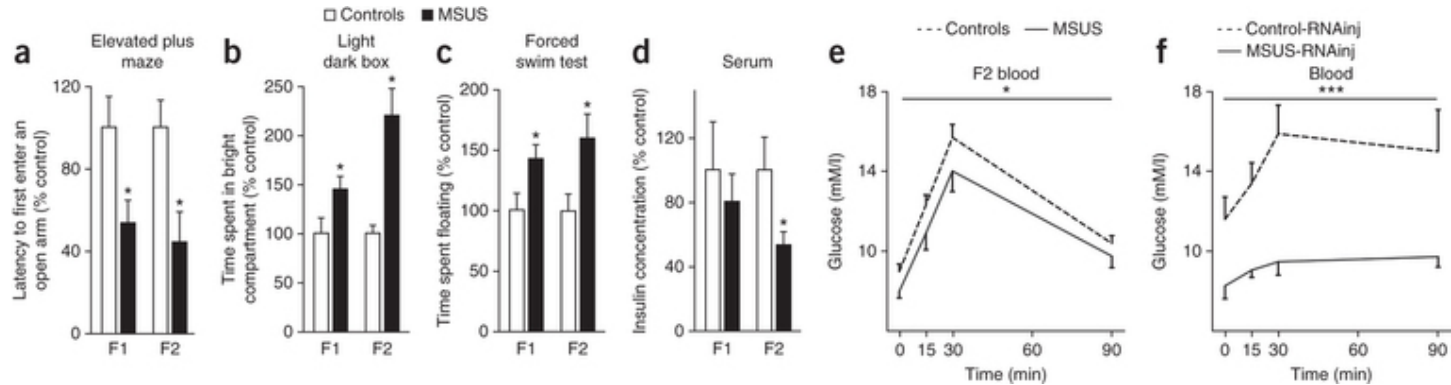
M = Age in Months

Boubred et al,
AJP 2007; 2009

Seasonal variation of methylation of metastable epialleles in infants according to maternal nutrition at conception in Gambia



Implication of sperm RNAs in transgenerational inheritance of the effects of early trauma in mice

