

Epigenetics and Developmental Plasticity

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How does variation in prenatal and postnatal experience lead to variation in phenotype?

Can these developmental effects persist across generations?

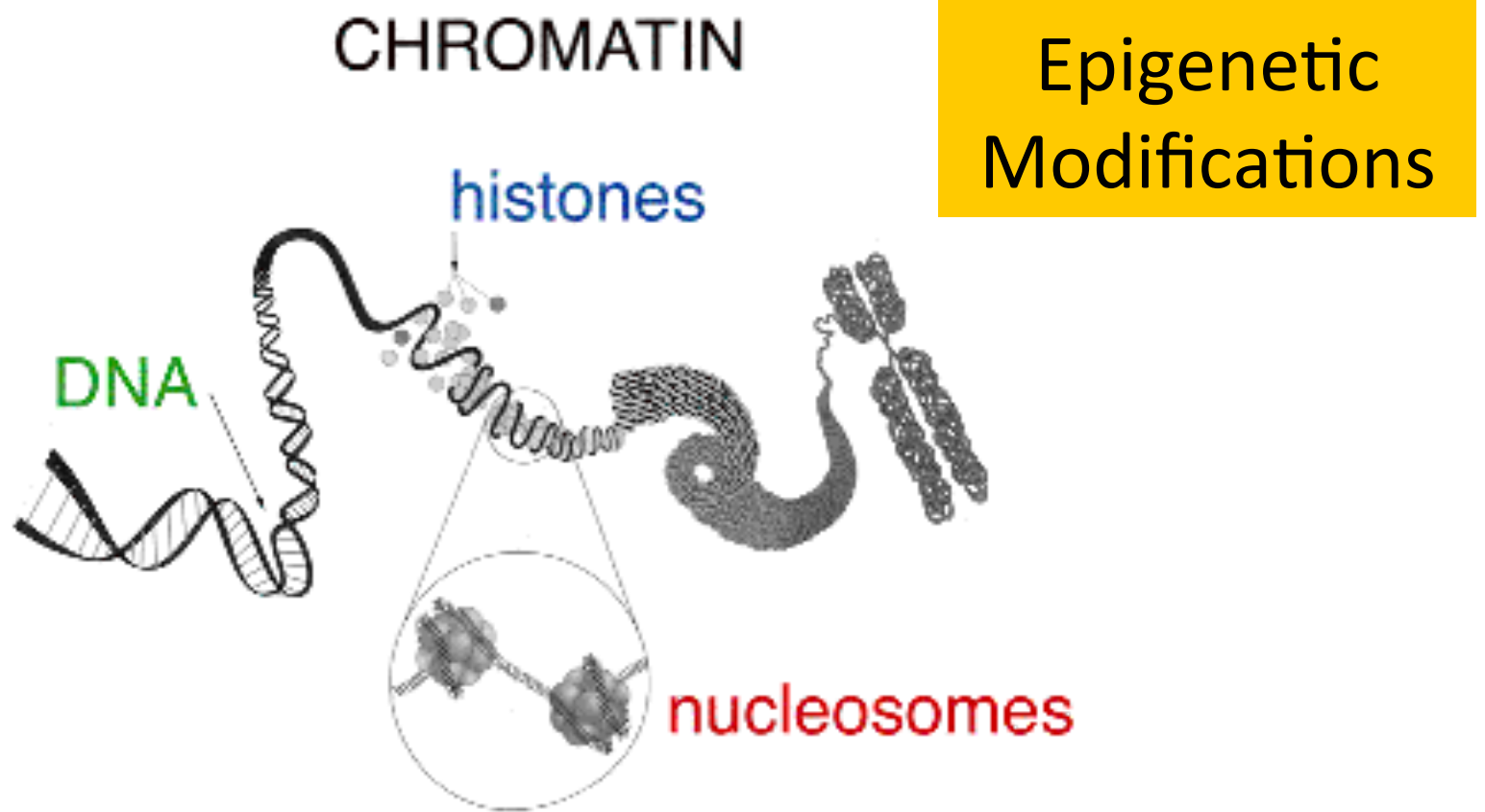
What is the adaptive significance of these within- and across-generation effects

prenatal & postnatal
experiences

long-term changes in
gene expression

altered
neurodevelopment
variations in stress,
cognition, social,
reproductive behavior

Through what mechanism can perinatal experiences induce long-term changes in gene expression in the brain?

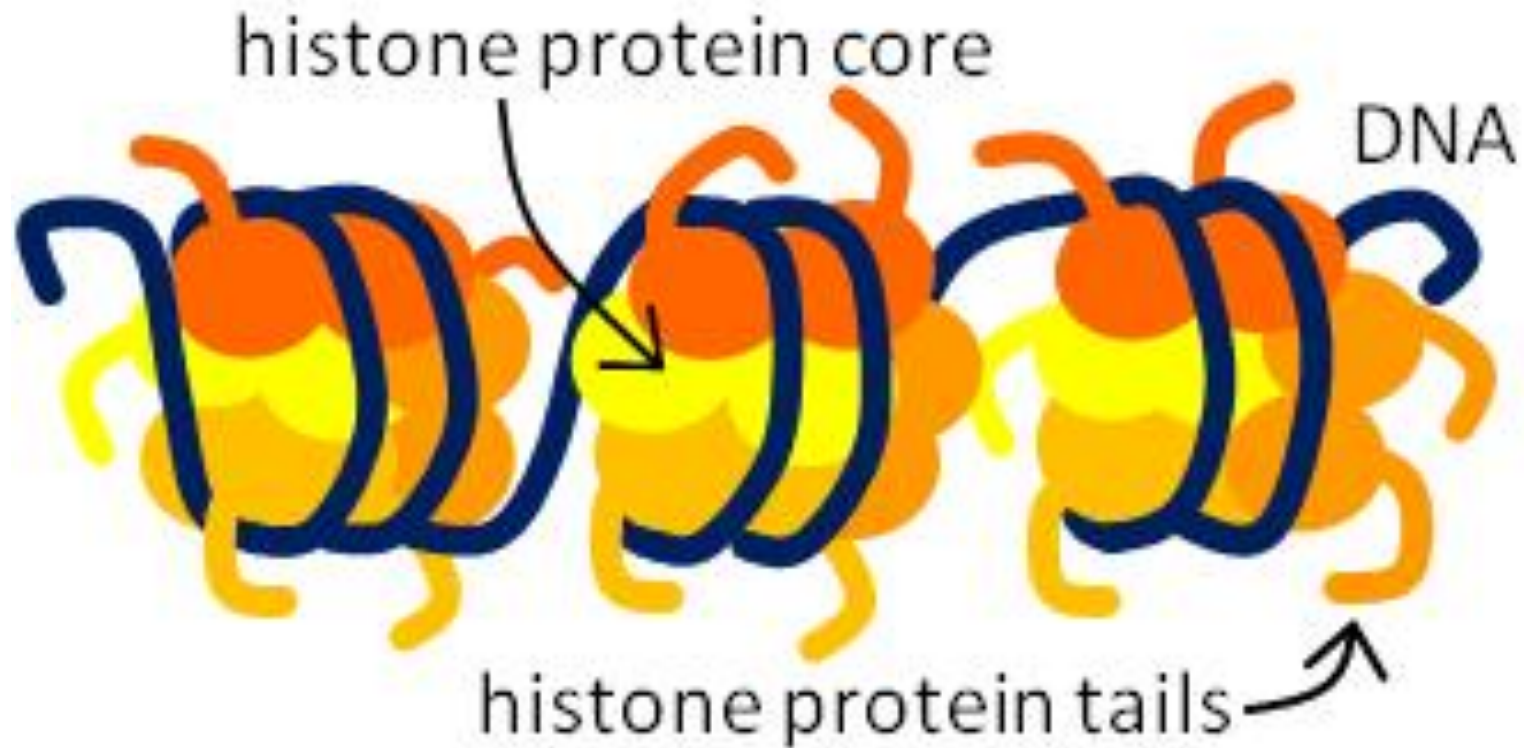


The many meanings of “Epigenetic”

