

Salve Omnes

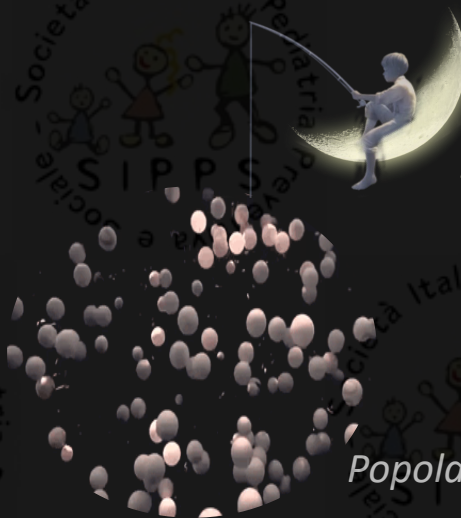


VERSO non DOVE

MICROCHIMERISMO

MISTERO

MISTERO



Bambino

Popolazione cellulare

Non ci sono misteri...
C'è soltanto l'insufficienza di dati o della mente.

Paul Valéry

MISTERO

L'uomo è l'oggetto più misterioso
e sconcertante scoperto dalla scienza.

Angel Ganivet

MISTERO

LIFE & DEATH



MISTERO

MISTERO

Si può “uccidere” la morte ?



MISTERO

Il Problema?

Trasferire 7 miliardesimi di DNA

La soluzione:

Attraverso la "riproduzione"

In che modo ?

Ammalandosi...

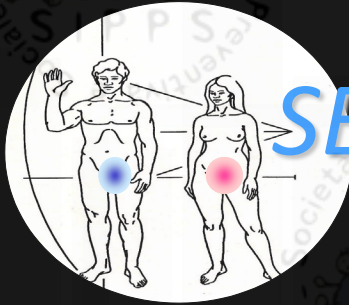
(la "riproduzione" è una malattia sessualmente trasmissibile)

Edward Bellamy

a viaggiare verso l'eternità...



"Che carini! A che servono?"



SESSUALITA'





220 cm

7 picogrammi

DNA

7 miliardesimi di un milligrammo.

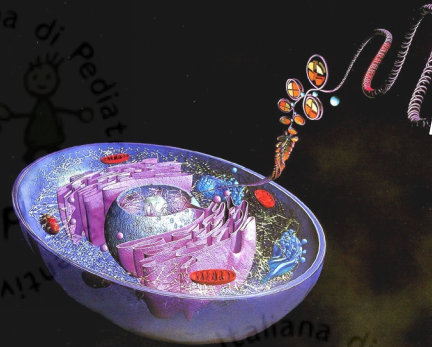


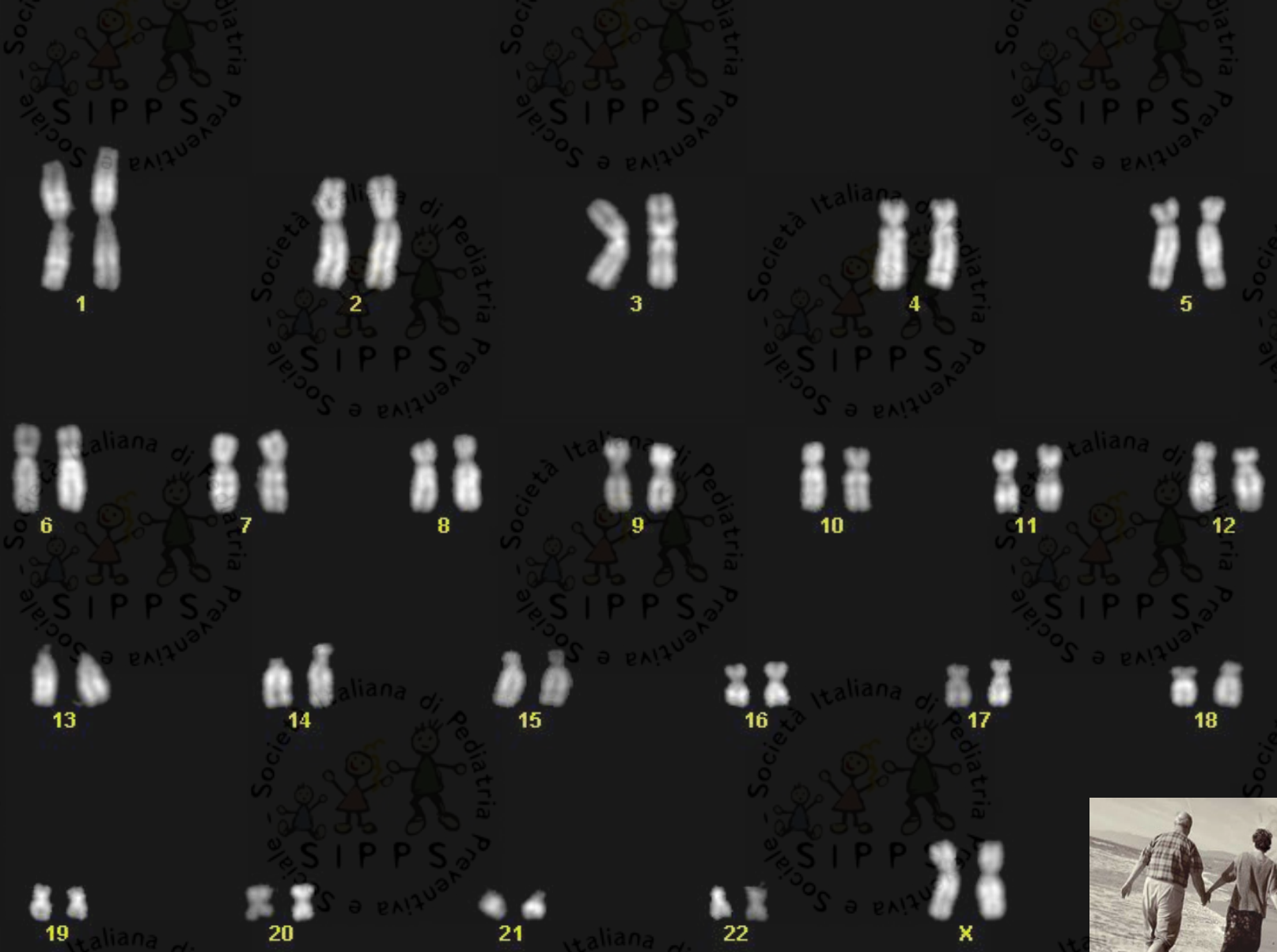
I nostri genitori

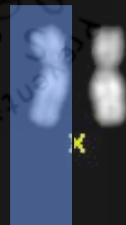
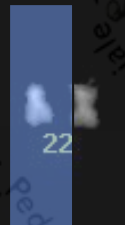
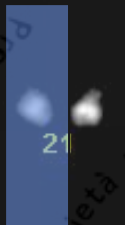
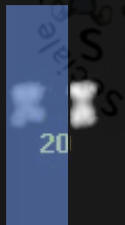
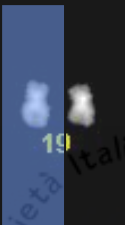
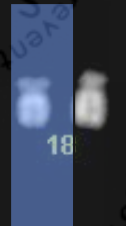
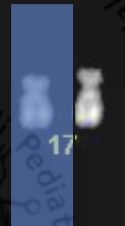
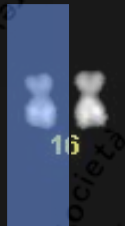
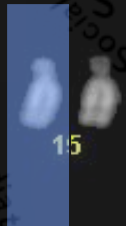
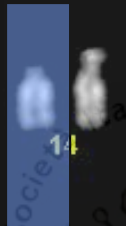
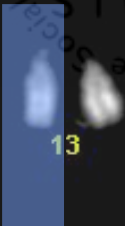
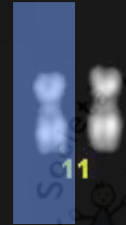
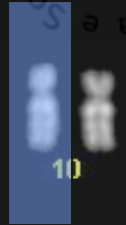
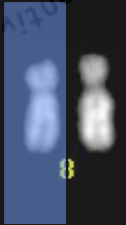
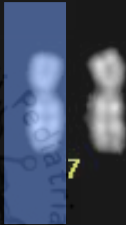
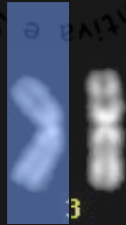
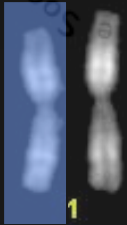


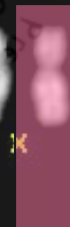
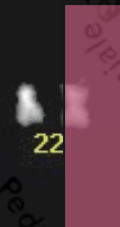
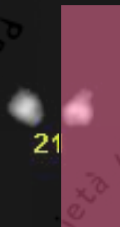
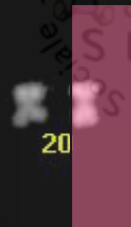
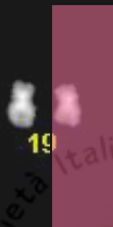
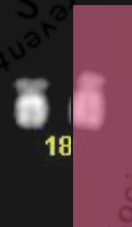
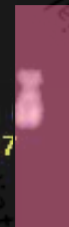
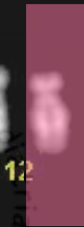
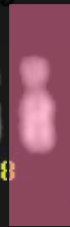
nel nostro DNA

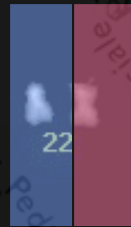
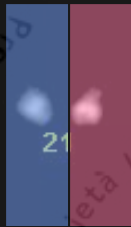
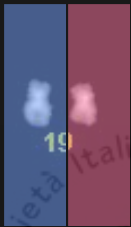
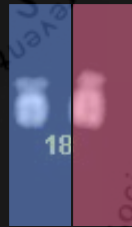
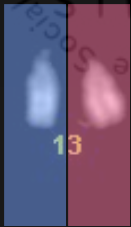
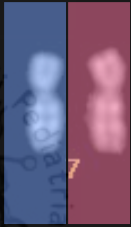
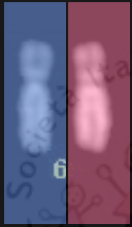
sono nelle nostre cellule













Etc...

$1/2$

$1/256$

$1/4$

$1/128$

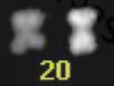
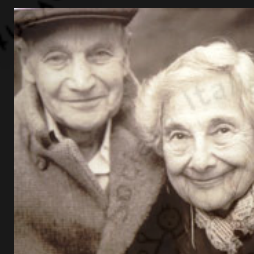


$1/8$

$1/64$

$1/32$

$1/16$

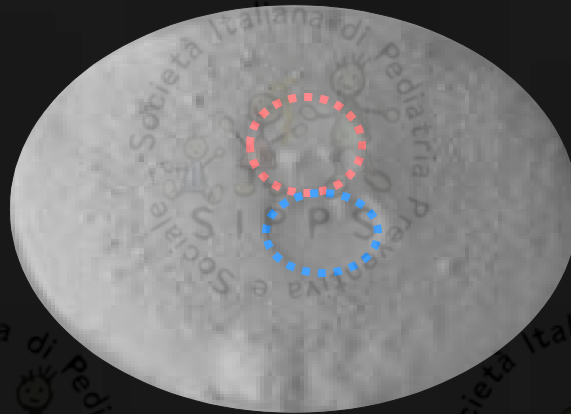


Non c'è niente di più "vecchio"
di una "nuova" vita

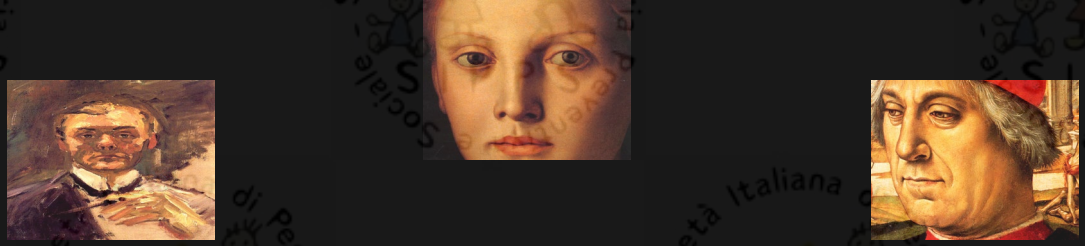


Morti riemergono dal passato ...

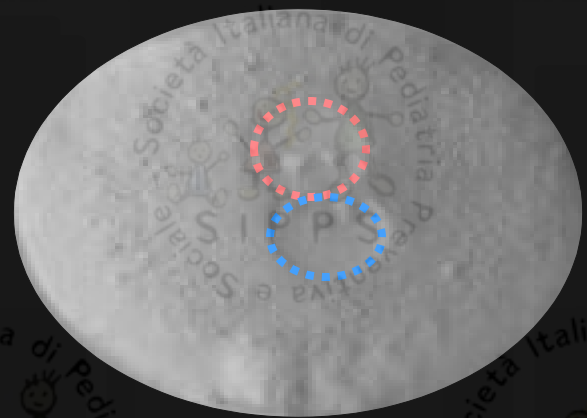
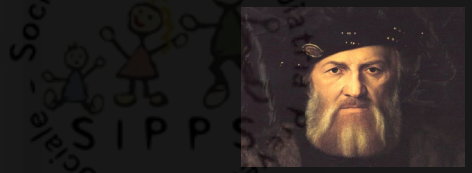
I nostri antenati erano presenti



Zigote



I nostri antenati erano presenti
ed ognuno offriva qualcosa di sé...



Zigote





capelli neri



capelli biondi



statura



occhi azzurri



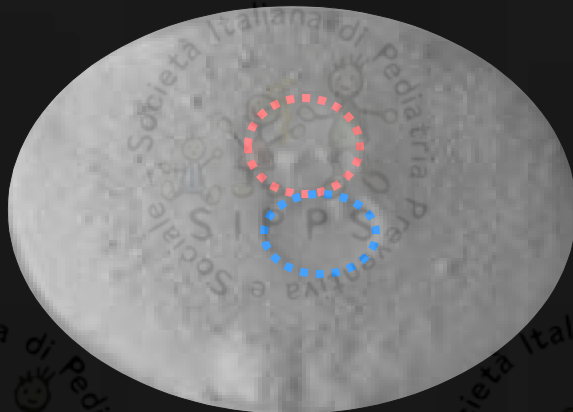
sangue



raffreddore



robustezza



tubercolosi



deformità




resistenza



daltonismo



vista acuta



Si definì così non soltanto il
nostro corpo
*ma anche buona porta
del nostro destino...*

calma

mansuetudine

iracondia

prepotenza

intelligenza

Avvedutezza commerciale

sentimento

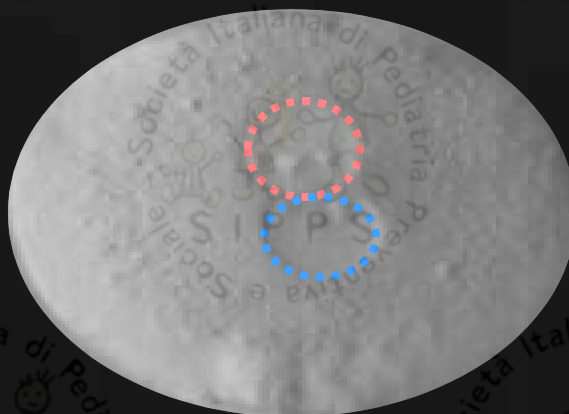
Visione poetica

musica

prodigalità

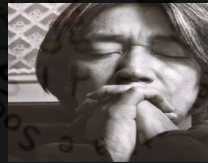
avarizia

matematica





mansuetudine



calma



iracondia



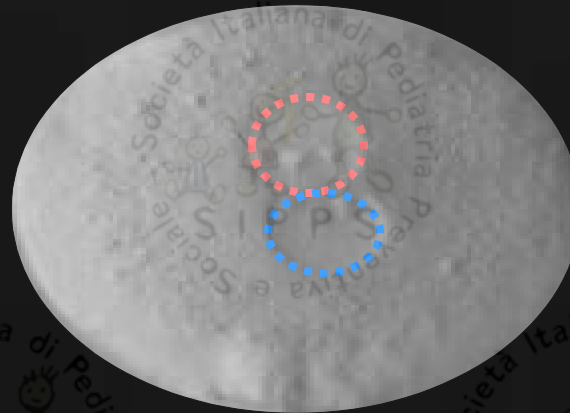
prepotenza



intelligenza



Avvedutezza commerciale



sentimento



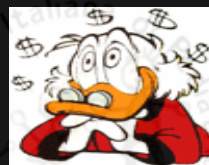
Visione poetica



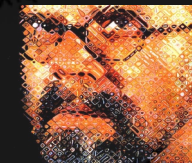
musica



prodigalità



avarizia

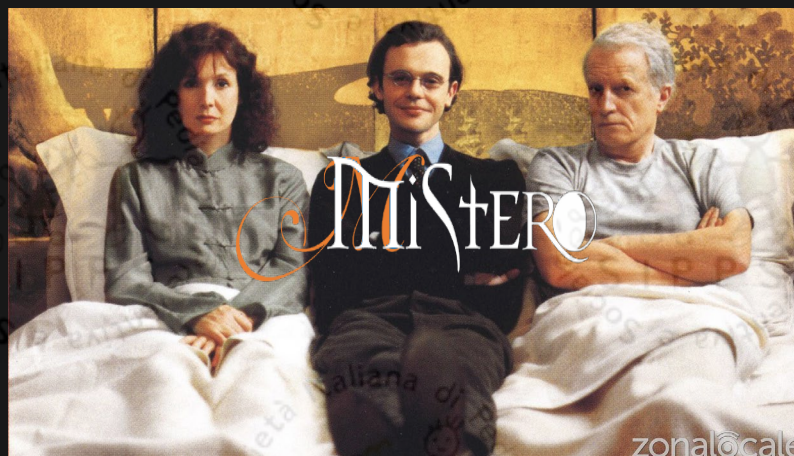


matematica



MISTERO

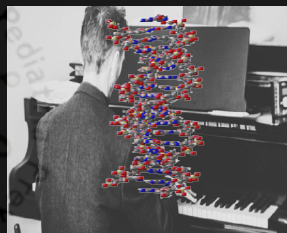
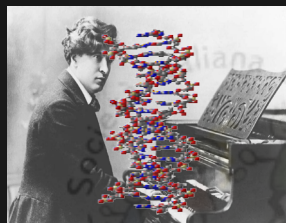
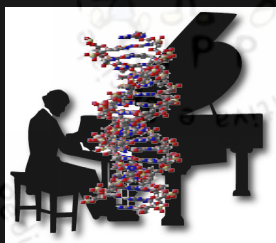




Ma da chi ha preso ?



Ma da chi ha preso ?



Ma da chi ha preso ?

2000 anni fa...

