Epigenetic mechanisms and DOHaD

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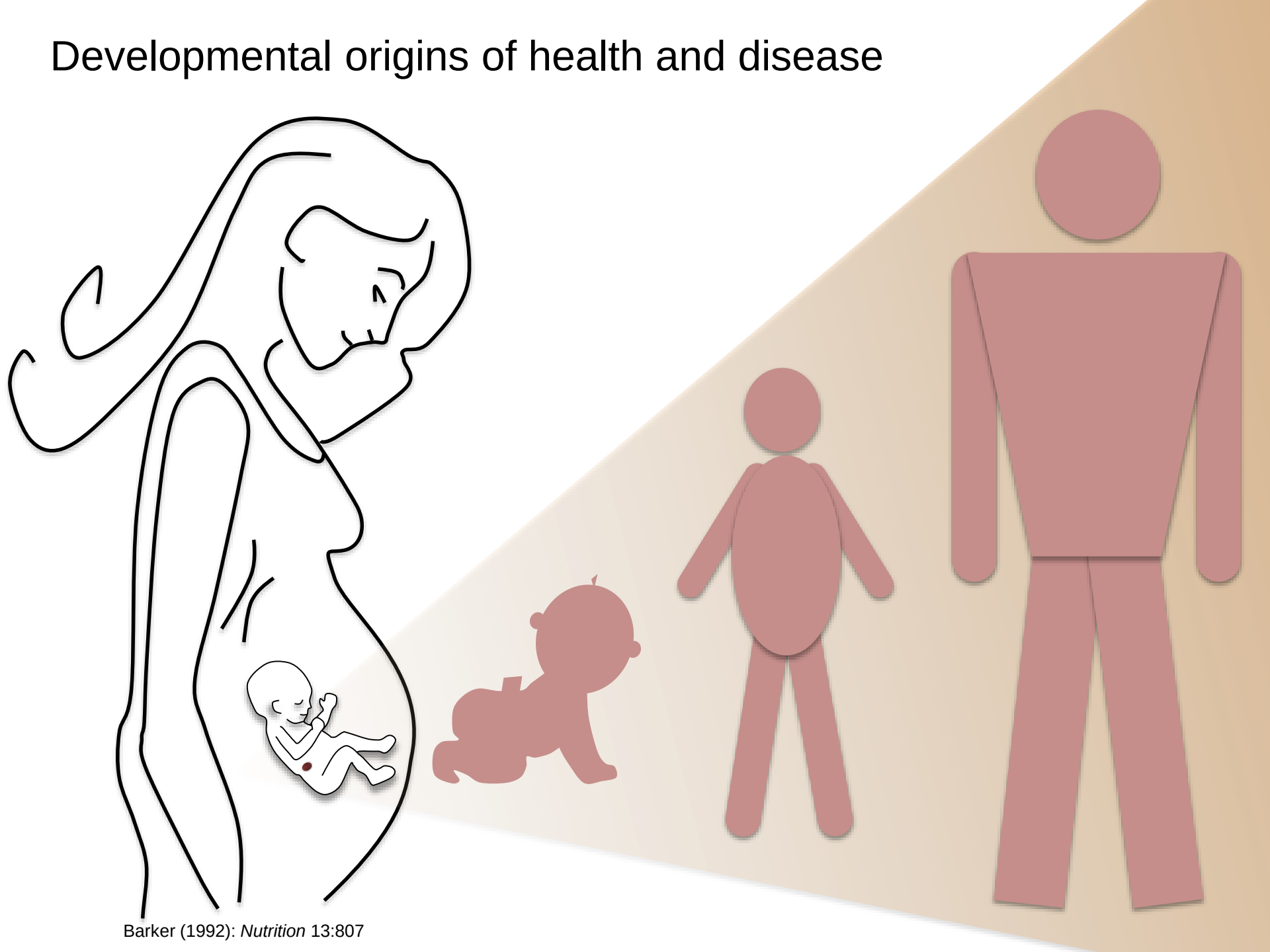