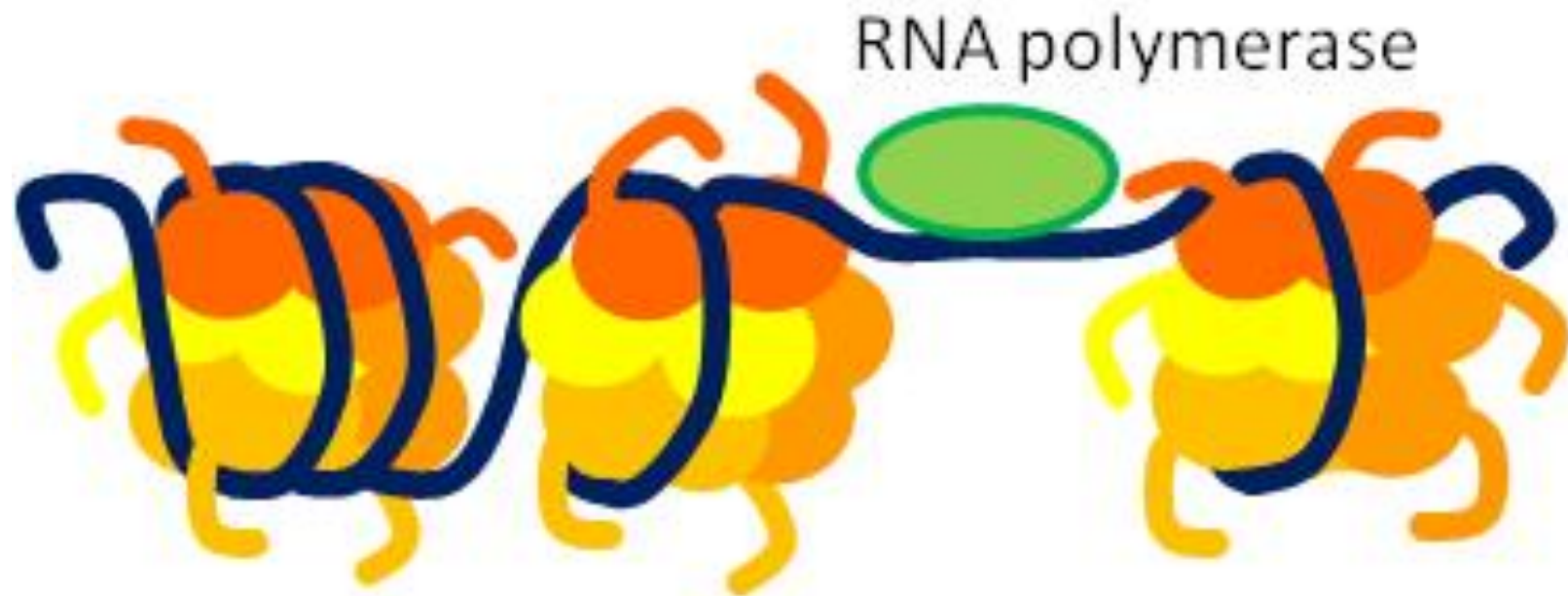
Waddington (1942): “the branch of biology which studies the causal interactions between genes and their products which bring the phenotype into being”

1. Environmentally-induced changes in gene expression
2. Phenotypic variations in cells and organisms that involve molecular mechanisms which alter gene transcription without altering gene sequence
3. Heritable molecular modifications to gene expression
4. Genomic imprinting

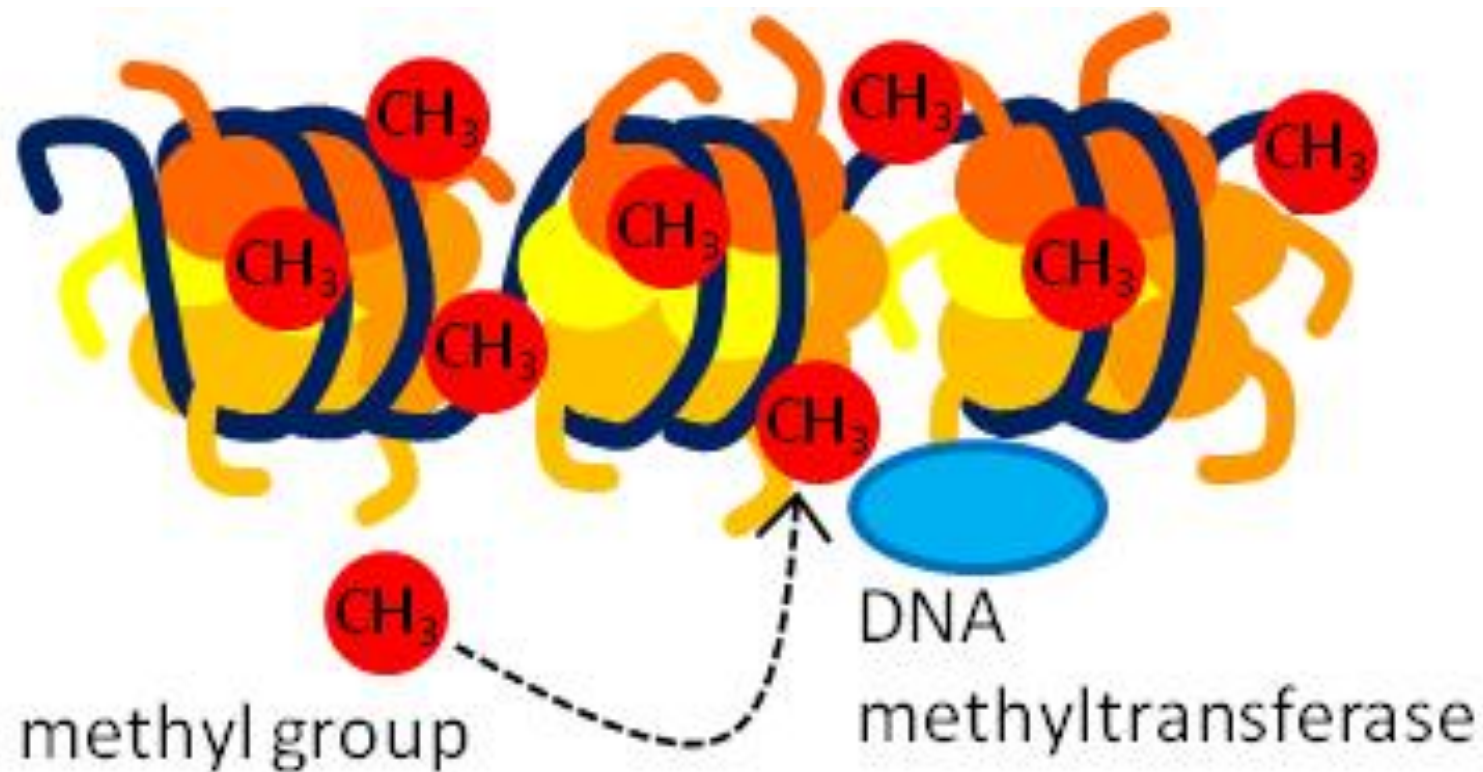
DNA is wrapped around a cluster of proteins called histones



