“Genetics loads the gun, Epigenetics pulls the trigger!”

DNA isn’t your destiny!

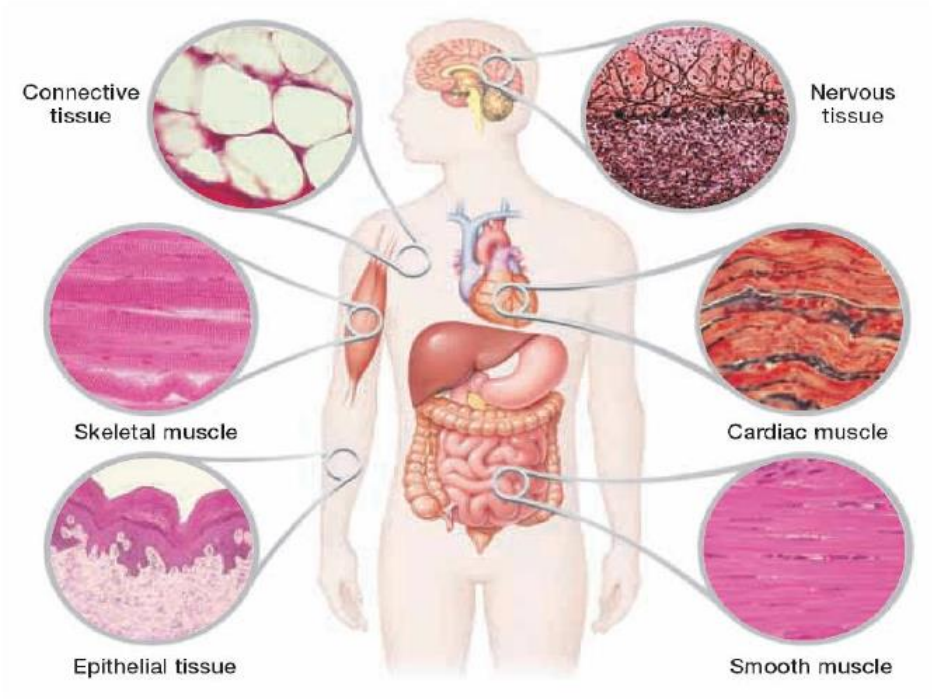
Dr Radhika Kandaswamy, PhD
Postdoctoral researcher
SGDP, KCL
@rkswamy16

Different species, not so different genome

50% 70% 90% 97% 98% 98-99%

Human Body Tissues

Same genome, different cells



And MZ twins,
What makes them different ?

Conrad Waddington 1942

"the interactions of genes with their environment that bring the phenotype into being"

epi = "on top of" (Greek)

Epigenetics

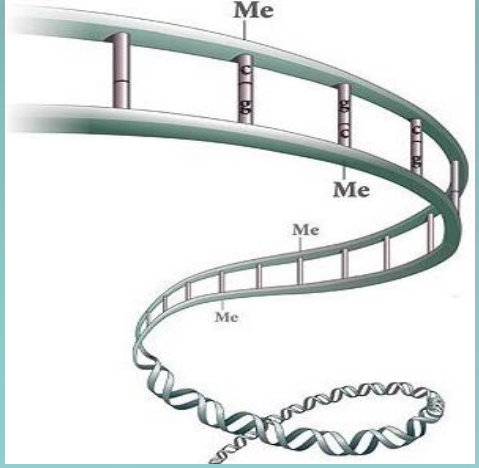
"…the reversible regulation of gene expression mediated principally through changes in DNA methylation and chromatin structure, occurring independently of the DNA sequence…"

Henikoff & Matzke 1997

Human Genome

"2.0×10^{13} mt"

That is the equivalent of nearly 70 trips from the earth to the sun and back!!!



