ROI
REGISTRO DEGLI
OSTEOPATI D'ITALIA

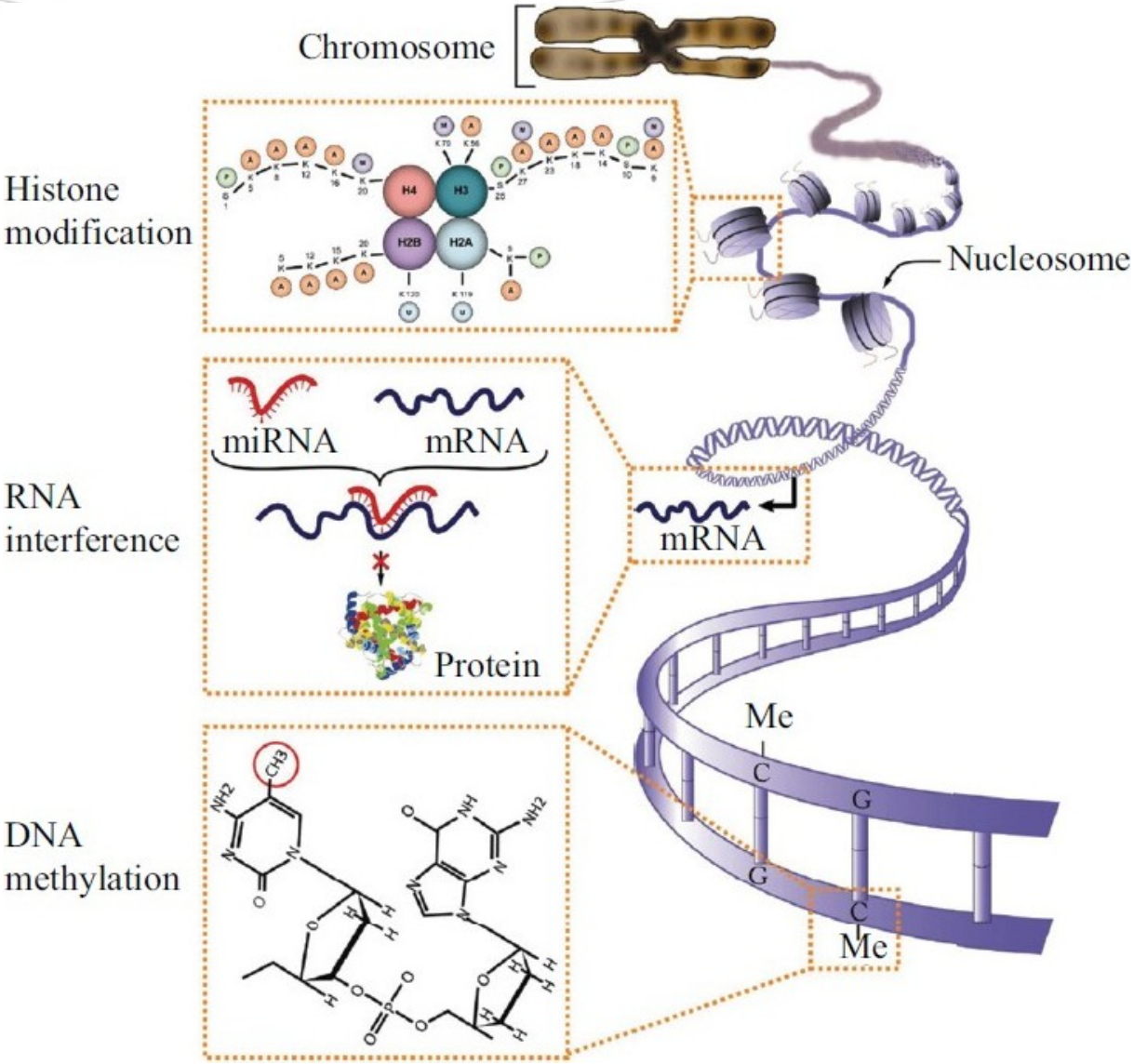
Epigenetica e salute umana

L. Stuppia, Genetica Medica
Università "G. d'Annunzio" Chieti-Pescara
stuppia@unich.it

DNA IS NOT DESTINY

The new science of epigenetics rewrites the rules of disease, heredity, and identity

By Ethan Watters


Chromosome
Histone modification
H4
H3
H2B
H2A
Nucleosome
RNA interference
miRNA
mRNA
Protein
mRNA
DNA methylation
CH3
NH2
Me
C
G
G
C
Me

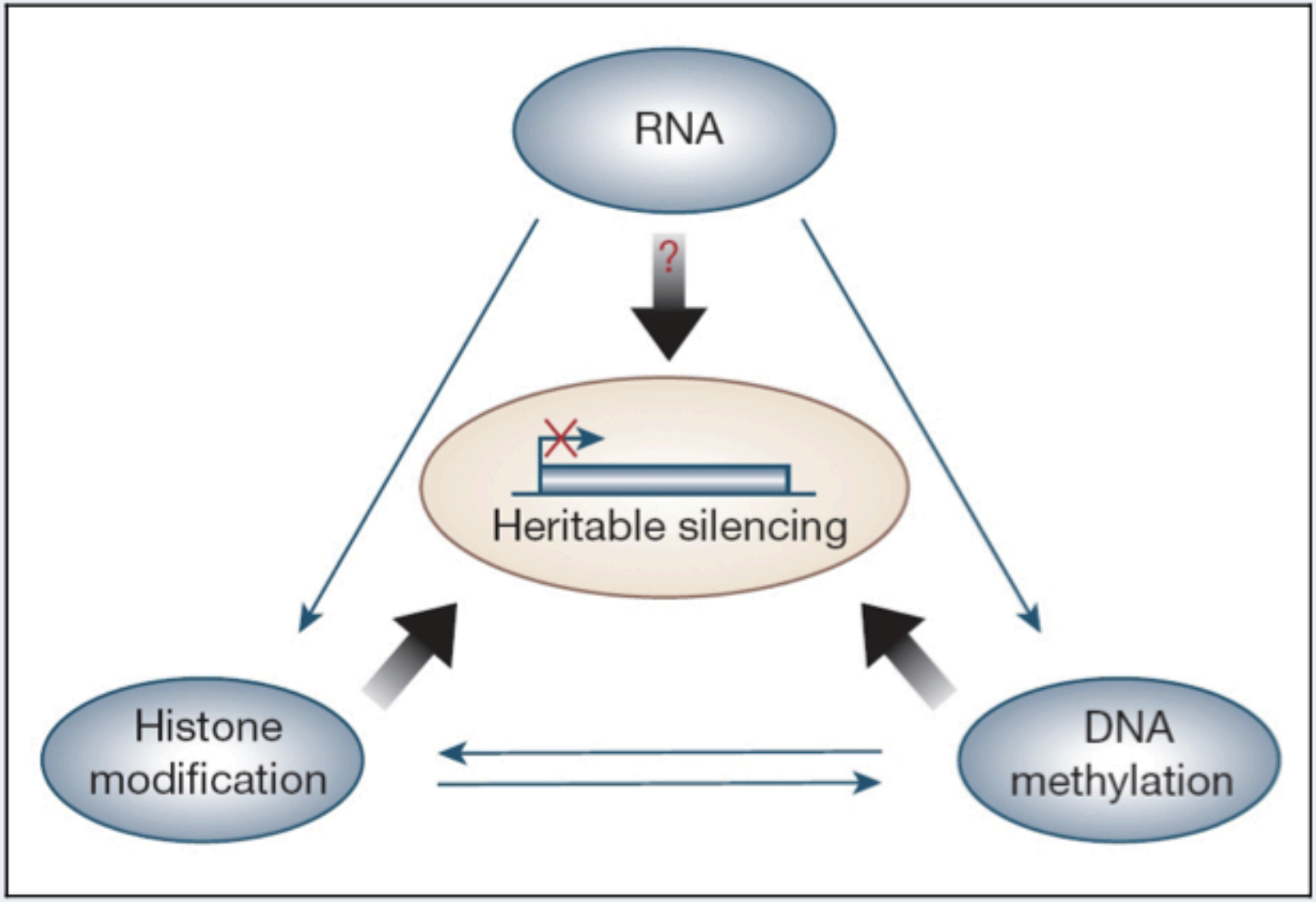
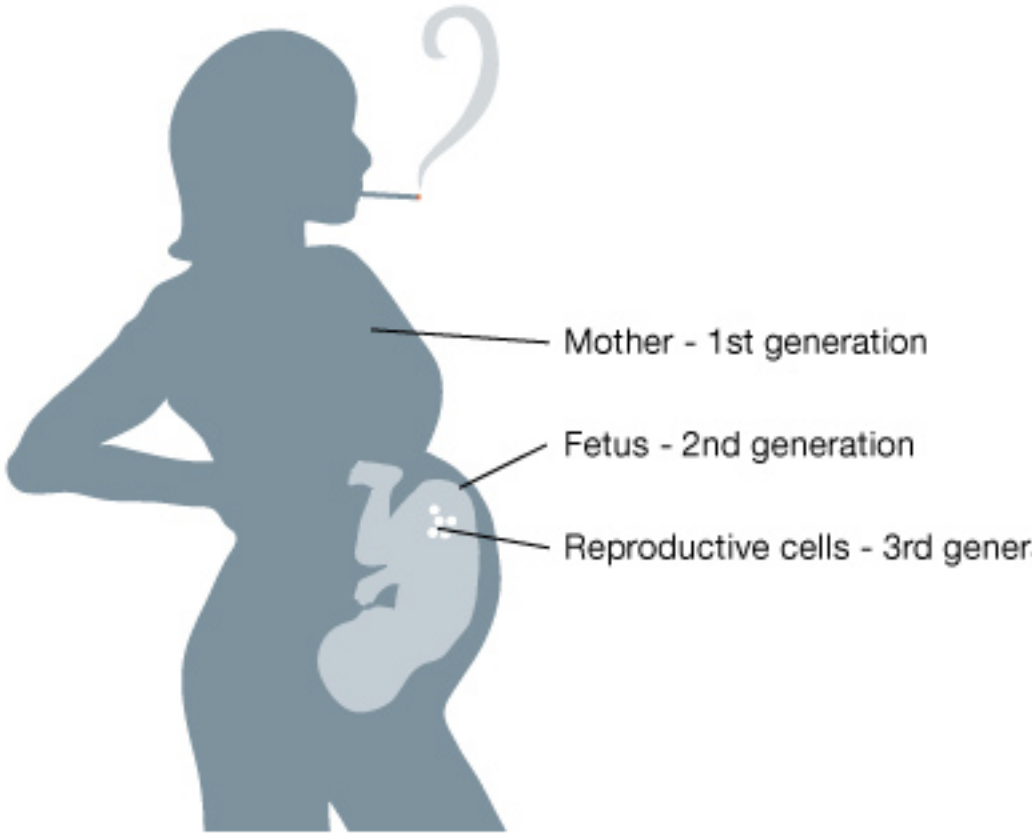


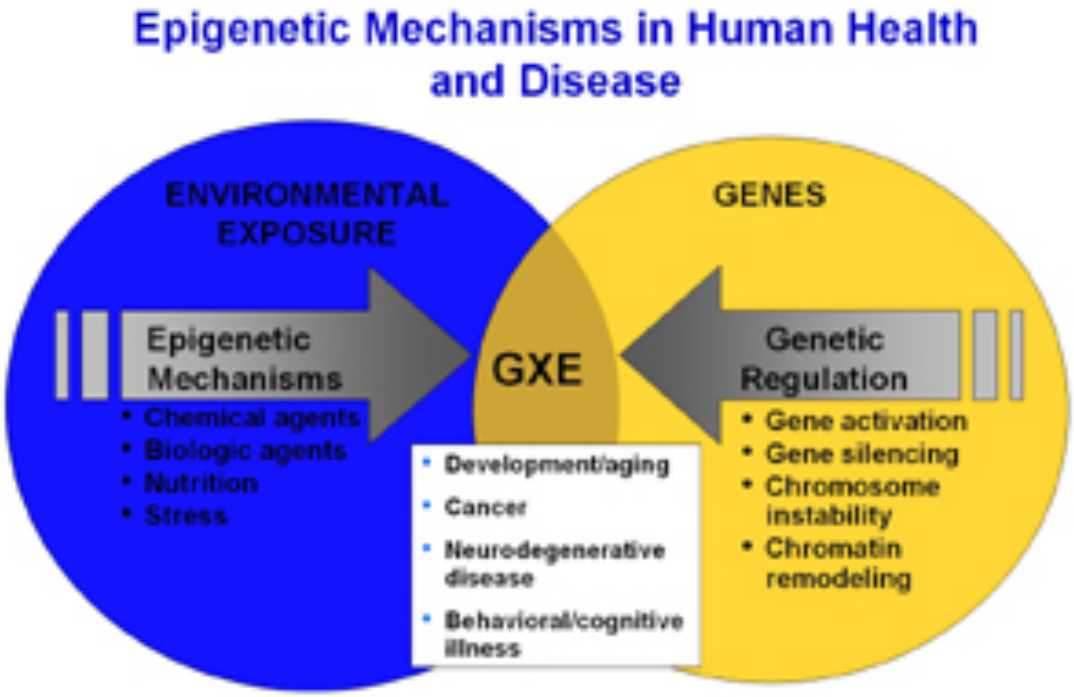
Figure 2. Three methods of Epigenetic silencing (Egger et al., 2004)

A phenomenon of methylation in plants.