Gene expression requires unwrapping of DNA

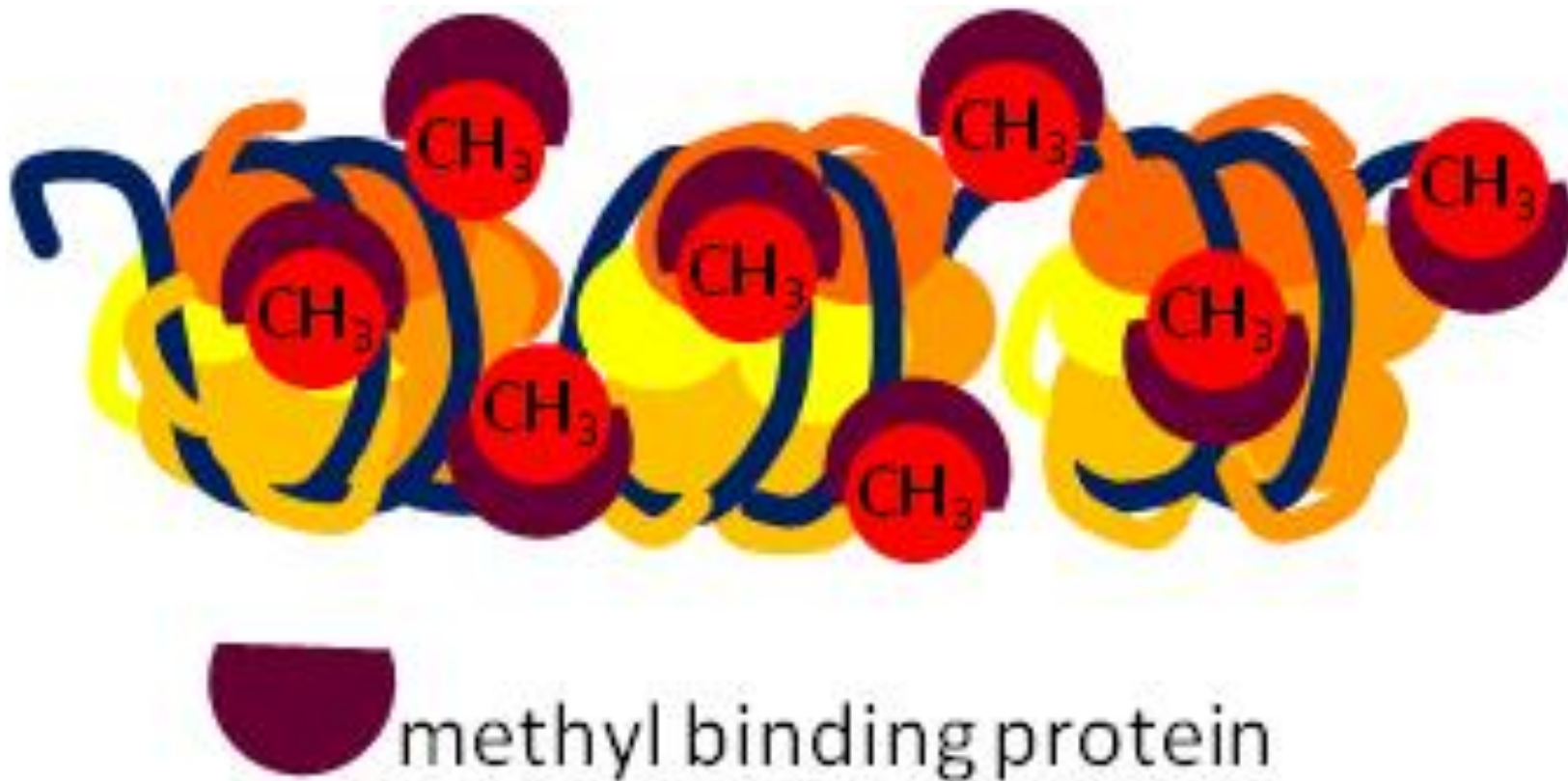


When methyl chemical groups attach to the DNA there is reduced accessibility to genes



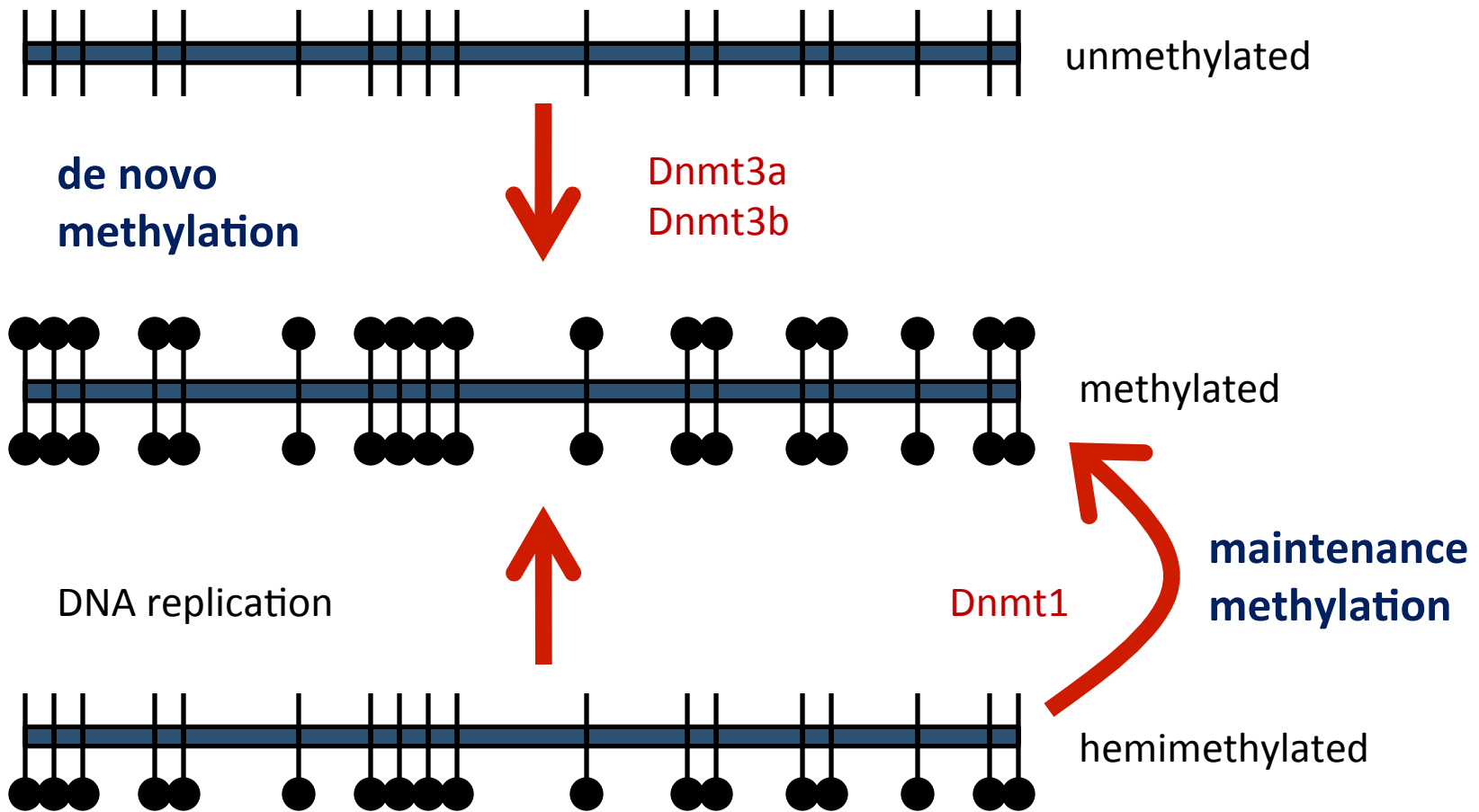
Champagne et al., (2009) *Current Opinion in Neurobiology*

