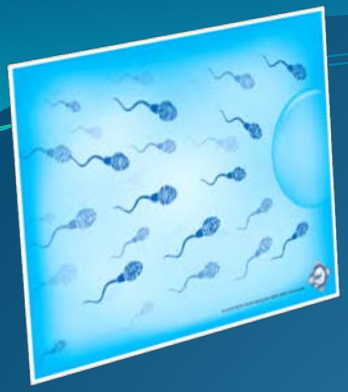
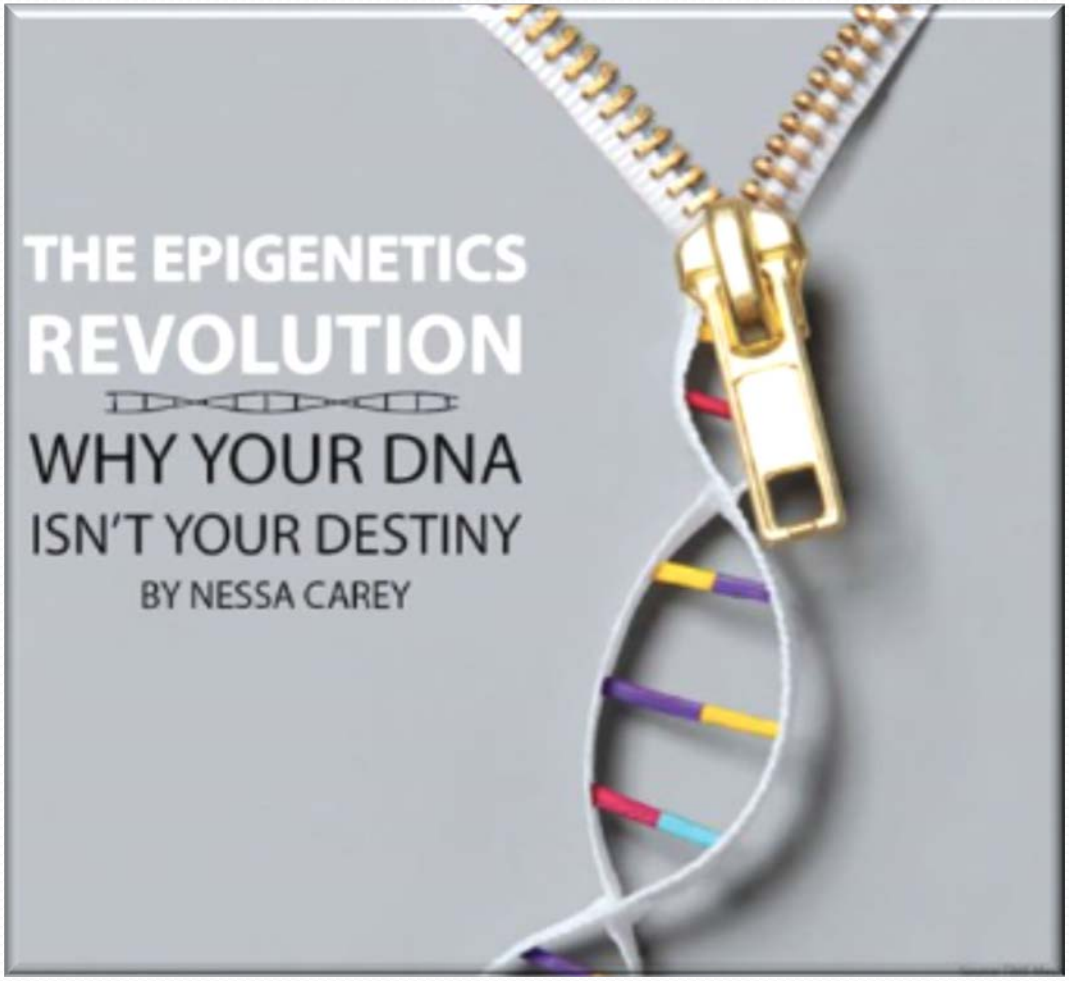