576.460.752.303.423.488



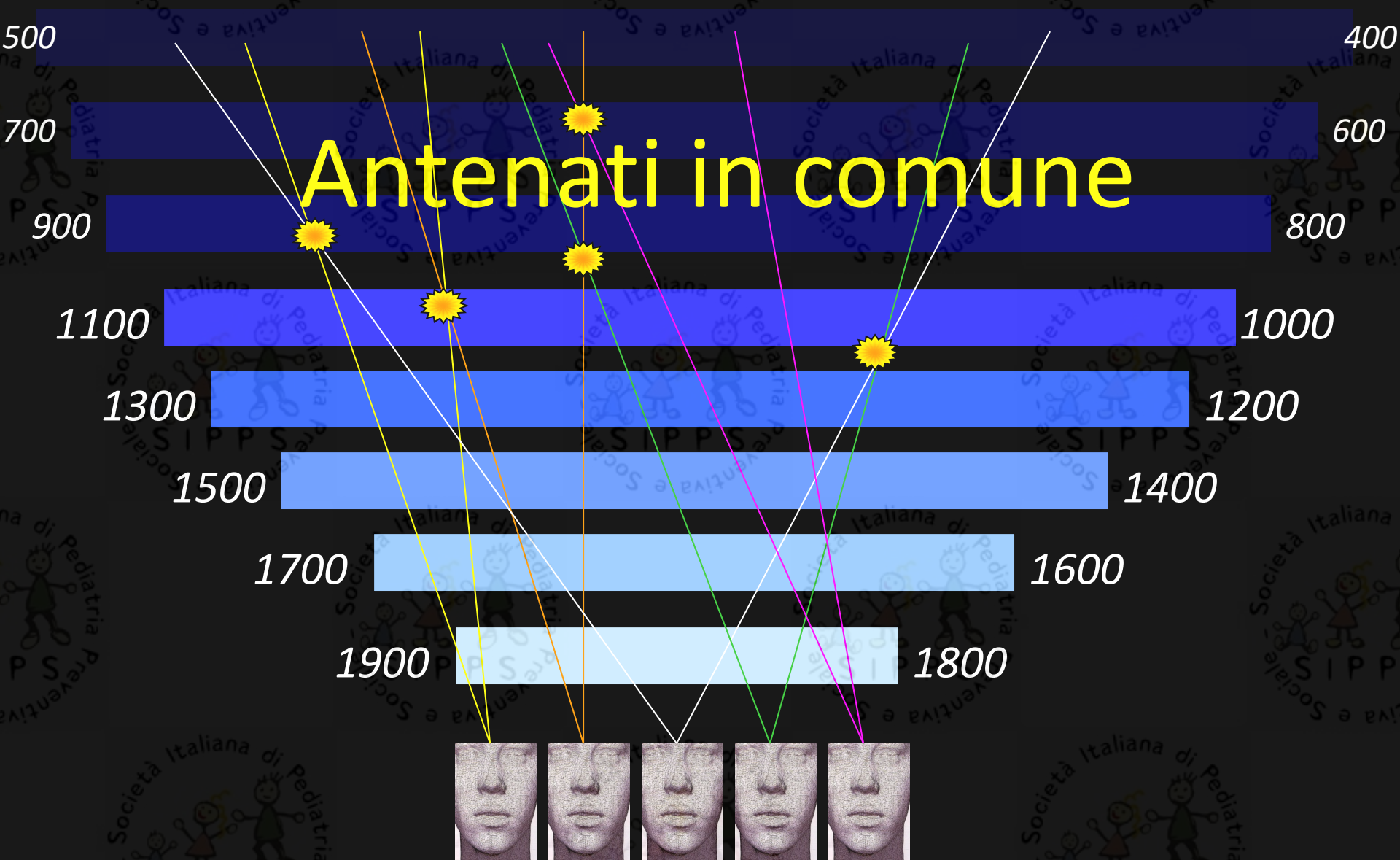
MISTERO

OGGI



8 MILIARDI

Antenati in comune



Inizia la ricerca



*dei nostri "fratelli biologici"
del "donatore compatibile"*

Daniel Davis



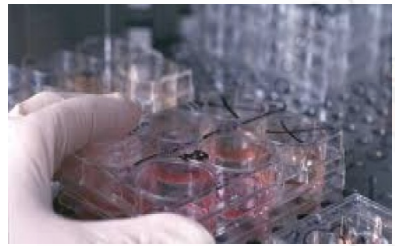


Antipatico a "pelle"





Antipatico a "pelle"

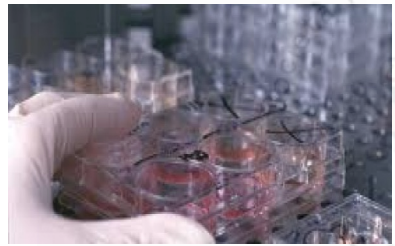


COMPATIBILITA' **MASSIMA**





Antipatico a "pelle"




COMPATIBILITA' MASSIMA



antipatico

ricevitore





ANTIPATIA come ANTIDOTO ad
un “incesto immunologico”



William Hazlitt

Le antipatie violente
sono sempre sospette,



tradiscono una segreta affinità.





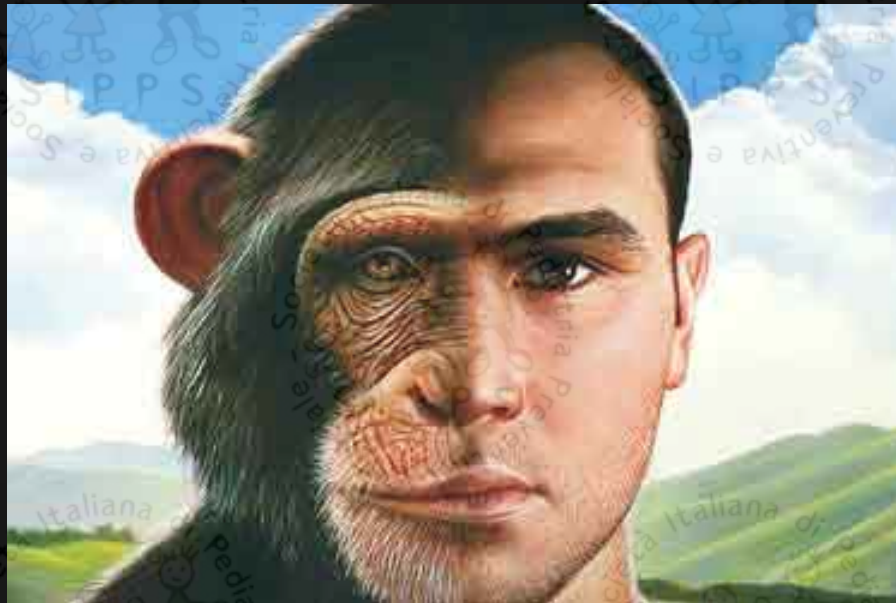
DNA

La storia dell'UMANITA'

Il DNA non ci dice solo da dove veniamo



Il DNA non ci dice solo da dove veniamo



*Ma anche chi erano, da dove venivano
e come vivevano i nostri antenati*

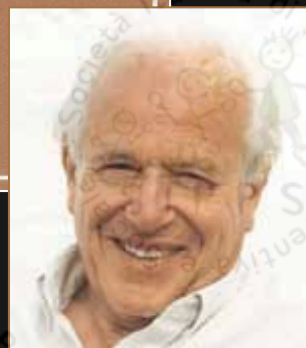
Biblioteca Scientifica 25

*Luigi Luca Cavalli-Sforza
Paolo Menozzi Alberto Piazza*

STORIA E GEOGRAFIA
DEI GENI UMANI



ADELPHI

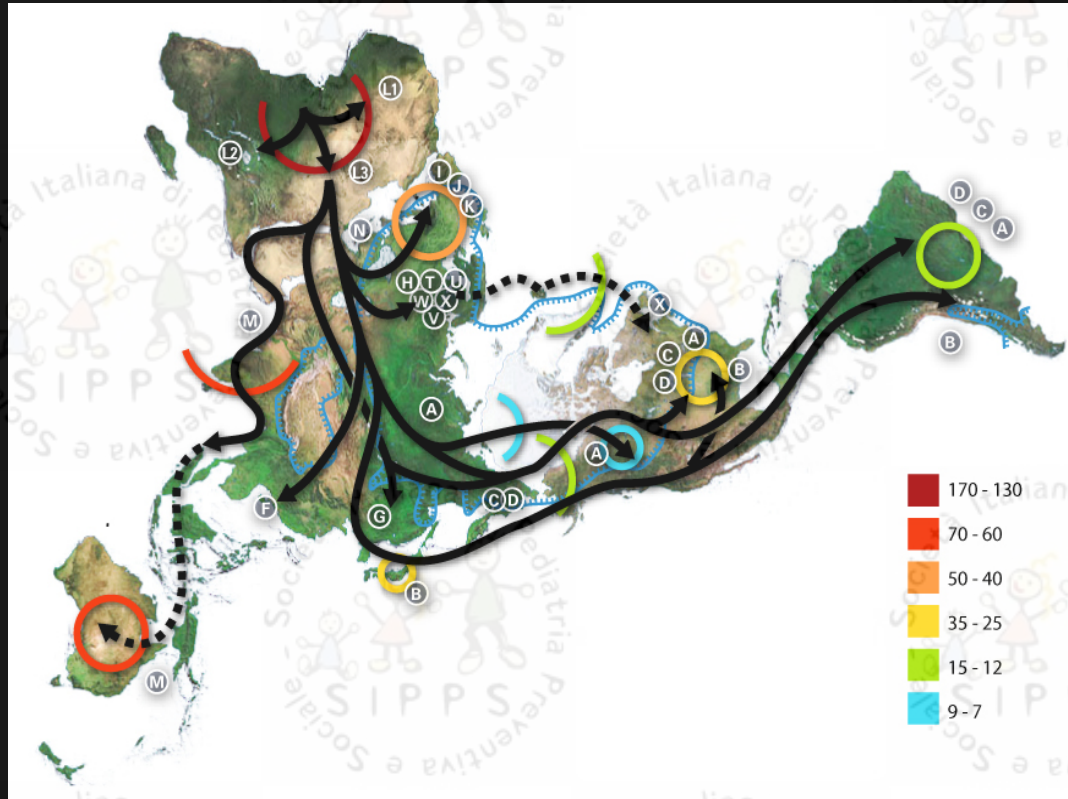


Le grandi migrazioni



*Sono
nel
nostro
DNA*

Dal Caucaso a Mergellina

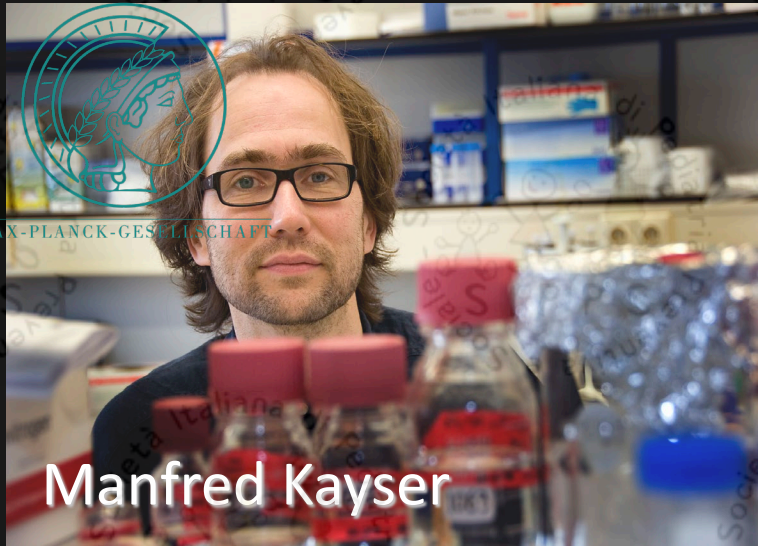
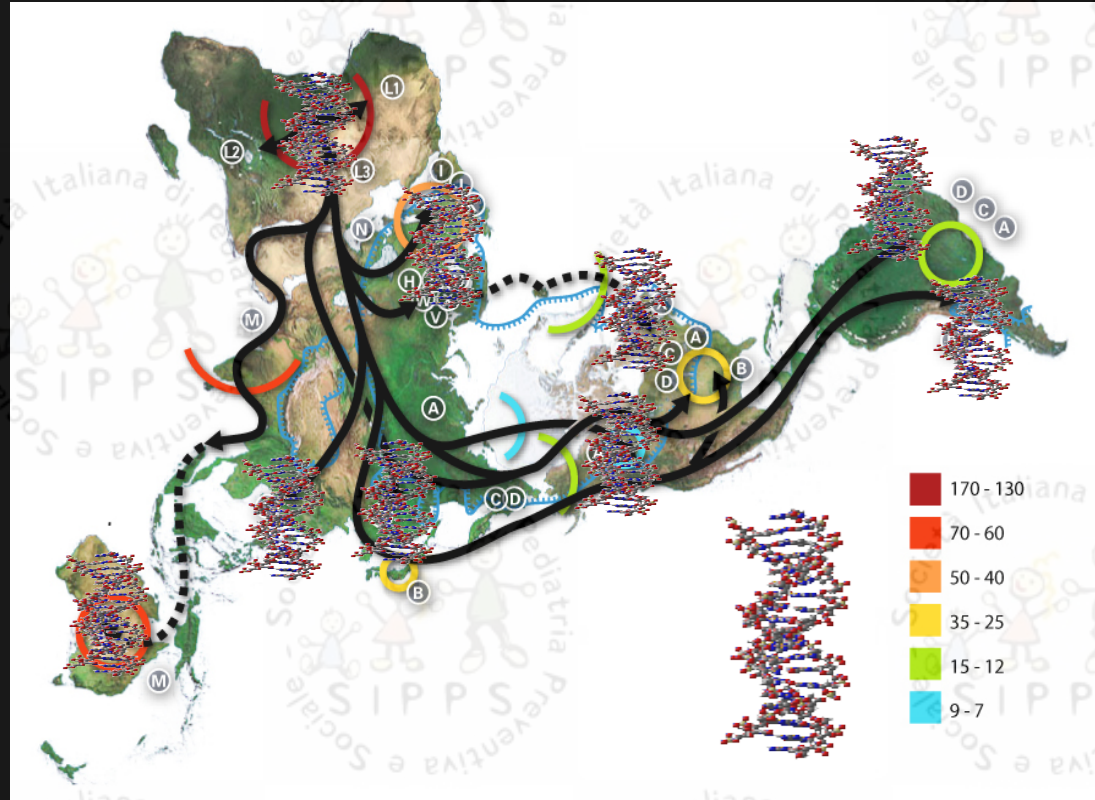


Manfred Kayser

Le grandi migrazioni



Dal Caucaso a Mergellina



MISTERO

La più alta concentrazione genetica di Longobardi ?



In alcuni paesini del Beneventano

MISTERO

Le più belle donne normanne ?



Le ragazze di Palermo



Genoma afro-americano



COLONIALISMO



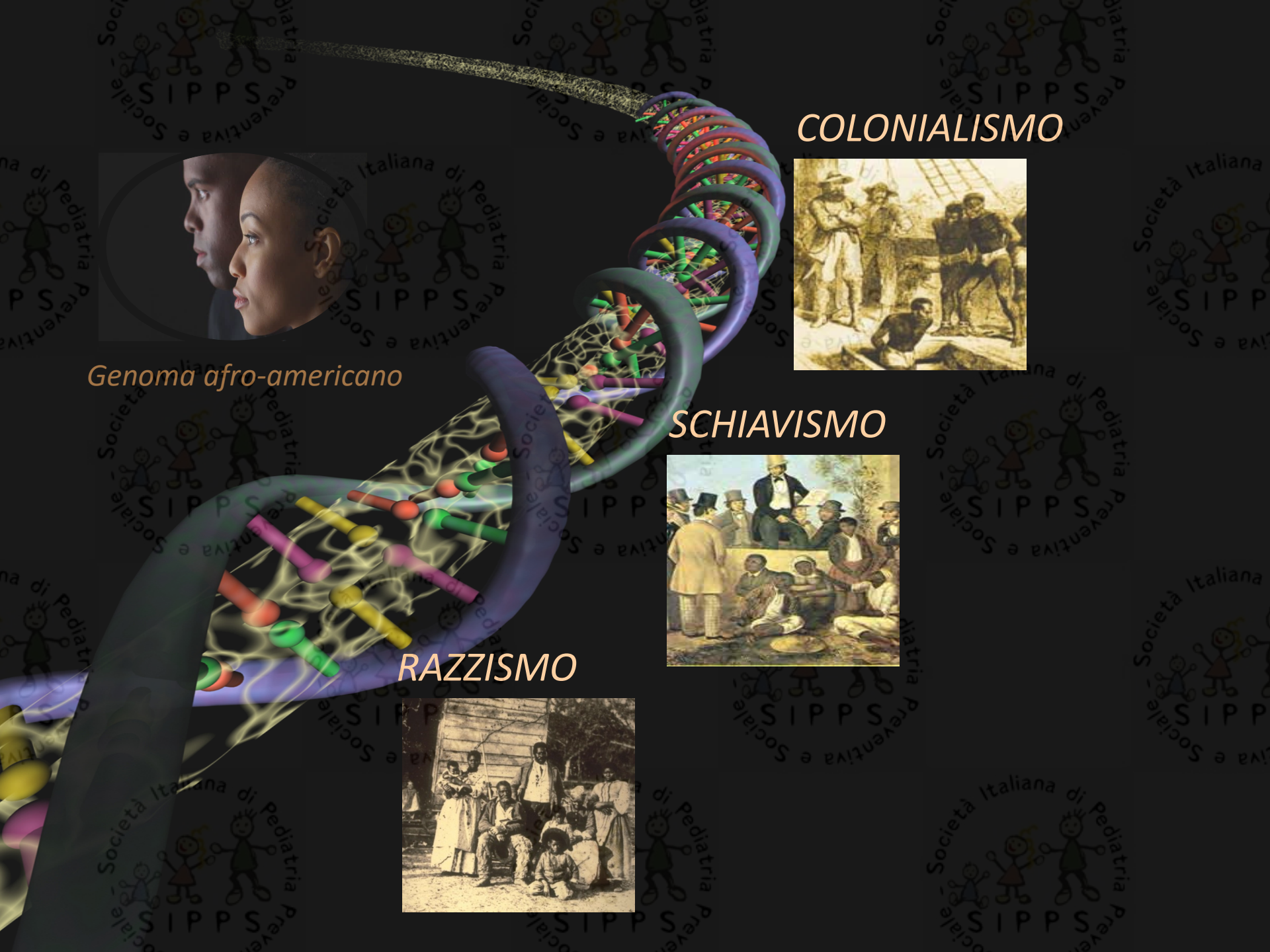
SCHIAVISMO



RAZZISMO



Genoma afro-americano





Genoma italo-americano





Genoma italo-americano

DISPERAZIONE



DISCRIMINAZIONE



PREGIUDIZI



*Siamo tutti emigranti...
da 2 milioni di anni*

MITOSI MITOSI

Il sogno di una cellula che si realizza

Jacques Monod

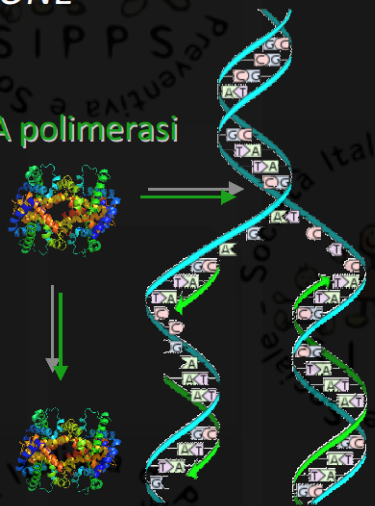


MITOSI MITOSI

R

REPLICAZIONE

DNA polimerasi



Le 3 prerogative di un gene

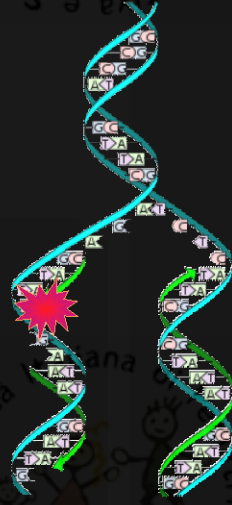


R.E.M.
musicwallpapers.net

That was just a dream
Just a dream
Just a dream, dream
Losing My Religion

M

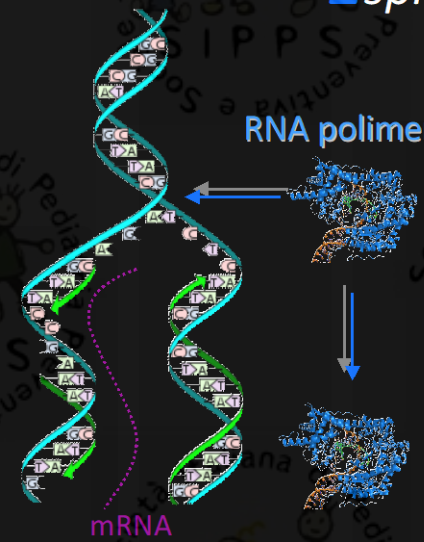
Muta



E

Espressione

RNA polimerasi



Metonimie pericolose:

Ce l'abbiamo nel DNA !

La **RNA polimerasi**
per la gestione del
quotidiano ?