Repression of gene expression can occur through DNA methylation

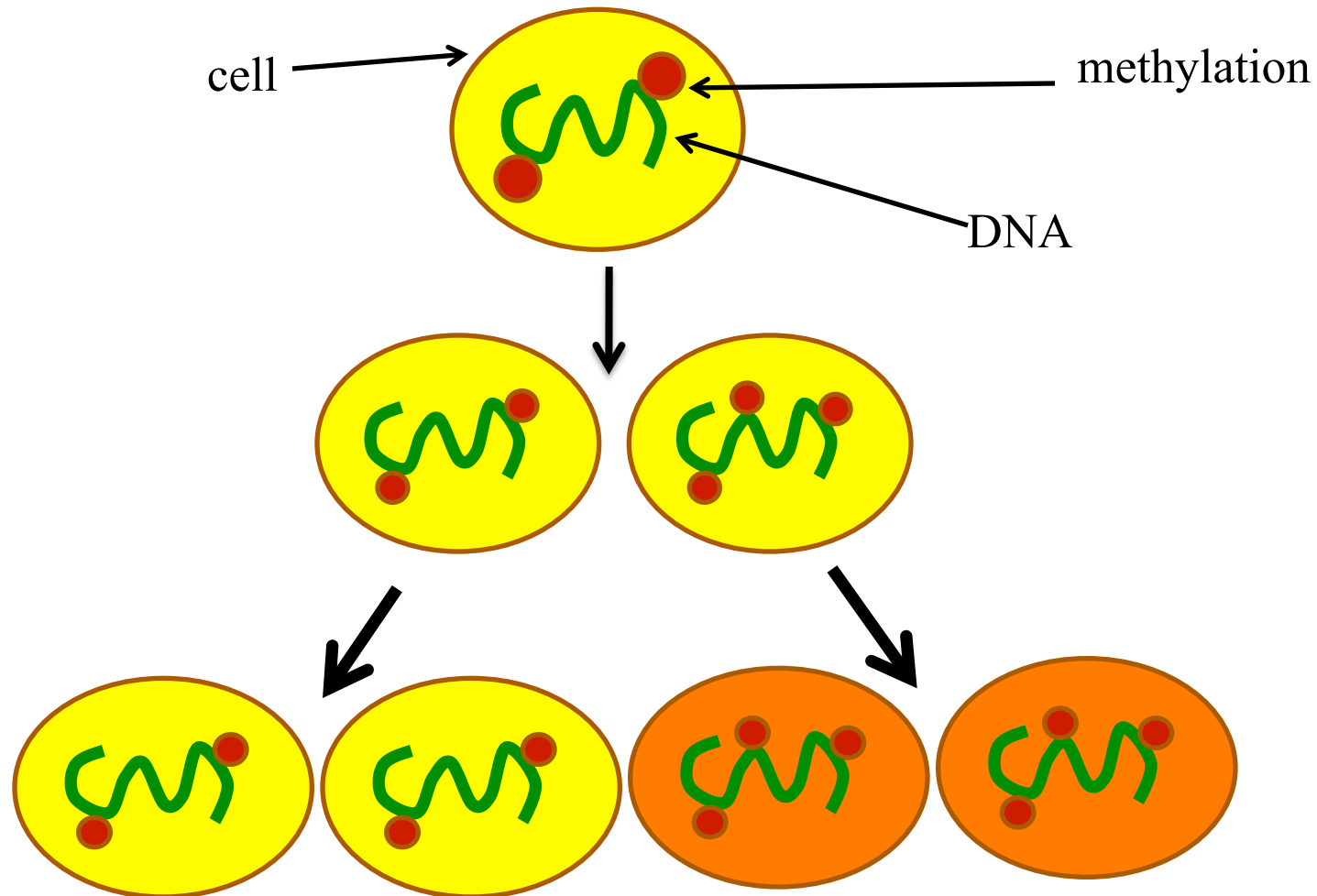


Champagne et al., (2009) *Current Opinion in Neurobiology*

2 Types of Methylation



Methylation is a stable modification to DNA which can be transmitted to daughter cells



DNA Methyltransferases

DNA Methyltransferase	Major Activity	Phenotype of loss-of-function mutations
DNMT1	Maintenance methylation of CpGs	<ul style="list-style-type: none">- genome wide loss of methylation- embryonic lethality- abnormal expression of imprinted genes
DNMT3a	De novo methylation of CpGs	<ul style="list-style-type: none">- postnatal lethality- failure to establish methylation imprints in male and female germ cells
DNMT3b	De novo methylation of CpGs	<ul style="list-style-type: none">- embryonic lethality- vascular and liver defects



Genetically Identical – Epigenetically Variable



Though twins are genetically identical and epigenetically similar when they are young, as they age they become more dissimilar in their epigenetic patterns

