

Consensus Help Human Early Life Prevention

Dal preconcepimento ai primi 24 mesi di vita

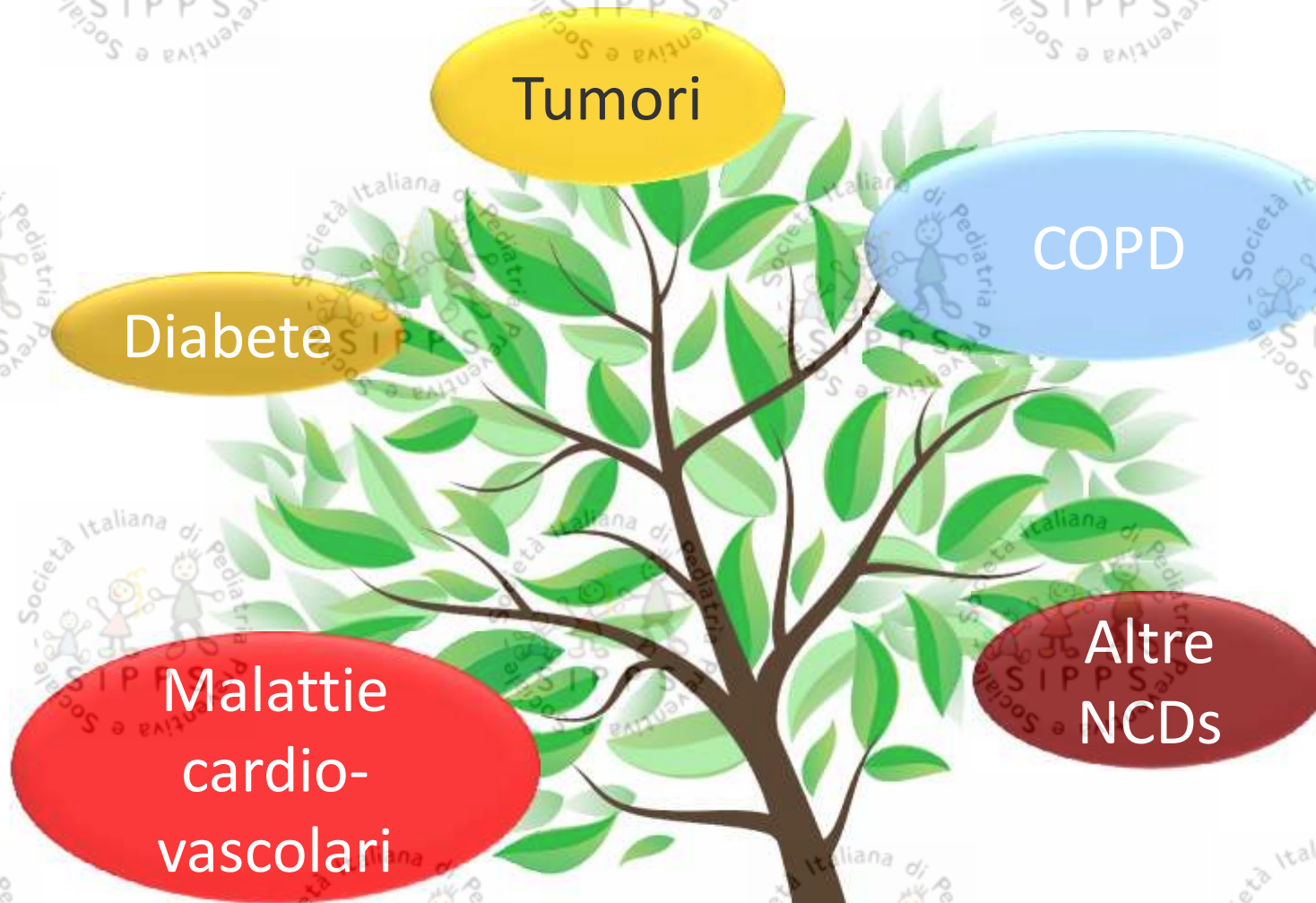
Alberto G. Ugazio

Istituto per la Salute del Bambino e dell'Adolescente



Le Nuove Sfide della Pediatria

Caserta, 2 Marzo 2017





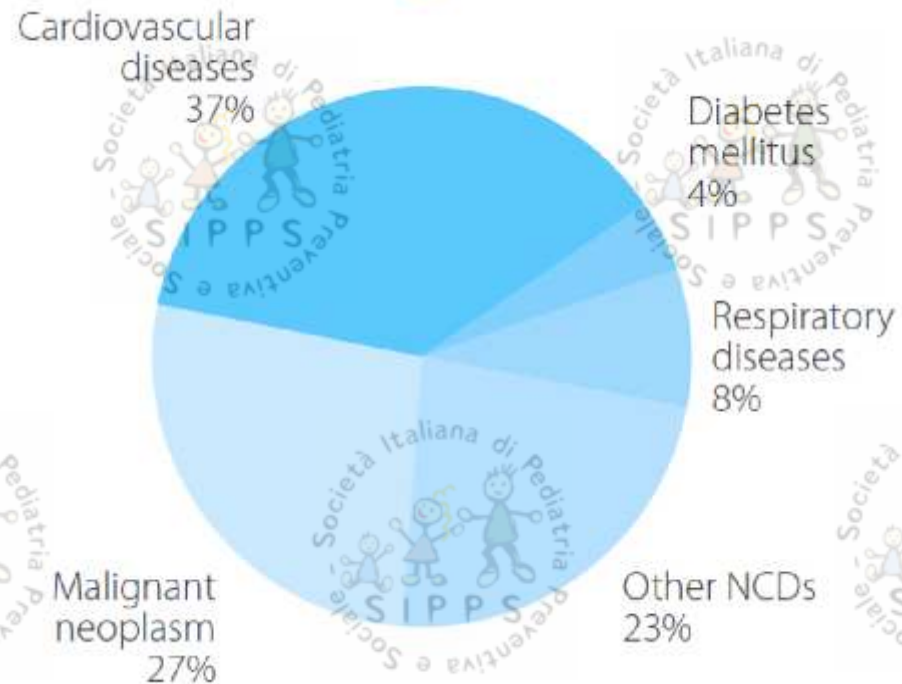
■ Decessi per malattie infettive ■ Decessi per NCD

Mortalità globale per NCDs nel 2012*

Popolazione globale
6.7 miliardi (+ 5.8%)

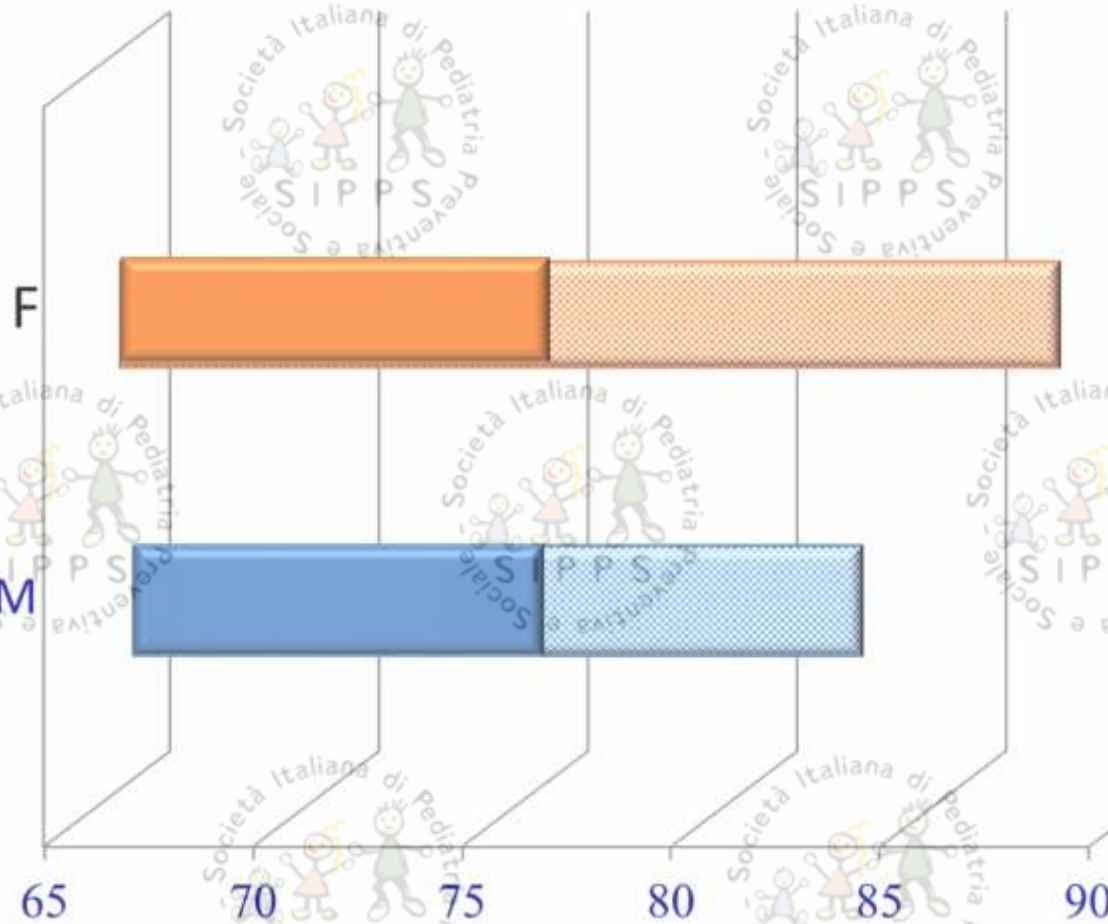
Mortalità globale
58 milioni (+ 1.7%)

Mortalità per NCDs
38 milioni (68%)



* WHO, 2017

EU 28, 2012: anni di vita in salute (■, ■) e aspettativa di vita (■, ■) all'età di 65 anni **



** Eurostat 2014



Tumori

COPD

Diabete

Malattie
cardio-
vascolari

Altre
NCDs

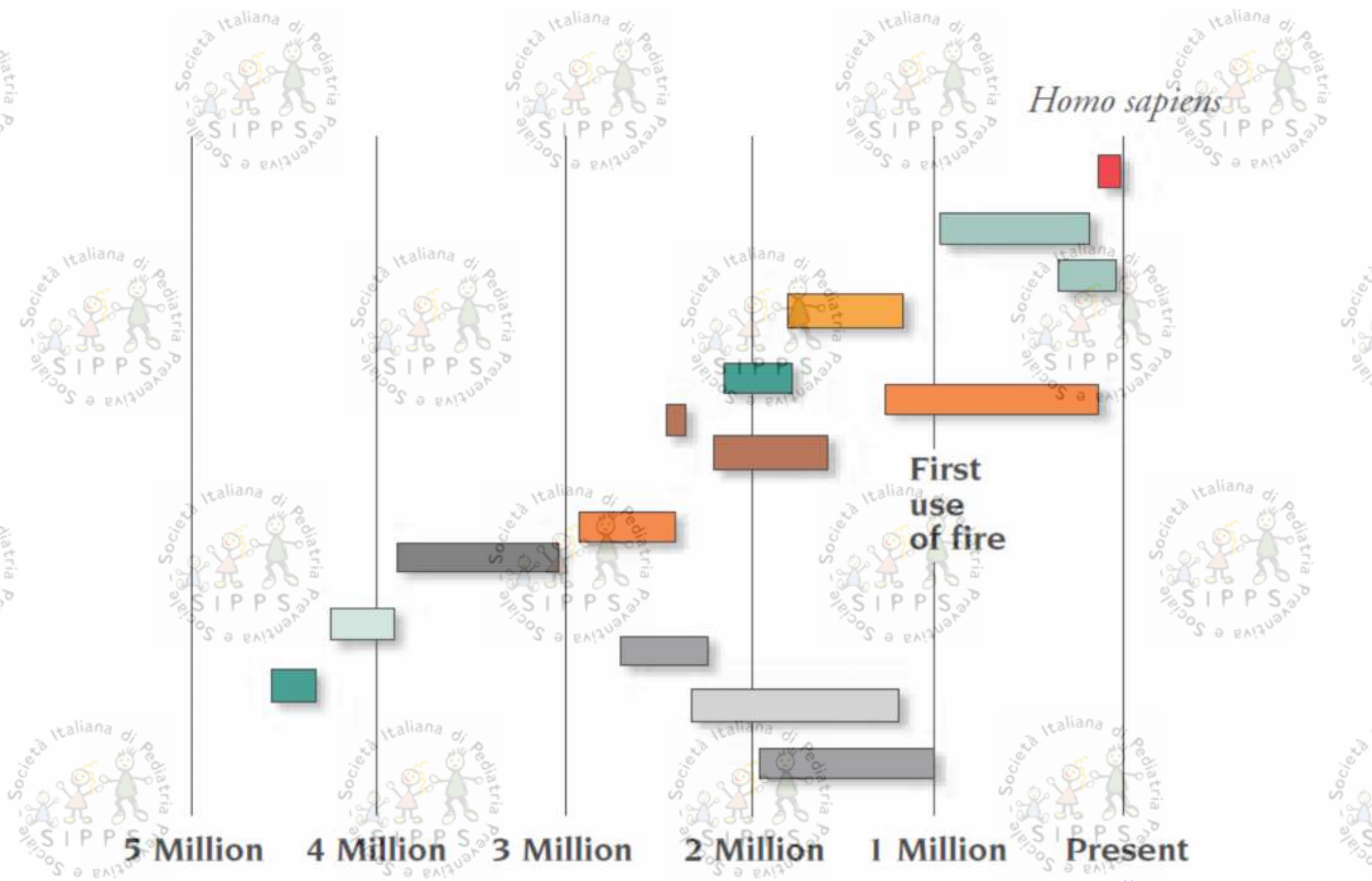
Genoma

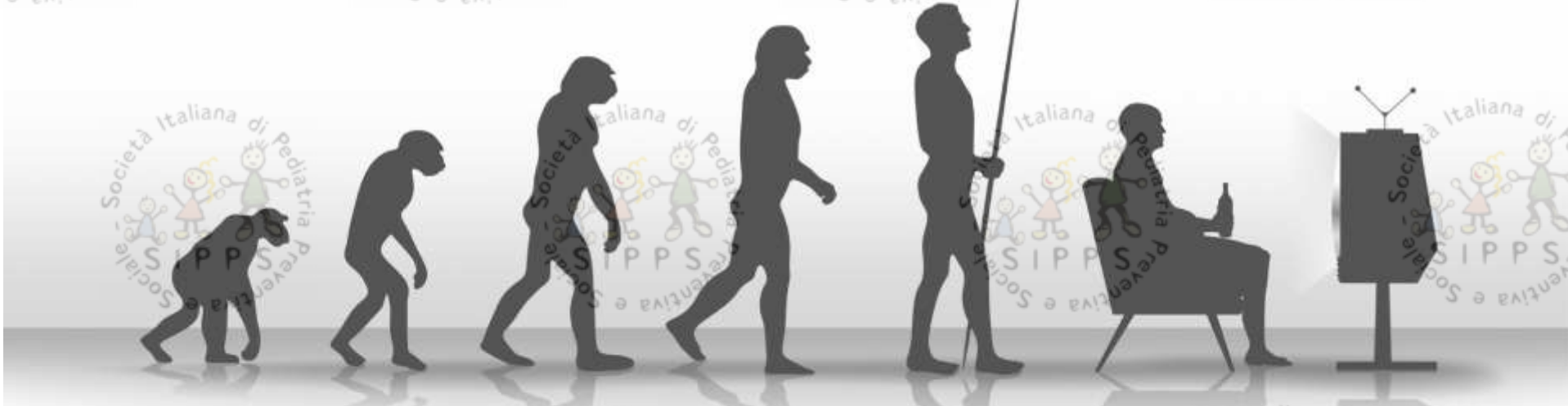
**Inattività
fisica**


Fumo

**Dieta
scorretta**




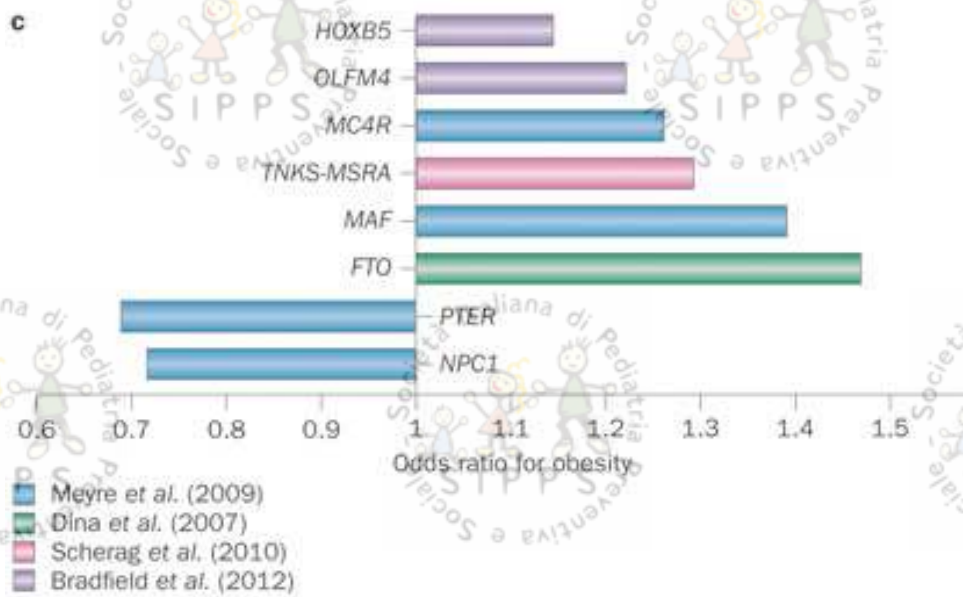
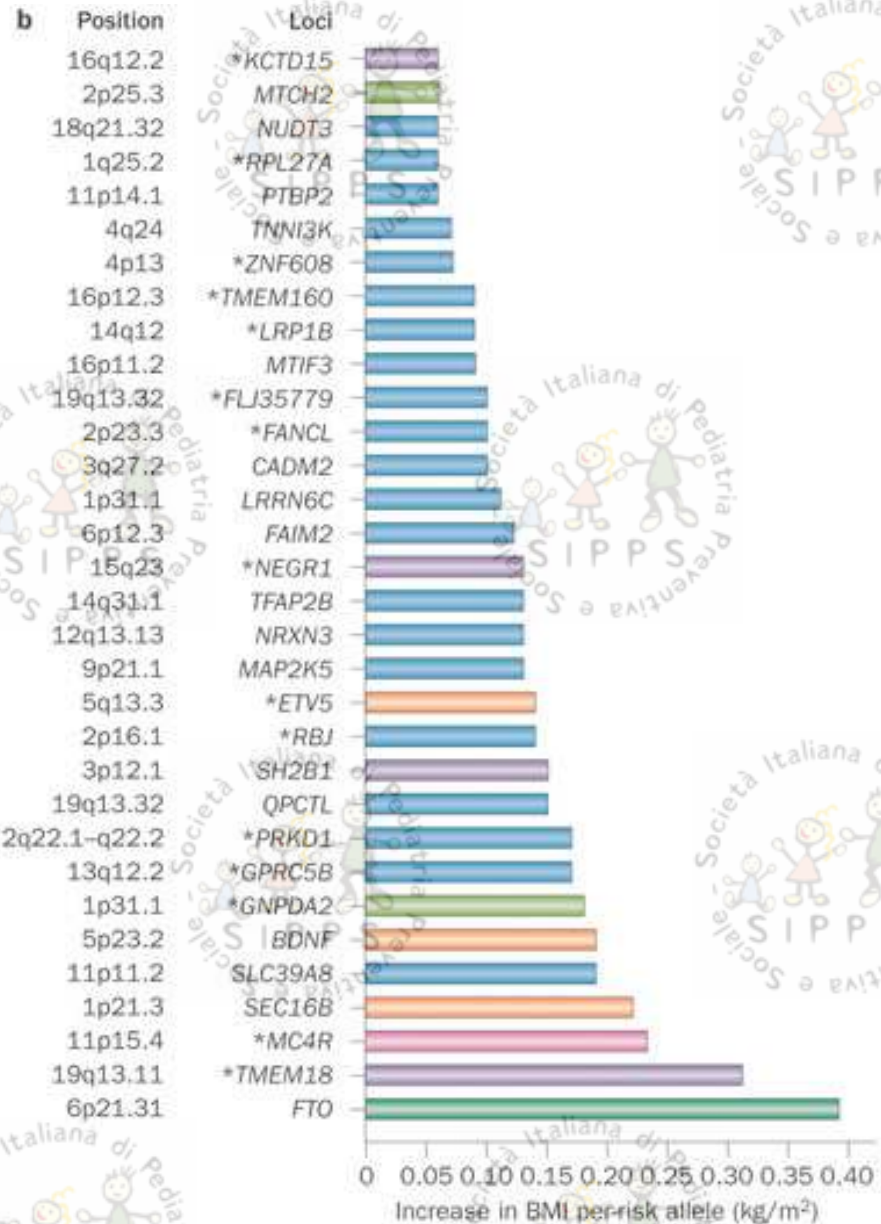
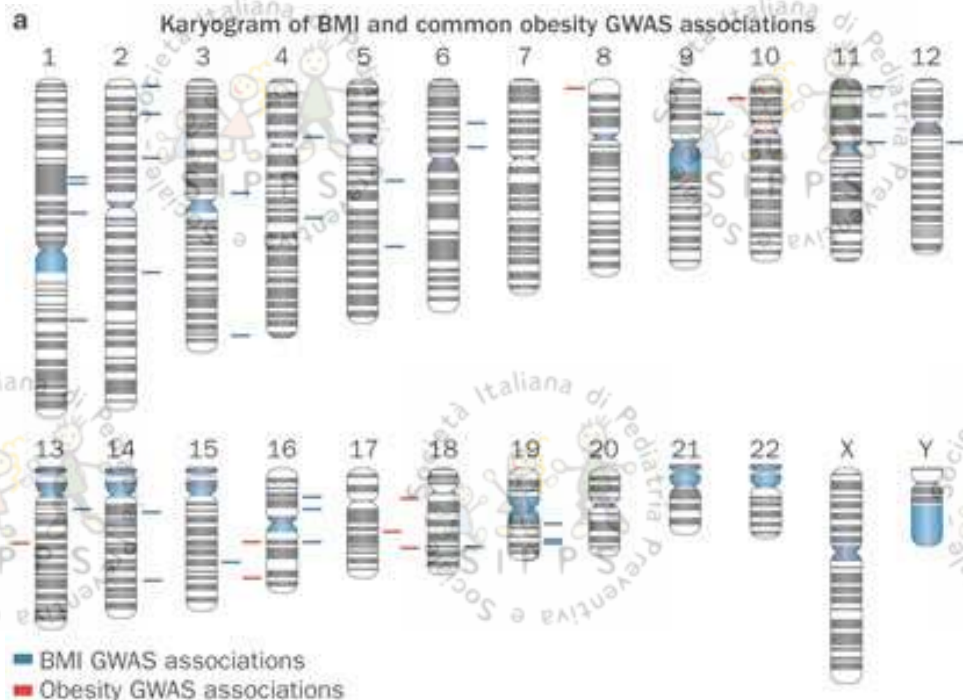




