CHAIRE ÉPIGÉNÉTIQUE ET MÉMOIRE CELLULAIRE

Année 2018-2019:

"Épigénétique, Environnement et Biodiversité"

11 Decembre 2018

Cours IV

Le role de l'épigénétique dans la plasticité phénotypique et l'évolution des réponses adaptatives

8/04/2019 (LORS DU COLLOQUE)
5) Épigénétique, Environnement et Biodiversité

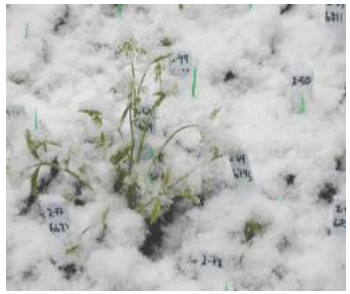
SUMMARY COURS III
Can the Environment induce or influence Epialleles?

Environmentally programmed epigenetic changes

1. Social insects : nutrition and pheromones - same genome gives rise to entirely different phenotypes (soldiers, common labourers, and queen); plant miRNAs in "beebread" fed to Workers; molecules affecting DNA methylation, histone acetylation (HDAC inhibitors) in Royal Jelly fed to Queens

2. Plants : climate-controlled programming - cold-induced flowering time (vernalisation); Polycomb proteins in memory of cold phase; heat in winter can have erasing effects

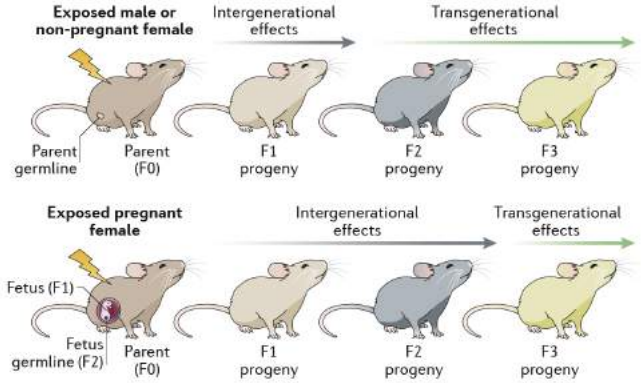





Reprogrammed at every generation

SUMMARY COURS III

Can the Environment induce Epigenetic memory across generations?

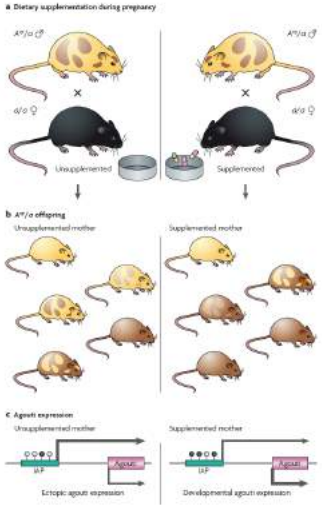


Transposable Elements: Targets for Early Nutritional Effects on Epigenetic Gene Regulation

Robert A. Waterland and Randy L. Jirtle*

Diet-induced hypermethylation at *agouti viable yellow* is not inherited transgenerationally through the female

Robert A. Waterland,[e-1] Michael Travisano,[1-2] and Kajal G. Tahiliani*



- Transposable elements are key targets in animals and plants for trans-generational effects
- Both spontaneous and environmentally induced

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SUMMARY COURS III

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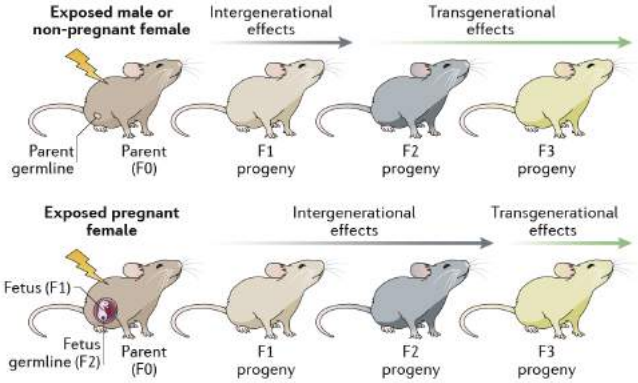

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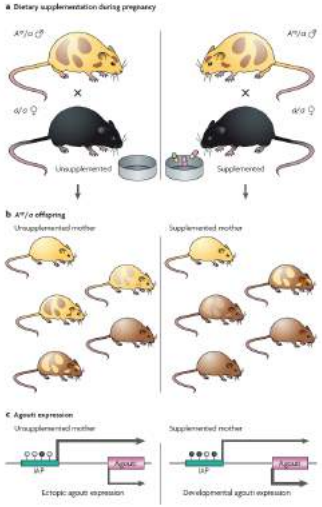

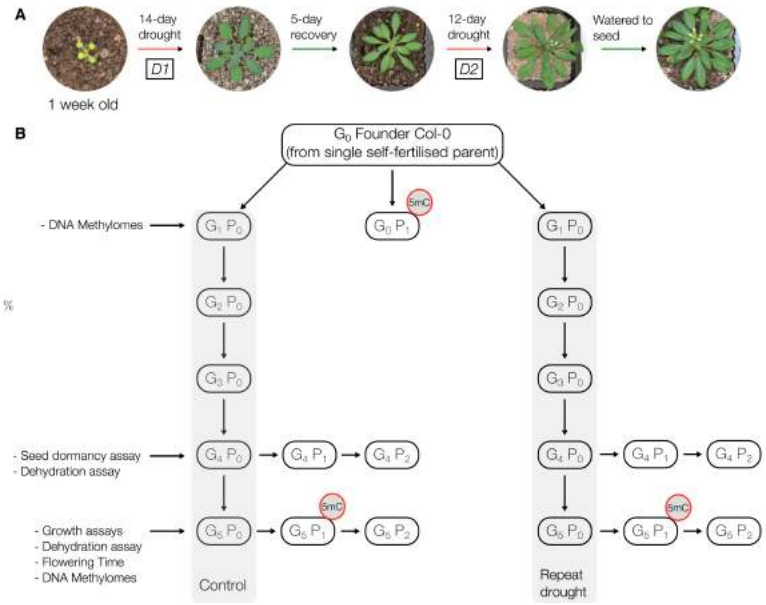

- Evidence of transgenerational drought stress memory for seed dormancy – elevated in both the direct seed of drought-stressed parents (72% enhanced dormancy) and to a lesser extend in seed produced from P1 progeny, from drought-exposed lineages, grown in the absence of stress (31% enhanced dormancy).
- DNA methylome is relatively *unaffected* by stress-induced changes.

E. Heard, December 2018

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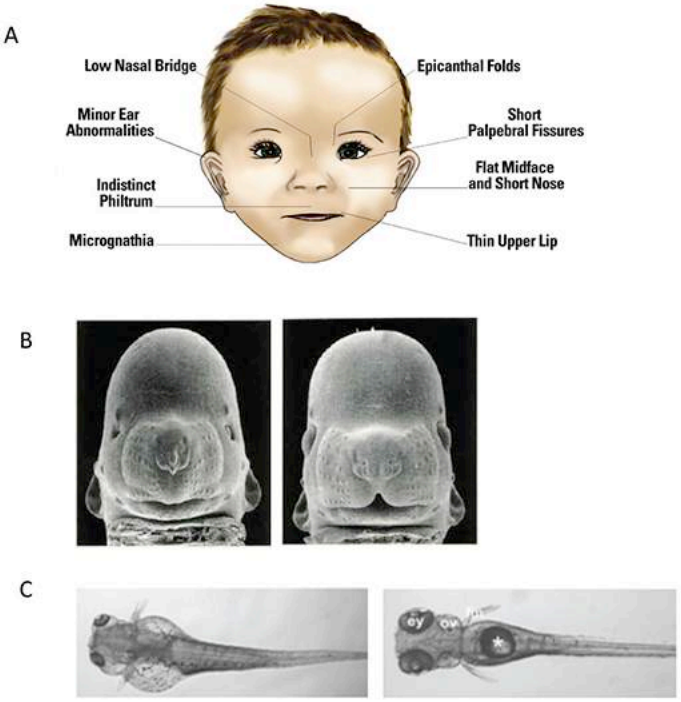
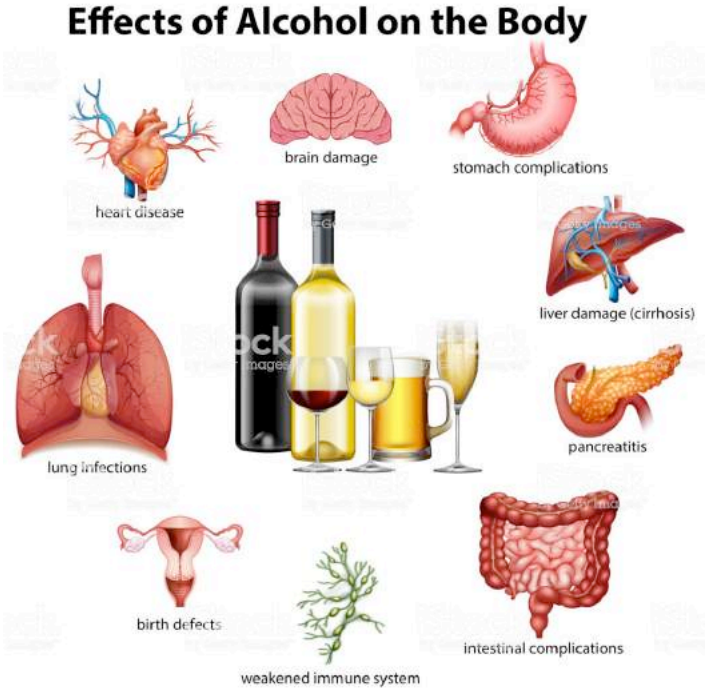
Can the Environment induce or influence Epialleles?

Maternal **ethanol consumption** alters the epigenotype and the phenotype of offspring

Ethanol induced post-natal growth restriction in fetal alcohol syndrome





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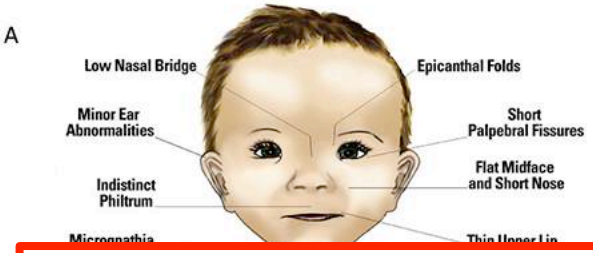
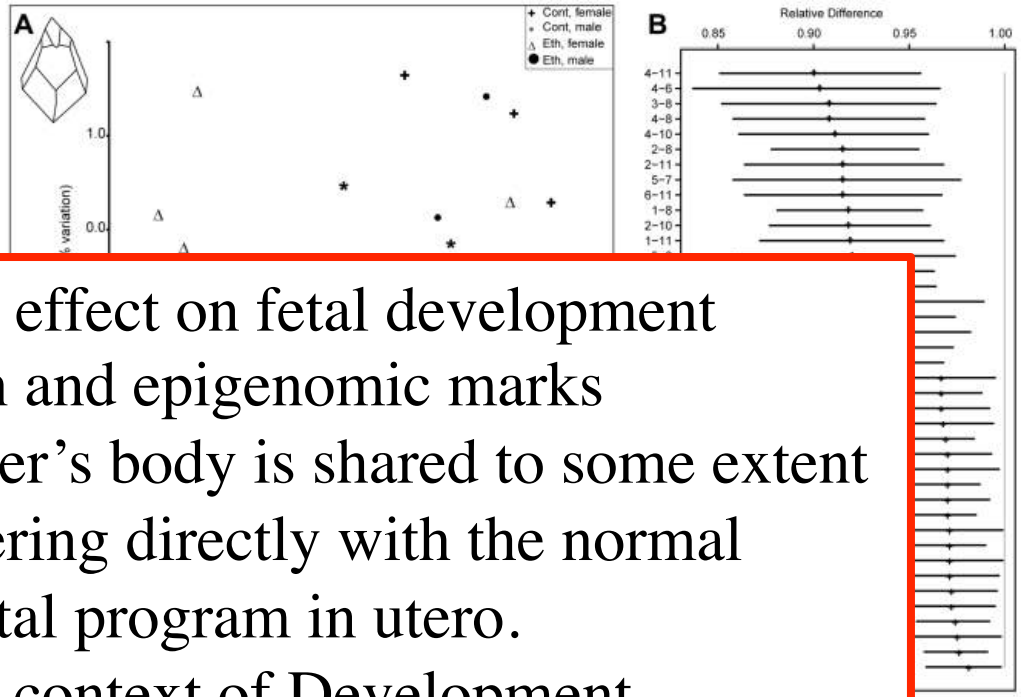


Quantitative analysis of the effects of gestational exposure to ethanol on Agouti locus, on epigenotype and on skull shape



Alcohol has a direct effect on fetal development gene expression and epigenomic marks

Stress on a pregnant mother's body is shared to some extent with the fetus, interfering directly with the normal developmental program in utero.