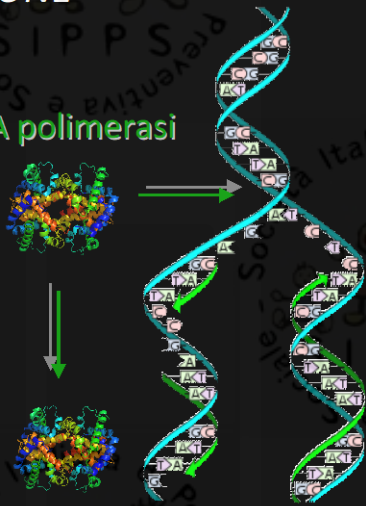
La **DNA polimerasi**
per la corenza della
dignità ?

Quante **Mutazioni**
hai collezionato nella tua vita ?

R

REPLICAZIONE

DNA polimerasi



Le 3 prerogative di un gene



RE.M
musicwallpapers.net

That was just a dream
Just a dream
Just a dream, dream
Losing My Religion

M

Muta



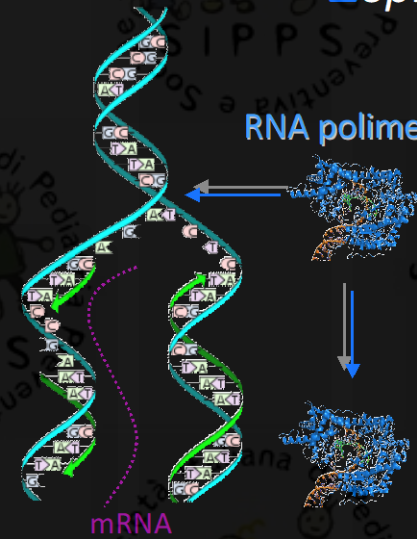
**Modificazione
EPIGENETICA**

Modificazione chimica covalente
EREDITABILE ma **REVERSIBILE**

E

Espressione

RNA polimerasi



GENOMA



HARDWARE

GENOMA

EPIGENOMA



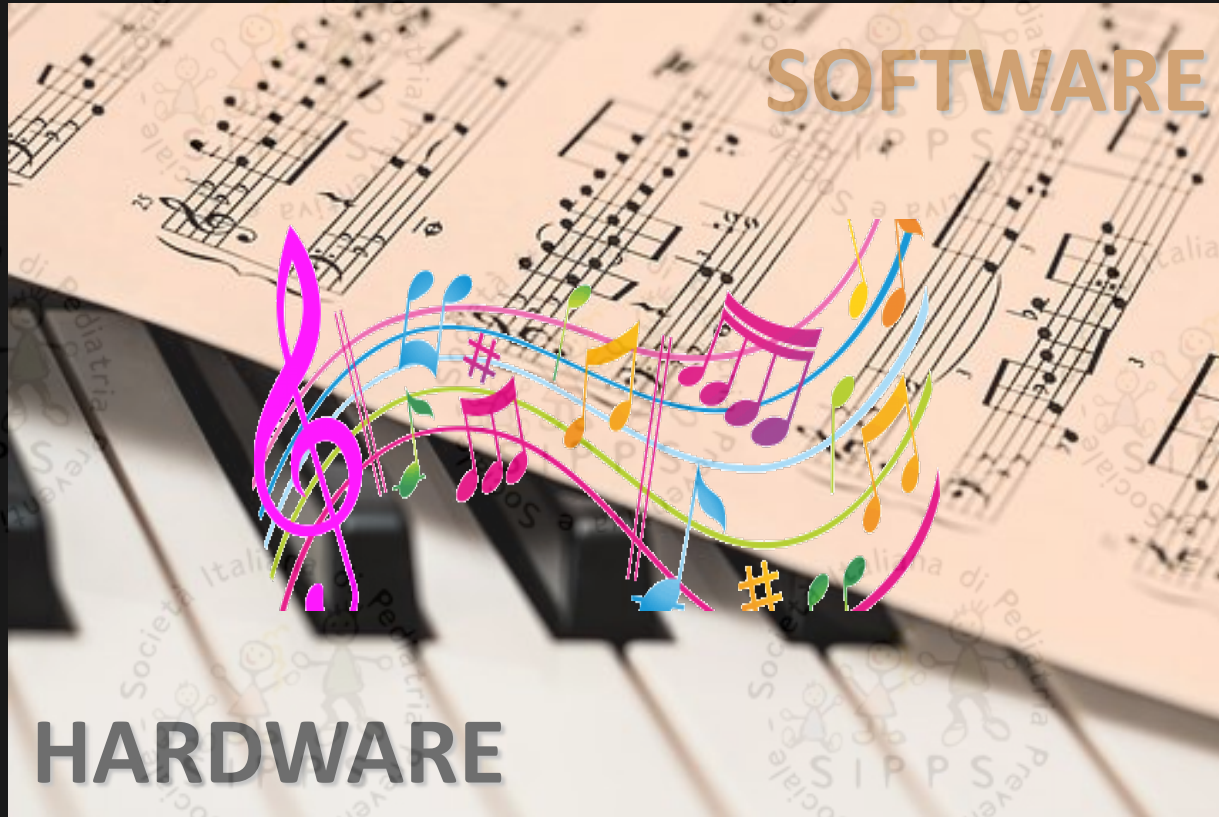


HARDWARE

DNA

STILE DI VITA

SOFTWARE



HARDWARE

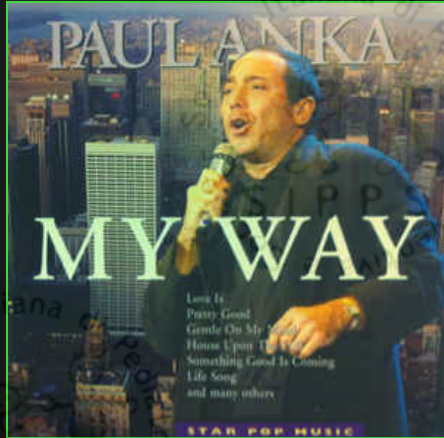
DNA



VERDI MESSA DA REQUIEM



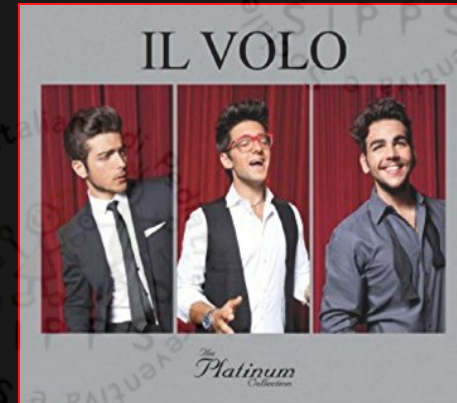
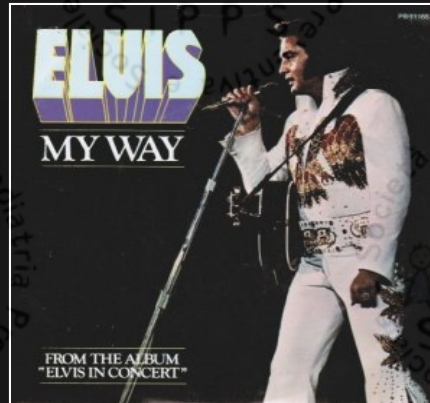
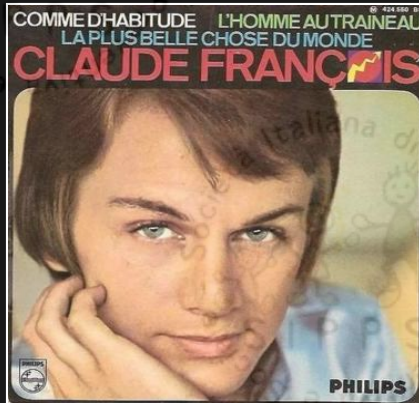
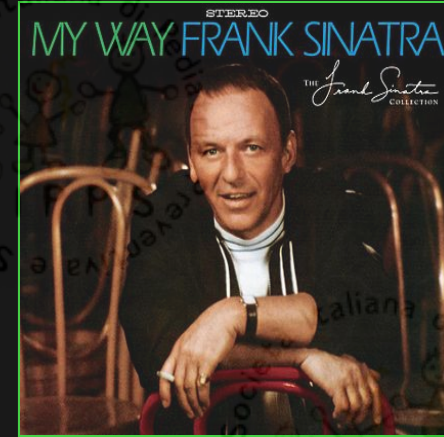
SOFTWARE



HARDWARE



SOFTWARE



Proto-HARDWARE

SOFTWARE

Polymorphisms
Polymorphisms
Polymorphisms



DNA

La data della nostra morte ?

TELOMERI



Raccontano cosa succede all'interno del **genoma**



Mol Ecol. 2013 Jan;22(1):249-59.

Telomere length and dynamics predict mortality in a wild longitudinal study.

Barrett EL et al.1

School of Biological Sciencesrk, Norwich, Norfolk UK.

Quanto durerà la nostra vita

Our results provide the first clear and unambiguous evidence of a relationship between telomere length and mortality in the wild, and substantiate the prediction that telomere length and shortening rate can act as an indicator of biological age further to chronological age when exploring life history questions in natural conditions

Adesso e nell'ora della nostra morte... MISTERO

Aging (Albany NY). 2016 Sep 28;8(9):1844-1865.

DNA methylation-based measures of biological age: meta-analysis predicting time to death.

Chen BH, Marioni RE, Colicino E, Peters MJ, Ward-Caviness CK, Tsai PC, Roetker NS, Just AC, Demerath EW, Guan W, Bressler J, Fornage M, Studenski S, Vandiver AR, Moore AZ, Tanaka T, Kiel DP, Liang L, Vokonas P, Schwartz J, Lunetta KL, Murabito JM, Bandinelli S, Hernandez DG, Melzer D, Nalls M, Pilling LC, Price TR, Singleton AB, Gieger C, Holle R, Kretschmer A, Kronenberg F, Kunze S, Linseisen J, Meisinger C, Rathmann W, Waldenberger M, Visscher PM, Shah S, Wray NR, McRae AF, Franco OH, Hofman A, Uitterlinden AG, Absher D, Assimes T, Levine ME, Lu AT, Tsao PS, Hou L, Manson JE, Carty CL, LaCroix AZ, Reiner AP, Spector TD, Feinberg AP, Levy D, Baccarelli A, van Meurs J, Bell JT, Peters A, Deary IJ, Pankow JS, Ferrucci L, Horvath S.

- (1) Longitudinal Studies Section, Translational Gerontology Branch, Baltimore, [USA](#).
- (2) The NHLBI's Framingham Heart Study, Framingham, MA 01702, [USA](#).
- (3) Population Sciences Branch, Division of Intramural Research, [USA](#).
- (4) Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, [UK](#).
- (5) Medical Genetics Section, Centre for Genomic and Experimental Medicine, [UK](#).
- (6) Queensland Brain Institute, University of Queensland, Brisbane, QLD, [Australia](#).
- (7) Laboratory of Environmental Epigenetics, Columbia University [USA](#).
- (8) Department of Internal Medicine, Erasmus University The [Netherlands](#).
- (9) Institute of Epidemiology II, Helmholtz Zentrum München, Neuherberg, [Germany](#).
- (10) Department of Twin Research and Genetic Epidemiology, Kings College London, (11) Division of Epidemiology and Community Health, [USA](#).
- (13) Human Genetics Center, University of Texas [USA](#).
- (14) Human Genome Sequencing Center, Baylor College of Medicine, [USA](#).
- (15) Center for Epigenetics, Johns Hopkins University, Baltimore, MD 21205, ; [USA](#).
- (16) Department of Medicine, Medical School, Boston, MA, ; [USA](#)
- (17) Institute for Aging Research, Hebrew Senior Life, Boston, MA 02215, [USA](#).
- (18) Department of Epidemiology, Harvard School of Public Health, Boston, [USA](#).
- (19) Department of Biostatistics, Harvard School of Public Health, Boston, [USA](#).
- (20) Department of Biostatistics, Boston, [USA](#)
- (21) Section of General Internal Medicine, University School of Medicine, [USA](#).
- (22) Geriatric Unit, Usl Centro Toscana Florence, [Italy](#).
- (23) Laboratory of Neurogenetics, Intramural Research Program, [USA](#)
- (24) Epidemiology and Public Health, Medical School, University of Exeter, RILD, Exeter EX2 5DW, ; [UK](#).
- (25) Research Unit of Molecular Epidemiology, Helmholtz Zentrum München, 85764 Neuherberg, [Germany](#).
- (26) Institute of Health Economics and Health Care Management, Helmholtz Zentrum München, 85764 Neuherberg, [Germany](#).
- (27) Division of Genetic Epidemiology, [Austria](#).
- (28) Institute for Biometrics and Epidemiology, [Germany](#).
- (29) University of Queensland Diamantina Institute, [Australia](#).
- (30) Department of Epidemiology, Erasmus University Medical Centre, [Netherlands](#).
- (31) HudsonAlpha Institute for Biotechnology, Huntsville, [USA](#).
- (32) Department of Medicine, Stanford University School of Medicine, [USA](#).
- (33) VA Palo Alto Health Care System, Palo Alto CA 94304, [USA](#).
- (34) Department of Preventive Medicine, [USA](#).
- (35) Robert H. Lurie Comprehensive Cancer Center, [USA](#).
- (36) Department of Medicine, Brigham and Women's Hospital, [USA](#).
- (37) Center for Translational Science Children's National Medical Center, [USA](#).
- (38) Department of Family Medicine and Public Health, [USA](#).
- 39) Department of Epidemiology, University of Washington [USA](#).
- (40) Public Health Sciences Division, Seattle, [USA](#).
- (41) Departments of Medicine, Molecular Biology/Genetics, [USA](#).
- (42) Department of Environmental Health, [USA](#).
- (43) Department of Psychology, University of Edinburgh, [UK](#).
- (44) Department of Biostatistics, School of Public Health, [USA](#).

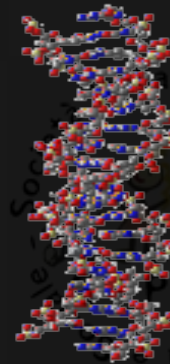
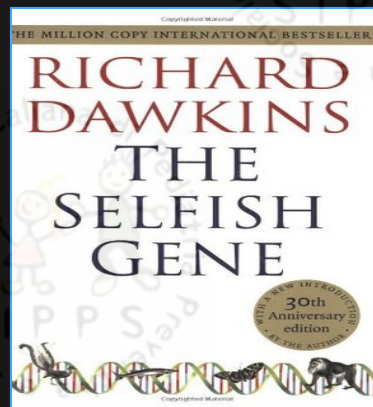
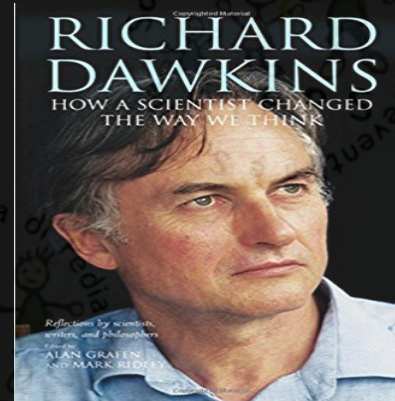


Salvo complicazioni, sto per morire.

Jules Renard

GENE EGOISTA

Il regista occulto delle nostre vite



La parte immortale di ogni essere vivente

IMMUNITA'

ASPETTO
ESTETICO

ORGOGGIO

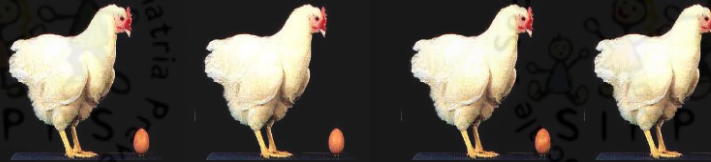
RESILIENCE

Ci spinge a riprodurci

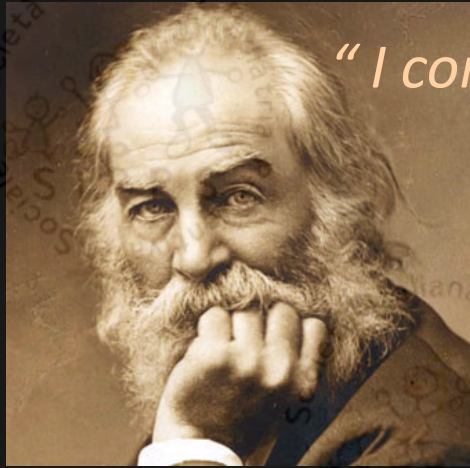
La gallina è un espediente al quale
l'uovo ricorre per fare un altro uovo

Samuel Butler

Piccoli pollai



Grandi dinastie



“I contain multitudes...”

Walt Whitman

Song of Myself



Claretta e Benito



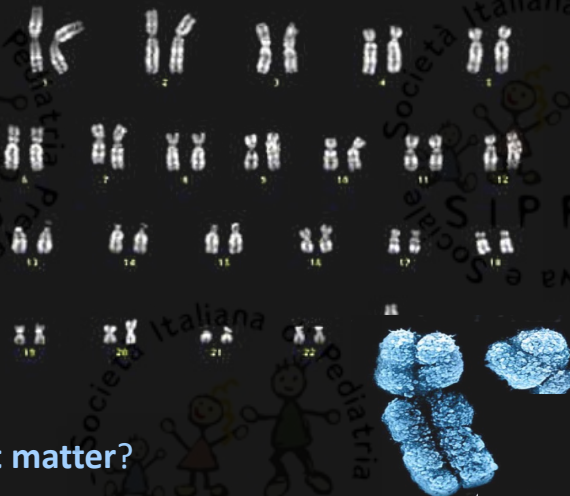
Benito

Claretta

MICROCHIMERISMO



Cariotipo



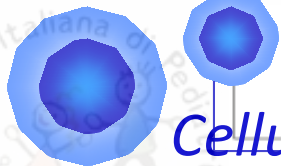
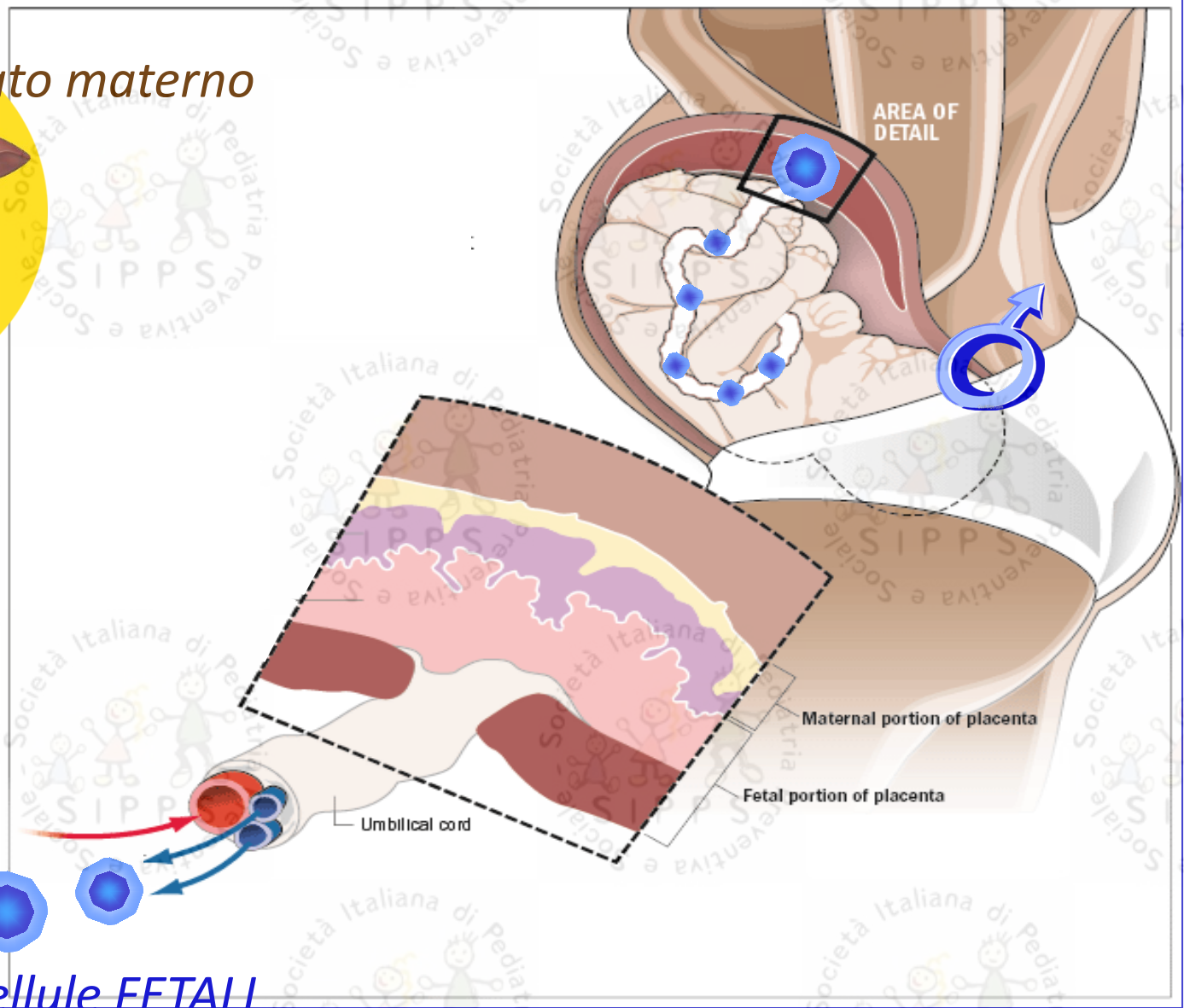
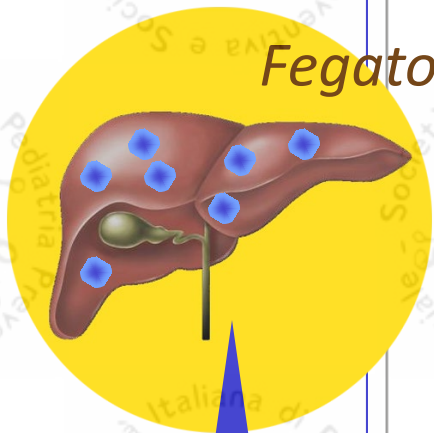
Geck Pet al

Symptomatic detection of chimerism: Y does it matter?