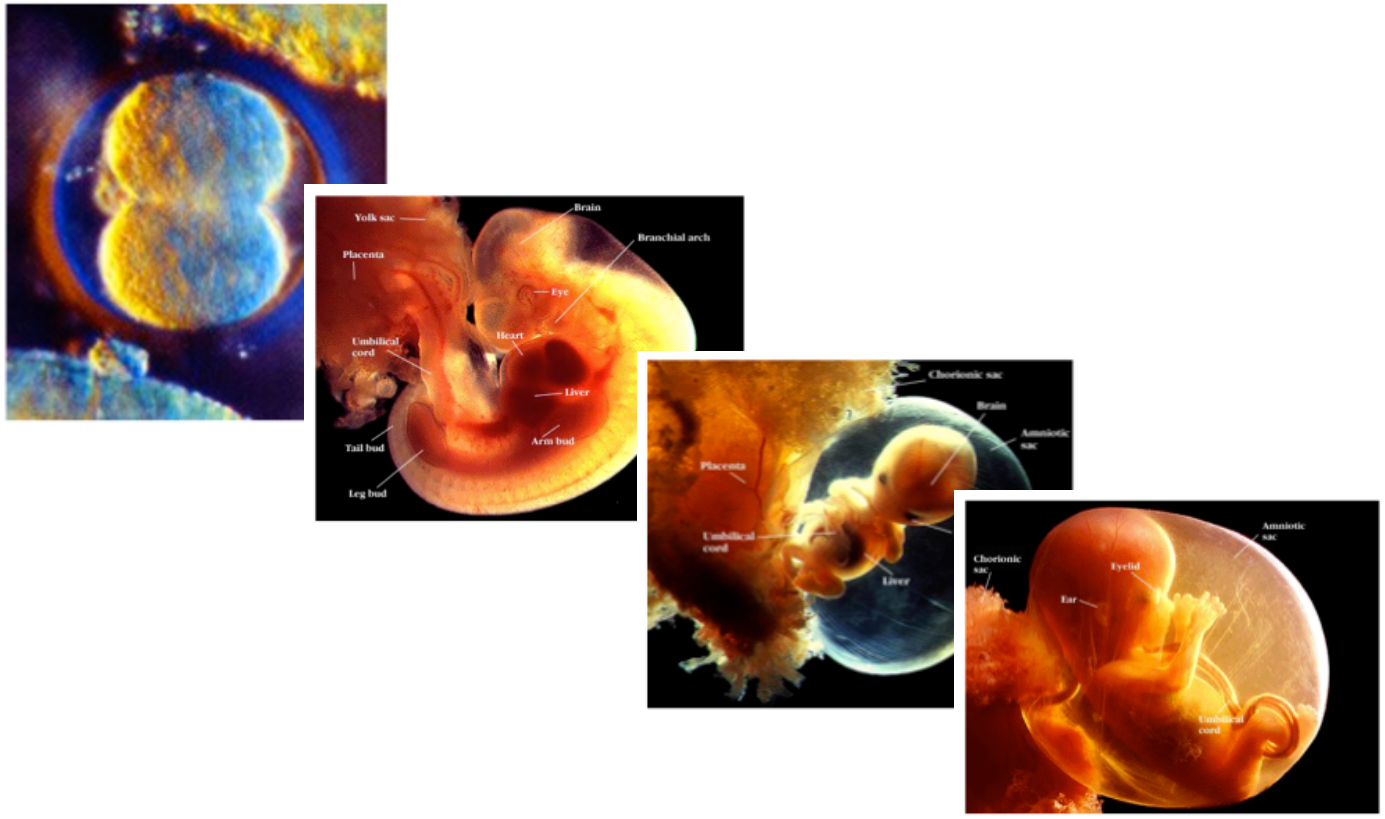

Epigenetics Warning:
What You Eat Today Could Harm
The Health of Your Children
and Grandchildren
DNA
AncestralChef.com


Mother - 1st generation
Fetus - 2nd generation
Reproductive cells - 3rd gener

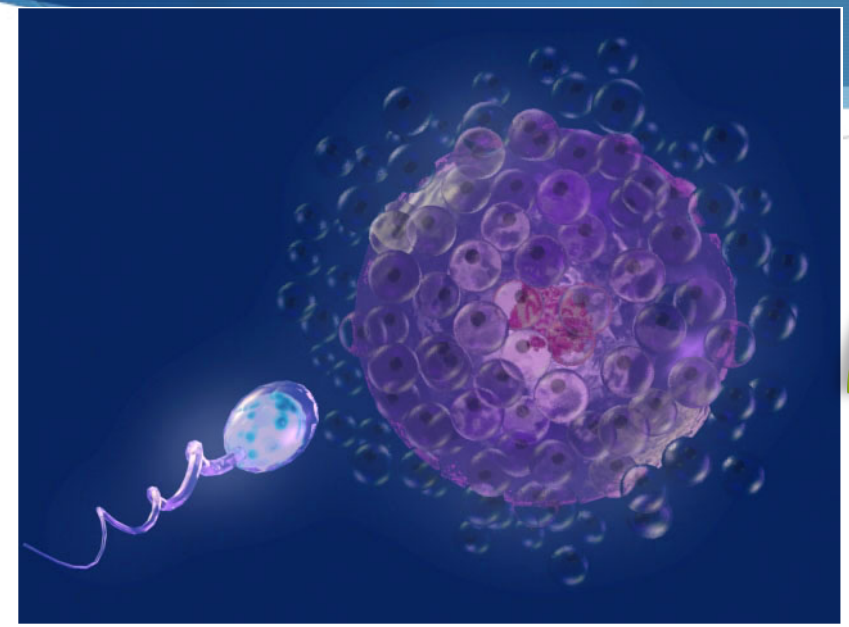
Epigenomica e salute umana



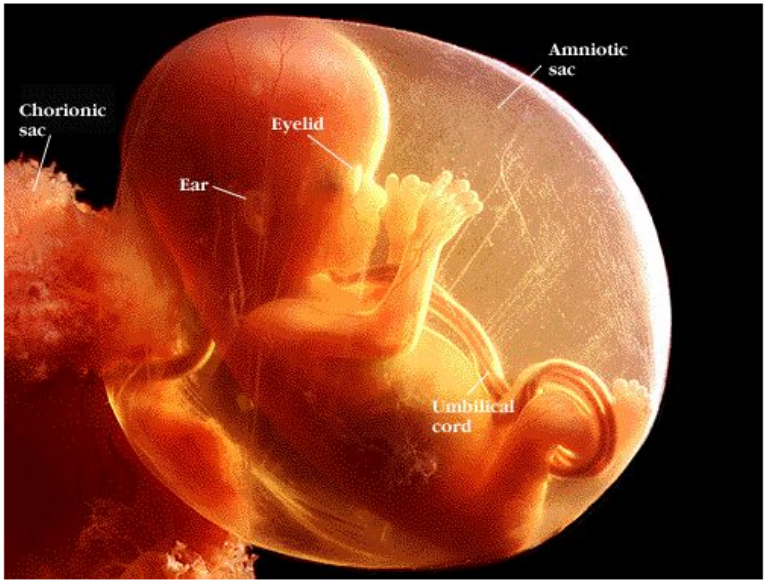
Epigenetica e sviluppo embrionale



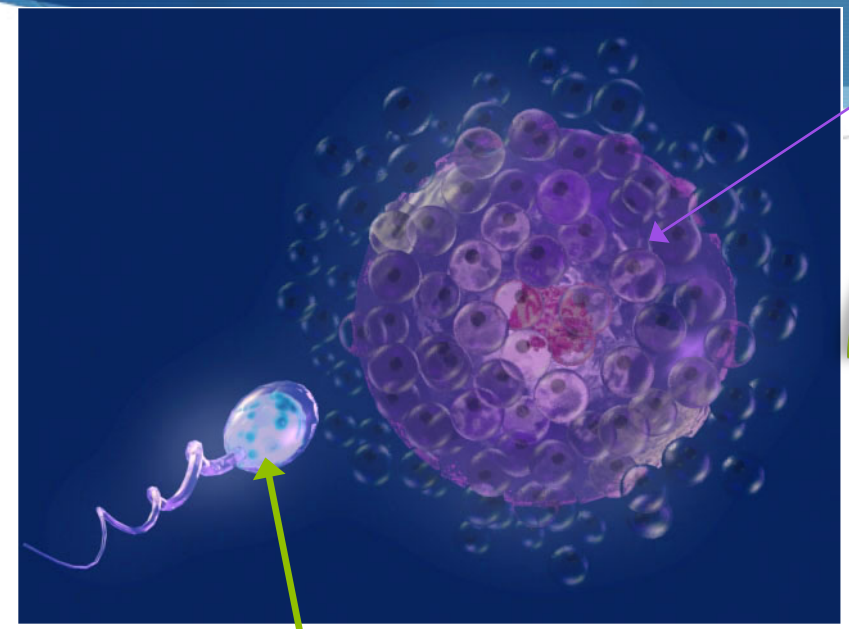
Riproduzione sessuata: la visione genetica



23+23=46



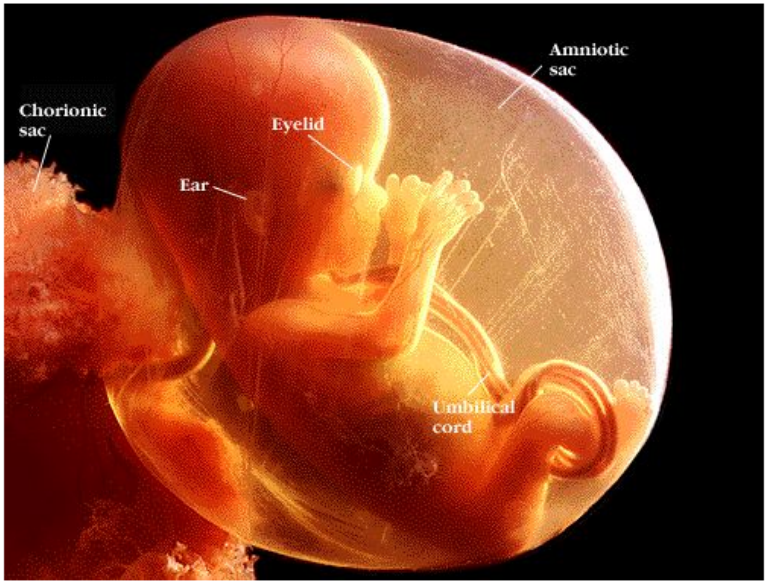
Riproduzione sessuata: la visione epigenetica