=> Epigenetic in context of Development

Not across multiple generations

Environmental polluants and Epigenetic alterations

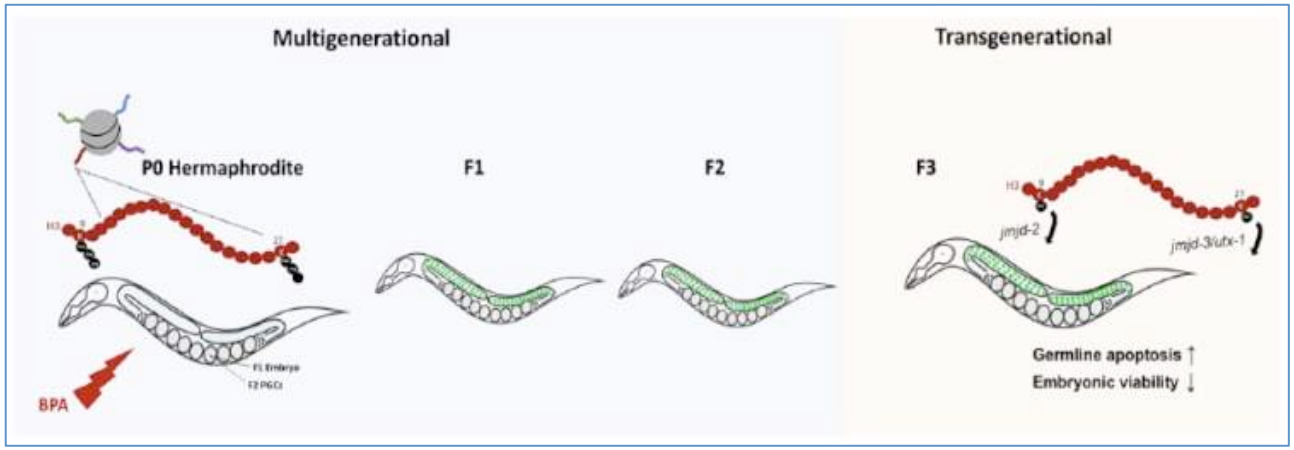
Endocrine disruptors

° BPA (Bisphenol A): plastics and resins, containers for food, drinks…
° Phtalates : associated with PVC, adhésives, glues, medical material, textiles, cosmetics, toys…
° Vinclozoline: fungicide used in agriculture

- Can interfere with hormonal pathways, signalling pathways involved in growth, differentiation and secondary sexual characteristics – can target: androgens and estrogens
- Thought to act during developmental sexual differentiation stages (*in utero*)
- Metabolic effects of gestational Exposure to BPA: early-life exposure to BPA is particularly effective in predisposing individuals to weight gain (Howdeshell et al. in 1999)
- In utero exposure to low doses of BPA (2.4 lg/kg) results in increased body weight
- Many studies have evaluated the effects of the exposure to this endocrine disruptor during pregnancy or pregnancy and lactation in terms of lipid and energy balance.
- Trans-generational effects have been reported – in mammals this remains highly controversial

What is the influence of the environment on epigenetic modifications and transmission of phenotypes?

The Memory of Environmental Chemical Exposure (Bisphenol A) in C. elegans depends on the Jumonji Demethylases jmjd-2 and jmjd-3/utx-1.



BPA exposures in C. elegans reduces the levels of the repressive histone marks H3K9me3 and H3K27me3, regulated by the demethylases jmjd-2 and jmjd-3/utx-1.

This causes a de-silencing effect and reproductive dysfunction observed from the P0 generation until the F4. The F3 generation represents the first generation where there was no direct contact with the environmental toxicant (BPA).

- How are artificial environmental cues biologically integrated and transgenerationally inherited?
- Bisphenol A (BPA) exposure causes the derepression of epigenomically silenced transgene in the germline for 5 generations, regardless of ancestral response.
- Chromatin immunoprecipitation sequencing (ChIP-seq), histone modification quantitation, and immunofluorescence assays revealed that this effect is associated with a reduction of the repressive marks H3K9me3 and H3K27me3 in whole worms and in germline nuclei in the F3, as well as with reproductive dysfunctions, including germline apoptosis and embryonic lethality.
- Targeting of the Jumonji demethylases JMJD-2 and JMJD-3/UTX-1 restores H3K9me3 and H3K27me3 levels, and alleviates the BPA-induced transgenerational effects.

- **=> A central role of repressive histone modifications in the inheritance of reproductive defects triggered by a common environmental chemical exposure**

Camacho J, et al (2018) Cell Rep 23:2392-2404. doi: 10.1016/j.celrep.2018.04.078.

Dietary influences on Epigenetic processes

Metabolic pathways linked to methylation (DNA, histones, etc)

Diet compound	Food source	DNA methylation	Histone modification
Folate	Leafy vegetables, fruits, fortified cereal	*	
B vitamins (B_2, B_6, B_{12})	Meat, nuts, various sources	*	
Methionine	Dairy products, nuts, fish	*	
Choline	Egg, milk, meat sources	*	
Betaine	Spinach, beets, wheat	*	
Phytoestrogen	Soy, legumes, cereal	*	*
Sulforaphane	Broccoli sprout		*
Diallyl sulfide	Garlic		*
Curcumin	Turmeric		*
EGCG	Green tea	*	*
Butyrate	Fermentation of dietary fiber in the digestive tract		*
Biotin	Egg yolk, animal liver		*

Nutrition can influence the availability of methyl-donors to a cell:

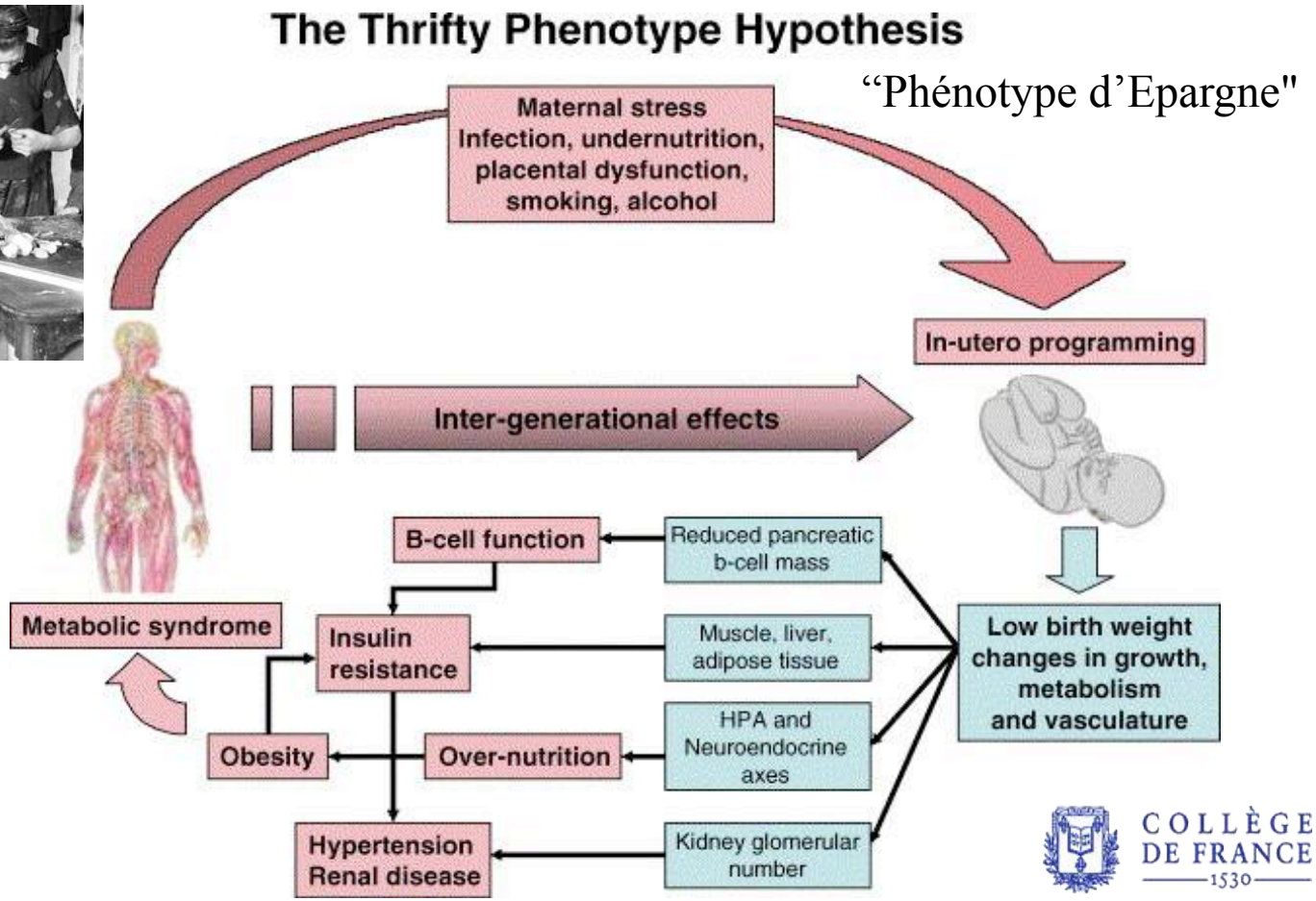
- Global effects?
- Certain regions more sensistive to such fluctuations?
- Impact during development and throughout life?

Can Nutrition induce or influence Epialleles?

Nutritional conditions during uterine development may have effects later in life, and influence the occurrence of adult metabolism and diseases

(Hales, C. N. & Barker, D. J. The thrifty phenotype hypothesis. *Br. Med. Bull.* 60, 5–20 (2001).

Eg Dutch famine – at the end of WWII, individuals exposed to famine during gestation had a poorer glucose tolerance than those born the year before the famine.



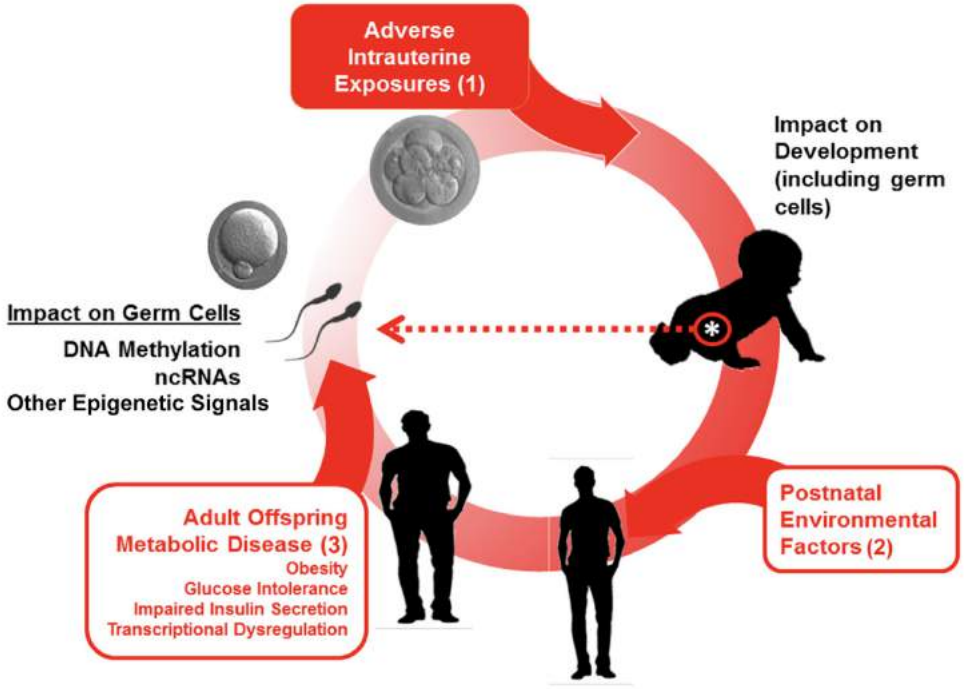
Epigenetic Mechanisms and Transmission of Metabolic Disease across Generations?