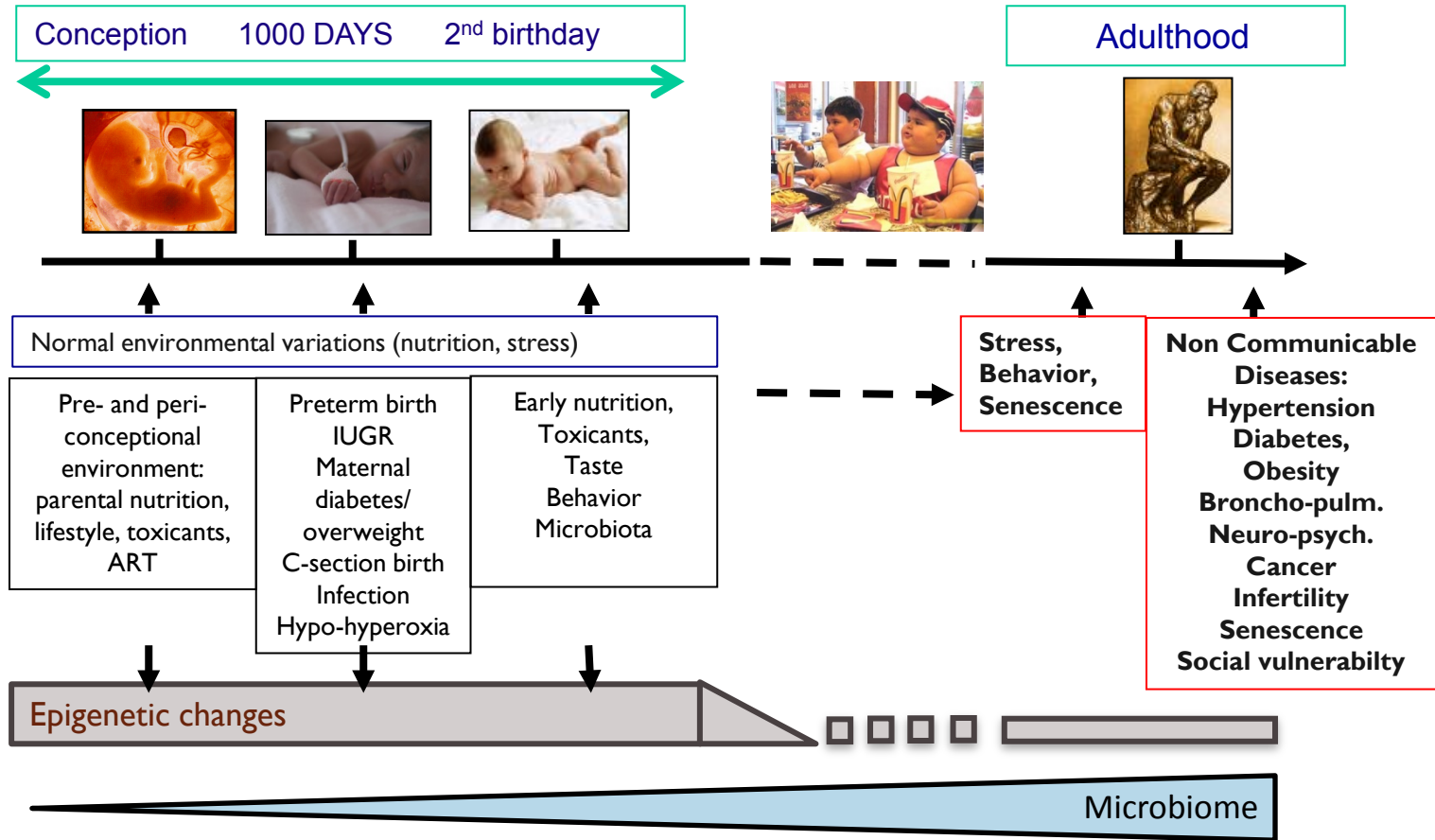


Behavioral and metabolic responses in “unpredictable maternal separation combined with unpredictable maternal stress” (MSUS) males across generations and in mice derived from RNA-injected oocytes.

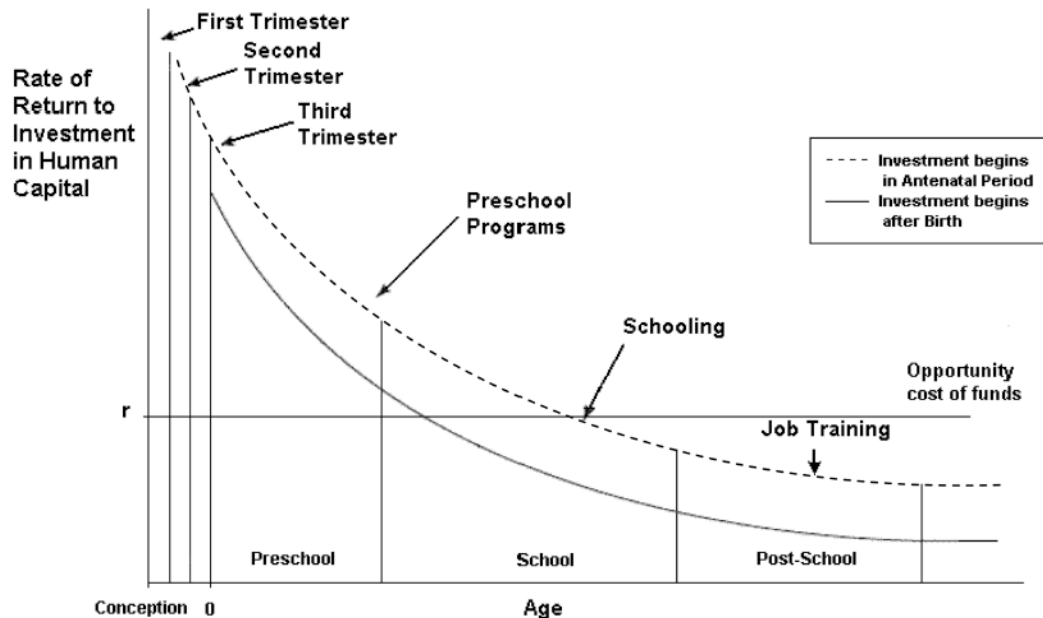
Gapp et al, Nature Neurosci 2014

Dad is having a much larger role in the whole process, rather than just delivering his genome and being done with it.