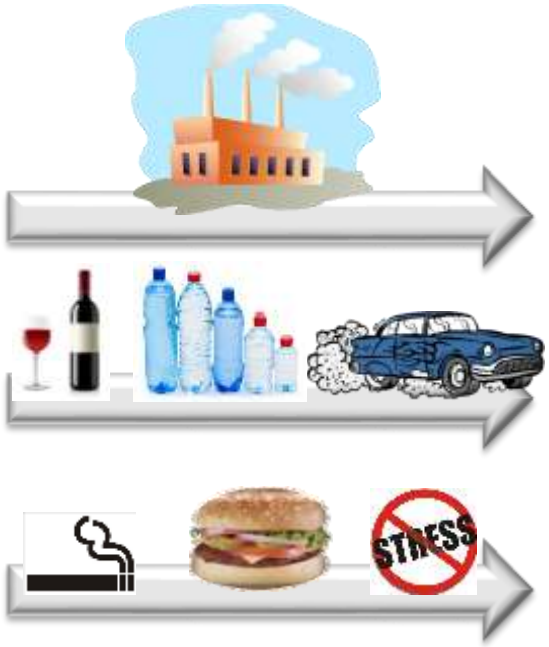
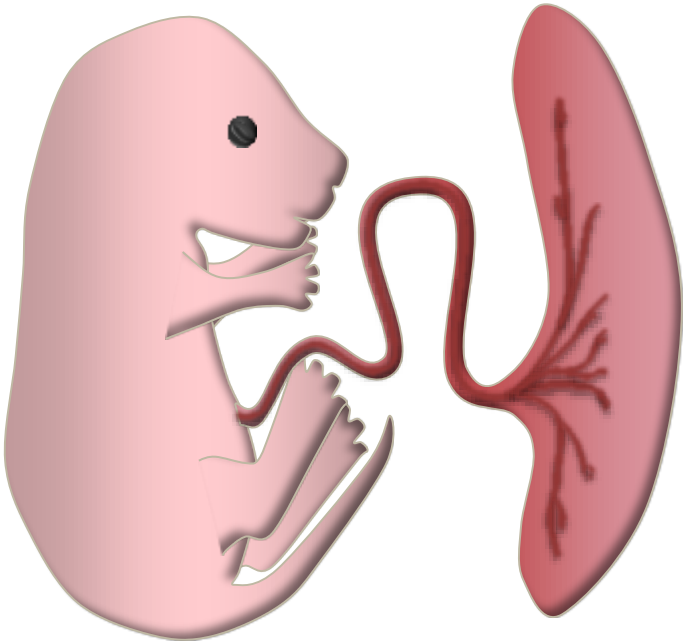
Developmental origins of health and disease