- Cell Metabolism
  Perspective

Epigenetic Mechanisms of Transmission of Metabolic Disease across Generations

Vicencia Micheline Sales,[1] Anne C. Ferguson-Smith,[2] and Mary-Elizabeth Patti[1,*]

- Both human and animal studies indicate that environmental exposures experienced during early life can robustly influence risk for adult disease.
- Environmental exposures experienced by parents during either intrauterine or postnatal life can also influence the health of their offspring, thus initiating a cycle of disease risk across generations.



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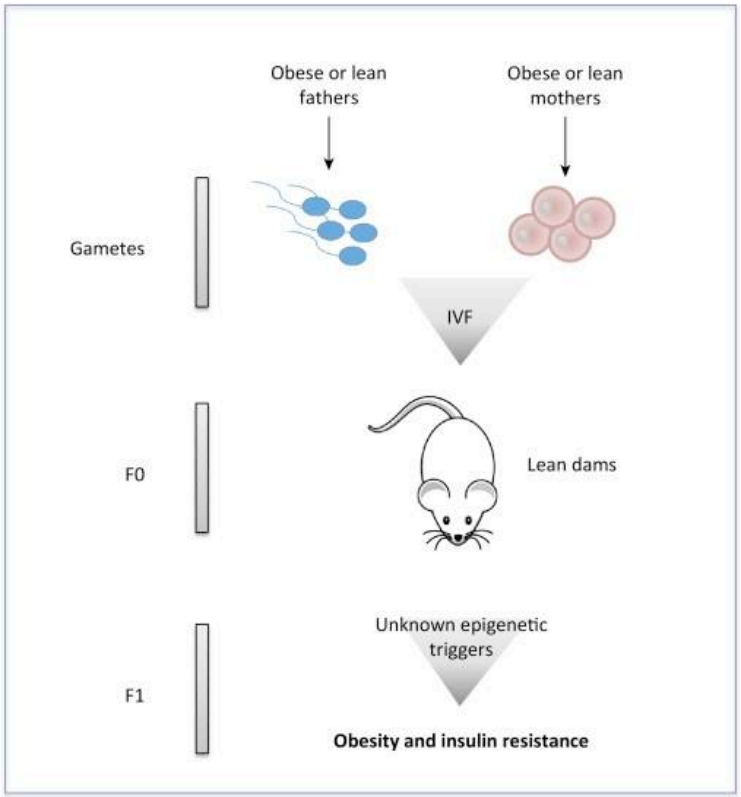
- Environmental exposures experienced by parents during either intrauterine or postnatal life can also influence the health of their offspring, thus initiating a cycle of disease risk across generations.
- Obesity and related metabolic problems can be inherited across generations through non-genetic mechanisms as shown by in vitro fertilization approaches.
- Exposure to a high-fat diet modifies egg and sperm epigenetic information, rendering progeny more prone to obesity.



HOW?

Epigenetic Mechanisms and Transmission of Metabolic Disease across Generations?

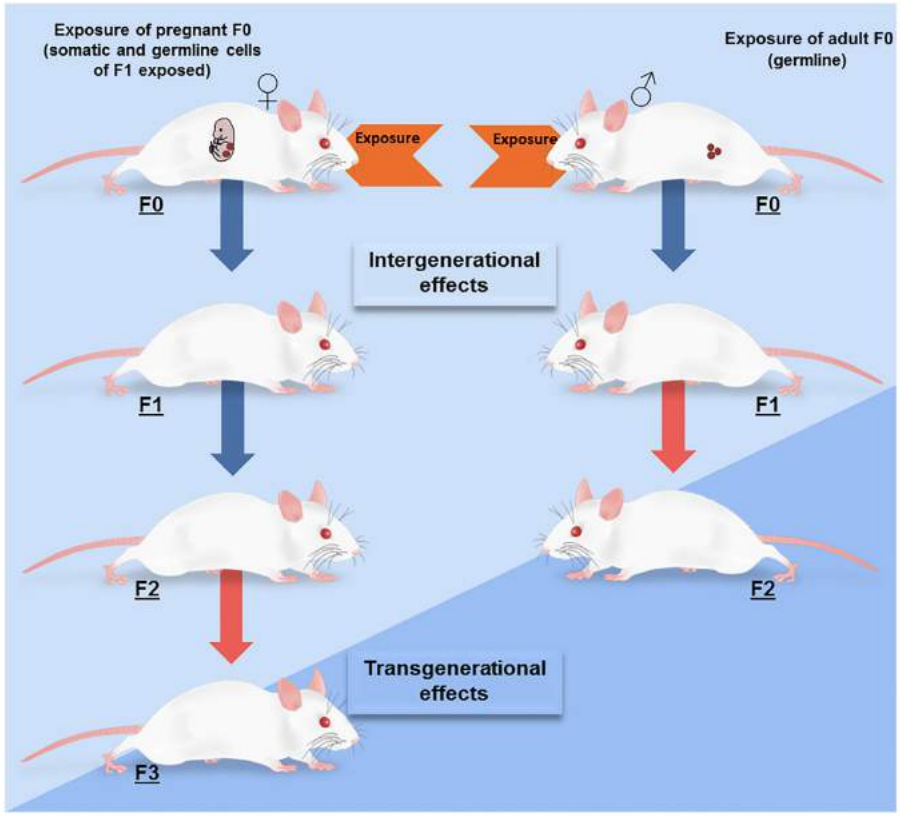
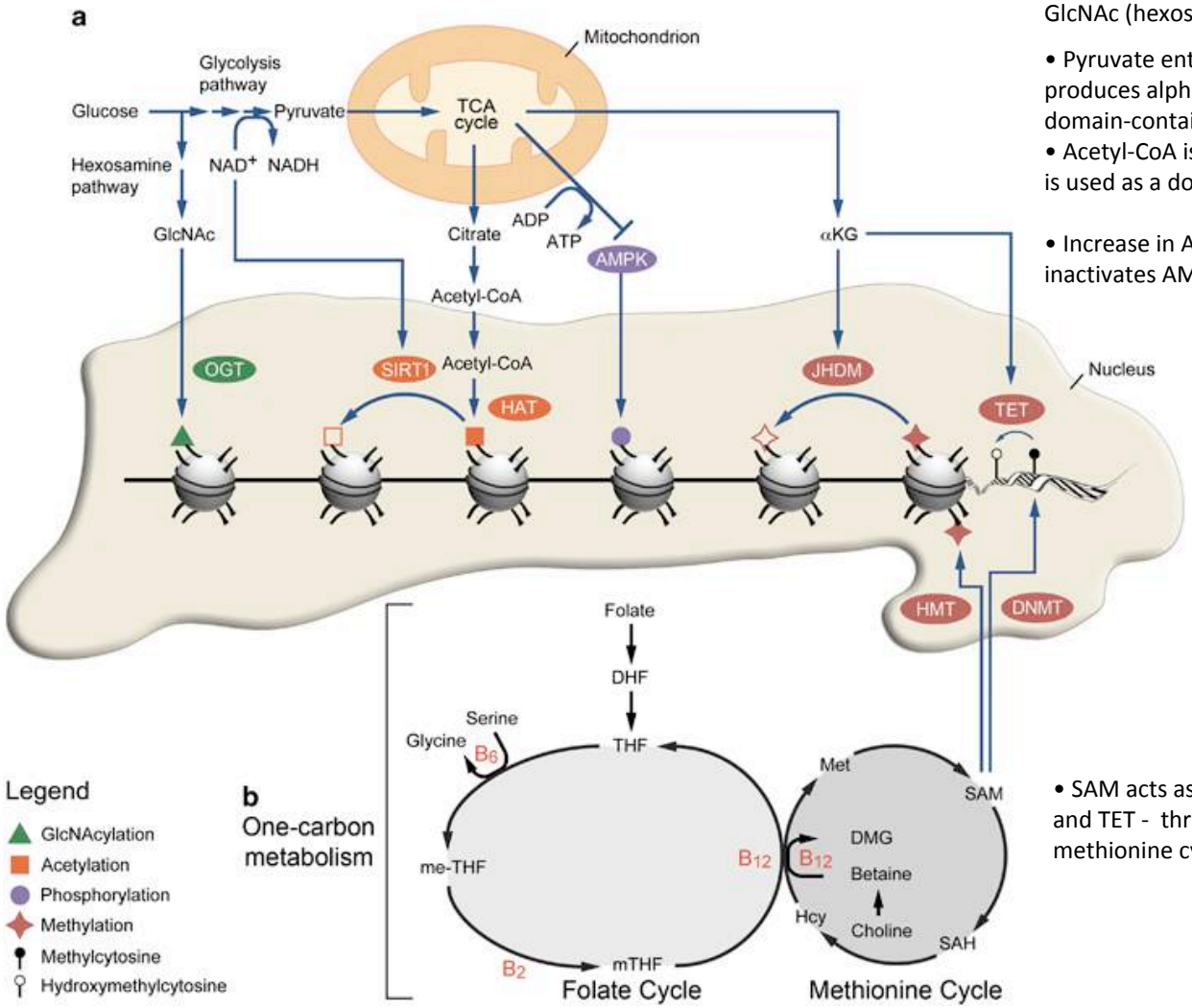


Table 1. Parental Contribution for Metabolic Disease Programming

	Maternal Lineage	Paternal Lineage
Nuclear DNA inheritance	Yes[a]	Yes[b]
Mitochondrial DNA inheritance	Yes[c,d]	No[e]
Epigenetic modification		
Germ cells	Yes[f,g]	Yes[h,i,j,k,l,m,n,o,p,q,r,s,t,u,v,w,x,y,z,aa,ab,ac]
Maternal environment during pregnancy		
Hormones	Yes[ad]	Not applicable
Nutrients	Yes[ae,af,ag,ah,ai,aj,ak,al,am,an,ao]	
Metabolism	Yes[ap,aq,ar,as]	
Uterine structure/function	Yes[af,au,av,aw]	
Behavior	Yes[ay,az]	
Chemical exposure	Yes[ba,bb]	
Milk composition	Yes[bc]	
Placental structure/function	Yes[bd,ay,be,bf]	Yes (paternal contribution to expression of placental development genes)[bg,bh]
Shared postnatal environment		
Diet	Yes[bi,bj]	Yes[bj]
Behavior	Yes[bk]	Yes[bk]
Environmental chemicals	Yes[bl]	Yes[bl]
Activity	Yes[bm]	Yes[bm]
Microbiome	Yes[bn]	Yes[bn]

What are the **epigenetic mechanisms** in germ cells that provide this non-DNA sequence based molecular legacy of prior environmental exposures and influence transcriptional regulation, developmental trajectories, and adult disease risk in offspring?

Metabolic pathways affect epigenetic mechanisms
=> may disturb chromatin states in germ line or development?