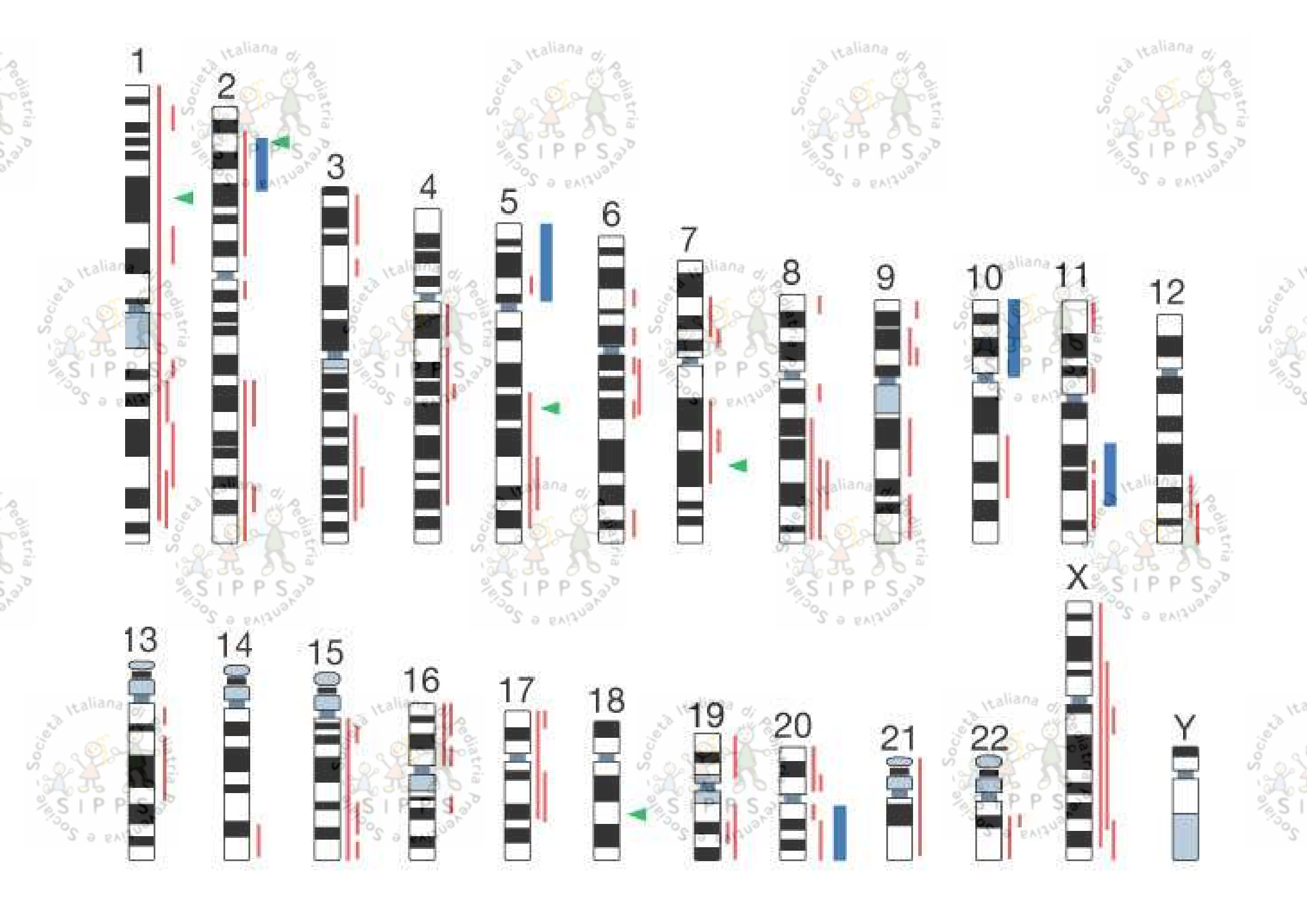


“...adult obesity and its complications
are largely a function of inherited
genetic susceptibility plus individual
choice in lifestyle.”





■ Frayling et al. (2007); Scuteri et al. (2007)
■ Willer et al. (2009); Thorleifsson et al. (2009)
■ Loos et al. (2008); Chambers et al. (2008)
■ Thorleifsson et al. (2009)
■ Speliotes et al. (2010)
■ Willer et al. (2009)



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19

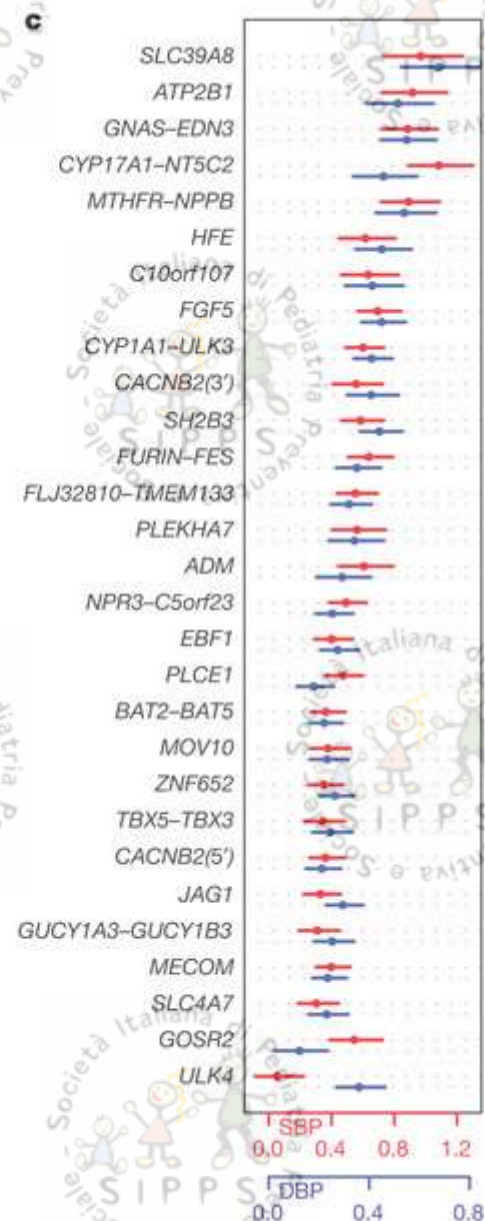
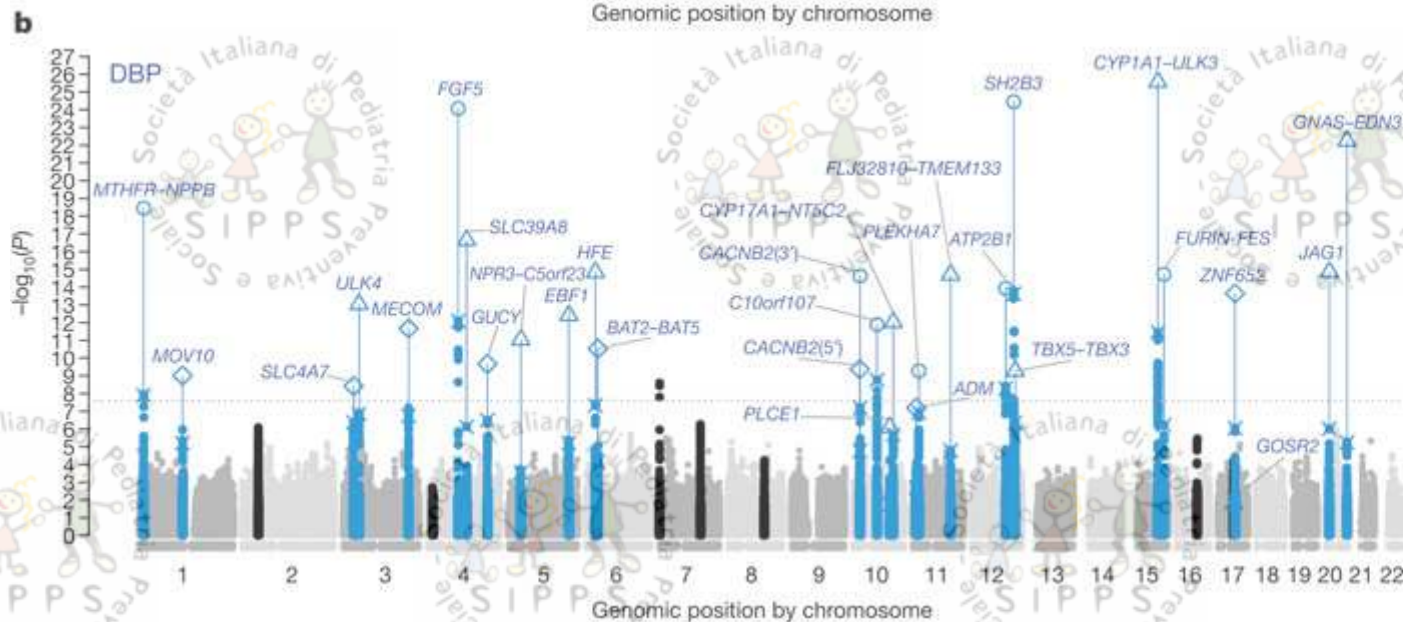
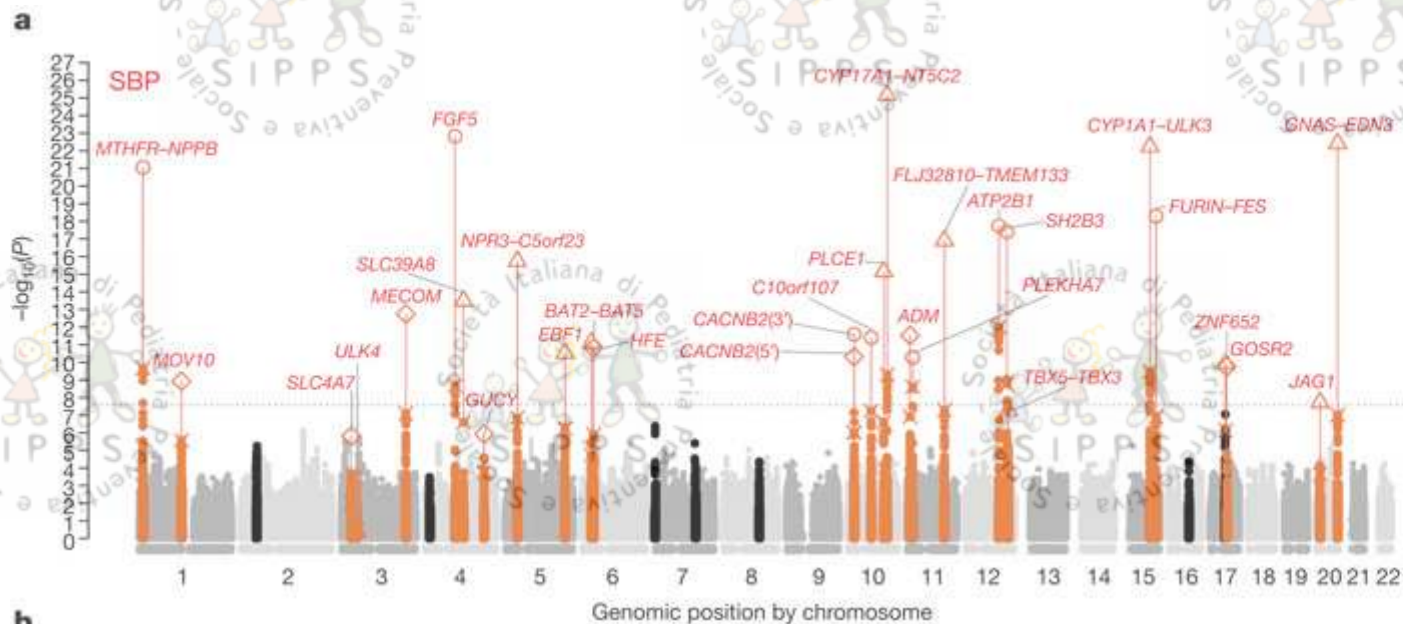
20

21

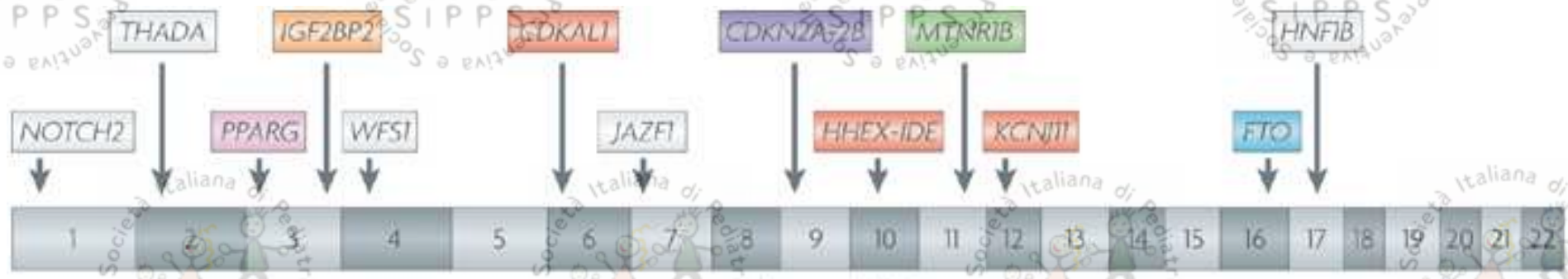
22

X

Y



Genome-wide association studies (GWAS): 18 genomic intervals confer increased risk to T2D in Caucasians