Barker (1992): *Nutrition* 13:807

GENE-ENVIRONMENT INTERACTION





HEALTH

EPIGENETICS

Epigenetic: heritable changes in gene expression caused by mechanisms that do not depend on changes in DNA sequences

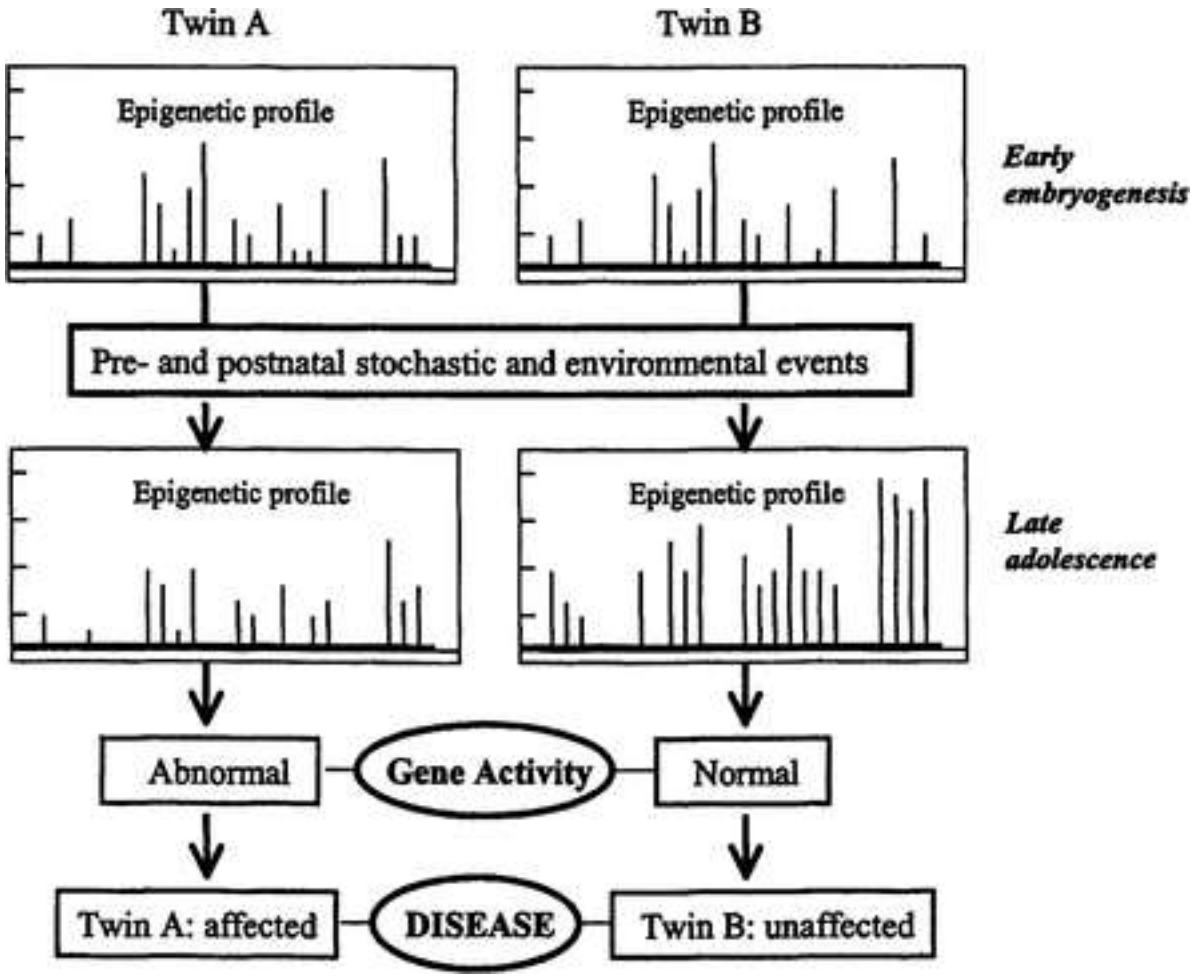
Genetics and disease

Normal (G/G)	AGATTCAGGCATATT AGATTCAGGCATATT
Carrier (G/A)	AGATTCAGGCATATT AGATTCAAGCATATT
Disease (A/A)	AGATTCAAGCATATT AGATTCAAGCATATT