- SIRT1 activity depends on NAD+/NADH ratio (glycolysis)
- OGT (O-linked N-acetylglucosamine transferase) uses GlcNAc (hexosamine path).
- Pyruvate entering the tricarboxylic acid (TCA) cycle produces alpha-ketoglutarate, a critical cofactor for Jumonji domain-containing histone demethylase and TETs.
- Acetyl-CoA is converted from citrate generated by TCA cycle is used as a donor by histone acetyltransferases.
- Increase in ATP/ADP ratio from the TCA cycle also inactivates AMPK (histone hosphorylation)
- SAM acts as a methyl donor for histone methyltransferases and TET - through the coordinate action of the folate and methionine cycles, one-carbon metabolism

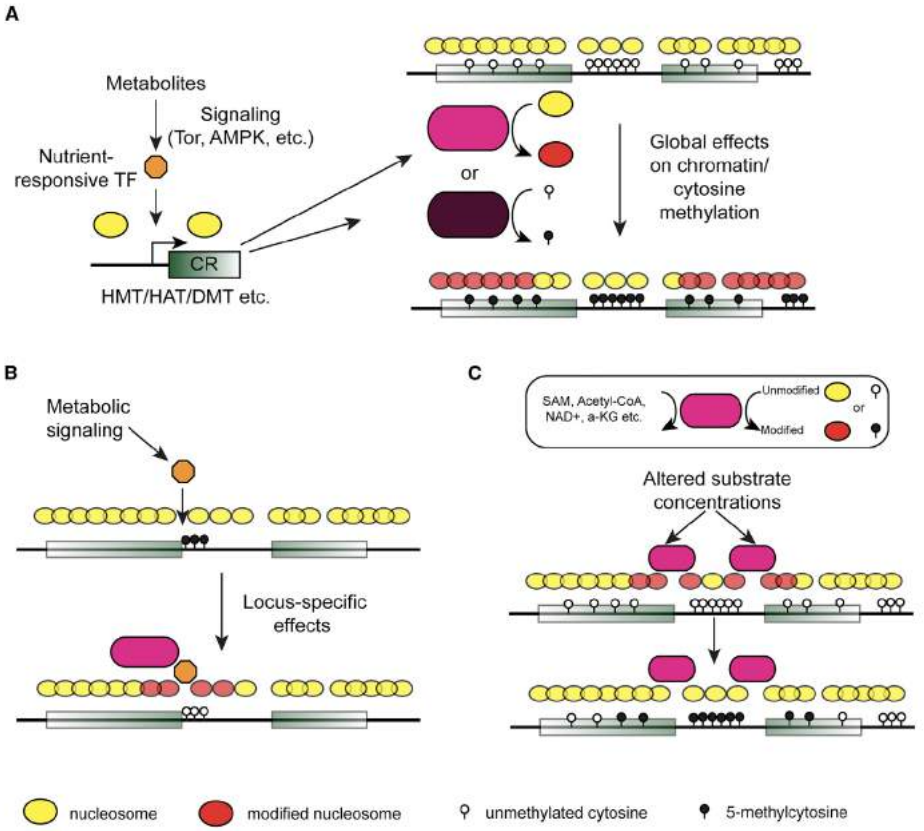
From Labbé et al, Oncogene 2015

Metabolic pathways affect epigenetic mechanisms
=> may disturb chromatin states in germ line or development?

Metabolic Inputs into the Epigenome

Upasna Sharma[1] and Oliver J. Rando[1,*]
[1]Department of Biochemistry and Molecular Pharmacology, University of Massachusetts Medical School, Worcester, MA 01605, USA
*Correspondence: oliver.rando@umassmed.edu
http://dx.doi.org/10.1016/j.cmet.2017.02.003

A number of molecular pathways play key roles in transmitting information in addition to the genomic sequence—epigenetic information—from one generation to the next. However, so-called epigenetic marks also impact an enormous variety of physiological processes, even under circumstances that do not result in heritable consequences. Perhaps inevitably, the epigenetic regulatory machinery is highly responsive to metabolic cues, as, for example, central metabolites are the substrates for the enzymes that catalyze the deposition of covalent modifications on histones, DNA, and RNA. Interestingly, in addition to the effects that metabolites exert over biological regulation in somatic cells, over the past decade multiple studies have shown that ancestral nutrition can alter the metabolic phenotype of offspring, raising the question of how metabolism regulates the epigenome of germ cells. Here, we review the widespread links between metabolism and epigenetic modifications, both in somatic cells and in the germline.



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Metabolic pathways affect epigenetic mechanisms
=> may disturb small RNAs in germ line or development?

Metabolic Inputs into the Epigenome

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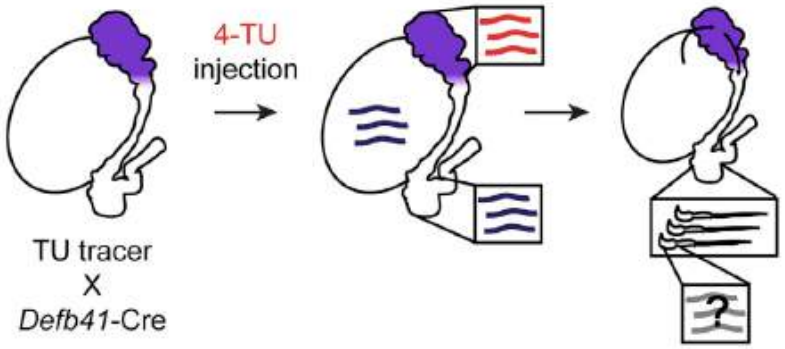
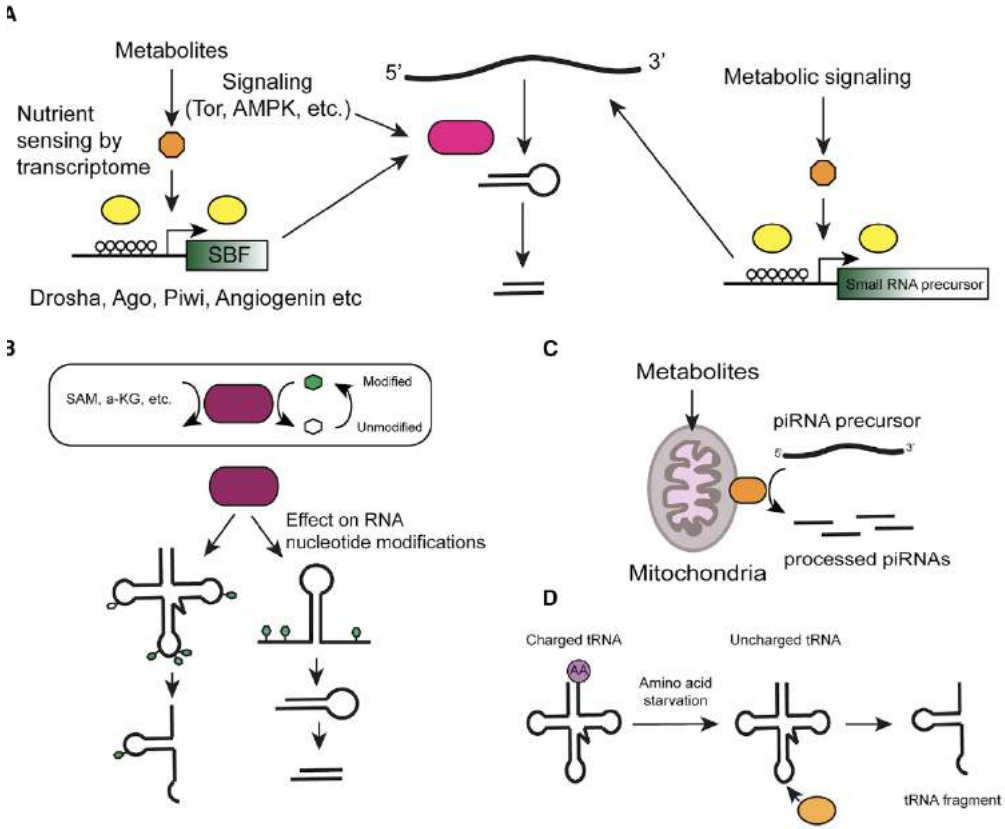
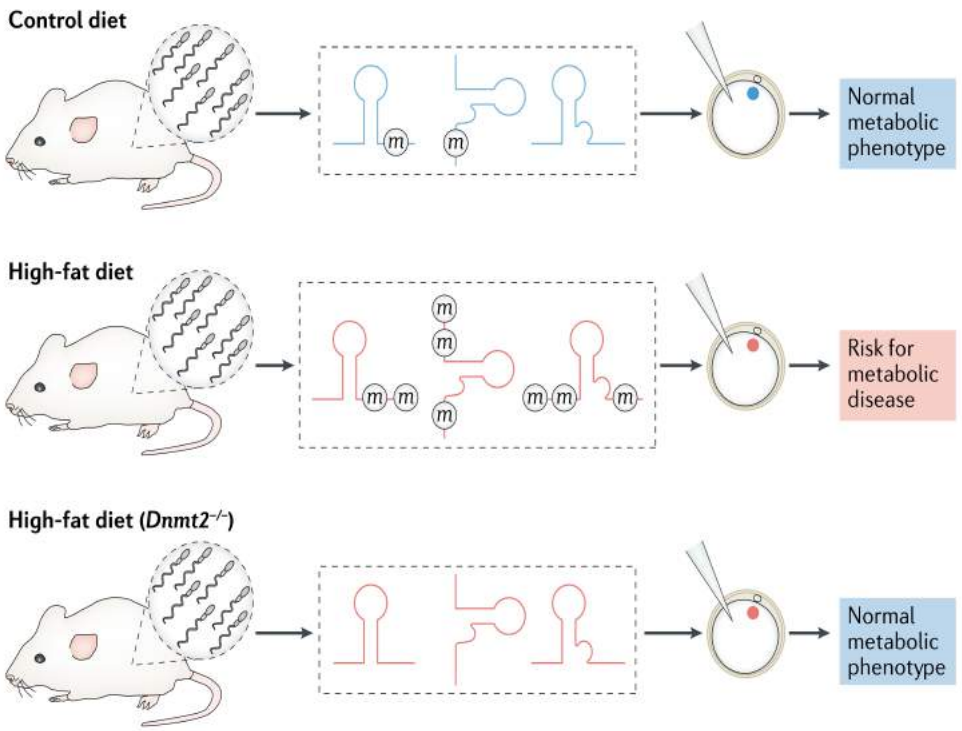




Novel epigenetic reprogramming events that occur during mammalian spermatogenesis: Transition from a piRNA-dominated stage of testicular spermatogenesis
To **tRNA fragment (tRF)** in epididymal sperm, and a transient loss of clustered microRNAs in the **caput epididymis.**
(Rando Lab 2018)

What is the influence of the environment on epigenetic modifications and their transmission?

Dad's diet – smRNA methylation signatures in sperm pass on disease risk



Zhang, Y. et al. Dnmt2 mediates intergenerational transmission of paternally acquired metabolic disorders through sperm small non-coding RNAs. Nat. Cell Biol. 20, 535–540 (2018).

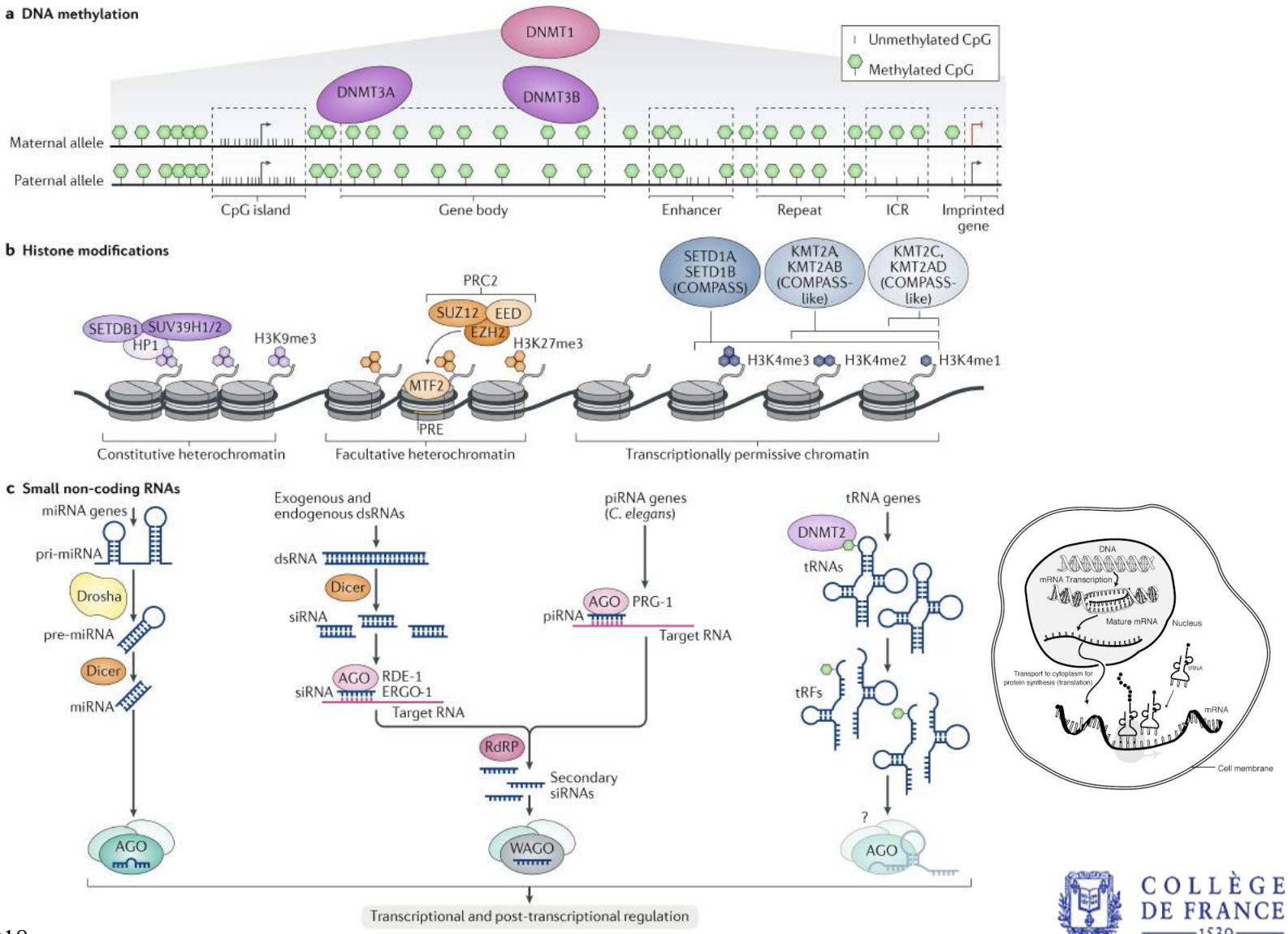
Changes in tRNA-derived small RNAs following a high-fat diet.