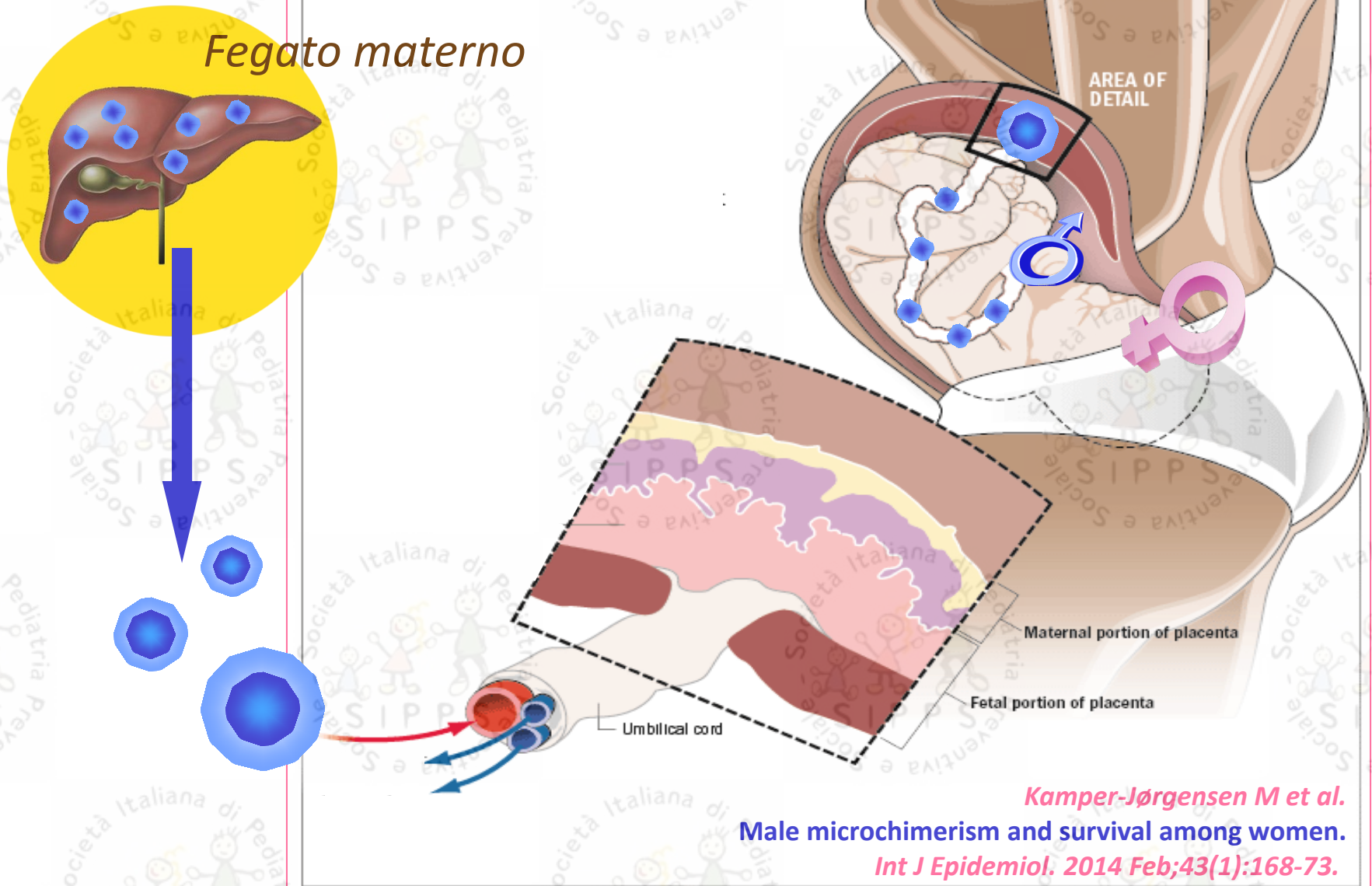
Chimerism. 2013 Oct-Dec;4(4):144-6

MISTERO

Prima gravidanza



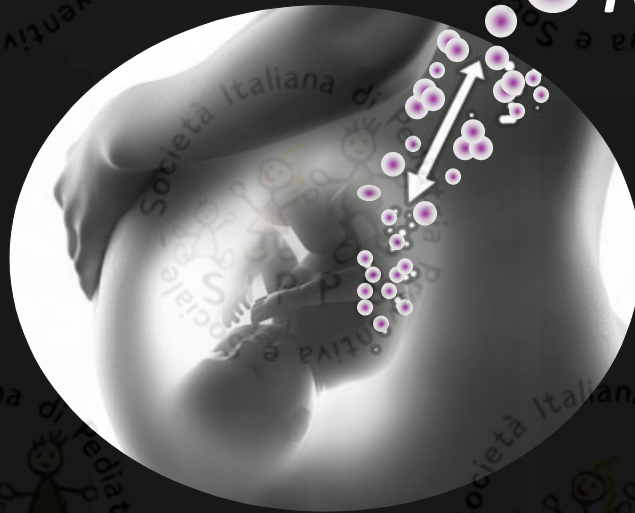
Seconda gravidanza





Passaggio trans-placentare

● Migrazione



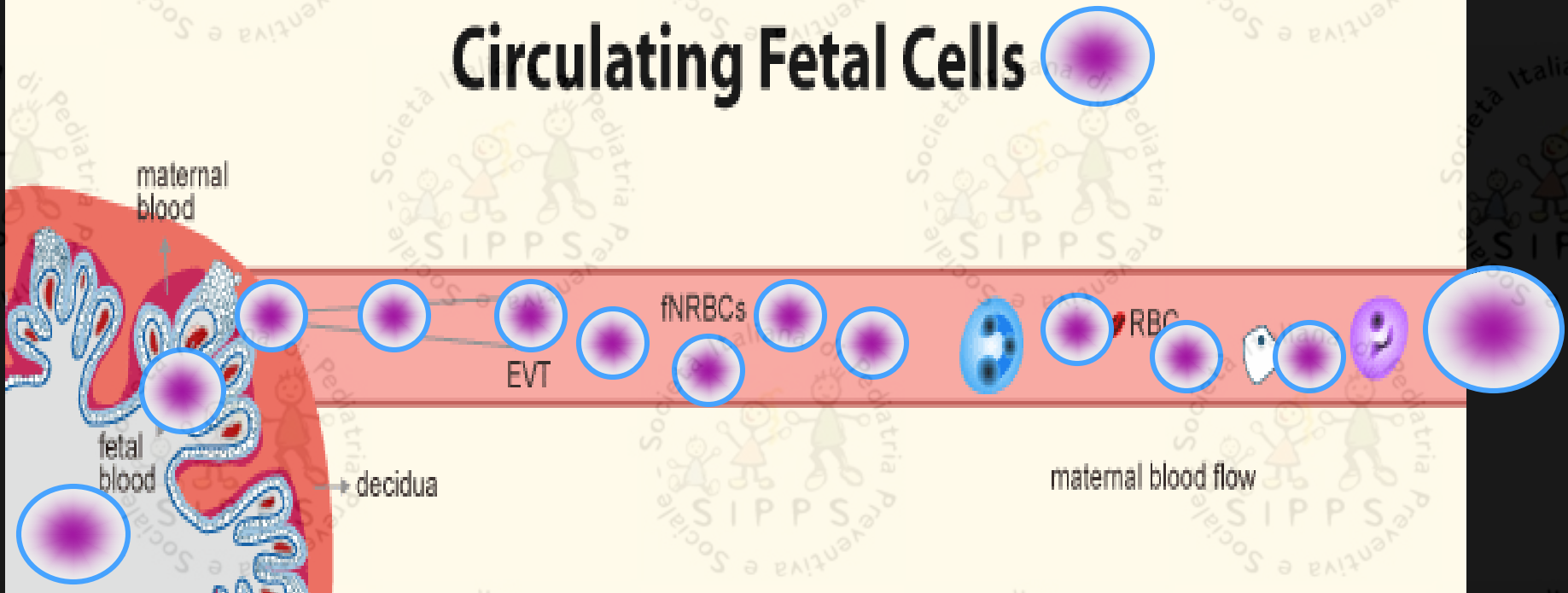
Stem Cell Rev. 2018 Oct;14(5):632-641.

Incognito: Are Microchimeric Fetal Stem Cells
that Cross Placental Barrier Real Emissaries of Peace?

Cismaru CA et al.

MISTERO

Circulating Fetal Cells



Coata G et al.

Persistence of male hematopoietic CD34+ cells in the circulation of women does not affect prenatal diagnostic techniques.

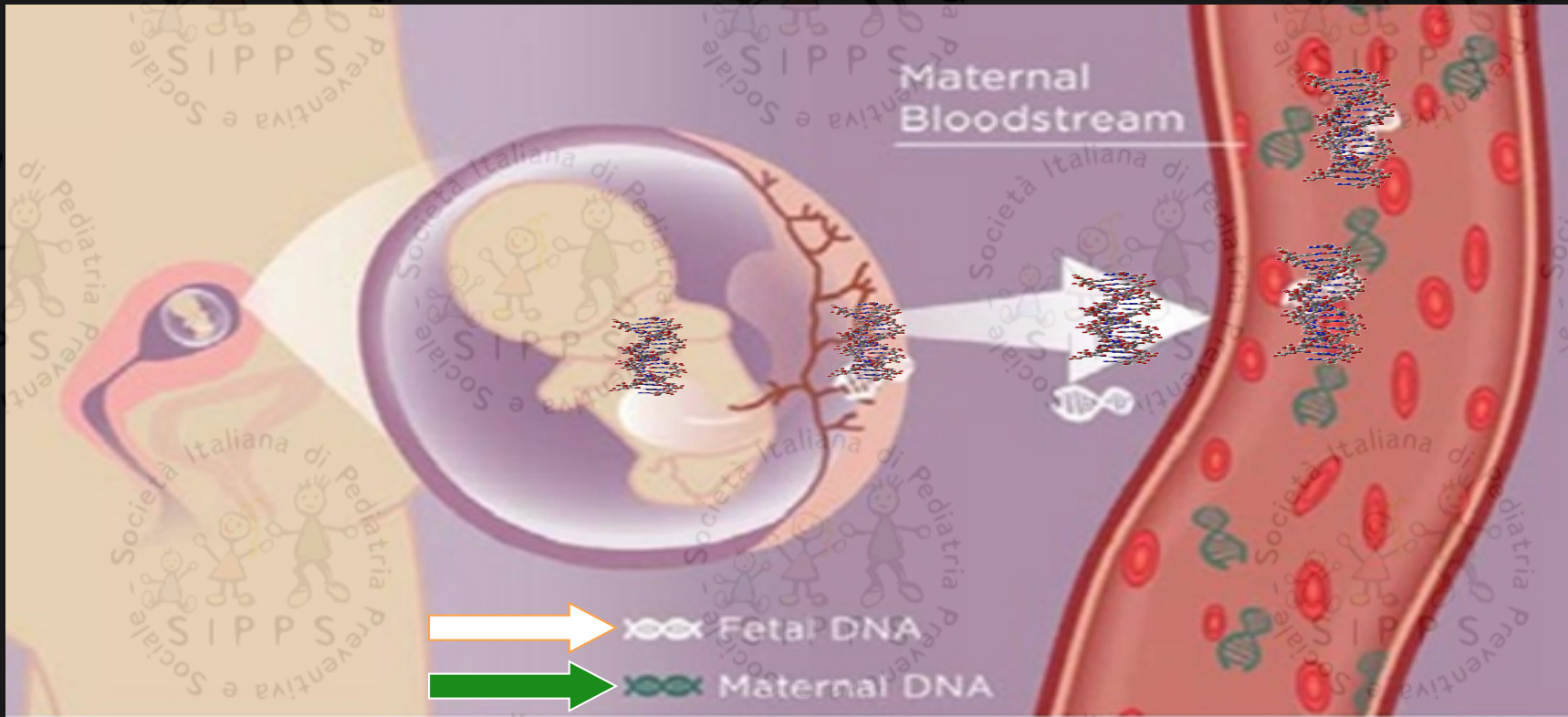
Am J Obstet Gynecol. 2009 May;200(5):528.e1

Mikhail MA et al.

High frequency of fetal cells within a primitive stem cell population in maternal blood.

Hum Reprod. 2008 Apr;23(4):928-33.





Breveglieri G et al.

Non-invasive Prenatal Testing Using Fetal DNA.

Mol Diagn Ther. 2019 Feb 2.

Stray J et al.

Isolation of Cell-Free DNA from Maternal Plasma.

Methods Mol Biol. 2019;1885:309-323.



Trends Mol Med. 2013 May;19(5):271-2.

Amniotic fluid stem cells and fetal cell microchimerism.

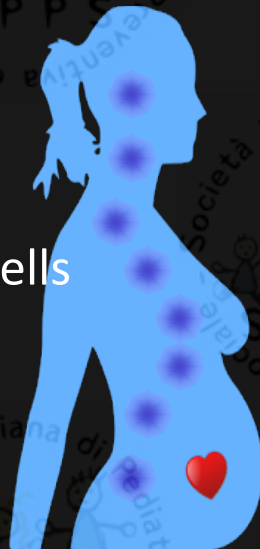
Rosner M et al.

-Medical Genetics, Medical University of Vienna, Austria.



During pregnancy, mobilized pluripotent fetal stem cells of yet unidentified in vivo significance float in the amniotic fluid

Circulating fetal cells



Fetal stem cells



We argue that circulating fetal cells and the pluripotent amniotic fluid cells might share a common origin.



Leiden University
Medical Center

Rijnink EC et al.

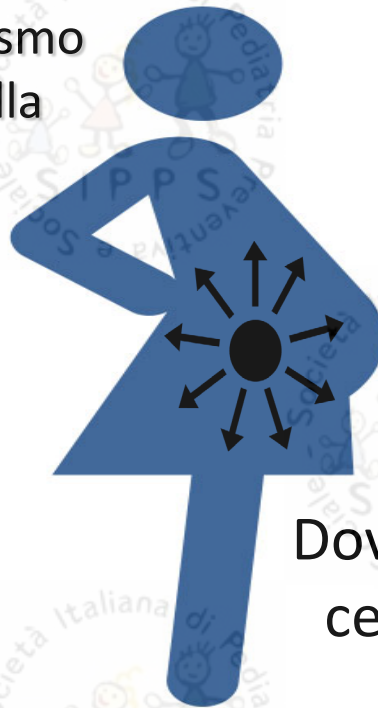
-Department of Pathology

-Department of Medical Statistics and Bio-Informatics

-Department of Obstetrics & Gynaecology

MiSTERO

Il Microchimerismo
è in relazione alla
gravidanza ?



Dove migrano le
cellule fetali ?

MiSTERO

26

donne decedute durante la gravidanza o entro 1 mese dalla nascita di un figlio.



Donne decedute

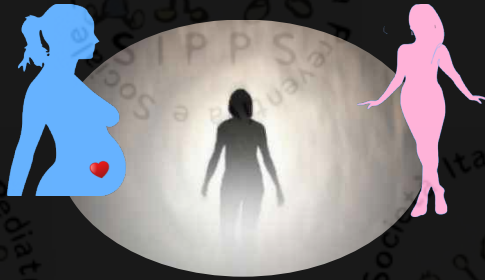
26

donne non gravide che avevano già avuto un figlio.



26

donne decedute durante la gravidanza o entro 1 mese dalla nascita di un figlio.



Donne decedute

26

donne non gravide che avevano già avuto un figlio



ibridazione in situ cromosoma

Y



Nuclei cromosomiali **positivi** per milione di nuclei segnati

Durante la gravidanza si realizza un aumento delle cellule chimeriche



ibridazione in situ cromosoma

Y





Mol Hum Reprod. 2015 Nov;21(11):857-64.

Tissue microchimerism is increased during pregnancy: a human autopsy study.

Rijnink EC et al.

Il Microchimerismo
è in relazione alla
gravidanza ?

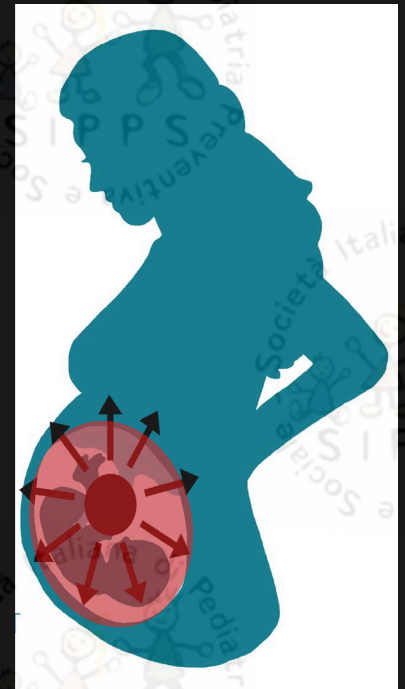


Dove migrano le
cellule fetali ?



Gammill HS et al.

*Department of Obstetrics Gynecology
Department of Pediatrics
Seattle Children's Hospital*



MISTERO

BAD

INFLUENCER



*Cosa può interferire con la
migrazione delle cellule fetali ?*

Placenta. 2017 Dec;60:130-133.

Microchimerism:

Defining and redefining the prepregnancy context: A review.

Gammill HS et al.

The amount, type, and persistence of
microchimerism are influenced by:

Obstetric characteristics

Pregnancy complications

Exposures to infection

and other factors...

Microchimerism



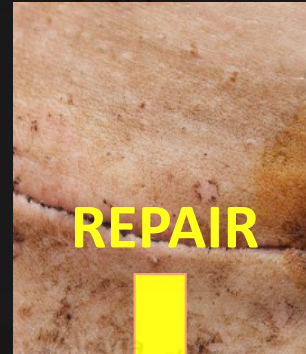


Chimeras. 2014;5(2):40-52.