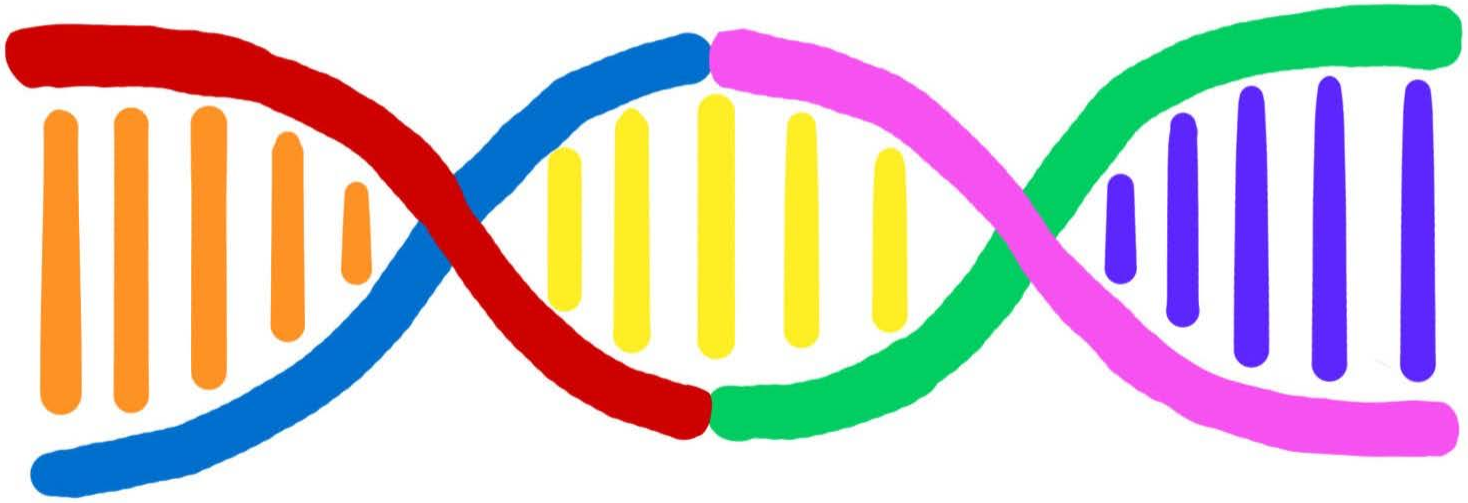
Eredità epigenetica transgenerazionale

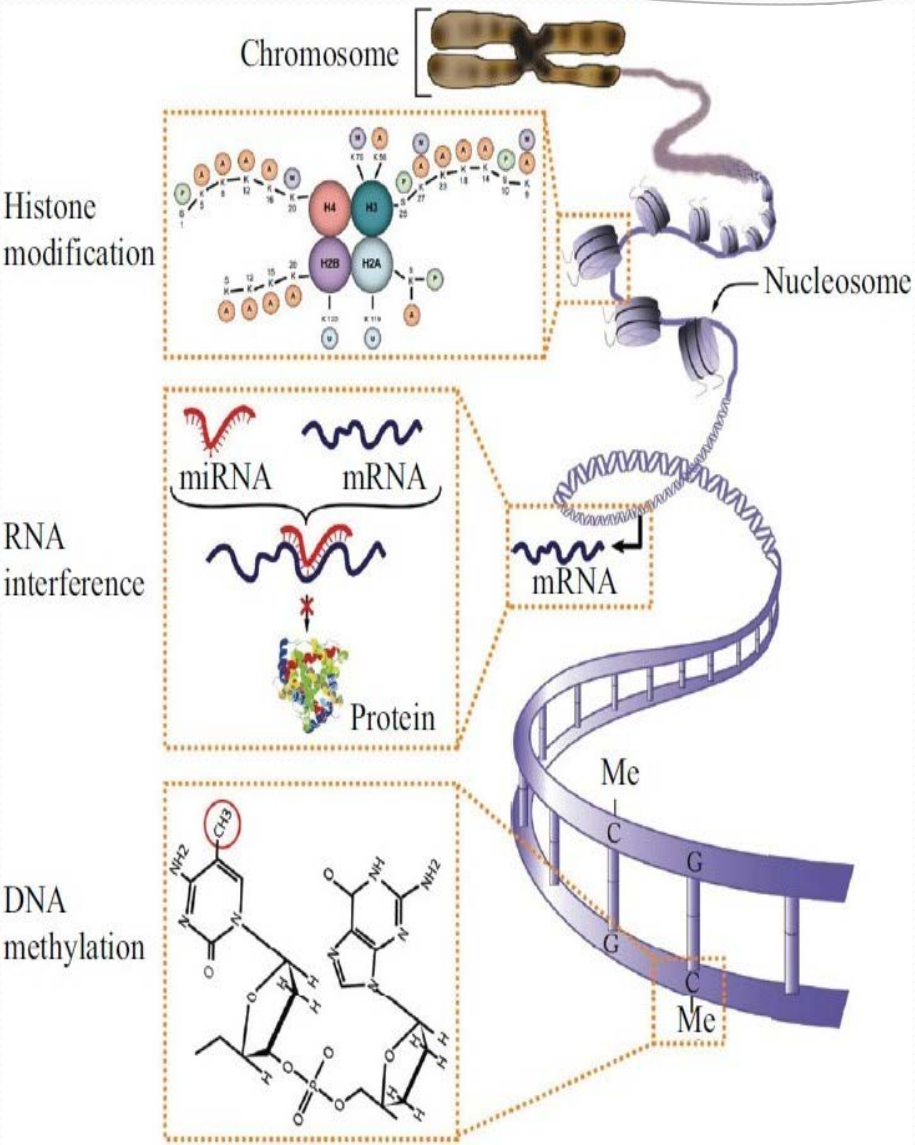


L. Stuppia, Medical Genetics
G. d'Annunzio University Chieti-Pescara, Italy

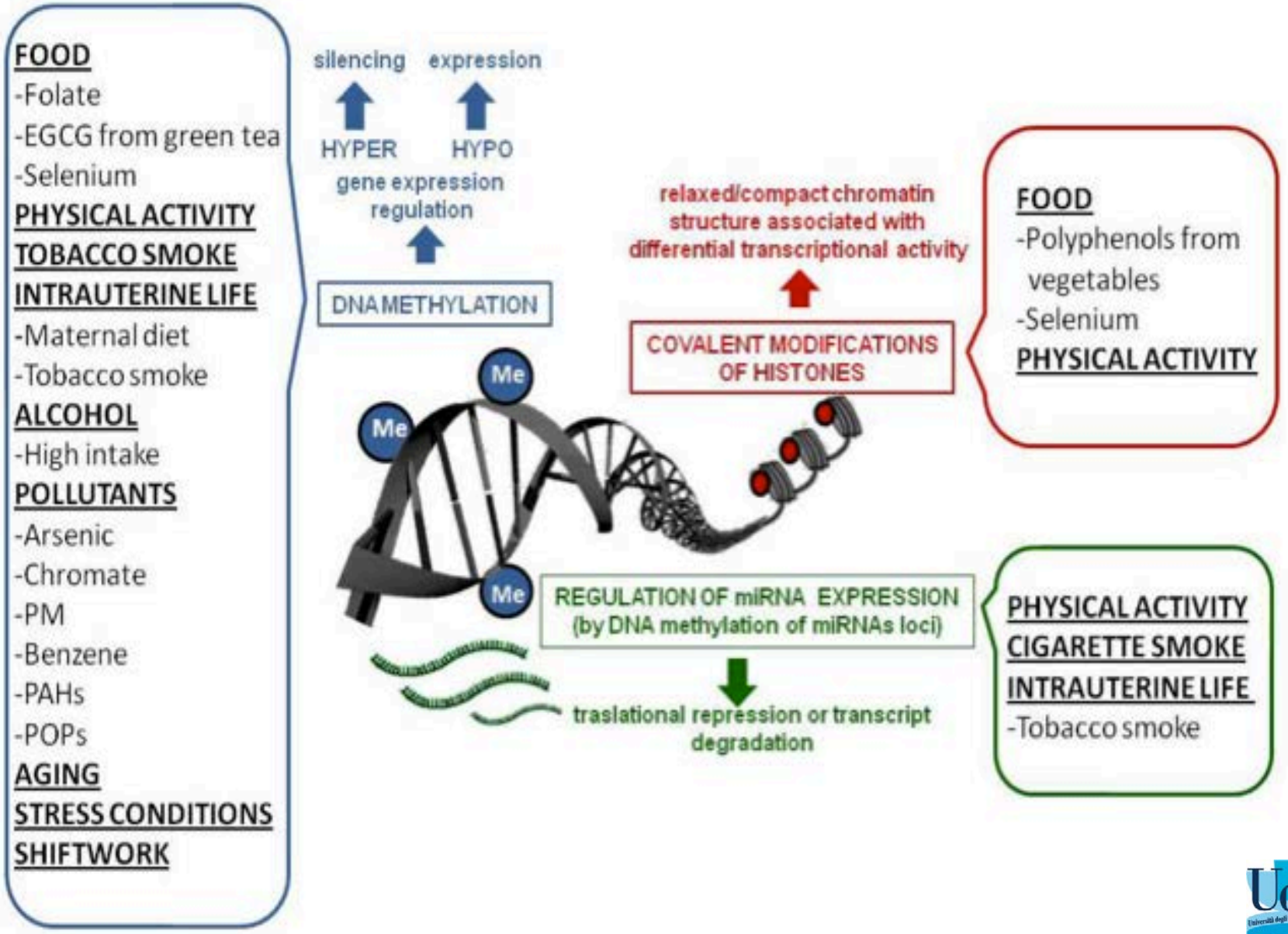

THE EPIGENETICS
REVOLUTION
WHY YOUR DNA
ISN'T YOUR DESTINY
BY NESSA CAREY

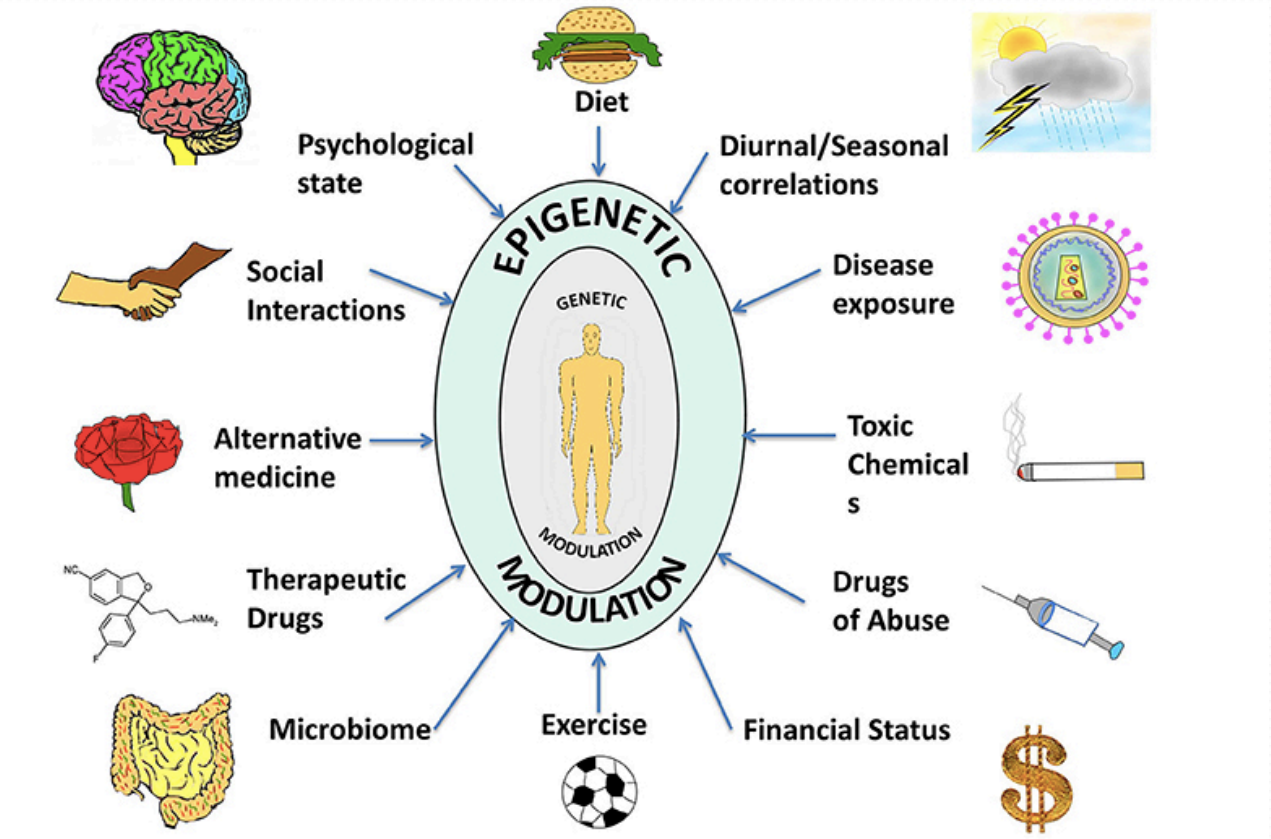
WHAT IS EPIGENETICS?




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

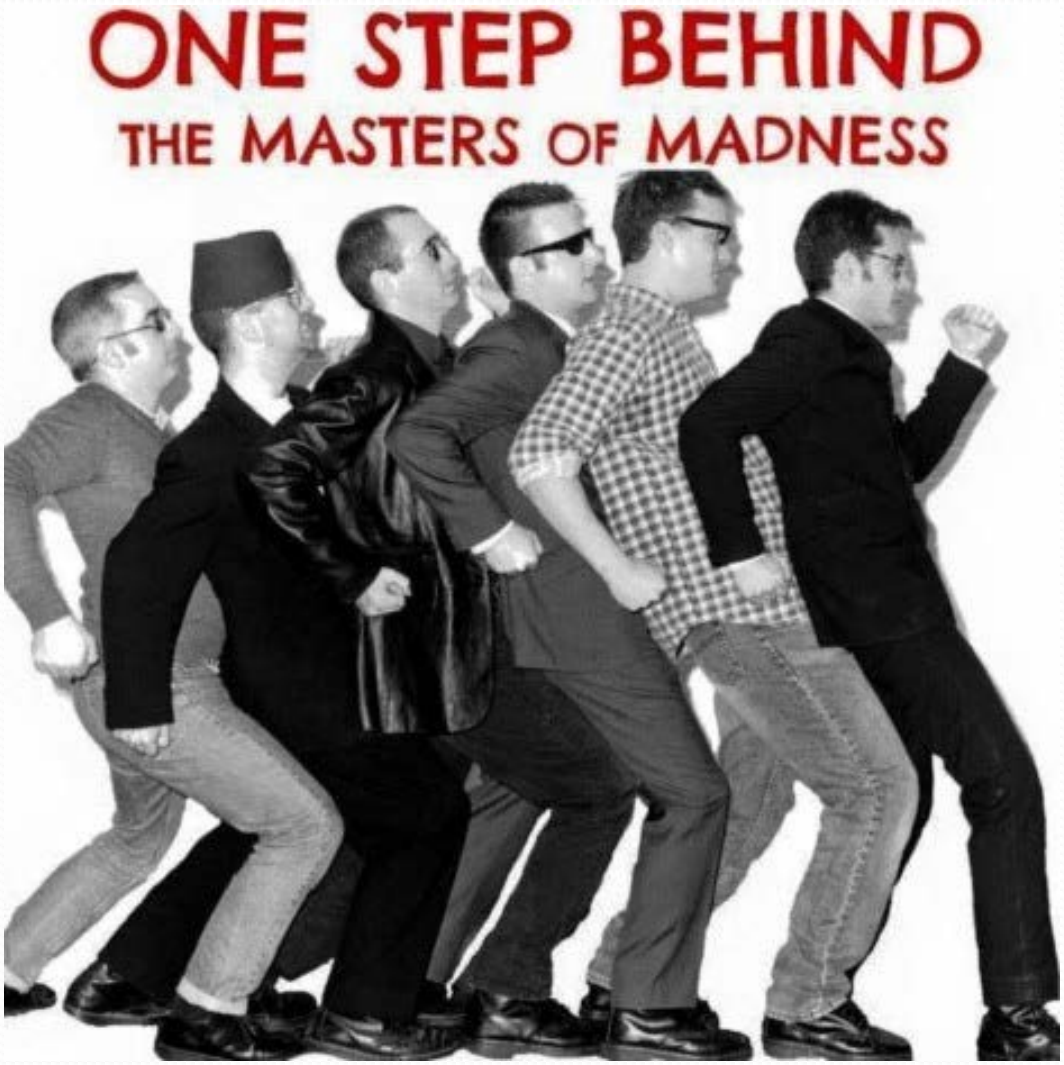
Epigenomics. 2011 June ; 3(3): 267–277.





Kanherkar et al. Front. Cell Dev. Biol., 2014


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


ONE STEP BEHIND
THE MASTERS OF MADNESS

Noncommunicable diseases

Fact sheet
Updated June 2017

World Health Organization

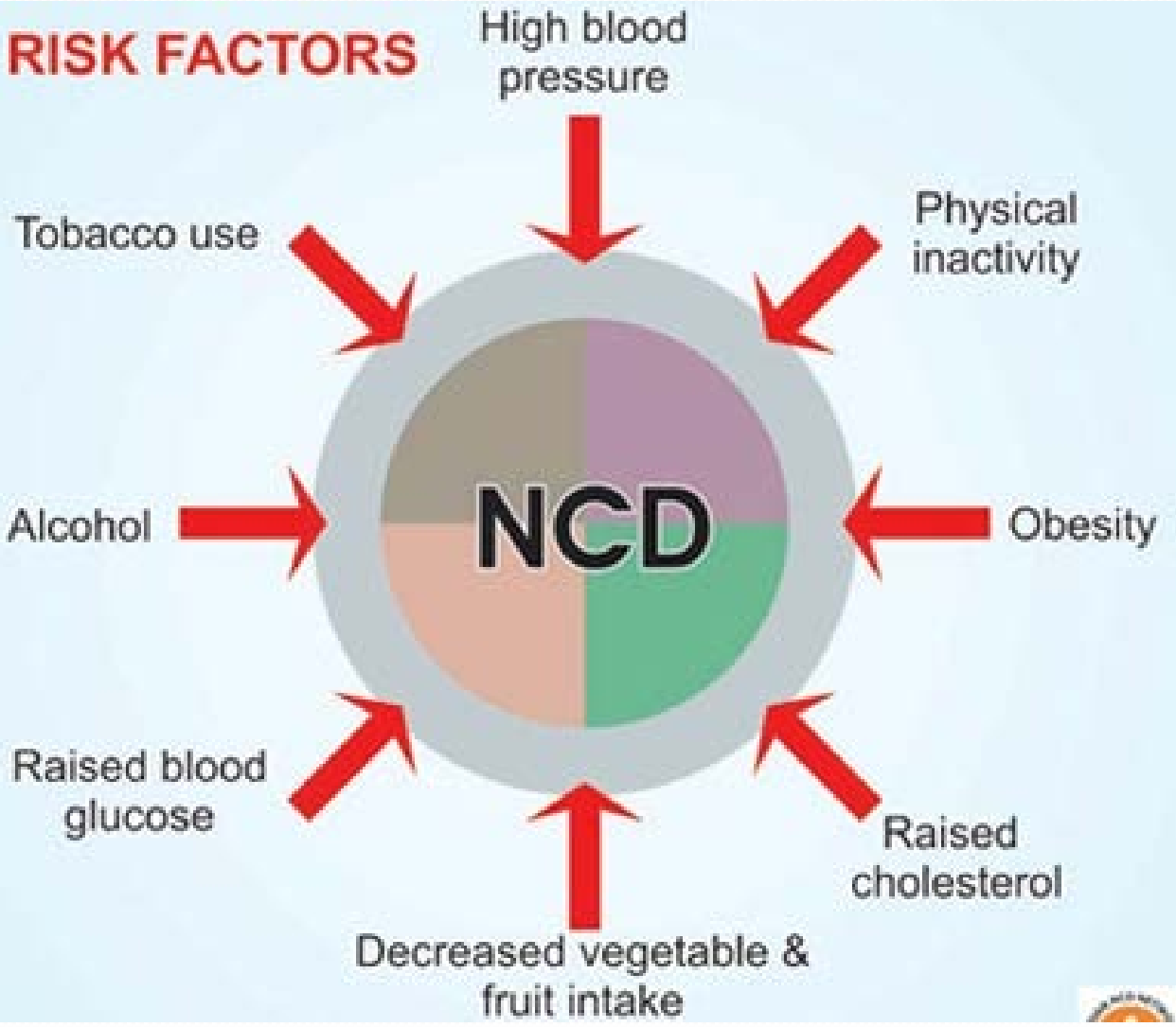
Key facts

- Noncommunicable diseases (NCDs) kill 40 million people each year, equivalent to 70% of all deaths globally.
- Each year, 15 million people die from a NCD between the ages of 30 and 69 years; over 80% of these "premature" deaths occur in low- and middle-income countries.
- Cardiovascular diseases account for most NCD deaths, or 17.7 million people annually, followed by cancers (8.8 million), respiratory diseases (3.9million), and diabetes (1.6 million).
- These 4 groups of diseases account for over 80% of all premature NCD deaths.
- Tobacco use, physical inactivity, the harmful use of alcohol and unhealthy diets all increase the risk of dying from a NCD.
- Detection, screening and treatment of NCDs, as well as palliative care, are key components of the response to NCDs.





E' tutta colpa tua?


RISK FACTORS
High blood pressure
Tobacco use
Physical inactivity
Alcohol
NCD
Obesity
Raised blood glucose
Raised cholesterol
Decreased vegetable & fruit intake







Le cose migliori della vita o sono illegali o immorali o fanno ingrassare **(O. Wilde)**









Barker hypothesis: fetal environment and early infant health permanently programme the body's metabolism and growth, and thus determine the pathologies of old age

The fetal and infant origins of adult disease

The womb may be more important than the home

A hundred years ago, when tuberculosis and rheumatic heart disease were common, the proposition that the childhood environment affects adult health would have been self evident. This proposition may still hold, even though infective disease has given place to degenerative disease.

