CONGRESSO REGIONALE
SID-AMD MARCHE 2025

SID Società Italiana di Diabetologia
fondata nel 1964

AMD MARCHE ASSOCIAZIONE MEDICI DIABETOLOGI

LA CURA DELLA PERSONA CON DIABETE NELL' ERA DELL' INTELLIGENZA ARTIFICIALE

TRAGUARDI, SFIDE E NUOVI ORIZZONTI

RESPONSABILE SCIENTIFICO Paola Canibus

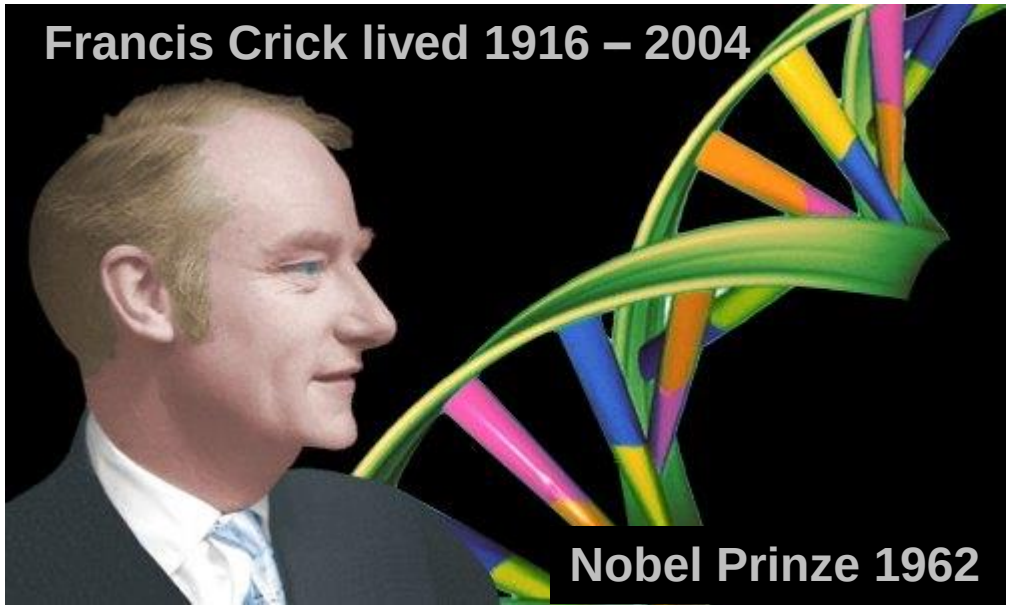
JESI (AN) | 11 ottobre 2025
Hotel Federico II

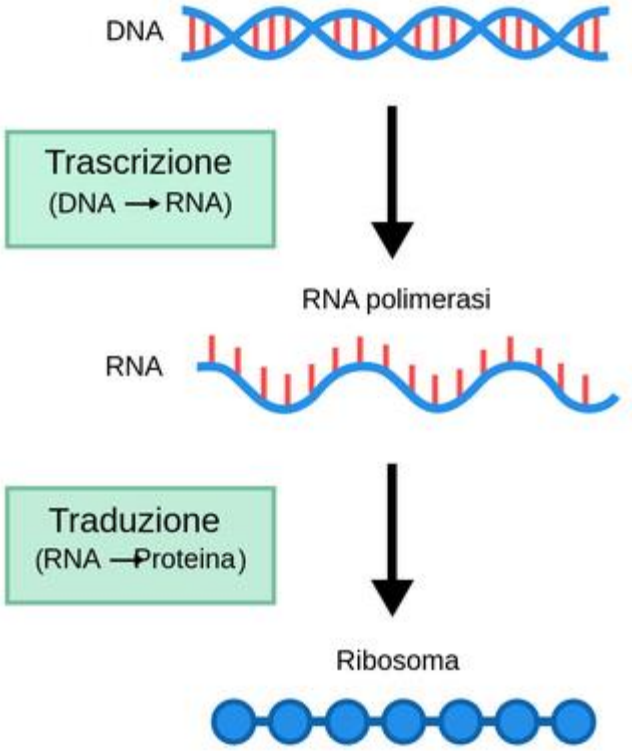
16.00 Genetica, epigenetica e disturbi del metabolismo
Franco Gregorio

DOGMA CENTRALE DELLA GENETICA:

il DNA è costituito da catene di geni
ciascuno dei quali contiene le informazioni per la sintesi di una proteina:
UN GENE → UNA PROTEINA

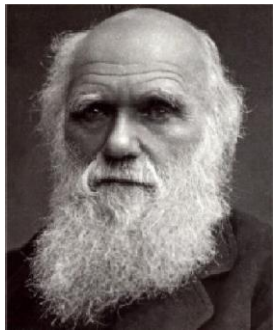
(postulato da Crick nel 1958)





I geni vengono trasmessi immodificati alla progenie.
Sono sostanzialmente stabili
ma occasionalmente possono andare incontro a mutazioni.

EVOLUZIONE



"The evolution of higher animals directly follows ...
from the war of nature,
from famine and death.."

C. Darwin "The Origin of Species", 1859

" Nothing in biology makes sense
except in the light of evolution."

Theodosius Dobzhansky, 1973

L'evoluzione seleziona quelle mutazioni spontanee
delle sequenze nucleotidiche del DNA
che rendono gli individui mutati meglio adattati all'ambiente.
Questi hanno maggiori possibilità di sopravvivere
e di i trasmettere così i propri (vantaggiosi) tratti genetici alla progenie.

E' un processo che impiega centinaia/migliaia di anni per verificarsi.

Una volta selezionata
la mutazione rimane cristallizzata nel genoma della discendenza.

Obesity and Diabetes in “the Land of Milk and Honey”

Kerin O’Dea — *Diab. Metab. Rev.* 8: 373-388; 1992

Adattamento genetico alla carenza alimentare

… **Food shortages were so common in human prehistory and history that they could be considered an inevitable fact of life.…and that selection could not provide for the eventuality of continuous surplus because it has simply never existed…**

Bruegel P. “Il Vecchio”
La terra del Latte e del Miele (1567)
Monaco, Alte Pinakothek

Palaeolitic diet represent the nutrition for which human beings are in essence ***genetically*** programmed….

Stile di vita ancestrale e collisione evolutiva.
Parte 1*: la scimmia cacciatrice

M. Sudano[1], F. Gregorio[2]
msudano_99@yahoo.it

[1] Servizio di Diabetologia e Malattie Metaboliche – ASUR Marche AV1 Urbino; [2] UOSD Malattie Metaboliche e Diabetologia Ospedale ASUR Marche, AV2, ZT6 "E. Profili" Fabriano (AN)

Parole chiave: Medicina evoluzionistica, Cacciatori-raccoglitori, Paleo-dieta, Genotipo parsimonioso, Insulino-resistenza
Key words: Evolutionary medicine, Hunter-gatherers, Paleo-diet, Thrifty genotype, Insulin-resistance

Il Giornale di AMD, 2013;16:411-419

Parte 2*: natural born runners

F. Gregorio[1], M. Sudano[2], D. Gregorio[3]
franco.gregorio@sanita.marche.it

[1] UOSD Malattie Metaboliche e Diabetologia Ospedale ASUR Marche, AV2, ZT6 "E. Profili" Fabriano (AN); [2] Servizio di Diabetologia e Malattie Metaboliche – ASUR Marche AV1 Urbino; [3] Corso Laurea in Scienze e Tecniche Psicologiche dei Processi Mentali, Università di Perugia

Parole chiave: Corsa aerobica, Caccia, Evoluzione homo
Key words: Endurance running, Unting, Hominid evolution

Il Giornale di AMD, 2014;17:24-32

MeDia 2015;15:72-83 72 SEZIONE DI FORMAZIONE PER L'AUTOVALUTAZIONE
AGGIORNAMENTO

Stile di vita ancestrale e collisione evolutiva
Parte 3 – L'acido urico: un'amicizia finita male

Franco Gregorio[1]
Maurizio Sudano[2]
Daniele Gregorio[3]

Paleodieta mediterranea e rivoluzione agricola

Mediterranean paleodiet and agricultural revolution

F. Gregorio[1], N. Musacchio[2], D. Gregorio[3], L. Richiardi[4]
franco.gregorio@sanita.marche.it

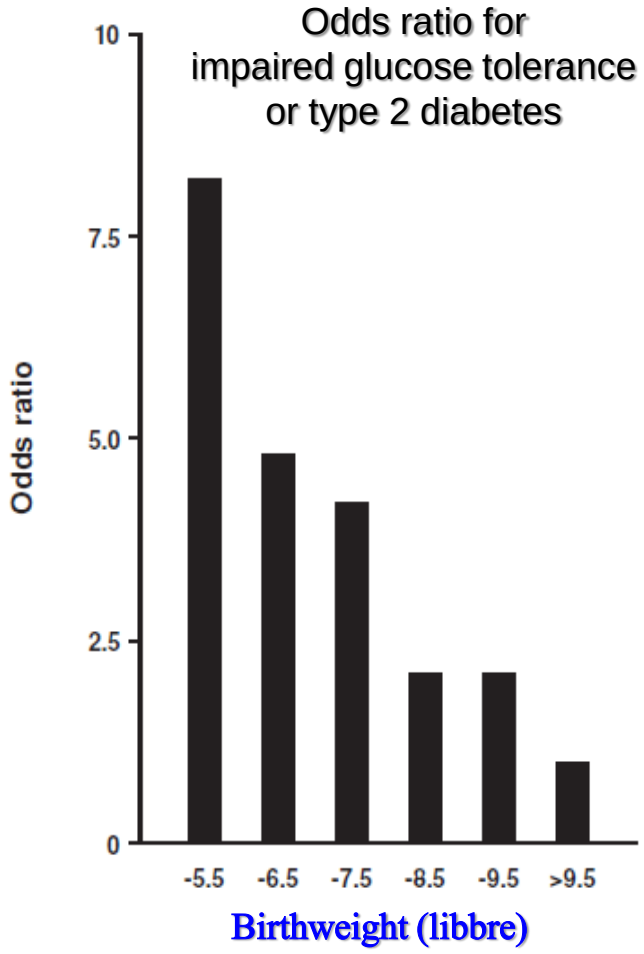
Può accadere
che una mutazione genetica inizialmente vantaggiosa
al modificarsi delle condizioni ambientali che l'hanno favorita
finisca con il diventare dannosa:
ma ormai è cristallizzata nel genoma e sostanzialmente irreversibile.

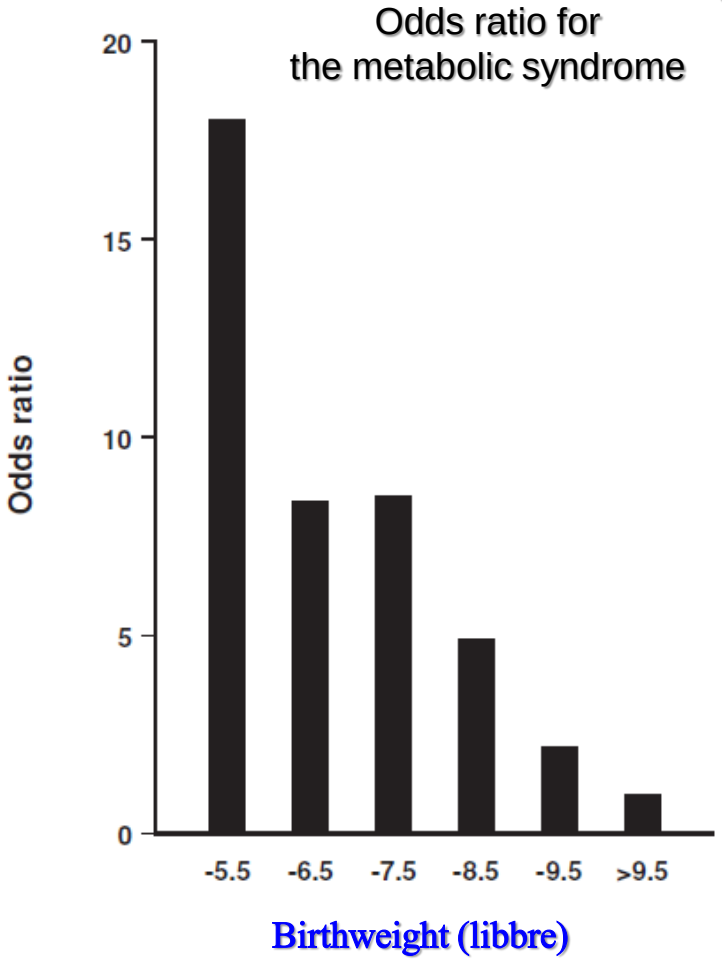
Il fenomeno è definito
Evolutionary Mismatch o Collisione Evolutiva

Barker hypothesis: poor nutrition in fetal and early life increases increase susceptibility to the development of Type 2 diabetes