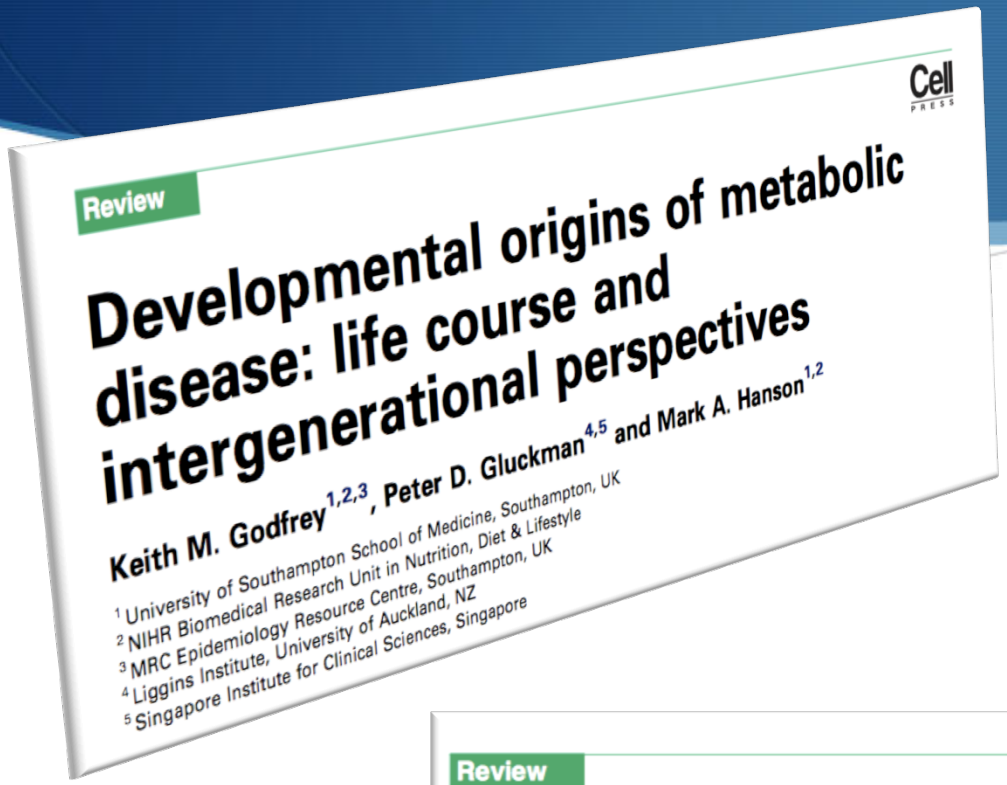
Stile di vita ed esposizioni ambientali materni

Variabile suscettibilità a patologie dell' infanzia o della età adulta

Stile di vita ed esposizioni ambientali paterni



Although the greatest increase occurs in adult life, the trajectory is set much earlier, being influenced by factors such as the mother's diet and body composition before and during pregnancy, and fetal, infant and childhood nutrition and development

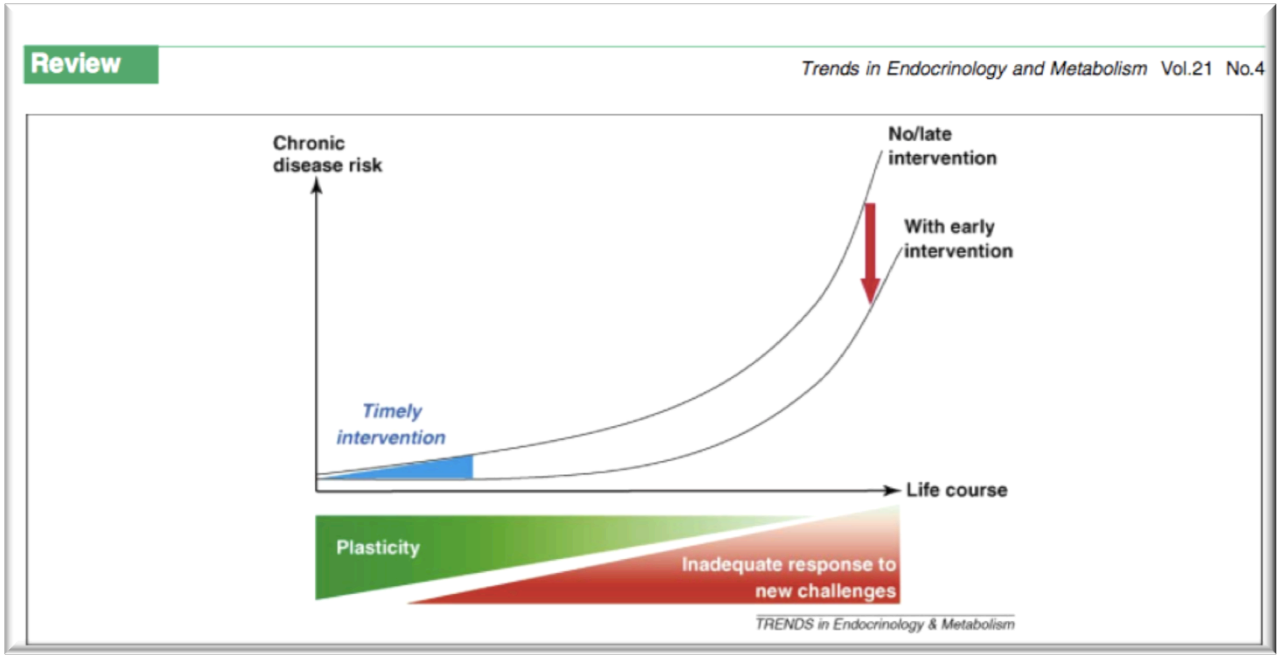

Review

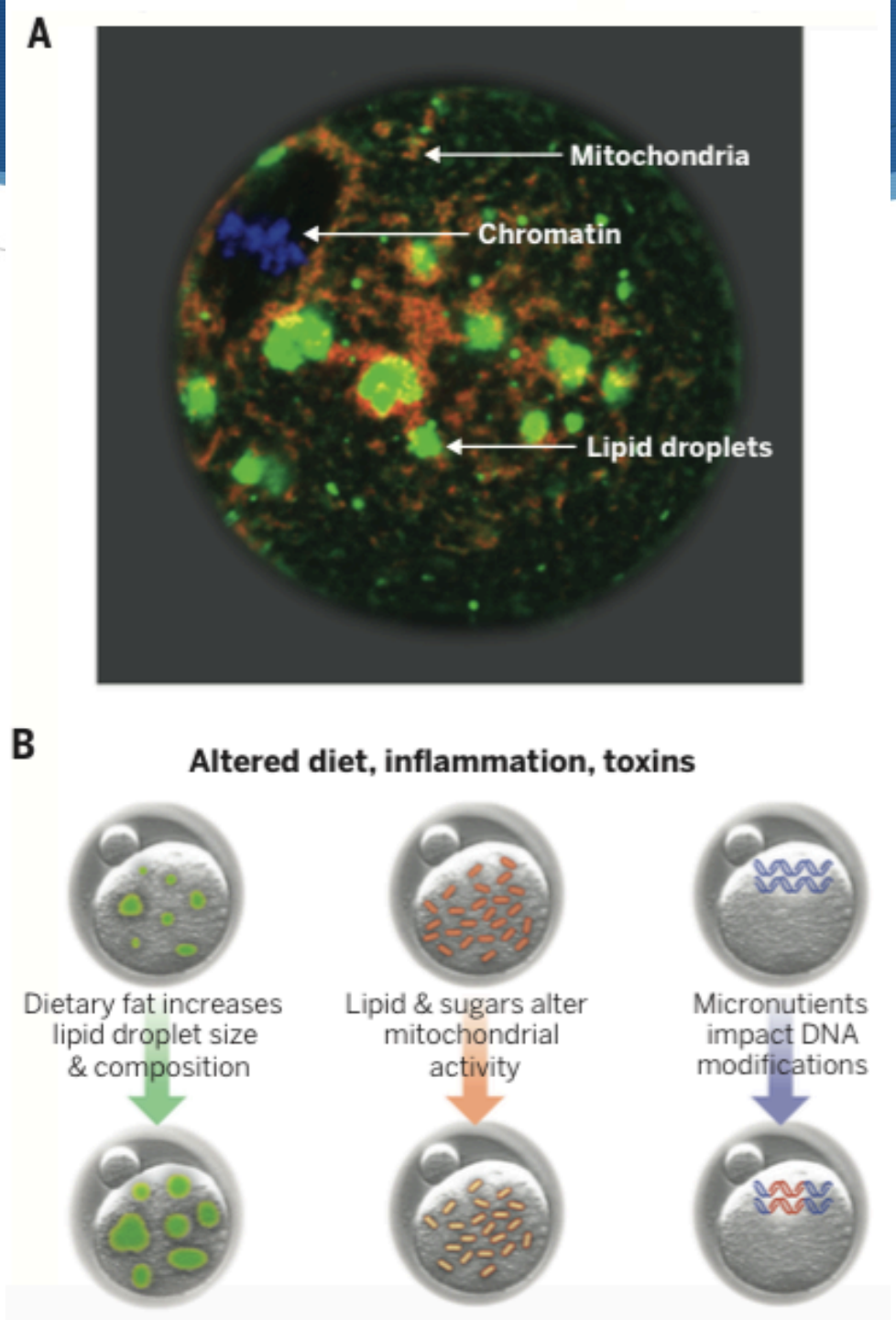
Cell PRESS

Developmental origins of metabolic disease: life course and intergenerational perspectives

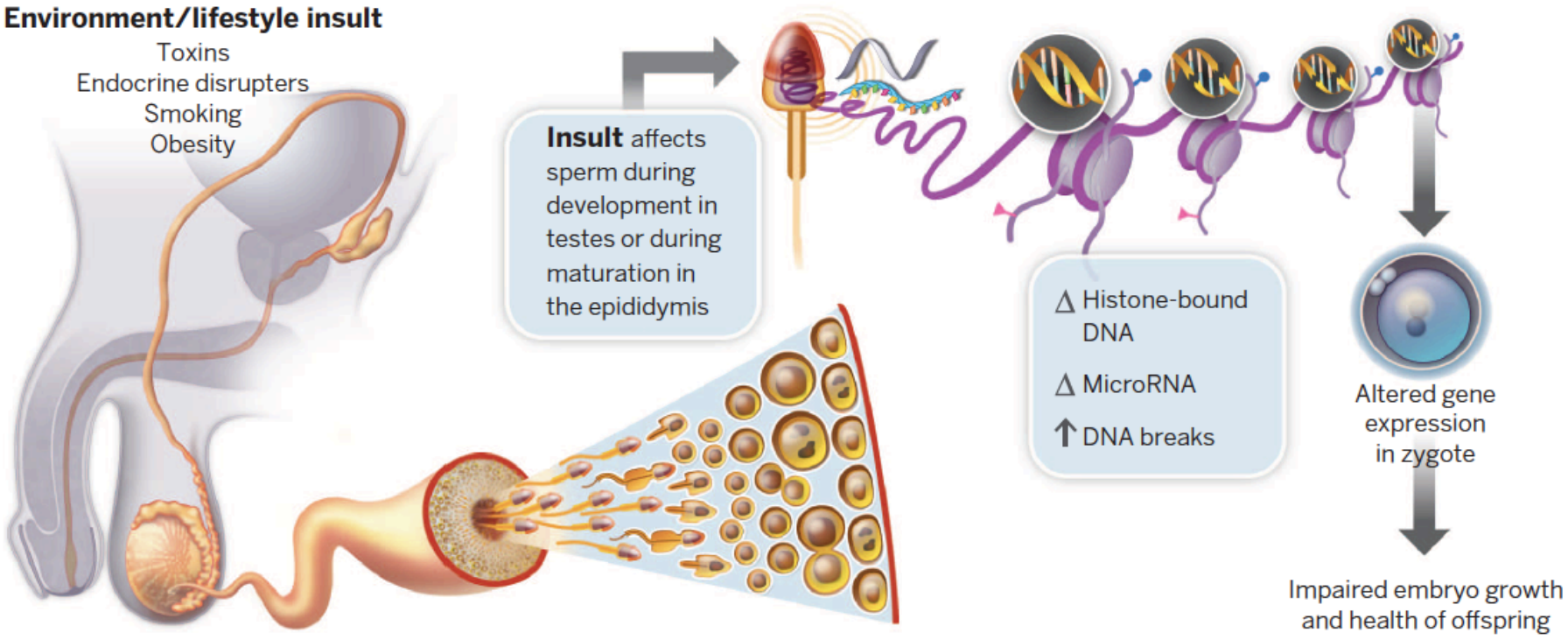
Keith M. Godfrey[1,2,3], Peter D. Gluckman[4,5] and Mark A. Hanson[1,2]

[1] University of Southampton School of Medicine, Southampton, UK
[2] NIHR Biomedical Research Unit in Nutrition, Diet & Lifestyle
[3] MRC Epidemiology Resource Centre, Southampton, UK
[4] Liggins Institute, University of Auckland, NZ
[5] Singapore Institute for Clinical Sciences, Singapore