Variation emerges across the lifespan

Mechanism of Perinatal Effects on Offspring Development

prenatal & postnatal
experiences

epigenetic variation

long-term changes in
gene expression



altered
neurodevelopment

variations in stress,
cognition, social,
reproductive behavior

Postnatal
Maternal
Care



Variation in
Brain &
Behavior





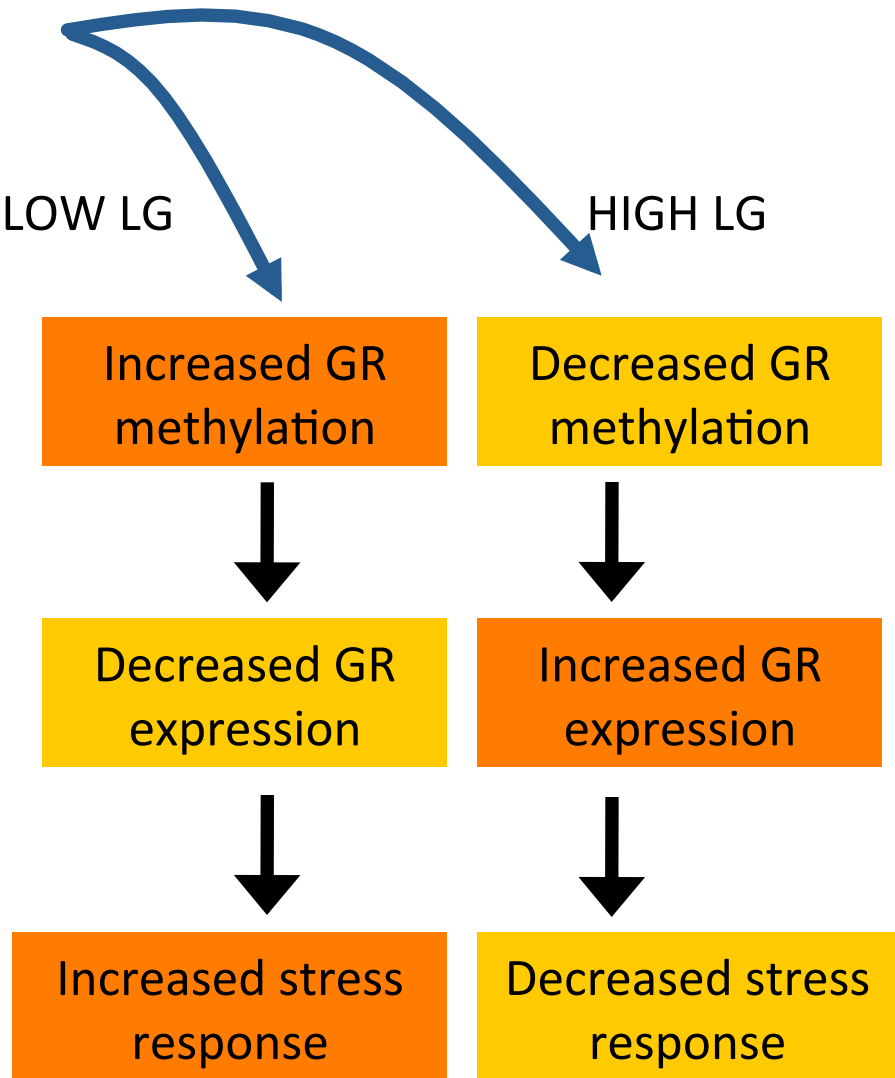


Maternal Licking/Grooming

LOW LG

HIGH LG

Cross-fostering studies confirm the influence of rearing environment on this epigenetic process



Research Paper

Prenatal exposure to maternal depression, neonatal methylation of human glucocorticoid receptor gene (*NR3C1*) and infant cortisol stress responses

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Key words: *NR3C1* methylation, prenatal maternal depression, hypothalamic pituitary adrenal, (HPA), infant stress response

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www.nature.com/tp

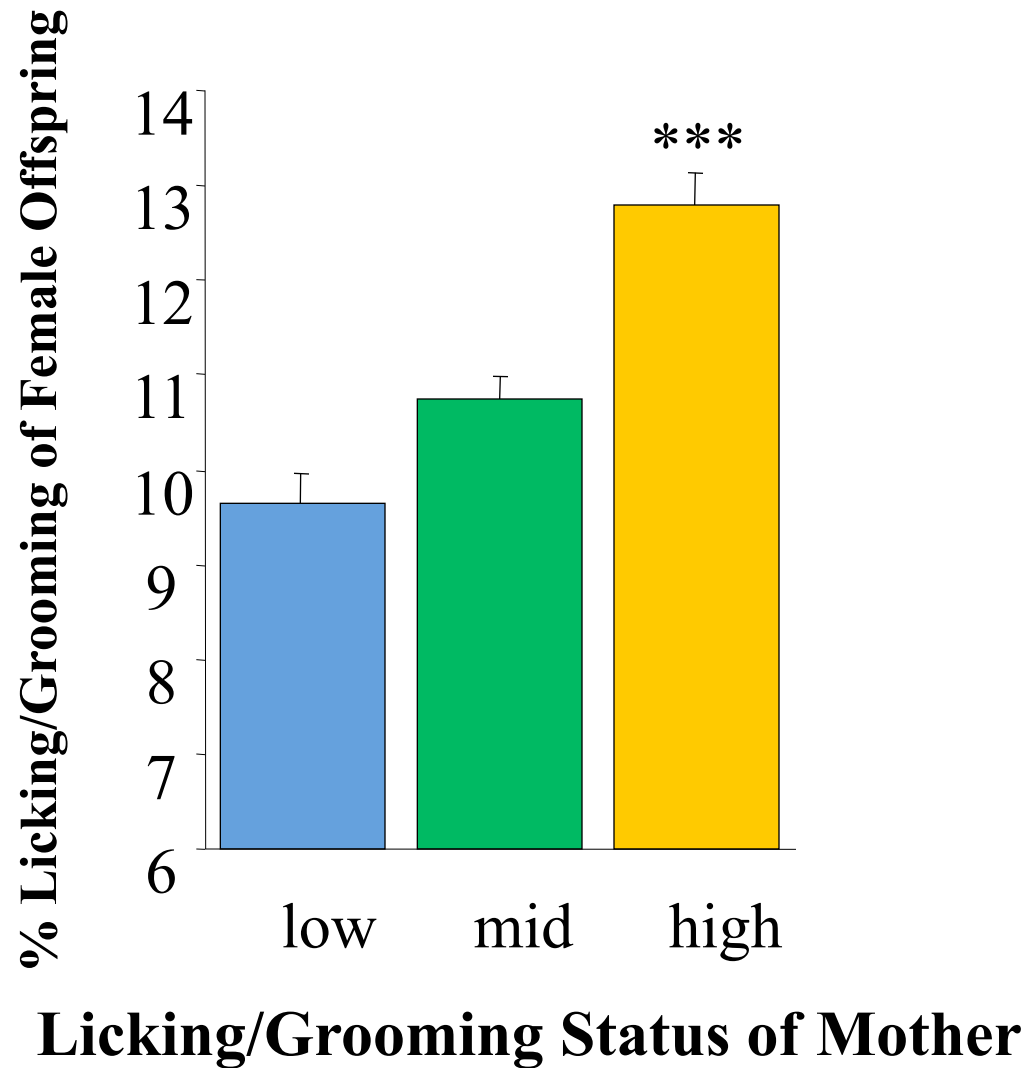


Transgenerational impact of intimate partner violence on methylation in the promoter of the glucocorticoid receptor