British Medical Bulletin 2001; **60**: 5–20

Le conseguenze impreviste della carestia fetale

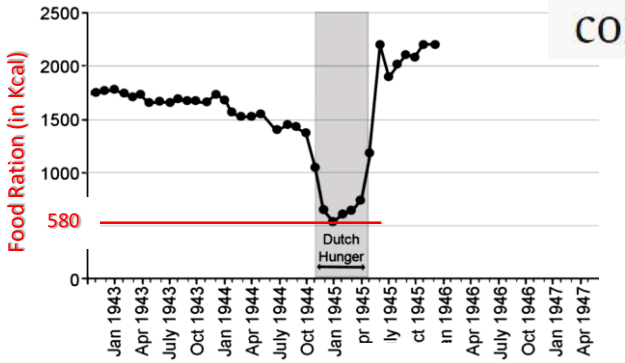


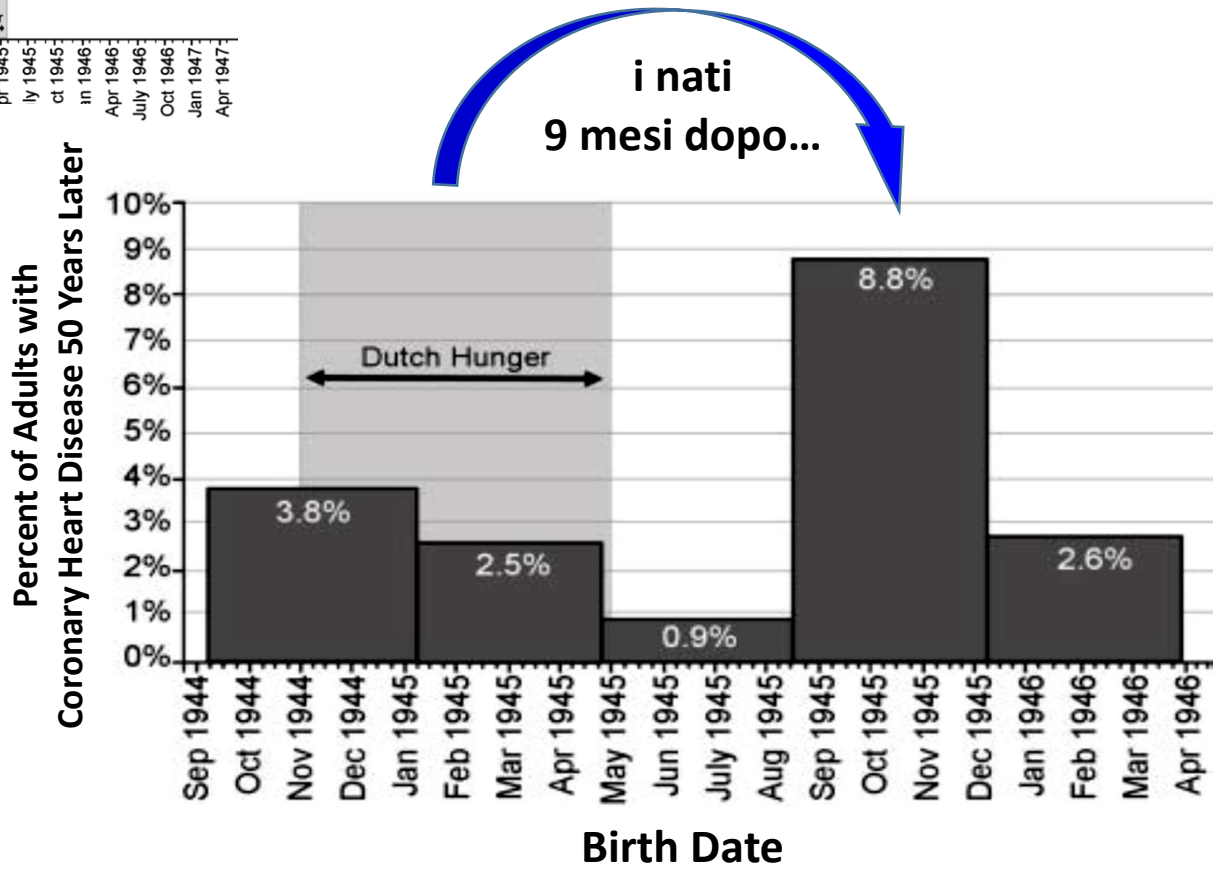


Le conseguenze
impreviste
della carestia fetale

The Dutch famine and its long-term consequences for adult health

› Early Hum Dev. 2006





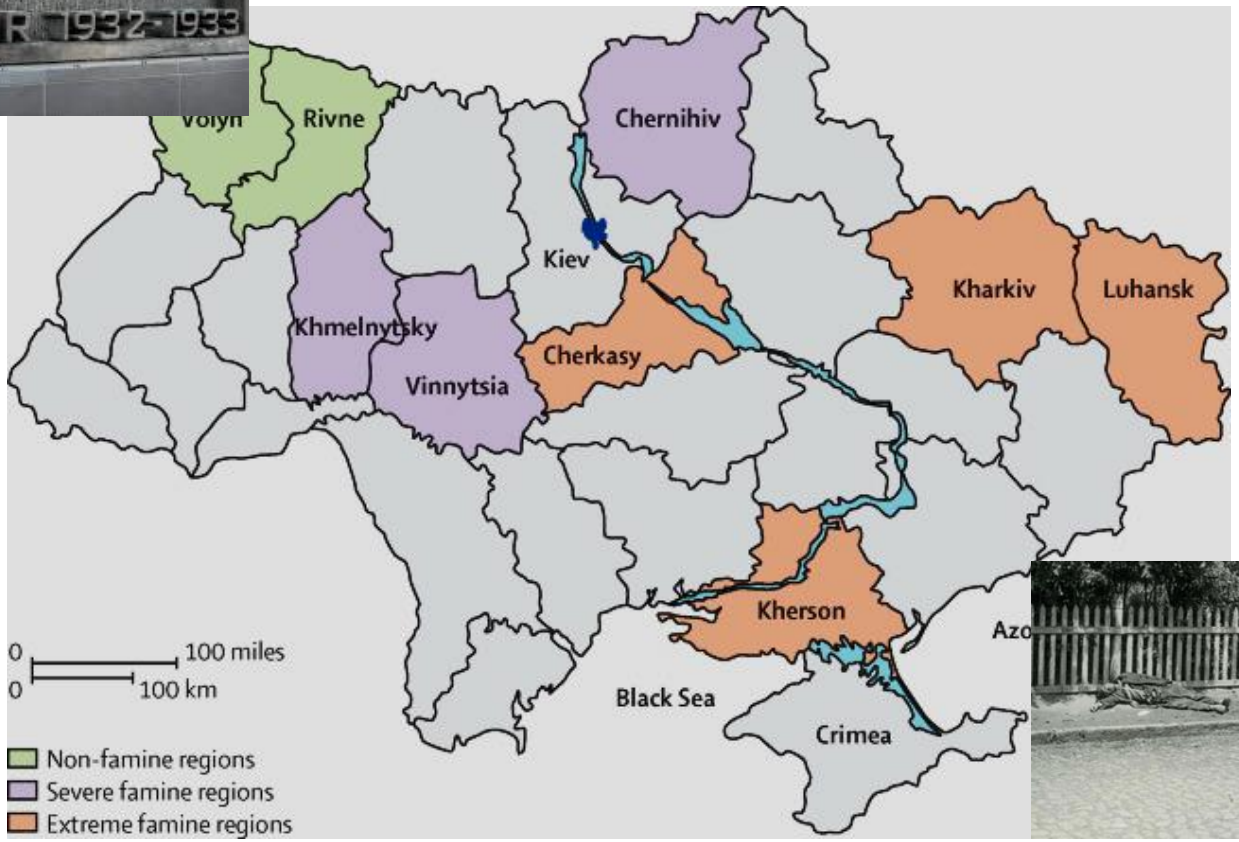
Non solo…..

Prenatal exposure to the Dutch famine is associated with a preference for fatty foods and a more atherogenic lipid profile

Am J Clin Nutr 2008;

Association between type 2 diabetes and prenatal exposure to the Ukraine famine of 1932–33: a retrospective cohort study The Lancet Diabetes & Endocrinology October 2015.

Le conseguenze impreviste della carestia fetale



Compared with births in other time periods, the OR for developing type 2 diabetes was:

- **1·47 in individuals born in the first half of 1934 in regions with extreme famine,**
- **1·26 in individuals born in regions with severe famine,**
- **and there was no increase (OR 1·00) in individuals born in regions with no famine.**

Review

Early-Life Nutritional Programming of Type 2 Diabetes: Experimental and Quasi-Experimental Evidence

Nutrients 2017

Le conseguenze impreviste della carestia fetale

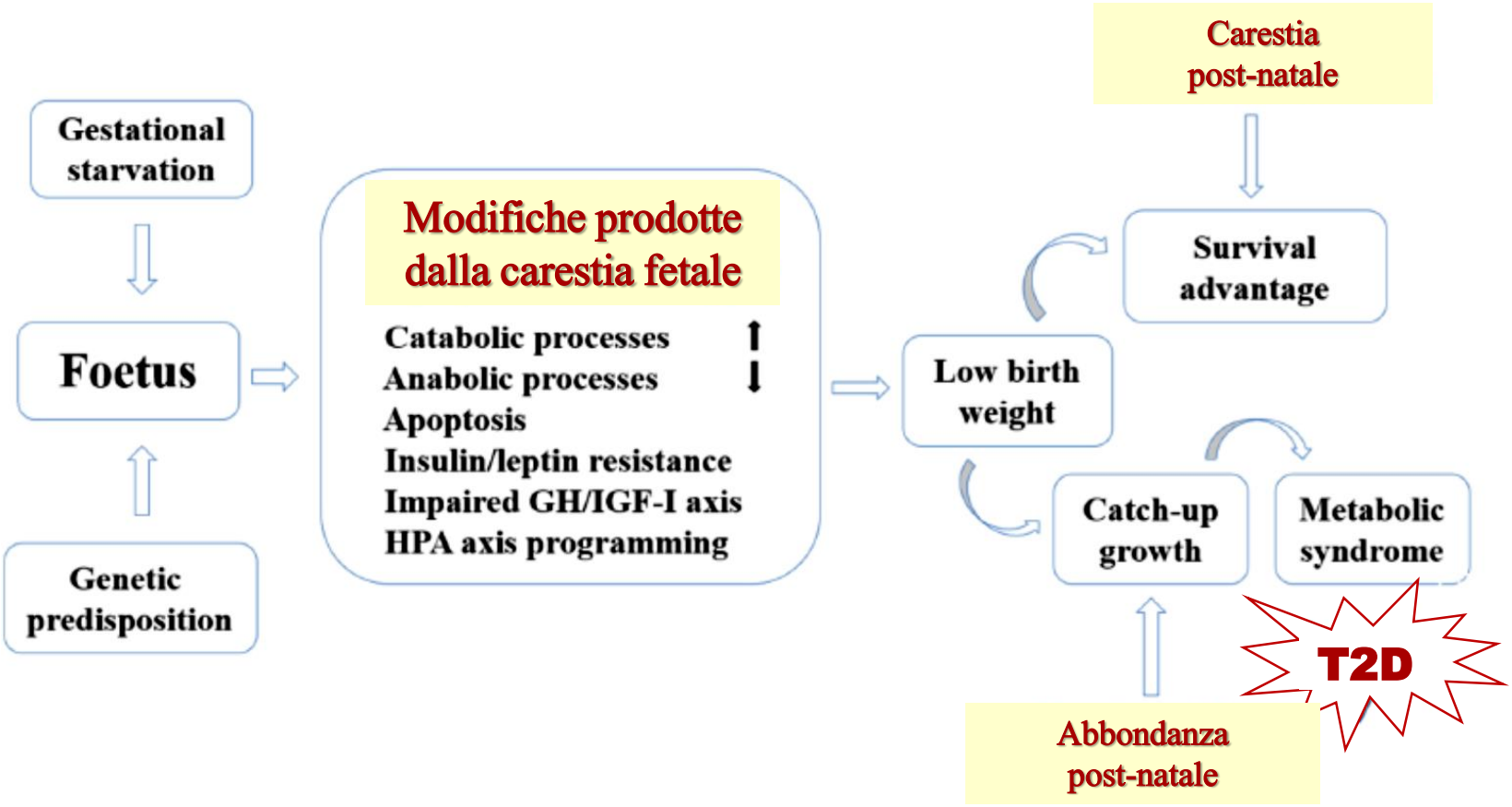
Country	Cause of Starvation	Period	Adult consequence
Netherlands ('Dutch Hunger Winter')	Nazi food embargo	1944–1945	Impaired glucose regulation Atherogenic lipid profiles Obesity, CVD T2D Lower *IGF2* methylation Changed methylation of *ABCA1*, *GNASAS*, *IL10*, *LEP*, *INSIGF* and *MEG3* genes
Austria	Empire's collapse Nazi food embargo Post-war period	1918–1919 1938 1946–1947	High risk of T2D
Ukraine ('Holodomor')	Agriculture collectivization	1932–1933	High risk of T2D
Russia	Leningrad Siege	1941–1944	Endothelial dysfunction, stronger influence of obesity on blood pressure Increasing incidence of T2D Atherosclerosis, arterial hypertension
China ('Great Leap Forward Famine')	Disastrous social agricultural reform	1959–1961	Hyperglycemia High risk of T2D
Nigeria ('Biafran Famine')	Civil war	1967–1970	Increased blood pressure, higher levels of p-glucose, increased waist circumference, overweight, high risks of impaired glucose regulation and systolic hypertension
Europe ('Holocaust')	Nazi genocide	1939–1945	Enhanced BMI, hypertension, dyslipidemia, high risk of T2D and CVD
Spain	Seasonal malnutrition	1935–1954	High systolic blood pressure
United Kingdom	Seasonal malnutrition	1920–1930	Obesity
Canada	Seasonal malnutrition	1943–1995	Obesity
United Kingdom	Seasonal malnutrition	1924–1943	Dyslipidaemia, insulin resistance and CVD
USA	Seasonal malnutrition	1968–1995	High risk of T2D

Le conseguenze impreviste della carestia fetale

Review

Early-Life Nutritional Programming of Type 2 Diabetes: Experimental and Quasi-Experimental Evidence

Nutrients 2017



Ricordiamo nuovamente il

DOGMA CENTRALE DELLA GENETICA:

il DNA è costituito da catene di geni
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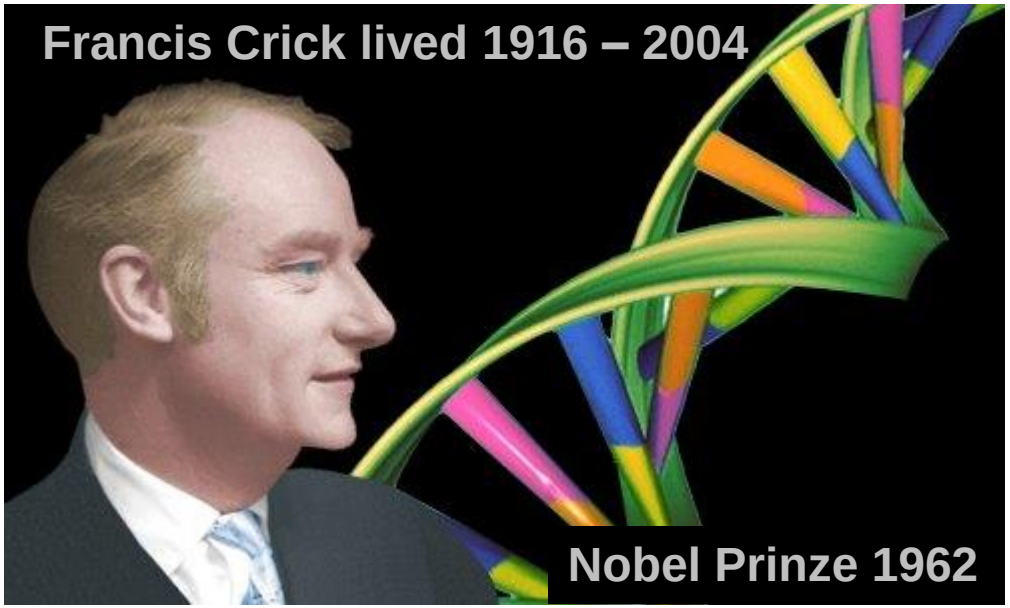
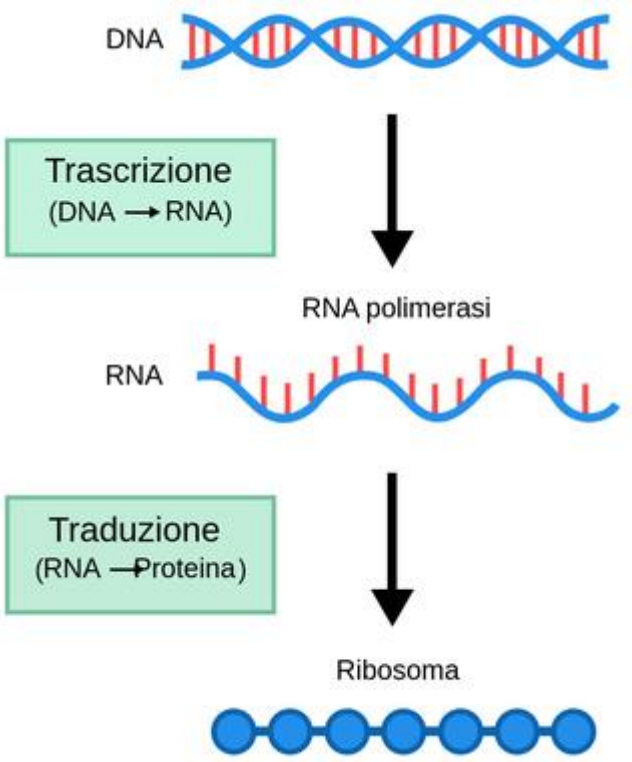
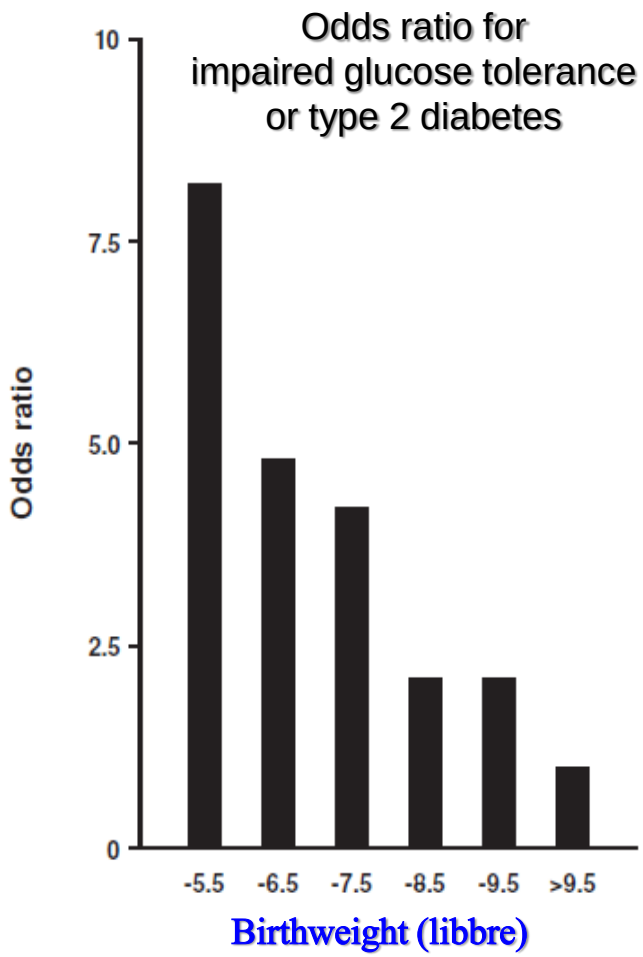
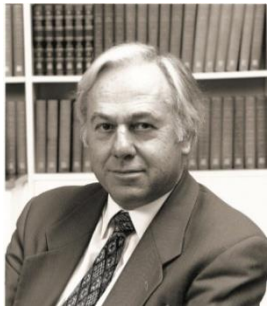




Però il dogma centrale della genetica non spiega (1° problema):

come può cambiare l'espressione genica nelle generazioni esposte a carestia fetale senza modifiche del DNA?