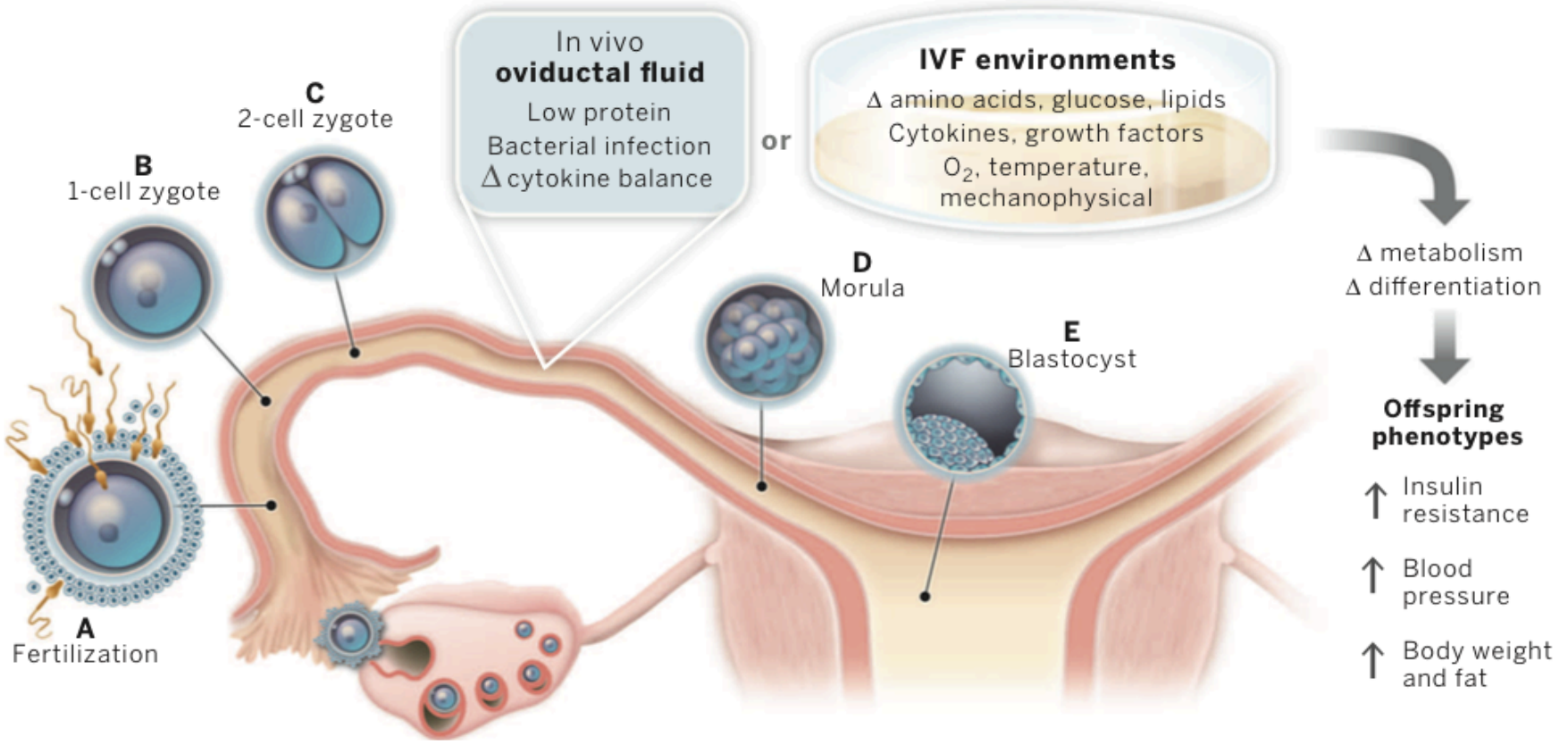


Lane et al., Science 2014

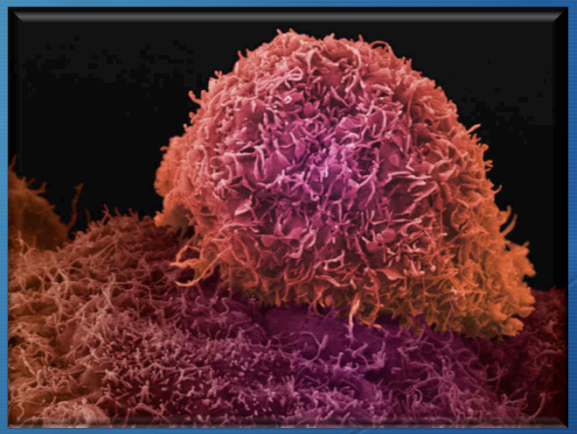

Environment/lifestyle insult
Toxins
Endocrine disrupters
Smoking
Obesity
Insult affects sperm during development in testes or during maturation in the epididymis
Δ Histone-bound DNA
Δ MicroRNA
↑ DNA breaks
Altered gene expression in zygote
Impaired embryo growth and health of offspring

Parenting from before conception

Michelle Lane, Rebecca L. Robker, Sarah A. Robertson*



Epigenetica e cancro



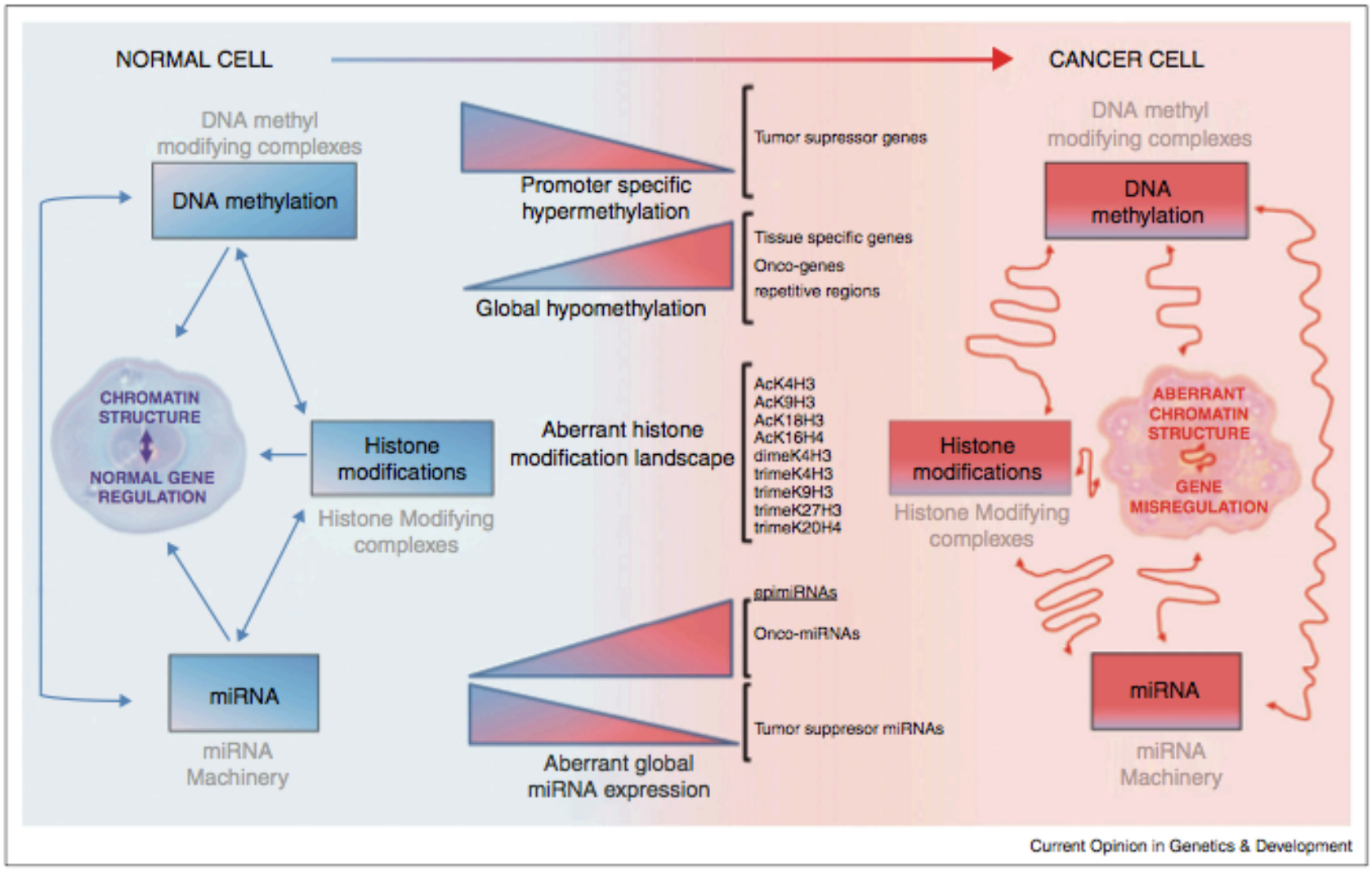
Available online at www.sciencedirect.com

SciVerse ScienceDirect

Current Opinion in Genetics & Development

Cancer epigenomics: beyond genomics

Juan Sandoval[1] and Manel Esteller[1,2,3]