Epigenetics and disease

AGATTCAGGCATATT AGATTCAGGCATATT

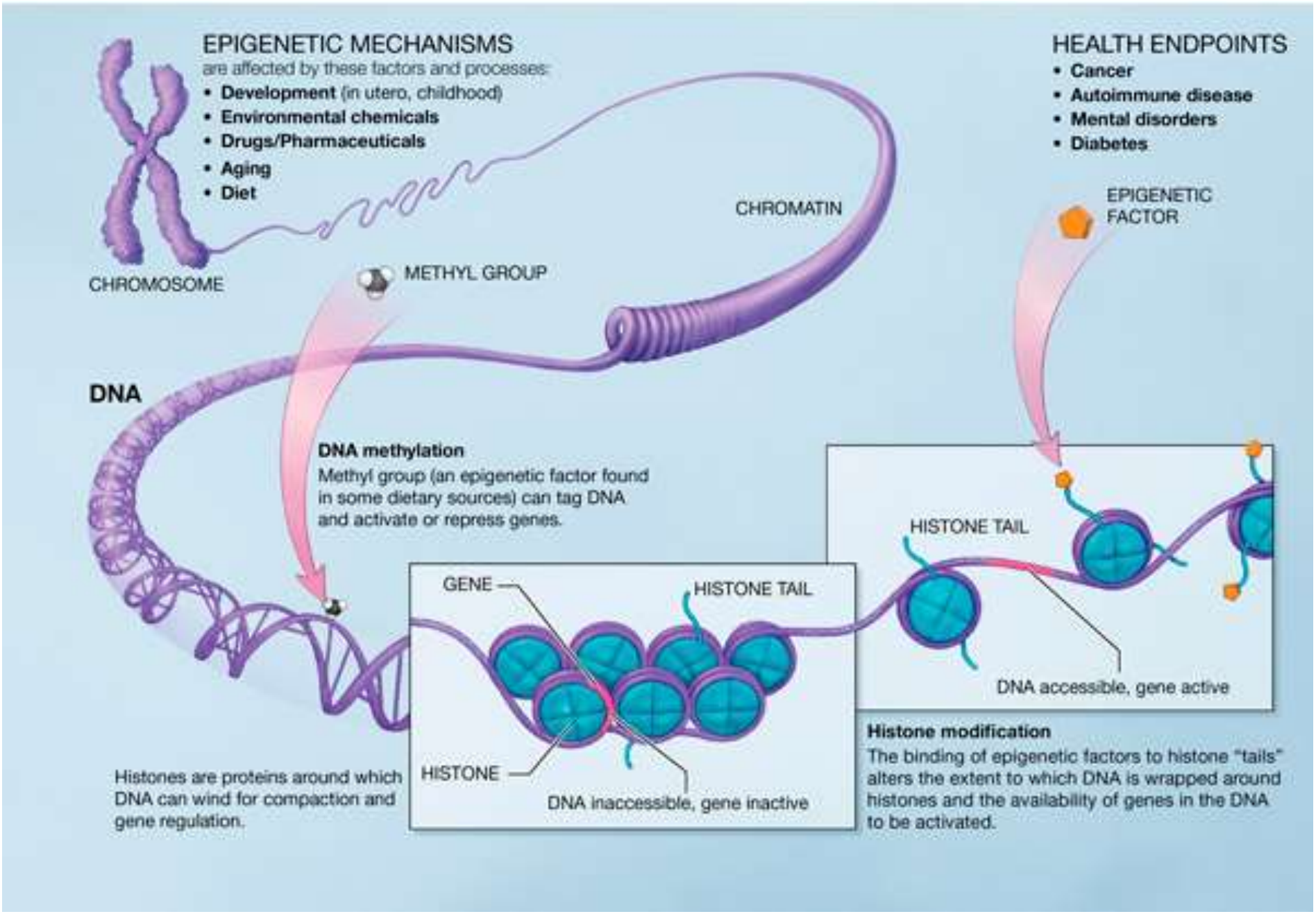
AGATTCAGGCATATT AGATTCAGGCATATT



Adapted from
Petronis et. al., 2003

Epigenetic mechanisms in mammalian development

- Lineage commitment
- Retrotransposon silencing
- X Chromosome inactivation
- **Genomic imprinting**