Poor nutrition in fetal and early infant life ....
greatly increase susceptibility
to the development of Type 2 diabetes

David J.P. Barker

Però il dogma centrale della genetica non spiega (2° problema):

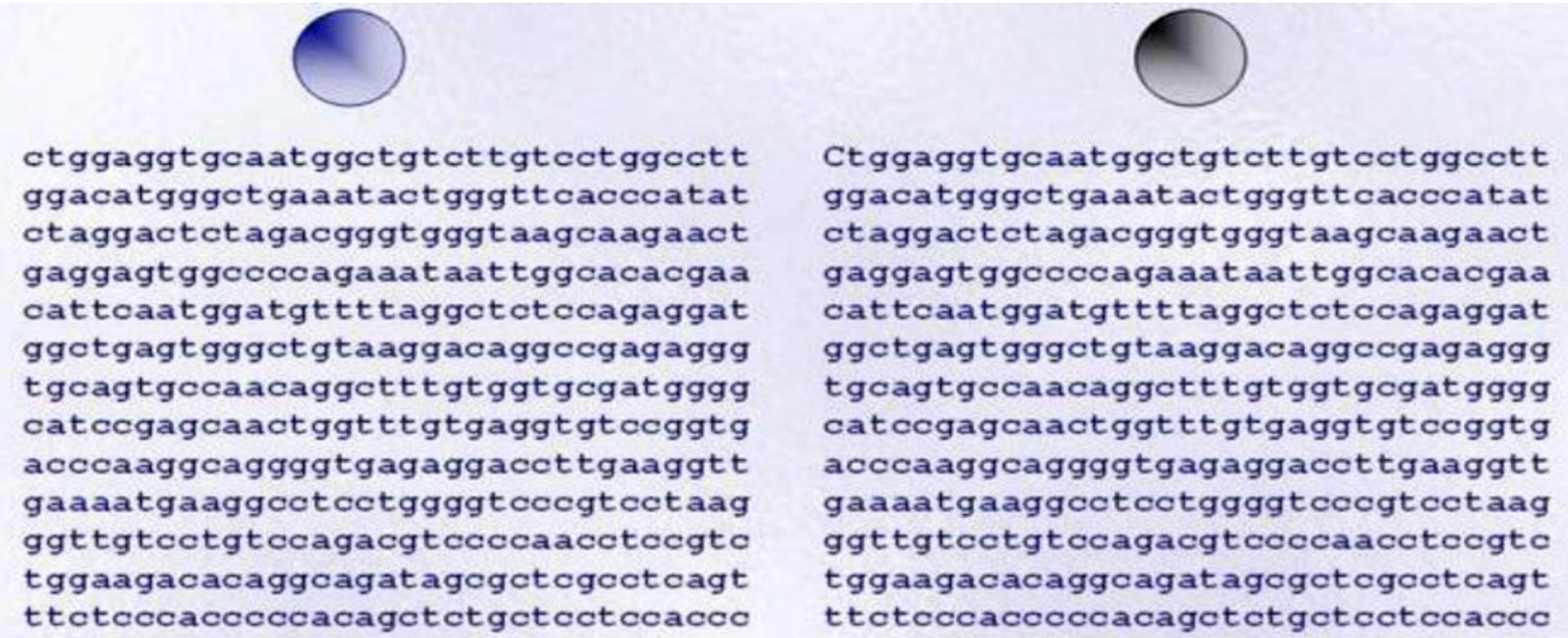
se il genoma dei gemelli monozigoti è identico come può essere così bassa la concordanza per malattie a base genetica?

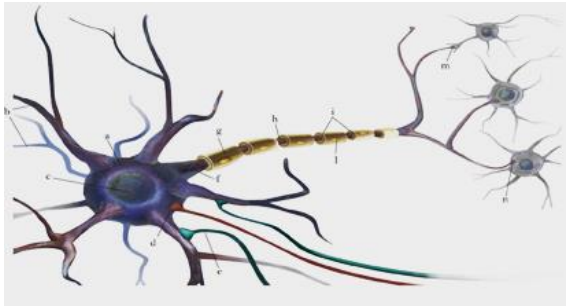
Concordance rates in monozygotic twins:

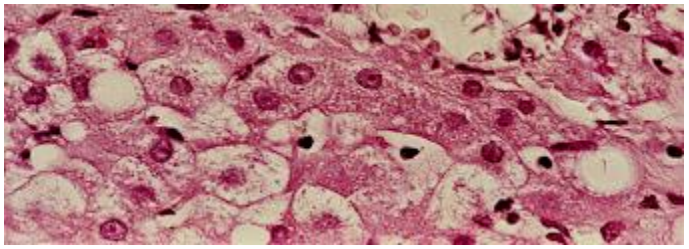
- 25% for multiple sclerosis,
- 40-50% for Type 1 diabetes
- 40-60% for BMI
- 50% for cancer in BRCA1 e BRCA2 mutations
- 50% for schizophrenia
- 60% for autism

Però il dogma centrale della genetica non spiega (3° *problema):*

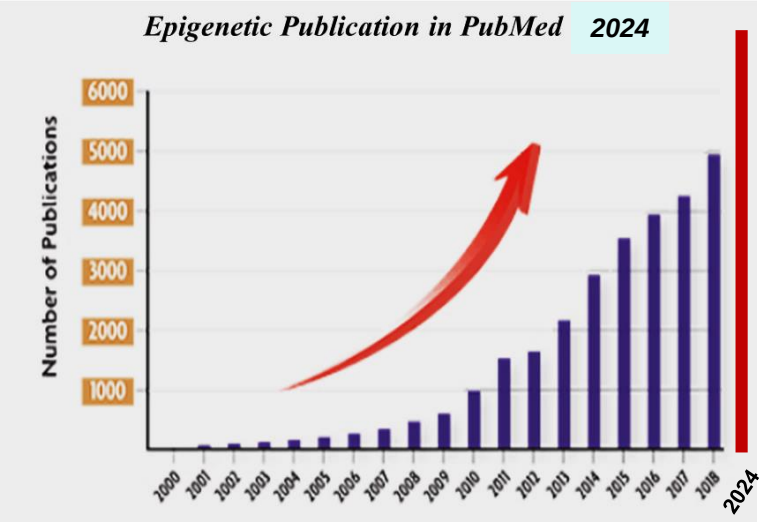
se il genoma è uguale in tutte le cellule come può cambiare l'espressione proteica e la morfologia da tessuto a tessuto?







Ma cos'è questa "EPIGENETICA" ??



the branch of biology which studies the causal interactions between genes and their products, which bring the phenotype into being

Conrad Hal Waddington, 1942

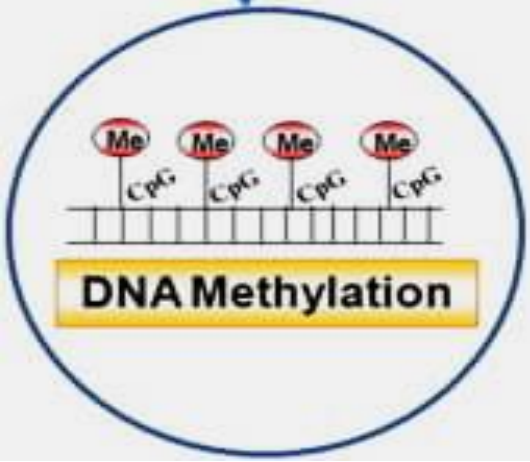
L'EPIGENETICA comprende
tutti i cambiamenti dell'espressione genica del DNA non dipendenti da modifiche della sua sequenza nucleotidica
ma indotte dall'ambiente (interno e/o esterno all'organismo).

Si tratta cioè di cambiamenti chimici a carico del DNA (e degli Istoni) ereditabili (da una cellula alla altra e da una generazione all'altra) che modificano l'espressione genica (e quindi il fenotipo) ma non modificano la sequenza nucleotidica del DNA.

Meccanismi dell'Epigenetica

Metilazione del DNA

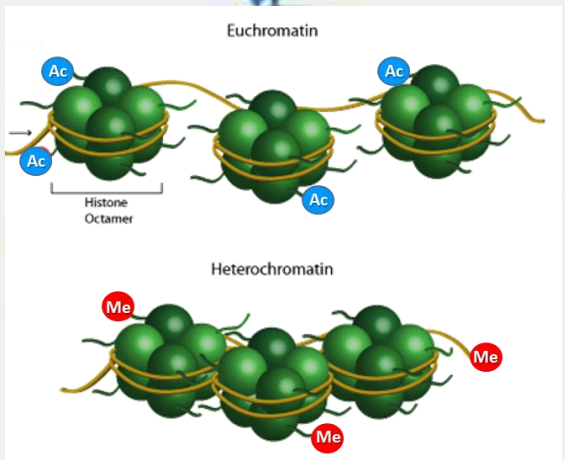
DNMTs



Modificazioni degli Istoni

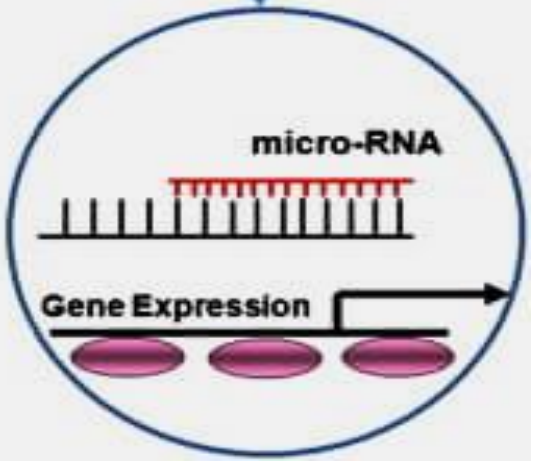
HATs
HMTs

HDACs
HDMs



RNA non codificante

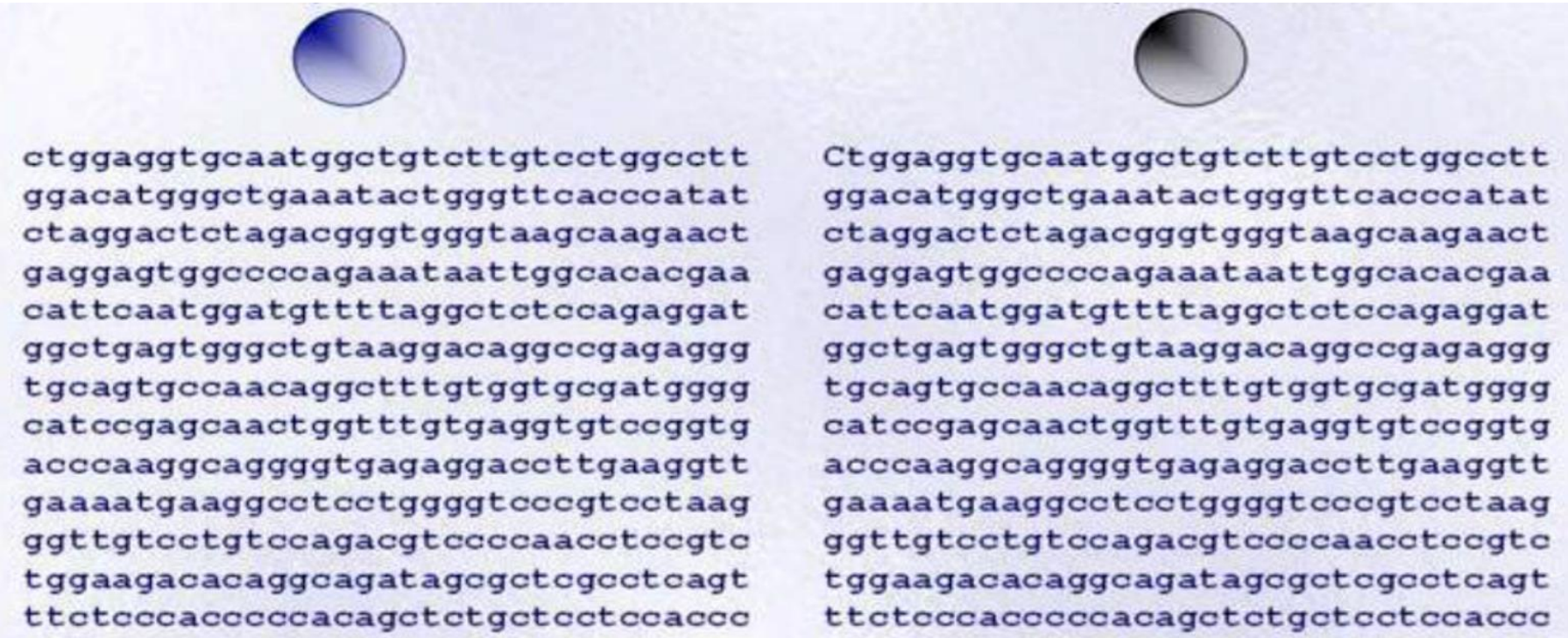
mi-RNAs

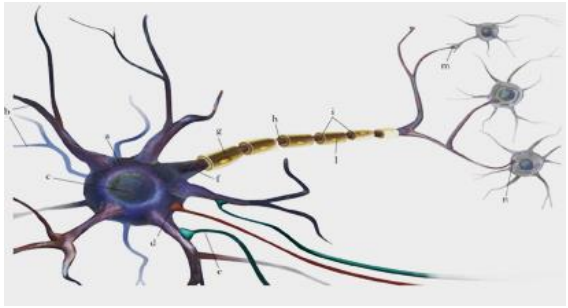


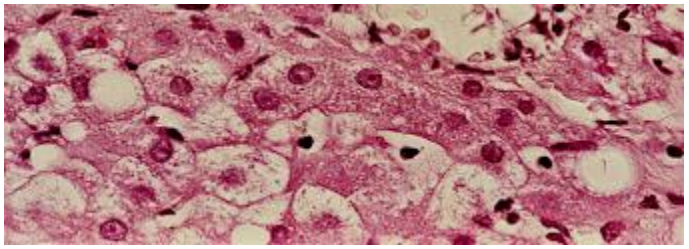
Histone Acetylation/Metilation

Riprendiamo il 3° interrogativo:

se il genoma è uguale in tutte le cellule come può cambiare l'espressione proteica e la morfologia da tessuto a tessuto?







DNA methylation

Cytosine C

Pluripotent cell

Unipotent cell

Methyl-Cytosine 5mC

ctggaggtgcaatggctgtcttgtcctggcctt
ggacatgggctgaaatactgggttcacccatat
ctaggactctagacgggtgggtaagcaagaact
gaggagtggccccagaaataattggcacacgaa
cattcaatggatgttttaggctctccagaggat
ggctgagtgggctgtaaggacaggccgagaggg
tgcagtgccaacaggctttgtggtgcgatgggg
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tggaagacacaggcagatagcgctcgcctcagt
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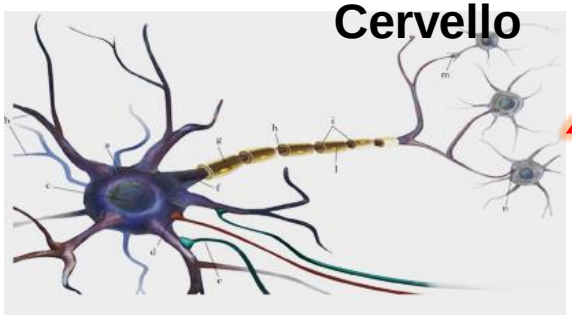
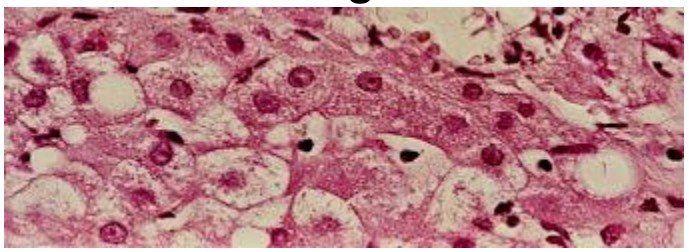
Cervello