Studies in Norway, Finland, Britain, and the United States have shown that death rates from cardiovascular disease are inversely related to adult height, and geographical differences in cardiovascular mortality are related to past differences in infant mortality.[1-7] These findings have been interpreted as evidence that adverse living conditions during childhood, such as poor housing and diet, increase the risk of ischaemic heart disease.[4] Case-control studies have generally supported this[8-12]: patients with myocardial infarction have higher infant death rates among their siblings,[8 9] are more likely to come from larger families, and are more likely to have fathers who were unemployed.[10] Now studies in Finland show that men with ischaemic heart disease had worse socioeconomic conditions in childhood (p 1121)[12]—an observation also made in Britain.[9]

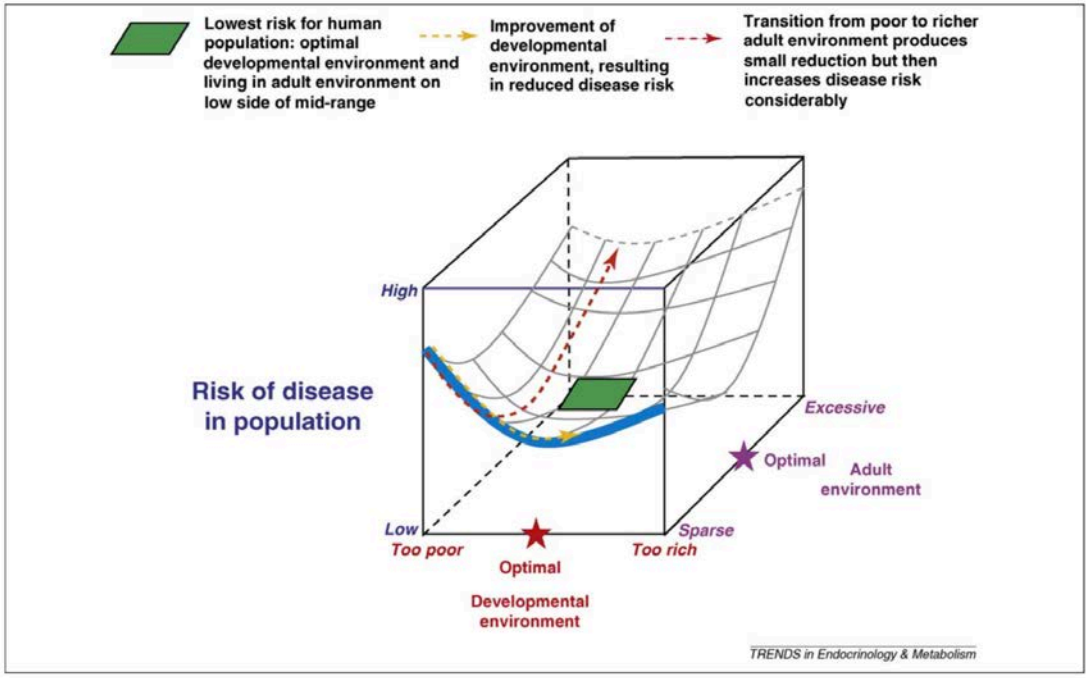
The completeness of infant mortality records in England and Wales from 1911 onwards has allowed detailed geographical comparisons of the relation between infant mortality 70 years ago and mortality from cardiovascular disease today. Differences in the death rates from cardiovascular disease among the 212 local authority areas of England and Wales are closely related to past differences in neonatal mortality.[6 13] Most neonatal deaths were associated with low birth weight, and rates were high in areas where mothers had poor health and high death rates during childbirth.[14 15] These findings suggested that research should be redirected towards the intrauterine environment rather than the environment in later childhood—housing, family income, diet, and other influences. The Medical Research Council employed a historian to search for old records of birth baboons.[16] Knowledge of the fetal processes that may determine programming is beginning to emerge.[20] A recent symposium heard evidence that diseases other than cardiovascular disease may also be determined by the maternal environment.[21] Schizophrenia and obstructive lung disease are two examples.

The old model of adult degenerative disease was based on the interaction between genes and an adverse environment in adult life. The new model that is developing will include programming by the environment in fetal and infant life.

D J P BARKER

Director,
MRC Environmental Epidemiology Unit,
University of Southampton,
Southampton General Hospital,
Southampton SO9 4XY

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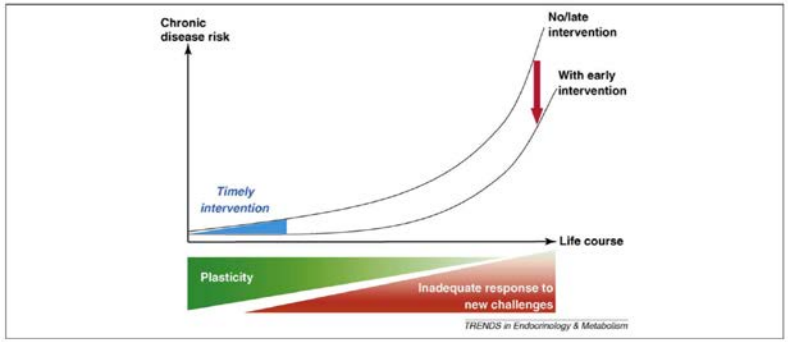


Review

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]




Environment Special:
The oceans—why 70% of our planet is in danger
The Facebook Movie:
The secret history of social networking
TIME
How the first nine months shape the rest of your life
The new science of fetal origins
BY ANNIE MURPHY PAUL



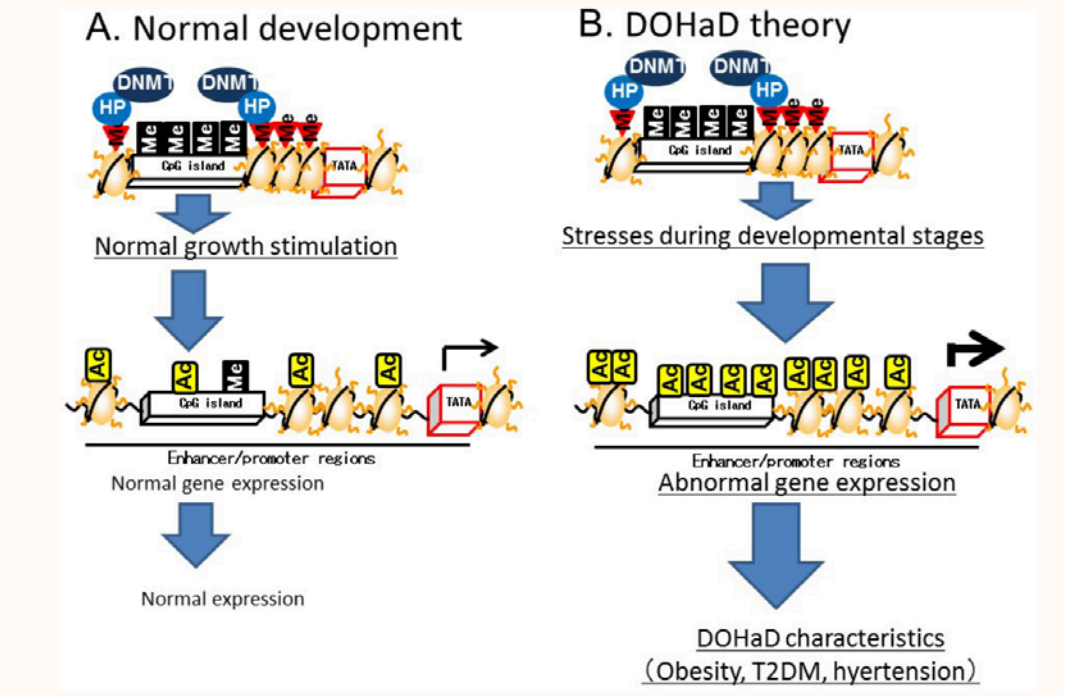
FIRST 1000 DAYS

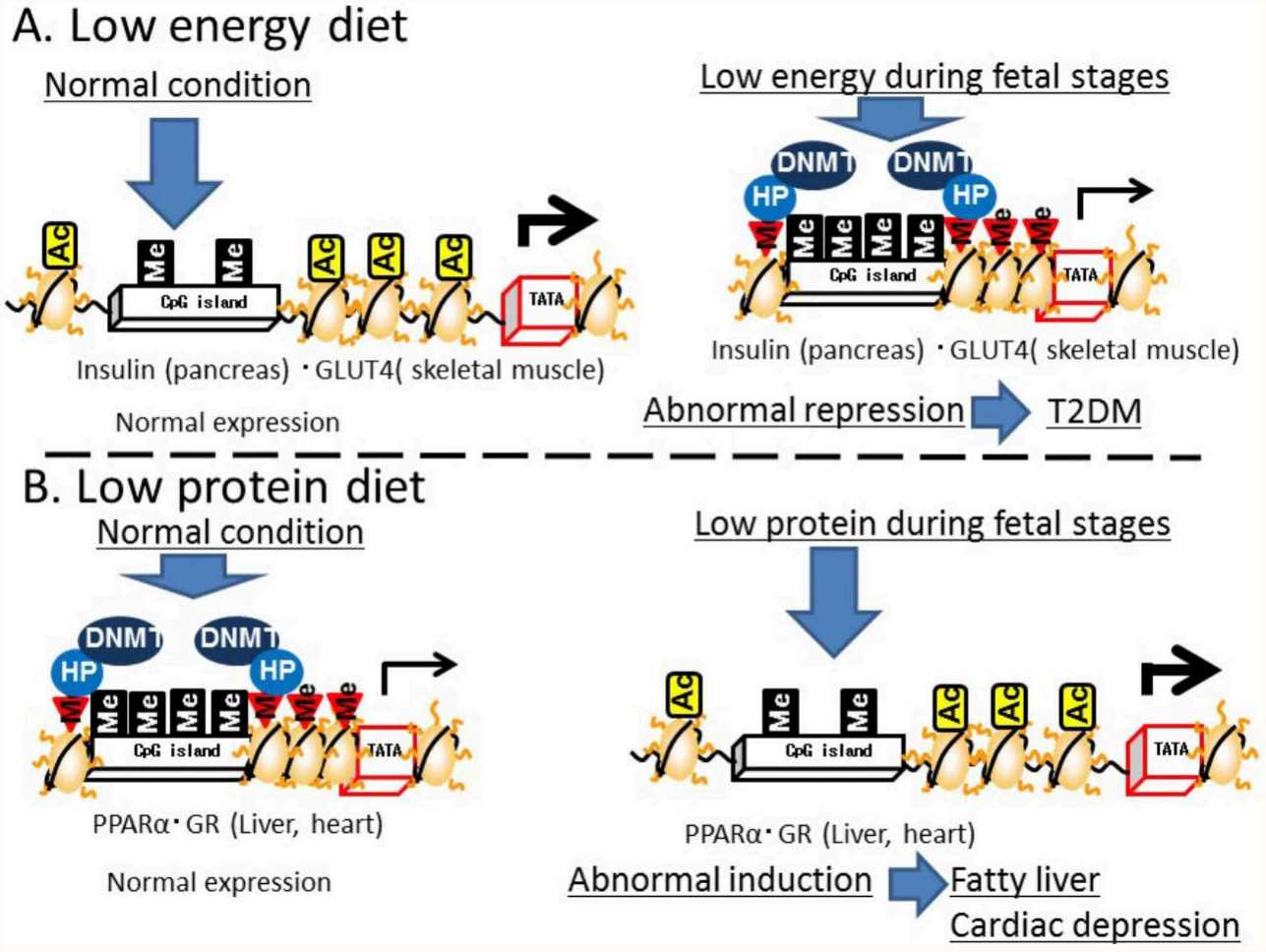
nutrition now, matters forever

Review

The Role of Epigenetics in Developmental Programming and the Developmental Origins of Health and Disease

Kazuki Mochizuki [1,*], Chihiro Imai [2], Noriko Sato [2], Takeo Kubota [3]





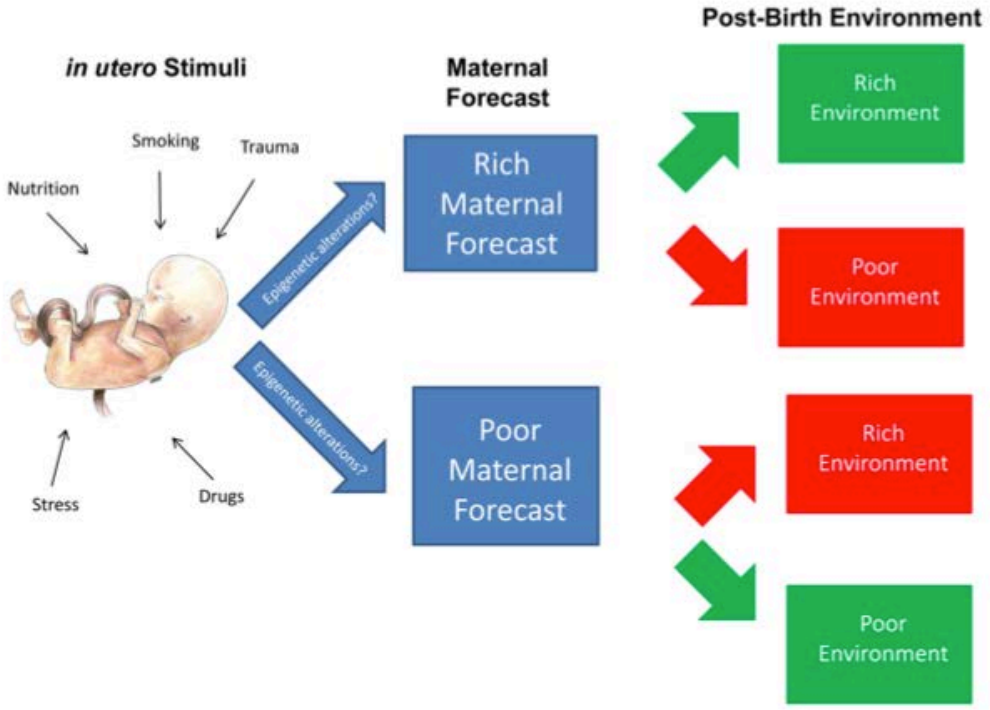
Malnutrition during the fetal period reduces insulin activity and induces impaired glucose tolerance iof the pancreas and skeletal muscle

Induction of PPARA and GR expression in the heart and liver could lead to cardiac muscle disorders and fatty liver

Published in final edited form as:
Dev Psychopathol. 2012 November ; 24(4): 1377–1390. doi:10.1017/S0954579412000776.