Nature Reviews | Genetics

Frazer K. A. et Al., 2009

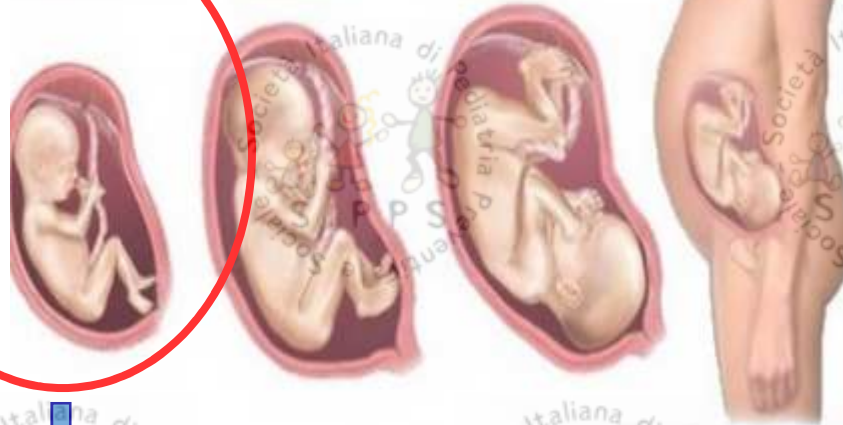
La carestia del 1944-45 in Olanda

Inverno 1944-45

Week 16

Week 20

Week 24

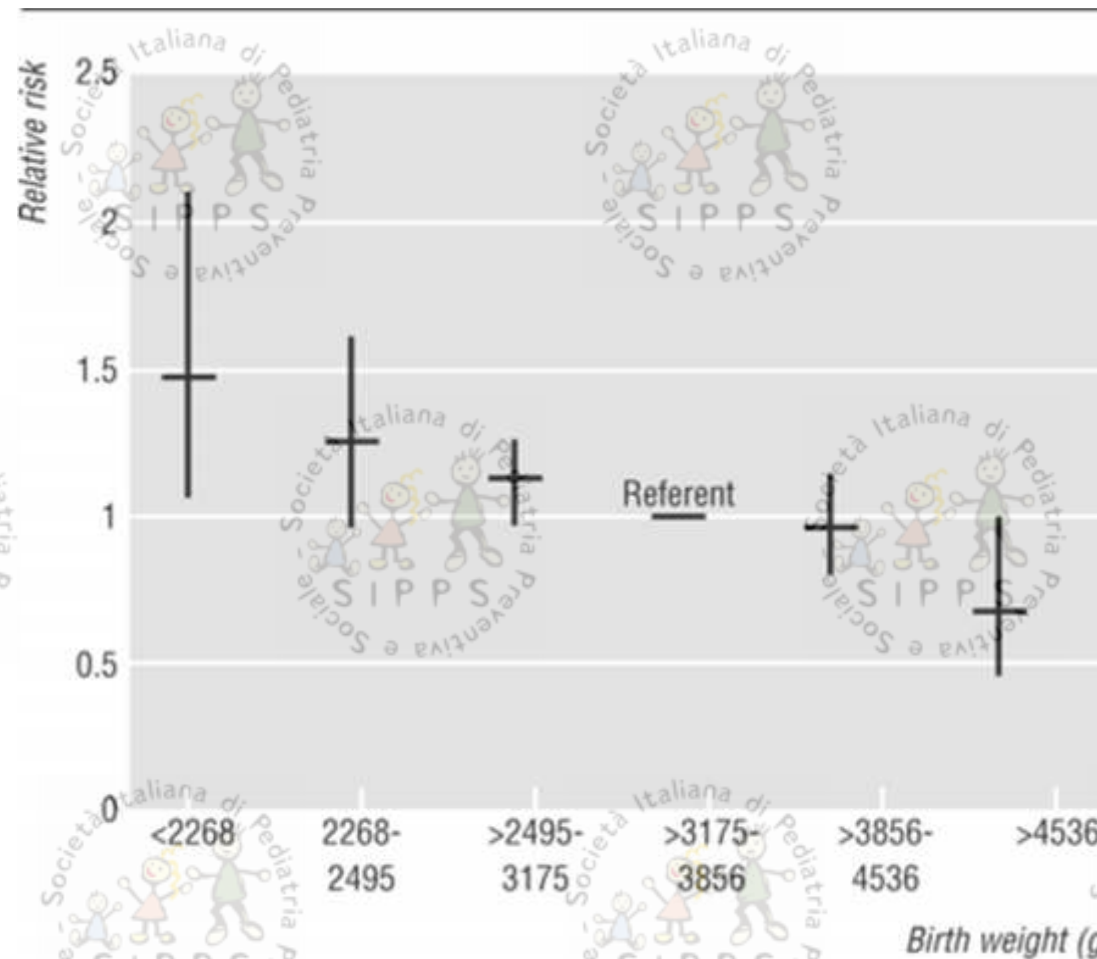


2003



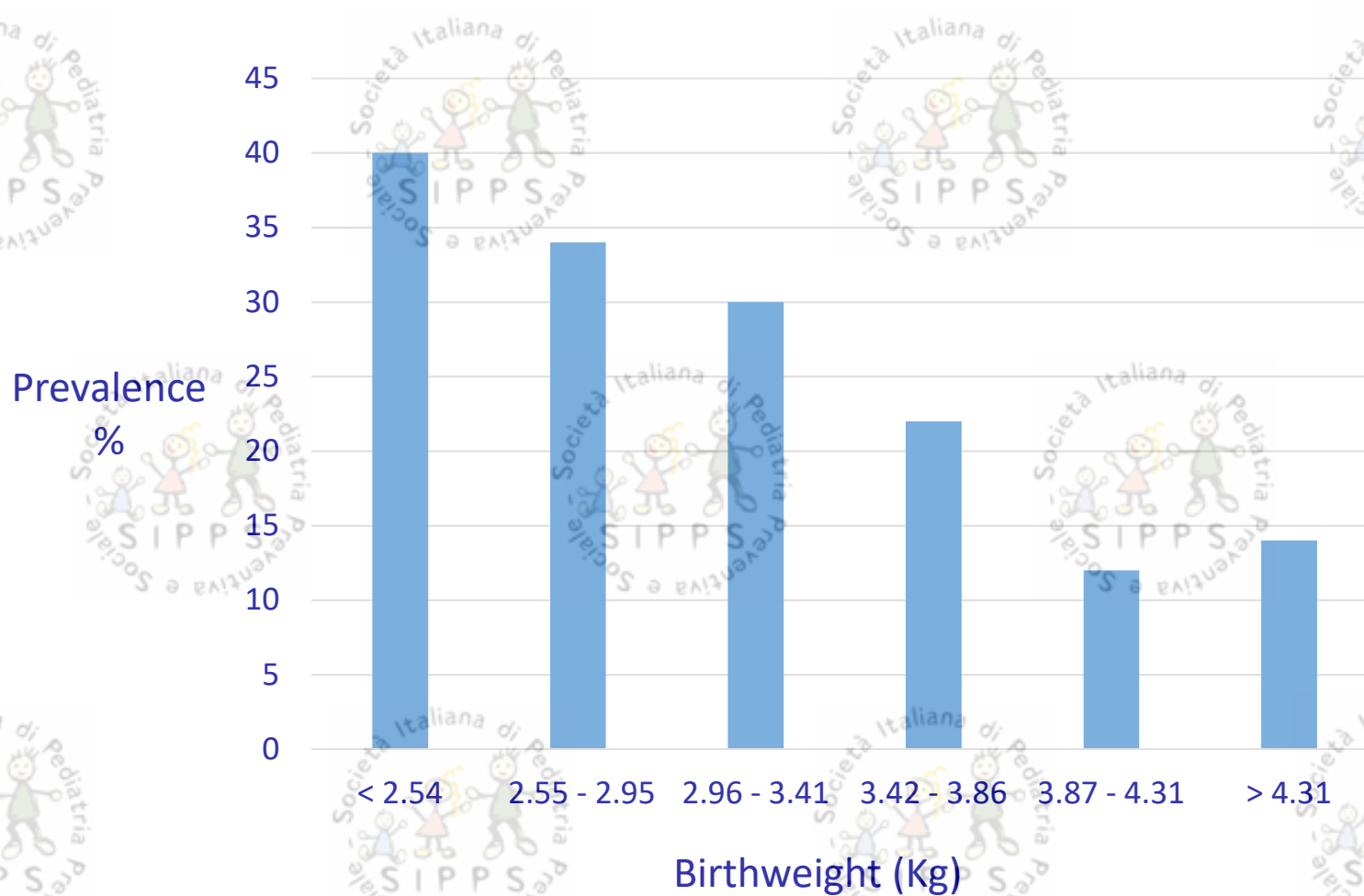
Elevata prevalenza di
sindrome metabolica,
sovrappeso, malattie
cardiovascolari e diabete
di tipo 2

Relative risk for non-fatal cardiovascular disease among 70,297 women aged 46 to 71.



Rich-Edwards J.W. Et al, 1997

Prevalence of NIDDM and impaired glucose tolerance in 370 men aged 59-70 years

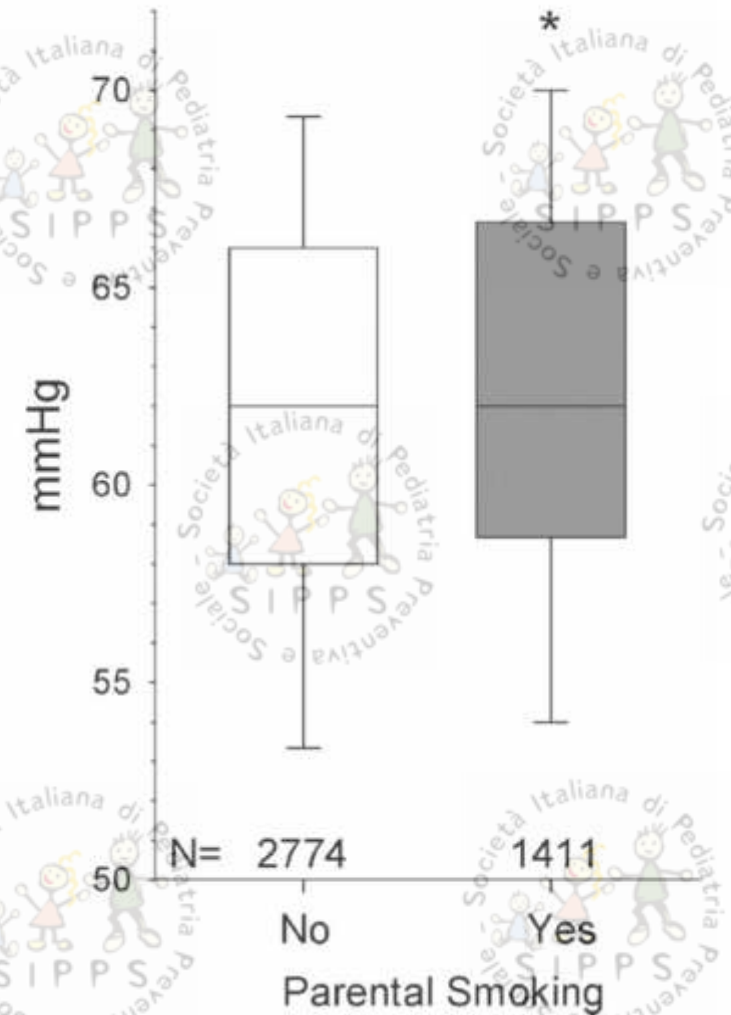
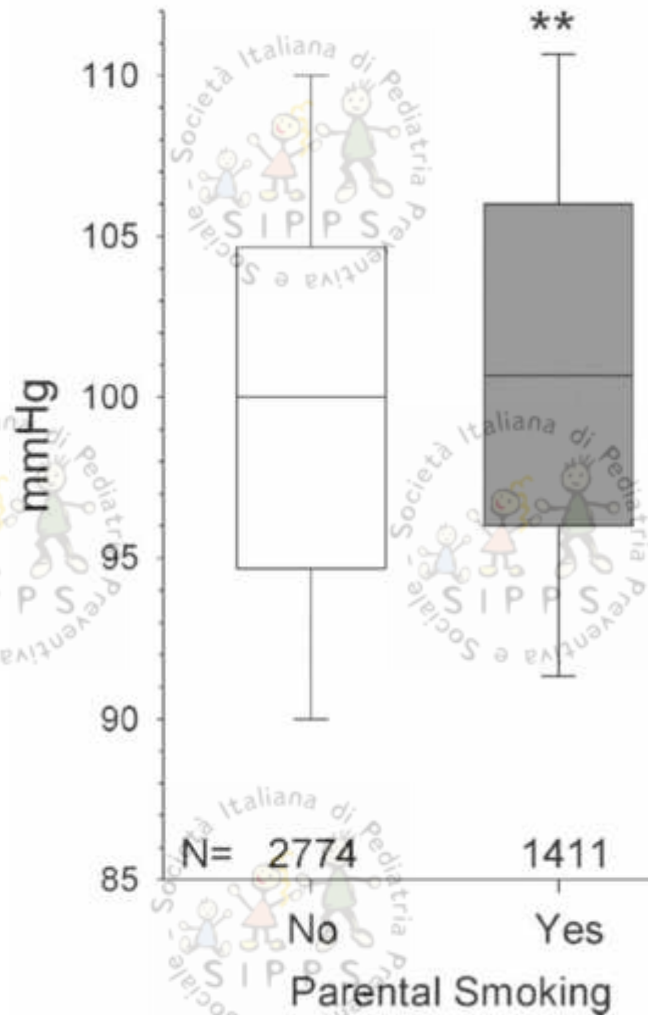


Godfrey K.M., 1998

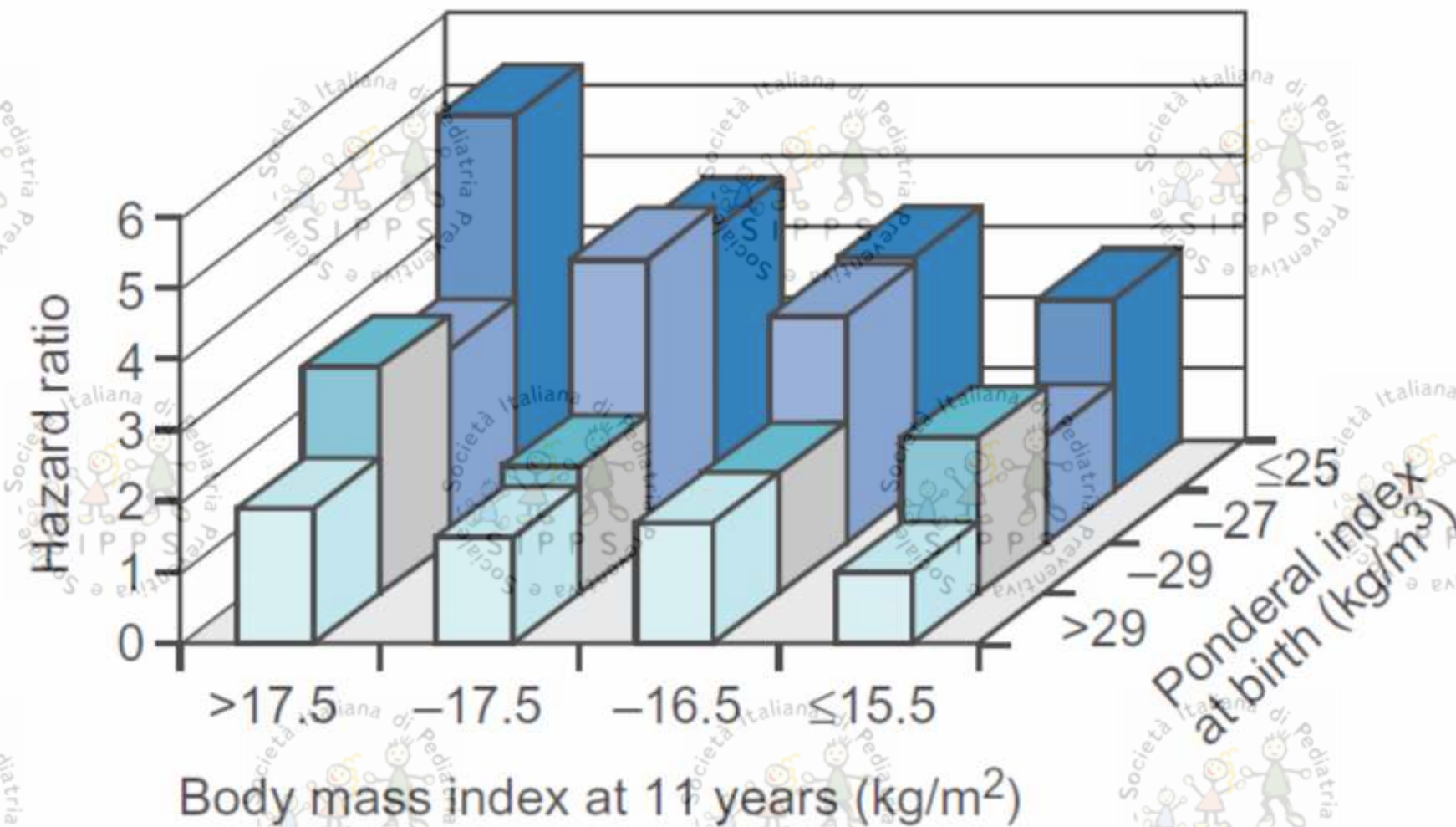
Influence of parental smoking on BP in preschool children

Systolic BP

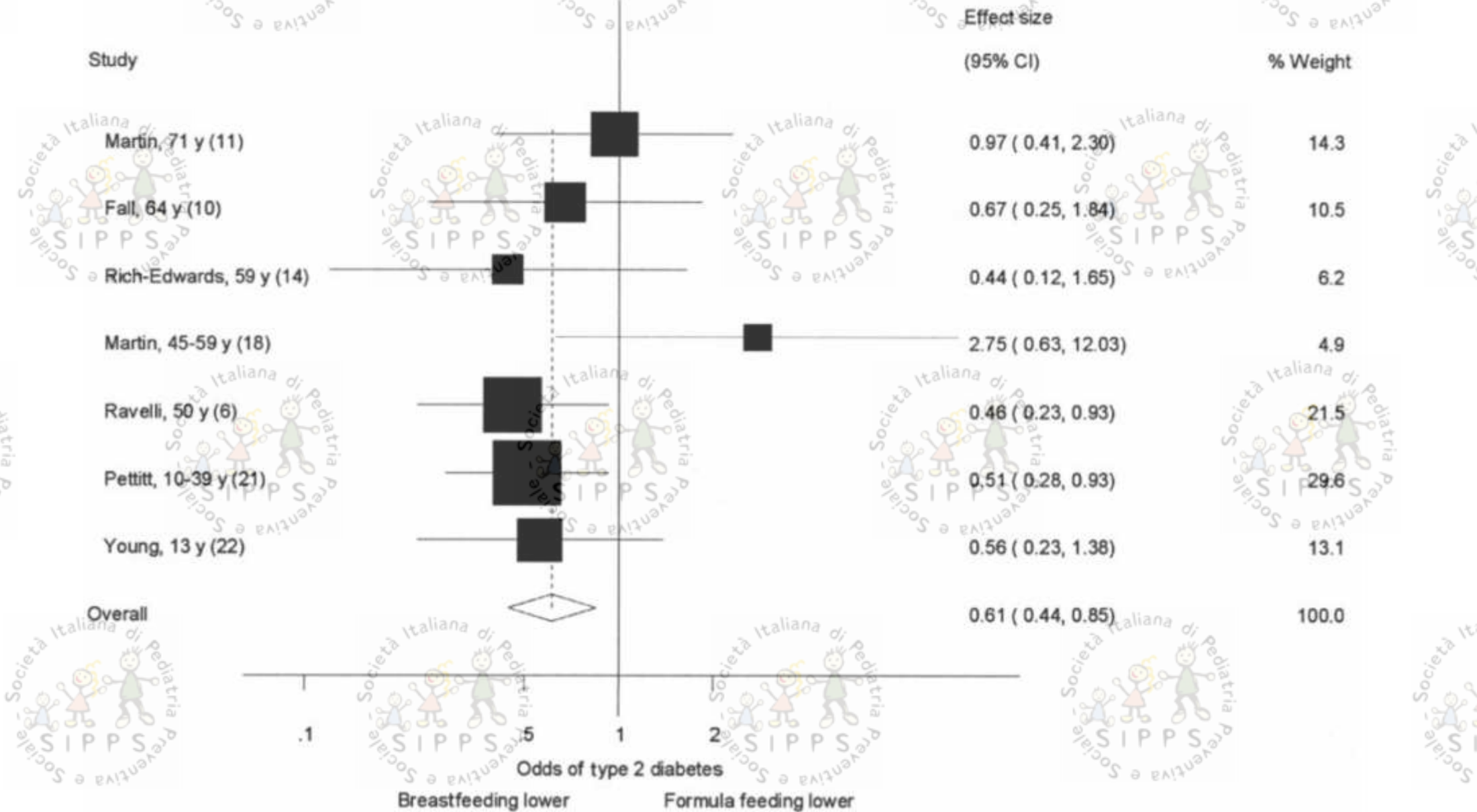
Diastolic BP



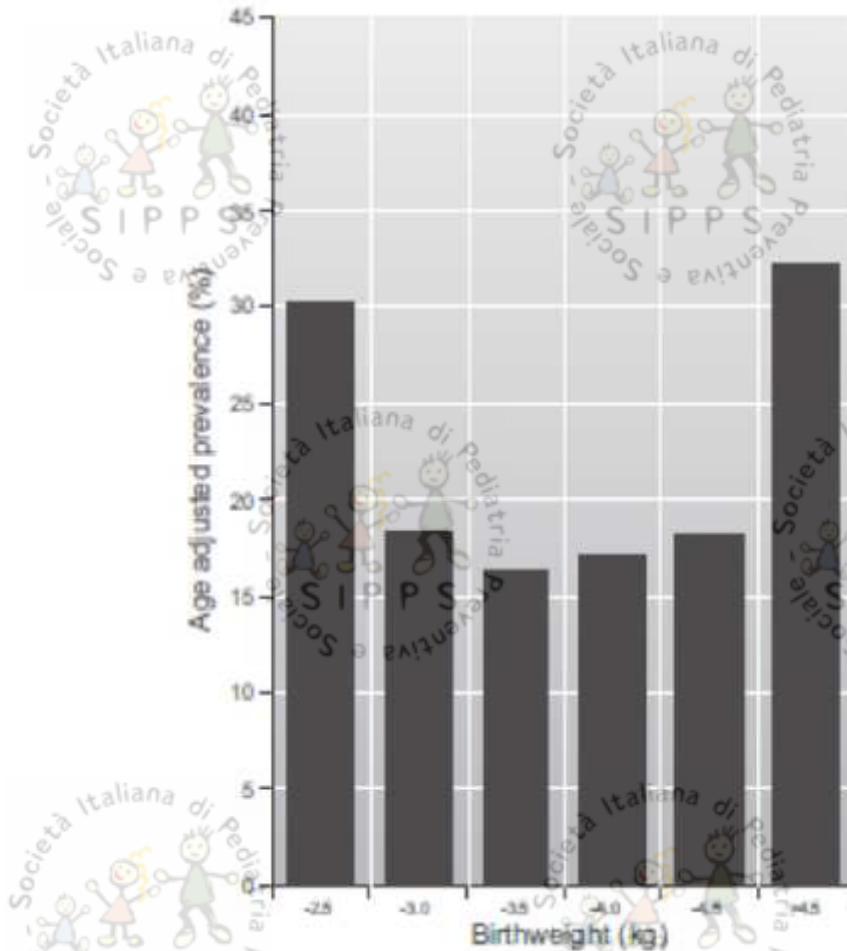
Hazard ratio for CHD among Finnish men of the HBCS



Diabetes and breast feeding

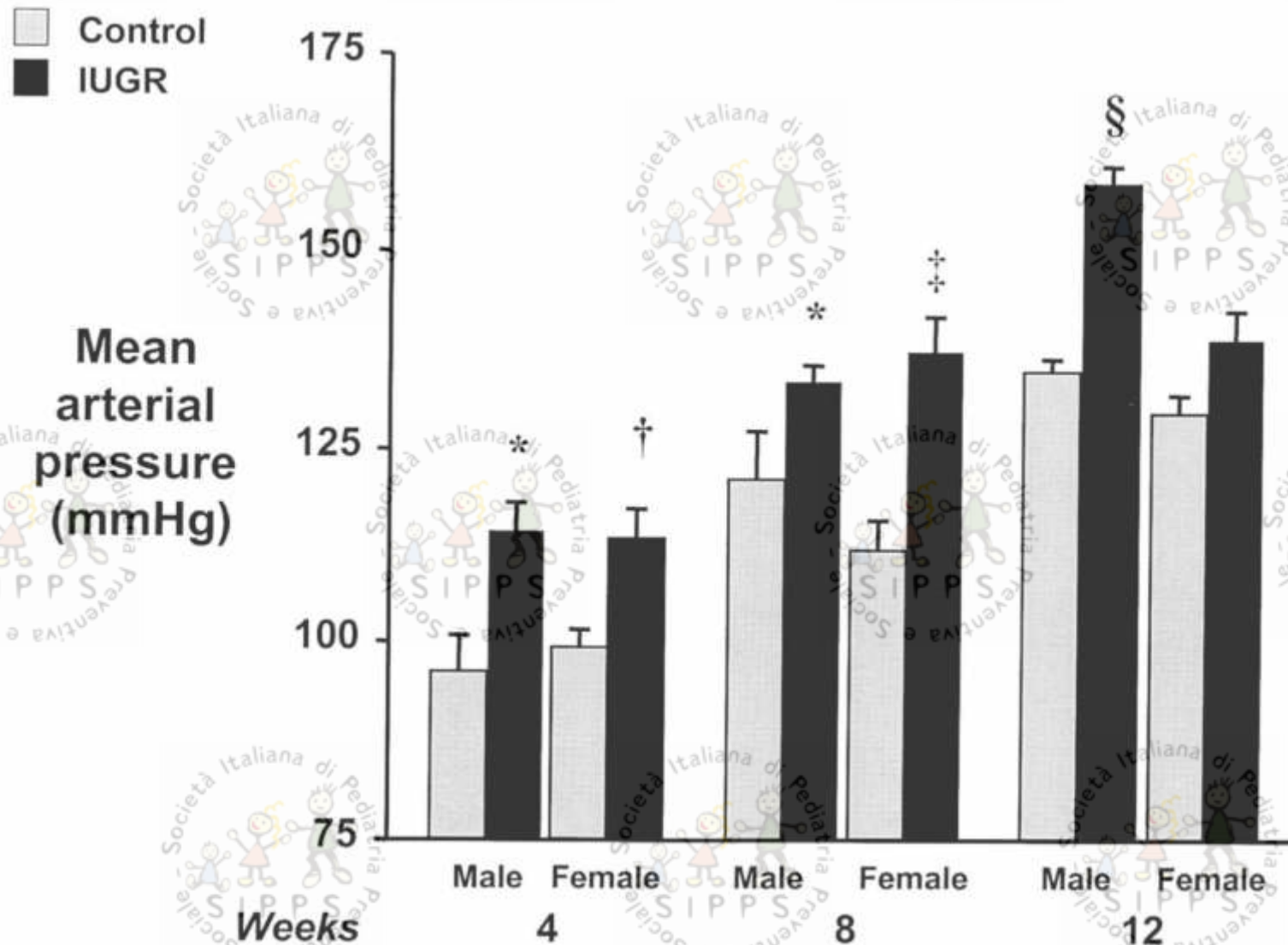


Prevalence of T2D in 1179 Pima Indians (age 20-39 yrs.) in relation to birthweight



McCance D. R. et al., 2000

MAP in rat models of IUGR induced by reduced uterine perfusion at 4, 8 and 12 weeks of age.