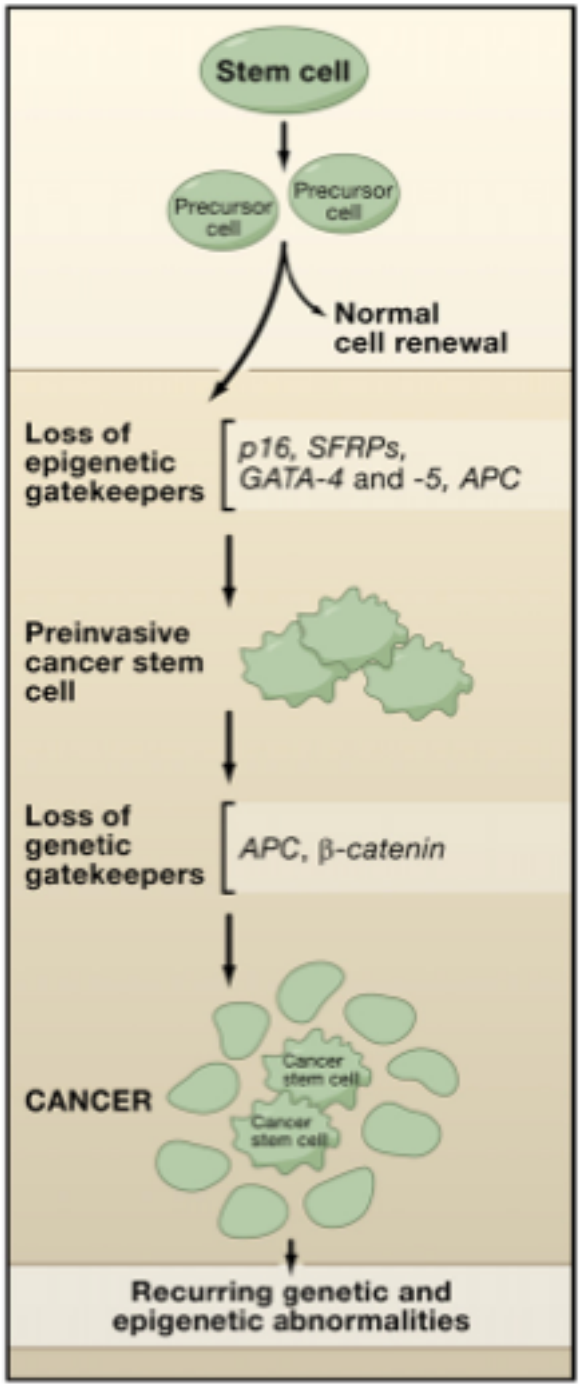
Leading Edge

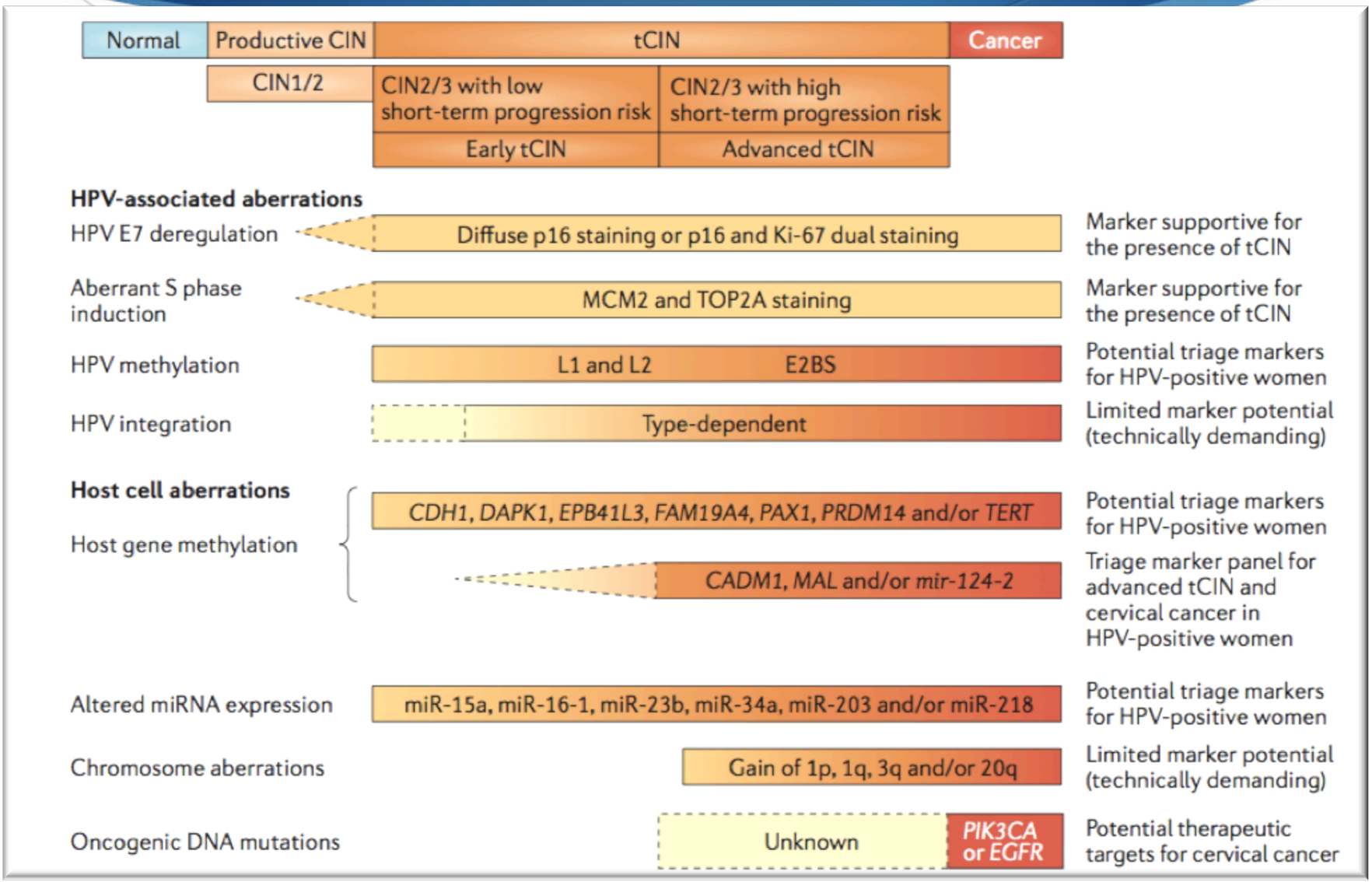
Review

Cell

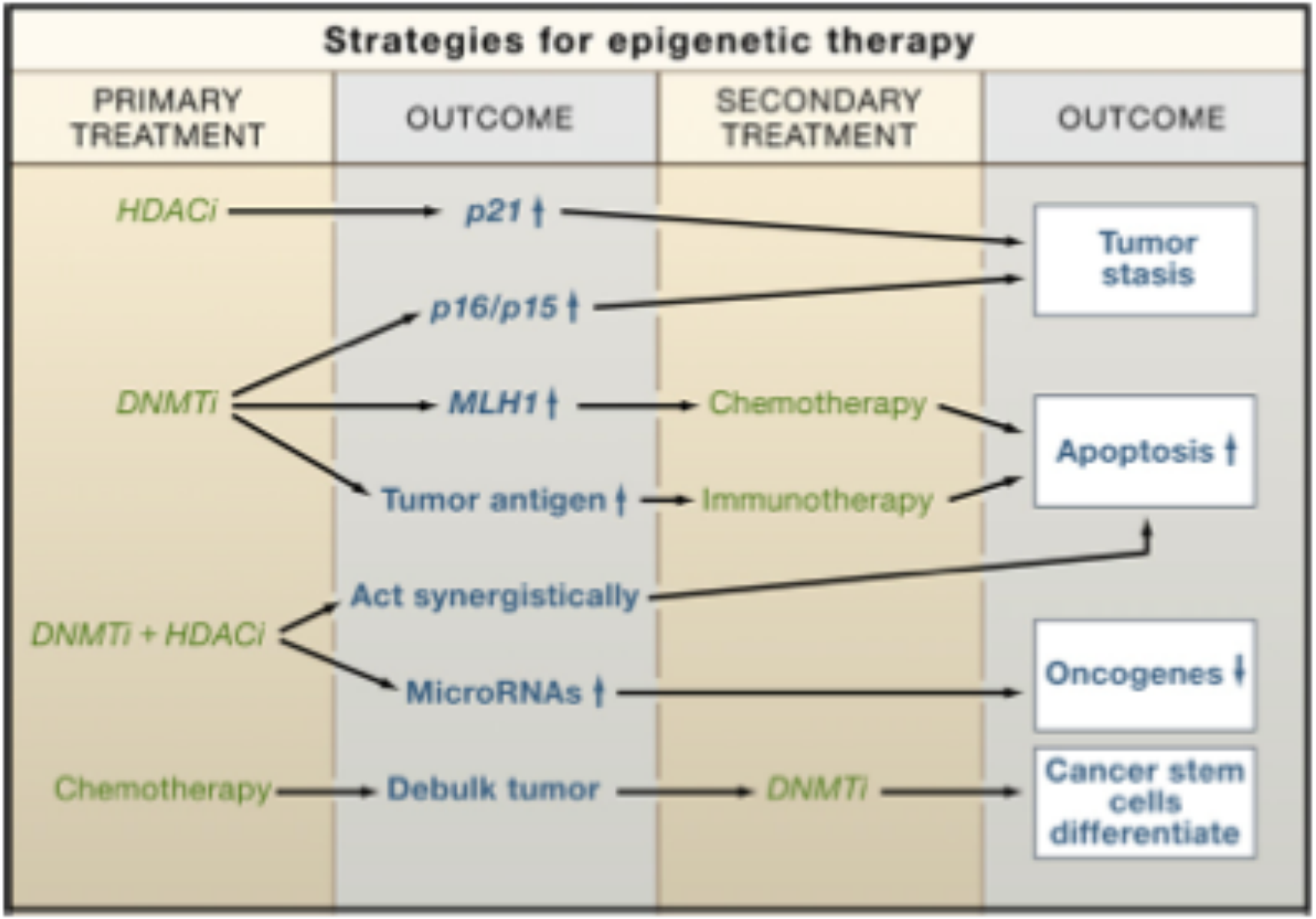
The Epigenomics of Cancer

Peter A. Jones[1,*] and Stephen B. Baylin[2,*]
[1] Department of Urology, Biochemistry, and Molecular Biology, USC/Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California, Los Angeles, CA 90089, USA
[2] Cancer Biology Program, The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Medical Institutions, Baltimore, MD 21231, USA
*Correspondence: jones_p@ccnt.usc.edu (P.A.J.), sbaylin@jhmi.edu (S.B.B.)
DOI 10.1016/j.cell.2007.01.029





Steembergen et al., 2014


Strategies for epigenetic therapy
PRIMARY TREATMENT
OUTCOME
SECONDARY TREATMENT
OUTCOME
HDACi
p21 ↑
Tumor stasis
p16/p15 ↑
DNMTi
MLH1 ↑
Chemotherapy
Apoptosis ↑
Tumor antigen ↑
Immunotherapy
Act synergistically
DNMTi + HDACi
MicroRNAs ↑
Oncogenes ↓
Chemotherapy
Debulk tumor
DNMTi
Cancer stem cells differentiate

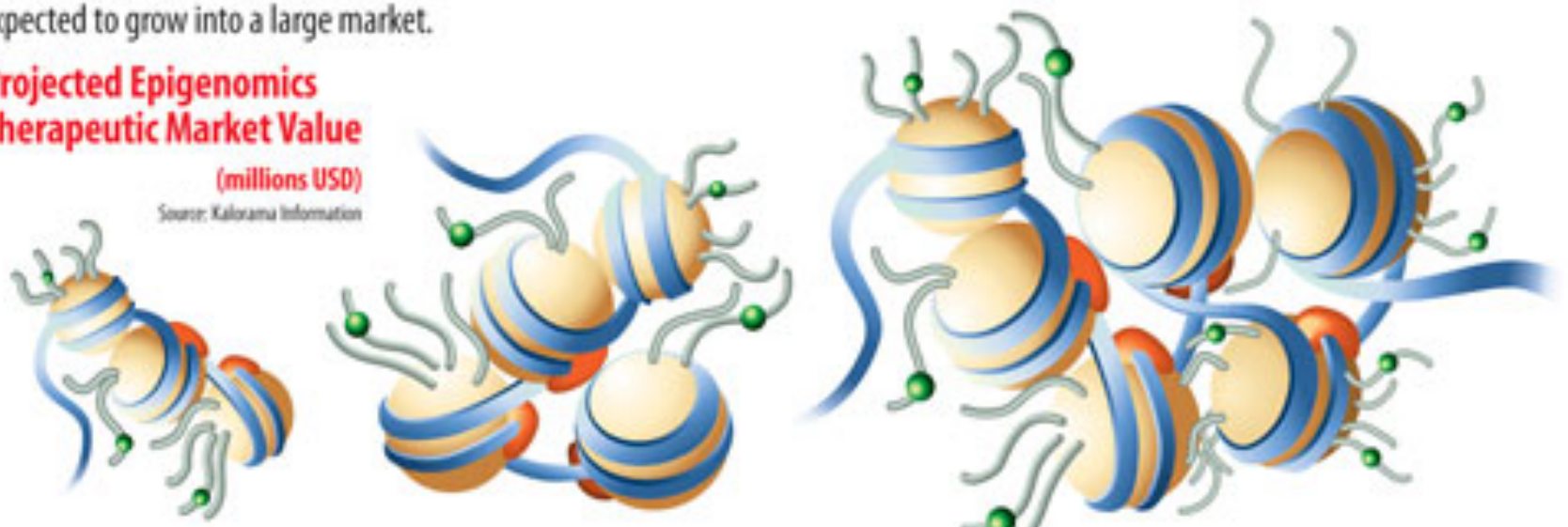
Epigenomics: Therapeutic Market Growth

The large-scale release of epimutagens into the environment may already be resulting in substantial damage to human and animal health. This represents a huge potential market for epigenomics drugs and diagnostics. Epigenetic diagnostics, therapeutics, and the tool-based technologies that supply these fields are expected to grow into a large market.

Projected Epigenomics Therapeutic Market Value

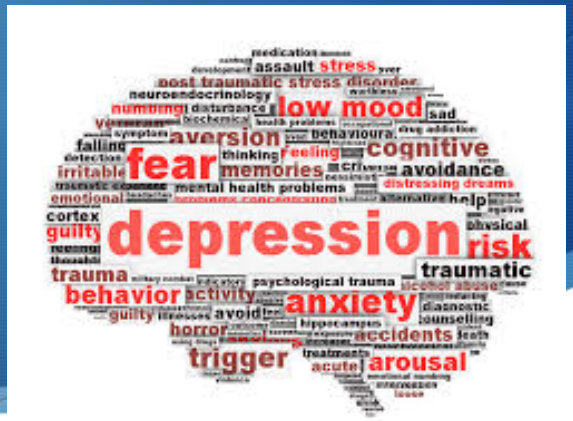
(millions USD)

Source: Kalorama Information



2011 $800 **2013 $1,000** **2017 $8,000**

Epigenetica e comportamento



Prader Willi Syndrome

Angelman Syndrome

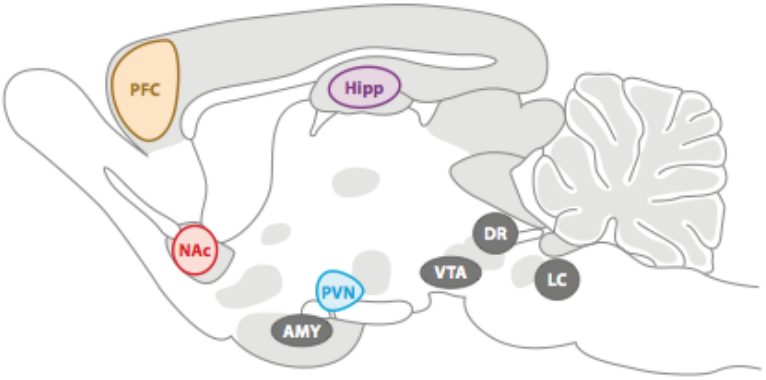
Stressful situation activates neuronal circuits, such as the hypothalamic-pituitary-adrenal (HPA) axis, the locus coeruleus, and the autonomic noradrenergic centers in the brain stem.