The Epigenetics of Maternal Cigarette Smoking During Pregnancy and Effects on Child Development

Valerie S. Knopik[1,2,*], **Matthew A. Maccani**[1,3,*], **Sarah Francazio**[1,4], and **John E. McGeary**[5,1,2]





SPECIAL SECTION PARENTING

REVIEW

Parenting from before conception

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

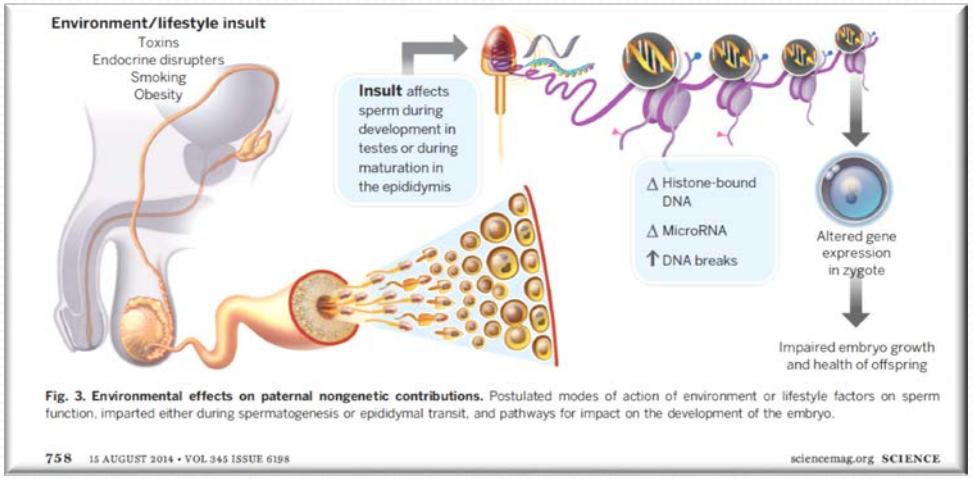
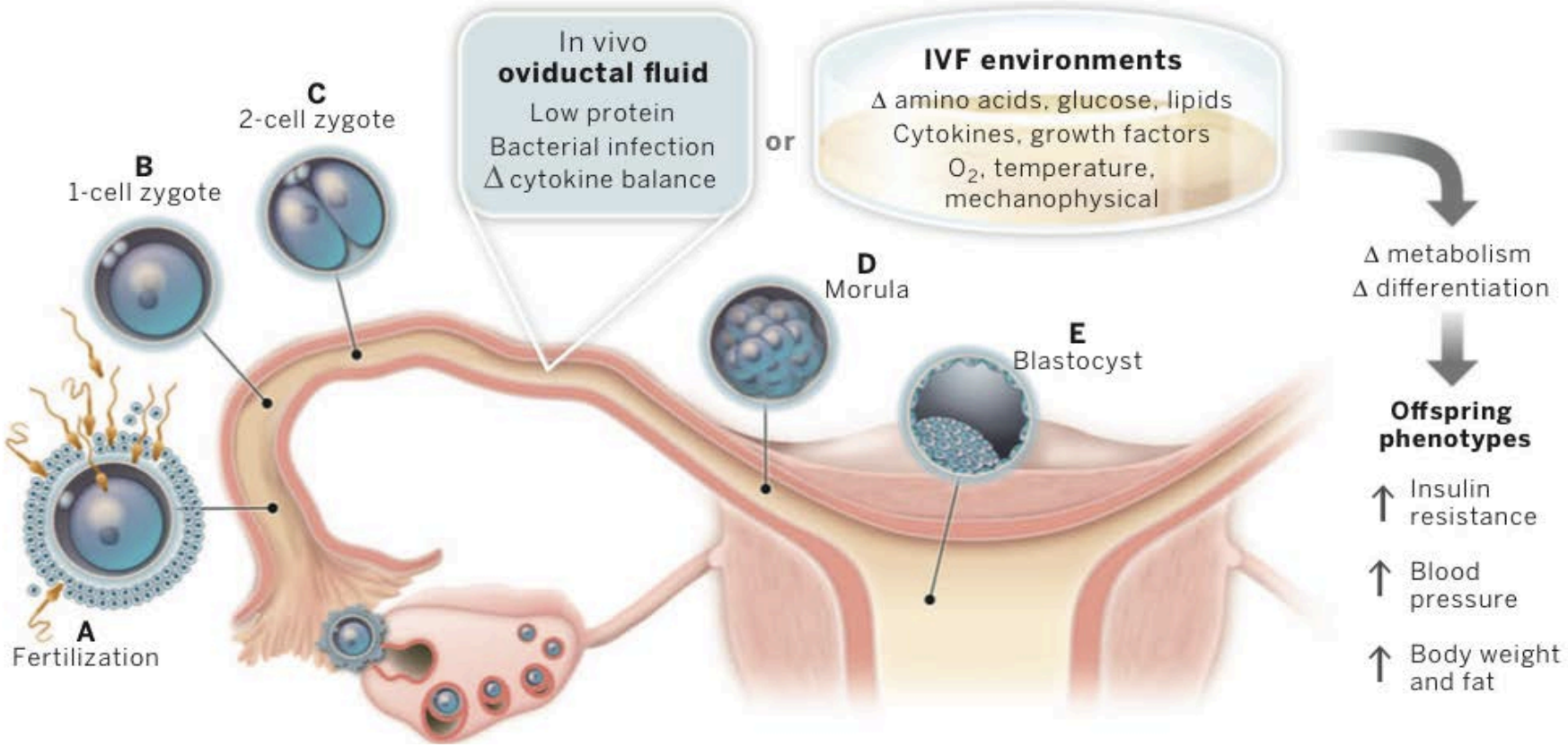


Fig. 3. Environmental effects on paternal nongenetic contributions. Postulated modes of action of environment or lifestyle factors on sperm function, imparted either during spermatogenesis or epididymal transit, and pathways for impact on the development of the embryo.

REVIEW

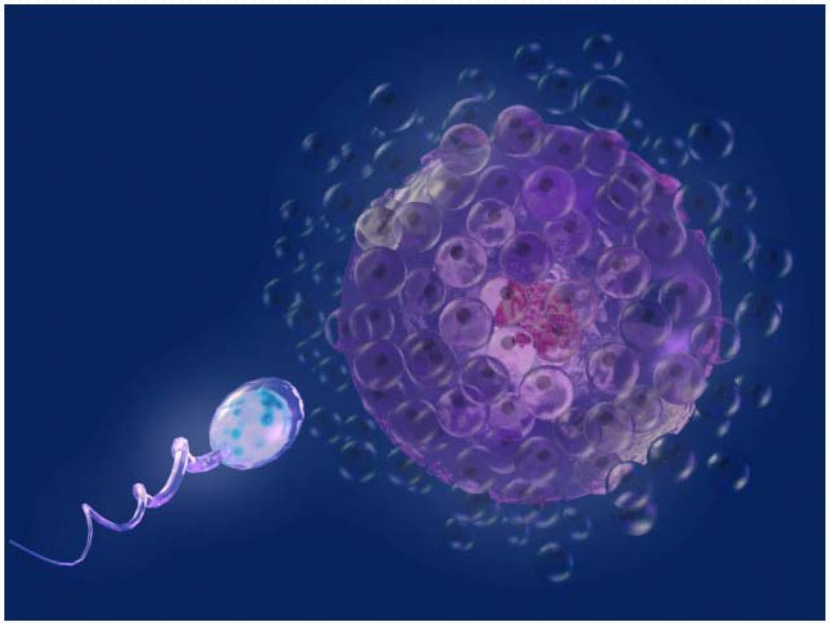
Parenting from before conception

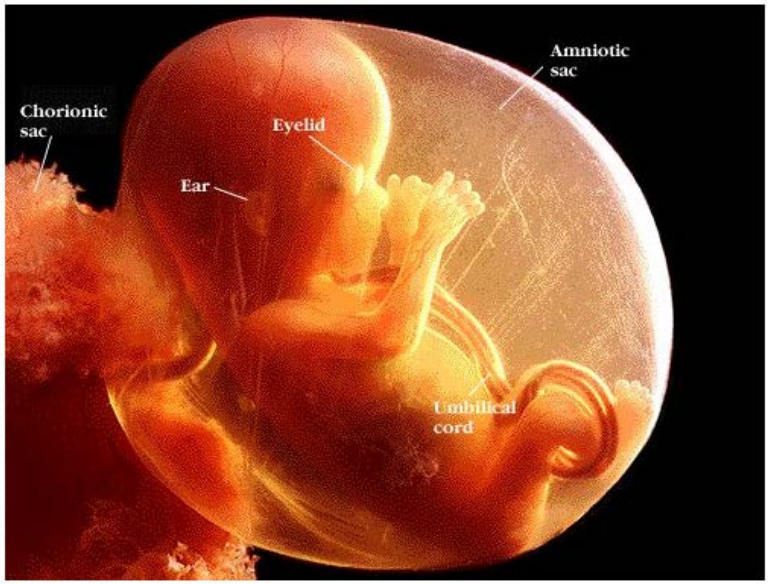
Michelle Lane, Rebecca L. Robker, Sarah A. Robertson*