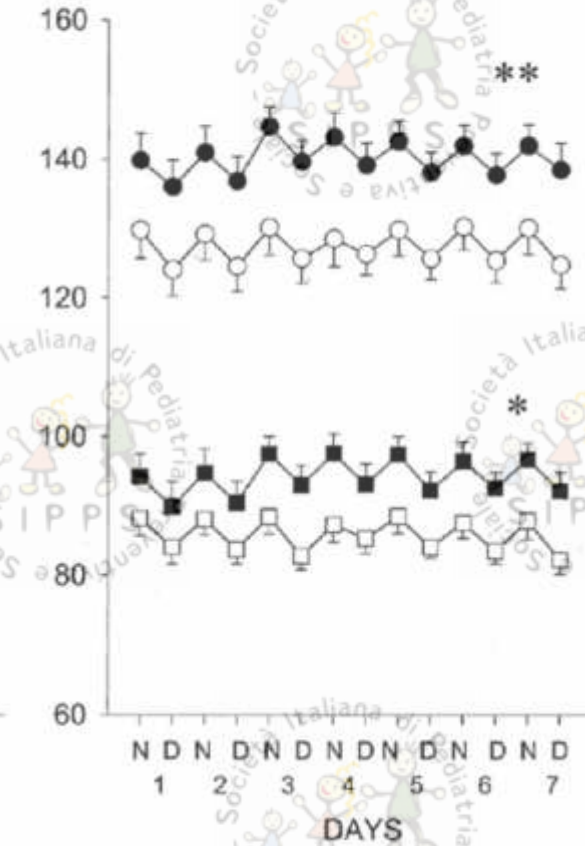
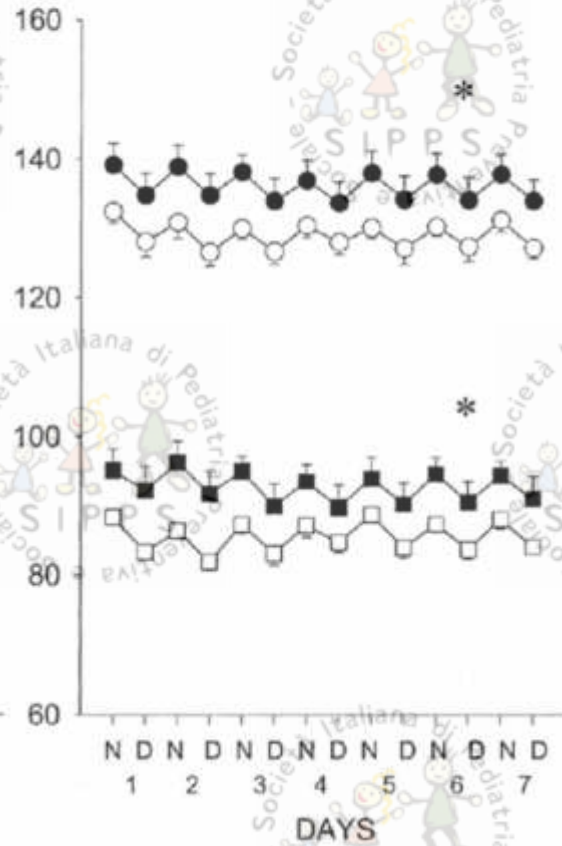
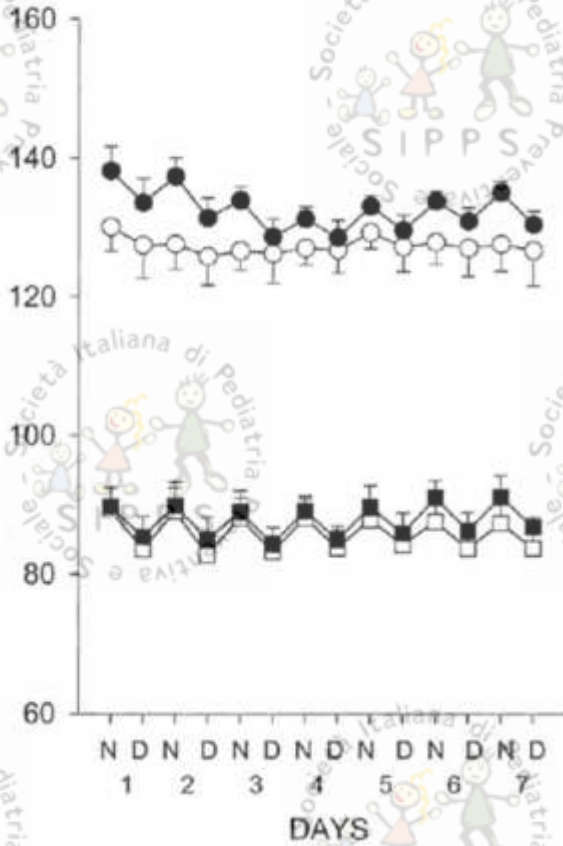
Systolic and diastolic blood pressure in offspring of lard-fed dams at 80, 180 and 360 days of age.

80 days

180 days

360 days

BLOOD PRESSURE (mmHg)



Alexander B. et al, 2015



DOHaD

Developmental Origin of Health and
Disease



Immediate Adaptive Responses (IAR)

Developmental plasticity



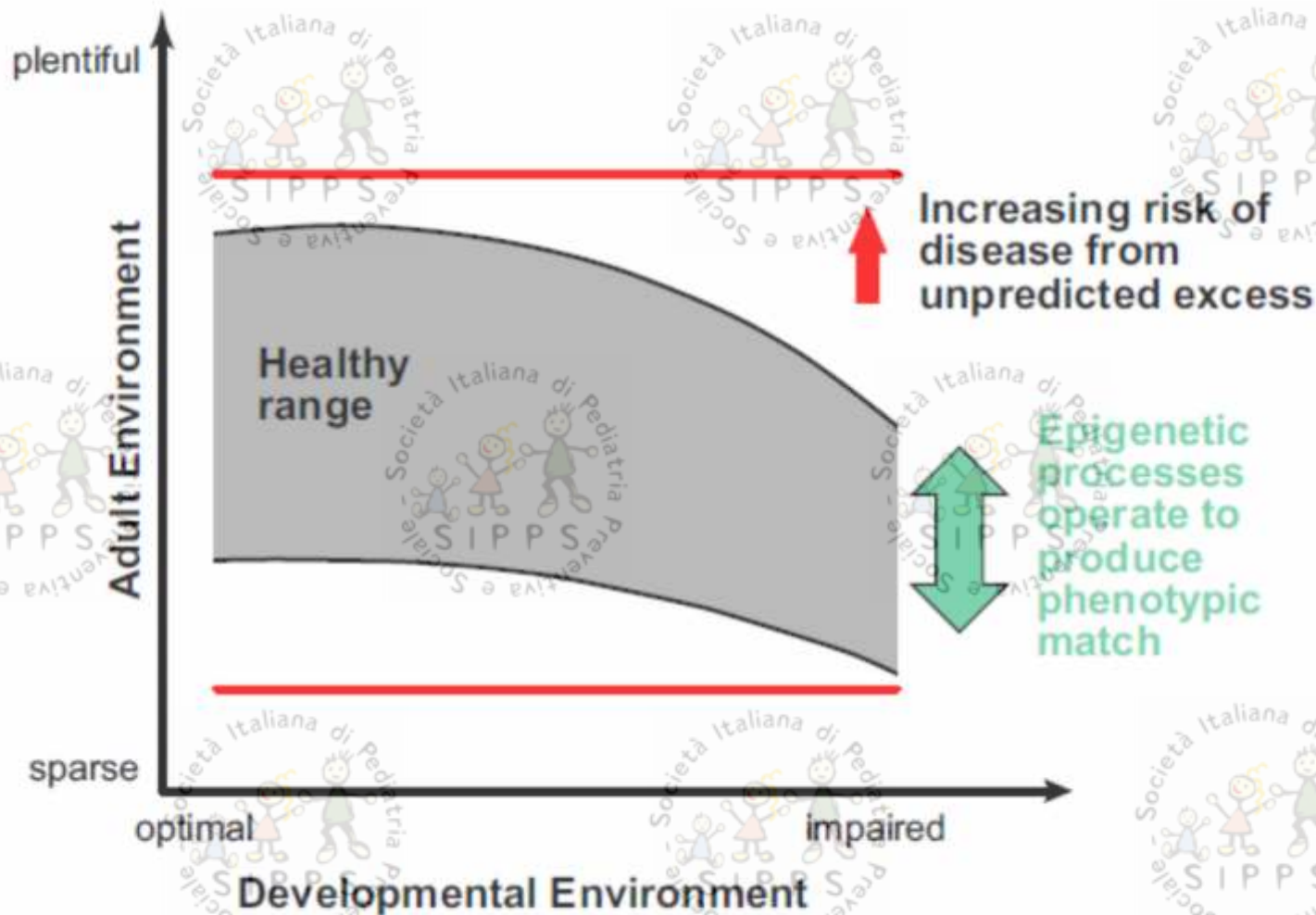
Predictive Adaptive Responses (PAR)



Developmental disruption



Rischio di NCD in rapporto alle disponibilità nutritive dell'ambiente



Hanson M. A., Gluckman P. D., 2014

Condizioni evolutivamente nuove che inducono «lacerazione dell'ontogenesi»

Obesità dei genitori

GDM

Nascita pretermine

Diabete di tipo 1 o 2

Fumo di sigaretta

Esposizione a tossine ambientali

Ipernutrizione del lattante

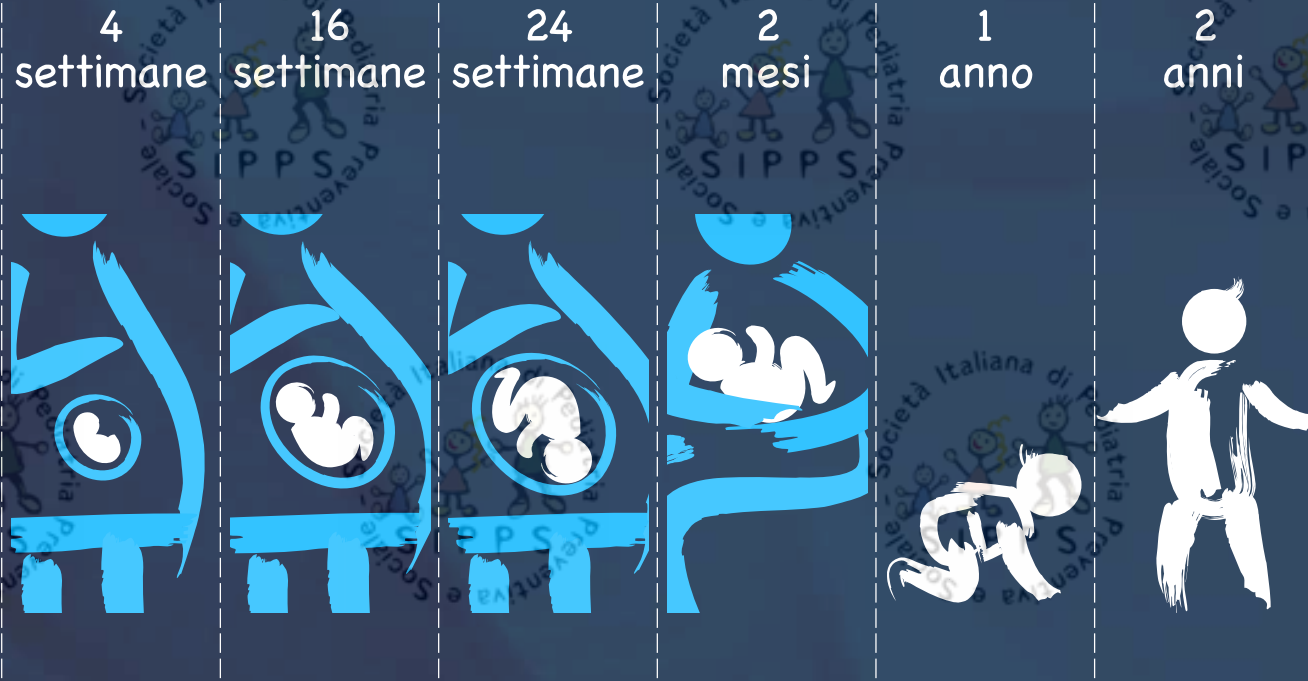
Il vantaggio conferito dalle PAR è evolutivistico
e deve quindi manifestarsi nel bambino e nel
giovane adulto.

Può trasformarsi in svantaggio (aumentato
rischio di andare incontro a malattia) una volta
superata l'età riproduttiva.

« La fase plastica dell'ontogenesi umana si estende dal concepimento fino allo svezzamento, periodo che in epoche premoderne durava almeno per i primi 2-3 anni di vita post-natale.»

Gluckman P.D., Hanson M. A. and Buklijas T., 2010

I primi mille giorni





LBW



NCDs





Genotipo

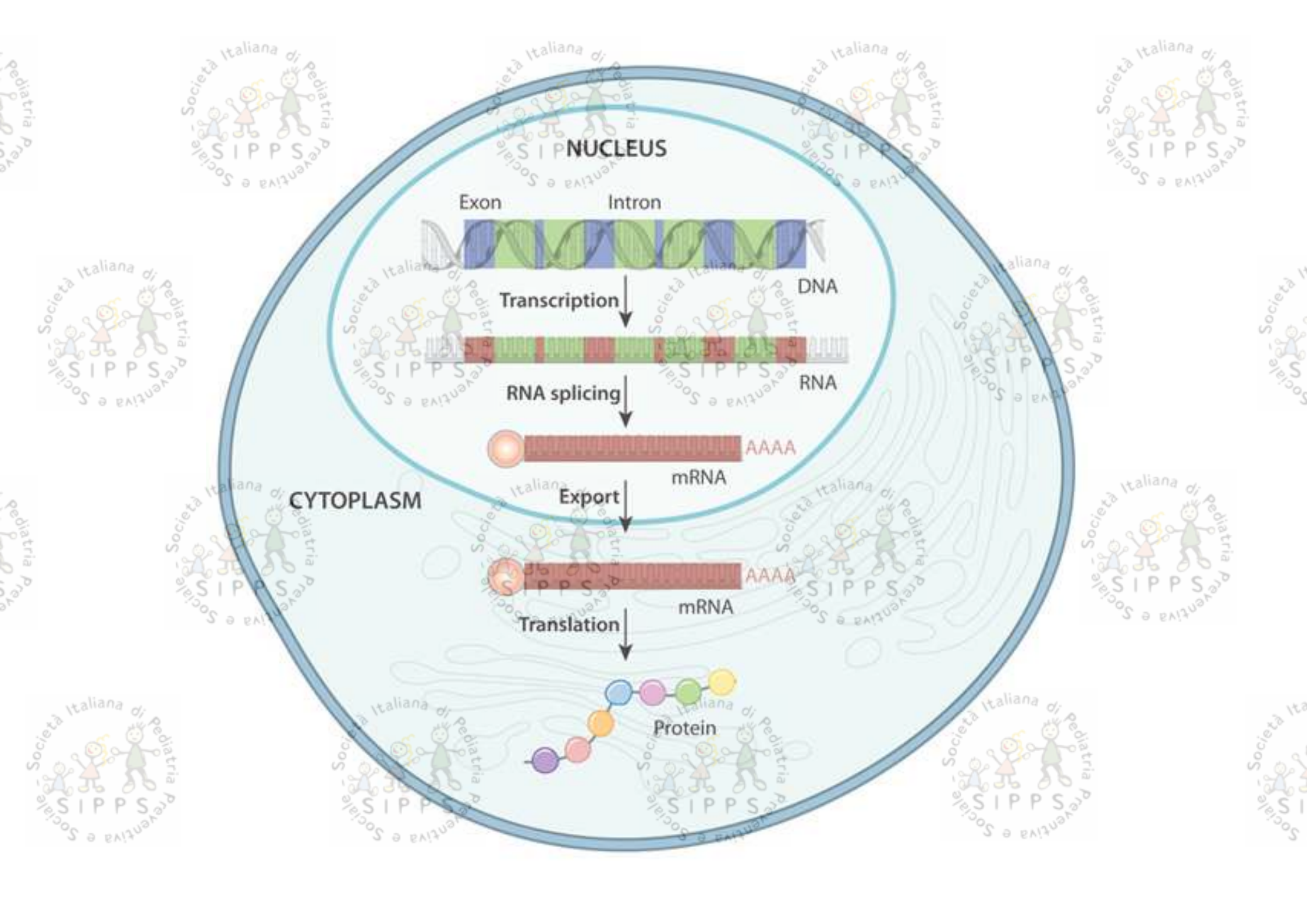
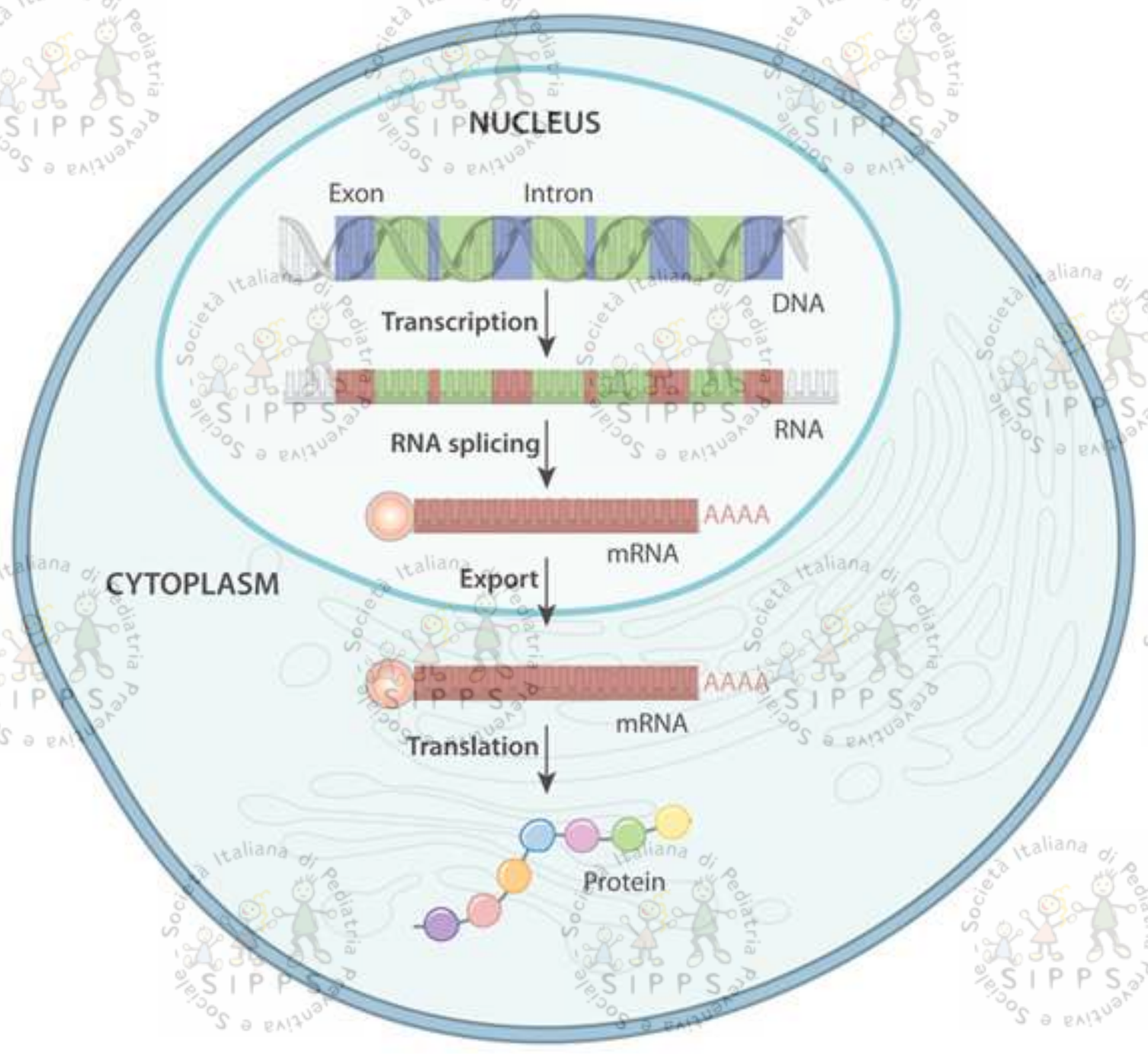