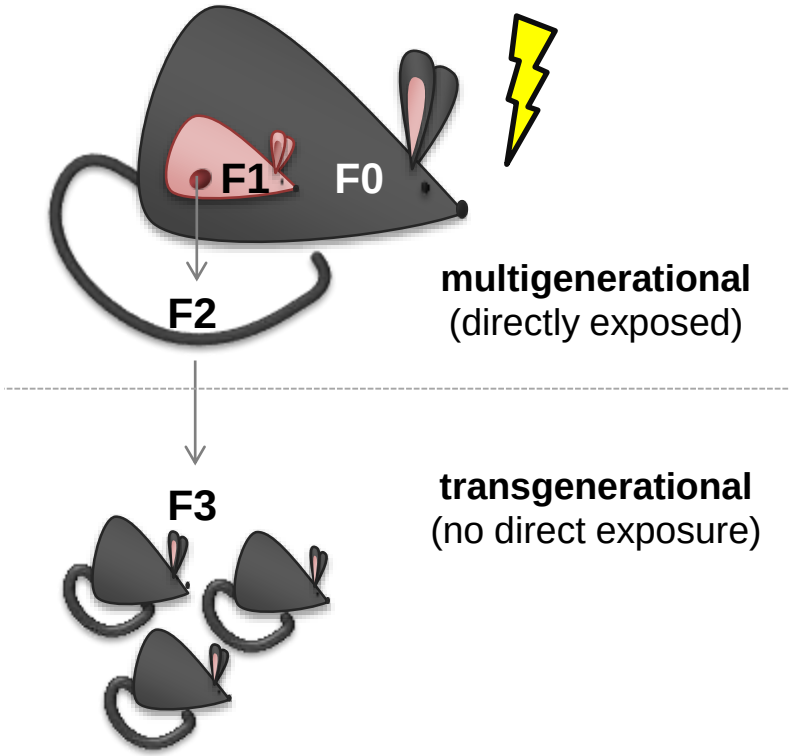
Germline epimutation

Parental genomic demethylation

Epigenetic drift / somatic epimutation

Developmental epigenetic programming

Waterland RA. *Nutr Rev* 2008



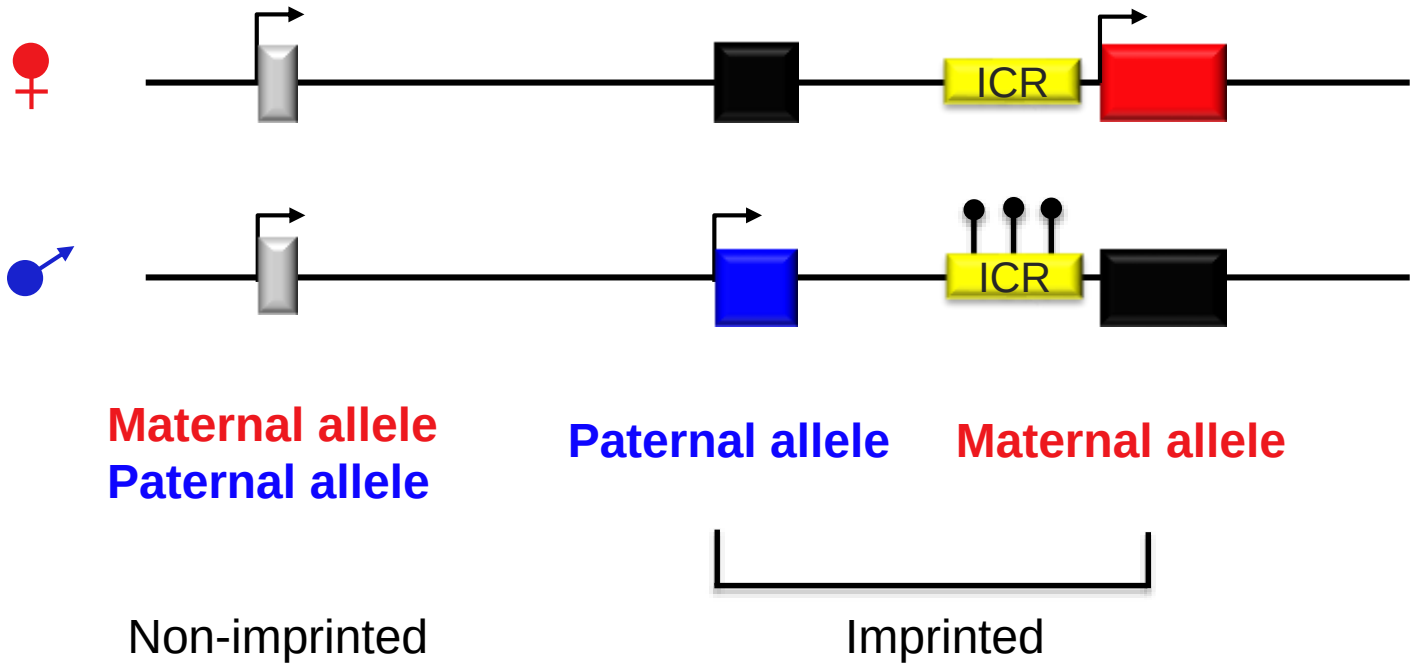
Adapted from Xin F. et al (2015) Seminars in Cell and Developmental Biology