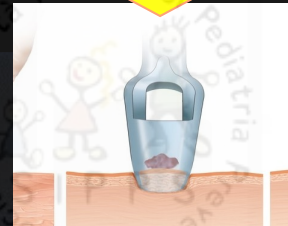
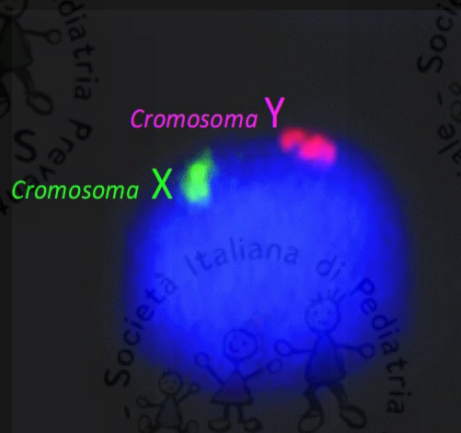
Microchimeric fetal cells play a role in maternal wound healing after pregnancy.

Mahmood U et al.

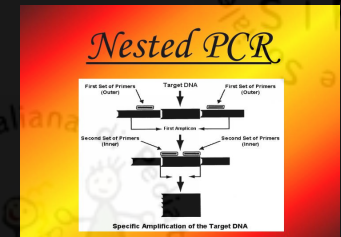
Anu Research Centre; Department of Obstetrics and Gynaecology; University College Cork; Cork University Maternity Hospital; Cork, Ireland.



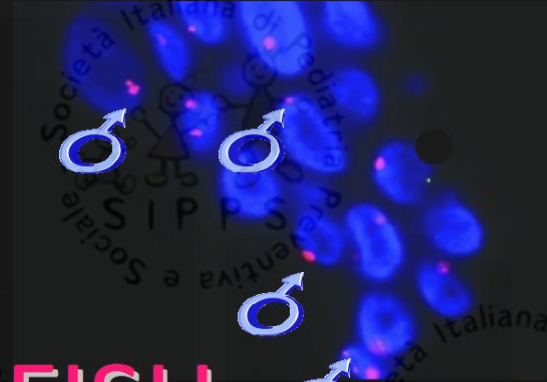
Cromosoma Y
Cromosoma X



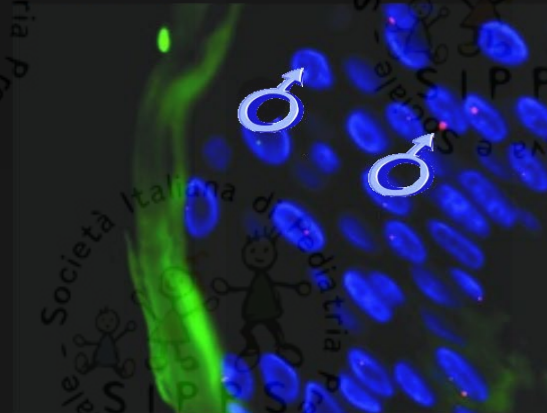
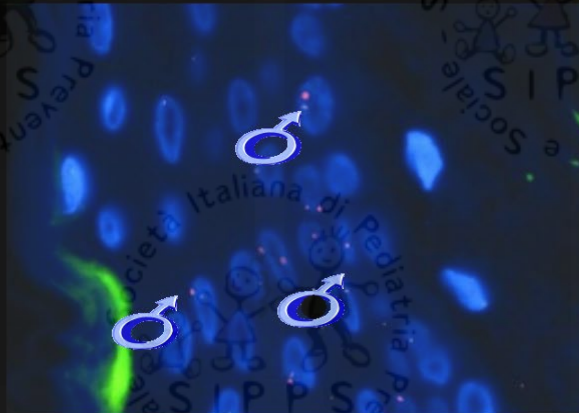
biopsie



Identificazione di cellule fetali “presunte maschili” in cicatrici CS materne guarite dopo la gravidanza



XY-FISH



fluorescence in situ hybridization

Presumibilmente in risposta a “segnali” prodotti da lesioni cutanee le cellule fetali migrano nell’area lesionata ed intervengono nella riparazione .



Saadai P et al.

*Division of Pediatric Surgery and The Fetal Treatment Center,
Department of Surgery, University of California, San Francisco, San Francisco,*

MISTERO

Pregnancy complications



Microchimerism?

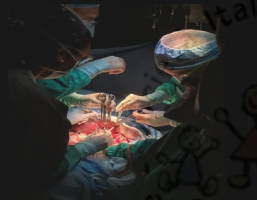
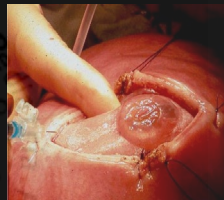
Maternal microchimerism levels were increased in patients who had open fetal surgery compared with controls



Open fetal surgery



Post natal repair



SPINA BIFIDA

Healthy controls



Patients who had fetal intervention at the time of delivery did not demonstrate increased microchimerism

Chimerism. 2012 Jul-Dec;3(3):1-3.

Increased maternal microchimerism after open fetal surgery.

Saadai P et al.

*Division of Pediatric Surgery and The Fetal Treatment Center,
Department of Surgery, University of California, San Francisco, San Francisco, CA, USA.*

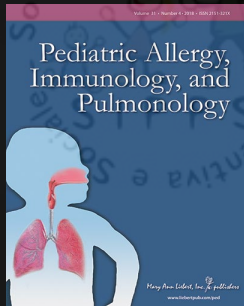


Microchimerism



MICROCHIMERISMO & Latte

Una relazione intrigante



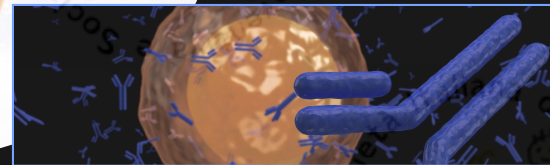
2018 Mar

Pediatr Allergy Immunol. 2018 Mar;29(2):133-143.

Breastmilk cell trafficking induces microchimerism-mediated immune system maturation in the infant.

Molès JP et al

- Pathogenesis and Control of Chronic Infections, INSERM, EFS, [Université de Montpellier](#), France.
- Department of Bacteriology-Virology and Department of Medical Information, [Montpellier](#), France.
- Department of Paediatrics and Child Health, School of Medicine, [University of Zambia](#).
- Institute for Medical Immunology, Université Libre de Bruxelles, [Belgium](#).
- Division of Infectious Diseases & International Health, Department of Medicine, University of Virginia, [USA](#).

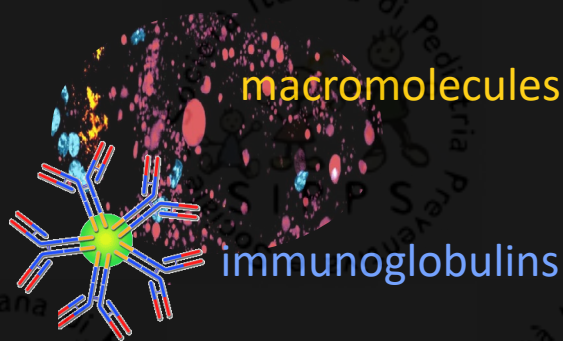


PERMEABILITA' INTESTINALE

First days

Post-partum

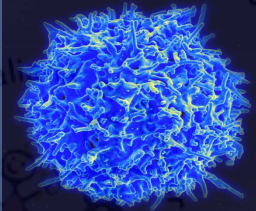
Neonatal period in response to local inflammation or introduction of a weaning food



Progenitor/stem cells **6%**

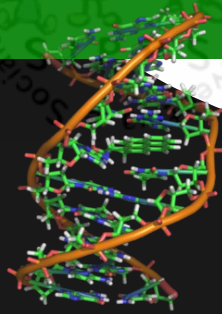


L'allattamento al seno genera cellule **T regolatorie (Treg)** che sopprimono l'immunità antimaterna.



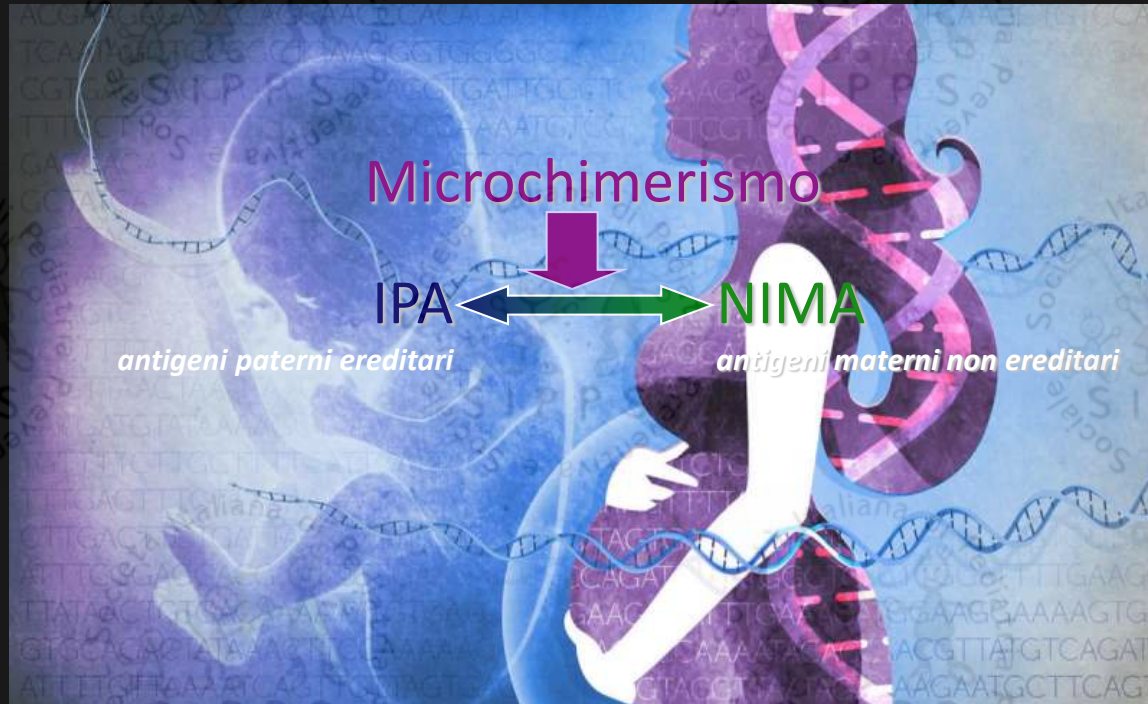
Il **microchimerismo delle cellule staminali** può indurre tolleranza agli **antigeni materni non ereditari (NIMA)**

Prodotti proteici derivati da geni polimorfici che le madri esprimono ma non la progenie.



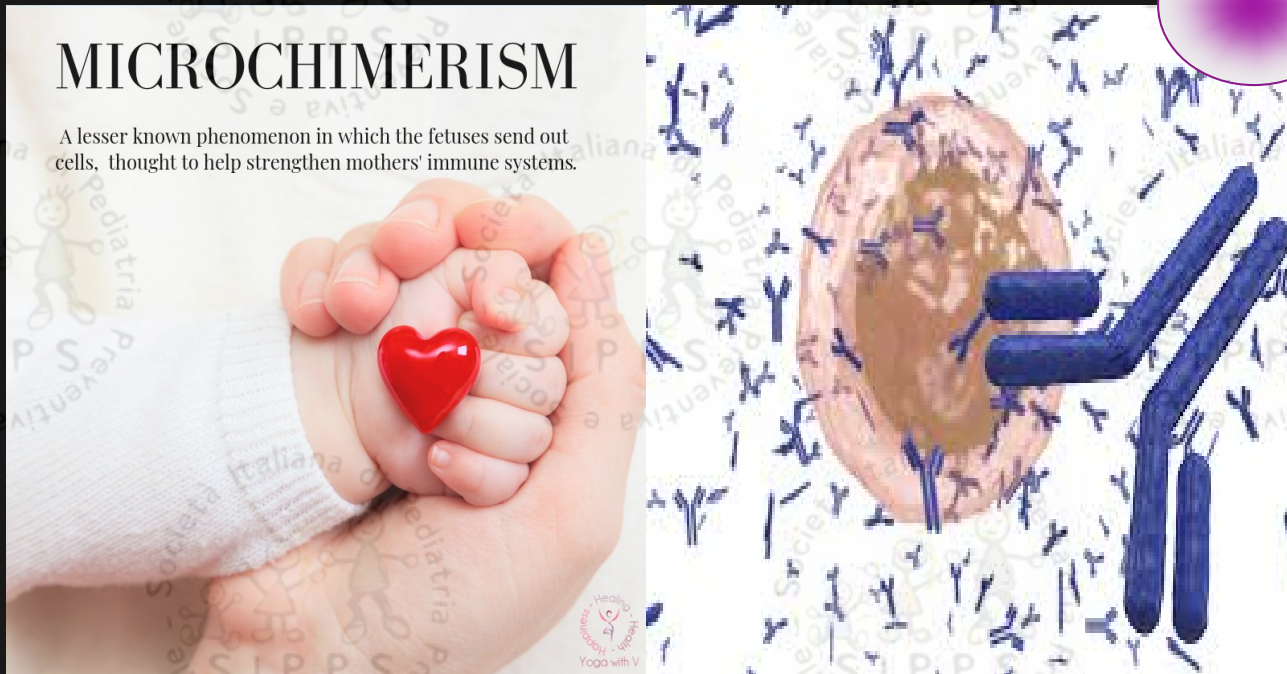
effetto **NIMA**

allotolleranza microchimerismo indotta



MICROCHIMERISM

A lesser known phenomenon in which the fetuses send out cells, thought to help strengthen mothers' immune systems.



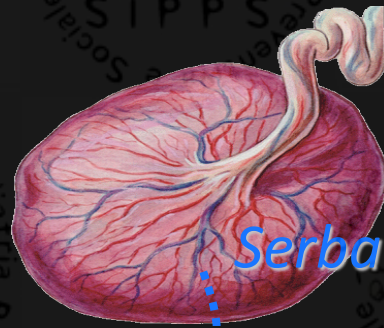


Esosomi





PLACENTA



PLACENTA

Serbatoio staminale

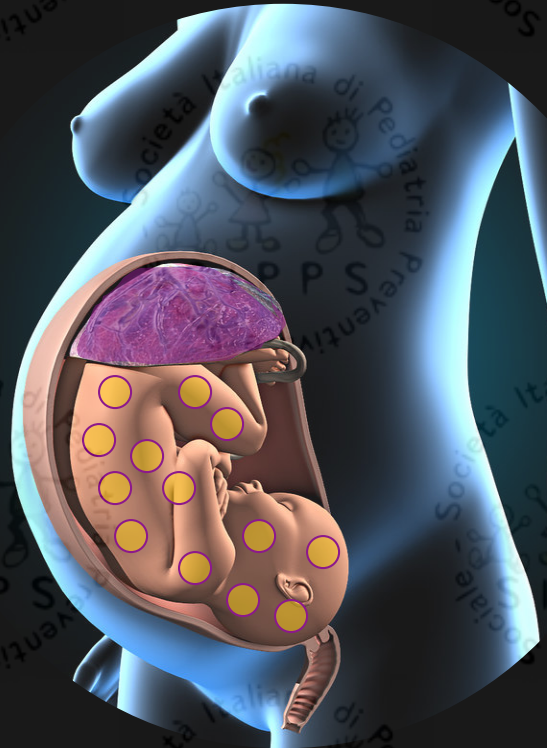


Prog Mol Biol Transl Sci. 2017;145:163-179.

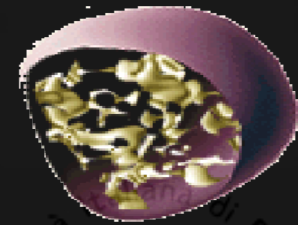
Role of **Exosomes** in Placental Homeostasis and Pregnancy Disorders.

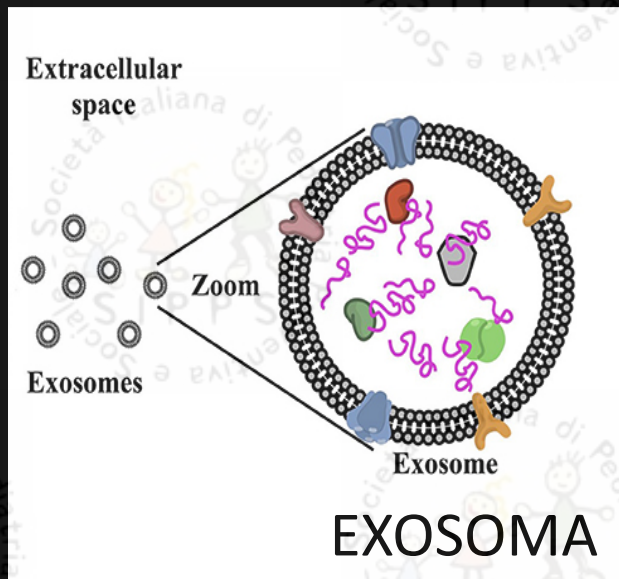
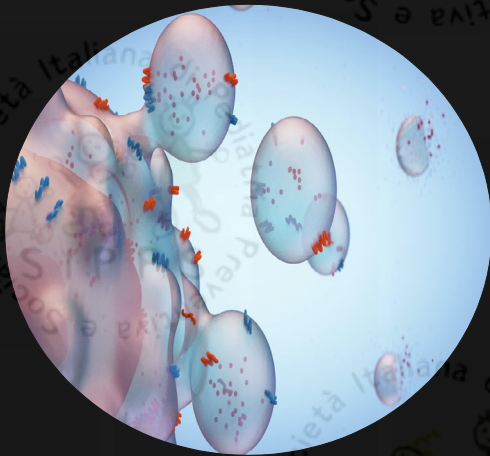
Salomon C

Le cellule placentari possono comunicare con i tessuti materni regolando la loro funzione



Attraverso il "sistema" delle **VESICOLE TRANSFER (EV)** extracellulari





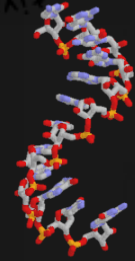
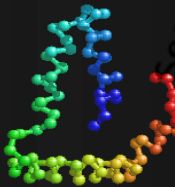
EXOSOMA



Proteine

Lipidi

miRNA



Markers
Epigenetici

Gli **EV** intervengono nella regolazione delle **risposte immunitarie** e regolano l'adattamento **materno-metabolico** alla gestazione

Sono dimostrabili nella circolazione materna dalla sesta settimana.



Liquid Biopsy

Aumentano nelle gravidanze complicate (*preeclampsia e nel diabete mellito gestazionale*)

Milk's Role as an Epigenetic Regulator in Health and Disease

Melnik BC

Il latte è il **principale modulatore epigenetico** dell'espressione genica un vero e proprio **"sistema dopante"** nello sviluppo dei mammiferi.



L'allattamento al seno attraverso il trasferimento di **miRNA** fornisce i segnali appropriati per un'adeguata *programmazione epigenetica* del neonato.



Boldo Melnik

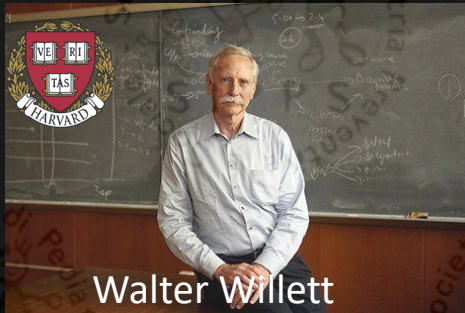
Department of Dermatology,
Environmental Medicine
and Health Theory,
*University of Osnabrück, Osnabrück,
Germany.*

Il consumo di latte promuove o aggrava
l' **acne vulgaris**

Alcuni esosomi del latte inducono
l'**obesità**, il **diabete di tipo 2**, il **cancro** e
numerose le malattie **neurodegenerative**

Il consumo di latte e prodotti lattiero-
caseari aumenta il rischio di **fratture ossee**
nelle persone di età avanzata

E' dimostrata una correlazione significativa
tra la dose di consumo di latte e il rischio di
mortalità



Walter Willett

Recent epidemiological research, especially of the Harvard group around Walter Willett provided strong evidence that dairy food and milk consumption increase the risk of bone (hip) fractures in people of higher age.