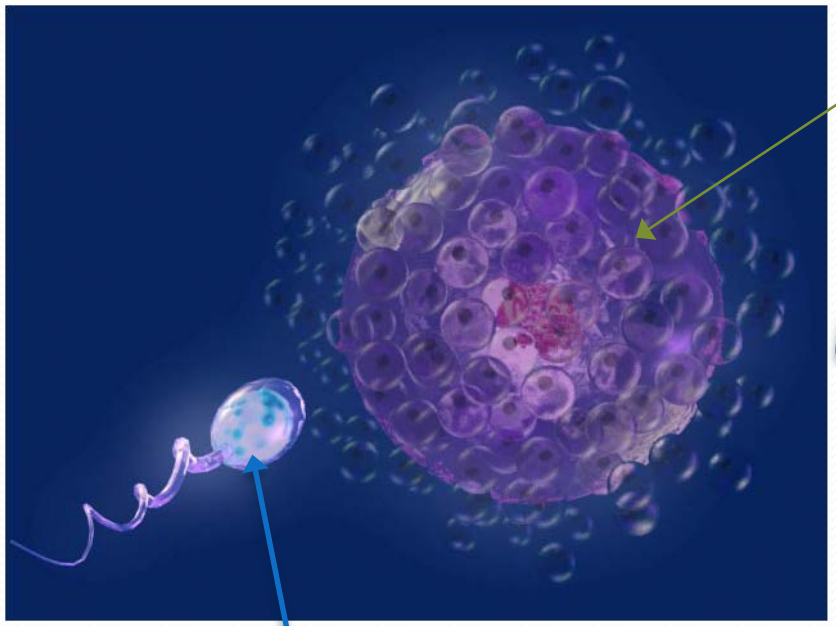
Human reproduction: the genetic vision

23+23=46



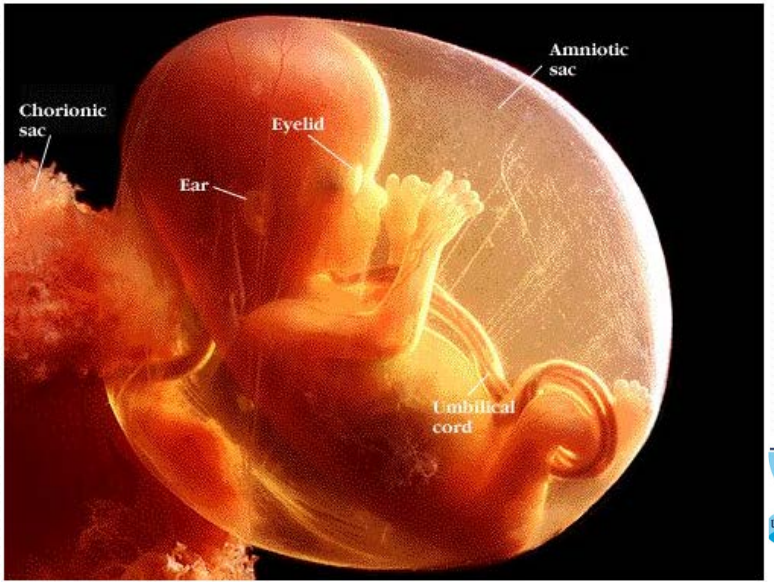


Human reproduction: the epigenetic vision

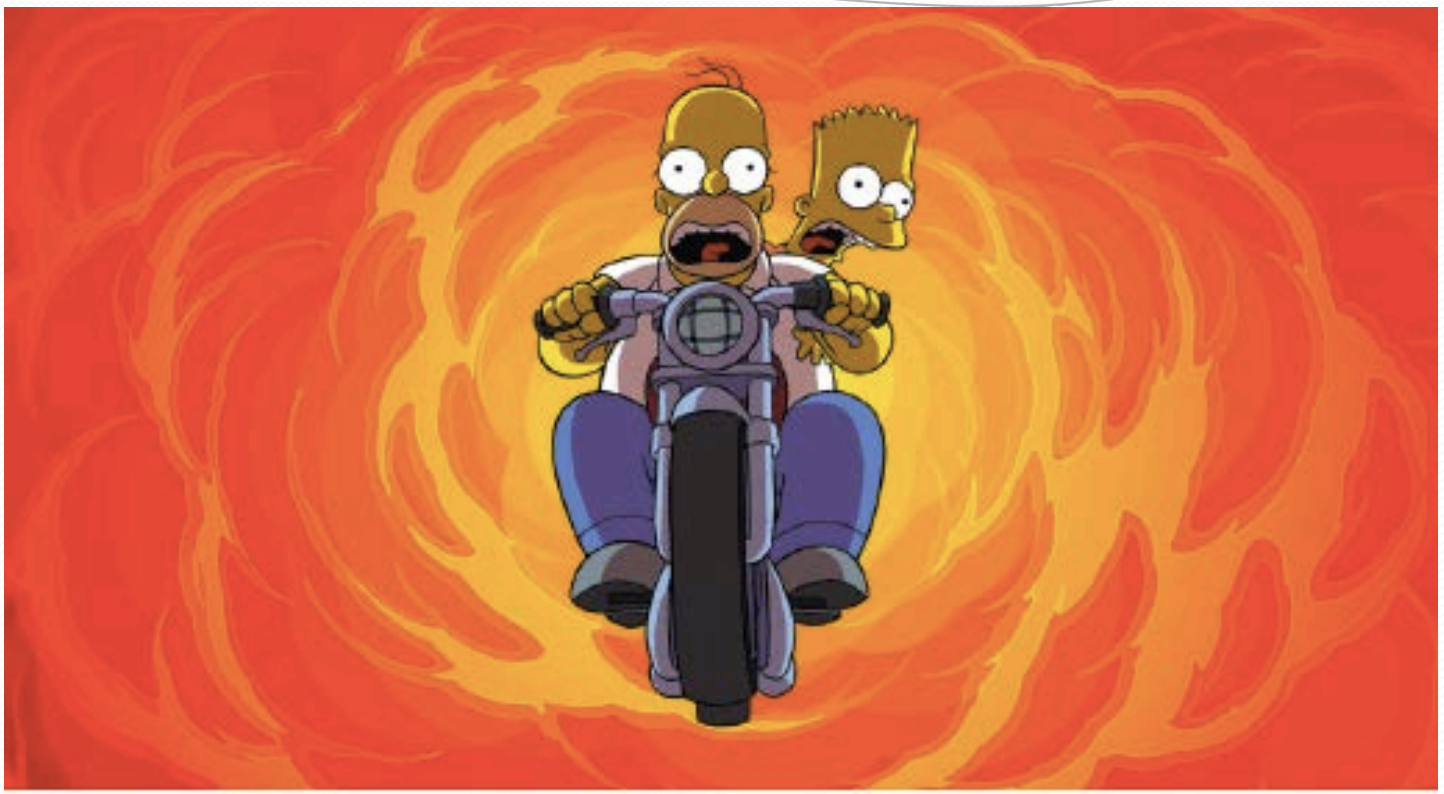


Maternal life style and environmental exposure

Different susceptibility to early or late onset diseases

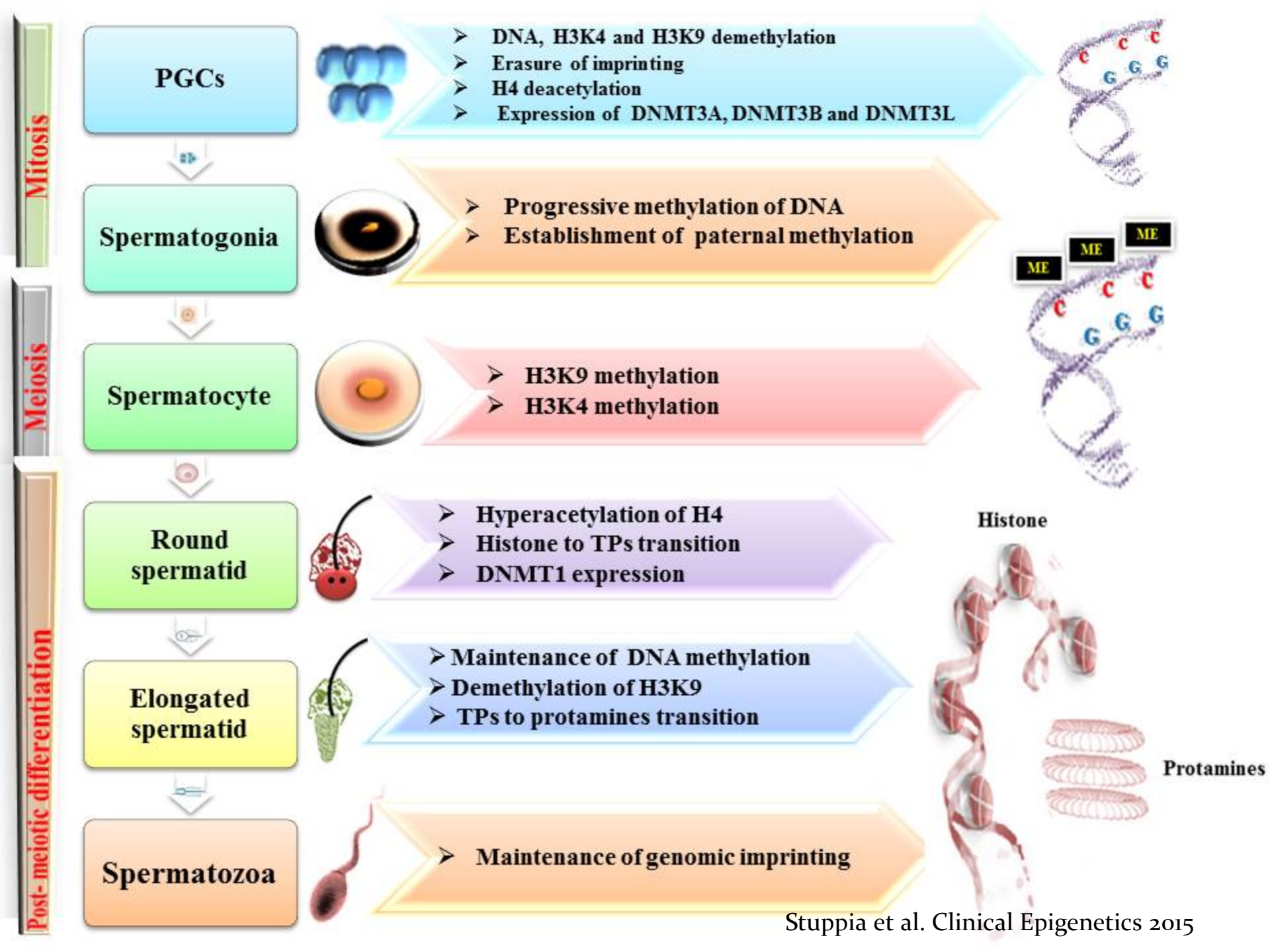


Paternal life style and environmental exposure



THE *SINS* OF THE FATHER

The roots of inheritance may extend beyond the genome, but the mechanisms remain a puzzle.



Stuppia et al. Clinical Epigenetics 2015

Stuppia et al. Clinical Epigenetics (2015) 7:120
DOI 10.1186/s13148-015-0155-4

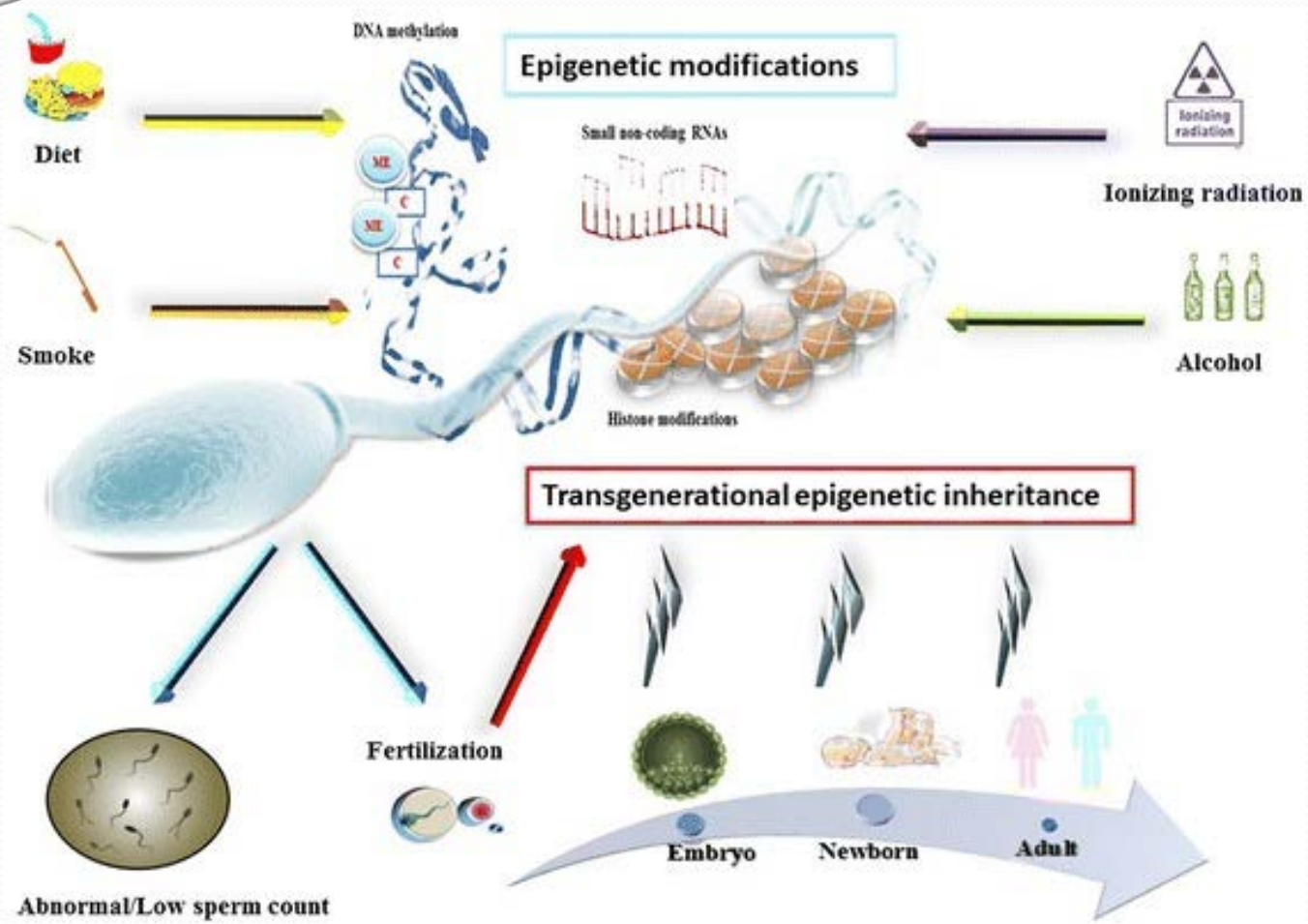
CLINICAL EPIGENETICS

Open Access

REVIEW

Epigenetics and male reproduction: the consequences of paternal lifestyle on fertility, embryo development, and children lifetime health

Liborio Stuppia[1,3*], Marica Franzago[1], Patrizia Ballerini[2], Valentina Gatta[1,3] and Ivana Antonucci[1,3]





THINK AGAIN

Insights & Perspectives

BioEssays

www.bioessays-journal.com

Epigenetics as a Driver of Developmental Origins of Health and Disease: Did We Forget the Fathers?

Adelheid Soubry

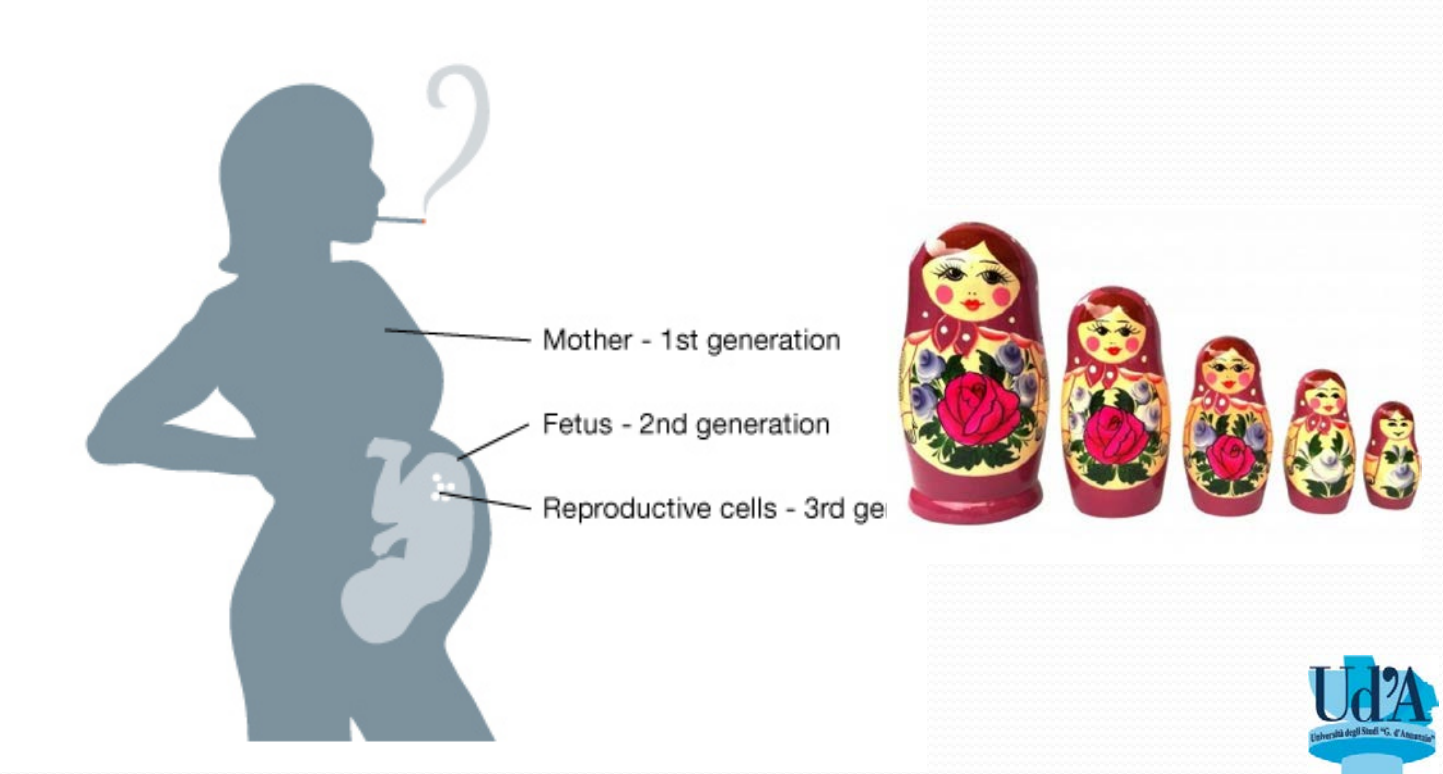
BioEssays 2018, 40, 1700113

«I suggest the term paternal exposome, as the origin of health and disease from paternal influences (or POHaD)»

Epigenetic inheritance which refers to the inheritance of information independent of the DNA sequence, is the most probable mechanism by which the environment could affect offspring

(Wei et al.,2014)

Transgenerational or *Intergenerational* epigenetic inheritance?