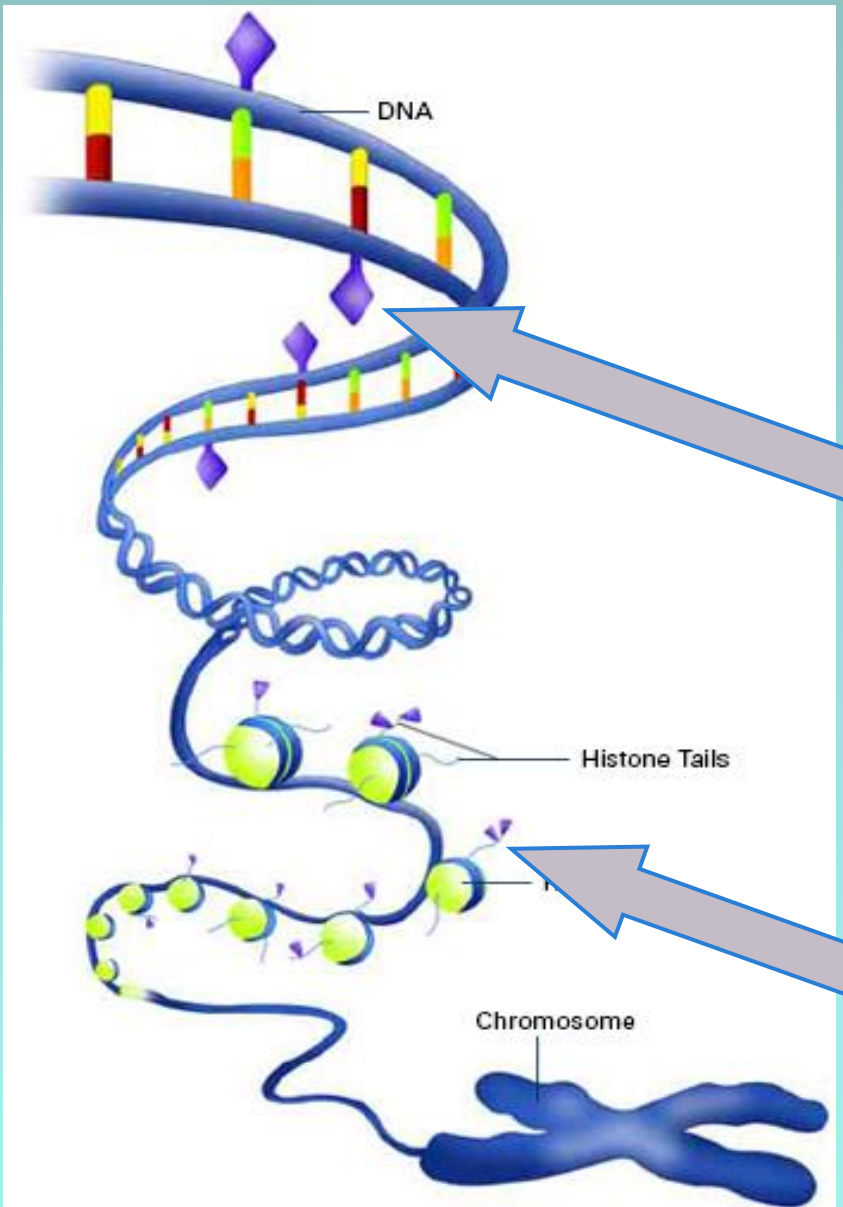
DNA Methylation
Histone modifications

Epi-genome

Environment

Phenotype

Epigenetic mechanisms: from chromosome to DNA



ncRNA

DNA methylation at Cytosine-p-Guanine island (CpG)

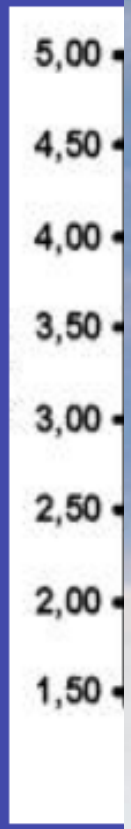
Histone modifications

Proc Natl Acad Sci

Epigenetic d

Fraga MF, Balles
C, Carlsson E, Po

Epigenetics Labora



Epigenetics: regulation of genomic activities

Scenario 'A'