Feskanich D, Bischoff-Ferrari HA, Frazier AL, **Willett WC.**

Milk consumption during teenage years and risk of hip fractures in older adults.

JAMA Pediatr. 2014 Jan;168(1):54-60.

Feskanich D, Meyer HE, Fung TT, Bischoff-Ferrari HA, **Willett WC.**

Milk and other dairy foods and risk of hip fracture in men and women.

Osteoporos Int. 2018 Feb;29(2):385-396.

Fung TT, Meyer HE, **Willett WC, Feskanich D.**

Protein intake and risk of hip fractures in postmenopausal women and men age 50 and older.

Osteoporos Int. 2017 Apr;28(4):1401-1411.



Karl Michaelsson of the Karolinska Institute showed a significant correlation between the dose of milk consumption and mortality risk.

Michaelsson K ET AL..

Milk intake and risk of mortality and fractures in women and men: cohort studies.

BMJ. 2014 Oct 28;349:g6015.

1



Deficient miRNA transfer

Artificial formula feeding

Disturbed postnatal epigenetic programming

➤ **Increased risk for diseases of civilization**

2



Physiological miRNA transfer

Breastfeeding

Appropriate postnatal epigenetic programming

➤ **Reduced risk for diseases of civilization**

3



Persistent miRNA transfer

Cow milk consumption

Persistent epigenomic disturbances

➤ **Increased risk for diseases of civilization**



4



Persistent + increased miRNA transfer

Milk of dairy cows increased in lactation performance

Persistent + increased epigenomic disturbances

➤ **Exaggerated risk for diseases of civilization**



J Transl Med. 2019 Jan 3;17(1):3.

Exosomes of pasteurized milk: potential pathogens of Western diseases.

Melnik BC & Schmitz G.

Department of Dermatology,
Environmental Medicine and Health Theory,
University of Osnabrück, Osnabrück, Germany.

Institute for Clinical Chemistry and Laboratory Medicine,
University Hospital Regensburg, University of Regensburg,
PMID: 30602375

**Exosomes of pasteurized milk
may represent new pathogens
that should not reach the human food chain.**





ESOSOMI

La pastorizzazione del latte vaccino protegge le vitamine termolabili e altri composti organici

Non altera gli esosomi bioattivi/ biodisponibili e le vescicole extracellulari di 40-120 nm

Tuttavia, le prove epidemiologiche e traslazionali presentate in questa revisione indicano che

OBESITA'

Ca.PROSTATA



DIABETE

Ca.FEGATO

PARKINSON

l'assunzione prolungata di esosomi attraverso il latte pastorizzato può portare un rischio per malattie croniche

OSTEOPOROSI

Ca.SENO



Gli esosomi promuovono l'induzione di *FoxP3*, il principale fattore di trascrizione delle cellule T regolatorie (Tregs)

miR-148a
miR-21
miR-29b
miR-155

TGF- β

FoxP3

CD4

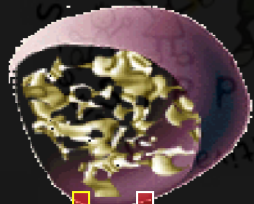
TREGs

TOLERANCE
induction

ALLERGY
prevention



Questo meccanismo previene lo sviluppo di allergie durante l'allattamento o il consumo di latte crudo durante la prima infanzia



Il *miR-21* e *miR-148a* sono promotori della adipogenesi

STAMINALE

miR-21



PPAR γ

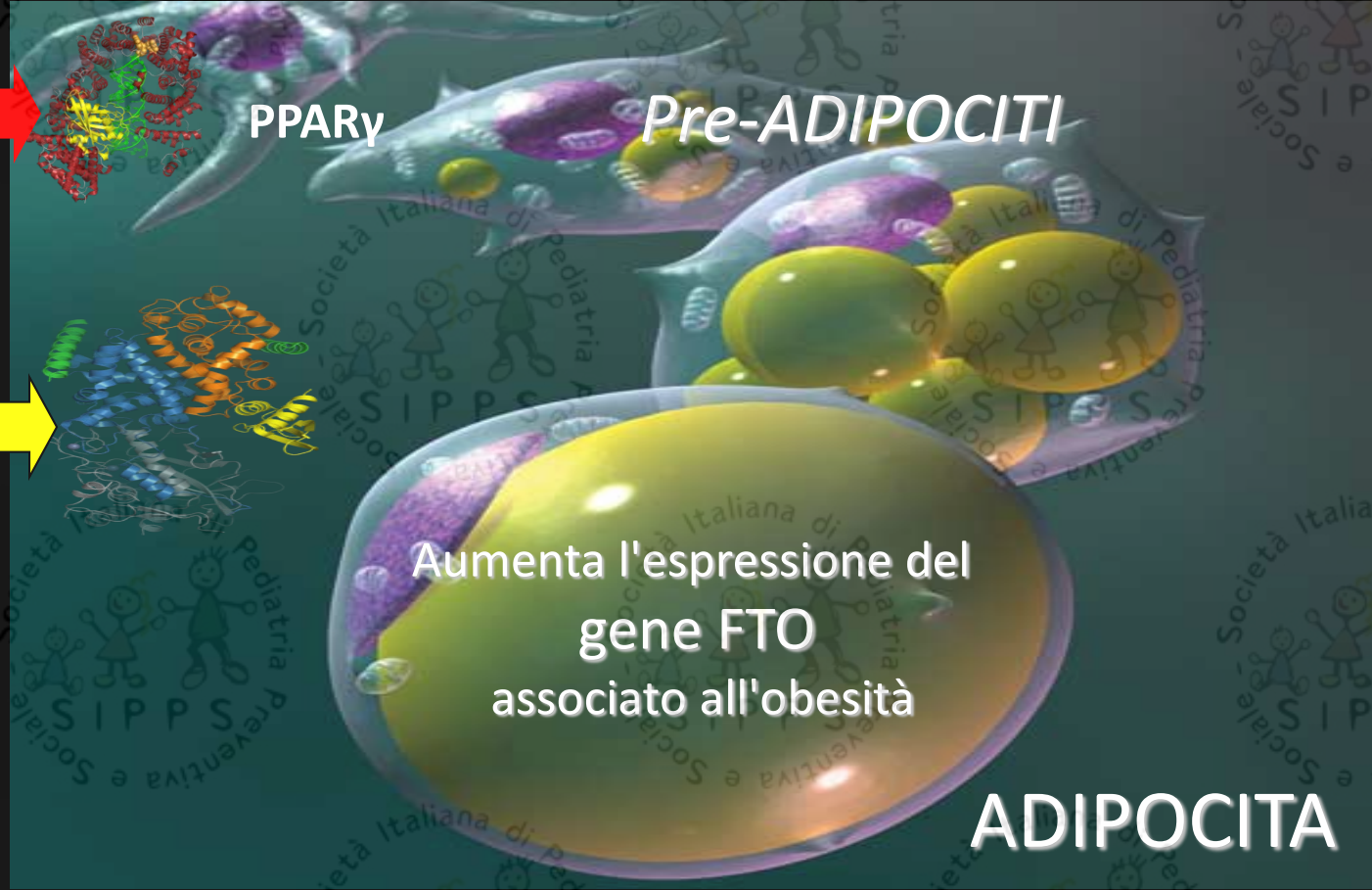
Pre-ADIPOCITI

miR-148a



Aumenta l'espressione del gene FTO associato all'obesità

ADIPOCITA



IOTALAMO

Feeding area CCKPZ receptor

IPERFAGIA

miR-148a

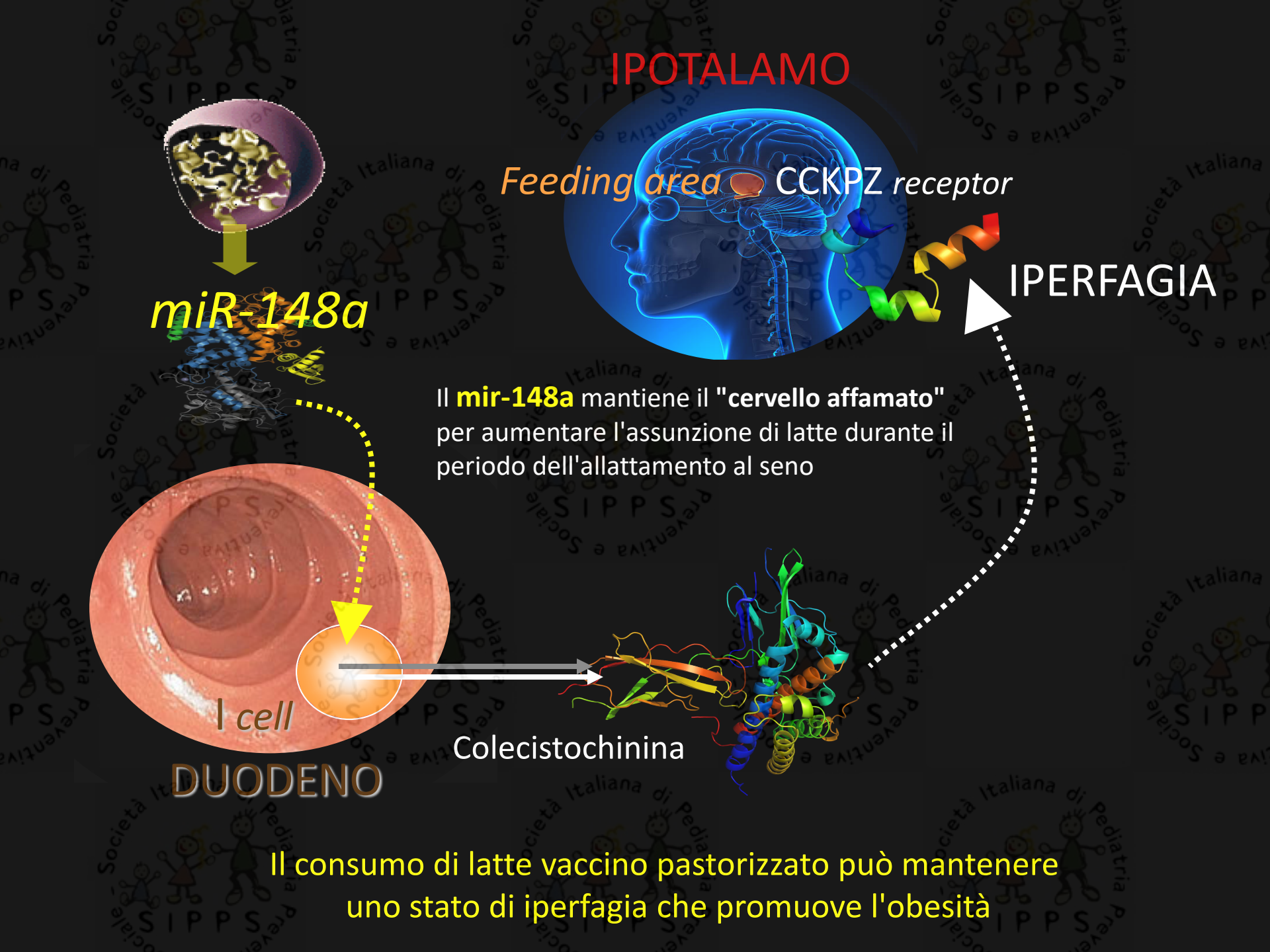
Il **mir-148a** mantiene il "cervello affamato"
per aumentare l'assunzione di latte durante il
periodo dell'allattamento al seno

I cell

Colecistochinina

DUODENO

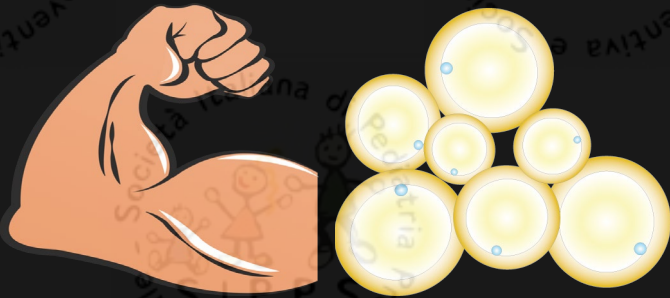
Il consumo di latte vaccino pastorizzato può mantenere
uno stato di iperfagia che promuove l'obesità



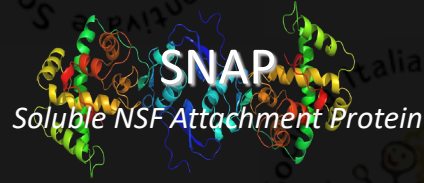
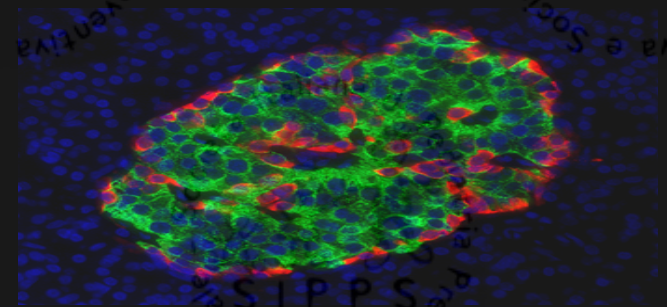


miR29b

Insulin responding peripheral cell



Insulin producing beta-cell



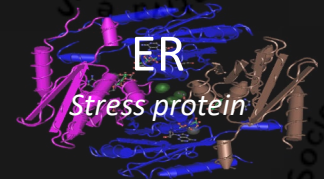
SNAP

Soluble NSF Attachment Protein

GLUT-1e4



Il **miR29b** promuove
l'insorgenza del
DIABETE tipo 2



ER

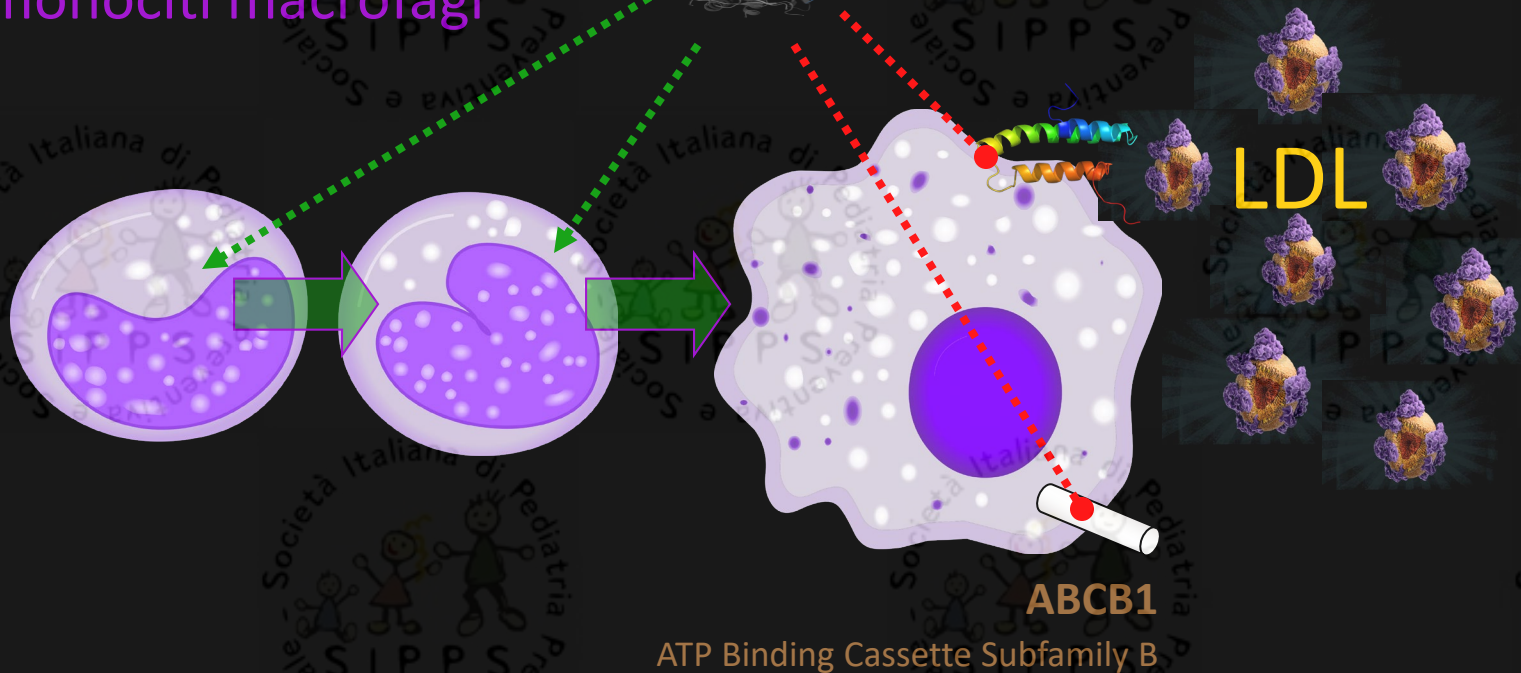
Stress protein



Apoptosi

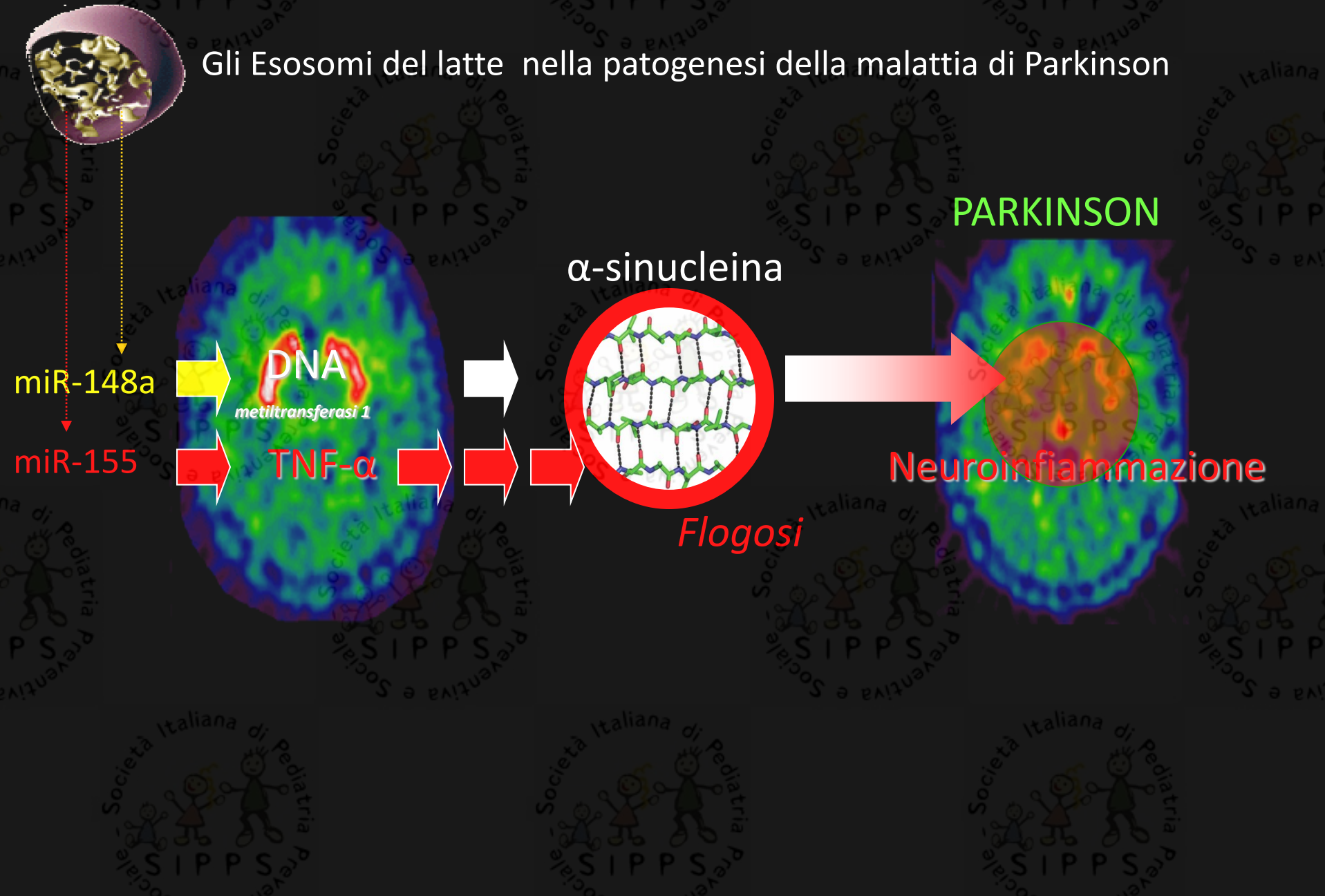
miR-148a stimola la
differenziazione
“monociti macrofagi”

miR-148

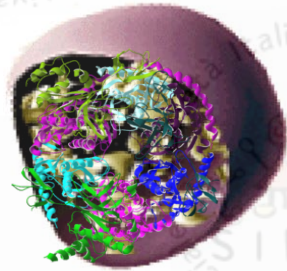


La soppressione mediata da **miR-148a** del **ABCA1**
attenua il trasporto inverso di colesterolo e quindi
promuove l'accumulo di lipidi nei macrofagi.