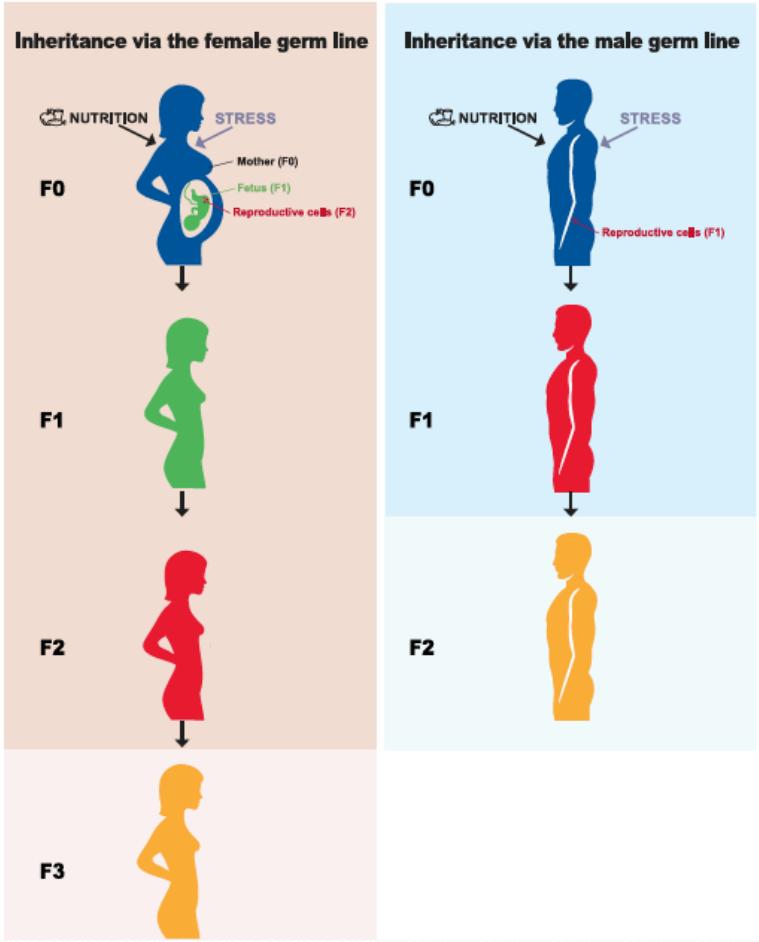


THE FASEB JOURNAL • REVIEW • www.fasebj.org

Transgenerational epigenetic inheritance in mammals: how good is the evidence?

Sanne D. van Otterdijk* and Karin B. Michels*,†,‡,1

*Institute for Prevention and Cancer Epidemiology, University Medical Center Freiburg, Freiburg, Germany; †Obstetrics and Gynecology Epidemiology Center, Department of Obstetrics, Gynecology and Reproductive Biology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; and ‡Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts



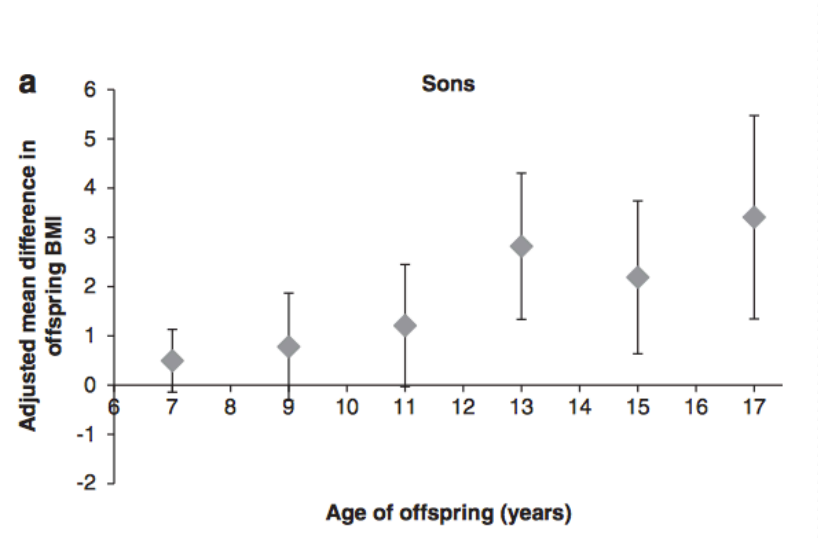
European Journal of Human Genetics (2014) 22, 1382–1386
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www.nature.com/ejhg

EJHG Open

ARTICLE

Prepubertal start of father's smoking and increased body fat in his sons: further characterisation of paternal transgenerational responses

Kate Northstone[1], Jean Golding[1,2], George Davey Smith[1,3], Laura L Miller[1] and Marcus Pembrey*[,1,2,4]



Published in final edited form as:
Int J Obes (Lond). 2016 March ; 40(3): 531–537. doi:10.1038/ijo.2015.186.

Is grand-parental smoking associated with adolescent obesity? A three-generational study

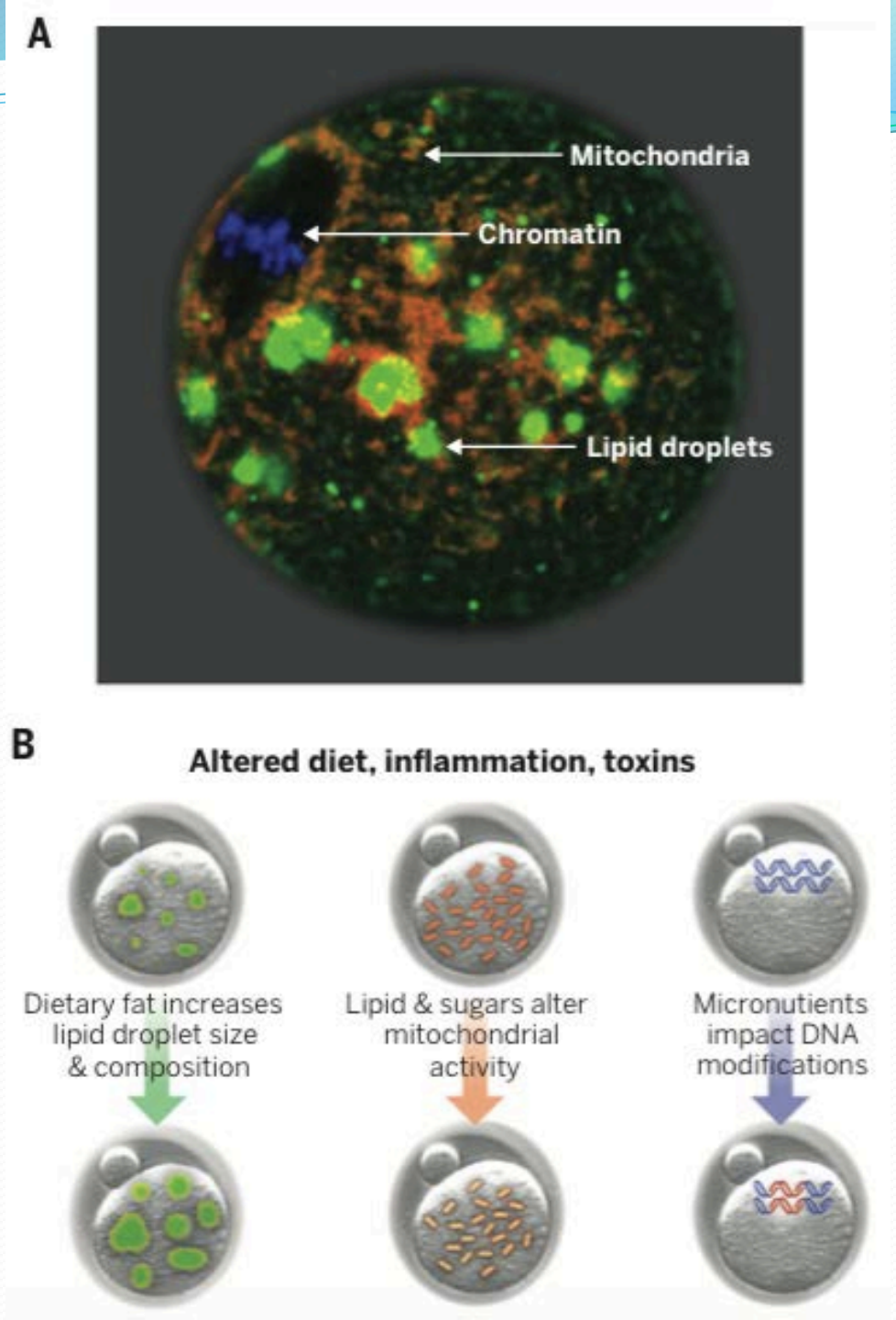
Marcelle M. Dougan, ScD[1], Alison E. Field, ScD[1,2,3], Janet W. Rich-Edwards, ScD[1,2,4], Susan E. Hankinson, ScD[1,2,5], Robert J. Glynn, PhD[6,7], Walter C. Willett, MD, DrPH[1,2,8], and Karin B. Michels, ScD, PhD[1,2,9]

Conclusions—Our findings suggest that the association between maternal smoking and offspring obesity may not persist beyond the first generation. However, grand-paternal smoking may affect overweight status of the granddaughter, likely through the association between grand-paternal smoking and maternal smoking.

Ex ovo omnia: all things come from eggs

(Lane et al., 2014)





Lane et al., Science 2014

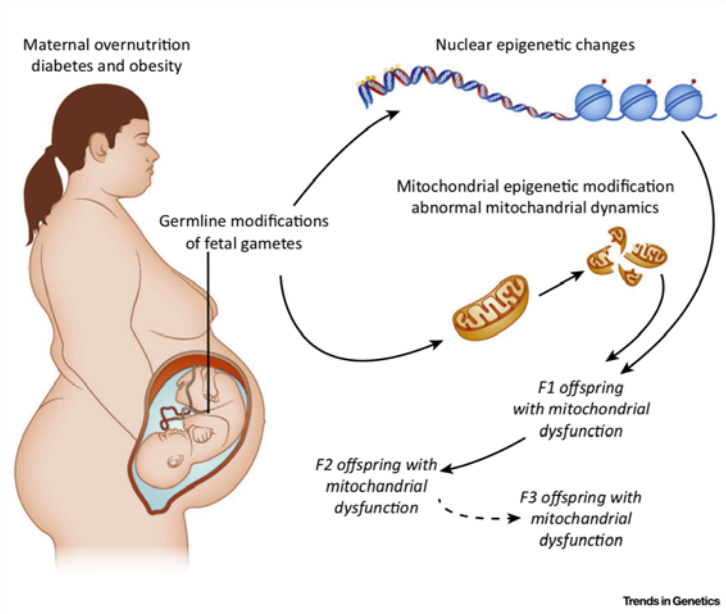
Trends in Genetics

CellPress

Review

Developmental and Transmittable Origins of Obesity-Associated Health Disorders

Arin K. Oestreich[1] and Kelle H. Moley[1,*]



Trends

Studies performed in both rodents and humans suggest that adverse maternal conditions during the pre- and perinatal period can cause long-term transgenerational epigenetic modifications in the offspring that mediate susceptibility to cardiometabolic disease.