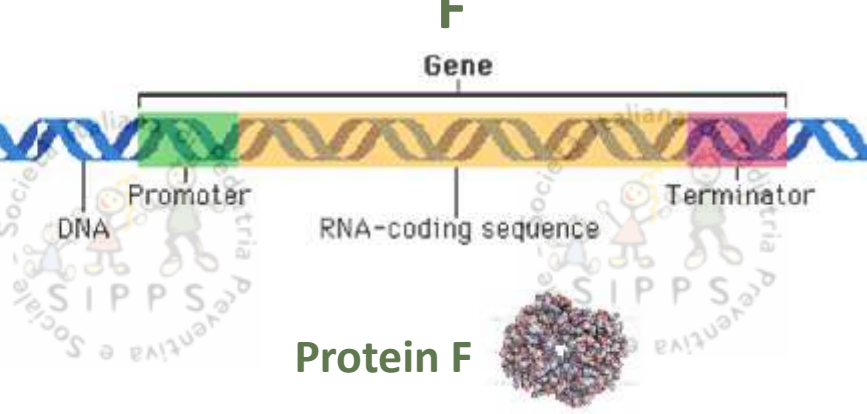
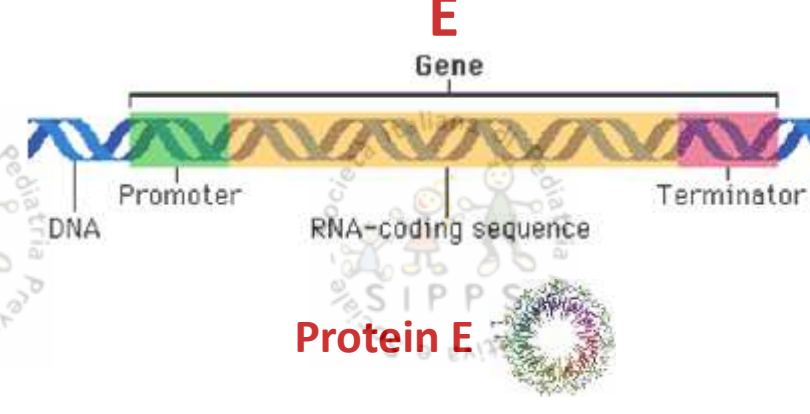
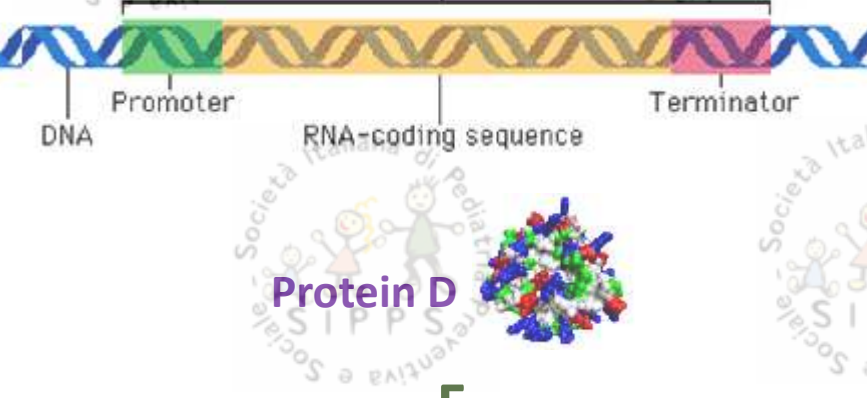
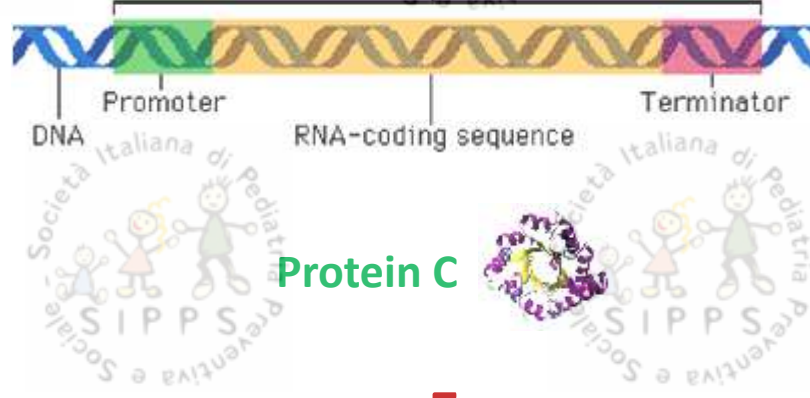
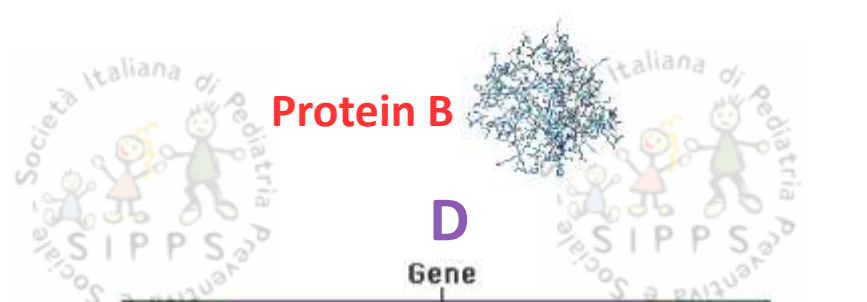
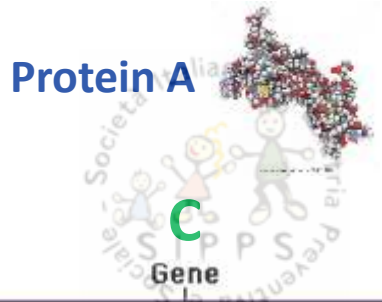
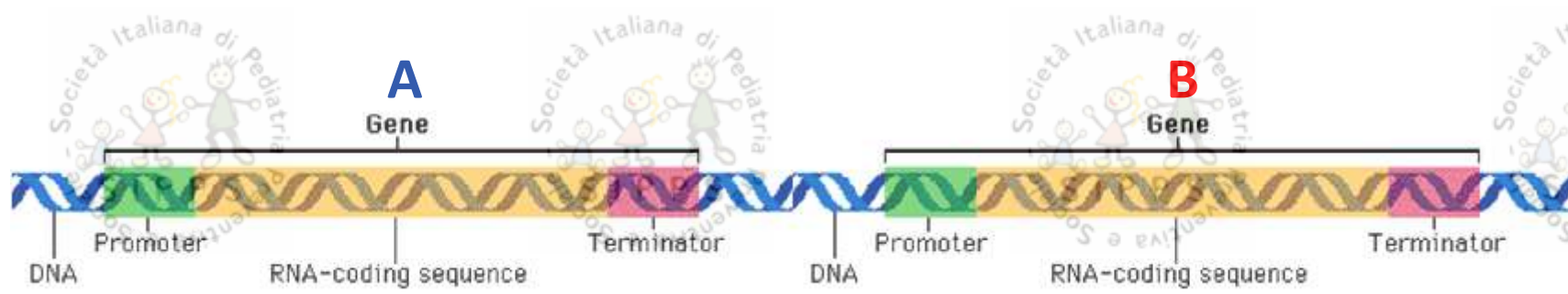
Ambiente



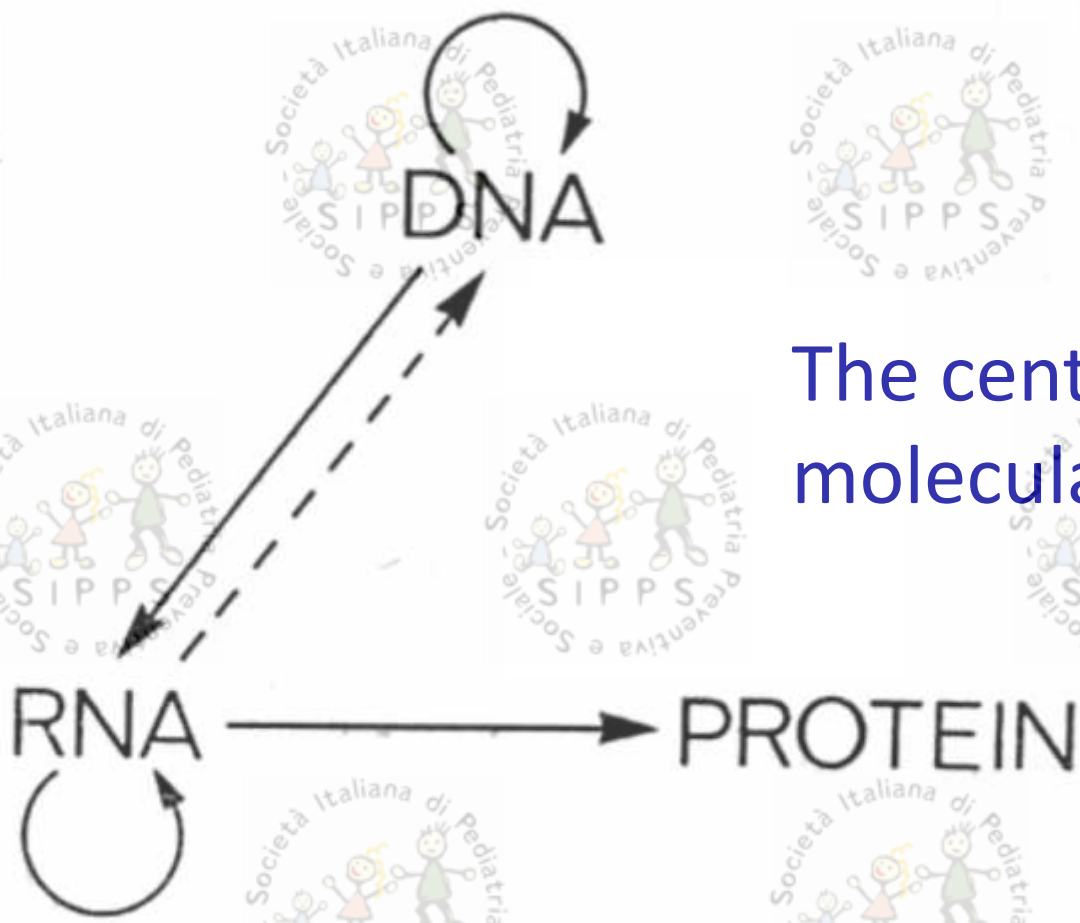
Fenotipo







The modern synthesis



The central dogma of molecular biology

Frances Crick, 1970

Progetto Genoma 1990



Science



THE HUMAN GENOME



AMERICAN ASSOCIATION OF PEDIATRIC SOCIETIES

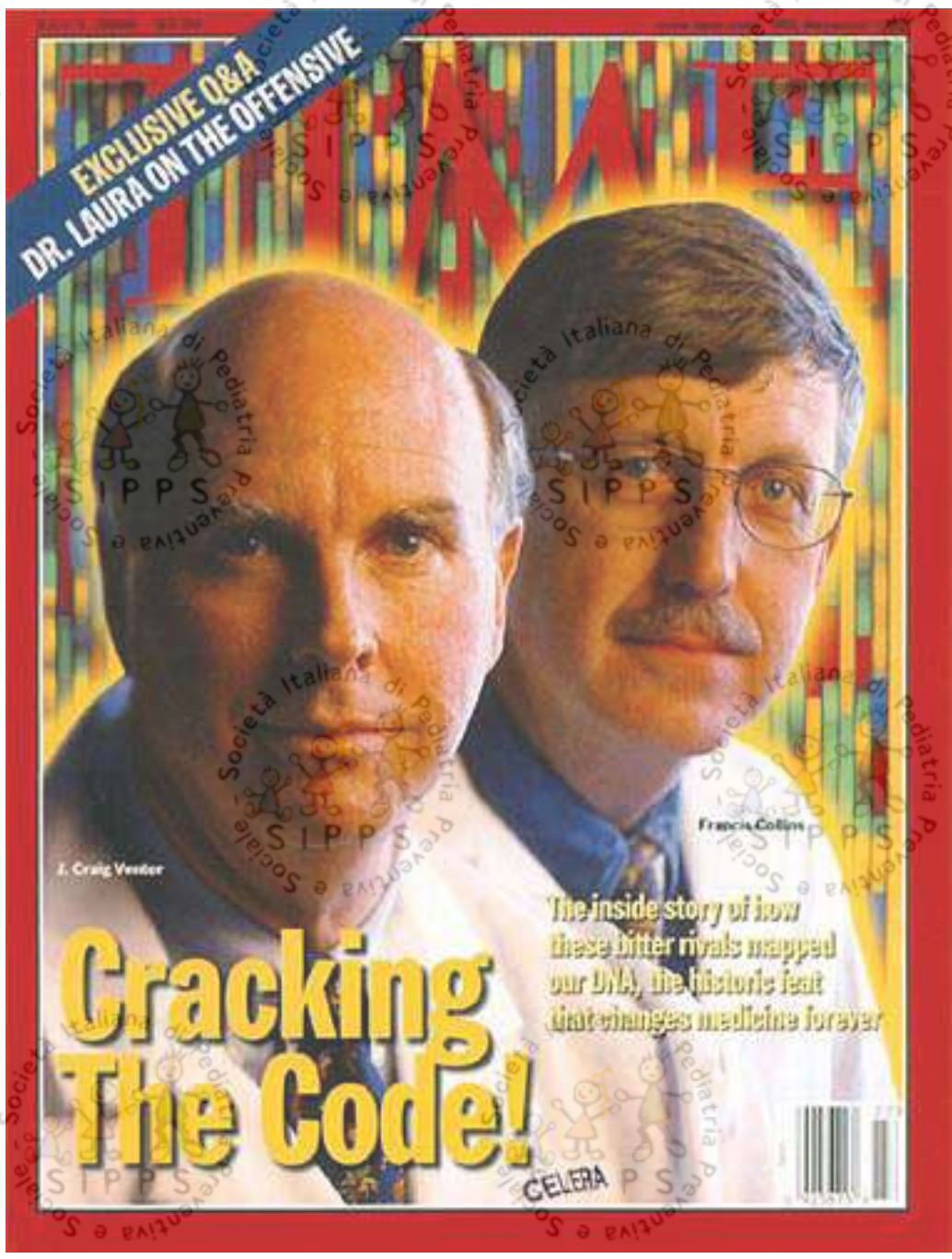
nature



the human genome

Genomics
Genetics
Molecular biology
Bioinformatics
Biochemistry
Developmental biology
Evolutionary biology
Cellular biology
Plant biology
Animal biology
Microbiology
Ecology
Environmental biology
Marine biology
Botany
Zoology

Macmillan
MAGAZINES



**EXCLUSIVE Q&A
DR. LAURA ON THE OFFENSIVE**

J. Craig Venter

Francis Collins

Cracking The Code!

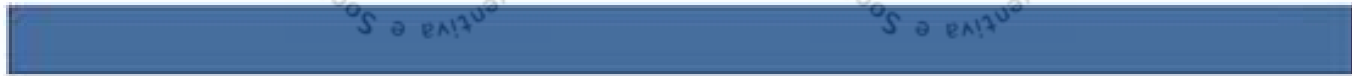
The inside story of how these bitter rivals mapped our DNA, the historic feat that changes medicine forever