The DNA sequence determines what specific mRNA molecules are synthesized

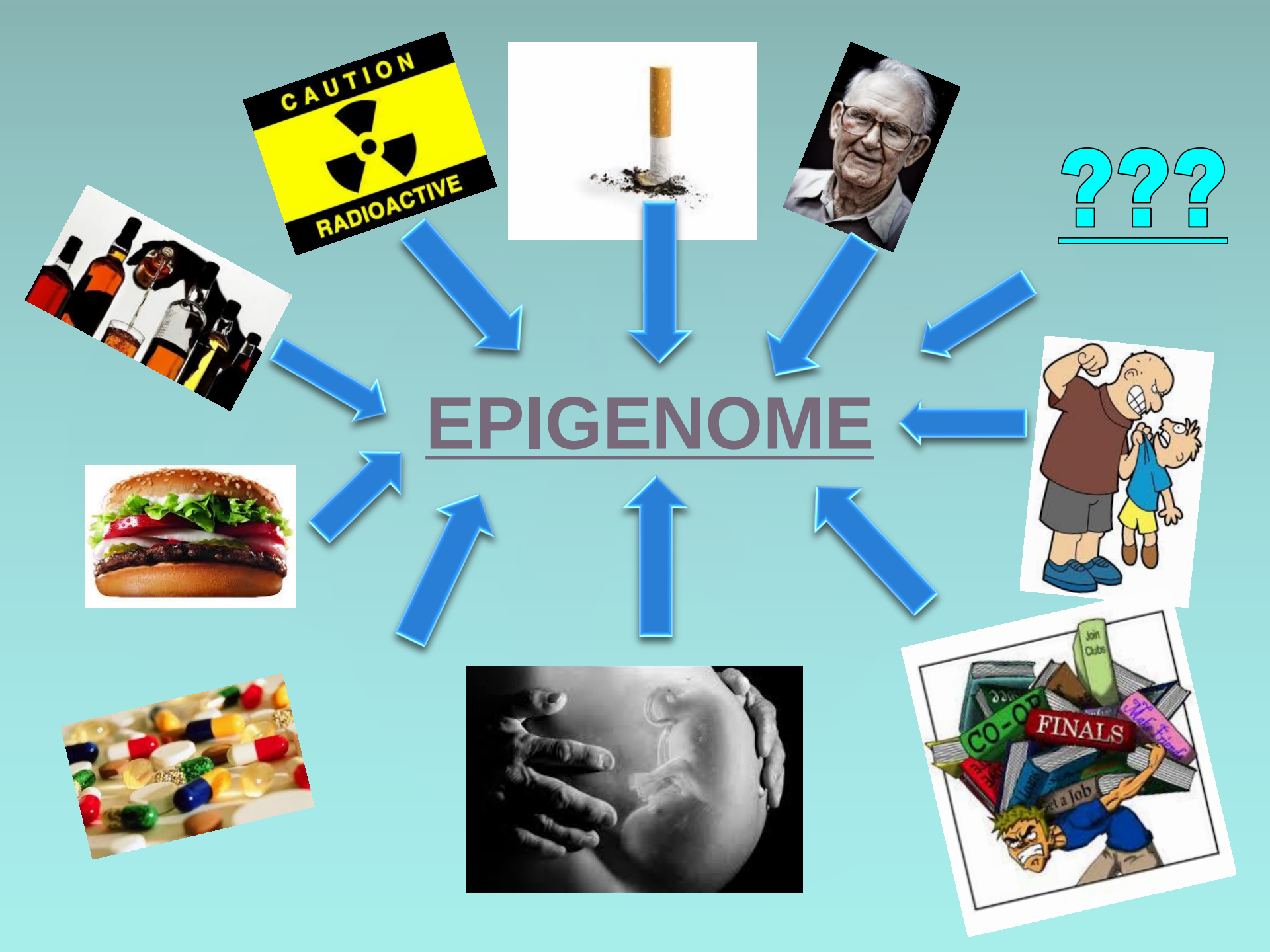
Epigenetics determines how much of the mRNA is made, and where and when it is synthesized

For example:

Cancer

Silencing (via hyper-methylation) of tumor suppressor genes and DNA repair genes

Global Hypo-methylation → expression of oncogenes, chromosome instability


CAUTION
RADIOACTIVE
???
EPIGENOME
FINALS
CO-OP
Join Clubs
Get a Job

Your DNAmet does not lie!!!