A high-fat diet in mice results in changes in **tRNA-derived small RNA** (tsRNA) expression profiles as well as increased methyl modifications at these tsRNAs, which when injected into zygotes result in phenotypes associated with metabolic disease risk.

This transmission is prevented in mice lacking DNA methyltransferase enzyme (DNMT2; *Dmnt2*–/–)

=> Methyl modifications for tsRNAs are required for the transmission of the environment memories of a high-fat diet.

Mechanisms of environmentally induced epigenetic transmission : methylation of RNA not DNA, and not associated with chromatin!



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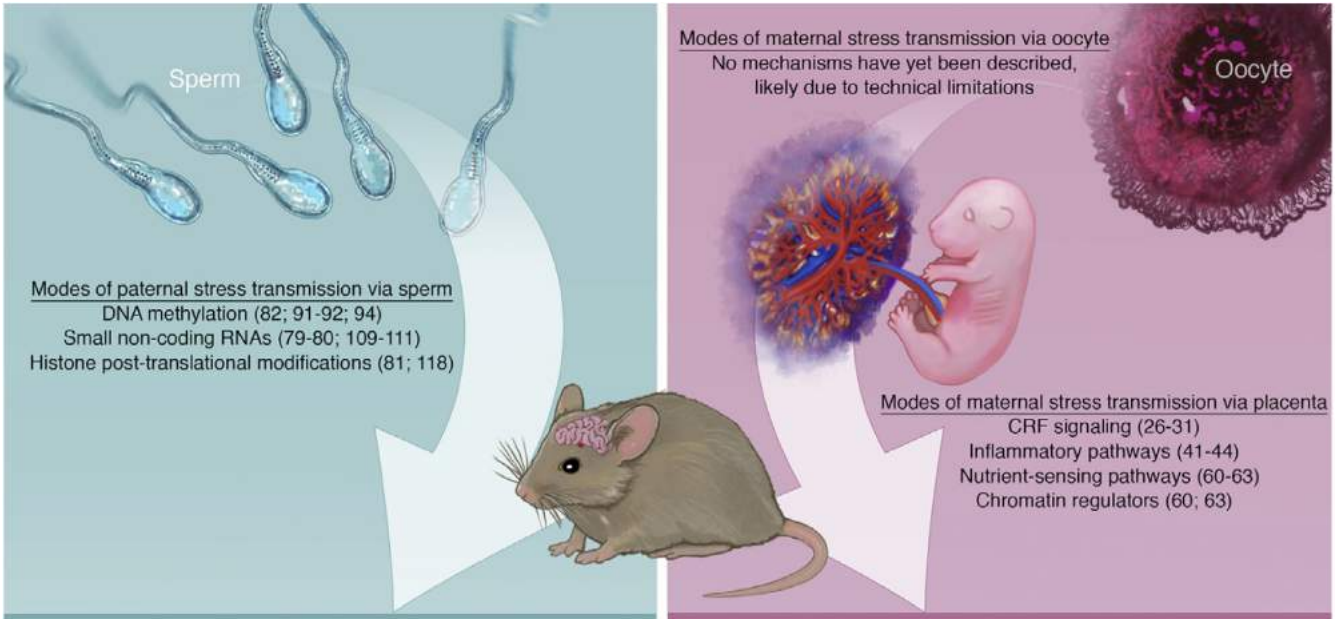
Summary: Metabolism and Epigenetic inheritance

- Central role for metabolites in many epigenetic processes
- Eg manipulation of α-KG levels in ESCs affects H3K27 and DNA demethylation, but not H3K4 demethylation (Carey et al., 2015) - but nothing is known about dietary effects on **germ cell** or **early developental** metabolism
- Many gaps in our ability to predict how diet affects the germline epigenome
- What are the concentrations of key metabolites in the germ cells of animals consuming various diets? Eg when mice are fed diets lacking methyl donors, how do levels of SAM change in the testis or ovary?
- And which methylases— Dnmts, histone methylases, and/or RNA methylases— are sensitive to these concentration changes?
- In most cases (in mammals) these cross-generation effects only proven to be short term ie inter-generational

Maternal and Paternal Stress: Epigenetic impact across generations?



Exposure	Species	Offspring outcomes	Ref
Swedish famine	H	Increased longevity and decreased risk for cardiovascular disease in grandsons	83-85; 98
Preconception trauma	H	Reduced cortisol levels, reduced GR sensitivity increased risk of depression and PTSD	74; 86
Chronic variable stress	M	Reduced HPA stress axis responsivity in male and female offspring	79
Social defeat	M	Increased depressive-like and anxiety-like behaviors, increased glucocorticoid levels	93
Odor-paired fear conditioning	M	Increased odor behavioral sensitivity in males	91
Maternal separation	M	Increased depressive-like behaviors; altered exploratory behavior	94
Dietary challenge	M	Metabolic dysfunction, developmental defects	78; 80; 82

Exposure	Species	Offspring outcomes	Ref
Psychological stress in pregnancy	H	Increased risk of ASD and schizophrenia in males; increased risk for affective disorders in females	13-19
Infection during pregnancy	H	Increased risk of ASD and schizophrenia in males	34-40
Childhood abuse	H	Increased disruptive behavior, externalizing behavioral problems	71-72; 75
Preconception trauma	H	Poor perceived emotional health, increased depressive and anxiety symptoms, increased PTSD risk, greater glucocorticoid sensitivity	73-74; 86
Prenatal chronic variable stress	M	Increased HPA stress axis sensitivity, cognitive dysfunction, metabolic dysfunction in males	21-23; 60
Prenatal infection	M	Social deficits; altered exploratory behavior; increased repetitive behaviors	42-43
Prenatal glucocorticoids	R	Impaired coping and learning; reduced growth	32-33

Maternal and Paternal Stress: Epigenetic impact across generations?

The Heritability of Trauma?

Parental Advisory: Maternal and Paternal Stress Can Impact Offspring Neurodevelopment

Jennifer C Chan, Bridget M. Nugent, and Tracy L. Bale

ABSTRACT

Parental stress exposures are implicated in the risk for offspring neurodevelopmental and neuropsychiatric disorders, prompting critical examination of preconception and prenatal periods as vulnerable to environmental insults such as stress. Evidence from human studies and animal models demonstrates the influence that both maternal and paternal stress exposures have in changing the course of offspring brain development. Mechanistic examination of modes of intergenerational transmission of exposure during pregnancy has pointed to alterations in placental signaling, including changes in inflammatory, nutrient-sensing, and epigenetic pathways. Transmission of preconception paternal stress exposure is associated with changes in epigenetic marks in sperm, with a primary focus on the reprogramming of DNA methylation, histone posttranslational modifications, and small noncoding RNAs. In this review, we discuss evidence supporting the important contribution of intergenerational parental stress in offspring neurodevelopment and disease risk, and the currently known epigenetic mechanisms underlying this transmission.

- Stress during pregnancy has been proposed to be associated with increased risks for autism spectrum disorder, schizophrenia, affective disorders, attention-deficit/ hyperactivity disorders in offspring, -and related to the specific stage of pregnancy in which stress experience occurred
- Placenta is a key source of corticotropin releasing factor (CRF) which feeds back to both the fetal and maternal pituitary
- How such stress might affect the developing brain epigenetically (eg COURS 2017) and whether there is any impact on the *germ line* remains an area of ongoing research.

Epigenetic Inheritance vs Behaviour

Mothers and fathers have tremendous influence on their children

Numerous studies show that maternal behavior/stress clearly has an impact on her progeny (parental effects – gene expression changes – *not* epigenetics)

From http://www.intechopen.com/books/

Important to distinguish between epigenetic trans-generational *effect* & epigenetic trans-generational *inheritance*. The former is a broad term incorporating all phenotypes in following generations that are not genetically determined…

Therefore, transfer of the acquired epigenetic phenotype is not through gametes and it is dependent upon consistency of the environmental condition.

D. Francis, J. Diorio, D. Liu, M.J. Meaney, Nongenomic transmission acrossgenerations of maternal behaviour and stress responses in the rat, Science286 (1999) 1155
Weaver, N. Cervoni, F.A. Champagne, A.C. D' Alessio, S. Sharma, J.R.Seckl, S. Dymov, M. Szyf, M.J. Meaney, Epigenetic programming by maternal behaviour, Nat. Neurosci. 7 (2004) 847–854.

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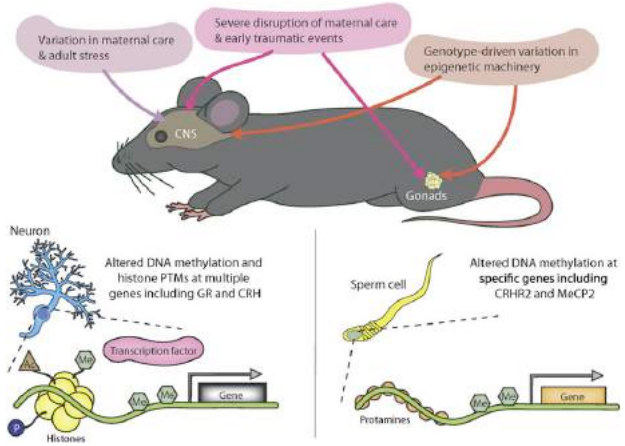
What about Fathers?

Does a pre- or post-natally stressed father
(who does not feed or raise the progeny and thus does not impose his behaviour)
nevertheless give rise to depressed progeny?

Epigenetic Inheritance vs Behaviour



Dietz et al (2011), behavioral changes in progeny from stressed (socially defeated males) only present after natural reproduction, and not after IVF…

⇒ **Stress-related vulnerabilities are not transmitted to subsequent generations through the gametes but rather through the mother's behavior to her pups - 'maternal provisioning' - which can be influenced the behavior of her mate (the father)**

Could be via physical aggression, pheromonal signaling, ultrasonic vocalization by the stressed male to the female => indicate inferiority or a degree of unfitness leading to subsequent decrease in maternal care …

Maternal and Paternal Stress: Epigenetic impact across generations?

The Heritability of Trauma?

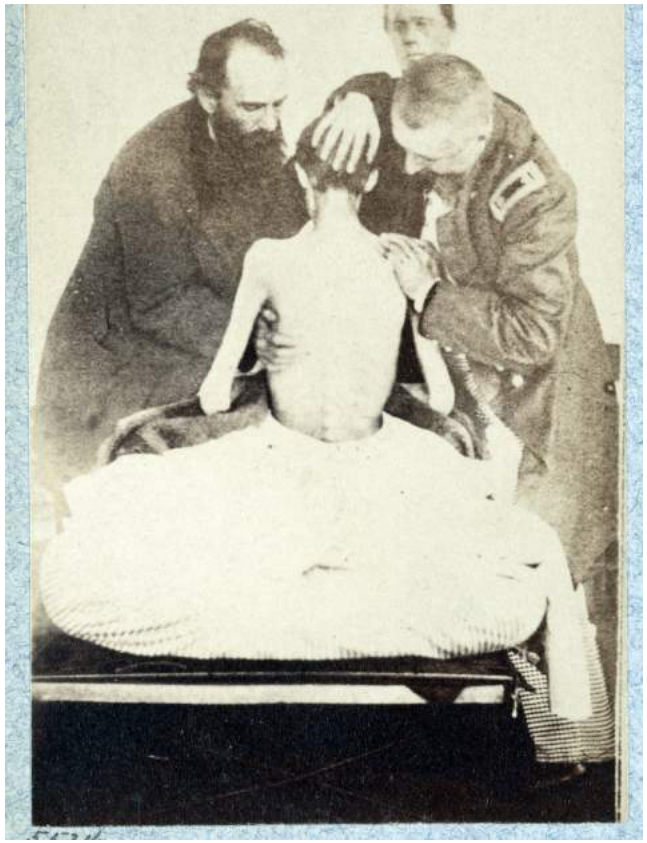
Can We Really Inherit Trauma?