CELEBRA





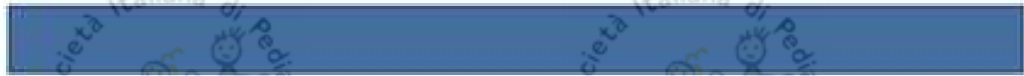
Grape



30,434



Human



22,333



Chicken



16,736



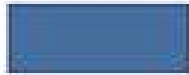
Fruit fly



14,889



Cow



4,149

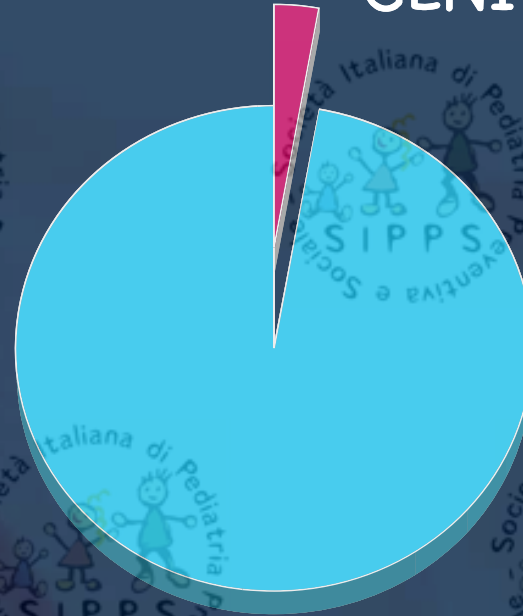


Influenza



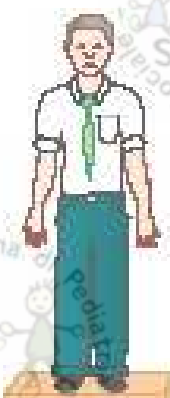
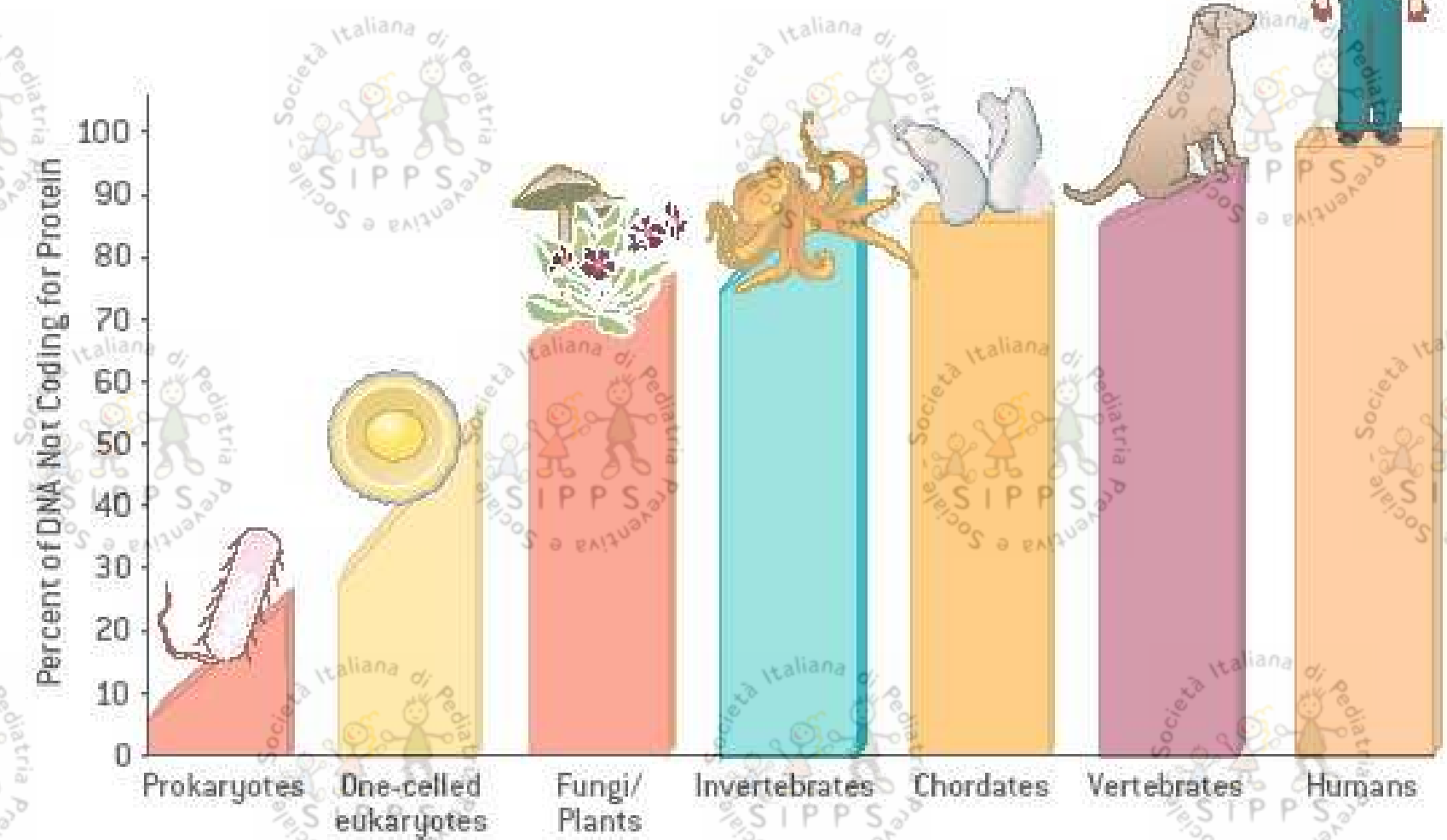
11

GENI 3%



DNA «NON CODIFICANTE»

97%



Joe Klein:
The CIA's
Afghan Disaster

Yemen: The
New Center
Of Terror

Why the Recession
Hasn't Been Cool
To Teens

JANUARY 13, 2011

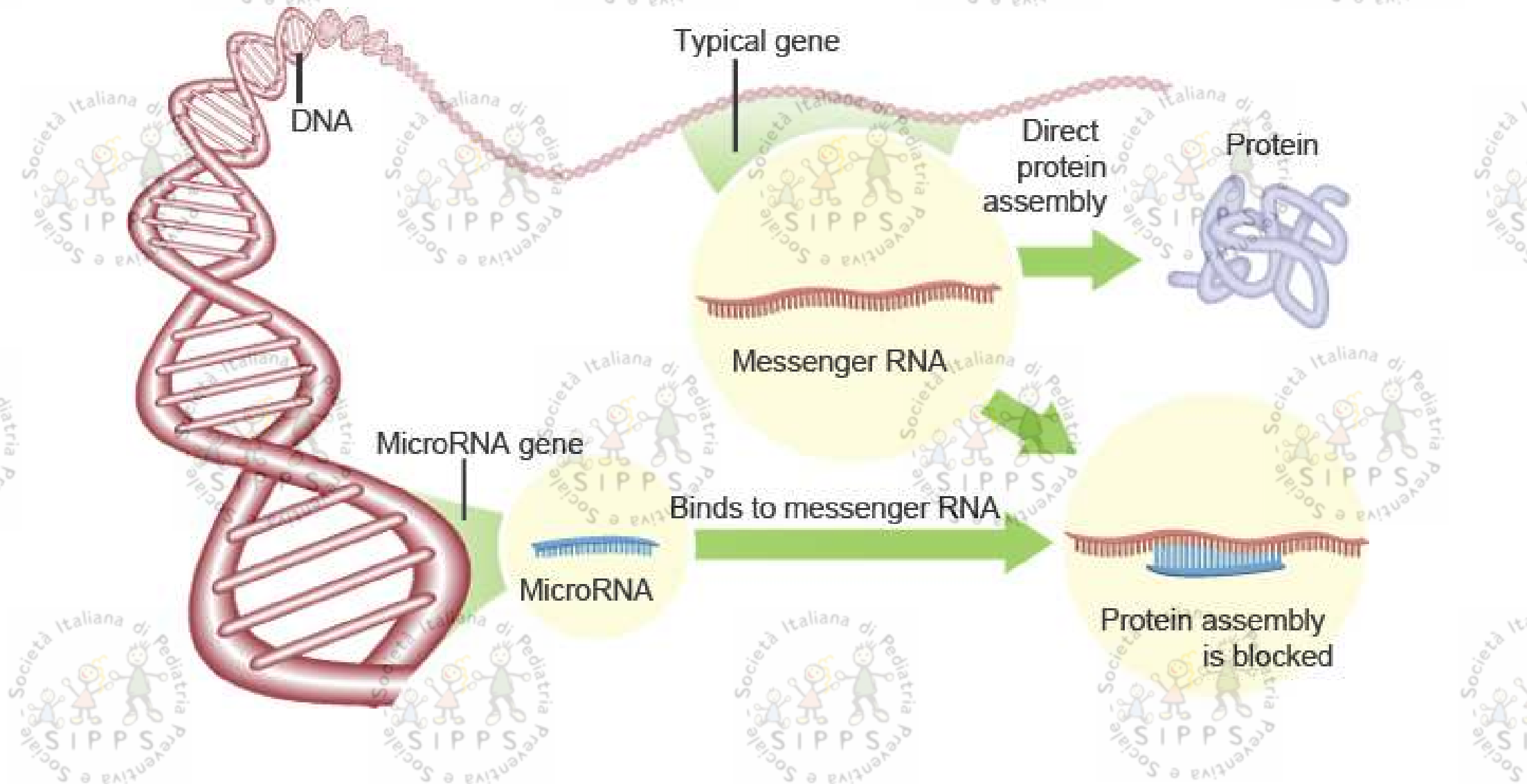
TIME

WHY YOUR DNA ISN'T YOUR DESTINY

The new science of epigenetics
reveals how the choices you
make can change your genes
—and those of your kids

BY JOHN CLOUD

Non-coding RNA: MIR



DNA methyl-transferases



Methylated DNA



Methylation

Acetylation

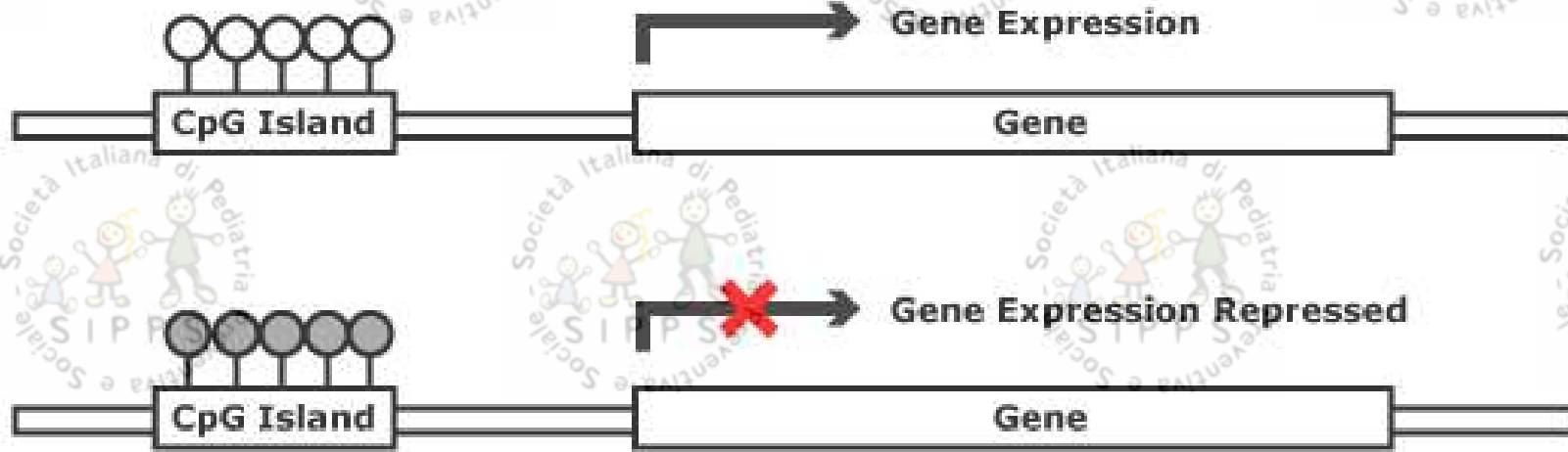
Unmethylated

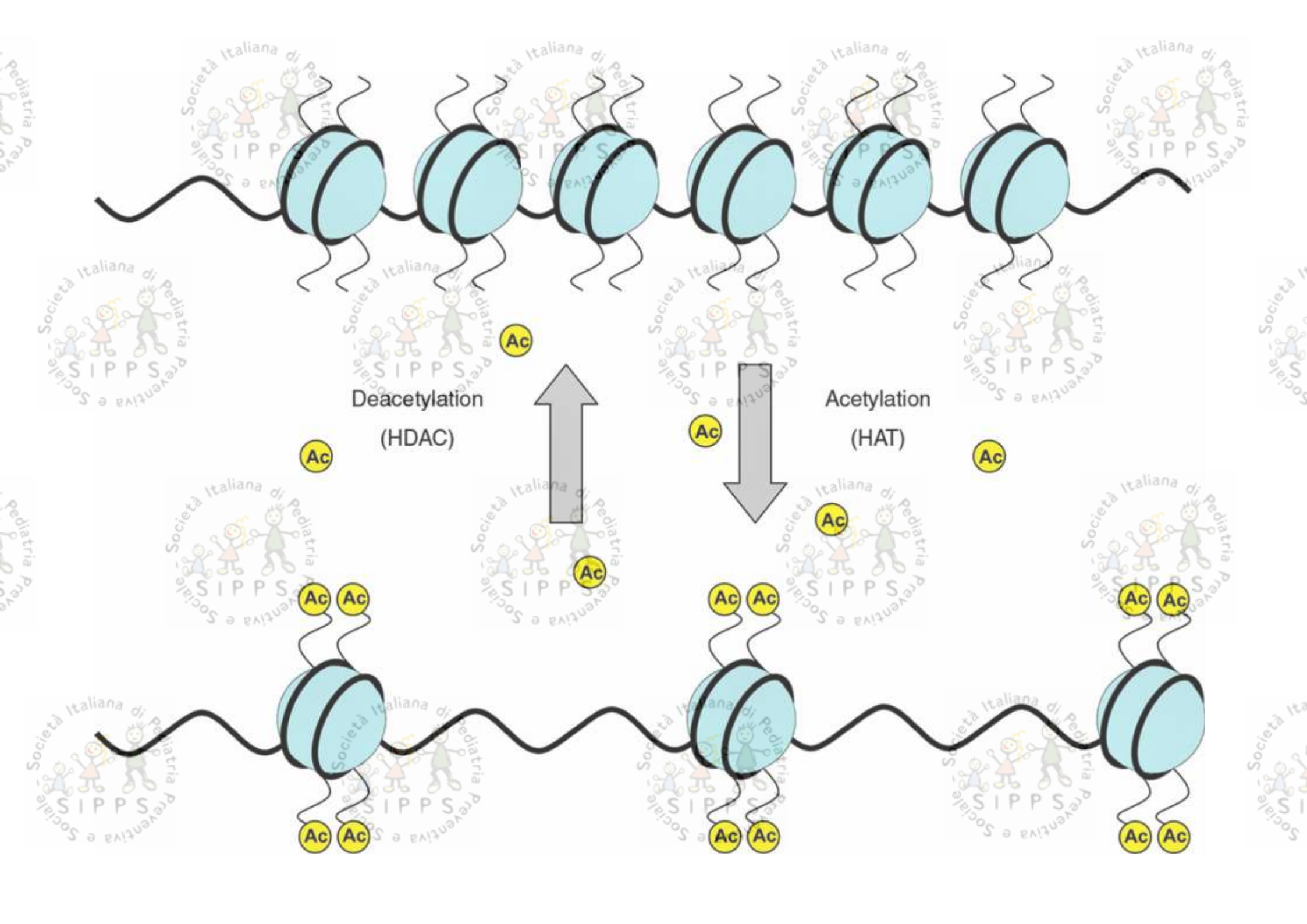


transcription

5'-CpG-3'

3'-GpC-5'





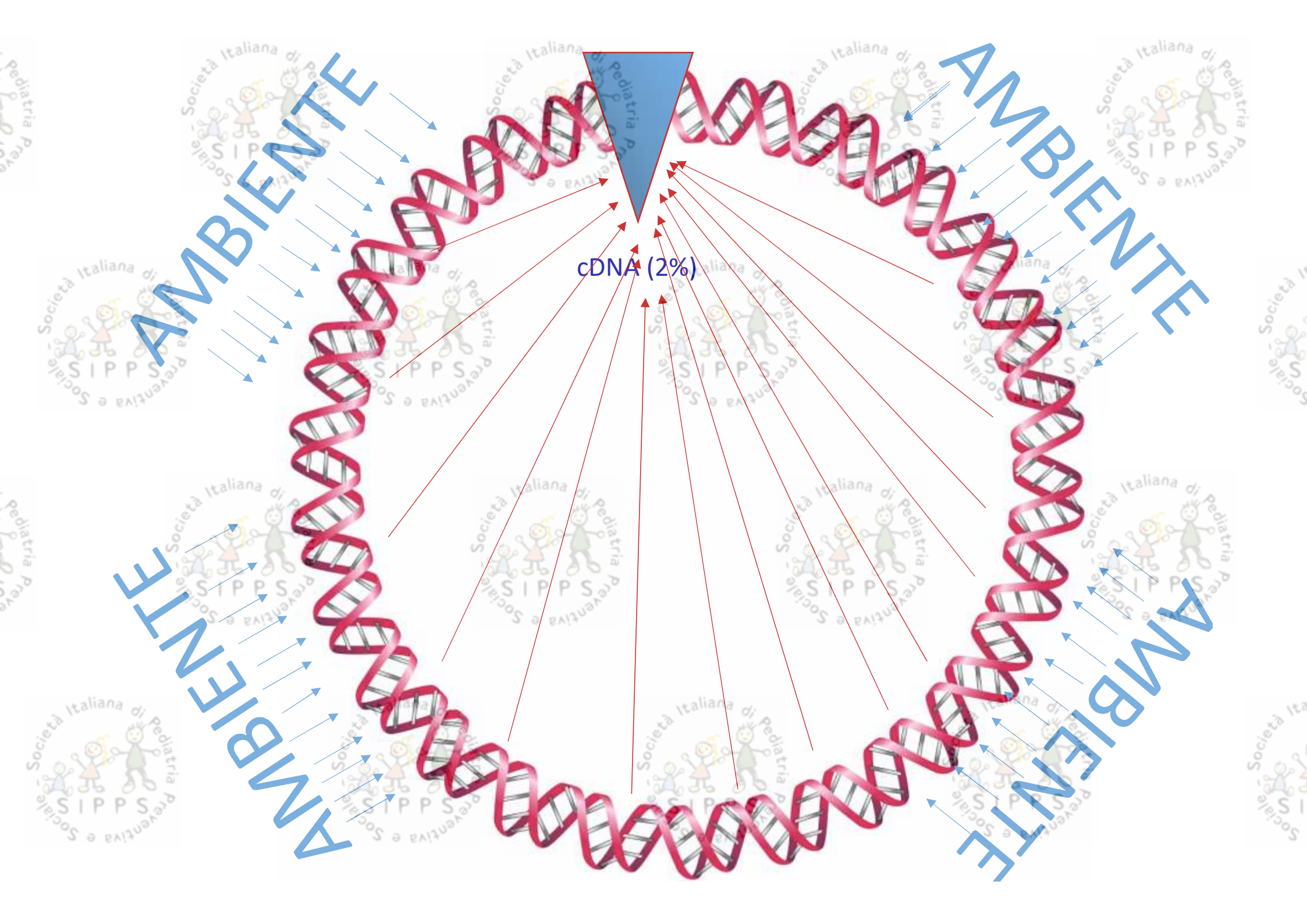
The background of the slide is a repeating pattern of the SIPPSS logo. Each logo is circular and contains the text 'Società Italiana di Pediatria Preventiva e Sociale' around the perimeter and 'SIPPSS' in the center. In the middle of the logo is a colorful illustration of three stylized children holding hands.

Evolutionary Developmental Biology

AMBIENTE

AMBIENTE

cDNA (2%)



Genotipo



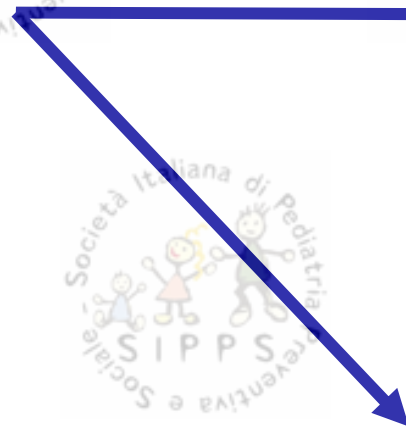
Developmental plasticity



Ambiente

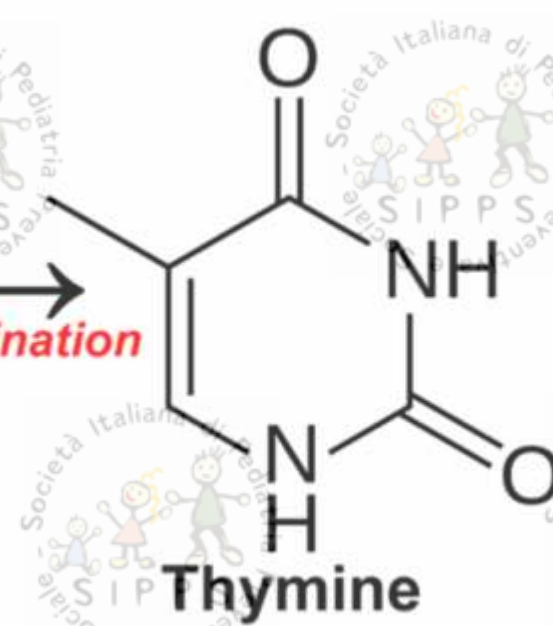
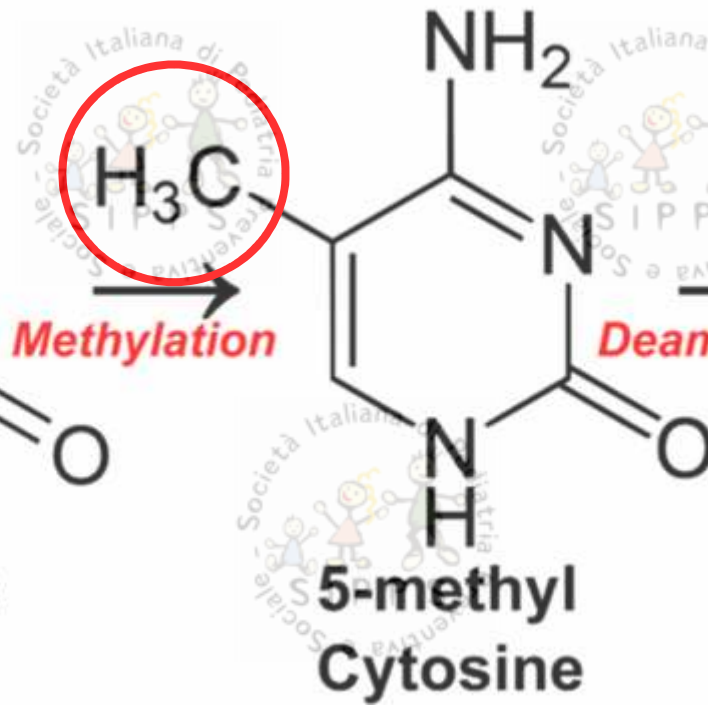
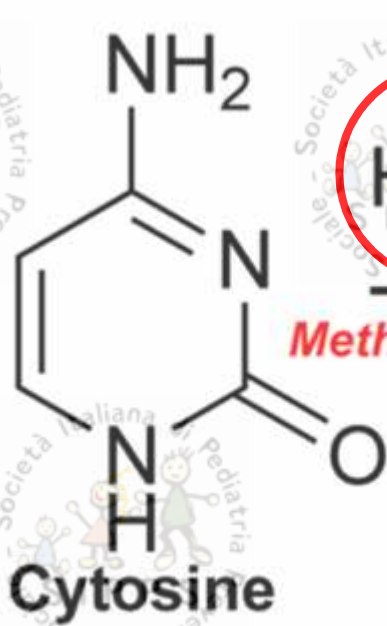