Developmental Programming & Developmental Origins of Health and Disease (DOHaD)

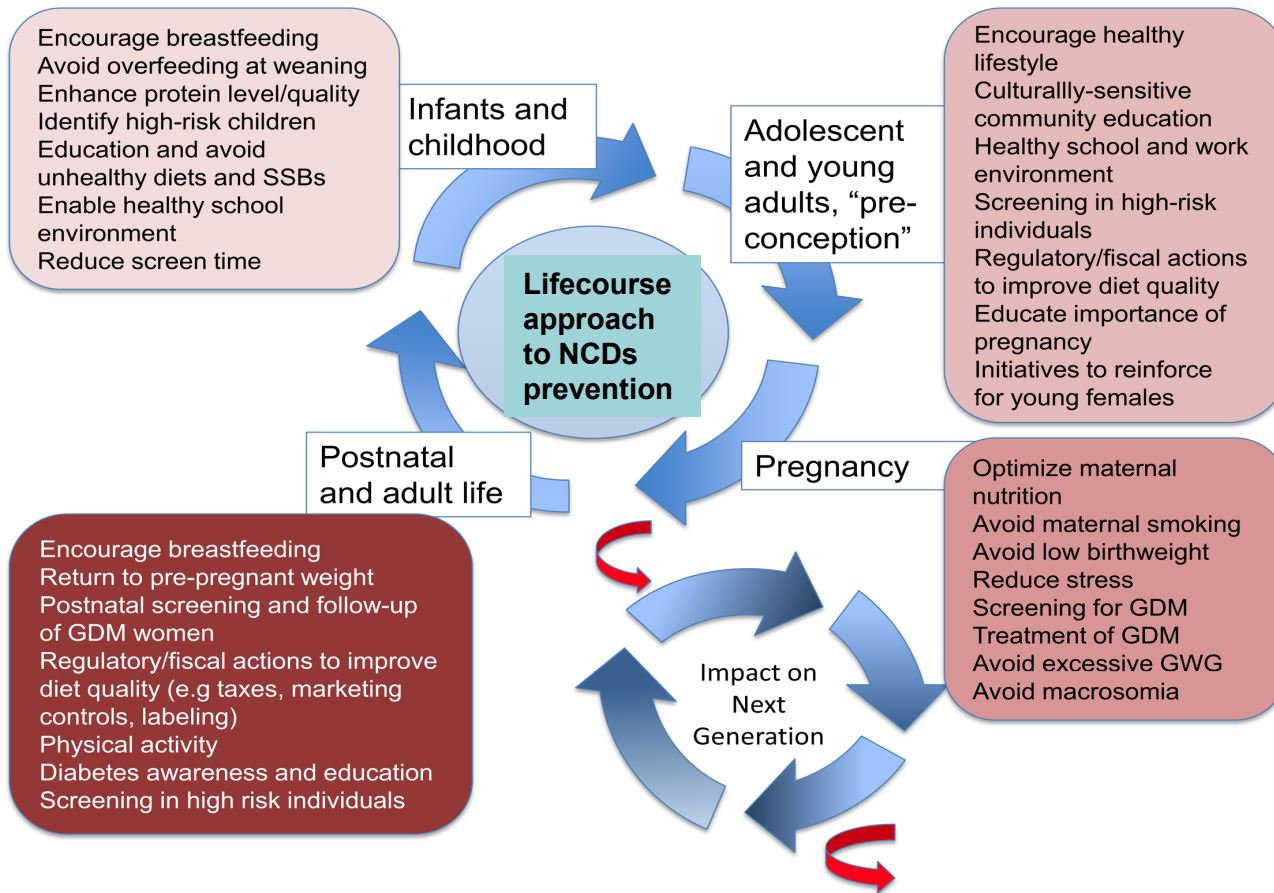


Rates of Return to Human Capital Investment Setting
Investment to be Equal across all Ages



Rates of return to human capital investment setting investment to be equal across all ages

Source: Carneiro and Heckman, 2003.



DOHaD Lab & Divisions of Pediatrics CHUV & FBM/UNIL, CH- Lausanne



- H Chehade
 - J-B Armengaud
 - C Yzydorczyk
 - U Simeoni
- Cardio-vascular,
Metabolic
Kidney, Immune
System, Nutrition,
Oxydative stress
Senescence
- B Siddeek
 - M Benahmed (INSERM-U895,
Nice)

Reproduction, Cancer
Epigenetics, ncRNA

Cooperation:

- Neonatology Lab, CHUV (J-F Tolsa, M Roth-Kleiner, A-C Peyter, S Gremlich)
- MRC Lifecourse Southampton (C Osmond)
- Heart Research Center, Portland (K Thornburg)
- INSERM 866 Dijon (C Vergely)
- INSERM 1076 Aix-Marseille University (F Dignat-George)