Fegato

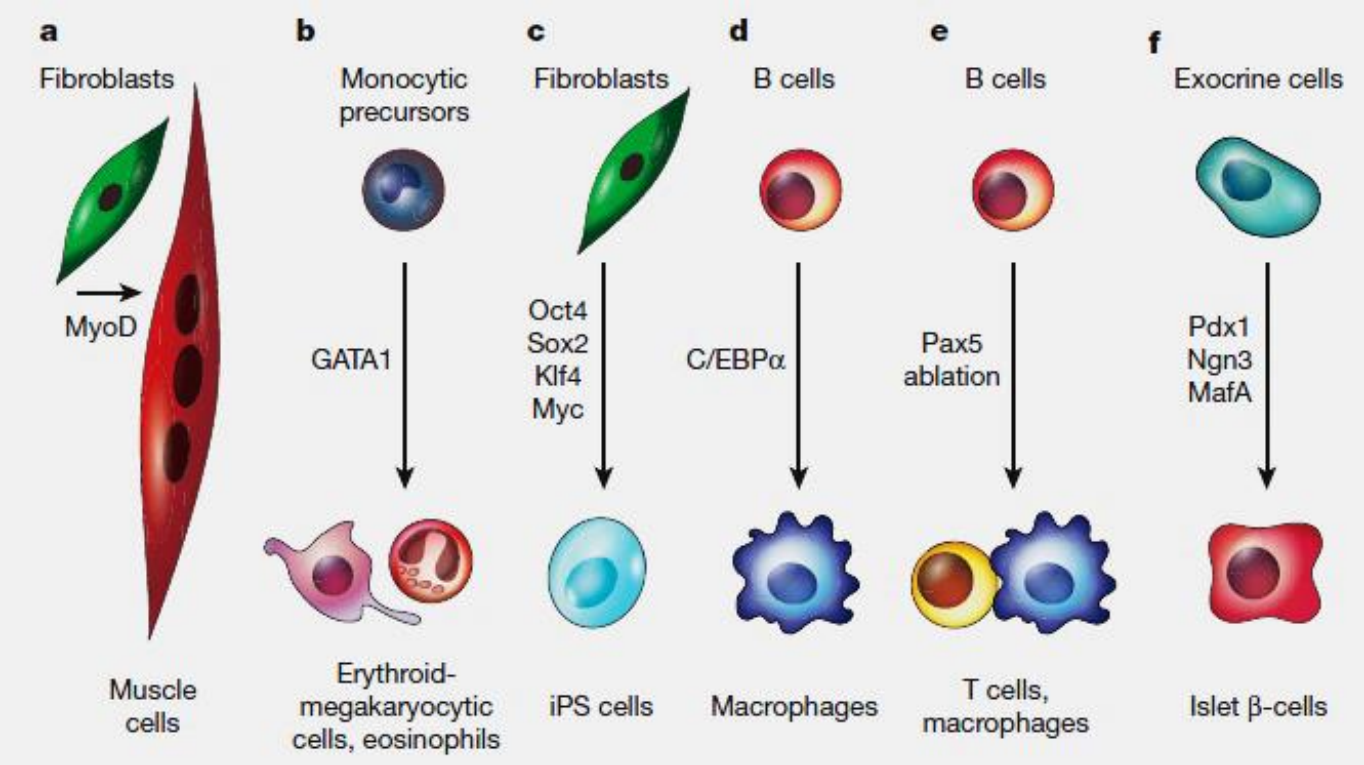


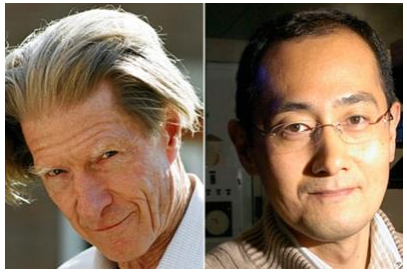
Forcing cells to change lineages

Thomas Graf[1] & Tariq Enver[2]

NATURE|Vol 462|3 December 2009

The ability to produce stem cells by induced pluripotency (iPS reprogramming) has rekindled an interest in earlier studies showing that transcription factors can directly convert specialized cells from one lineage to another. Lineage reprogramming has become a powerful tool to study cell fate choice during differentiation, akin to inducing mutations for the discovery of gene functions. The lessons learnt provide a rubric for how cells may be manipulated for therapeutic purposes.





The Nobel Prize in Physiology or Medicine 2012 jointly to J.B.Gurdon and S.Yamanaka for the discovery that mature cells can be reprogrammed to become pluripotent

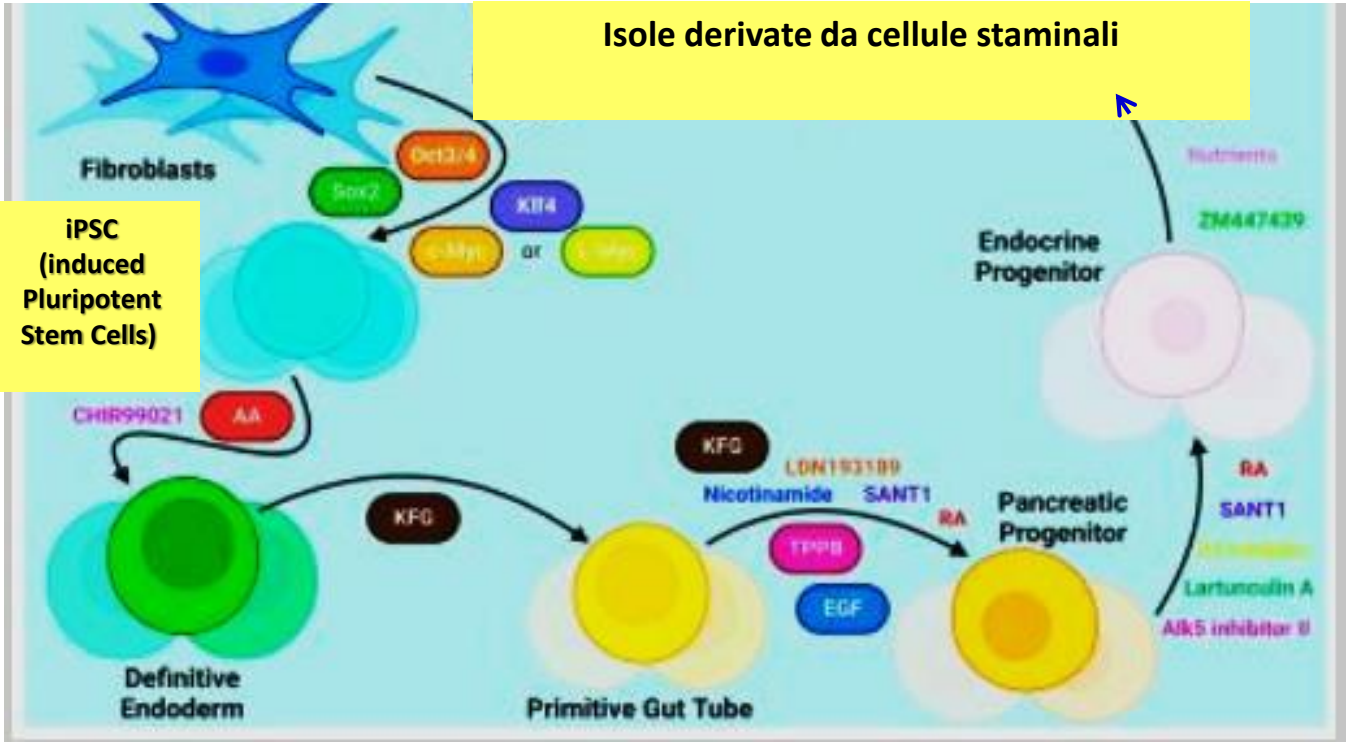
Direct conversion of human fibroblasts to dopaminergic neurons PNAS | June 21, 2011 |

Direct conversion of human fibroblasts into functional osteoblasts by defined factors PNAS | May 12, 2015

Review

Challenges of CRISPR/Cas-Based Cell Therapy for Type 1 Diabetes: How Not to Engineer a "Trojan Horse"

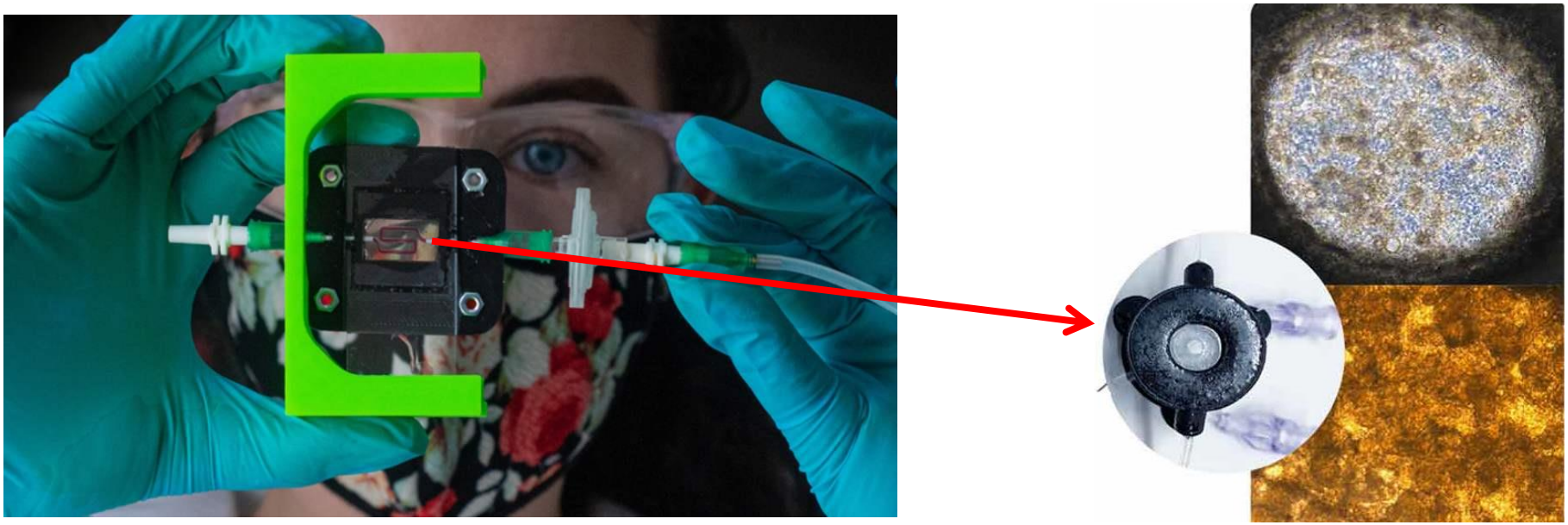
Int. J. Mol. Sci. 2023,



The generation of hypoimmunogenic iPSC (induced pluripotent stem cells) seems to be a more universal approach...

Hypoimmunogenic iPSCs' engineering is a multi-step process involving the knockout or knockin of several genes.
The CRISPR/Cas systems are best suited for such a complex task.

Gli Organ-on-Chip (OoC) sono sistemi miniaturizzati che consentono di riprodurre gli organi e di mimare la loro interazione biologici. I chip sono piastre che contengono al loro interno uno o più tipi di cellule.



Da iPCS pancreatiche inserite all'interno di un idrogel stampato in 3D biocompatibile si stanno testando (per ora su topi diabetici) OoC capaci di essere vascolarizzato così di riprodurre più da vicino la struttura di un vero pancreas

Epigenetic silencing of triple negative breast cancer hallmarks by Withaferin A

Oncotarget, 2017,

Toh *et al. Molecular Cancer* (2017) 16:29
DOI 10.1186/s12943-017-0596-9

Molecular Cancer

REVIEW **Open Access**

Epigenetics in cancer stem cells

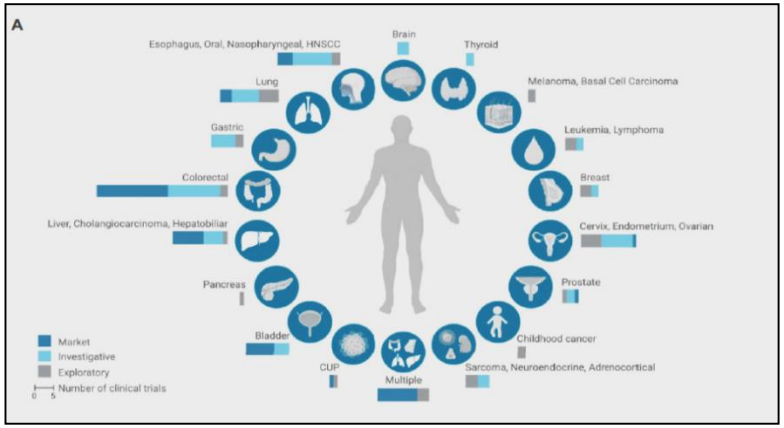
REVIEW ARTICLE *Signal Transduction and Targeted Therapy* (2025) www.nature.com/

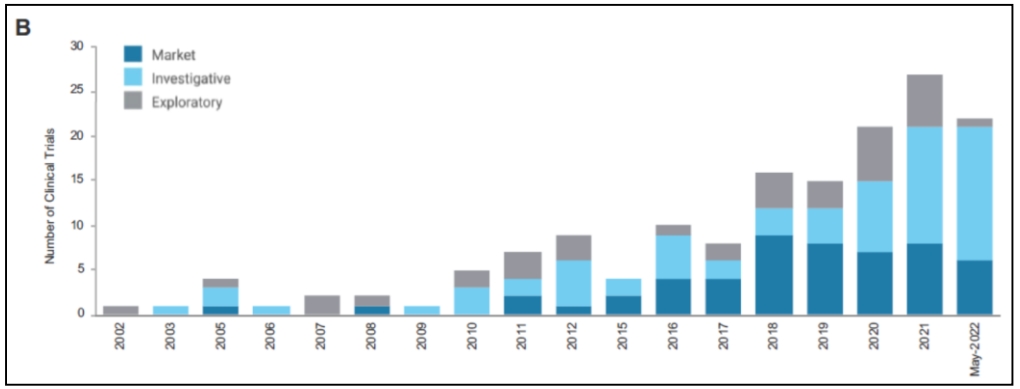
Epigenetic regulation of cancer stemness

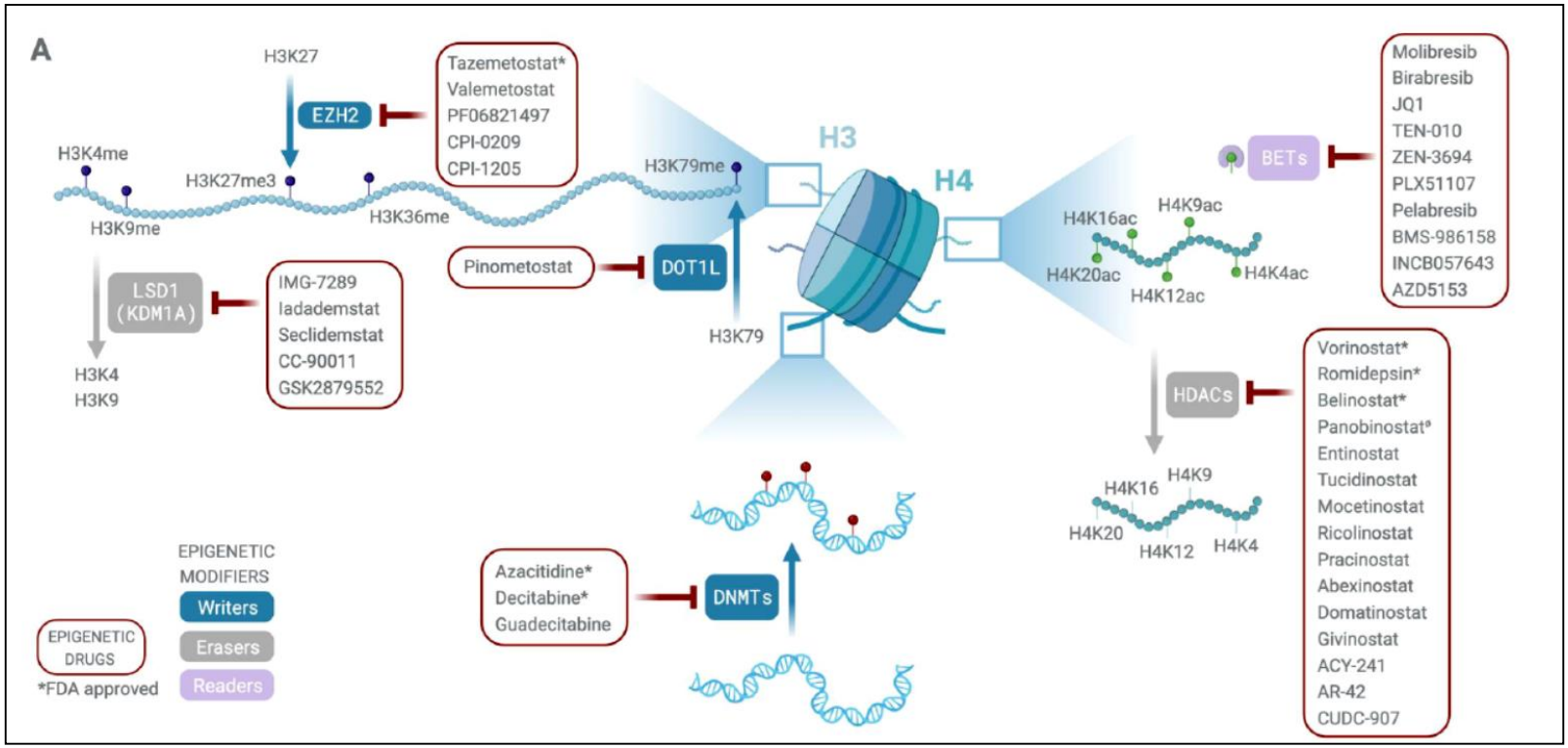
In molti tumori è stata dimostrata la presenza di cellule staminali cancerose
che danno origine a tutte le altre cellule tumorali
comprese quelle che provvedono
al sostegno citoarchitettonico, nutrizionale e vascolare del tumore
proprio come fanno le normali cellule staminali per riparare un tessuto dopo una lesione

Cancer epigenetics in clinical practice

Cancer J Clin. 2023;73:376–424.