Headlines suggest that the epigenetic marks of trauma can be passed from one generation to the next. But the evidence, at least in humans, is circumstantial at best.

The New York Times

Study of Civil War prisoners that came to a remarkable conclusion. Male children of abused war prisoners were about 10 % more likely to die than their peers were, in any given year after middle age, the study reported.

Costa et al (2018) Inter-generational transmission of paternal trauma among US Civil War ex-POWs.
PNAS 115(44): 11215–11220.



« The findings, the authors concluded, supported an "epigenetic explanation." The idea is that trauma can leave a chemical mark on a person's genes, which then is passed down to subsequent generations. The mark doesn't directly damage the gene; there's no mutation. Instead it alters the mechanism by which the gene is converted into functioning proteins, or expressed. The alteration isn't genetic. It's epigenetic. «

Maternal and Paternal Stress: Epigenetic impact across generations?

The Heritability of Trauma?

Genetic predisposition?
Cultural transmission?
« Epigenetic » transmission?

Current Psychiatry Reports (2018) 20: 115
https://doi.org/10.1007/s11920-018-0980-1

GENETIC DISORDERS (F GOES, SECTION EDITOR)

Robust Findings From 25 Years of PTSD Genetics Research

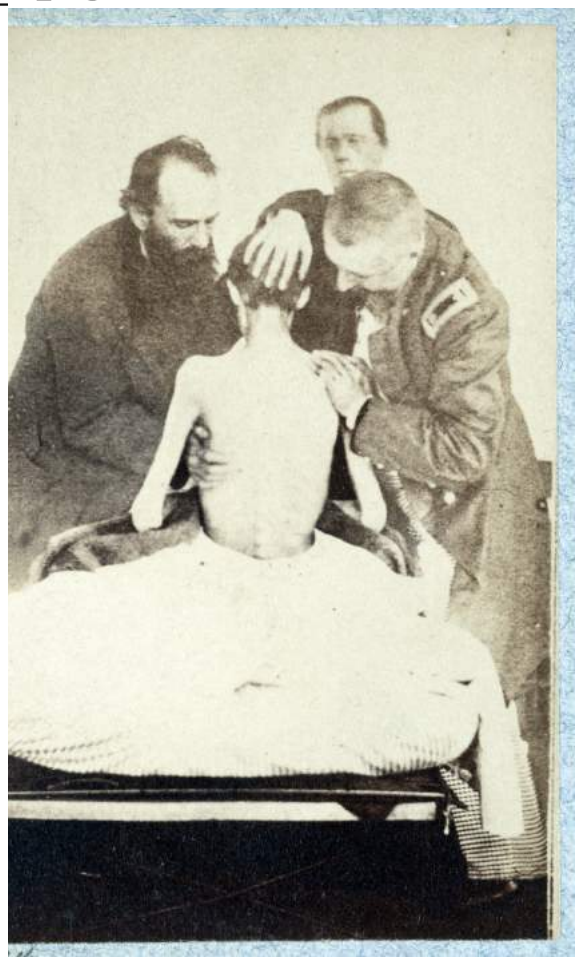
Laramie E. Duncan[1] · Bryna N. Cooper[2] · Hanyang Shen[1]

Twin studies from 25 years ago established that Post traumatic stress disorder (PTSD) is also genetically influenced

Genome-wide association studies (GWAS) encompassing tens of thousands of participants enabled the first molecular genetic heritability and genetic correlation estimates for PTSD in 2017.

In 2018, highly promising loci for PTSD were reported, including variants in and near the *CAMKV, KANSL1*, and *TCF4* genes (involved in brain functions?)

NB Sex differences in PSTD
(see COURS 2018)
Stress induce TE activation in the brain
(see COURS 2017)



Robust Molecular Genetic Findings for PTSD Are Emerging

Million Veterans Program

The Million Veterans Program [51] (MVP) biobank is one of the world's leading repositories of genetic and phenotypic information, and is an unprecedented resource for the study of PTSD. A conference abstract on MVP GWAS of PTSD re-experience symptoms has been published [12••] and additional results about other PTSD phenotypes measured within MVP will be available in future publications. Regarding PTSD re-experiencing symptoms, MVP researchers examined a sample of 146,660 European-ancestry participants and 19,983 African-ancestry participants. This dataset afforded the discovery of eight loci at the level of genome-wide significance (i.e.,

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What is the influence of the environment on epigenetic modifications and their transmission?

- « *The question of whether and how the effects of* ***cultural trauma*** *can be transmitted intergenerationally from parents to offspring, or even to later generations, has evoked interest and controversy in academic and popular forums.*
- *Recent methodological advances have spurred investigations of potential epigenetic mechanisms for this inheritance, representing an exciting area of emergent research.*
- *Epigenetics has been described as the means through which environmental influences "get under the skin," directing transcriptional activity and influencing the expression or suppression of genes.*
- *Over the past decade, this complex environment-biology interface has shown increasing promise as a potential pathway for the intergenerational transmission of the effects of trauma.* »

Many challenges facing research on trauma:
Rather than searching for putative *epigenetic* mechanisms, the societal implications of genetic predispositions and the relevance of cultural narratives need to be discussed
As do the remarkable possibilities of resilience and adaptivity that humans can have!

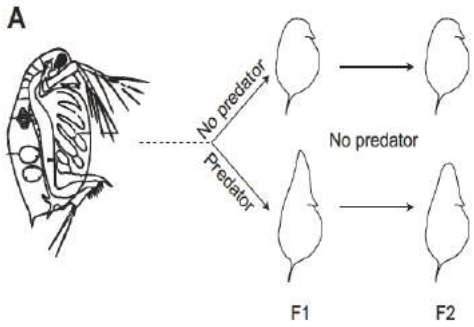
2018 Dec;30(5):1763-1777. doi: 10.1017/

The role of Epigenetics in Phenotypic Plasticity and the Evolution of Adapative Responses

The role of Epigenetics in Phenotypic Plasticity and the Evolution of Adapative Responses

Epigenetic processes extend the phenotypic options of a genotype by fine-tuning gene expression and triggering development of alternative phenotypes:
Development, phenotypic plasticity …

Environmentally-induced and spontaneous stochastic modifications (epimutations) are two fundamentally different mechanisms enabling epigenetic variation (COURS I and II)

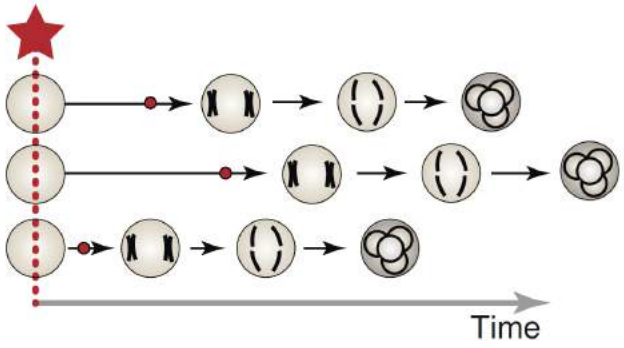


Environmentally-induced epimutation
Daphina: can grow as parthenogenotes
Exposure to chemical signals from predators, induces protective cranial structures « *Helmets* » (*casques*)
Phenotype can be transmitted to subsequent generation in absence of predator signal…

Stochastic epimutation
Upon nutrient starvation (red star), individual yeast cells in a population undergo sporulation in an unsynchronized fashion (horizontal profiles).

Bet-Hedging: heterogeneity in sporulation timing is linked to **expression noise** in the master regulator *Ime1p (*Meiosis-inducing protein 1)

This favors the maintenance of non-sporulated cells that are pre-adapted in case of reversion to nutrient-rich conditions.



The role of Epigenetics in Phenotypic Plasticity and the Evolution of Adapative Responses

Epigenetic processes extend the phenotypic options of a genotype by fine-tuning gene expression and triggering development of alternative phenotypes:
Development, phenotypic plasticity …

Environmentally-induced and spontaneous stochastic modifications (epimutations) are two fundamentally different mechanisms enabling epigenetic variation (COURS I and II)

(1) **Environmentally induced epigenetic variation** has been proposed to mediate **phenotypic plasticity**: following perception of an environmental signal, specific genes may be epigenetically silenced or activated, resulting in a modified and environment-specific phenotype (see for example Verhoeven and Preite 2014).

Phenotypic plasticity would be selected for dealing with predictable environmental changes, for example, when environmental conditions change between generations but remain stable within a generation

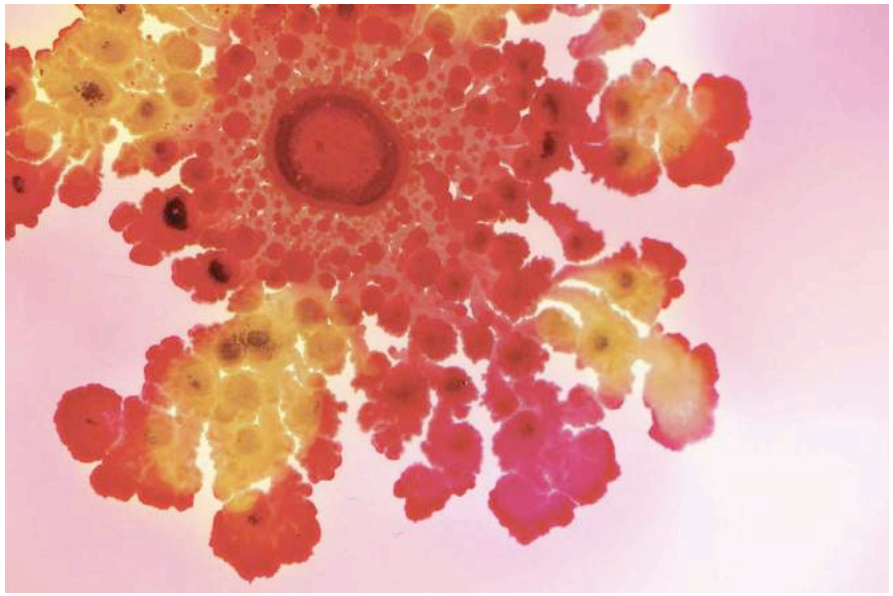
(2) **Stochastic epigenetic changes** can also result in the production of different phenotypes (eg Cubas et al. 1999; Miura et al. 2009) - epimutations can be 10^4 times higher than somatin mutations, can vary a lot and can increase in some cases under environmental stress

Bet hedging could be selected for unpredictable environmental changes - risk-spreading strategy is based on the stochastic production of phenotypically variable offspring, irrespective of environmental conditions (Slatkin 1974; Veening et al. 2008; de Jong et al. 2011)

Variation in the predictability of environmental conditions may be encountered, compromise between plasticity and bet-hedging strategies may be optimal.

E

Phenotypic plasticity in Bacteria: bet hedging and epigenetics



Bacterial World, Oxford University Museum of Natural History, to 28 May 2019

Adapt and survive: bacteria such as Paenibacilla promote crop growth
New Scientist Dec. 5th 2018 - Soonhee Moon/Tal Danino

Inducible and reversible phenotypic switching in Paenibacillus dendritiformis

Phase variation in Bacteria:

Genetic or Epigenetic? Can be BOTH!