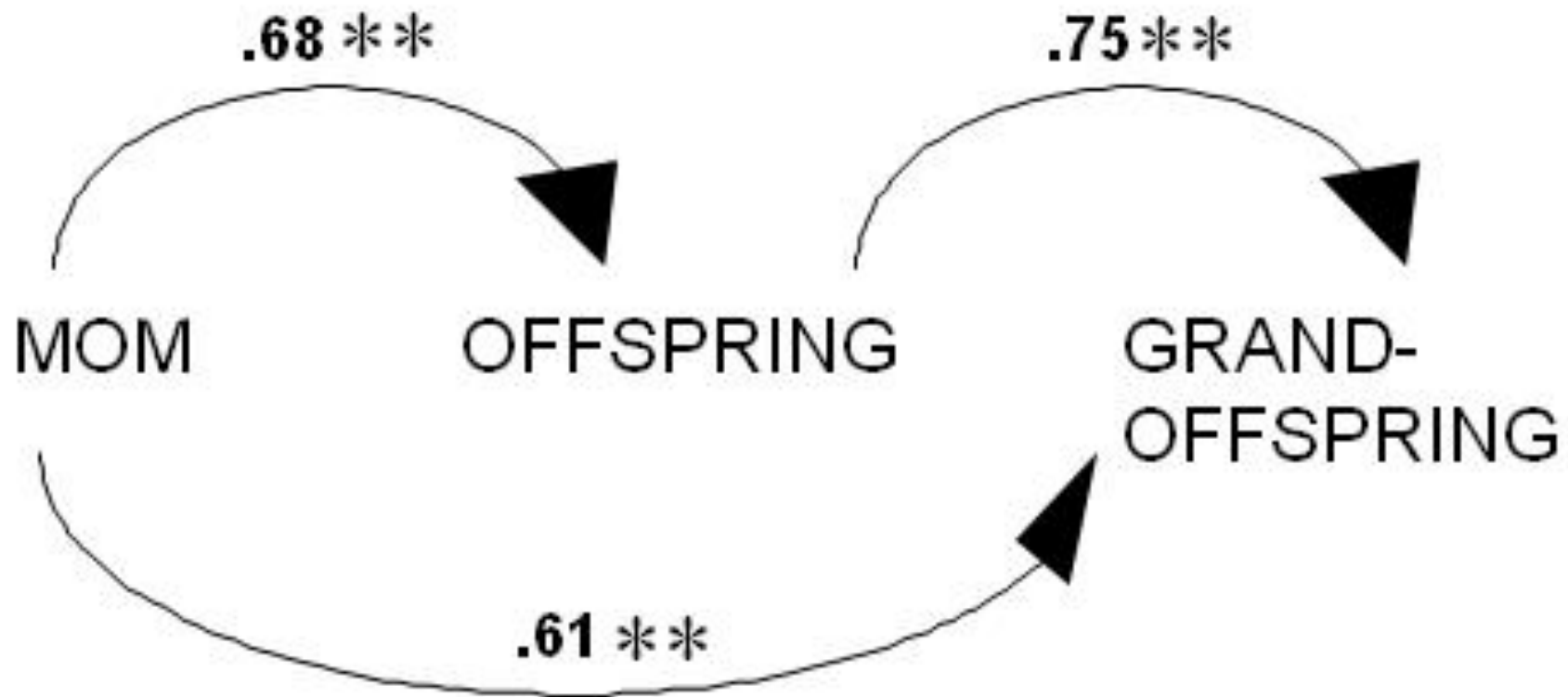
KM Radtke^{1,2,4}, M Ruf^{1,4}, HM Gunter^{2,3,4}, K Dohrmann¹, M Schauer¹, A Meyer² and T Elbert¹

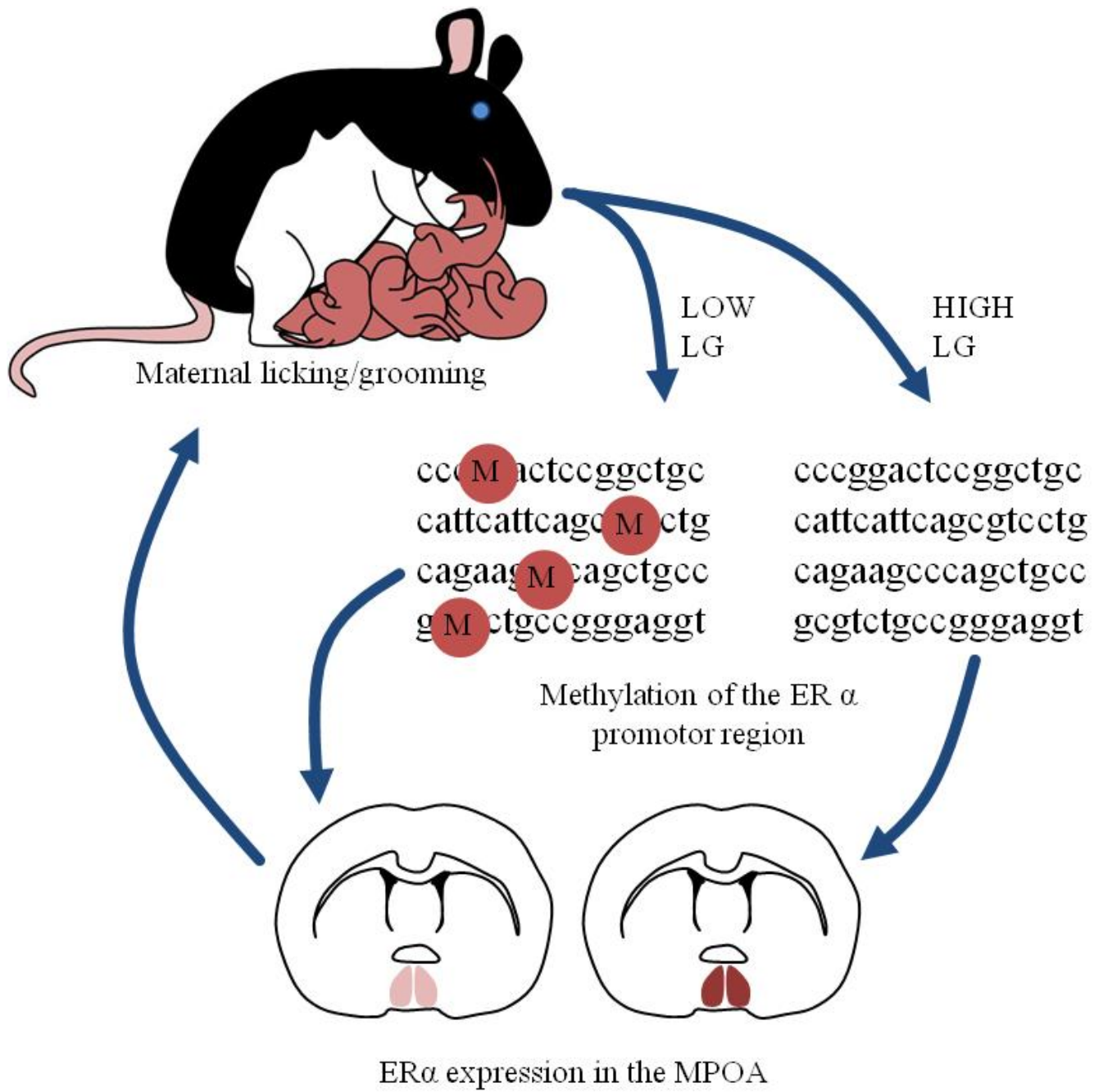
Transmission of Phenotype from Parents to Offspring