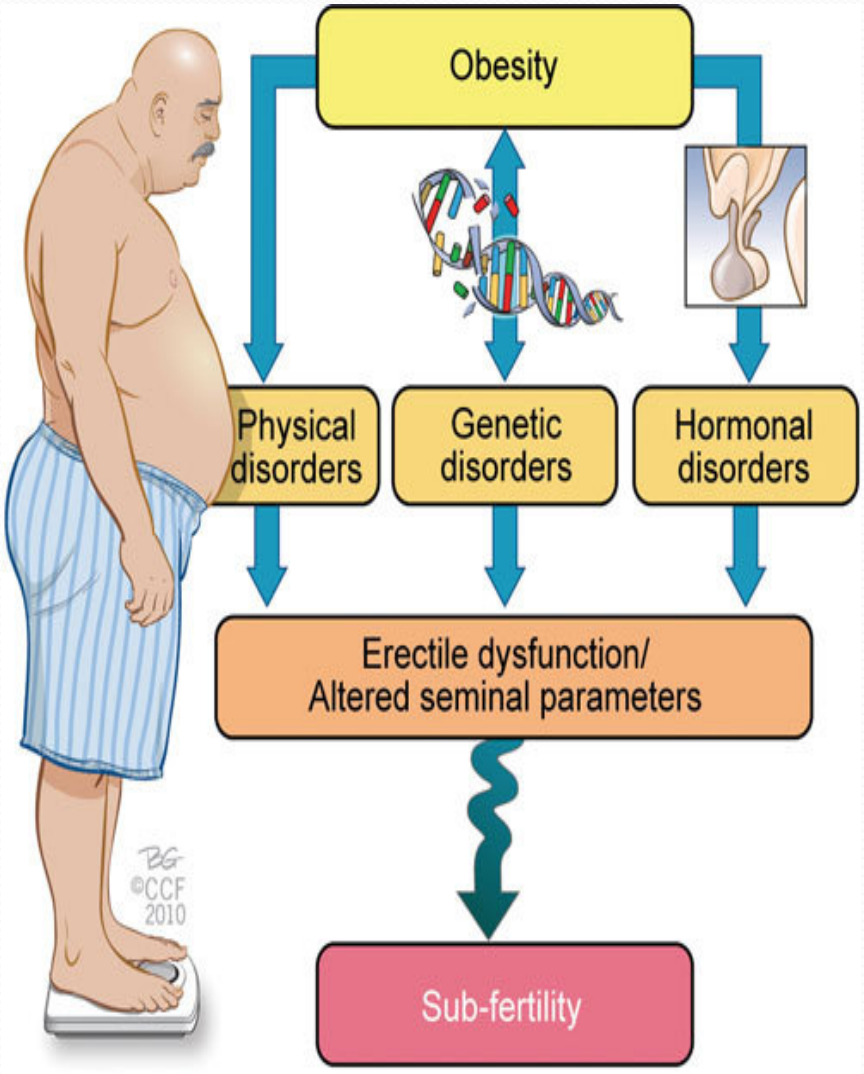
An adverse maternal environment exposes three generations and is transmitted epigenetically through the germline only if the F3 offspring are affected.

Rare regulatory sequences that escape systematic DNA demethylation and others that are able to maintain histone marks in the primordial germ cells represent a potential mechanism for non-imprinted transgenerational epigenetic inheritance.

Inheritance of damaged oocyte mitochondria is an important potential transgenerational mechanism to consider because they are passed exclusively from the mother and contain mitochondrial DNA subject to epigenetic regulation.

Ud'A
Università degli Studi "G. d'Annunzio"

The effects of obesity on male infertility and the mechanisms involved



Asian Journal of Andrology (2010) 12: 480–489
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www.nature.com/aja

Review

Obesity: modern man's fertility nemesis

Stephanie Cabler[1], Ashok Agarwal[1], Margot Flint[2], Stefan S. Du Plessis[2]

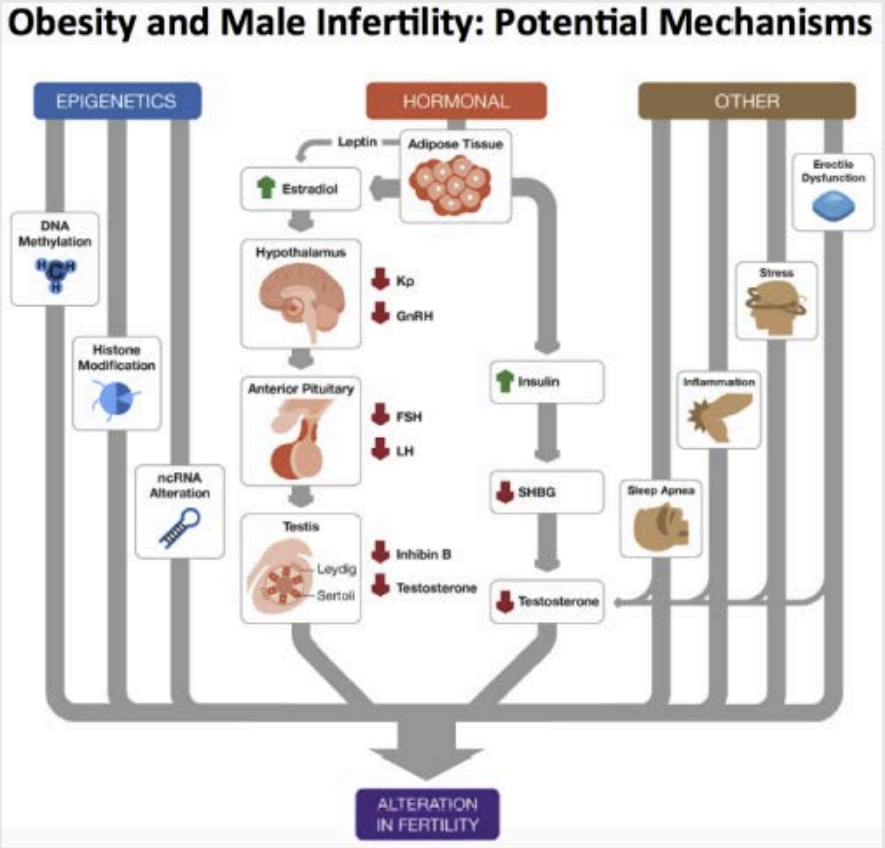
[1] *Center for Reproductive Medicine, The Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, USA*
[2] *Division of Medical Physiology, Faculty of Health Sciences, Stellenbosch University, PO Box 19063, Tygerberg 7505, South Africa*

Obesity, male infertility, and the sperm epigenome

James R. Craig, M.D.,[a,b] Timothy G. Jenkins, Ph.D.,[a] Douglas T. Carrell, Ph.D., H.C.L.D.,[a,c,d] and James M. Hotaling, M.D., M.S., F.E.C.S.M.[a,b,c]

[a] Division of Urology, Department of Surgery, [b] Center for Men's Health and Reconstructive Surgery, and [c] Department of Obstetrics and Gynecology, University of Utah; and [d] Department of Human Genetics, University of Utah School of Medicine, Salt Lake City, Utah

FIGURE 2



Obesity and male infertility: mechanisms. Obesity operates through multiple pathways to alter male reproductive potential. It creates epigenetic changes, some of which can influence subsequent generations. In addition, it alters the male androgenic axis, influences a host of other "neohormones," and raises insulin levels. Finally, it has been linked to erectile dysfunction and causes stress, inflammation and sleep apnea, all of which can further reduce male fertility. Kp = kisspeptin.

Craig. Obesity and sperm epigenetics. Fertil Steril 2017.

Soubry *et al. Clinical Epigenetics* (2016) 8:51
DOI 10.1186/s13148-016-0217-2

Clinical Epigenetics

RESEARCH Open Access

Obesity-related DNA methylation at imprinted genes in human sperm: Results from the TIEGER study

Adelheid Soubry[1*], Lisa Guo[2], Zhiqing Huang[2], Cathrine Hoyo[3], Stephanie Romanus[1], Thomas Price[4] and Susan K. Murphy[2,5*]

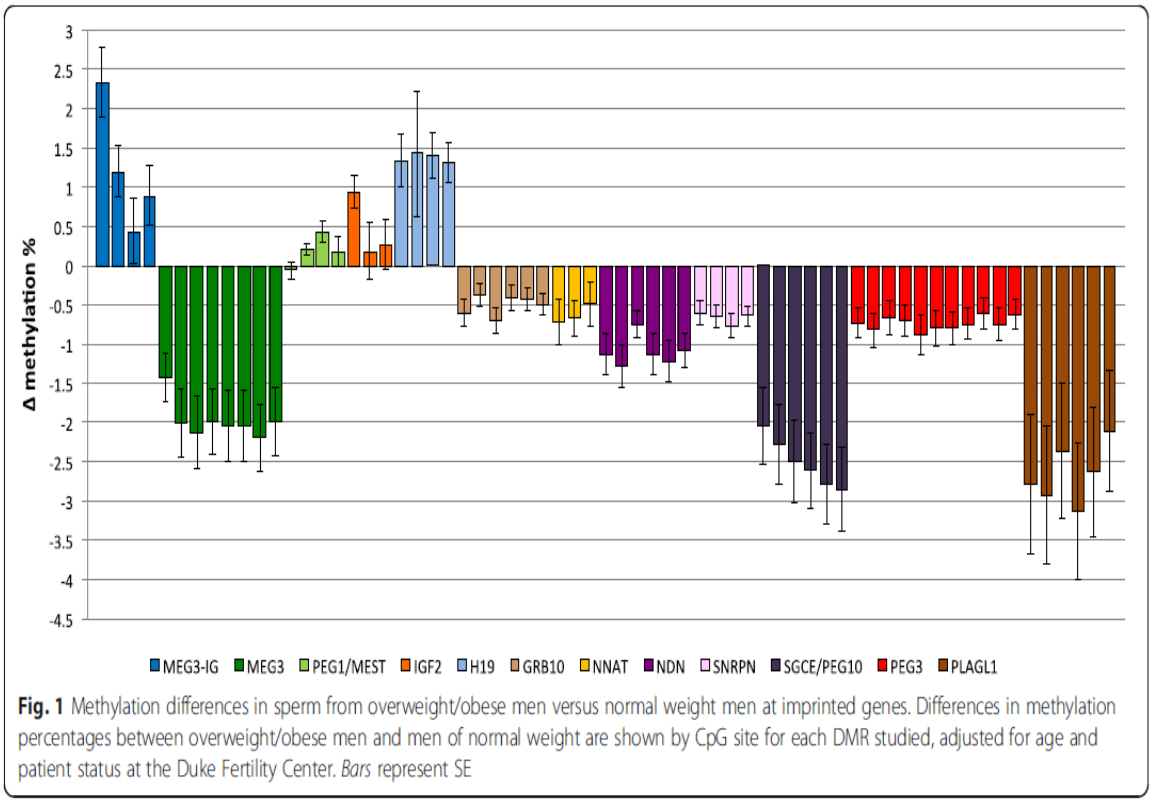
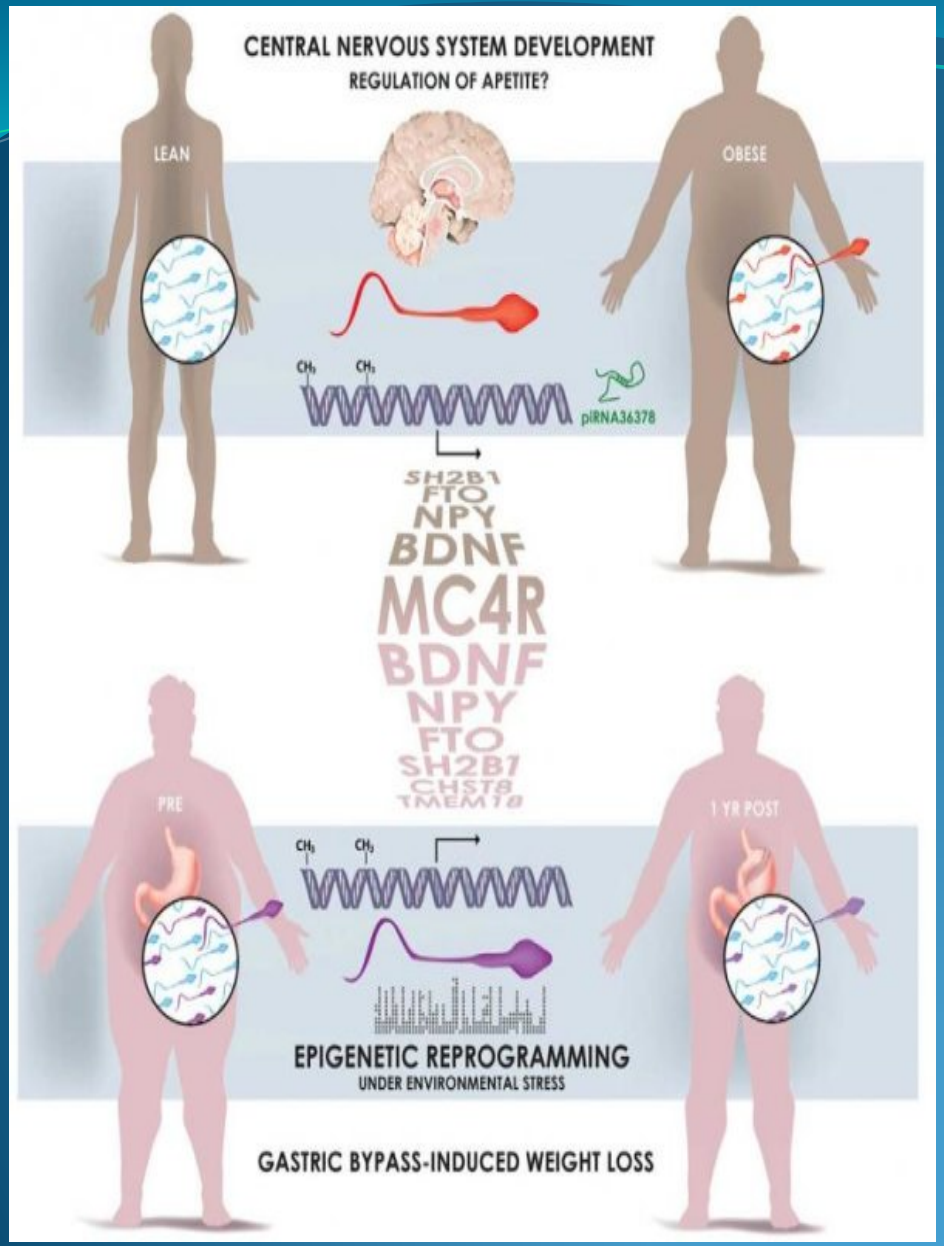