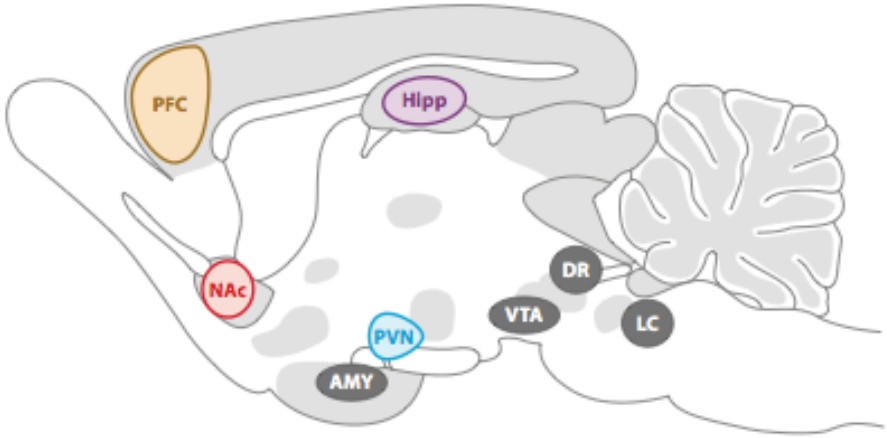
Stress targets numerous limbic brain regions, such as the prefrontal cortex, hippocampus, amygdala, and ventral striatum.

These changes in the central nervous system directly affect learning and memory, alertness, arousal, and perhaps basal anxiety, and they promote adaptive behavioral responses to subsequent stresses.

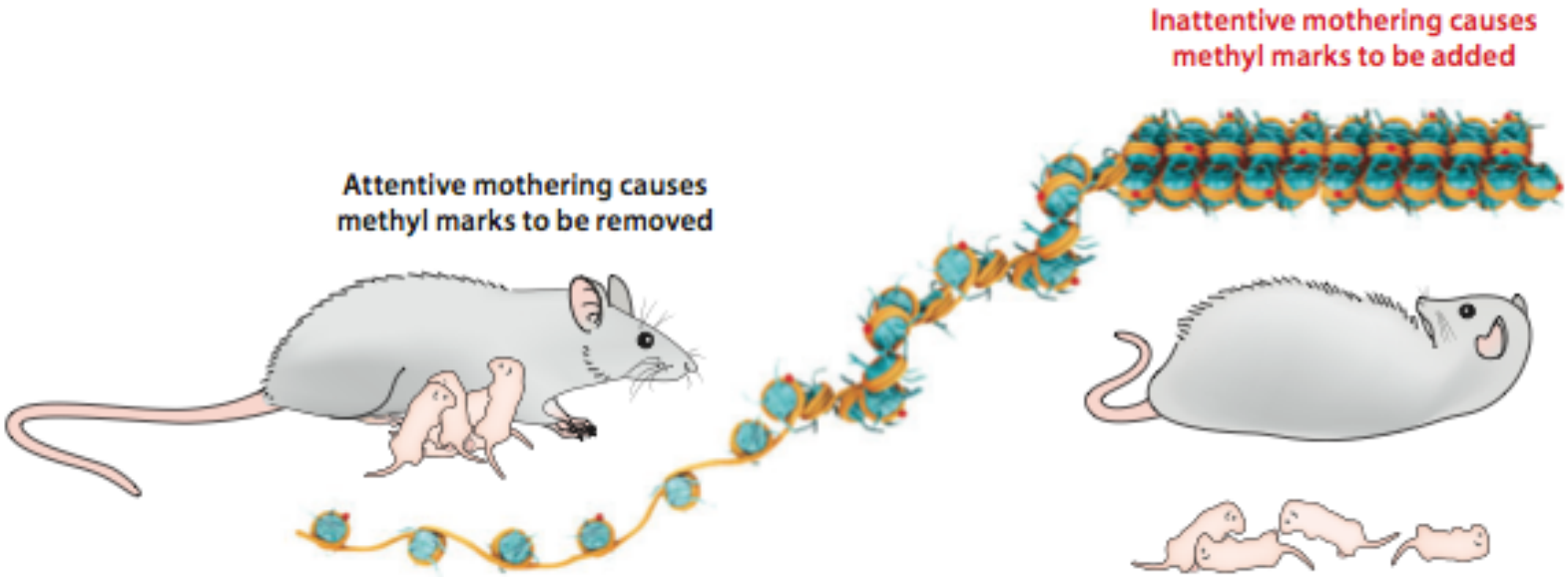
Epigenetic Mechanisms of Depression and Antidepressant Action

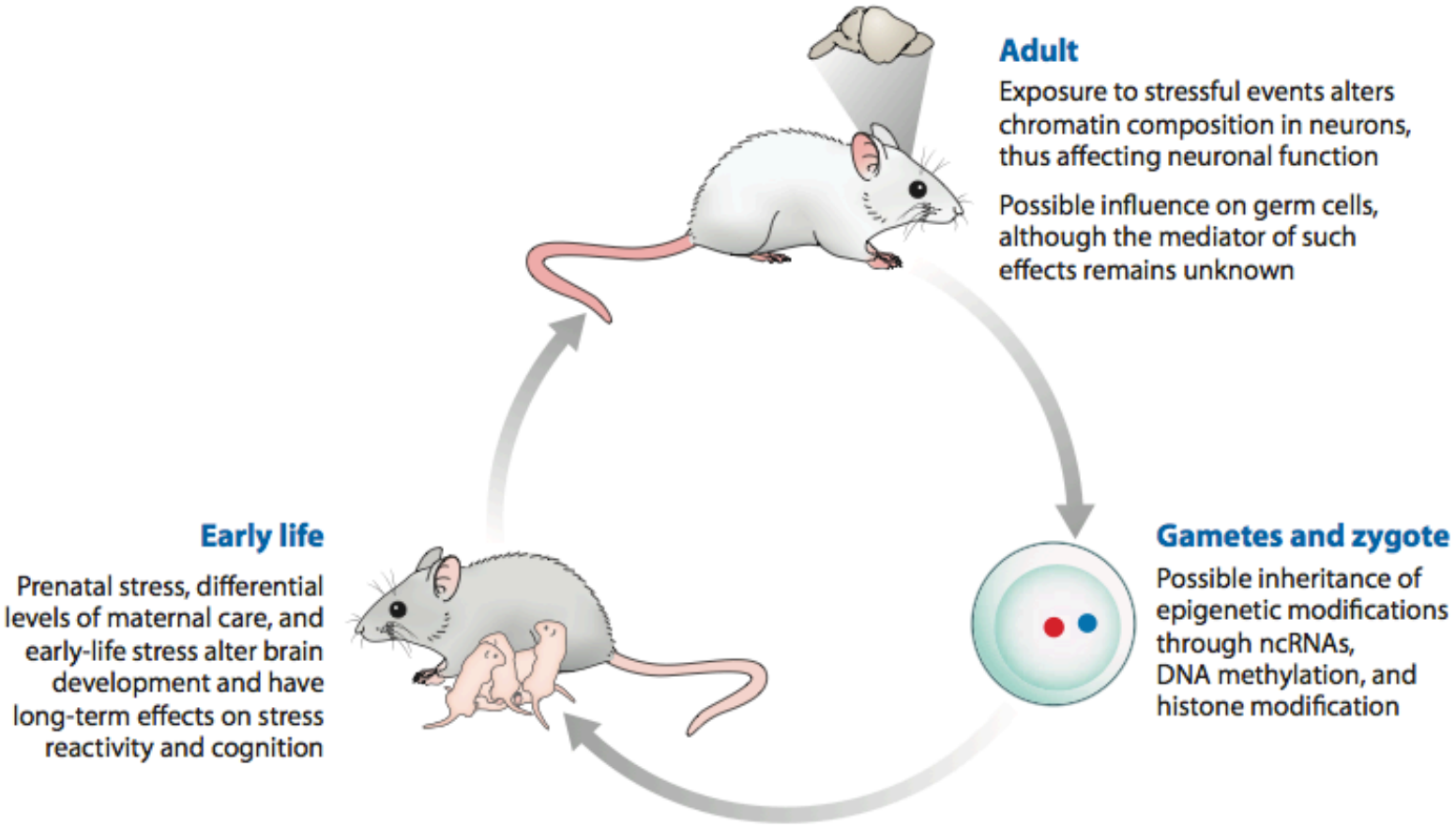
Vincent Vialou, Jian Feng, Alfred J. Robison, and Eric J. Nestler





Gene	Region	MeDNA	Associated mechanisms	Behavioral paradigm
BDNF ↓	Hipp	↑		Predator stress[105]
BDNF ↓	PFC	↑		Early-life stress[146]
CRF ↓	PVN	↑		Chronic mild stress (females)[103]
CRF ↑		↓		Social defeat (reversed by imipramine)[31]
P11 ↓	PFC	↑		FSL depression model[110]
P11 ↑		↓		FSL with escitalopram[110]
GDNF	NAc	↑		Social defeat – sus and res[108]
GDNF ↓			↑ MeCP2/HDAC2	Social defeat – sus only[108]
GDNF ↑			↑ MeCP2/CREB	Social defeat – res only[108]
AVP ↑	PVN		↓ MeCP2	Maternal separation[144]
GR ↑	Hipp	↓		High LG (maternal attention)[151]


Inattentive mothering causes
methyl marks to be added
Attentive mothering causes
methyl marks to be removed


Adult
Exposure to stressful events alters chromatin composition in neurons, thus affecting neuronal function
Possible influence on germ cells, although the mediator of such effects remains unknown
Gametes and zygote
Possible inheritance of epigenetic modifications through ncRNAs, DNA methylation, and histone modification
Early life
Prenatal stress, differential levels of maternal care, and early-life stress alter brain development and have long-term effects on stress reactivity and cognition

Journal of
Clinical Pharmacy and Therapeutics

Journal of Clinical Pharmacy and Therapeutics, 2012, **37**, 499–501 doi: 10.1111/j.1365-2710.2012.01346.x

Commentary

Role of epigenetics in pharmacotherapy, psychotherapy and nutritional management of mental disorders

J. Peedicayil MD
Department of Pharmacology and Clinical Pharmacology, Christian Medical College, Vellore, India

Received 2 January 2012, Accepted 23 February 2012

Keywords: **epigenetics, mental disorders, nutrition, pharmacotherapy, psychotherapy**

Epigenetica e disturbi del SNC

Neuropharmacology 68 (2013) 2–82

Contents lists available at SciVerse ScienceDirect

Neuropharmacology

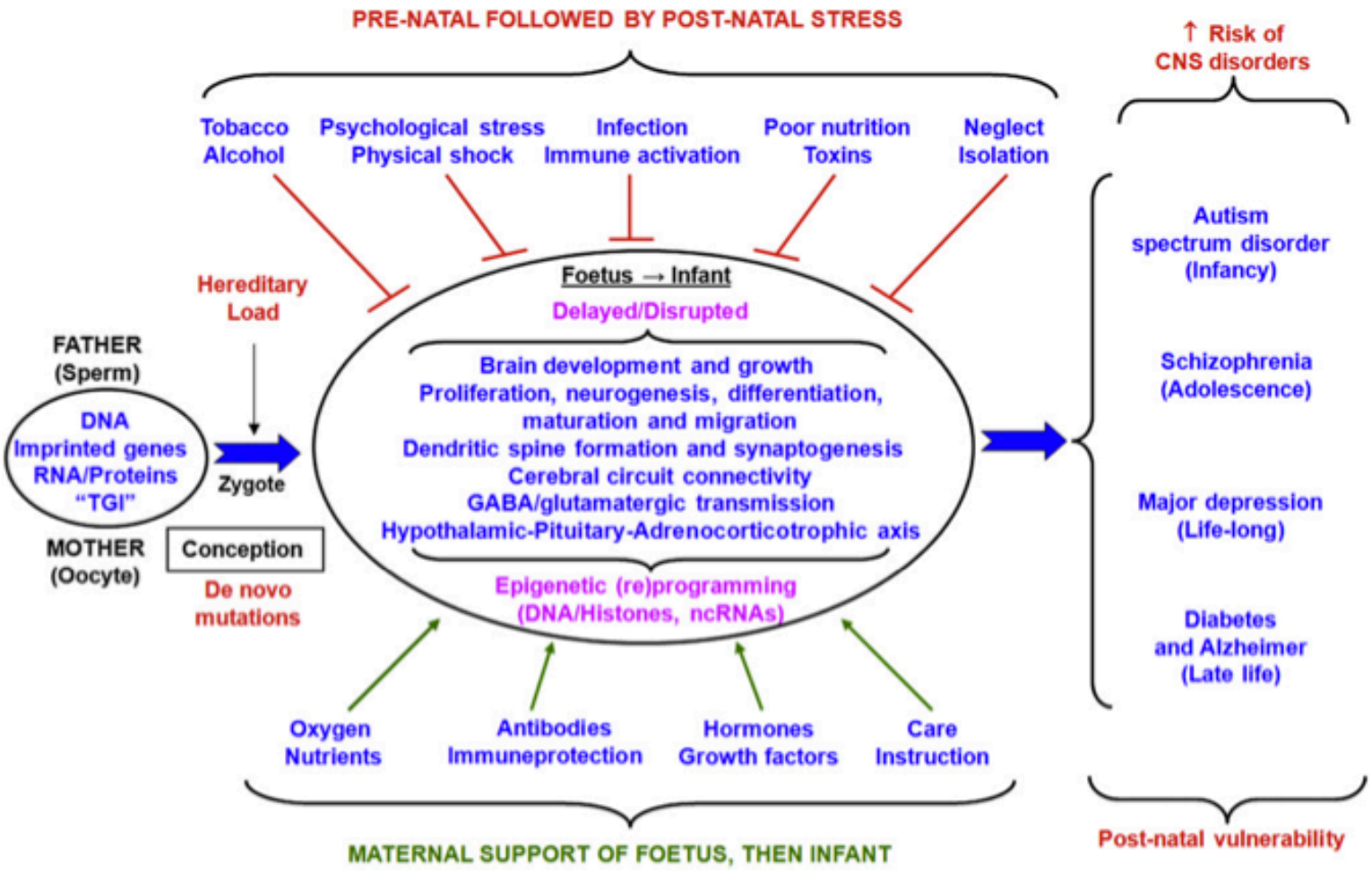
journal homepage: www.elsevier.com/locate/neuropharm