Epigenetic mechanisms in mammalian development

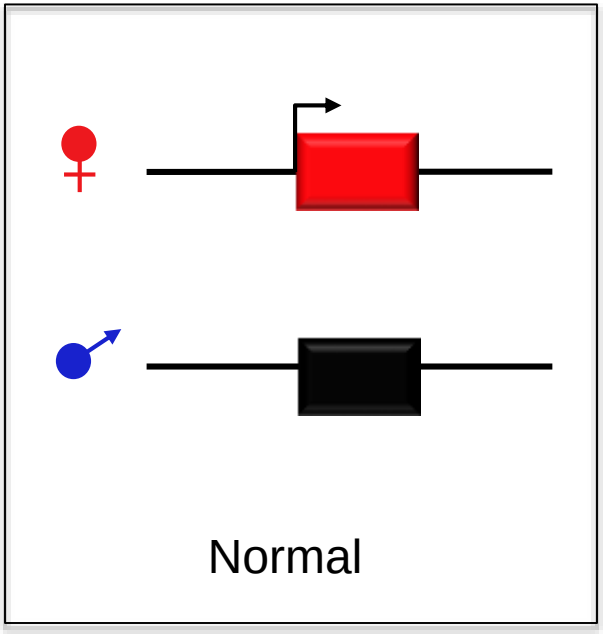
- Lineage commitment
- Retrotransposon silencing
- X Chromosome inactivation
- **Genomic imprinting**