Fenotipo





**“Il futuro inizia oggi,
non domani.”**

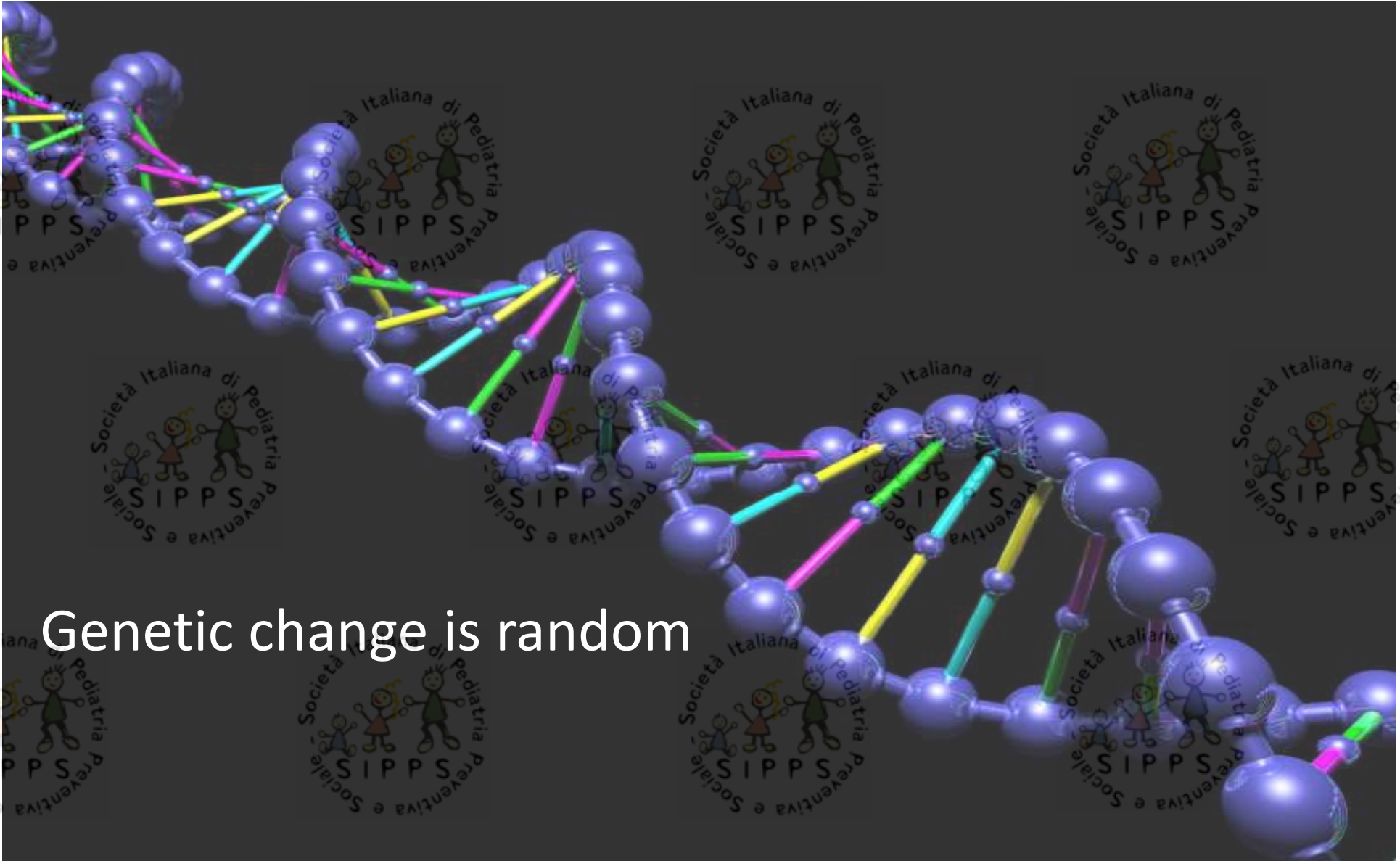


Health Literacy

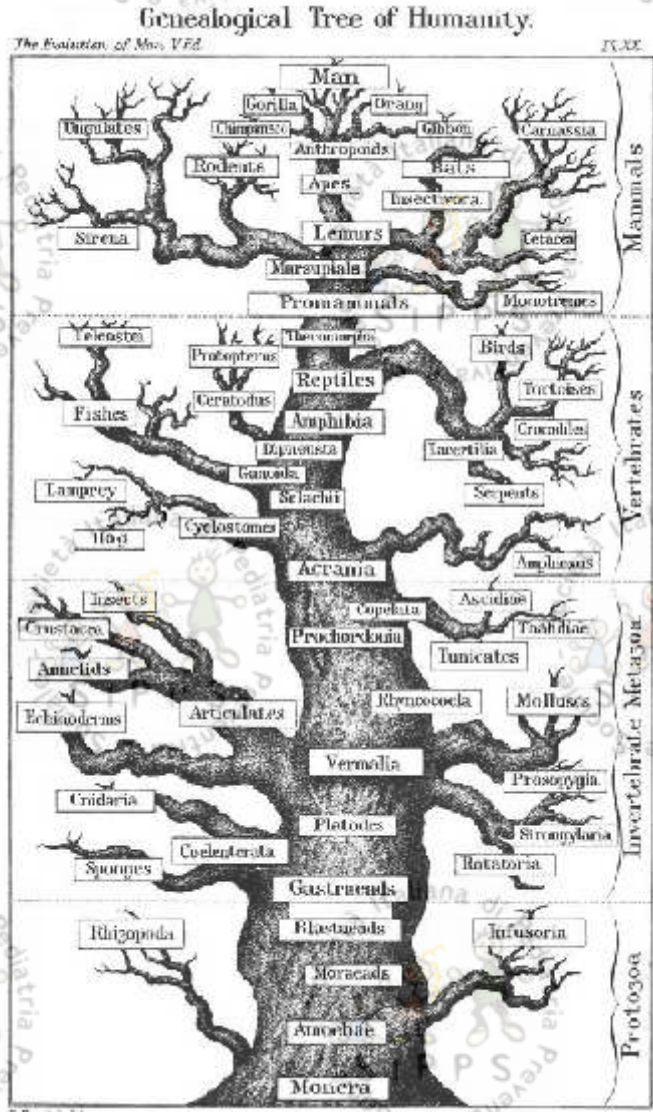
“Cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health.”

WHO, 2009

The modern synthesis



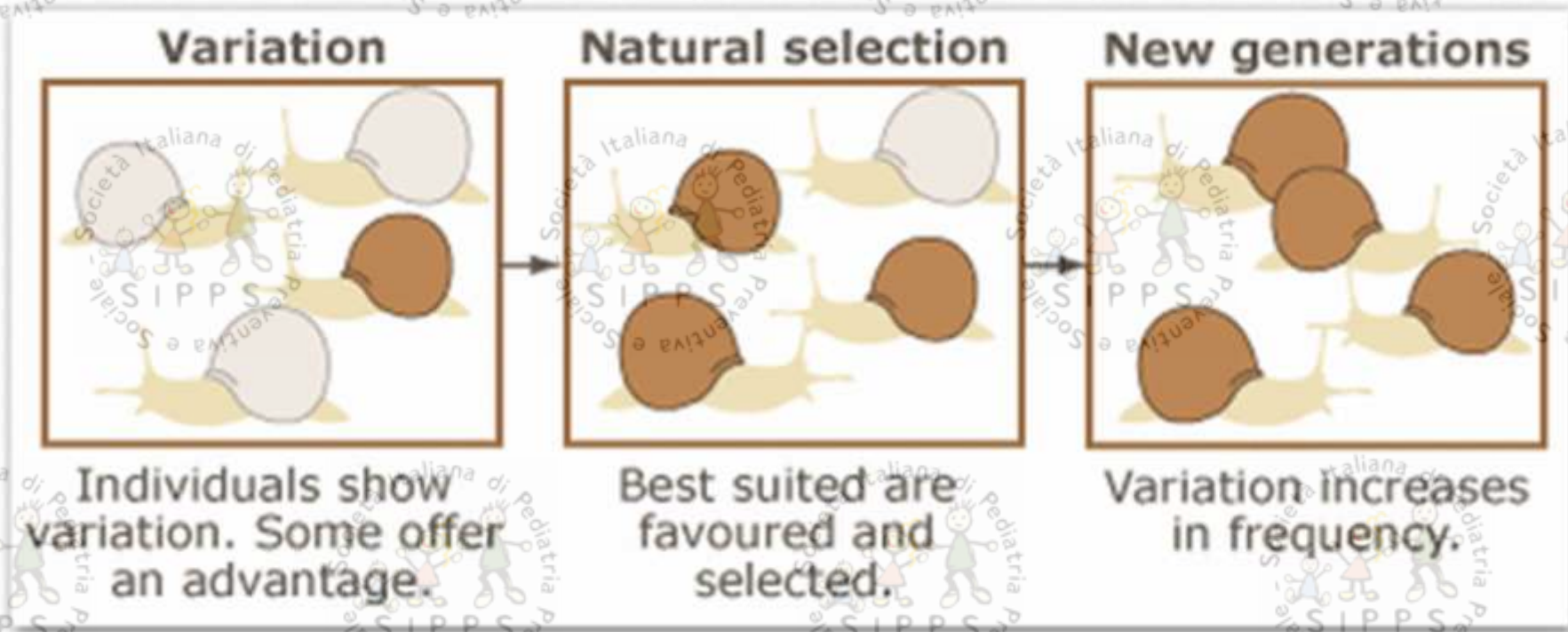
The modern synthesis

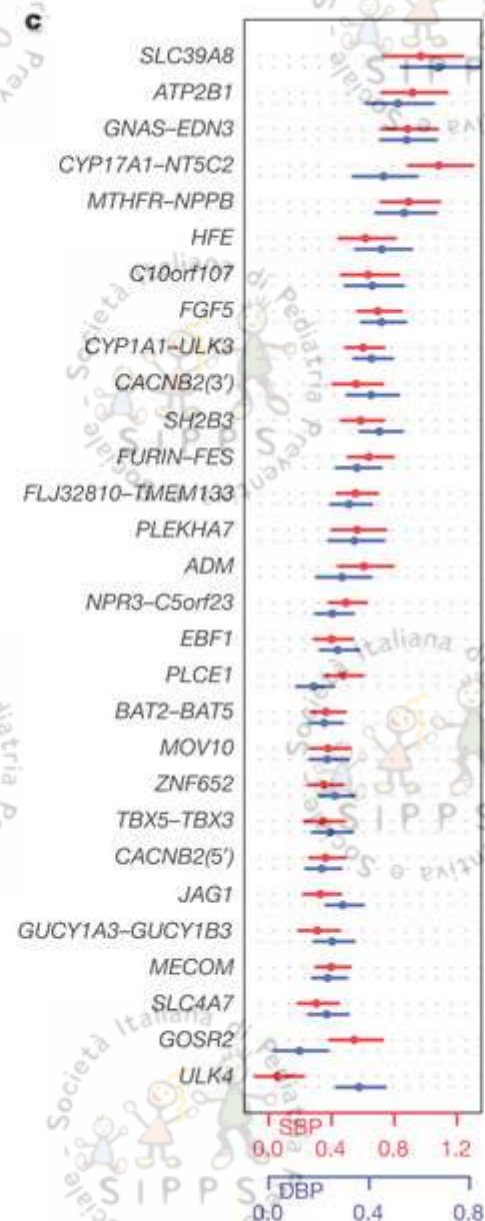
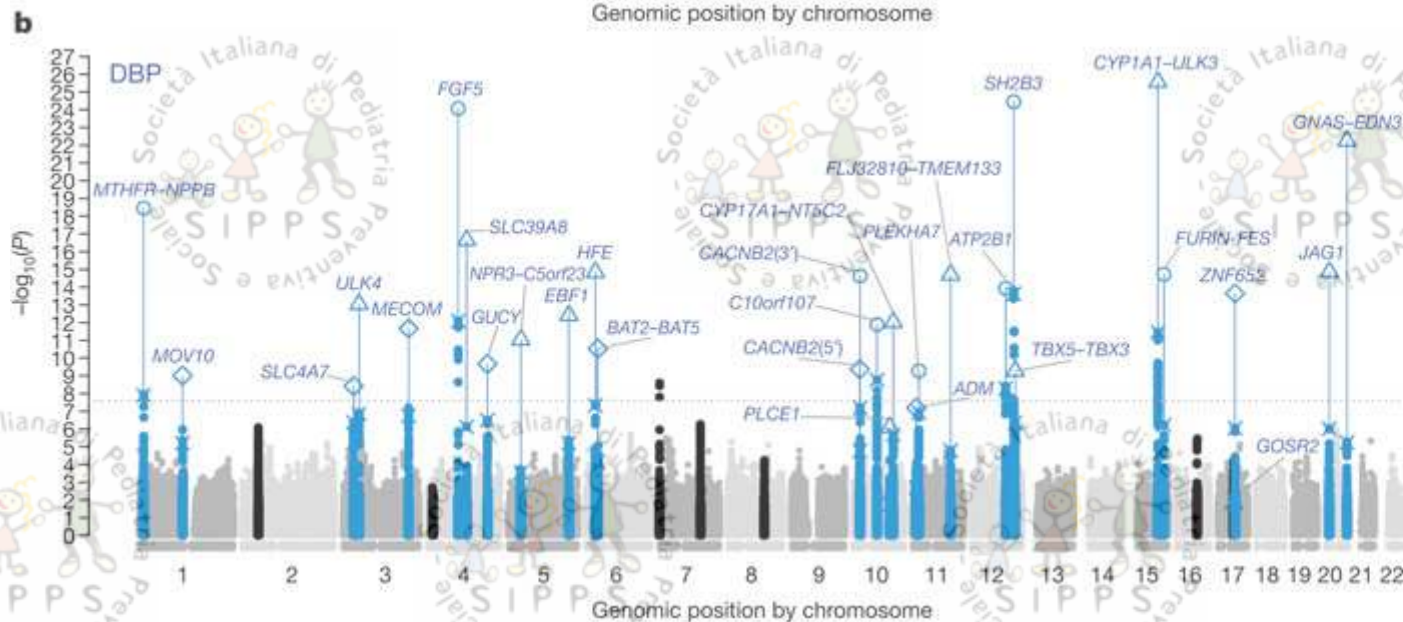
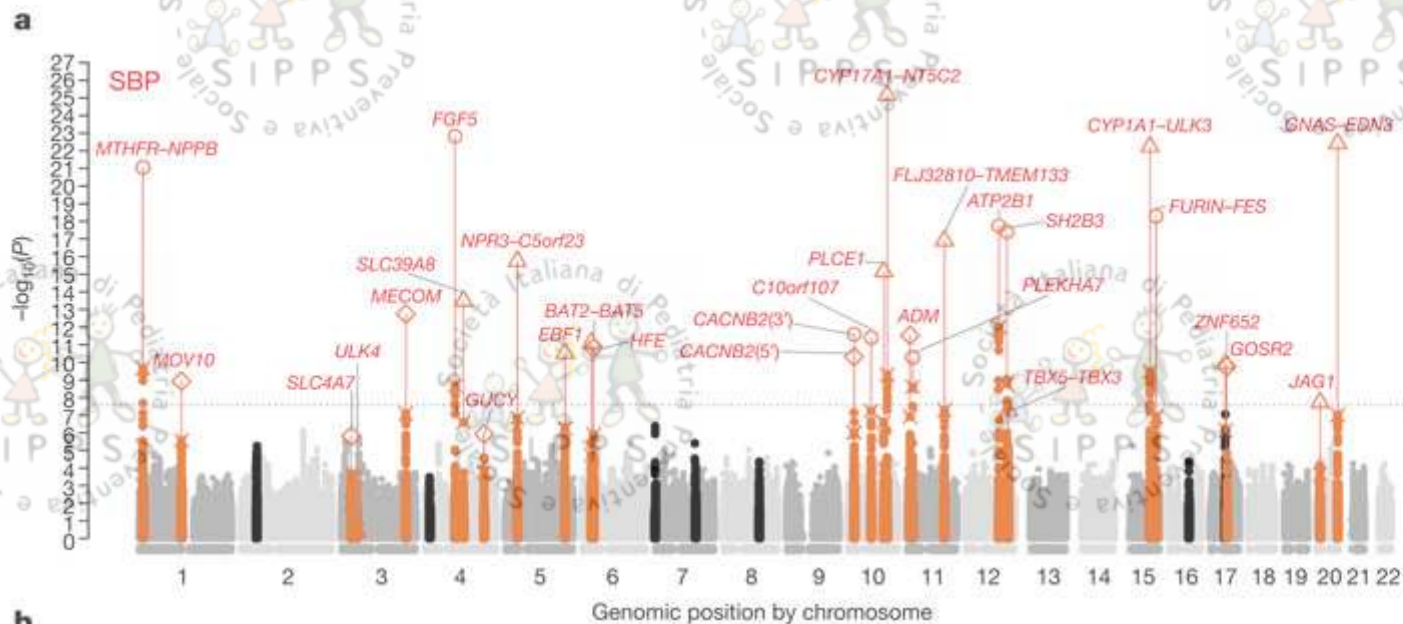


Genetic change is gradual

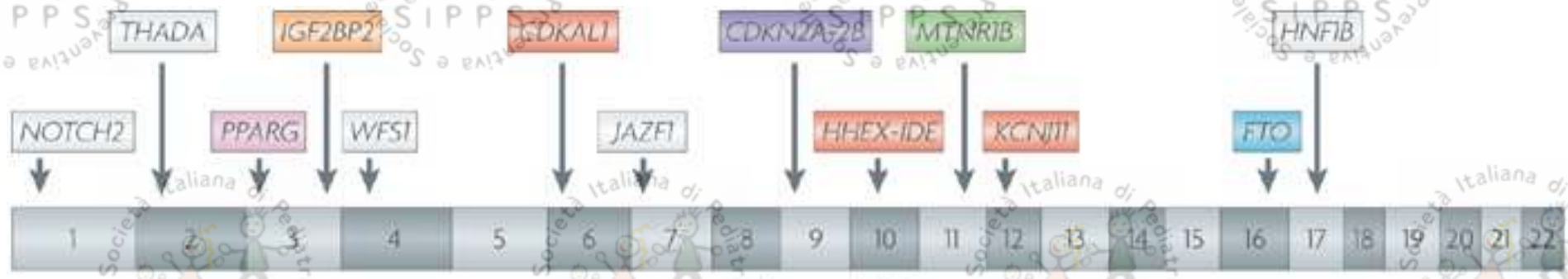
The modern synthesis

Natural selection of «advantageous» alleles





Genome-wide association studies (GWAS): 18 genomic intervals confer increased risk to T2D in Caucasians



Nature Reviews | Genetics

Frazer K. A. et Al., 2009

The background of the slide is a repeating pattern of the SIPPSS logo. The logo is circular and features three stylized figures (a blue baby, a pink girl, and a green boy) holding hands. The text 'SIPPSS' is written in a large, bold, sans-serif font across the middle of the circle. The full name 'Società Italiana di Pediatria Preventiva e Sociale' is written around the perimeter of the circle.