- Do you smoke? Have you really stopped ?
- Are you really as young as you say?
- Do you drink alcohol?
- Do you really go to the gym?
- Do you follow a healthy diet?

EWAS data: Epigenome wide association study of DNA met

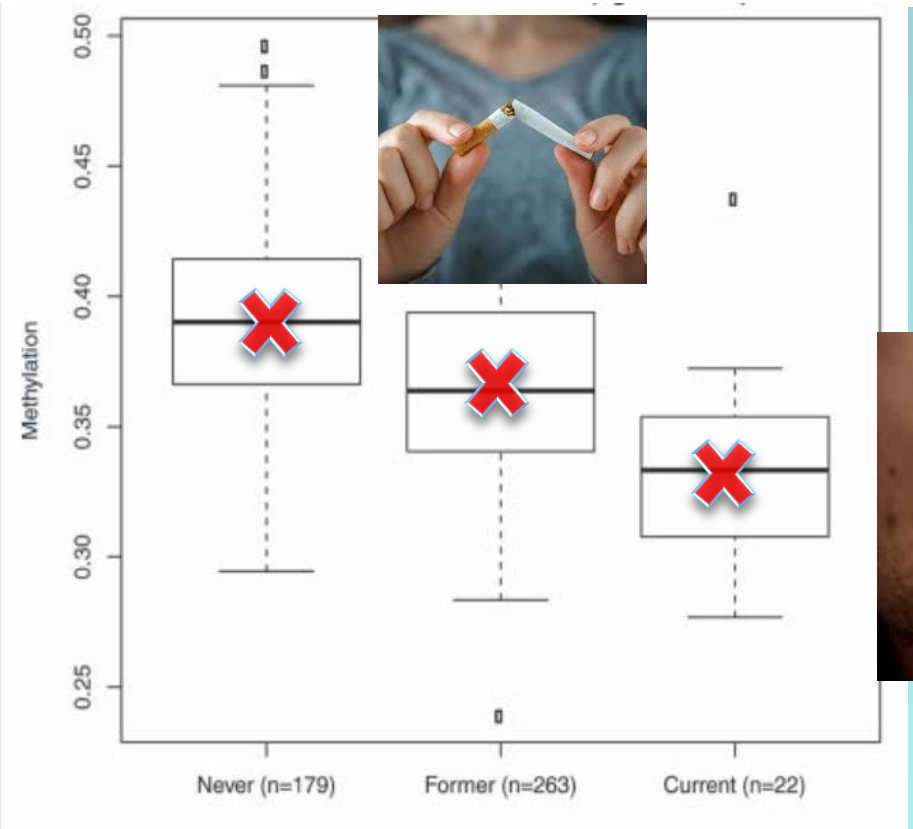
DNAmet smoking score

RESEARCH PAPER

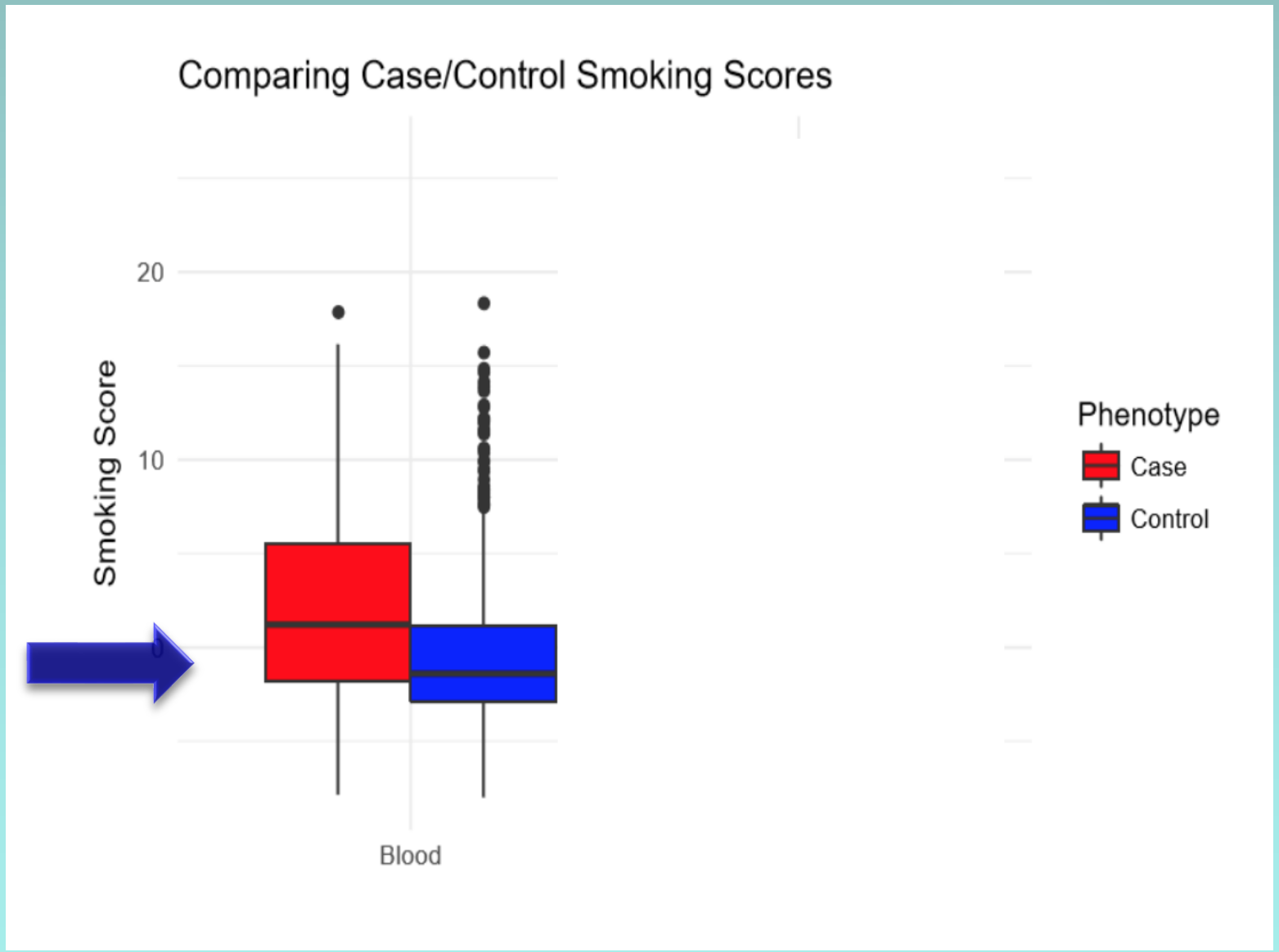
Epigenetics 9:10, 1382–1396; October 2014; © 2014 Taylor & Francis Group, LLC