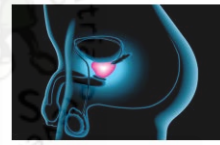
Gli Esosomi del latte nella patogenesi della malattia di Parkinson



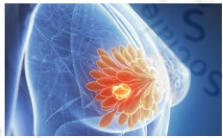
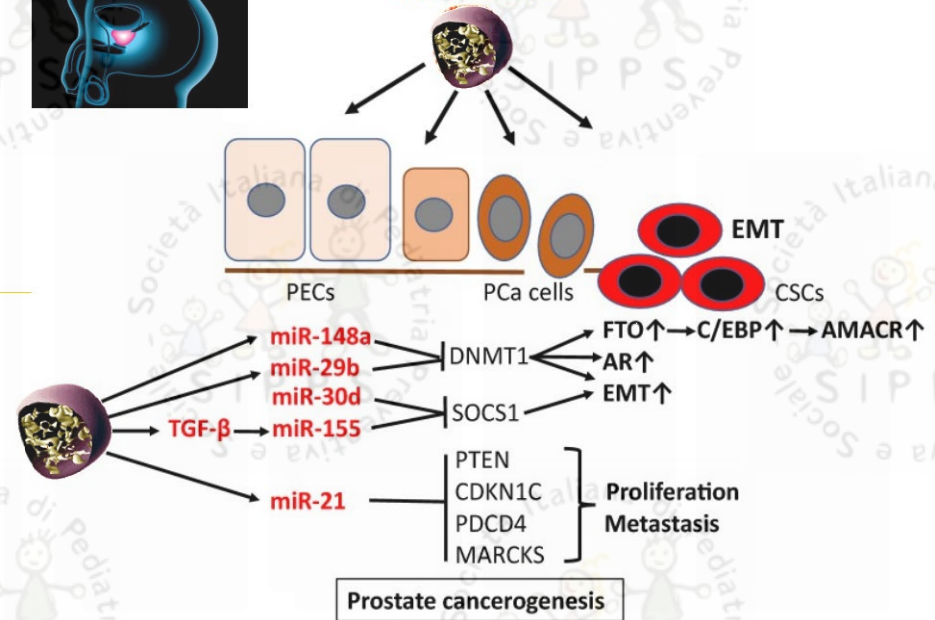
MILK EXOSOMES



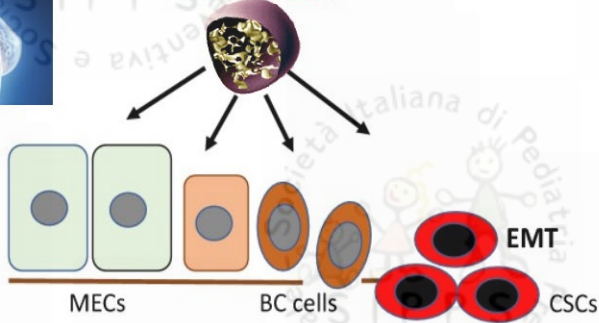
miR



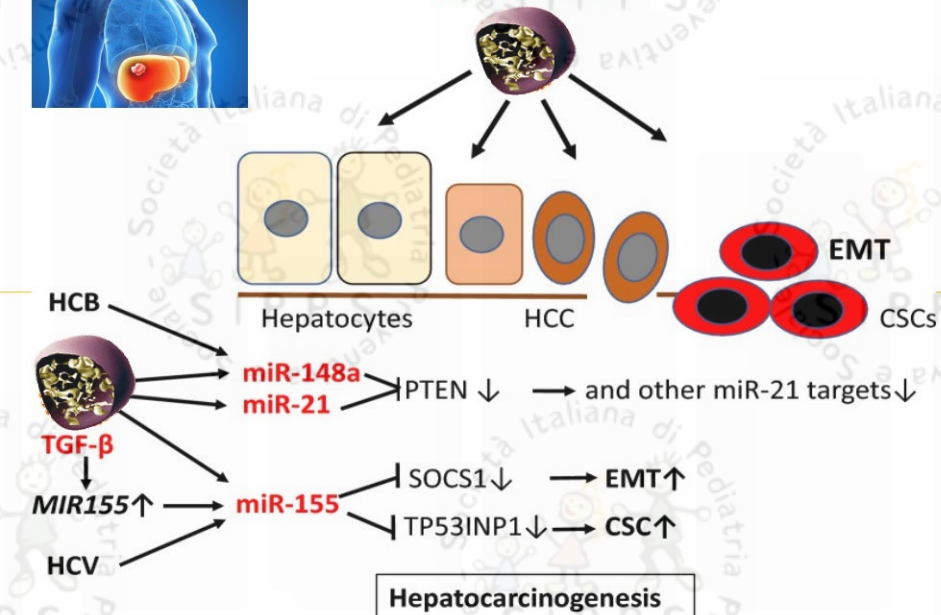
Milk exosomes



Milk exosomes



Milk exosomes





EXOSOMES *free*

Dal *Microchimerismo* al:

MICROCHIOMA

Nat Rev Immunol. 2017 Aug;17(8):483-494.

Immunological implications of pregnancy-induced microchimerism.

Kinder JM et al.

- Division of Infectious Disease, Cincinnati Children's Hospital & Perinatal Institute. USA.

-Laboratory for Experimental Feto-Maternal Medicine,

- Department of Obstetrics and Prenatal Medicine, University Medical Center Hamburg-Eppendorf, Germany.

Le **cellule microchimiche** esprimono tratti antigenici non ereditari e familiari rilevanti non sono "**ricordi**" **casuali** della gravidanza



sono **intenzionalmente mantenute** nelle madri e nella loro prole per promuovere l'idoneità genetica migliorando l'esito delle future gravidanze

grazie ad un **MICROCHIOMA** biologicamente attivo formato da cellule geneticamente estranee.

Protezione

Ca. Mammario
Neoplasie epiteliali

Tumori



Autoimmuni

Tiroidite di Hashimoto
Malattia di Graves



Aggravamento

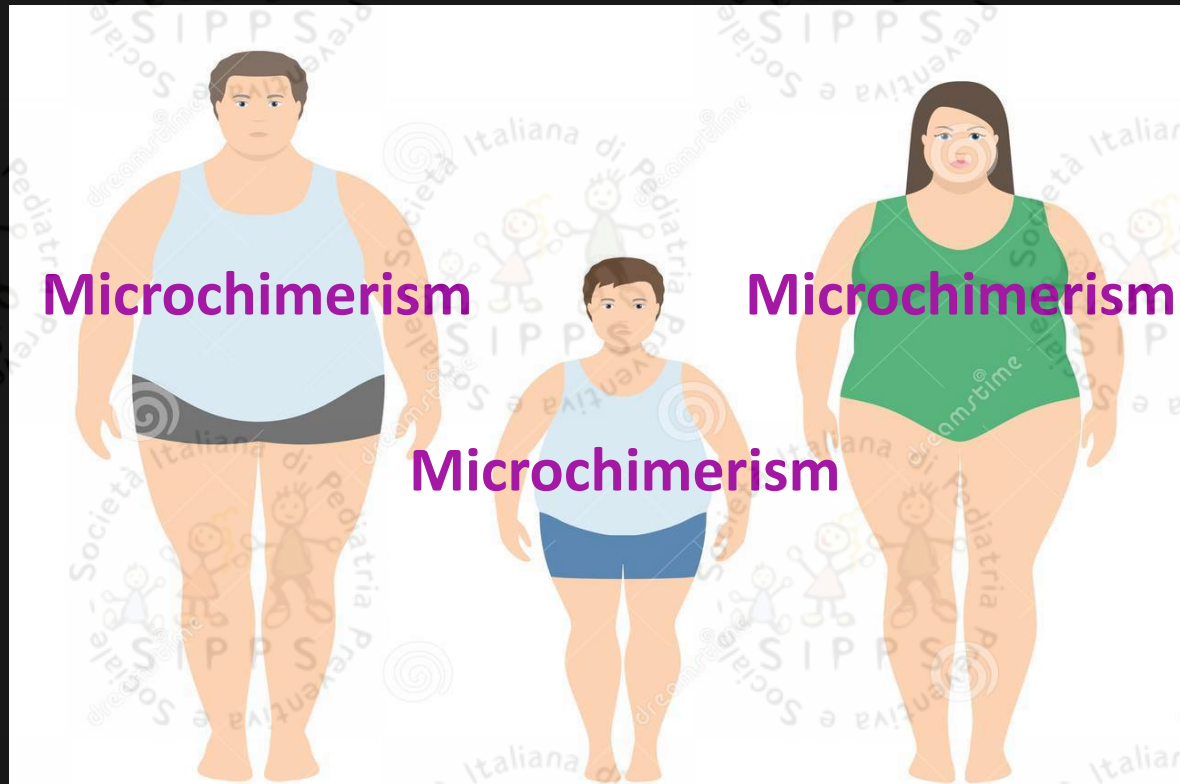




Med Hypotheses. 2012 Apr;78(4):528-32.

A role for microchimerism in **obesity** and evolution?

Schnitzler M



Bioessays. 2015 Oct;37(10):1106-18.

Fetal microchimerism and maternal health: a review and evolutionary analysis of cooperation and conflict beyond the womb.

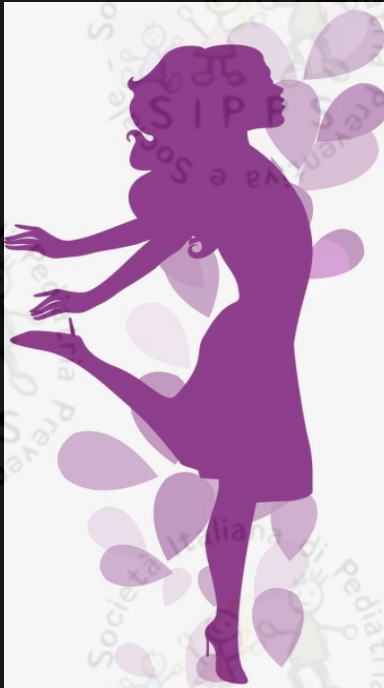
Boddy AM et al.

-Department of Psychology, Arizona State University, Tempe, AZ, USA.

-Center for Evolution and Cancer, University of California San Francisco, San Francisco, CA, USA.

-Center for Evolution and Medicine, The Biodesign Institute, Arizona State University, USA.

-School of Life Sciences, Arizona State University, Tempe, AZ, USA.



Salute emotiva e materna

Migliorano la produzione di latte

Funzione tiroidea

Malattia autoimmune

Guarigione delle ferite

Prevenzione neoplasie

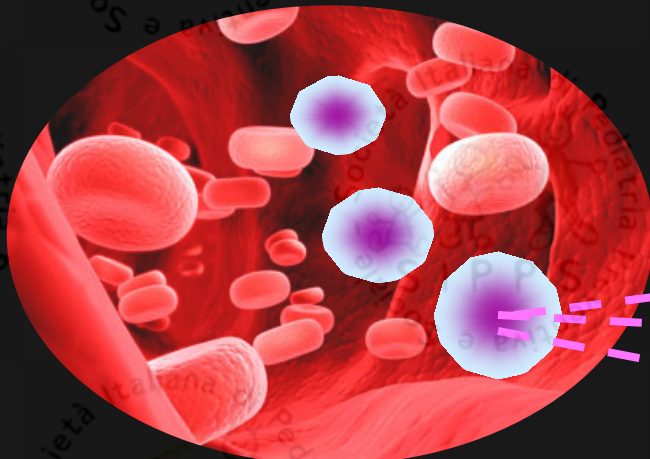
J Clin Endocrinol Metab. 2012 May;97(5):1452-61.

Microchimerism and endocrine disorders.

Fugazzola L et al.

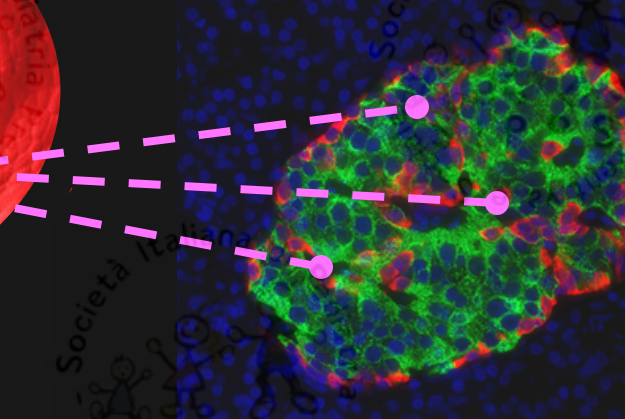
Department of Medical Sciences, University of Milan,
Istituto di Ricovero e Cura a Carattere Scientifico Ca' Granda, Milan, Italy.

Diabete di tipo 1



le cellule microchimeriche circolanti sono statisticamente superiori rispetto ai controlli.

Insula di Langherans



Le β -cellule femminili sono state ipotizzate come bersagli di autoimmunità



Gynecol Obstet Fertil. 2011 Apr;39(4):224-31.

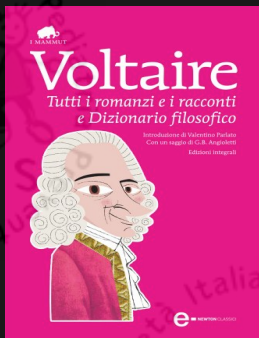
Is fetal microchimerism beneficial for the fetus or the mother

Boyon C

Eur J Obstet Gynecol Reprod Biol. 2011 Oct;158(2):148-52.

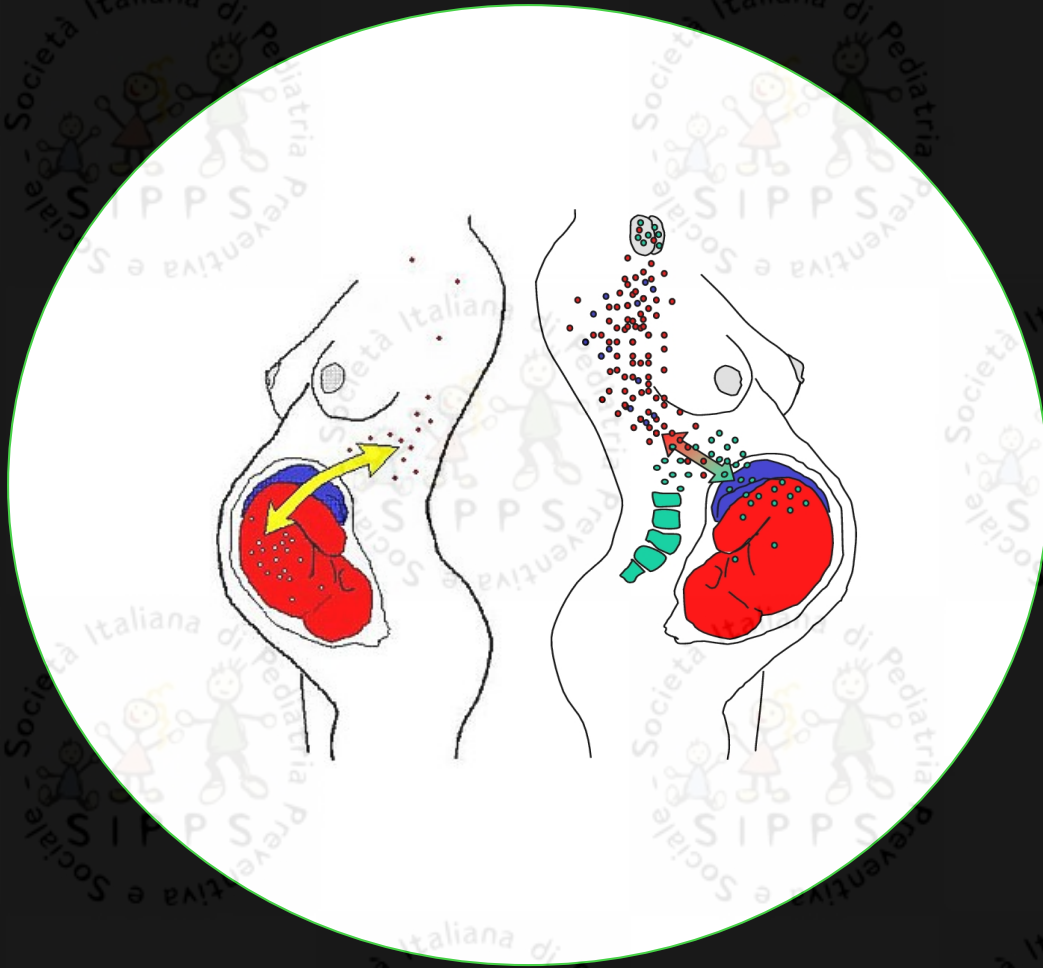
Fetal microchimerism: benevolence or malevolence for the mother?