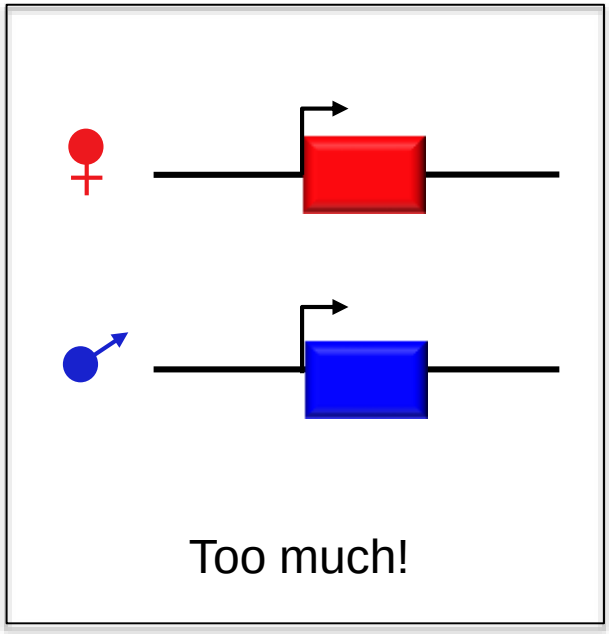
Genomic Imprinting

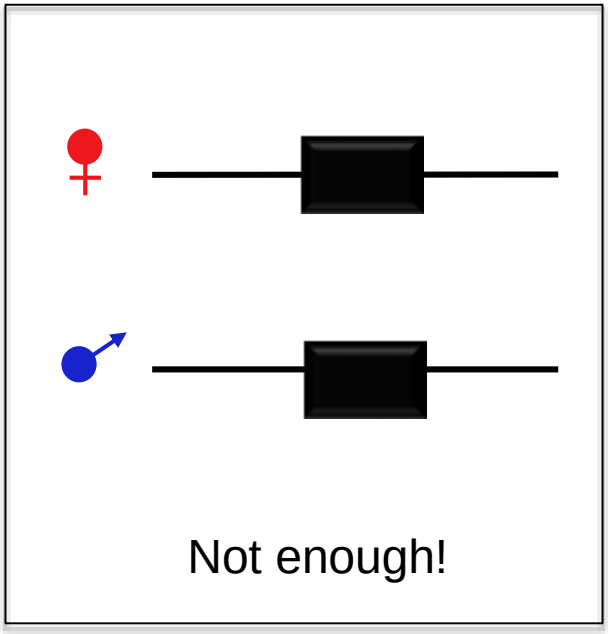
The unequal expression of the maternal and paternal alleles of a gene



Dosage is important!







Abnormal imprinting disrupts development

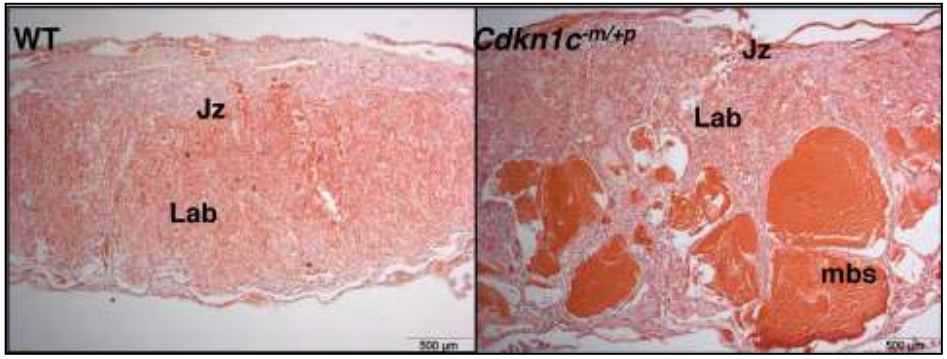
Fetal growth

Charalambous et al (2003).

Mutant WT

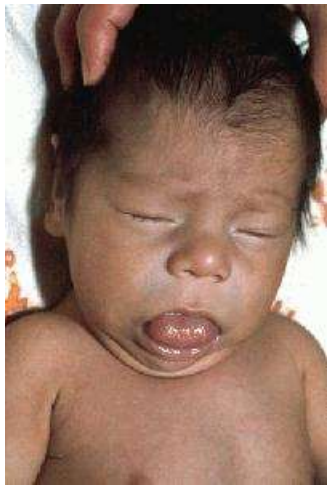
Placental development

Tunster et al (2011)