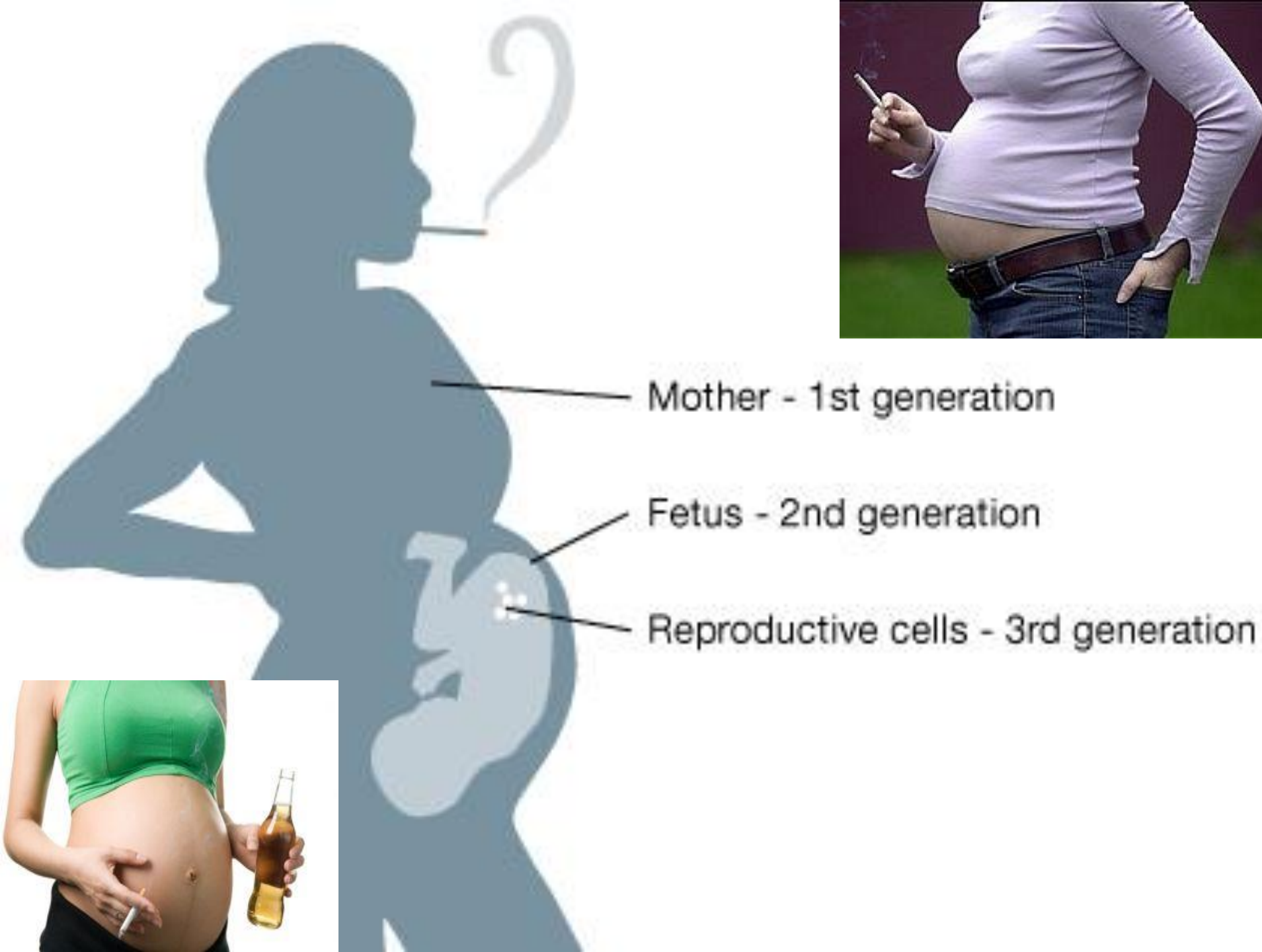
Cigarette smoking reduces DNA methylation levels at multiple genomic loci but the effect is partially reversible upon cessation

Loukia G Tsaprouni[1,2,†], Tsun-Po Yang[1,3,†], Jordana Bell[4], Katherine J Dick[5,6], Stavroula Kanoni[7], James Nisbet[1], Ana Viñuela[4], Elin Grundberg[8], Christopher P Nelson[5,6], Eshwar Meduri[1,4], Alfonso Buil[9], Francois Cambien[10], Christian Hengstenberg[11], Jeanette Erdmann[12], Heribert Schunkert[13], Alison H Goodall[5,6], Willem H Ouwehand[1,14], Emmanouil Dermitzakis[9], Tim D Spector[4], Nilesh J Samani[5,6], and Panos Deloukas[1,7,15,*]