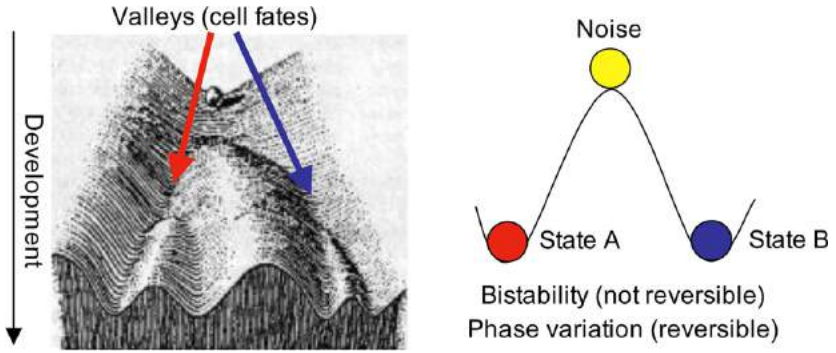


FIGURE 1. *Left panel*, Waddington's artistic drawing of an "epigenetic landscape" as a ball that falls to stable valleys from unstable ridges (adapted from Ref. 1). *Right panel*, bistability viewed as the fall of a ball from an unstable state on a ridge to a stable state in a valley. In phase variation, the valley state is metastable, and the ball periodically returns to the ridge.

COURS V (lors du Colloque)

Epigenetic diversity may increase the productivity and stability of plant populations?

Epigenetic variations may be involved in the control of plant developmental processes and participate in shaping phenotypic plasticity to the environment.

Intense breeding has eroded genetic diversity, and epigenetic diversity may be a new source of phenotypic variation to improve adaptation to changing environments and ensure the yield and quality of crops.

Biological diversity within species can be an important driver of population and ecosystem functioning. Until now, such within-species diversity effects have been attributed to underlying variation in DNA sequence. However, within-species differences, and thus potentially functional biodiversity, can also be created by epigenetic variation.

(Bosdorff 2013)

Epigenetic diversity may increase the productivity and stability of plant populations?

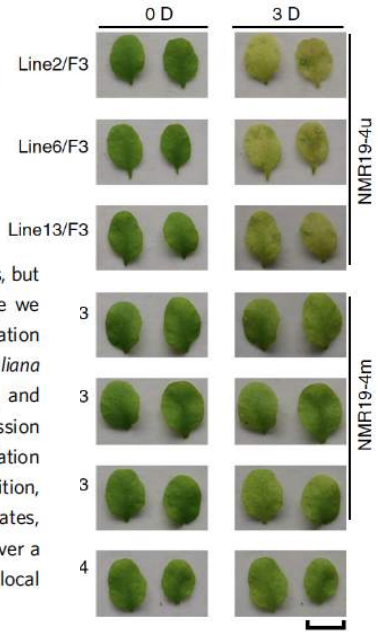
ARTICLE

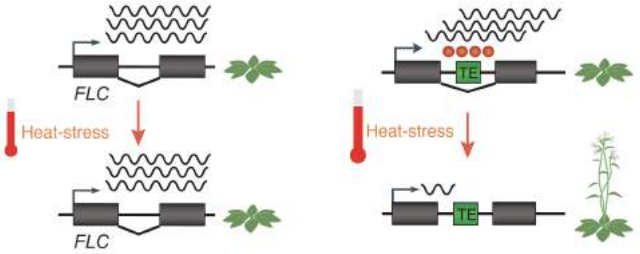
DOI: 10.1038/s41467-018-02839-3 OPEN

A naturally occurring epiallele associates with leaf senescence and local climate adaptation in *Arabidopsis* accessions

Li He[1,2], Wenwu Wu[1,4], Gaurav Zinta[1], Lan Yang[1], Dong Wang[1], Renyi Liu[1], Huiming Zhang[1], Zhimin Zheng[1], Huan Huang[1], Qingzhu Zhang[1,5] & Jian-Kang Zhu[1,3]

Epigenetic variation has been proposed to facilitate adaptation to changing environments, but evidence that natural epialleles contribute to adaptive evolution has been lacking. Here we identify a retrotransposon, named "NMR19" (naturally occurring DNA methylation variation region 19), whose methylation and genomic location vary among *Arabidopsis thaliana* accessions. We classify NMR19 as NMR19-4 and NMR19-16 based on its location, and uncover NMR19-4 as an epiallele that controls leaf senescence by regulating the expression of *PHEOPHYTIN PHEOPHORBIDE HYDROLASE* (*PPH*). We find that the DNA methylation status of NMR19-4 is stably inherited and independent of genetic variation. In addition, further analysis indicates that DNA methylation of NMR19-4 correlates with local climates, implying that NMR19-4 is an environmentally associated epiallele. In summary, we discover a novel epiallele, and provide mechanistic insights into its origin and potential function in local climate adaptation.





A TE insertion enables plants to skip the vernalization requirement and **to flower in response to extreme heat-stress**
Quadrana, Colot (unpublished)

Hyperosmotic stress memory in Arabidopsis is mediated by distinct epigenetically labile sites in the genome and is restricted in the male germline by DNA glycosylase activity

Anjar Wibowo[1†], Claude Becker[2†], Gianpiero Marconi[1,3], Julius Durr[1], Jonathan Price[1], Jorg Hagmann[2], Ranjith Papareddy[1], Hadi Putra[1], Jorge Kageyama[2], Jorg Becker[4], Detlef Weigel[2], Jose Gutierrez-Marcos[1*]

Improved salt resistance of progeny from parents exposed to hyperosmotic stress in the next generation (***but not beyond***)

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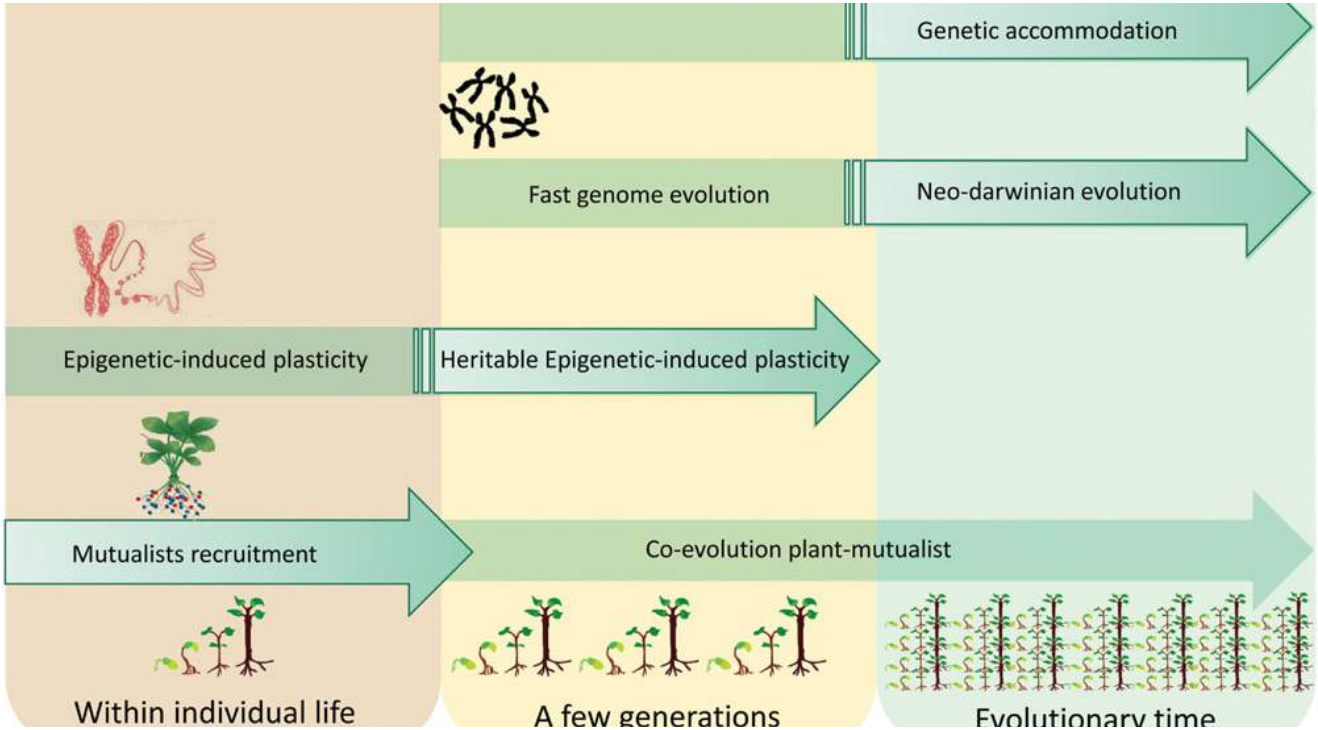
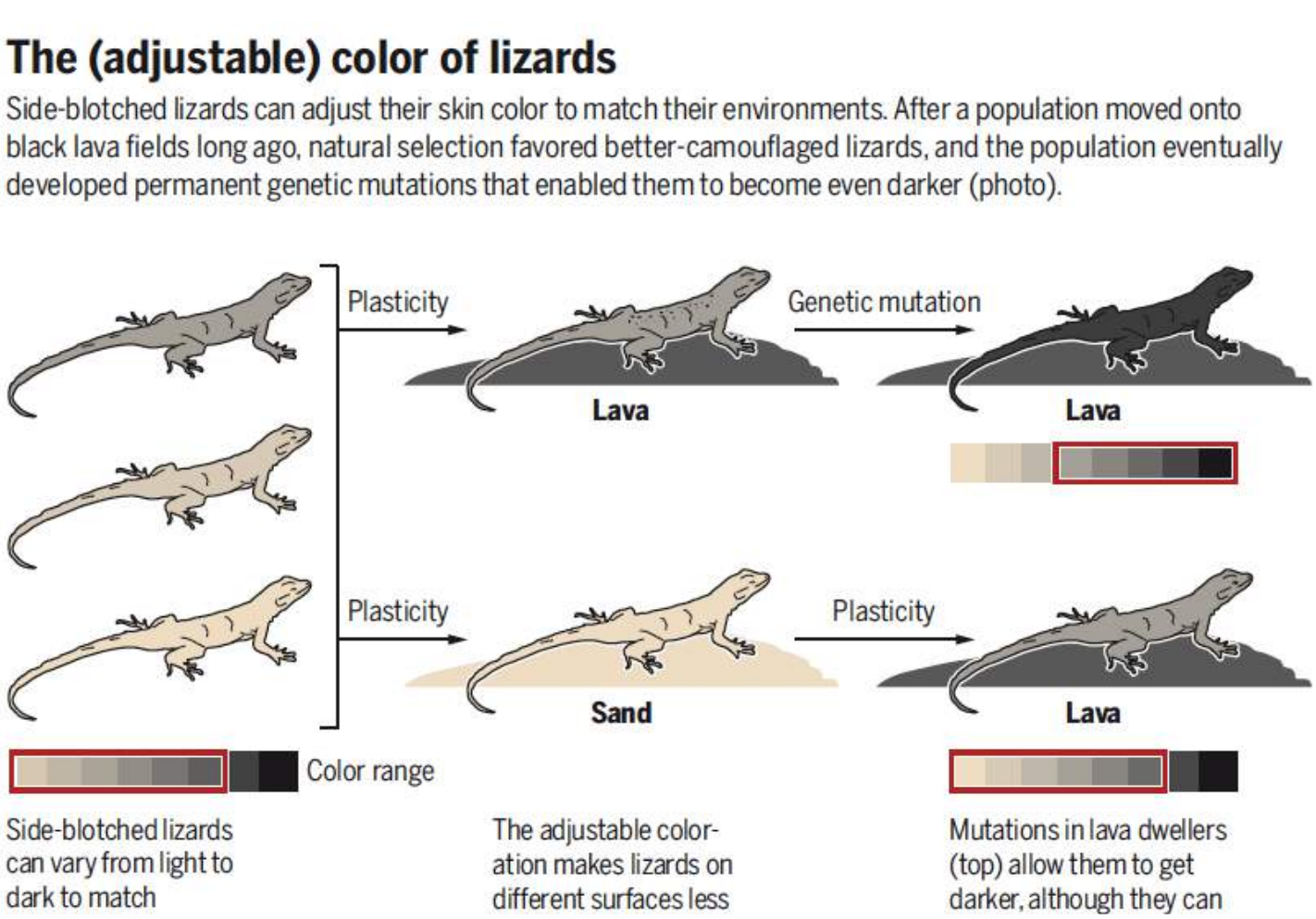
The role of Epigenetics in Phenotypic Plasticity and the Evolution of Adapative Responses

- « Phenotypic plasticity" enables individual animals to alter their appearance or behavior enough to survive in a new environment.
- Eventually, new adaptations promoting survival arise in the population through genetic changes and natural selection, which acts on the population over generations.
- Known as the "Baldwin effect" after the psychologist James Mark Baldwin, who presented the idea in 1896.