WT Mutant

Growth



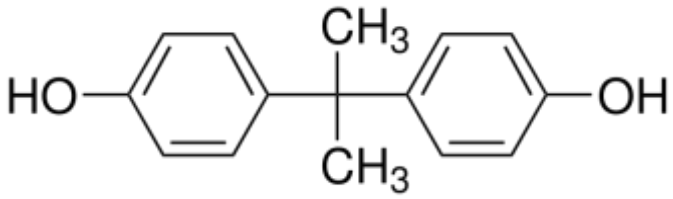
Beckwith-Wiedemann Syndrome

Neurobehavioral development

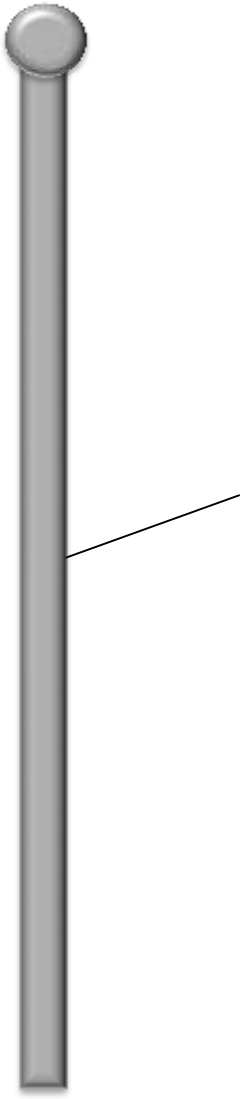
Prader-Willi Syndrome

Angelman Syndrome

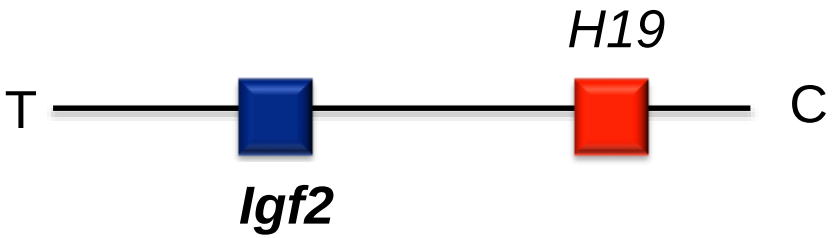
A model of environmental exposure: Bisphenol A is ubiquitous in the environment

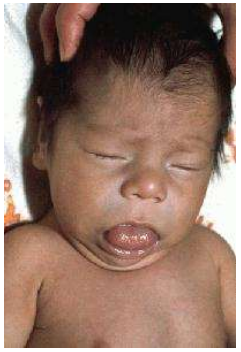


MOUSE
CHR 7



H19/Igf2 domain:





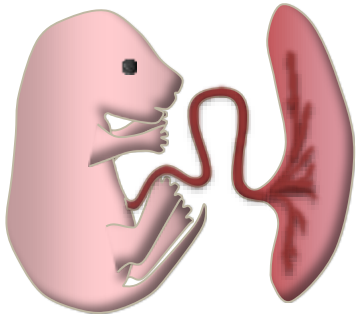
-insulin-like growth factor

-fetal growth

-misregulation linked to disease

-**BPA exposure alters DNA methylation and expression (Susiarjo et al 2013: PLoS Genetics)**

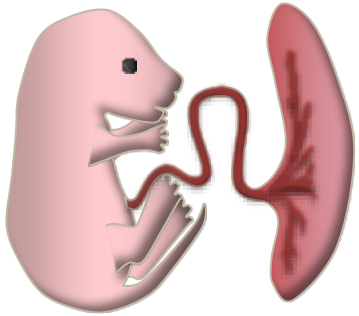
Igf2 normally expressed



Control

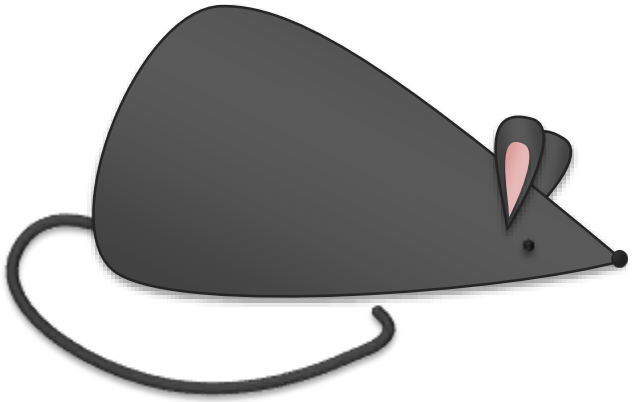
Healthy

Igf2 overproduced



BPA-exposed

Adult onset obesity
Glucose intolerance
Insulin resistance



Susiarjo et al (2015): Endocrinology