EWAS smoking score: the EUGEI example




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

Nutrition and epigenetics

Agouti gene

Mother fed control diet:
gene unmethylated

Mother fed folic acid diet:
gene methylated

Waterland & Jirtle 2003

Nutrition and epigenetics

The New York Times

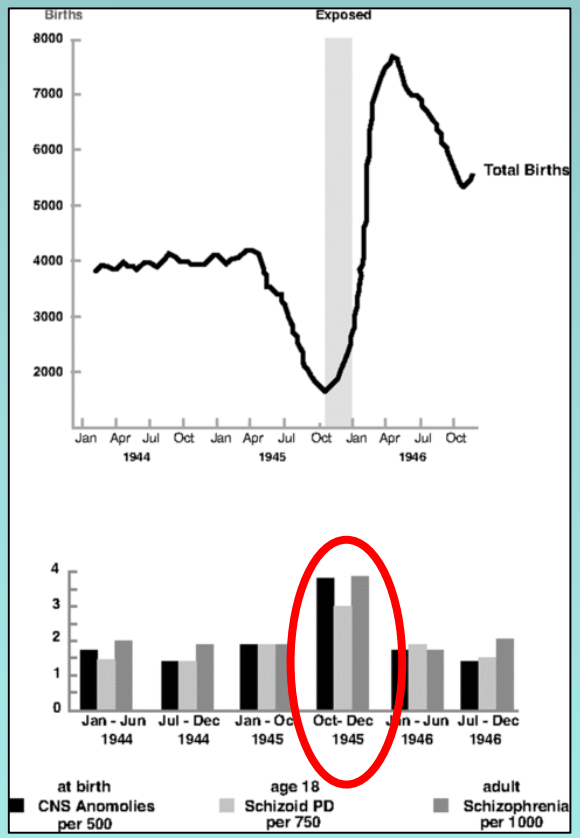
MATTER

The Famine Ended 70 Years Ago, but Dutch Genes Still Bear Scars

A victim of starvation during the Dutch famine of 1944-45. Women pregnant during the period gave birth to babies who were affected by health problems throughout their lives.
Hulton Archive/Getty Images

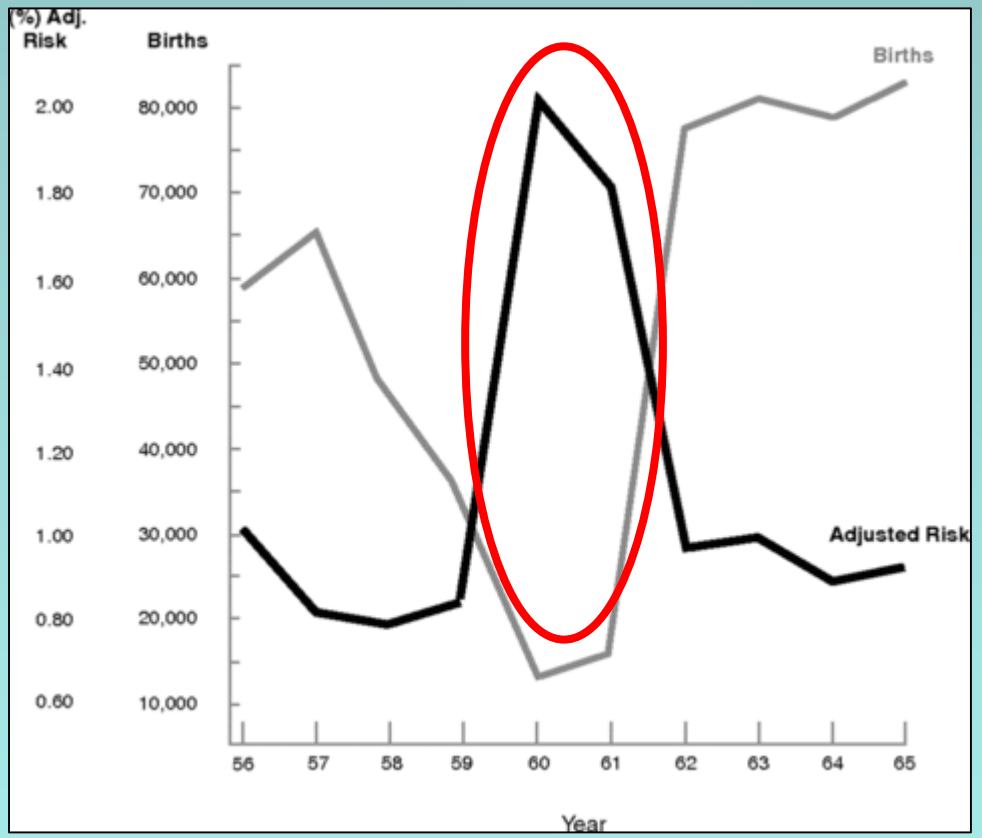
Perinatal malnutrition and schizophrenia