The role of Epigenetics in Phenotypic Plasticity and the Evolution of Adapative Responses



Some lizards switch
sandy and lava surfa
Both varieties can a
their new surroundi
just a few weeks.
Some lizards from a
not get as dark on la
dwellers, suggesting
lizards' ability to cha

- Individual side-blotched lizards can change colors in a new environment - darker on lava, lighter on sand – in weeks
- Epigenetic mechanisms? not known
- *PREP* and *PRKA1A* genes regulate coloration and differ between populations on and off the lava
- Mutations in the population adapted to the lava flow make these lizards darker than others.
- One of the most detailed example of the Baldwin effect occurring in a wild population.

The role of Epigenetics in Phenotypic Plasticity and the Evolution of Adapative Responses

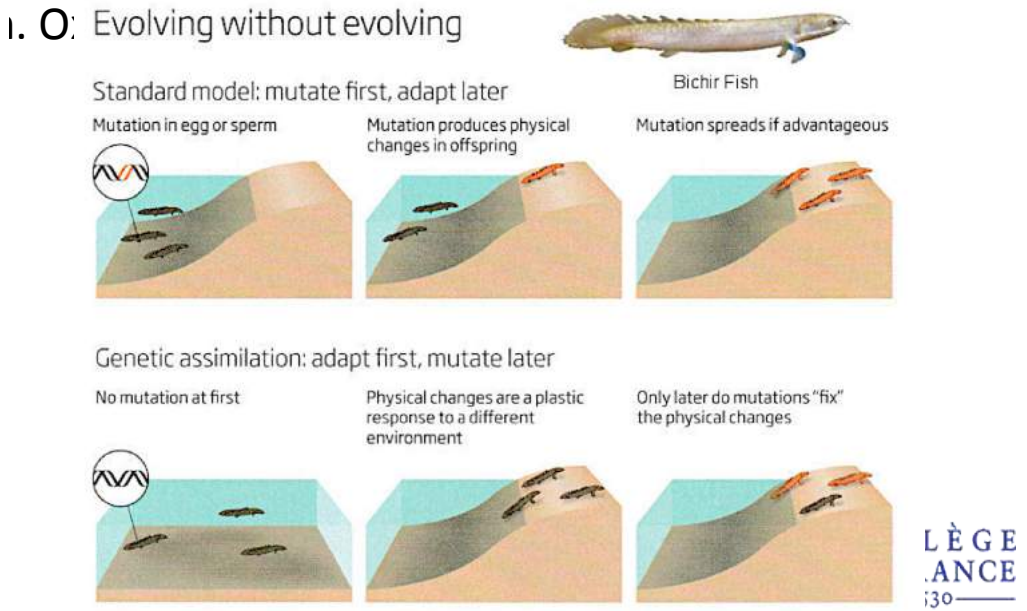
- Can acquired traits be inherited? (as posited by Lamarck?!)
- No – phenotypic plasticity is DNA sequence based (transcriptional noise, epimutations) and is in itself an adaptive trait
- In some environments when an "acquired" trait does become permanent, it is due to mutations that "fixed" the plastic trait— genetic assimilation.
- Mary Jane West-Eberhard suggested in 2003 (based on work on wasps, and butterflies) that phenotypic plasticity might set the stage for permanent adjustments: some of those genetic changes would simply increase the proportion of the most flexible individuals, while others might favor a specific trait

Lamarck was right in emphasizing that fast, flexible responses to the environment— ie phenotypic plasticity— can drive lasting change

However mutations must fix these changes:

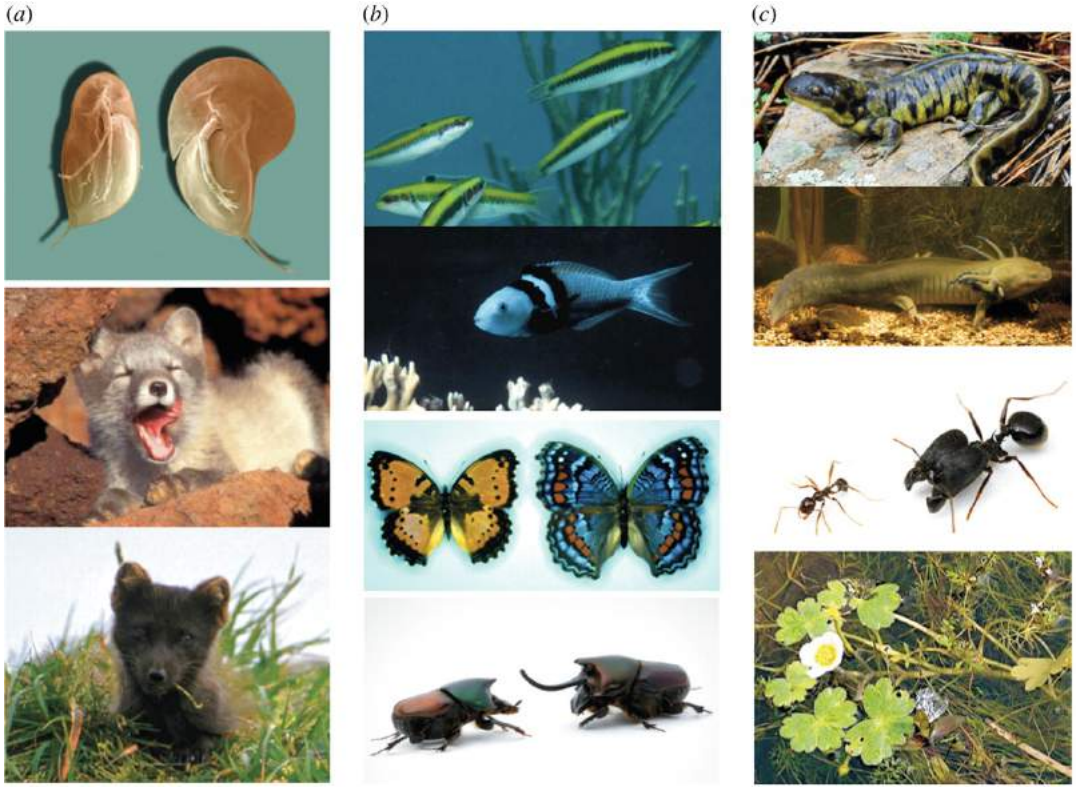
⇒ Mutations are still important drivers of evolution

⇒ Responses to the environment may be the precursors and the mutations are followers…?



Biodiversity – from genotype to phenotypes : The role of epigenetics?

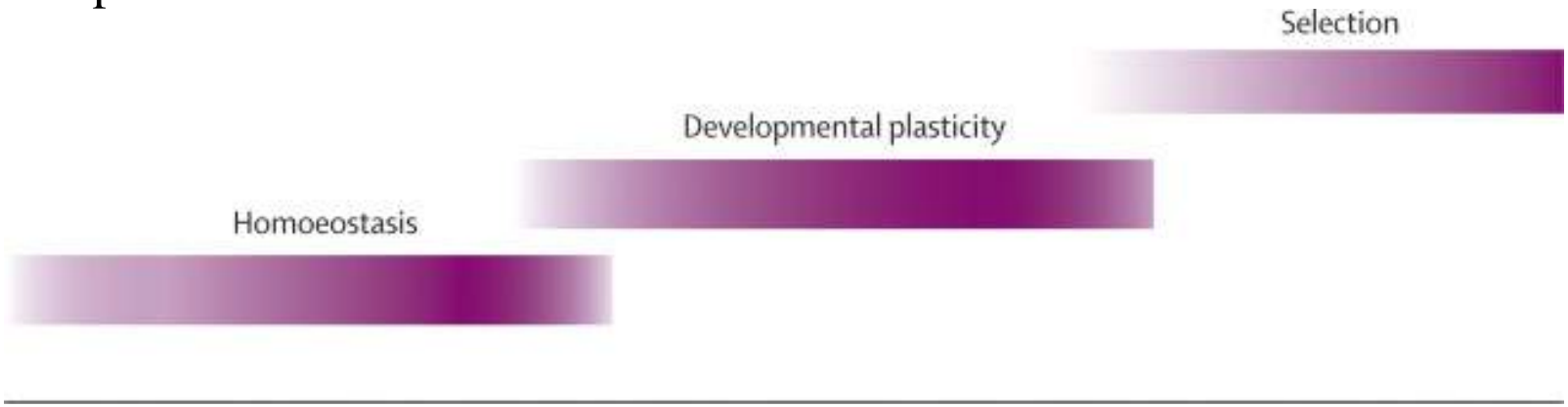
Same Genotype - very different Phenotypes
Environmentally induced before, during, or after development
Selected for in the course of Evolution



Armin P. Moczek et al. Proc. R. Soc. B 2011;rspb.2011.0971

SUMMARY: Epigenetics in life phase transitions

- Biodiversity within species (phenotypic variation) regarded with some suspicion as genetic determinism prevailed…
- Most species can display some degree of phenotypic plasticity
- It can be functional (and potentially adaptive), neutral, or deleterious
- Can be restricted to a few minutes, to a whole life time, or to many generations
  ⇒ Implications for evolution



- Such plasticity can be subject to Natural Selection (Eg insects are the most diverse kingdom because of their remarkable phenotypic plasticity)

- Understanding this level of biodiversity will be key to understand life, and how it can (or cannot) adapt to the rapid, manmade changes we are imposing.

Synthesizing the role of epigenetics in the response and adaptation of species to climate change in freshwater ecosystems

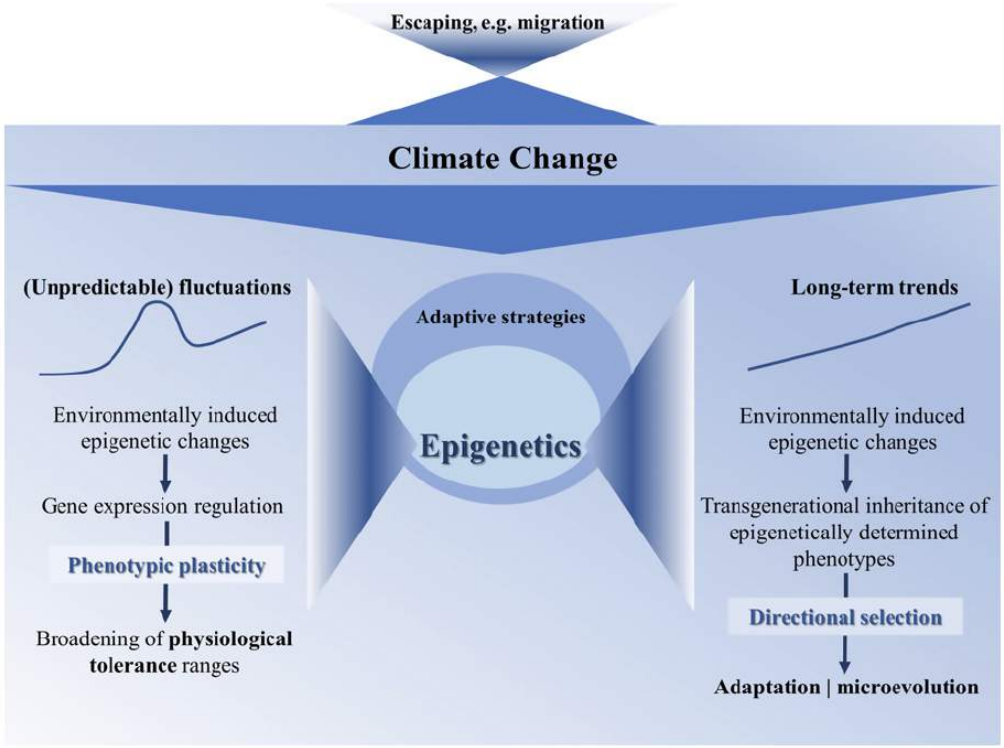


FIGURE 1 Conceptual diagram representing the role of epigenetics as an adaptive strategy by freshwater organisms while coping to environmental stressors deriving from climate change

We are the first generation of scientists with the tools to address the dimensions of biodiversity on Earth… and ironically we may be the last generation with the opportunity to discover and understand Earth's biodiversity before it is irrevocably changed or lost.

James Collins, February 13, 2009

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Année 2018-2019:

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