Molecular mechanisms responsible for antitumor effects of epigenetic drugs

Riprendiamo il 2° interrogativo:

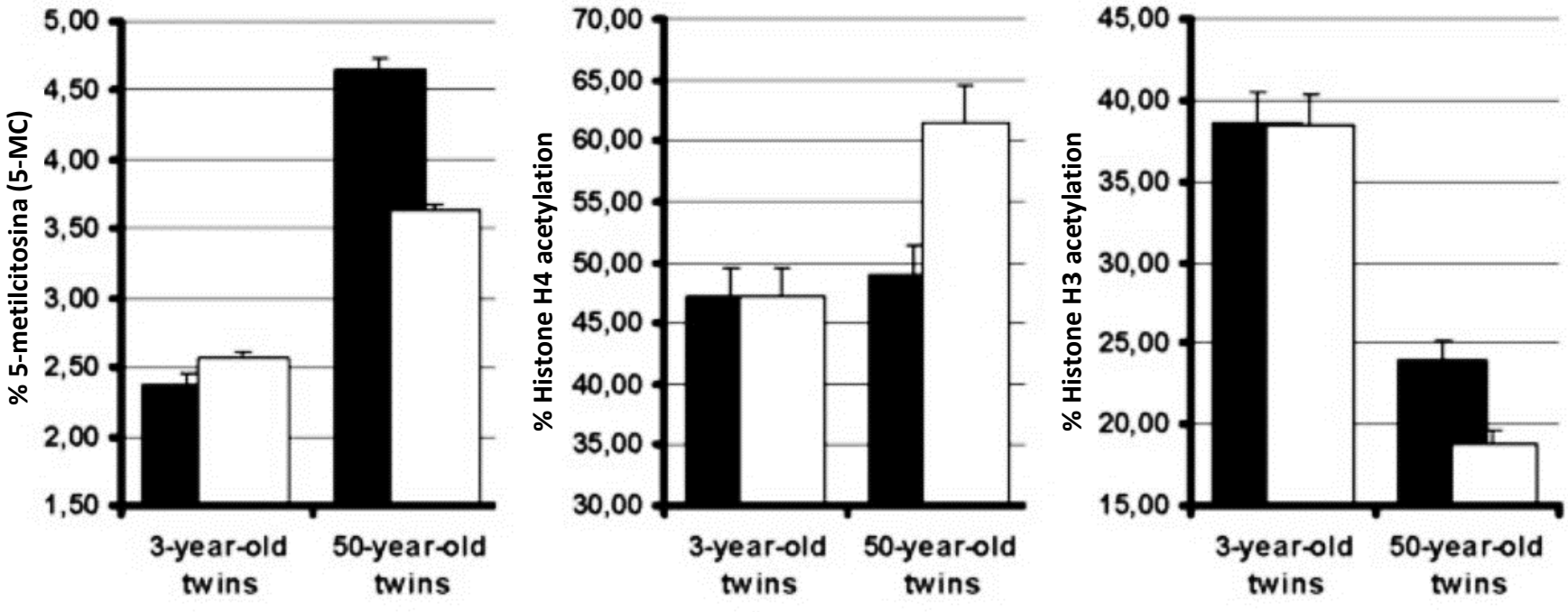
se il genoma dei gemelli monozigoti è identico
come può essere così bassa
la concordanza per malattie a base genetica?

Concordance rates in monozygotic twins:

- 25% for multiple sclerosis,
- 40-50% for Type 1 diabetes
- 40-60 for BMI
- 50% for cancer in BRCA1 e BRCA2 mutations
- 50% for schizophrenia
- 60% for autism

Epigenetic differences arise during the lifetime of monozygotic twins

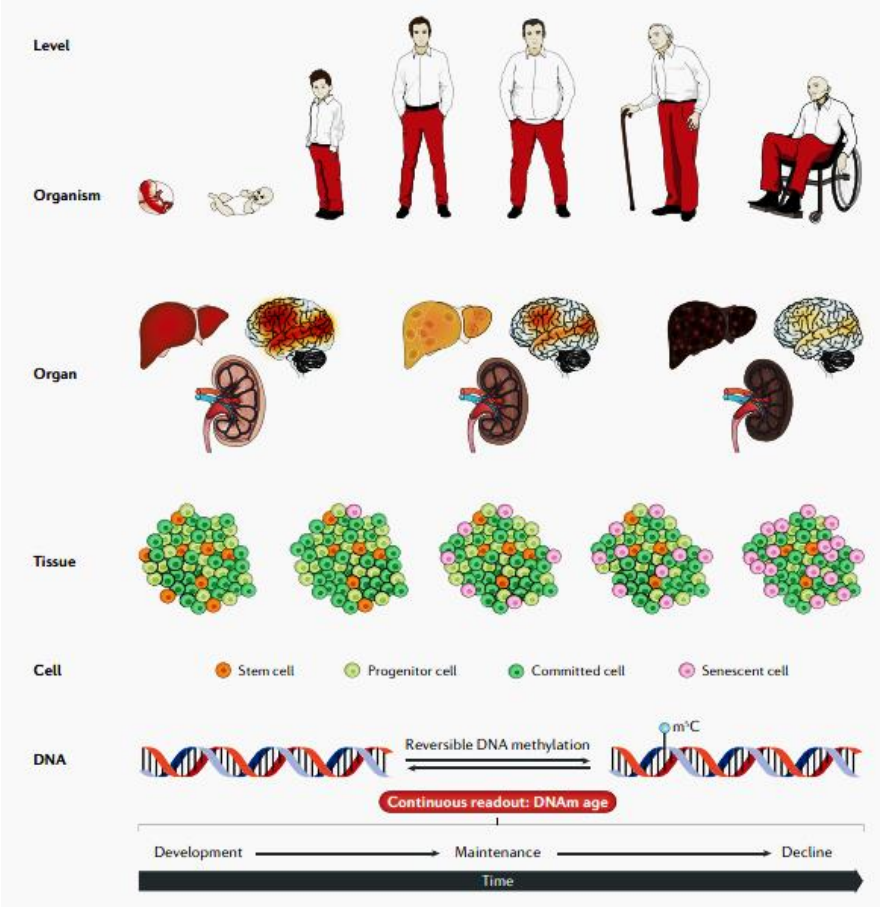
PNAS | July 26, 2005 |



Comunque i gemelli monozigoti hanno sempre meno differenze nella metilazione del DNA rispetto ai gemelli dizigoti

(Zdravkovic et al, J Intern Med 2002; 252: 247-54.)

Perché il tuo DNA non è il tuo destino



EPIGENETICS

DNA methylation-based biomarkers and the epigenetic clock theory of ageing

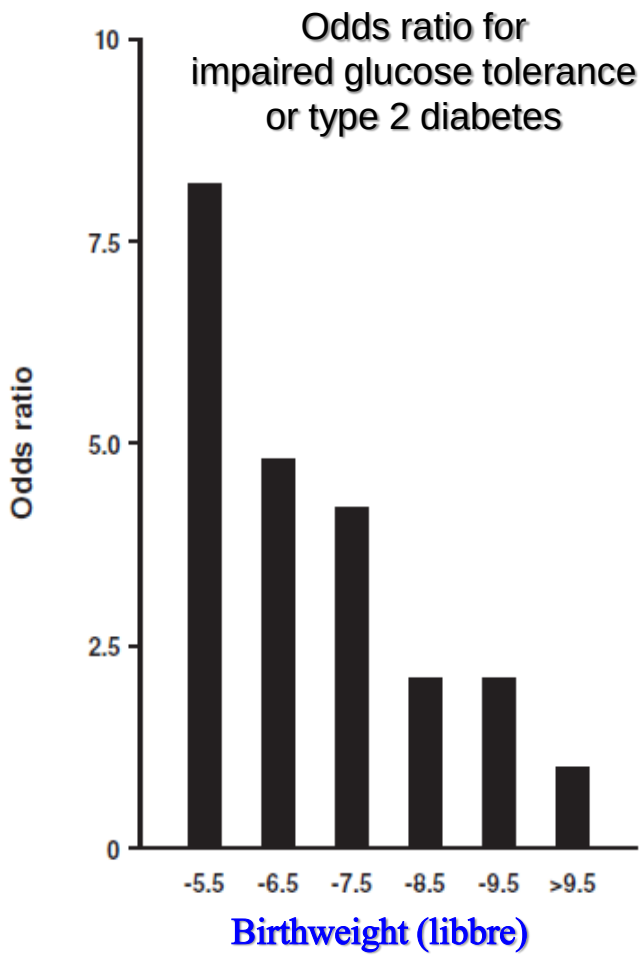
NATURE REVIEWS | GENETICS 2018

Steve Horvath[1,2] and Kenneth Raj[3]*

Fig. 3 | **Tissue function versus DNA methylation-based age.** DNA methylation-based (DNAm) age is a continuous readout of molecular processes that play a role in development, tissue maintenance and, ultimately, decline. DNAm age increases as stem and progenitor cells undergo differentiation to produce more committed cells for growth during the early developmental years and for replenishment of committed cells during the maintenance years (after 20 years).

Riprendiamo il 1° interrogativo:

come può cambiare l'espressione genica nelle generazioni esposte a carestia fetale senza modifiche del DNA?



Poor nutrition in fetal and early infant life ....
greatly increase susceptibility
to the development of Type 2 diabetes

Charles Nicholas Hales, 1992,

Epigenetics of Royalty

Science. 2008 Mar 28;319(5871):1827-30. doi: 10.1126/science.1153069. Epub 2008 Mar 13

Nutritional control of reproductive status in honeybees via DNA methylation

PLoS Biol 8(11): 2010

Diet and Cell Size Both Affect Queen-Worker Differentiation through DNA Methylation in Honey Bees (*Apis mellifera*, Apidae)

PLoS on April 2011

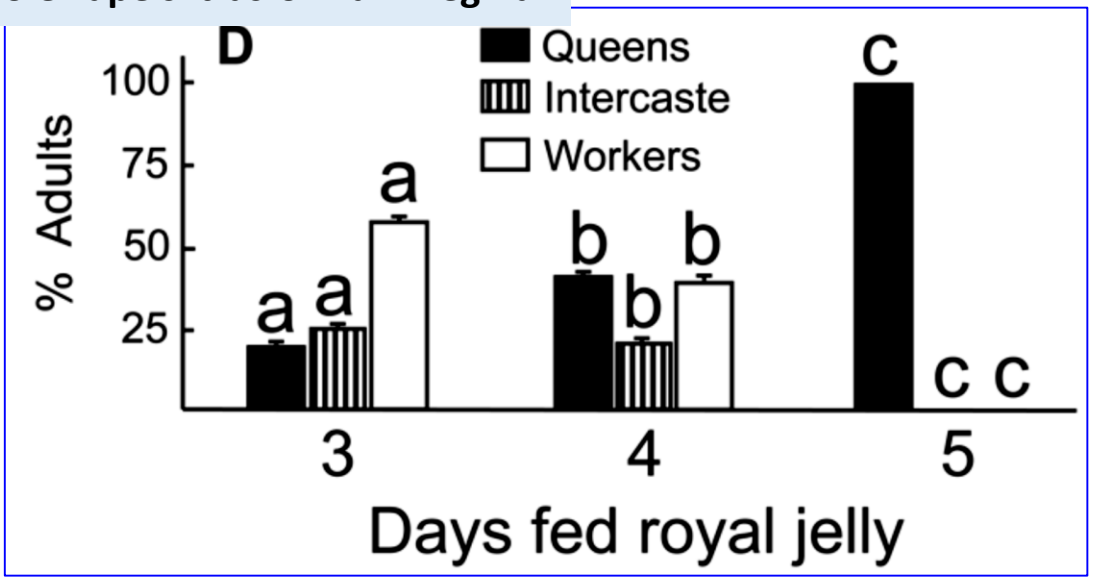
SOLO LE LARVE ALIMENTATE CON PAPPA REALE SVILUPPANO REGINE

Il gene dinactina p62 esprime i geni necessari per la trasformazione in regina.

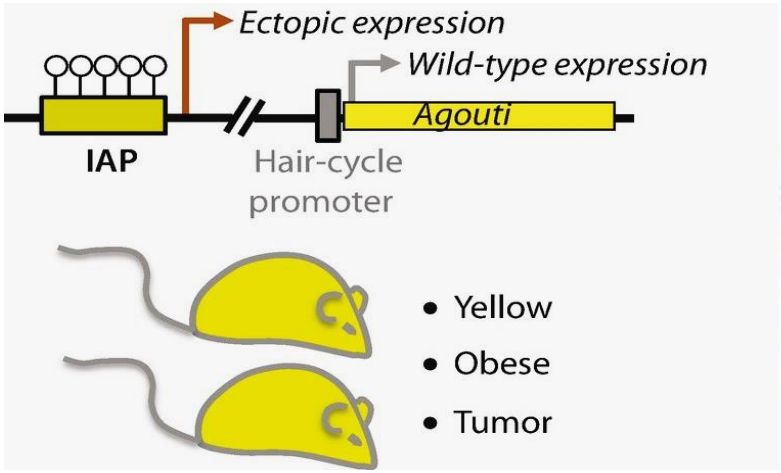
La DNMT3 determina la metilazione (= inattivazione) del gene dinactina p62

La pappa reale riduce l'attività di DNMT3 e quindi diminuisce la metilazione del gene dinactina p62.

Il gene viene derepresso e l'ape si trasforma in regina.



The agouti mouse model: an epigenetic biosensor for nutritional and environmental alterations on the fetal epigenome *Nutr Rev.* 2008 August



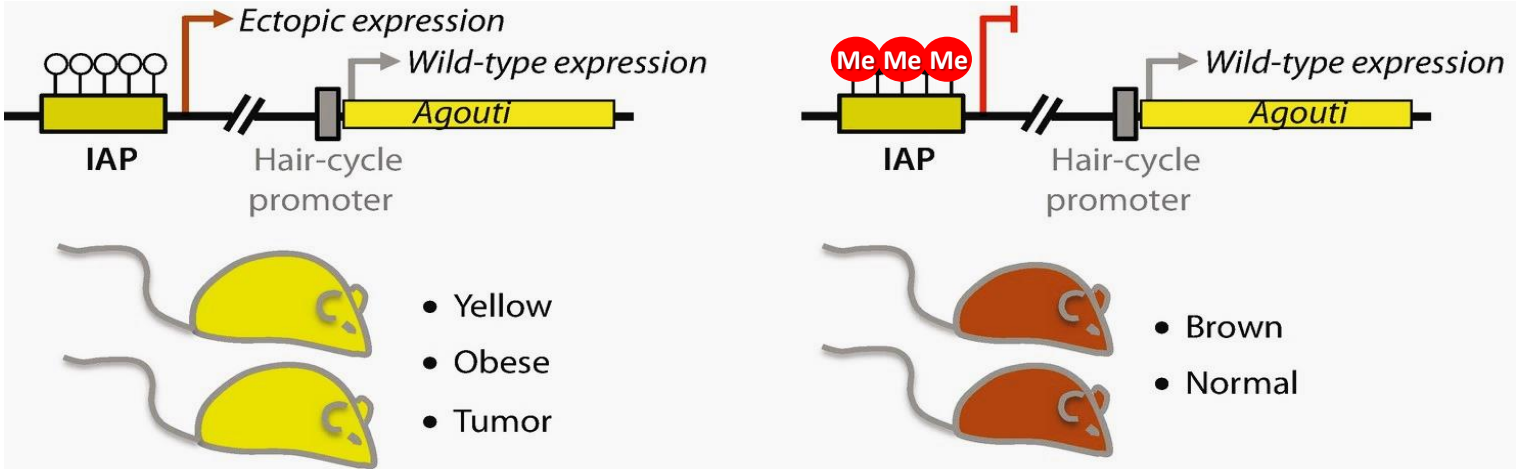
Questo topo presenta un gene, detto Agouti, responsabile del colore marrone del manto.

E' attivo solo per un breve periodo durante lo sviluppo: in seguito viene silenziato.

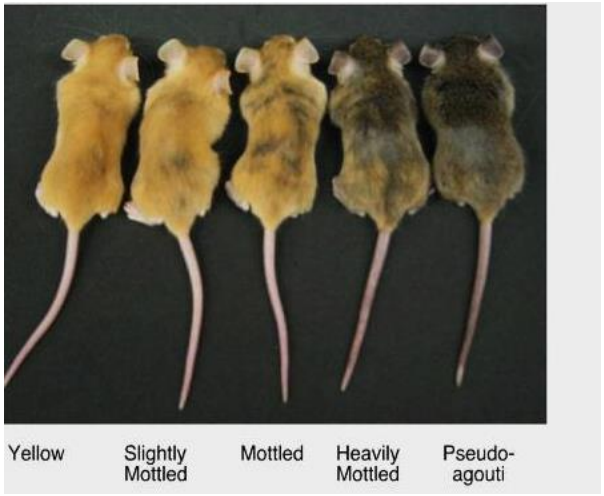
A monte di questo gene si è verificato l'inserimento di un retrotrasposone (IAP).