Mother & Offspring LG Behavior

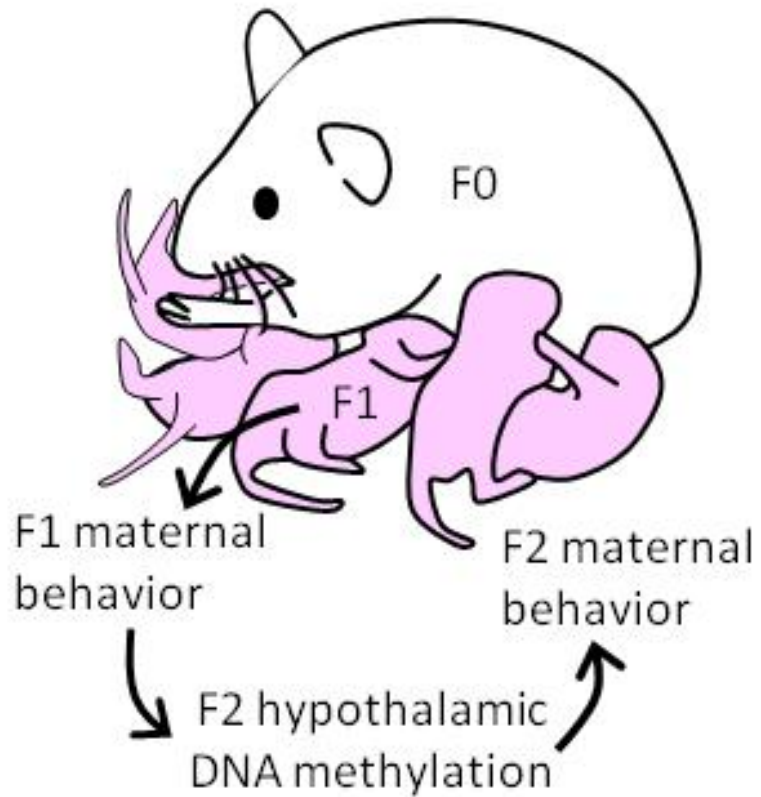


Correlation between mother, offspring, and grand-offspring LG

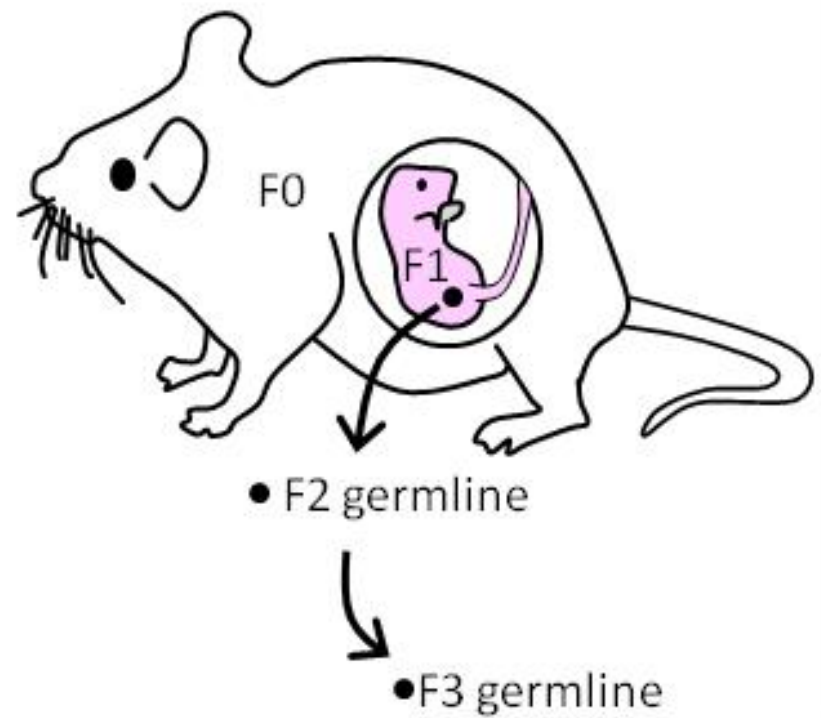




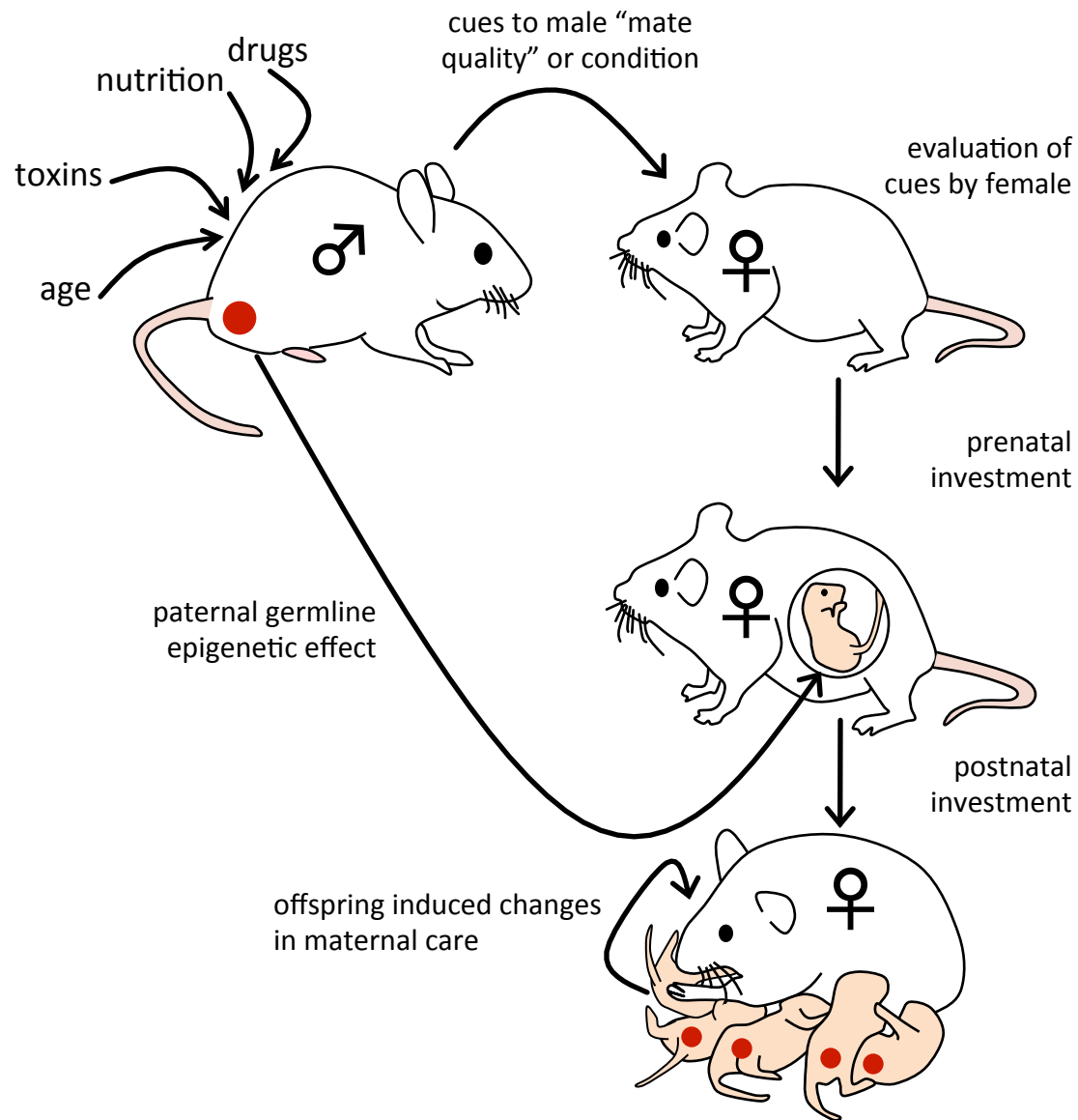
Experience-dependent inheritance

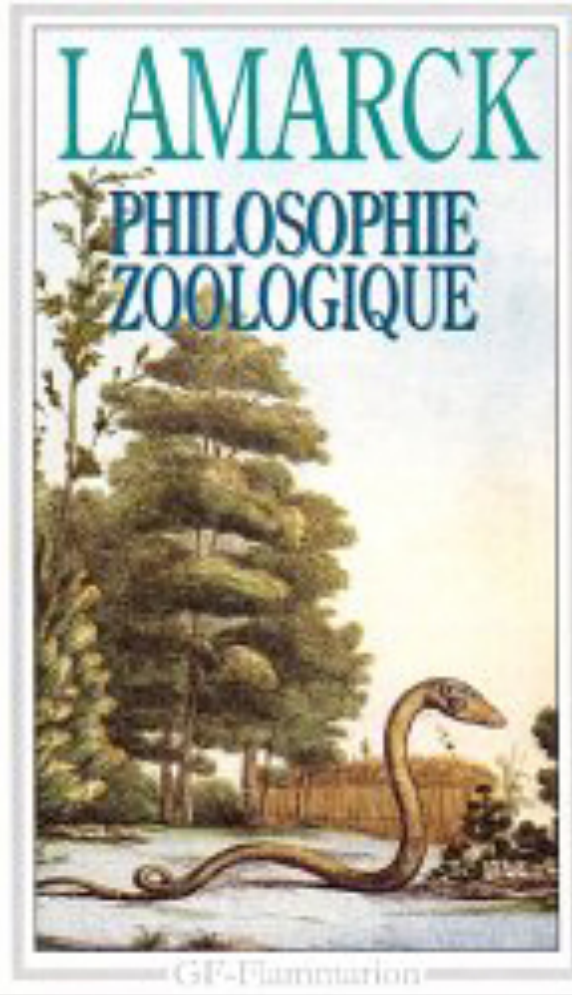


Germline inheritance



Interaction between maternal, paternal, & offspring characteristics/ influences





THE INHERITANCE OF ACQUIRED CHARACTERISTICS

PAUL KAMMERER



The case of the missing heritability

When scientists opened up the human genome, they expected to find the genetic components of common traits and diseases. But they were nowhere to be seen. **Brendan Maher** shines a light on six places where the missing loot could be stashed away.

Adaptive Significance

bad parenting strategy

LOW LG