Invited review

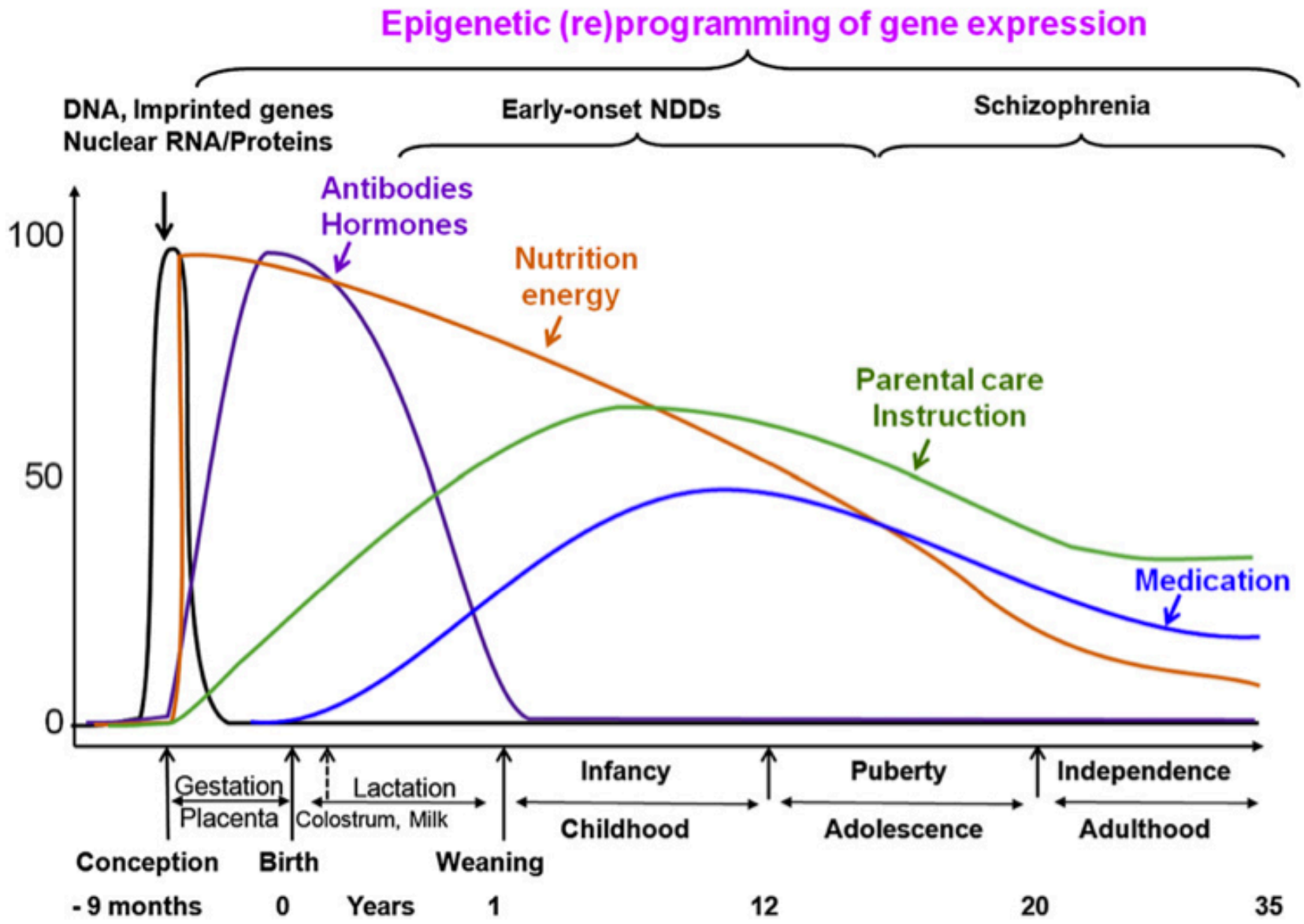
An epigenetic framework for neurodevelopmental disorders: From pathogenesis to potential therapy

Mark J. Millan*

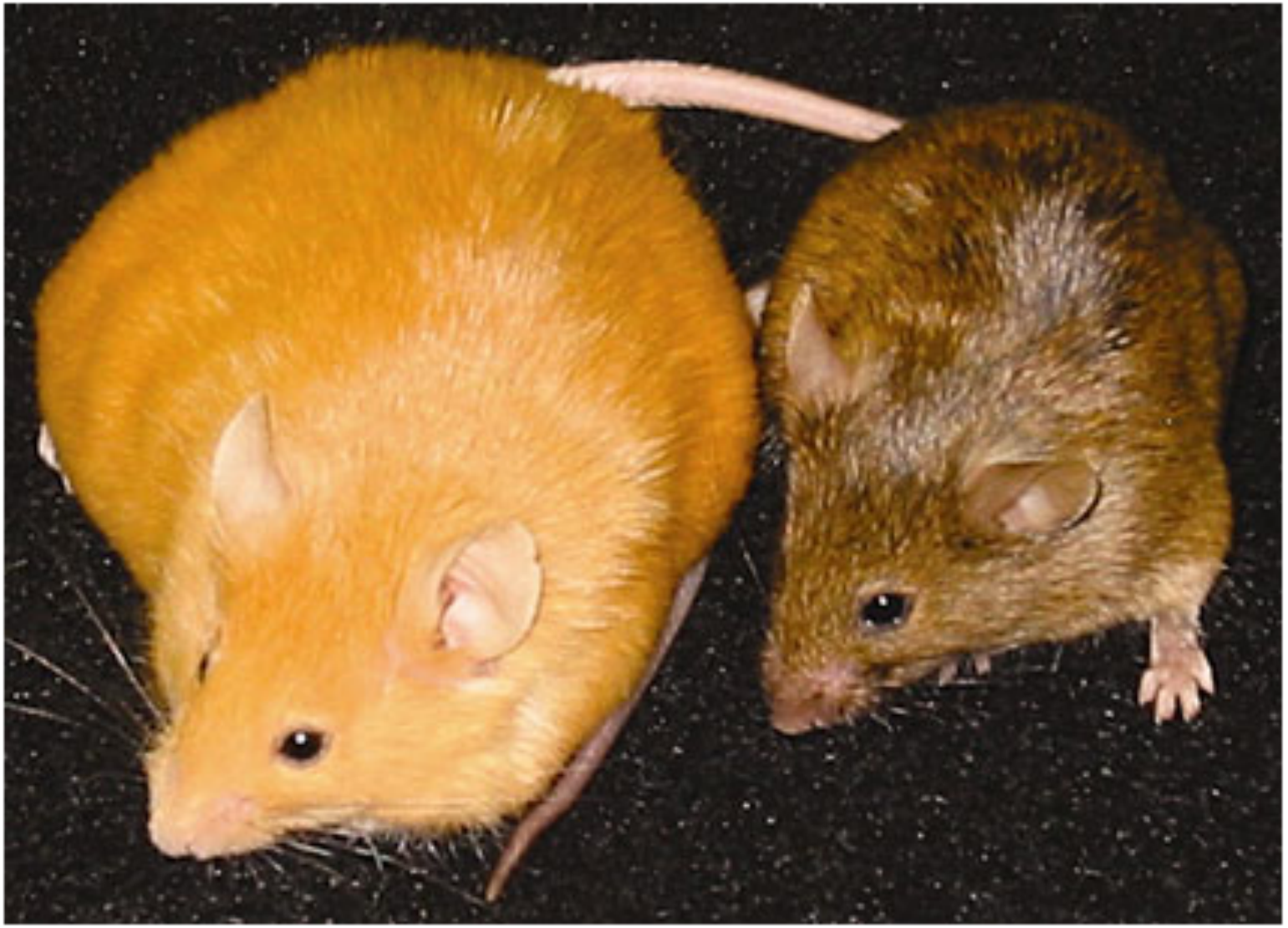
Unit for Research and Discovery in Neuroscience, IDR Servier, 125 chemin de ronde, 78290 Croissy sur Seine, Paris, France



M.J. Millan / Neuropharmacology 68 (2013) 2–82



Modificazioni epigenetiche: quali fattori ambientali?



CORRIERE DELLA SERA
SETTE

Data 19-10-2012
Pagina 124
Foglio 1

Ricerca Da guerre e carestie la scoperta che sul nascituro influisce anche la dieta dell'uomo

Il cibo del padre ricade sulla salute del figlio

Un'alimentazione più o meno ricca addirittura durante la pubertà modifica le capacità "espressive" del Dna. Modifiche trasmesse poi alla prole

di **Franca Porciani**

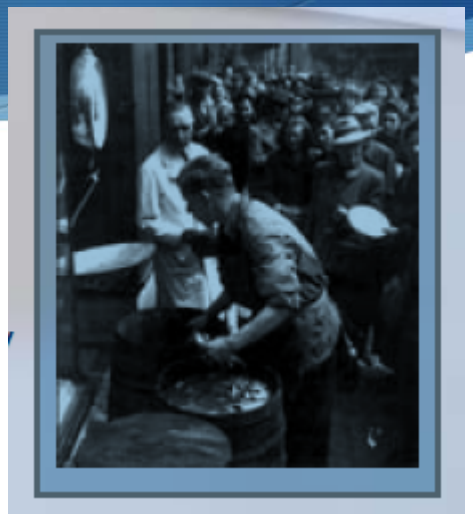
Non c'erano contatti con il mondo esterno nei rigidi mesi d'inverno a Overkalix a quei tempi. Se il raccolto era stato abbondante, si mangiava a sufficienza, se era stato scarso, un po' di fame era inevitabile. È stato così fino agli inizi del Novecento in questo paese di 4.000 anime nel cuore della Lapponia svedese, la regione più a nord a ridosso del Circolo Polare Artico, vicino al fiume Kalix, famoso per la pesca al salmone. Quando era chiusa nella morsa del mar Baltico ghiacciato, diventava irraggiungibile. Una situazione eccezionale che ha stimolato l'attenzione di un genetista svedese, Lars Olov Bygren, che insieme al collega inglese Marcus Pembrey ha correlato i certificati di nascita e di morte della popolazione (li ha trovati a partire dal lontano 1799) con l'andamento dei raccolti, di conseguenza con la disponibilità di cibo durante l'inverno.