Un promotore criptico nell'estremità prossimale dell'IAP (A^{vy}) promuove la trascrizione prolungata ed ectopica di Agouti che porta a pelliccia gialla, obesità e carcinogenesi.

The agouti mouse model: an epigenetic biosensor for nutritional and environmental alterations on the fetal epigenome *Nutr Rev.* 2008 August



Il retrotrasposone (IAP) può essere inattivato attraverso metilazione: in tal modo il gene Agouti non viene espresso e il topo è marrone e sano



A seguito di un'alimentazione ricca di donatori di metili (acido folico, betaina, Vit B12) la metilazione viene facilitata e il topo è marrone e sano

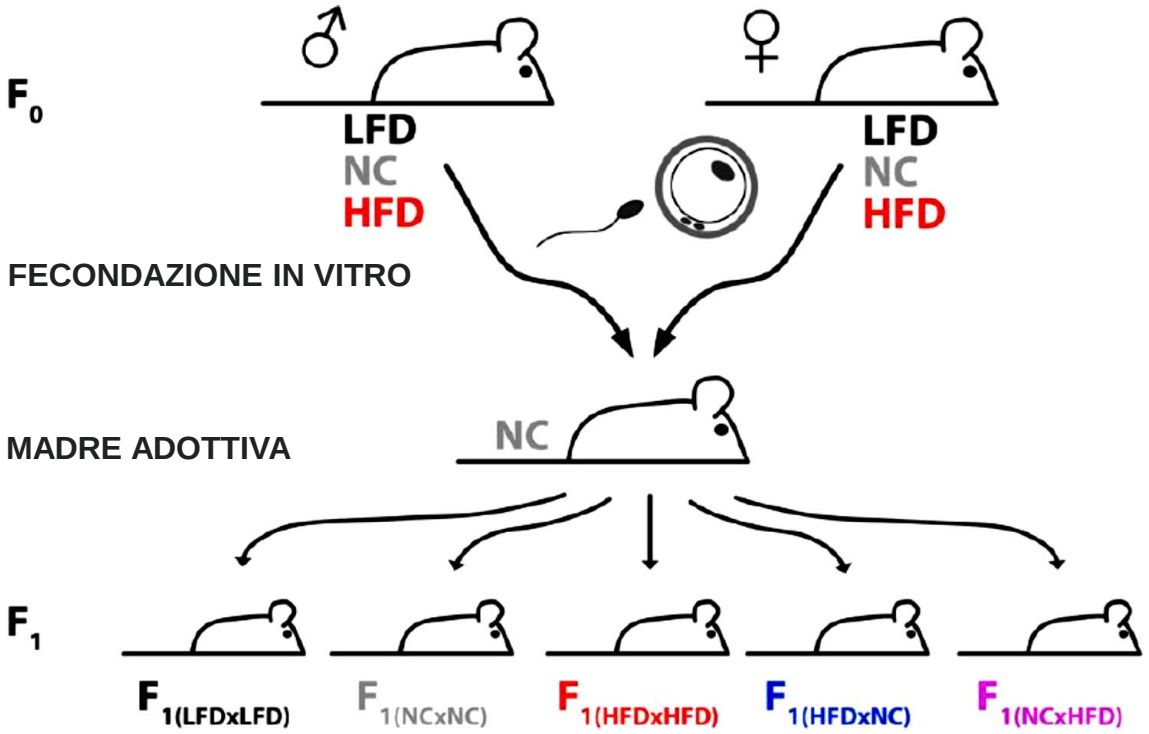
Per gradi intermedi di metilazione si hanno fenotipi intermedi dal giallo (non metilato) al marrone (metilato).

Epigenetic germline inheritance of diet-induced obesity and insulin resistance

NATURE GENETICS VOLUME 48 | NUMBER 5 | MAY 2016

EPIGENETICA TRANSGENERAZIONALE

LFD: dieta basso contenuto di grassi
NC: dieta normale
HFD: dieta ad alto contenuto di grassi



Parental diets (father x mother)

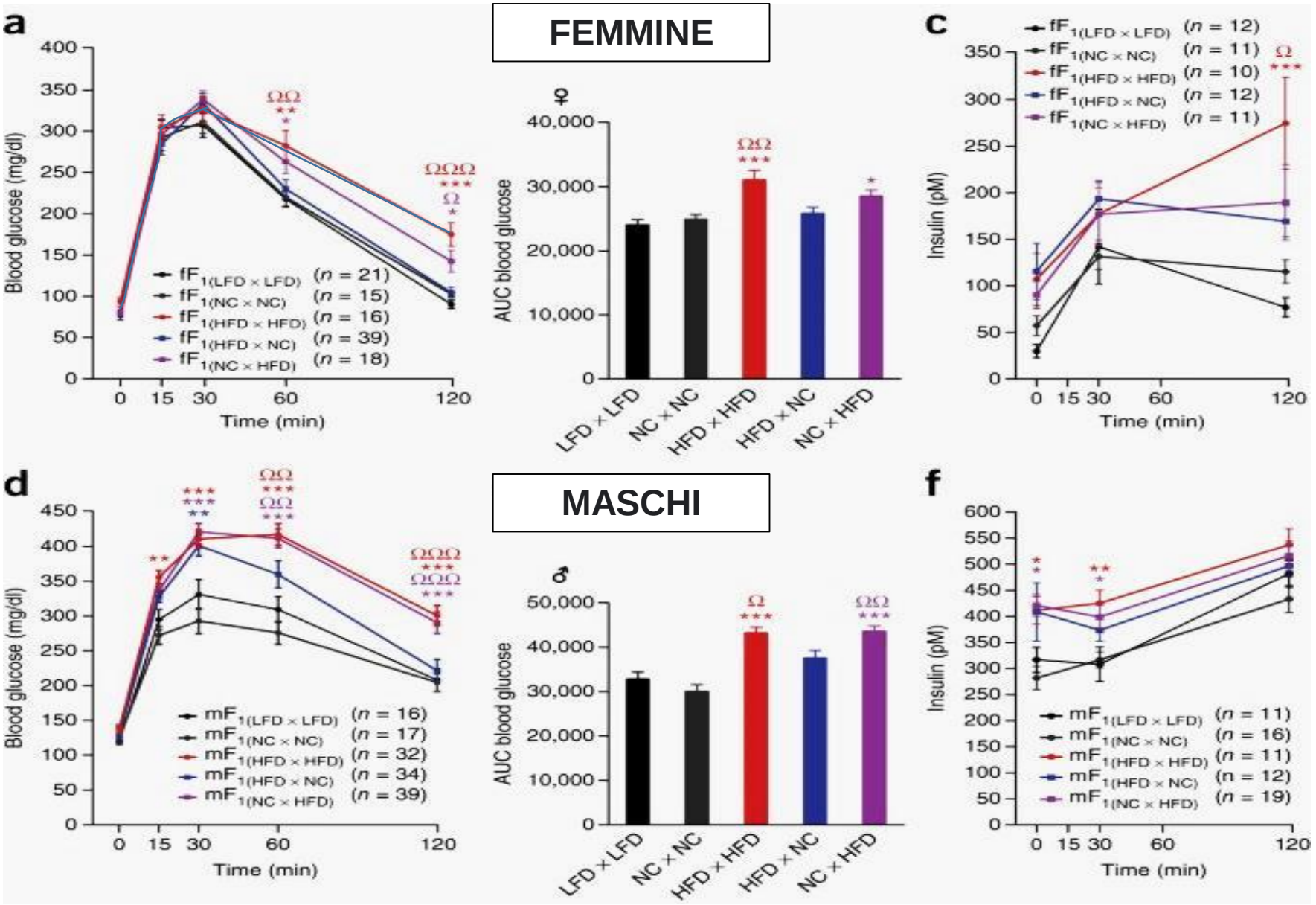
Two-cell embryos were transferred into healthy foster mothers that were maintained on an NC diet.

All offspring (F_1) were weaned and kept on an NC diet until 9 weeks of age.

At 9 weeks of age, all F_1 offspring were placed on an HFD diet until 15 weeks of age.

Epigenetic germline inheritance of diet-induced obesity and insulin resistance

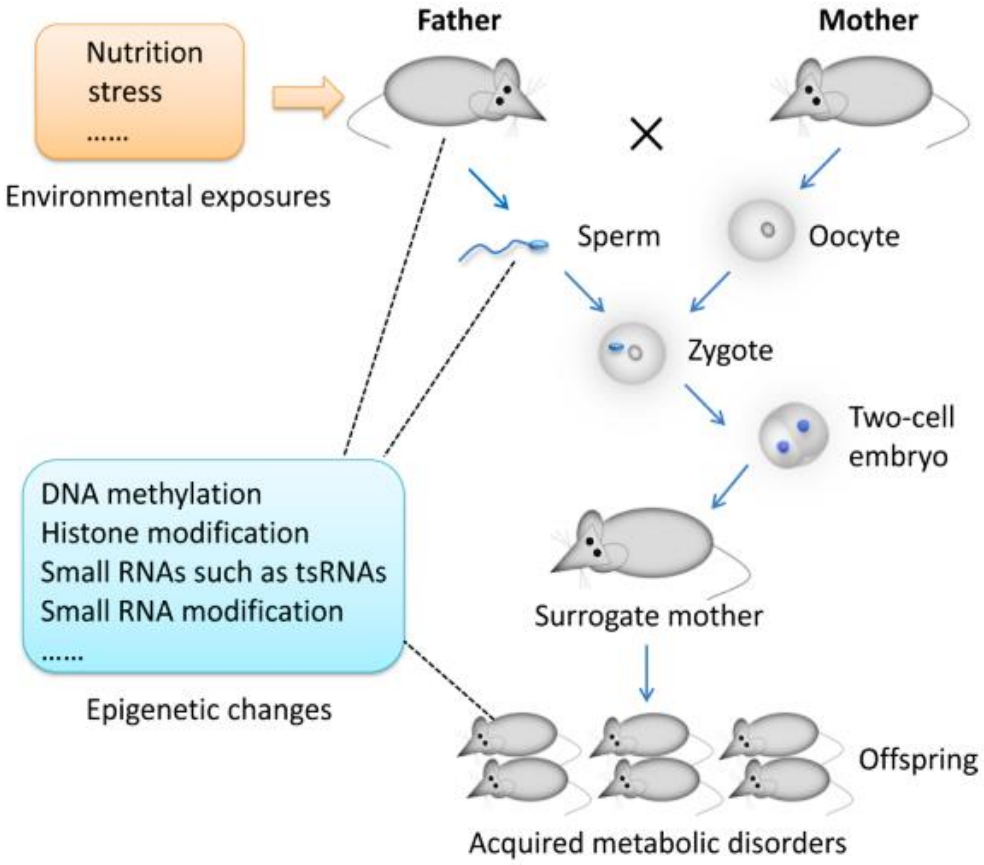
NATURE GENETICS VOLUME 48 | NUMBER 5 | MAY 2016



EPIGENETICA TRANSGENERAZIONALE

Sperm tsRNAs and acquired metabolic disorders

Journal of Endocrinology
(2016) **230**, F13–F18

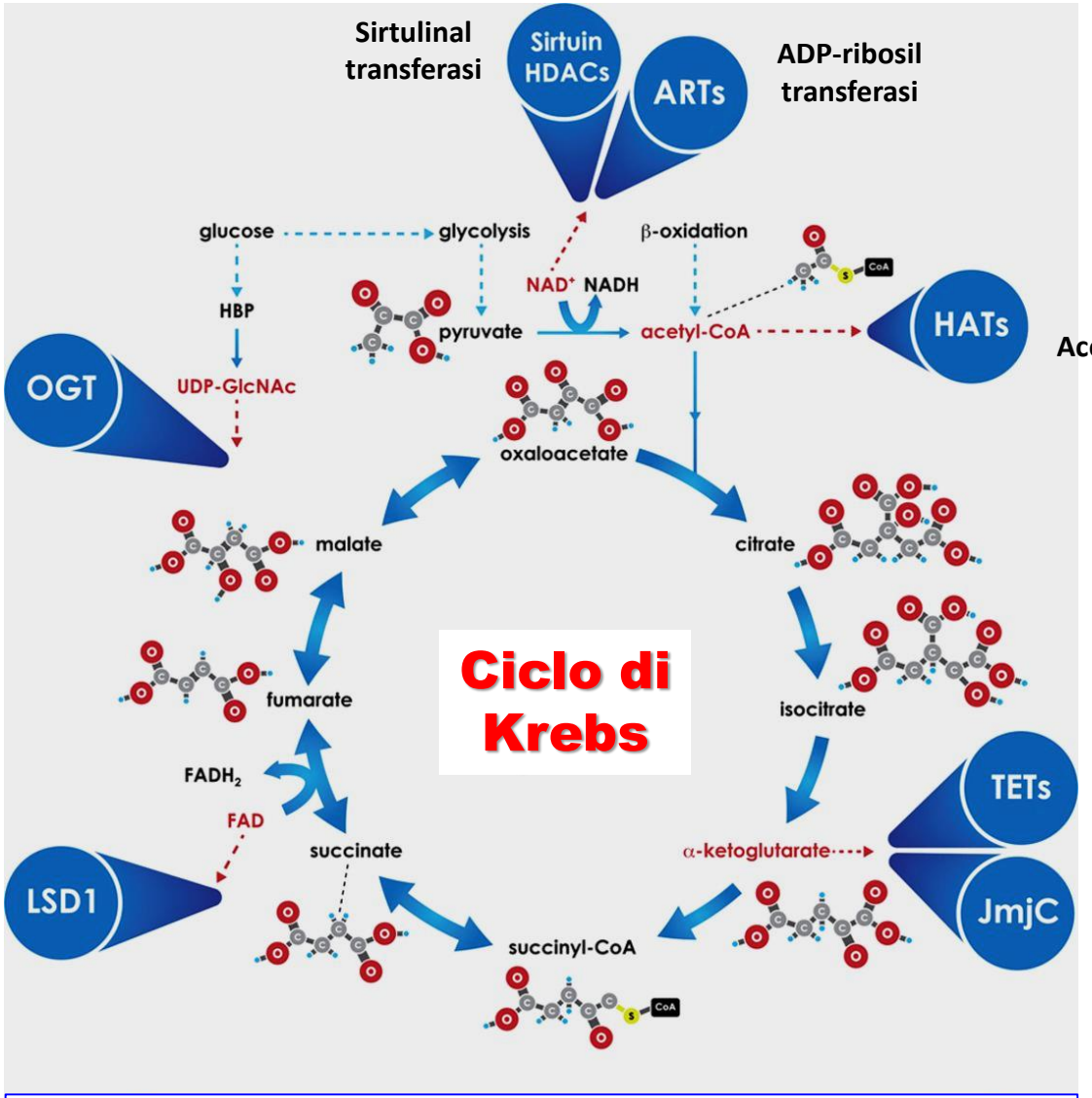


Small non-coding RNA (sncRNAs) trasferiti da ratti maschi sottoposti a dieta con alto contenuto di grassi, tramite iniezioni di sperma, in zigoti da ratti con dieta bilanciata hanno causato sindrome metabolica nella prole allevata con dieta bilanciata.

I disturbi metabolici nel F_1 progenie non erano correlati alla metilazione del DNA nelle isole CpG.

Pertanto gli sncRNA degli spermatozoi rappresentano un fattore epigenetico paterno indipendente che può mediare direttamente l'ereditarietà intergenerazionale dei disturbi metabolici indotti dalla dieta.