Increased GR
methylation



Decreased GR
expression



Increased stress
response

HIGH LG

Decreased GR
methylation

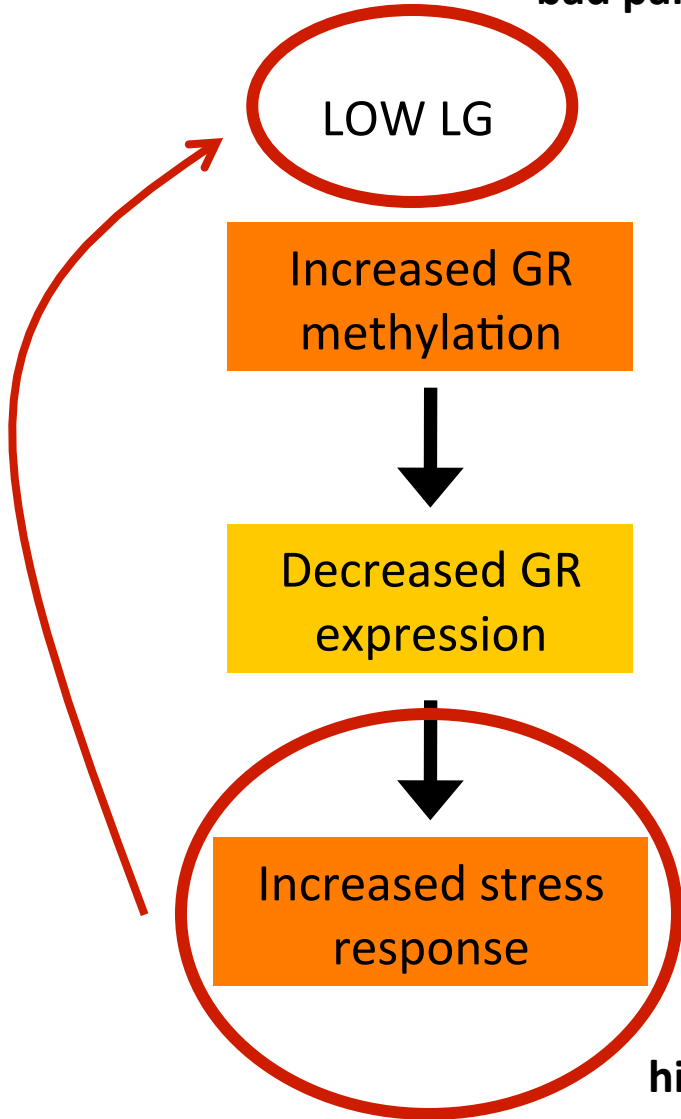


Increased GR
expression



Decreased stress
response

high stress is "bad"



maternal care

low

high

elevated ER α mRNA in
the AVPVn



estrogen induced LH,
GnRH, & pER α



early puberty



elevated sexual
receptivity



high fecundity

elevated ER α in the
MPOA



estrogen induced OTR &
cfos in the MPOA



high maternal care

Prenatal Nutrition & Social Status



Worker honey bee



Queen honey bee



Drone honey bee

Nutritional Control of Reproductive Status in Honeybees via DNA Methylation

R. Kucharski,* J. Maleszka,* S. Foret, R. Maleszka†

Blocking DNMT3 leads to more Queens than Workers

~~abnormal vs. normal~~

match vs. mismatch