Fig. 1 Methylation differences in sperm from overweight/obese men versus normal weight men at imprinted genes. Differences in methylation percentages between overweight/obese men and men of normal weight are shown by CpG site for each DMR studied, adjusted for age and patient status at the Duke Fertility Center. *Bars* represent SE



Cell Metabolism

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Short Article

Obesity and Bariatric Surgery Drive Epigenetic Variation of Spermatozoa in Humans

Ida Donkin[1, 10], Soetkin Versteyhe[1, 10], Lars R. Ingerslev[1], Kui Qian[1], Mie Mechta[1], Loa Nordkap[2], Brynjulf Mortensen[3, 4, 9], Emil Vincent R. Appel[1], Niels Jørgensen[2], Viggo B. Kristiansen[5], Torben Hansen[1], Christopher T. Workman[6, 7], Juleen R. Zierath[1, 8], Romain Barrès[1,]

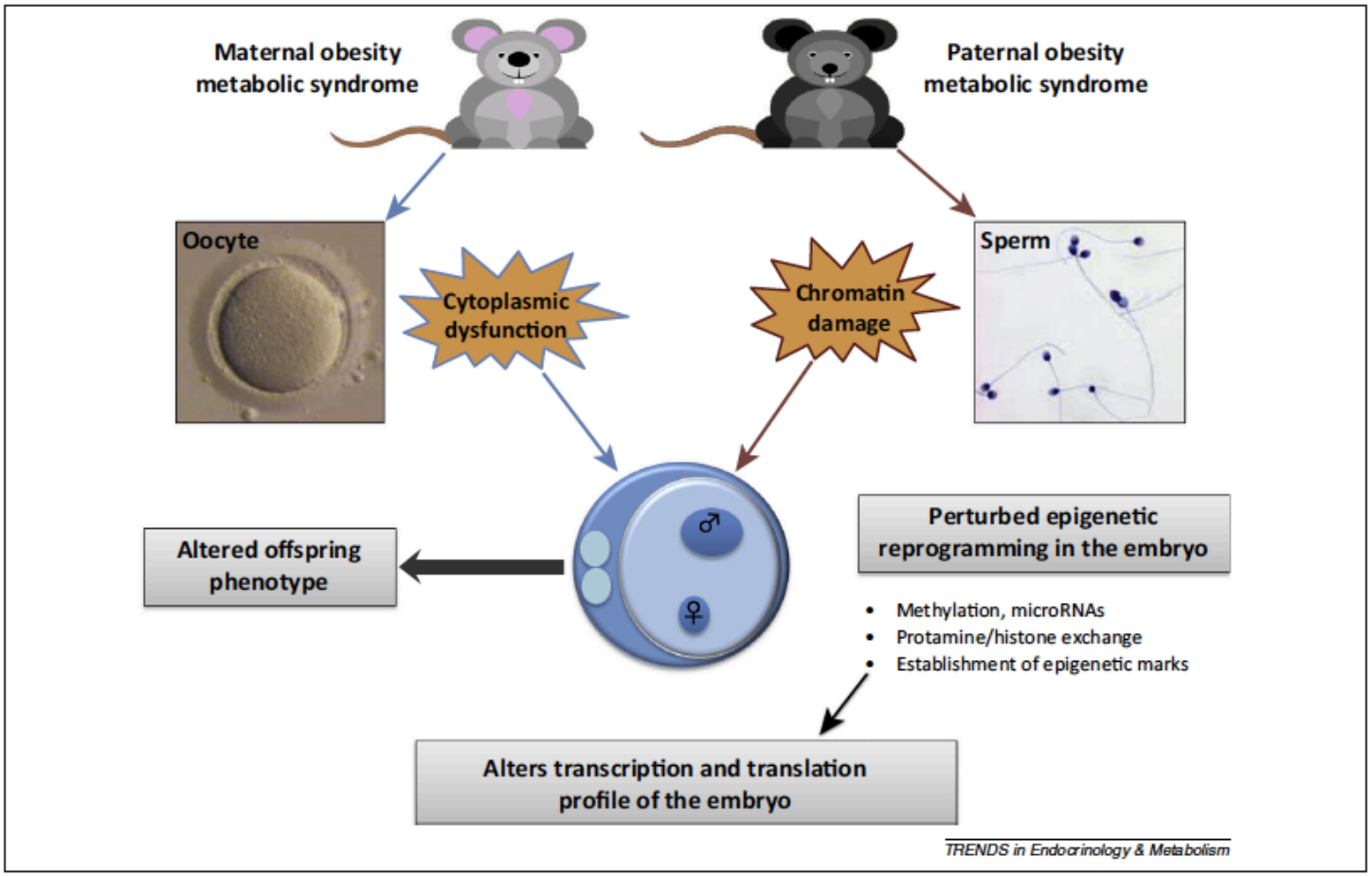
This figure shows how spermatozoa from obese men carry a distinct epigenetic signature compared to lean men, in particular at genes controlling brain development and function. The sperm methylome is dynamically remodeled after gastric-bypass-induced weight loss, notably at gene regions implicated in the central control of appetite.

CellPress
Review

Peri-conception parental obesity, reproductive health, and transgenerational impacts

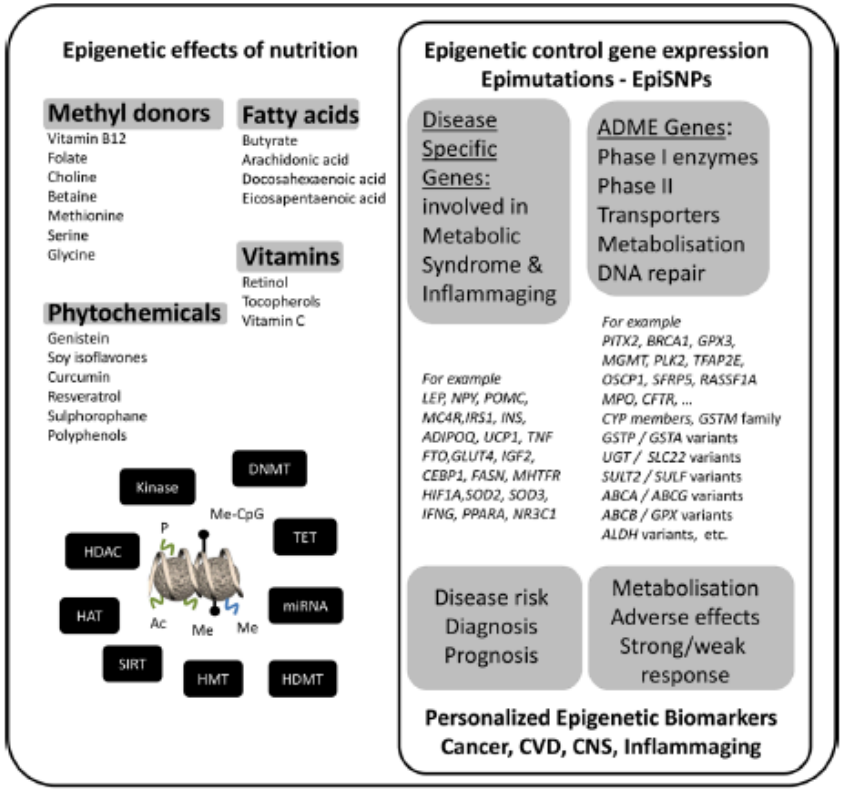
Michelle Lane[1,2,4], Deirdre L. Zander-Fox[1,3], Rebecca L. Robker[1], and Nicole O. McPherson[1,3,4]

[1] Robinson Research Institute, School of Paediatrics and Reproductive Health, University of Adelaide, Adelaide, South Australia
[2] Monash IVF Group, Richmond, Victoria, Australia
[3] Repromed, Dulwich, South Australia
[4] Freemasons Centre for Men's Health, University of Adelaide, Adelaide, South Australia



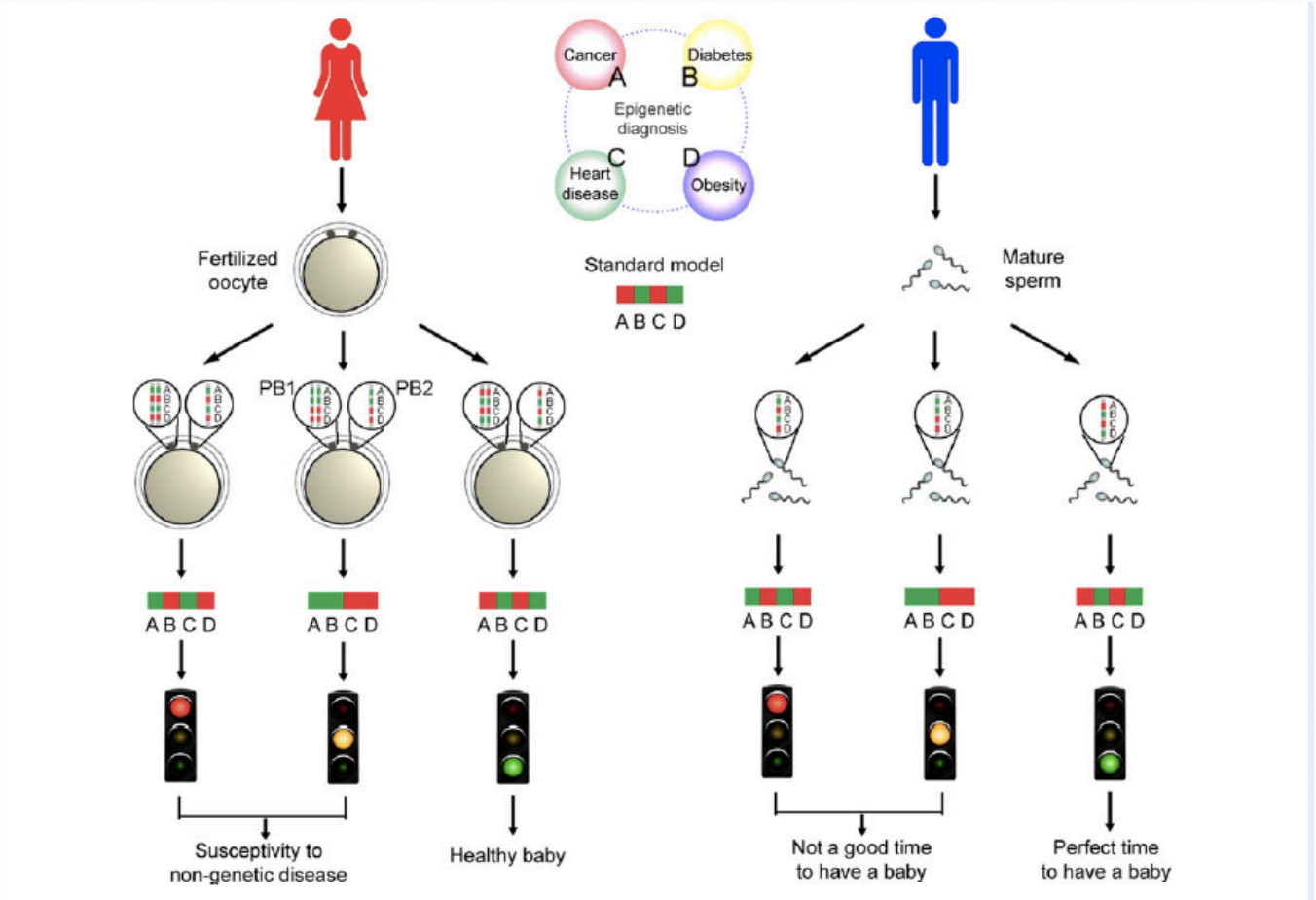


Nutritional Epigenetics



Personalized Nutrition


human reproduction update
Environmental epigenetic inheritance through gametes and implications for human reproduction
Yanchang Wei[1], Heide Schatten[2], and Qing-Yuan Sun[1,*]


Cancer
A
Diabetes
B
Epigenetic diagnosis
C
Heart disease
D
Obesity
Standard model
A B C D
Fertilized oocyte
PB1
PB2
Mature sperm
A B C D
A B C D
A B C D
A B C D
A B C D
A B C D
Susceptivity to non-genetic disease
Healthy baby
Not a good time to have a baby
Perfect time to have a baby


Reproductive health
development
services
pregnancy
maternal
aborted
implies
social
sexual
capability
reassignment
stateadopted
woman
international
year
morbidity
men
improve
research
abortion
antenatal
attempting
counseling
approach
legal
education
debate
planning
infertility
prevention
poorest
infirmity
deaths
term
fundamental
discursive
safe
mutilation
safer
endorses
childbirth
fetuses
access
improving
reconfirmed
health
consensus
methods
pandemic
strategy
sex
stated
birth
population
couples
physical
mortality
part
reproduce
definition
acceptable
family
absence
satisfying
mental
silent
countries
linkages
sexuality
care
control
target
reproductive
coercion
disparities
groups
indicators
unsafe
collate
broadened
childbearing
estimates
prevalence

You shall not bow down to them or worship them;
for I, the Lord your God, am a jealous God,
punishing the children for the sin of the parents
to the third and fourth generation of those who hate me

(Esodus, 20.5)