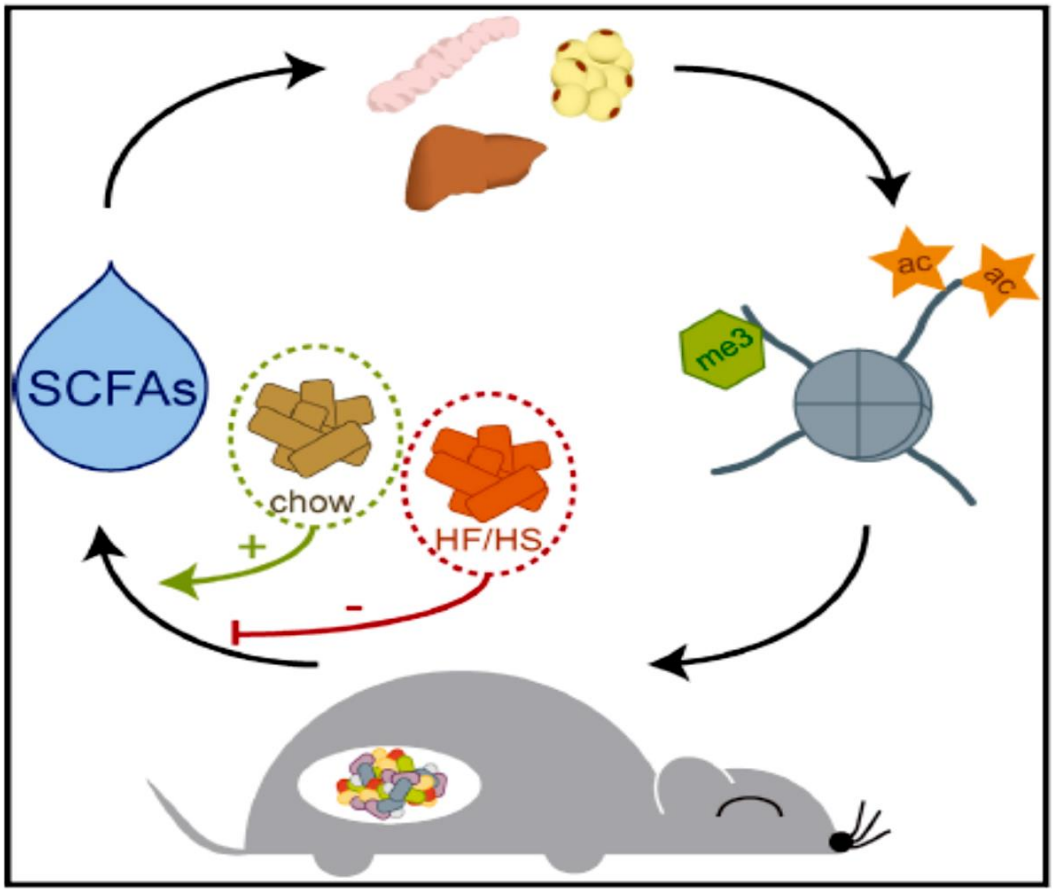
Epigenetics and Metabolism Circulation Research 2015



Gli intermedi del metabolismo energetico
sono tutti cofattori per modifiche epigenetiche

Diet-Microbiota Interactions Mediate Global Epigenetic Programming in Multiple Host Tissues

Molecular Cell 2016



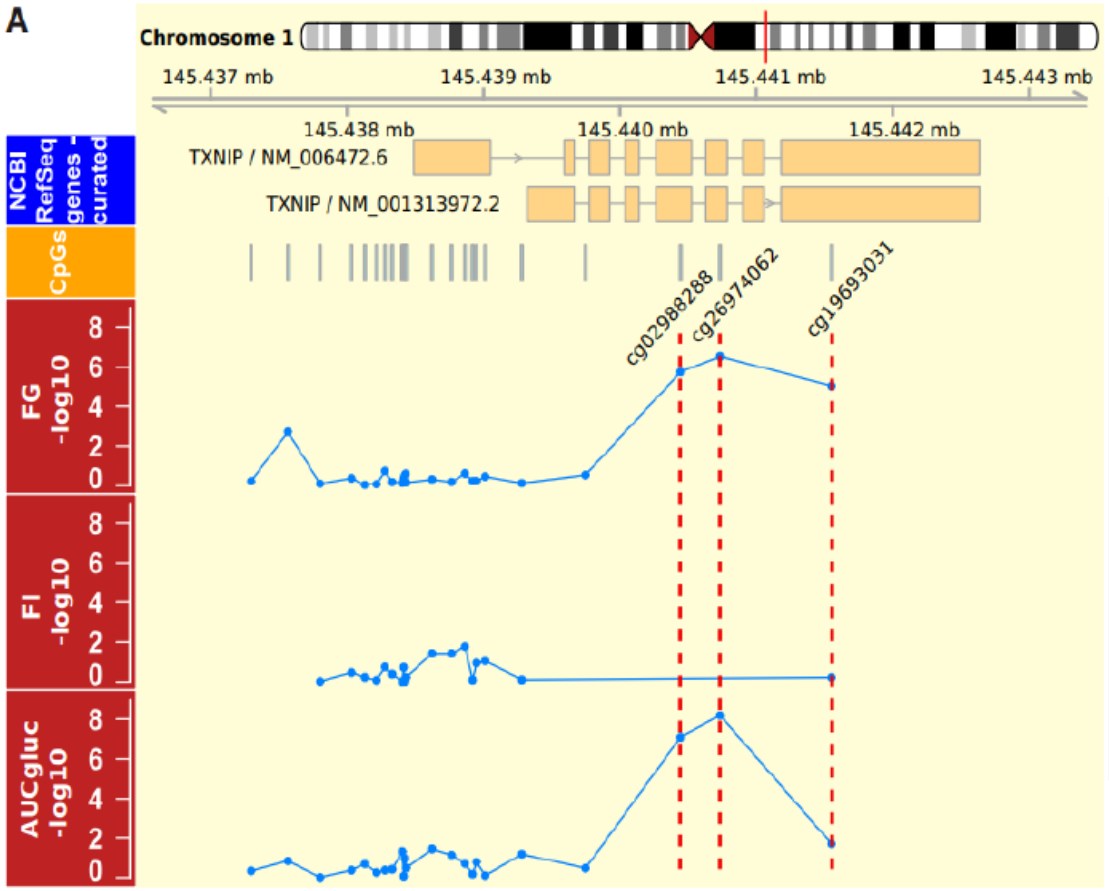
Highlights

- Gut microbiota alter host histone acetylation and methylation in multiple tissues
- Western diet suppresses microbiota-driven SCFA production and chromatin effects
- SCFAs recapitulate microbiota-driven chromatin and transcriptional effects

Maternal Glycemic Dysregulation During Pregnancy and Neonatal Blood DNA Methylation: Metaanalyses of Epigenome-Wide Association Studies

Diabetes Care 2022;

A



ANTIOXIDANTS & REDOX SIGNALING
Volume 36, Numbers 13–15, 2022

Thioredoxin-Interacting Protein in Cancer and Diabetes

TABLE 1. KEY NOTES OF THIS REVIEW

(1) *Txnip* is the gene to protect from starvation.
(2) *Txnip* is the most representative gene induced by glucose.
(3) Txnip suppresses glucose uptake.
(4) Txnip accumulation worsens diabetes.
(5) Txnip acts as a tumor suppressor largely through the control of glucose utilization.
(6) Txnip expression is regulated in multilayered mechanisms such as transcription, microRNA, mRNA stabilization, and protein degradation.
(7) Txnip promotes autophagy.
(8) Txnip may regulate mRNA and long noncoding RNA expression.
(9) Alpha arrestin family proteins regulate intracellular trafficking, including endocytosis and microvesicular formation.

mRNA, messenger RNA; Txnip, thioredoxin-interacting protein.

Conclusioni: L'iperglicemia materna è associata ad ipometilazione di TXNIP nel feto, con conseguente aumentato rischio di iperglicemia e diabete nella vita adulta.

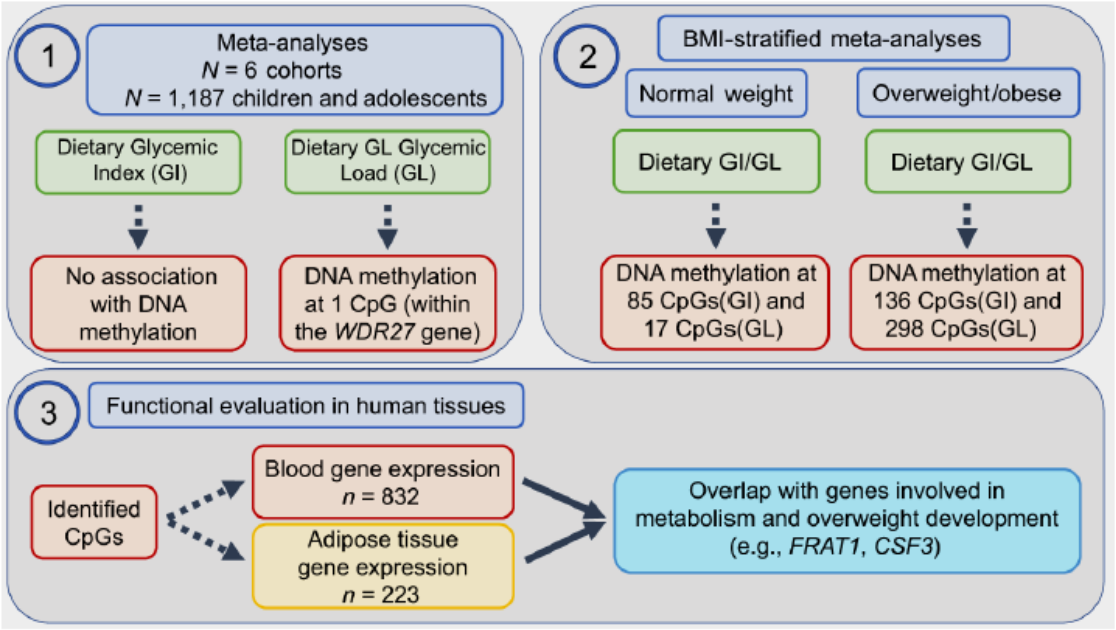
Diabetes Care Diabetes Care 2023;

Epigenome-Wide Meta-analysis Reveals Associations Between Dietary Glycemic Index and Glycemic Load and DNA Methylation in Children and Adolescents of Different Body Sizes

OBJECTIVE Dietary glycemic index (GI) and glycemic load (GL) are associated with cardiometabolic health in children and adolescents, with distinct effects in people with increased BMI.

DNA methylation (DNAm) may mediate these effects.

Thus, we conducted meta-analyses of epigenome-wide association studies (EWAS) between dietary GI and GL and blood DNAm of children and adolescents.



CONCLUSIONS We identified 537 associations between dietary GI and GL and blood DNAm, mainly in children and adolescents with overweight or obesity.

High-GI and/or -GL diets may influence epigenetic gene regulation and thereby promote metabolic derangements in young people with increased BMI

La prima strategia preventiva delle malattie è

all'inizio della vita

DOHaD sta per "Developmental Origins of Health and Disease" :
le esposizioni ambientali durante il periodo prenatale e i primi anni di vita
(i "primi mille giorni")
influenzano permanentemente la salute e aumentano il rischio di malattie croniche nell'età adulta
(Barker DJ et al., Int J Epidemiol 2002)

Heindel et al. Environmental Health (2015) 14:54
DOI 10.1186/s12940-015-0042-7

ENVIRONMENTAL HEALTH

COMMENTARY Open Access

Parma consensus statement on metabolic disruptors

Summary and conclusions

The Parma workshop helped to focus this emerging field by developing an overarching hypothesis for the role of environmental chemicals in the current worldwide epidemics of obesity, diabetes and related metabolic diseases.

EXTERNAL SCIENTIFIC REPORT

Literature review on epidemiological studies linking exposure to pesticides and health effects[1]

Available online: www.efsa.europa.eu/publications

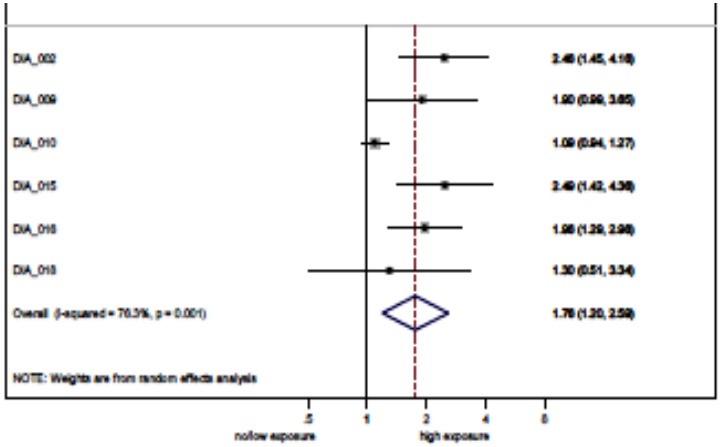


Figure 36: Summary odds ratio (OR) for the association between DDT exposure and type 1 diabetes

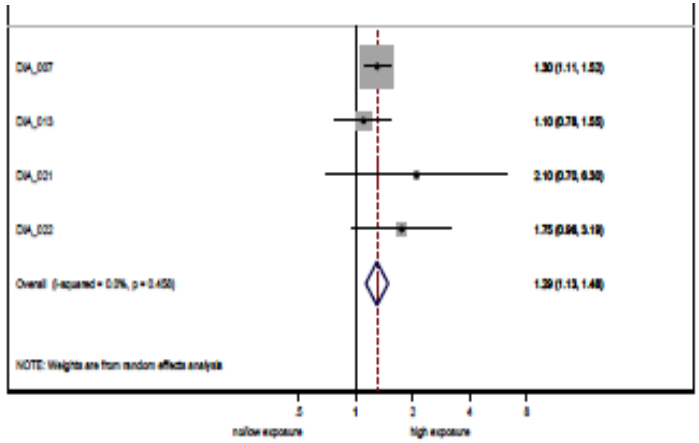


Figure 37: Summary odds ratio (OR) for the association between DDE exposure and type 2 diabetes

Cancer Risk and Parental Pesticide Application in Children of Agricultural Health Study Participants

Environmental Health Perspectives • VOLUME 112 | NUMBER 5 | April 2004

An increased risk of cancer was detected among children whose fathers did not use chemically resistant gloves (OR = **1.98**) compared with children whose fathers used gloves.

	Observed no. of cancer cases	Expected no. of cancer cases	Standardized incidence ratio	95% CI
TOTAL[a]	50	36.87	1,36	1.03–1.79
Leukemia[c]	9	9.88	0.91	0.47–1.75
Lymphoma	9	4.13	2.18	1.13–4.19
Hodgkin's	5	1.96	2.56	1.06–6.14
Non-Hodgkin's	2	1.70	1.18	0.29–4.70
Burkitt's	2	0.37	2.67	0.37–19.0
Brain tumors[d]	11	6.87	1.60	0.89–2.89
Neuroblastoma	3	2.39	1.26	0.40–3.89
Retinoblastoma	2	1.22	1.63	0.41–6.53
Wilms tumor	3	1.92	1.56	0.50–4.84
Bone tumors	4	1.82	2.19	0.82–5.84
Soft-tissue tumors	3	2.57	1.17	0.38–3.62
Germ cell tumors	5	1.71	2.34	0.88–6.24

[a]Cancer rates for Iowa 1975–1998 were used as reference standard in calculation of standardized incidence ratios.

CORRIERE DELLA SERA

9 feb 2024

Unione europea, la riforma abbandonata sui pesticidi (dopo le proteste dei trattori): stop ai divieti vicino alle scuole

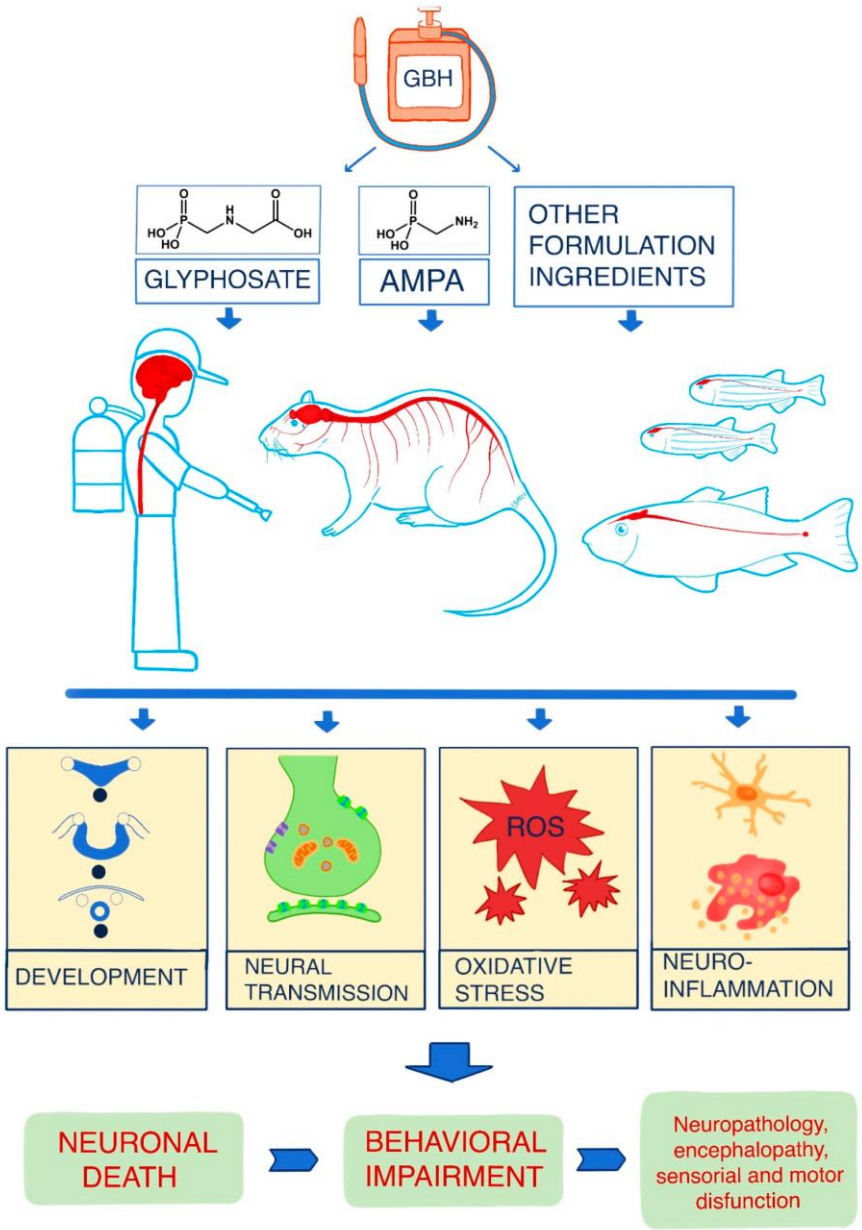
Dall'obiettivo di dimezzarli entro il 2030 al divieto di usarli in aree "sensibili" come parchi, scuole e ospedali: tutte le misure ritirate dall'Ue per andare incontro alle proteste degli agricoltori

Sia gli agricoltori sia chi utilizza professionalmente i pesticidi, secondo la proposta, avrebbero dovuto privilegiare metodi alternativi e più ecologici per prevenire le infestazioni. Le alternative avrebbero dovuto essere definite da ciascun Paese membro tramite norme specifiche per ogni coltura. **Tra i metodi alternativi elencati nella normativa, c'erano ad esempio la rotazione delle colture e il ricorso a tecniche di agricoltura di precisione.**

Review

Toxic Effects of Glyphosate on the Nervous System: A Systematic Review

Int. J. Mol. Sci. **2022,**



Summary …..The doses of glyphosate that produce these neurotoxic effects vary widely but are lower than the limits set by regulatory agencies. Although there are important discrepancies between the analyzed findings**, it is unequivocal that exposure to glyphosate produces important alterations in the structure and function of the nervous system of humans,** rodents, fish, and invertebrates.