Effetti imprevisti. Il risultato? I due ricercatori hanno scoperto che quando i ragazzi fra i nove e i dodici anni, epoca cruciale

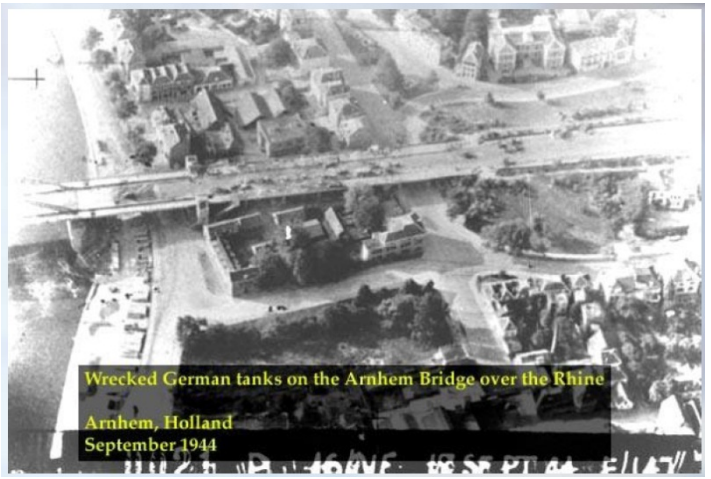
LARS TUNDIN / AGENZIA VU

Tre generazioni. Il genetista svedese Lars Olov Bygren, autore dello studio su Overkalix, che ha scoperto l'influenza della dieta dell'uomo sulla prole, con il figlio Magnus e il nipote Ludvig nella sua casa a Stoccolma.

di ricerche, quello sull'epigenetica (*epi*, sopra, in greco, e genetica) ovvero quanto gli stimoli ambientali possono modificare le capacità "espressive" del nostro Dna, senza arrivare a intaccarne la composizione. È una sorta di nuova scienza, in gran parte da esplorare, che dimostra come sia forte l'ambiente: i geni non si autocontrollano, ma sono controllati dall'ambiente, da quanto e come mangiamo prima di tutto», spiega Liborio Stuppia, professore di genetica medica alla facoltà di psicologia dell'università di Chieti, uno dei primi ad interessarsi in Italia di questa nuova branca. Ma oltre agli inverni lapponi, una vicenda a noi più vicina ci fa capire l'importanza dell'epigenetica: la carestia olandese dell'inverno '44-'45 quando il Paese, già vittima dell'occupazione nazista, restò prigioniero dell'embargo sul trasporto di cibo voluto da Hitler, che lo costrinse all'inverno "della fame". *Hongerwinter* in fiammingo, mesi in cui la gente, ridotta alla stremo, si nutrì di gatti, ratti, alla fine di bulbi di tulipano.



L'embargo nazista sulla Olanda occidentale alla fine della II Guerra Mondiale causò 30.000 morti per malnutrizione…



60 anni dopo….

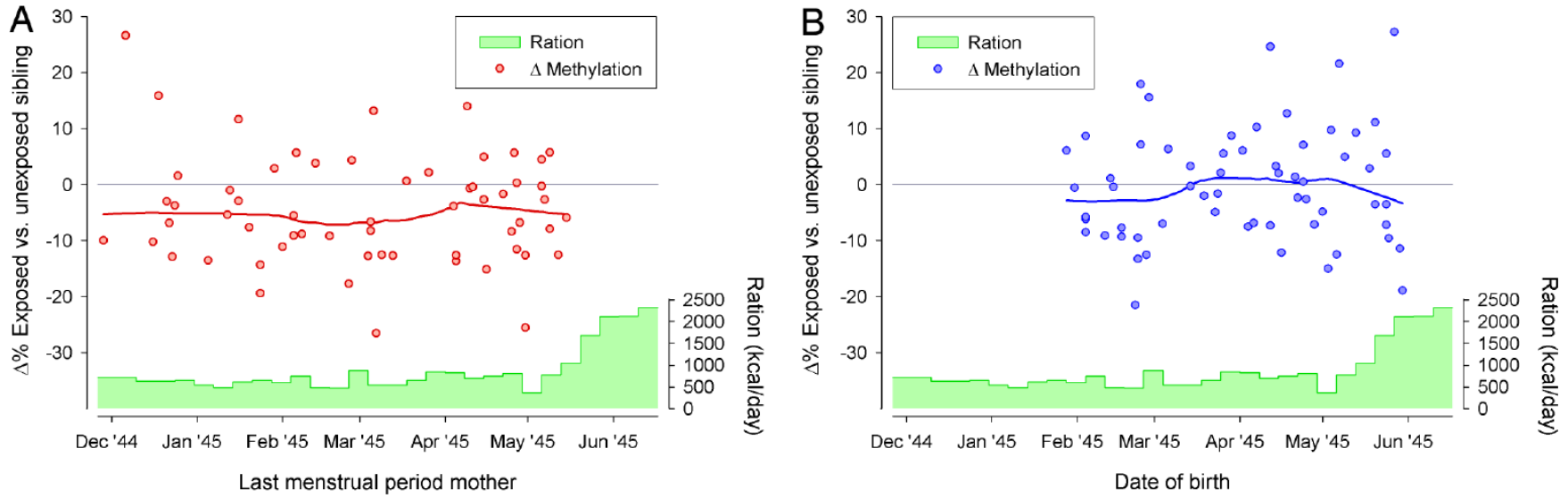
PNAS

Persistent epigenetic differences associated with prenatal exposure to famine in humans

Bastiaan T. Heijmans[a,1,2], Elmar W. Tobi[a,2], Aryeh D. Stein[b], Hein Putter[c], Gerard J. Blauw[d], Ezra S. Susser[e,f], P. Eline Slagboom[a], and L. H. Lumey[e,1]

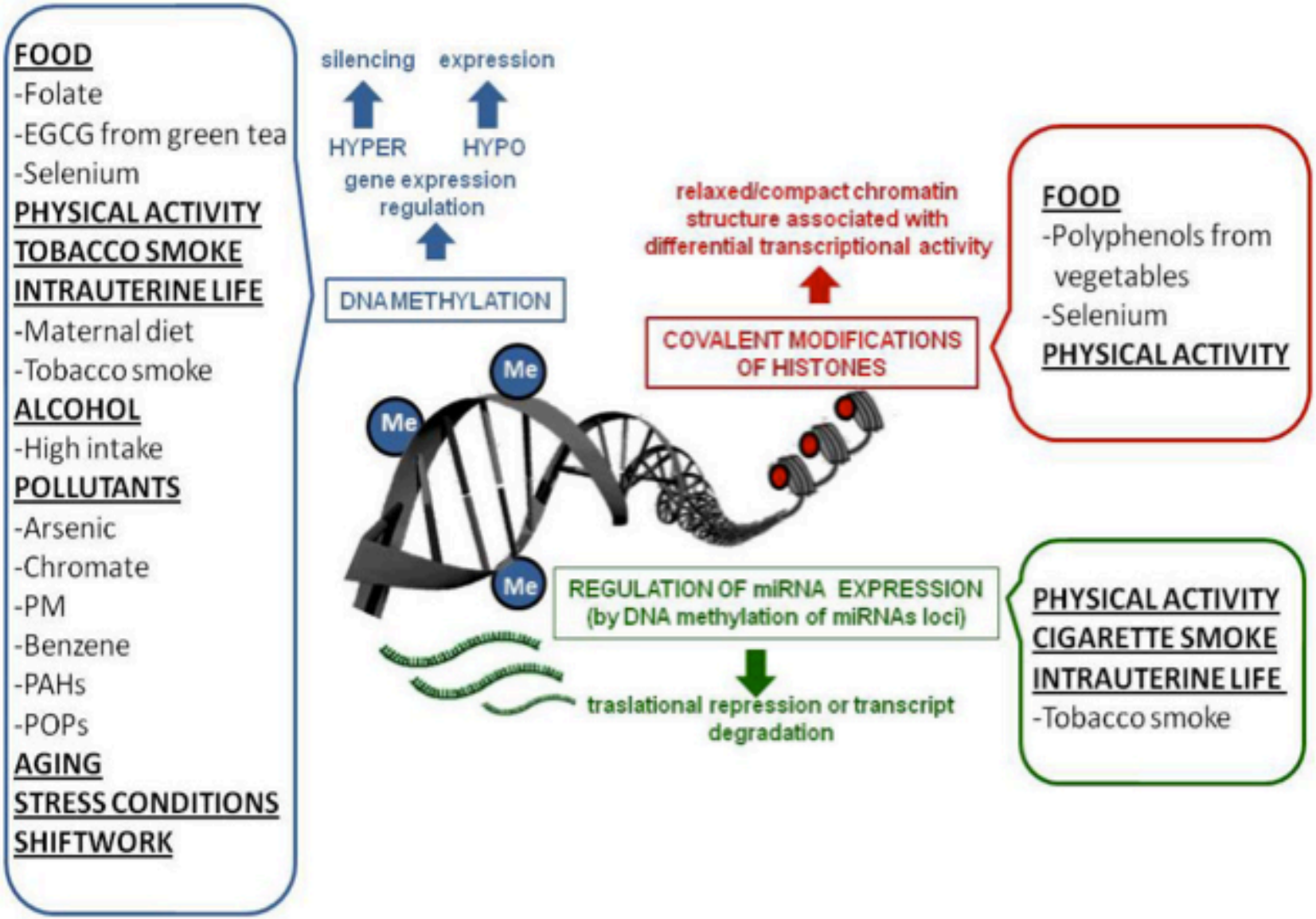
Departments of [a]Molecular Epidemiology, [c]Medical Statistics, and [d]Gerontology and Geriatrics, Leiden University Medical Center, Leiden, The Netherlands; [b]Hubert Department of Global Health, Rollins School of Public Health, Emory University Atlanta, GA 30322; [e]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY 10032; and [f]New York State Psychiatric Institute, New York, NY 10032

Edited by Charles R. Cantor, Sequenom Inc., San Diego, CA, and approved September 17, 2008 (received for review July 7, 2008)

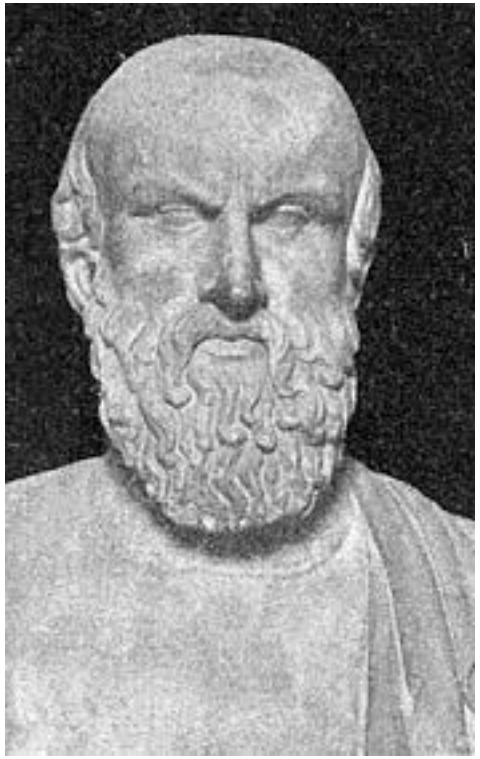


Ridotta metilazione del gene IGF2 negli individui concepiti durante la carestia

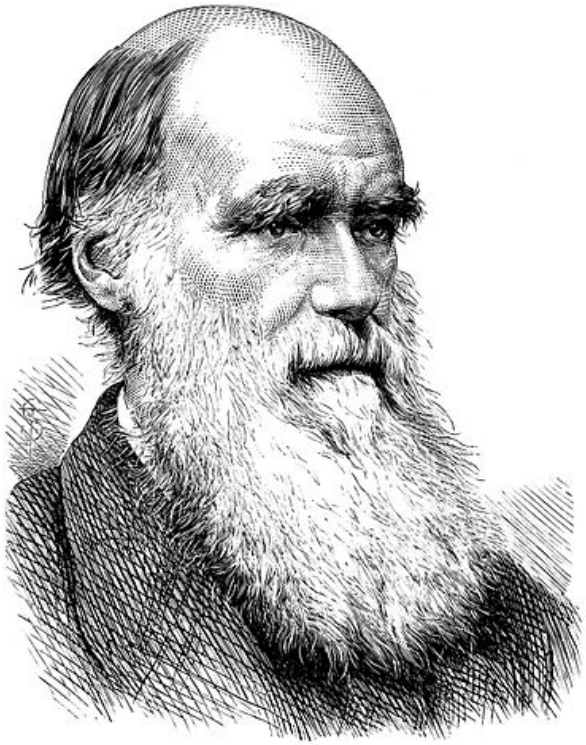
Epigenomics. 2011 June ; 3(3): 267–277.



L'uomo non deve essere ὑβριστής – ubristès – "smodato/tracotante", perché questo è un atteggiamento che dispiace molto agli dèi, i quali puniscono tale uomo, e può passare anche molto tempo, prima che giunga la punizione, ma bisogna tenere sempre ben presente che "Zeus punisce, anche se tardi". Per questo motivo le colpe dei padri ricadono sui figli.




DAMN YOU, EPIGENOME.
BUTTER PECAN



Charles Robert Darwin (1809 – 1882)

Jean Baptiste de Lamarck (1744-1829)