The problem of «missing heritability»



LBW



NCDs



Genotipo



Ambiente



Fenotipo





International Society for Developmental Origins of Health and Disease

www.dohadsoc.org

The Cape Town Manifesto – November 2015

A HEALTHY START BUILDS A BRIGHT FUTURE

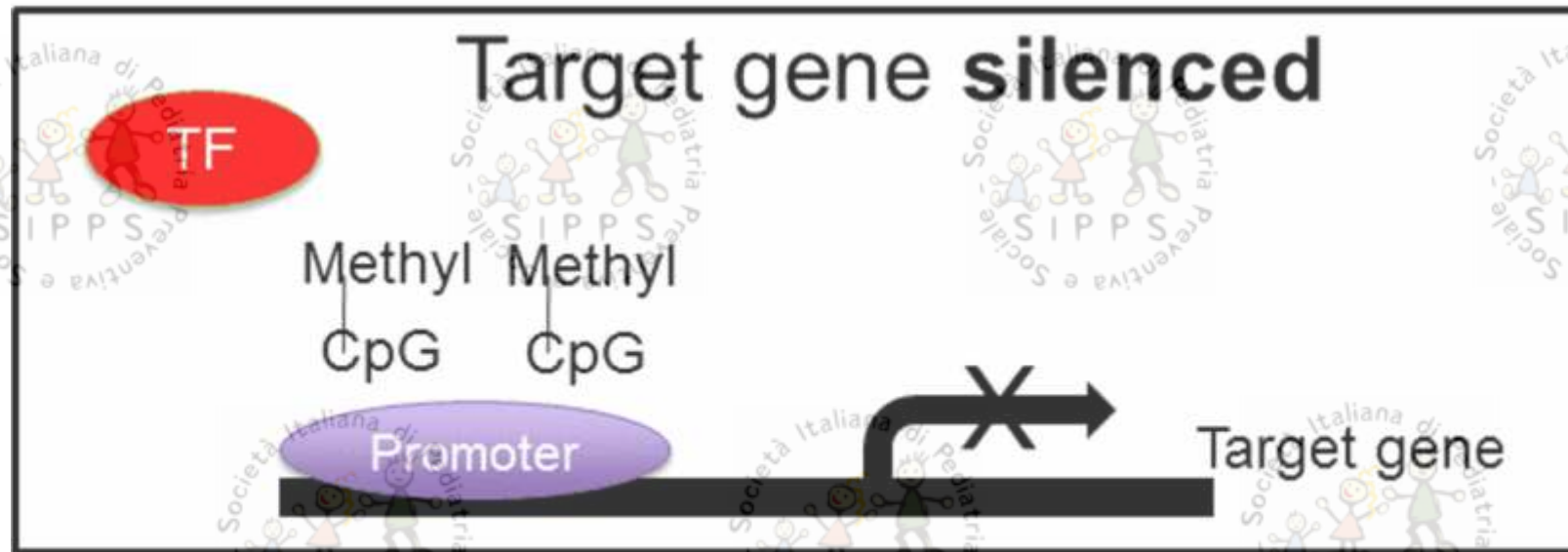
Research in the field of Developmental Origins of Health and Disease (DOHaD) shows that the environment in which the embryo, fetus and young child grow and develop influences not only life course health and wellbeing but also the risk of later non-communicable diseases (NCDs). Important aspects of the environment include maternal, fetal and infant malnutrition (including excess or insufficient macro- and micronutrients), toxins (e.g. maternal smoking or environmental chemical exposure), pregnancy in teenagers or older women and psychological or physiological stress. The NCDs include obesity, type 2 diabetes, hypertension, coronary heart disease, chronic lung and kidney disease, musculoskeletal disorders, some cancers and some mental illness.

Mothers are central to these inter-generational effects on health, because the embryo, fetus and young child depend on them for nutrition and nurturing. However, unhealthy behaviour and exposure to harmful environments in fathers may also increase the risk of NCDs in the next generation, through biological effects on the sperm as well as social factors.

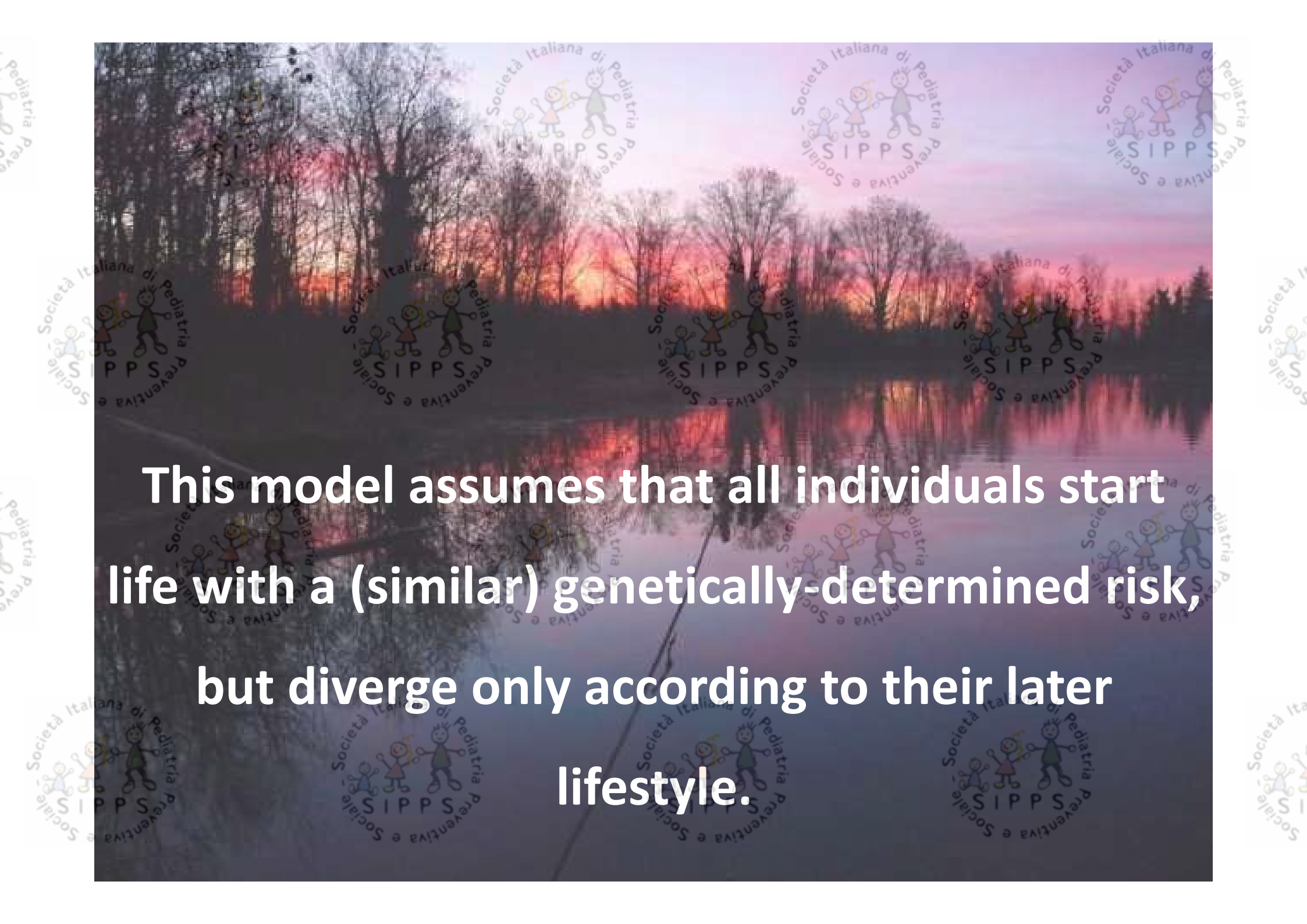
Target gene expressed




Target gene silenced



(Fry, 2011)



This model assumes that all individuals start life with a (similar) genetically-determined risk, but diverge only according to their later lifestyle.



“... attempts to reduce the burden of NCDs by promoting weight loss and changing adult lifestyles have been relatively unsuccessful at a public health level.”

Hanson M. A. and Gluckman P. D., 2014

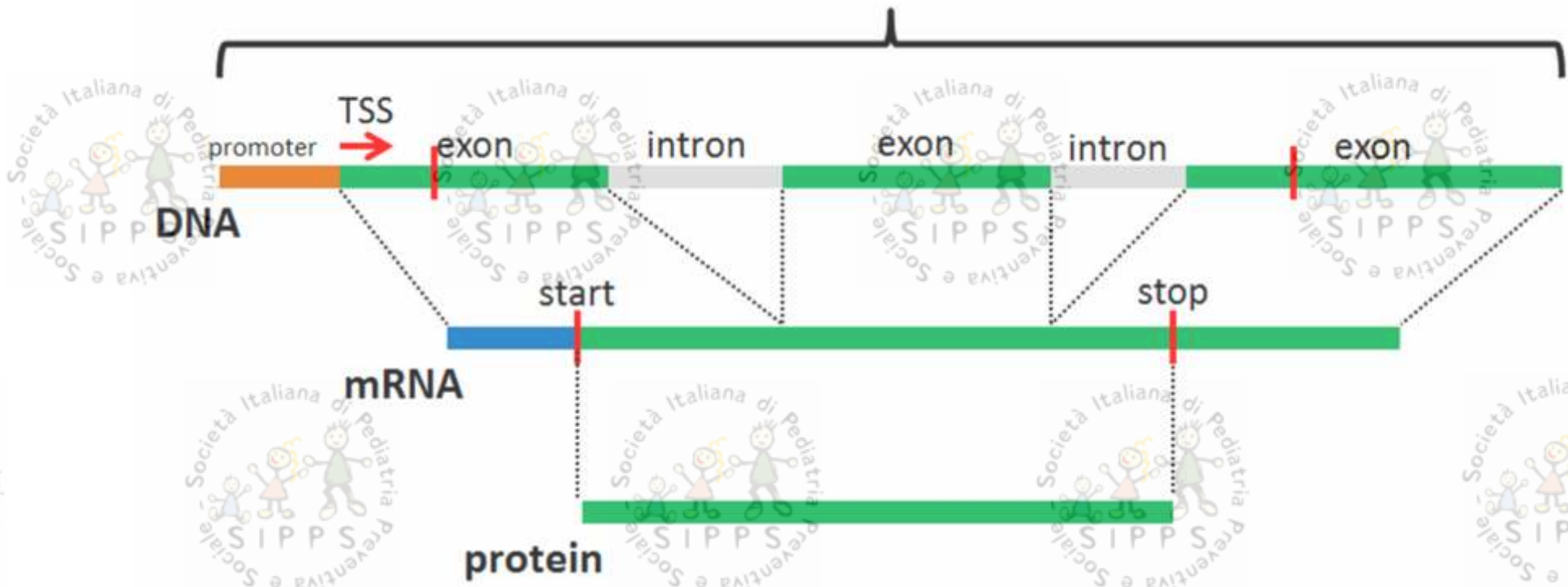


literacy
Health
education
engagement
patient
communication
learning
skills
information
assessment
tools
behaviour
resources
surroundings
change
tips
health
October
HealthEd
surveying
numeracy



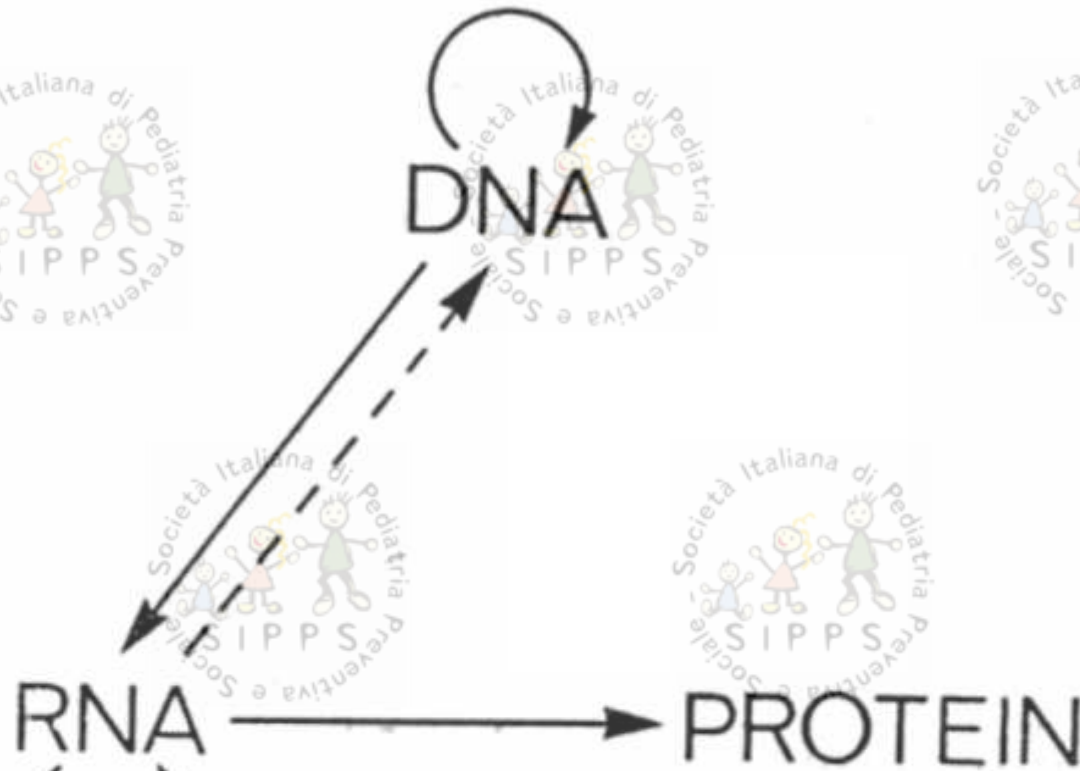
Stile di vita salutare

"Gene"



TSS: Transcription Start Site

Central Dogma of Molecular Biology

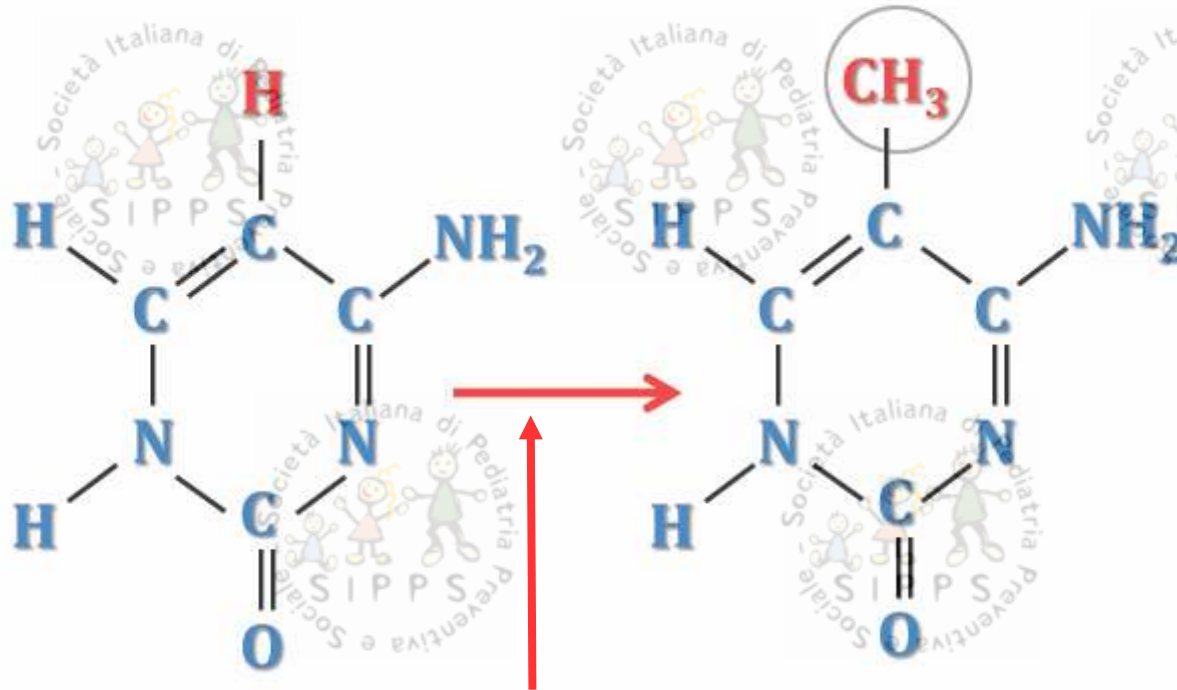


Frances Crick, 1970



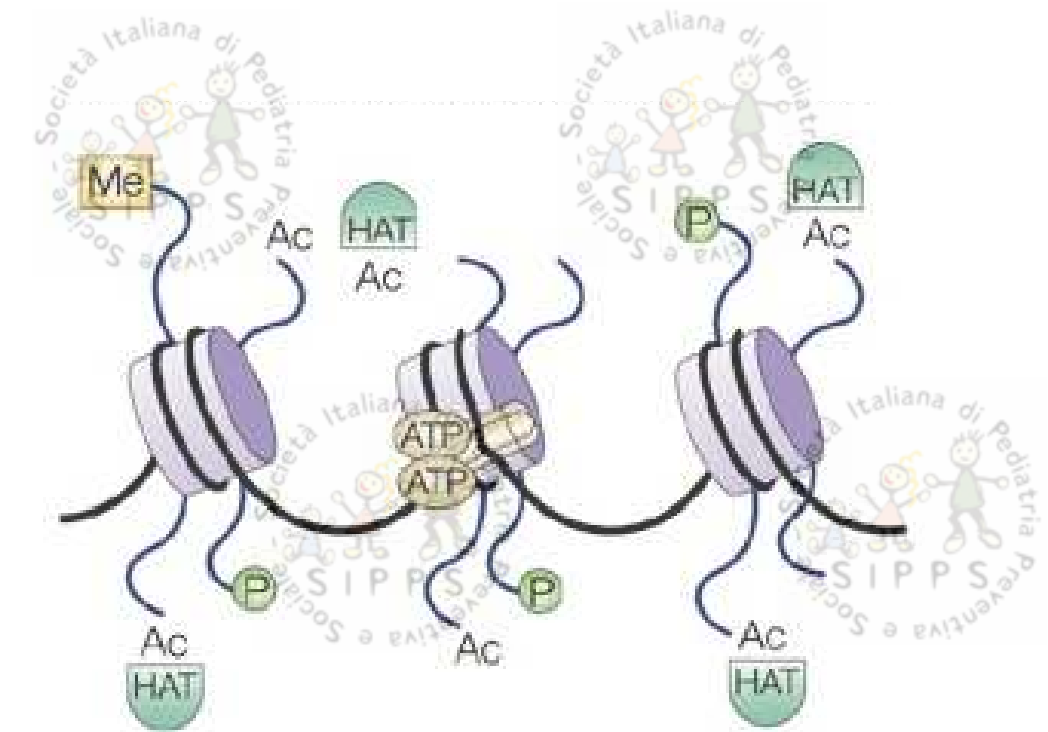
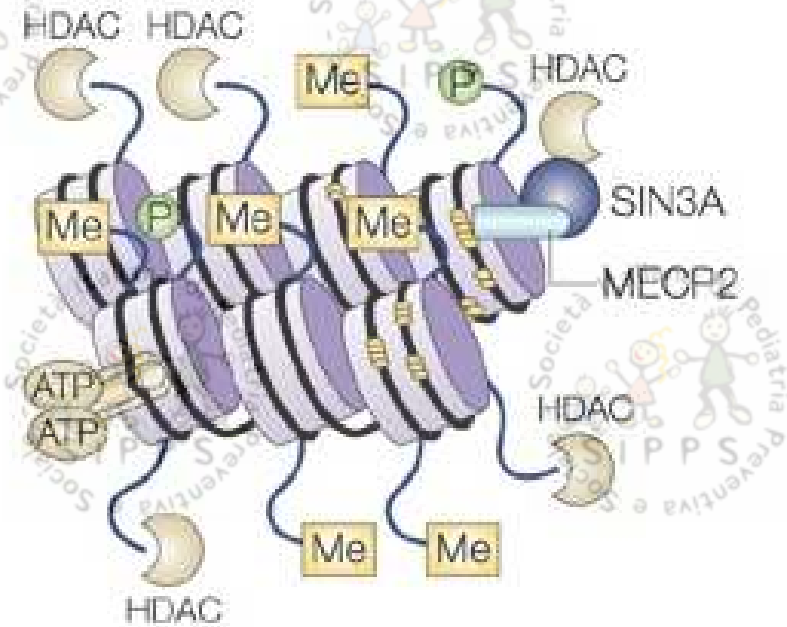
Unmethylated Cytosine

Methylated Cytosine



Metiltransferasi

Acetilazione e deacetilazione degli istoni



HDAC: Histone deacetylase
HAT: Histone AcetylTransferase

L'epigenetica