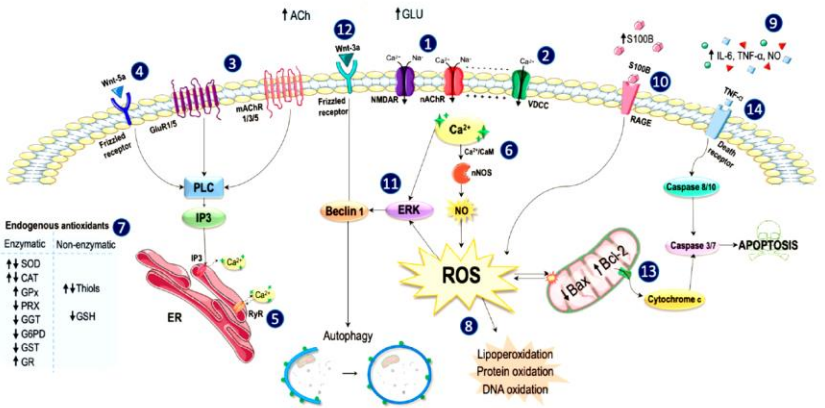


Figure 4. Possible mechanism of action of glyphosate or GBH in the nervous system. The presence

Epigenetic Changes Associated With Exposure to Glyphosate-Based Herbicides in Mammals

Frontiers in Endocrinology

May 2021

Compound	Modification	Tissue/Cell	Main Effects
Humans			
Glyphosate	DNA methylation (33)	**Cell Mononucl Perif**	Decrease global 5mC percentage Increase methylation of p53 promoter
Glyphosate	DNA methylation (34)	**Cell Mononucl Perif**	Decrease global 5mC percentage Change methylation pattern of p21 and p53 promoters Alter the expression genes involved in regulation of cell cycle (CCND1, p16, P21, and P53) and apoptosis (BCL2)
Glyphosate	DNA methylation (35)	**Linea Cellulare Mammella Normale**	DNA hypomethylation occurring *via* TET pathway Changes in methylation patterns of MTRNRL2 and DUX4 genes Exposure to glyphosate and miRNA 182-5p induced tumor development in 50% mice TET inhibitor prevents tumor formation in glyphosate-miR 182-5p-cells
AMPA and Glyphosate	DNA methylation and histone modification (36)	**Cell Mononucl Perif**	Changes in the expression of DNMT1 and HDAC3 by glyphosate and AMPA Changes in the expression of DMNT3A by glyphosate
AMPA	DNA methylation (36)	**Cell Mononucl Perif**	Decrease global 5mC percentage Change methylation pattern of p21 and p53 promoters Increase the expression of CCND1
Rodents			
GBH	DNA methylation (37)	Rat mammary gland	Alter mammary gland development Decrease ERα protein and mRNA expression (transcripts OS, O, OT, and E1) Changes in methylation patterns of ERα promoters in post-puberal animals
GBH	DNA methylation and histone modification (38)	Rat uterus	Increase ERα mRNA during pre-implantation period Increase the relative abundance of ERα-O transcript variant Alter methylation status and histone post-transductional modifications in the O promoter of ERα gene.
GBH	miRNA (39)	Mouse brain (PFC)	55 upregulated and 19 downregulated miRNAs Alter Wnt/β-catenin and Notch pathways
GBH	circRNA (40)	Mouse brain (Hip)	330 upregulated and 333 downregulated circRNAs
Glyphosate	DNA methylation (41)	Rat sperm	Increase pathologies in F2 and F3 (prostate, ovarian and kidney diseases, obesity, birth abnormalities, and tumor growth) DMRs in sperm
Glyphosate	DNA methylation and histone modification (42)	Rat sperm	DMRs and DHRs in F3 generation.

DHRs, Differential histone retention sites; DMRs, Differential DNA methylation sites; DNMT, DNA methyltransferase; HDAC, histone deacetylase; PBMCs, Peripheral Blood Mononuclear Cells; PFC, Prefrontal Cortex; Hip, Hippocampus.

… e non è poi tanto difficile procurarsi il glifosato…

adama DISERBANTE Totale ERBICIDA GLIFOSATE SISTEMICO 500 ML

Marca: adama

4,4 ★★★★½ 2.750 voti | Cerca in questa pagina

900+ acquistati nel mese scorso

12[85] € (25,70€ / l)

I prezzi degli articoli in vendita su Amazon includono l'IVA. In base all'indirizzo di spedizione, l'IVA potrebbe variare durante il processo di acquisto. Per maggiori informazioni clicca qui.

Marchio	adama
Peso articolo	100 Grammi
Volume liquido	100 Millilitri, 500 Millilitri
Forma articolo	Liquido
Ingredienti attivi	Glifosate

12[85] € (25,70€ / l)

Consegna GRATUITA **3 - 4 luglio**. Maggiori informazioni

Consegna a Camerata Picena 60020: aggiorna luogo

Disponibilità immediata

Quantità: 1

Aggiungi al carrello

Acquista ora

Spedizione AGRIFER S.R.L.

MONSANTO 5 Litri di Roundup Power 2.0 erbicida Post-Emergenza Glifosate Acido Puro 360 gr/lt (10 X 500 ML)

Marca: MONSANTO

4,3 ★★★★½ 261 voti

100+ acquistati nel mese scorso

-11% 79[50] € (15,90€ / l)

Prezzo mediano: ~~89,00€~~

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Marchio	MONSANTO
Peso articolo	360 Grammi
Volume liquido	500 Millilitri

79[50] € (15,90€ / l)

Consegna a 11,50 € **3 - 4 luglio**. Maggiori informazioni

Consegna a Camerata Picena 60020: aggiorna luogo

Disponibilità immediata

Quantità: 1

Aggiungi al carrello

Acquista ora

Spedizione Agrifarm2.0

Venditore Agrifarm2.0

Resi Restituibile entro 30 giorni dal ricevimento

il Salvagente

Leader nei Test di laboratorio contro le truffe ai consumatori

…..mandando in laboratorio su 20 marche di spaghetti... in 7 prodotti abbiamo trovato tracce di glifosato e in 6 (omissis…) il grano veniva anche da paesi extraeuropei. Dal Canada? Per alcuni campioni di pasta il sospetto è forte ma non abbiamo la certezza perché la normativa sull'etichettatura consente alle aziende di poter genericamente indicare la provenienza "Ue" e/o "non Ue"

FOOD ADDITIVES & CONTAMINANTS: PART A
2023, VOL. 40, NO. 11, 1459–1469
https://doi.org/10.1080/19440049.2023.2264976

Diverging fates of cadmium and glyphosate during pasta cooking

GLIFOSATO Mean ± standard deviation ($n = 3$) glyphosate in pasta (dry weight) and cooking water sampled at various time points during cooking. Pasta was prepared from test materials B [application of glyphosate-containing herbicide product at <30% grain moisture content (MC)] and C (application at >30% MC). Unique superscripts indicate means were significantly different (one-way ANOVA, $p < 0.001$).

	Durum test material			
	Test material B		Test material C	
Cooking time (min)	Pasta (mg/kg)	Cooking water (pg/µL)	Pasta (mg/kg)	Cooking water (pg/µL)
0	0.335 ± 0.003^{a}	$<3^{a}$	0.633 ± 0.002^{a}	$<0.003^{a}$
3	0.189 ± 0.001^{b}	15.7 ± 0.1^{a}	0.369 ± 0.005^{b}	29.3 ± 0.5^{b}
5	0.166 ± 0.001^{c}	21.1 ± 0.5^{b}	0.321 ± 0.001^{c}	39 ± 2^{c}
7	0.150 ± 0.001^{d}	25.3 ± 0.3^{b}	0.283 ± 0.003^{d}	47 ± 1^{d}
9	0.136 ± 0.001^{e}	31.1 ± 0.6^{b}	0.254 ± 0.005^{e}	54 ± 4^{e}
11	0.124 ± 0.003^{f}	35 ± 2^{b}	0.240 ± 0.009^{f}	63 ± 3^{f}
13	0.111 ± 0.001^{g}	37 ± 2^{b}	0.218 ± 0.005^{g}	73 ± 3^{g}
15	0.105 ± 0.003^{h}	41 ± 2^{b}	0.201 ± 0.005^{h}	74 ± 1^{h}

CADMIO Mean ± standard deviation ($n = 3$) cadmium in pasta (dry weight) and cooking water sampled at various time points during cooking. Pasta was prepared from test materials representing a high cadmium accumulating variety (A) and a low cadmium accumulating variety (B, C). Unique superscripts indicate means were significantly different (one-way ANOVA, $p < 0.001$).

	Durum test material					
	Test material A		Test material B		Test material C	
Cooking time (min)	Pasta (mg/kg)	Cooking water (pg/µL)	Pasta (mg/kg)	Cooking water (pg/µL)	Pasta (mg/kg)	Cooking water (pg/µL)
0	0.159 ± 0.002^{a}	$<0.1^{a}$	0.048 ± 0.001^{a}	$<0.1^{a}$	0.054 ± 0.001^{a}	$<0.1^{a}$
3	0.170 ± 0.003^{a}	0.45 ± 0.02^{b}	0.059 ± 0.002^{a}	0.203 ± 0.003^{a}	0.052 ± 0.001^{a}	0.167 ± 0.004^{a}
5	0.171 ± 0.004^{a}	0.57 ± 0.03^{c}	0.064 ± 0.009^{a}	0.32 ± 0.02^{ab}	0.054 ± 0.002^{a}	0.23 ± 0.01^{ab}
7	0.176 ± 0.001^{a}	0.68 ± 0.03^{d}	0.063 ± 0.004^{a}	0.35 ± 0.02^{ab}	0.054 ± 0.003^{a}	0.272 ± 0.005^{ab}
9	0.176 ± 0.002^{a}	0.75 ± 0.03^{e}	0.063 ± 0.004^{a}	0.39 ± 0.02^{ab}	0.056 ± 0.003^{a}	0.32 ± 0.01^{ab}
11	0.176 ± 0.004^{a}	0.85 ± 0.03^{f}	0.0600 ± 0.0002^{a}	0.41 ± 0.01^{ab}	0.059 ± 0.005^{a}	0.33 ± 0.02^{ab}
13	0.176 ± 0.002^{a}	0.96 ± 0.07^{g}	0.061 ± 0.002^{a}	0.42 ± 0.01^{b}	0.056 ± 0.002^{a}	0.362 ± 0.005^{b}
15	0.178 ± 0.003^{a}	0.98 ± 0.02^{h}	0.060 ± 0.001^{a}	0.41 ± 0.02^{b}	0.057 ± 0.006^{a}	0.36 ± 0.01^{b}

JAMA Network Open

May 23, 2024

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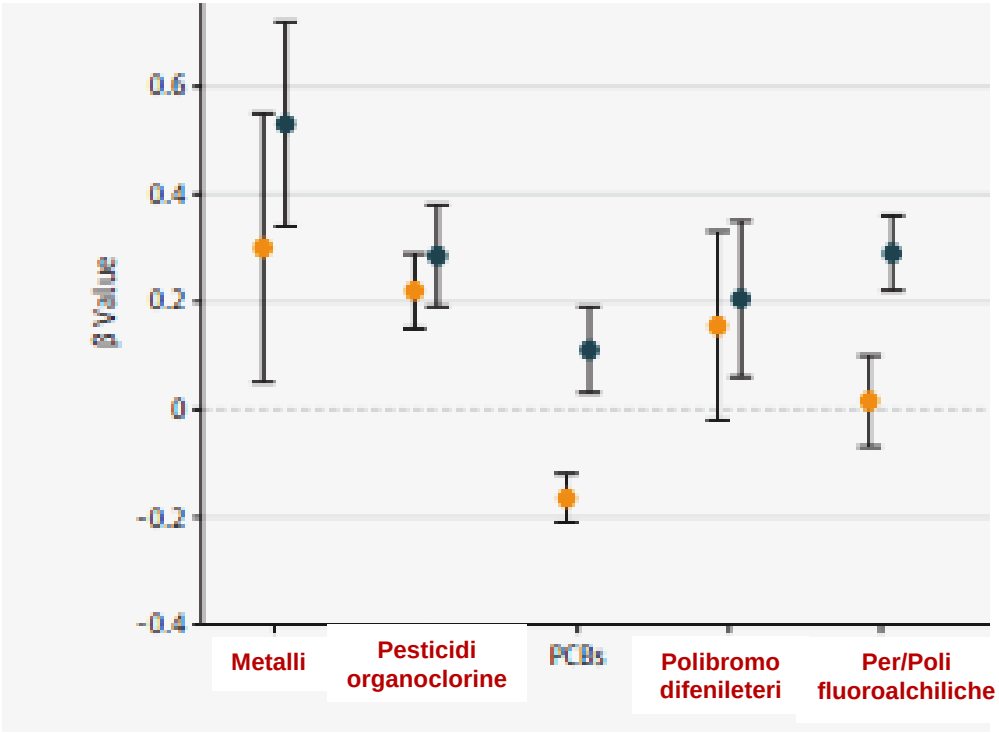
Prenatal Exposure to Chemical Mixtures and Metabolic Syndrome Risk in Children

Figure 2. Associations of Prenatal Chemical Mixtures With Metabolic Syndrome (MetS) Score Stratified by Sex



Folate concentrations and serum perfluoroalkyl and polyfluoroalkyl substance concentrations in adolescents and adults in the USA (National Health and Nutrition Examination Study 2003–16): an observational study

Lancet Planet Health 2023;

	Unadjusted percentage change (95% CI)	
Folate in red blood cells‡		
PFOA	−36·43% (−41·41 to −31·04)	−7·34% (−16·57 to 2·91)
PFOS	−65·00% (−68·00 to −61·00)	−24·36% (−33·21 to −14·34)
PFNA	−18·74% (−28·83 to −7·23)	−13·00% (−21·87 to −3·12)
PFHxS	−27·18% (−37·67 to −14·92)	−12·29% (−26·12 to 4·12)
Folate in serum‡		
PFOA	−16·19% (−21·50 to −10·51)	3·82% (−2·32 to 10·34)
PFOS	−43·70% (−48·67 to −38·25)	−11·57% (−17·87 to −4·79)
PFNA	−5·62% (−13·71 to 3·21)	−1·25% (−7·14 to 5·01)
PFHxS	−13·12% (−24·03 to −0·64)	−3·94% (−15·51 to 9·20)

Reduction in PFAS levels for 2,7 fold increase in folate among adolescents adjusted for age, sex, ethnicity, BMI etc

Negative associations exist for PFAS concentrations in plasma and serum in relation to dietary intake of soy, beans, grain, spinach, vegetables, and fruits, which are foods containing high amounts of folate

Interpretation In this large-scale, nationally representative study, **we found consistent inverse associations for most examined serum PFAS compounds in relation to folate concentrations** measured in either red blood cells or serum among both adolescents and adults. These findings are supported by mechanistic in-vitro studies that show the potential of PFAS to compete with folate for several transporters implicated in PFAS toxicokinetics.
If confirmed in experimental settings, these findings could have important implications for interventions to reduce the accumulated PFAS body burden and mitigate the related adverse health effects.

GRAZIE PER L'ATTENZIONE