Dutch hunger winter (1944-1945)



Drop in birth rate increase in schizophrenia in those conceived during famine

Chinese leap forward famine (1959-1961)



Birth rate plummets due to famine and risk for schizophrenia doubles for those born in these years

Brown & Susser et al 2008

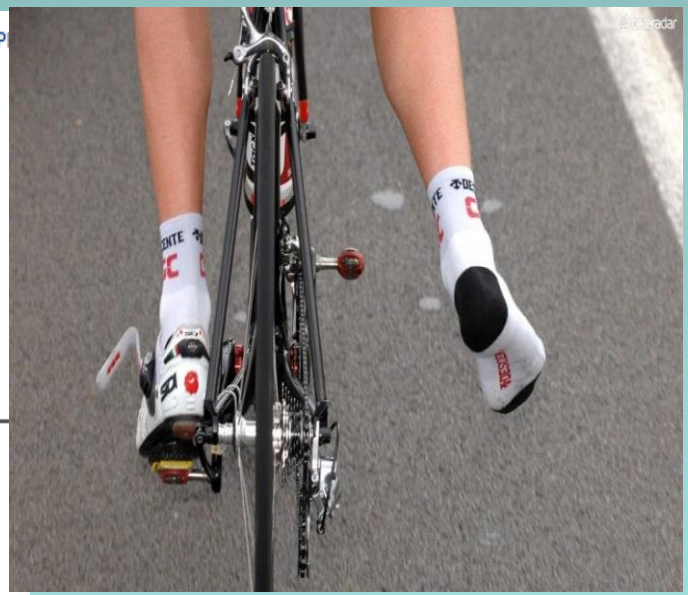
DNAmet and Exercise

RESEARCH PAP

Epigenetics 9:12, 1557–1569; December 2014; Published with license by Taylor & Francis Group, LLC

An integrative analysis reveals coordinated reprogramming of the epigenome and the transcriptome in human skeletal muscle after training

Maléne E Lindholm[1,*,†], Francesco Marabita[2,*,†], David Gomez-Cabrero[2], Helene Rundqvist[3], Tomas J Ekström[4],



Karolinska Institute:
23 men and women to bicycle using only one leg for 45 minutes, four times a week over three months.

Muscle biopsies before and after the experiment

new methylation-gene expression patterns on genes associated with insulin response, inflammation and energy metabolism

EWAS and RNA-seq

Pidsley *et al. Genome Biology*
http://genomebiology.com/20

RESEARCH

Methylomi
supports a
schizophre

Ruth Pidsley[1,2], Joana Vi
Gustavo Turecki[4], Leona

DOI 10.1186/s13059-016-1041-x

Genome Biology

RESEARCH Open Access

An integrated genetic-epigenetic analysis of schizophrenia: evidence for co-localization of genetic associations and differential DNA methylation

Eilis Hannon[1], Emma Dempster[1], Joana Viana[1], Joe Burrage[1], Adam R. Smith[1], Ruby Macdonald[1], David St Clair[2], Colette Mustard[3], Gerome Breen[4], Sebastian Therman[5], Jaakko Kaprio[5,6,7], Timothea Toulopoulou[8], Hilleke E. Hulshoff Pol[9], Marc M. Bohlken[9], Rene S. Kahn[9], Igor Nenadic[10], Christina M. Hultman[11], Robin M. Murray[4], David A. Collier[4,12], Nick Bass[13], Hugh Gurling[13], Andrew McQuillin[13], Leonard Schalkwyk[4,14] and Jonathan Mill[1,4,15*]

"We have identified multiple differentially methylated positions and regions consistently associated with schizophrenia across the three cohorts; these effects are independent of important confounders such as smoking. We also show that epigenetic variation at multiple loci across the genome contributes to the polygenic nature of schizophrenia"

Gene and environment contribute towards mental illness

QUESTIONS?