Boyon C(1)



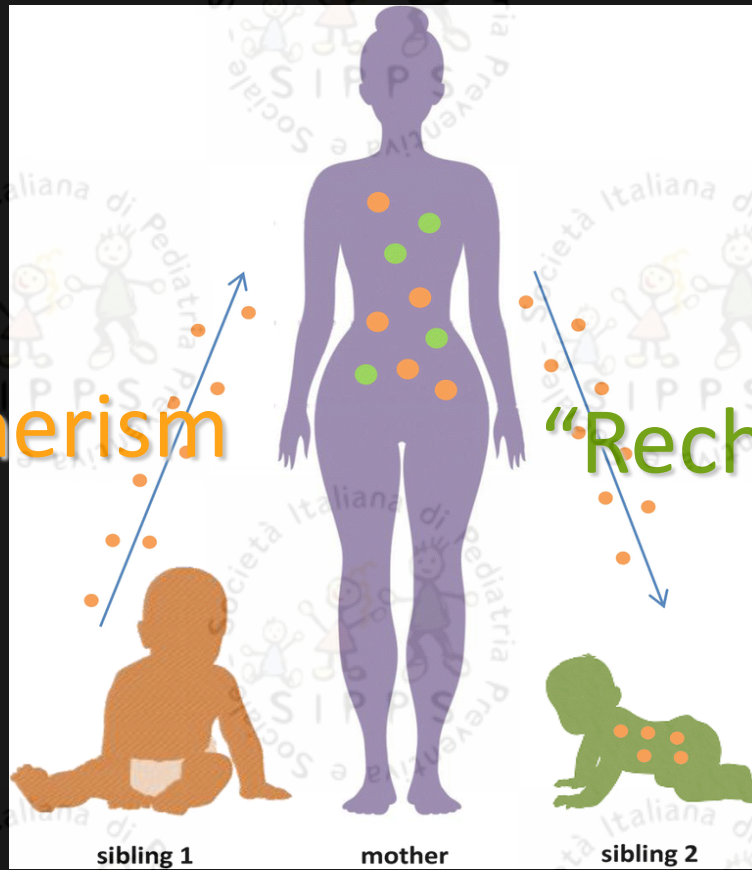
Candide

Il dubbio non è piacevole, ma la certezza è ridicola



Chimerism

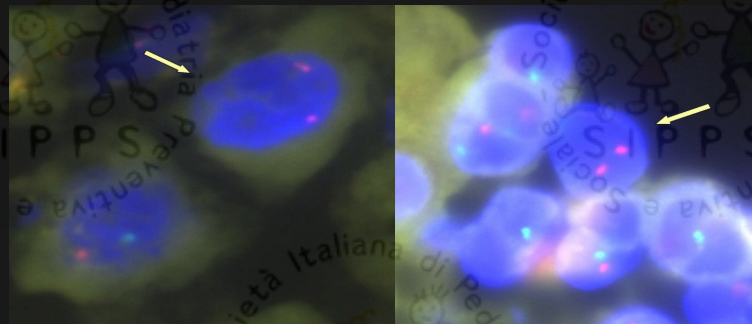
“Rechimerism”



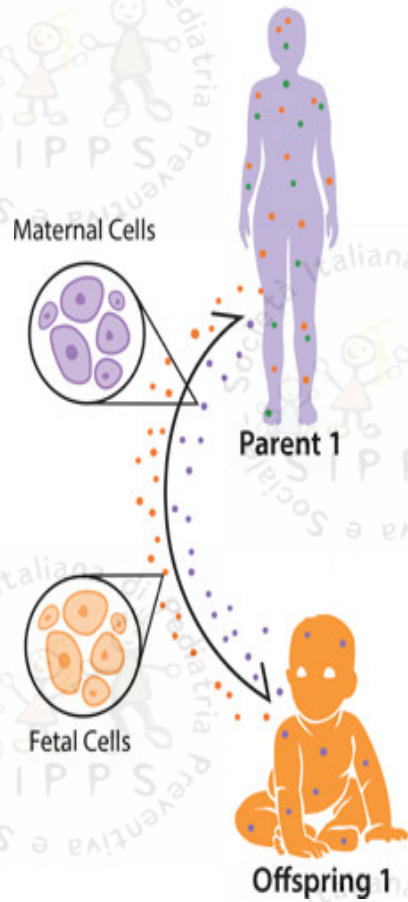
sibling 1

mother

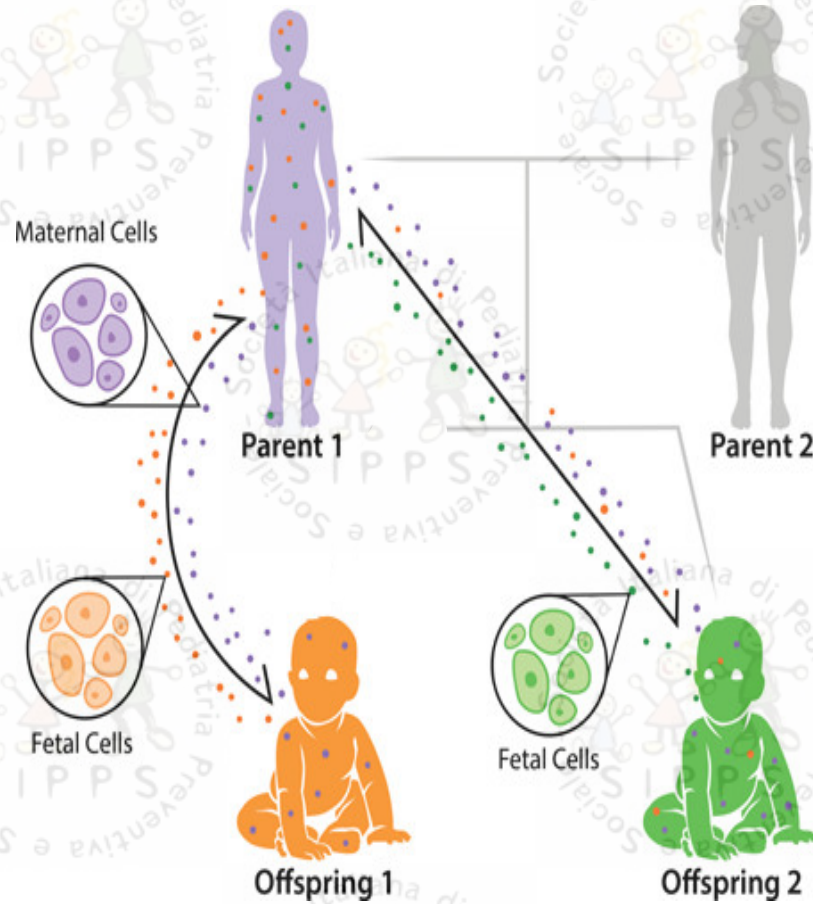
sibling 2

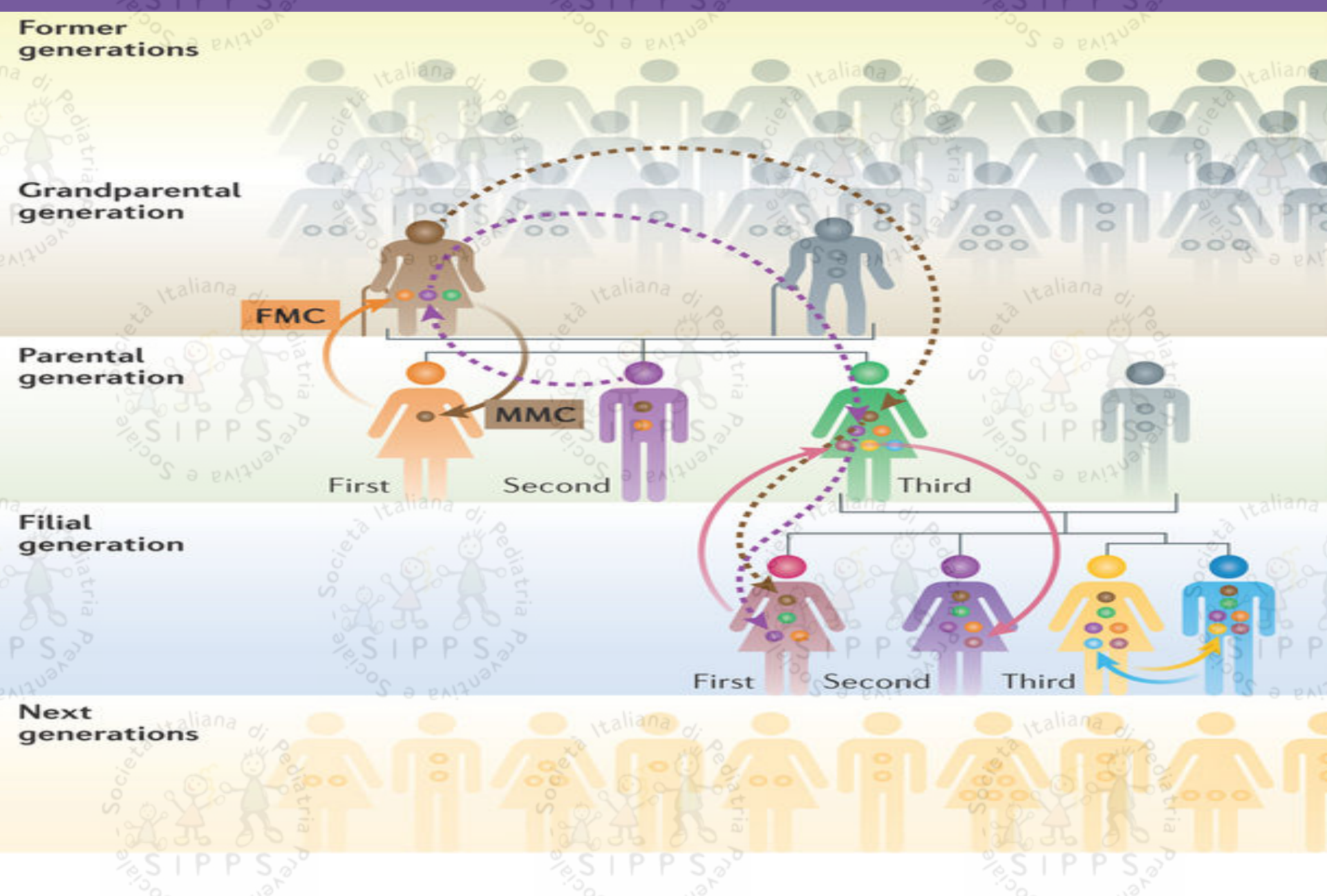


MICROCHIMERISMO



MICROCHIMERISMO





Cellule che viaggiano nel tempo...



PLoS One. 2011;6(8):e24101.

Pregnancy, microchimerism, and the maternal grandmother.

Gammill HS et al.

Division of Clinical Research, Fred Hutchinson Cancer Research Center
Seattle, Washington, United States of America.

Trasferimento genico



Transgenerazionale



Followed
longitudinally

HLA-genotyped



DRB1
DQA1
DQB1



DRB1
DQA1
DQB1



DRB1
DQA1
DQB1

PCR real time





HLA-genotyped



DRB1
DQA1
DQB1



DRB1
DQA1
DQB1

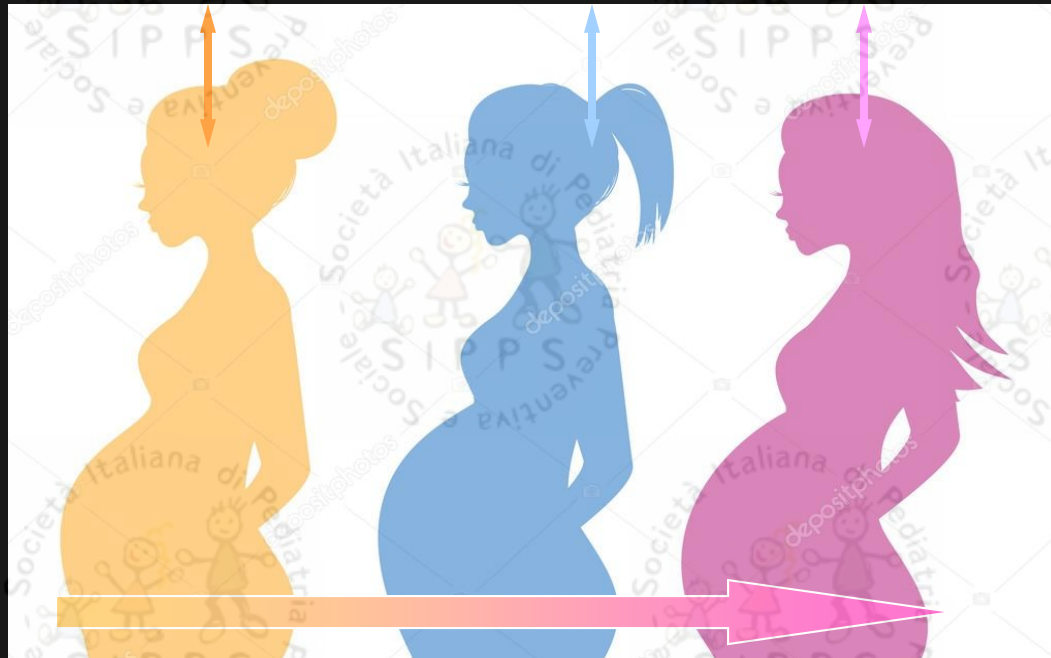


DRB1
DQA1
DQB1

PCR real time



Followed
longitudinally



Il trasferimento del **microchioma delle nonne** è rilevabile durante una gravidanza “normale” e diminuisce in preeclampsia e rappresenta un marker di un sano adattamento materno alla gravidanza.

Chimerism. 2013 Jan-Mar;4(1):18-9.

We are all born as microchimera.

Dierselhuis M et al.

*Department of Pediatrics, Leiden University Medical Center
The Netherlands.*

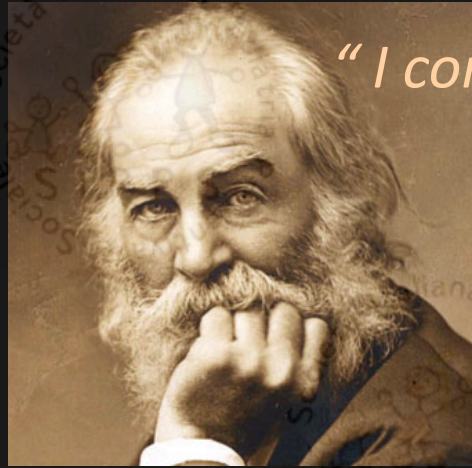
Nobody is born naïve: we are all microchimera's.



Il passaggio tran-materno delle cellule dai fratelli maggiori è una possibile fonte di

Microchimerismo non fetale

nelle donne nullipare



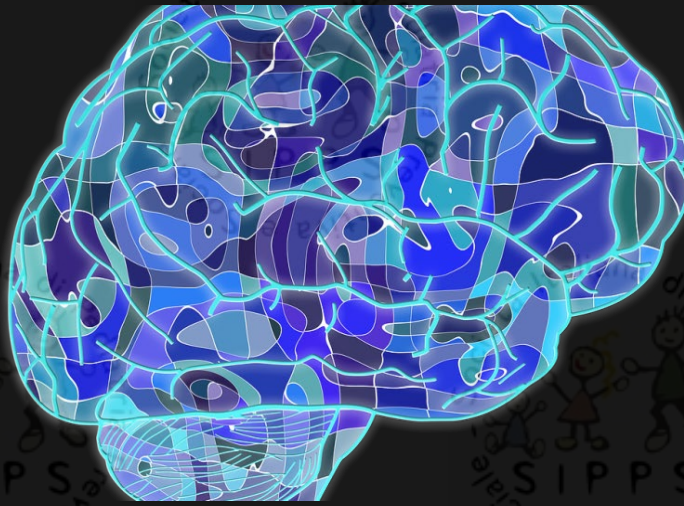
“I contain multitudes...”

Walt Whitman

Song of Myself



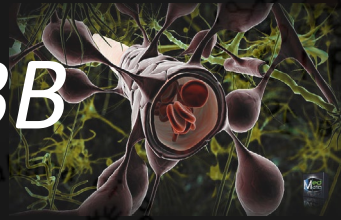
Déjà vu





*Transport across
Blood Brain Barrier*

Transport across BBB



Dawe GS et al

Cell migration from baby to mother.

Cell Adh Migr. 2007 Jan-Mar;1(1):19-27..

Tanaka A et al.

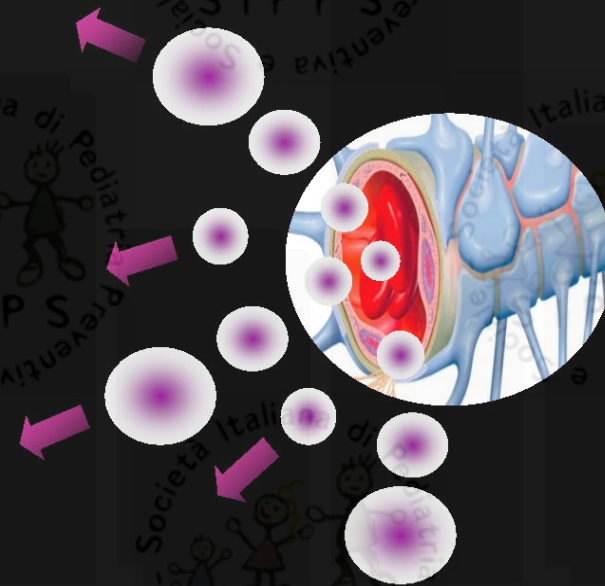
Fetal microchimerisms in the mother:
immunologic implications.

Liver Transpl. 2000 Mar;6(2):138-43.

Boyon C et al.

Is fetal microchimerism beneficial for the
fetus or the mother

Gynecol Obstet Fertil. 2011 Apr;39(4):224-31..

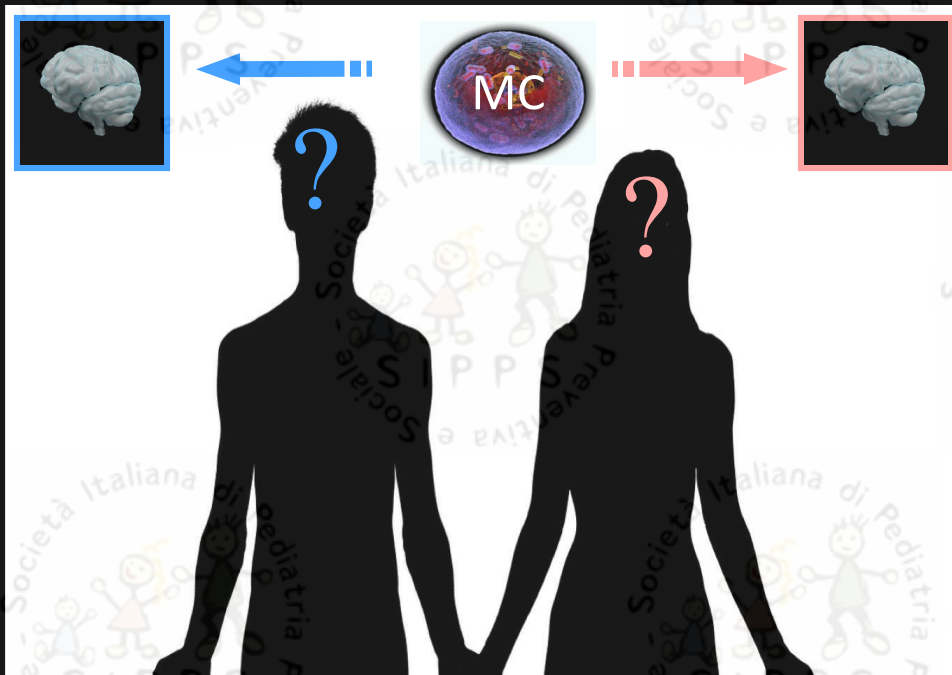


Chimerism. 2013 Jan-Mar;4(1):32-3.

Microchimerism in the human brain: more questions than answers.

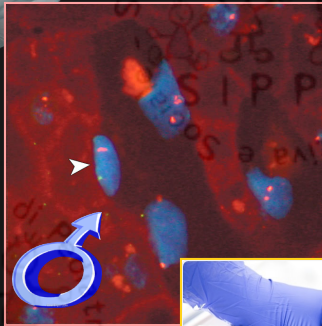
Chan Wfet al.

Department of Biochemistry, University of Alberta, Edmonton, AB Canada.





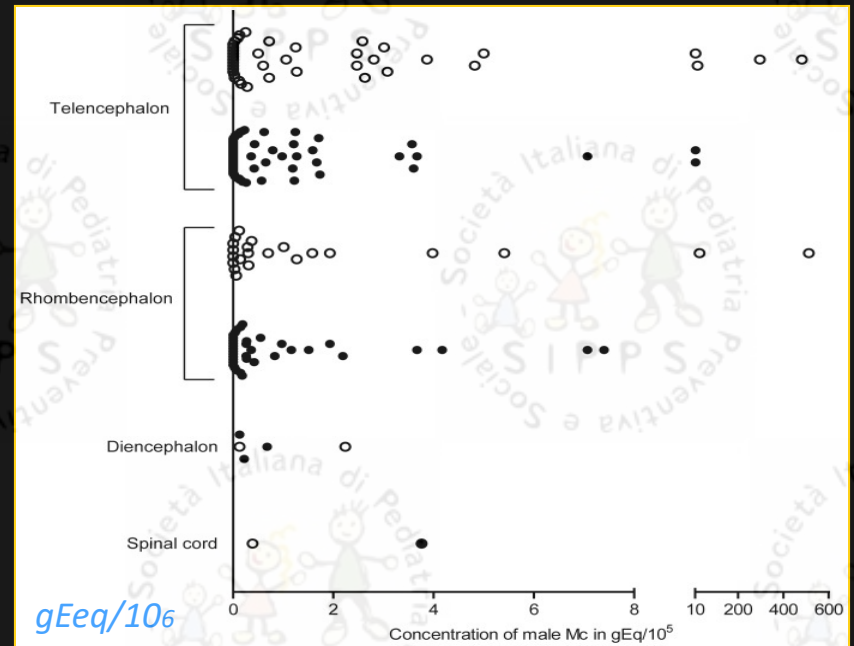
male MC



PCR quantitativa
in tempo reale

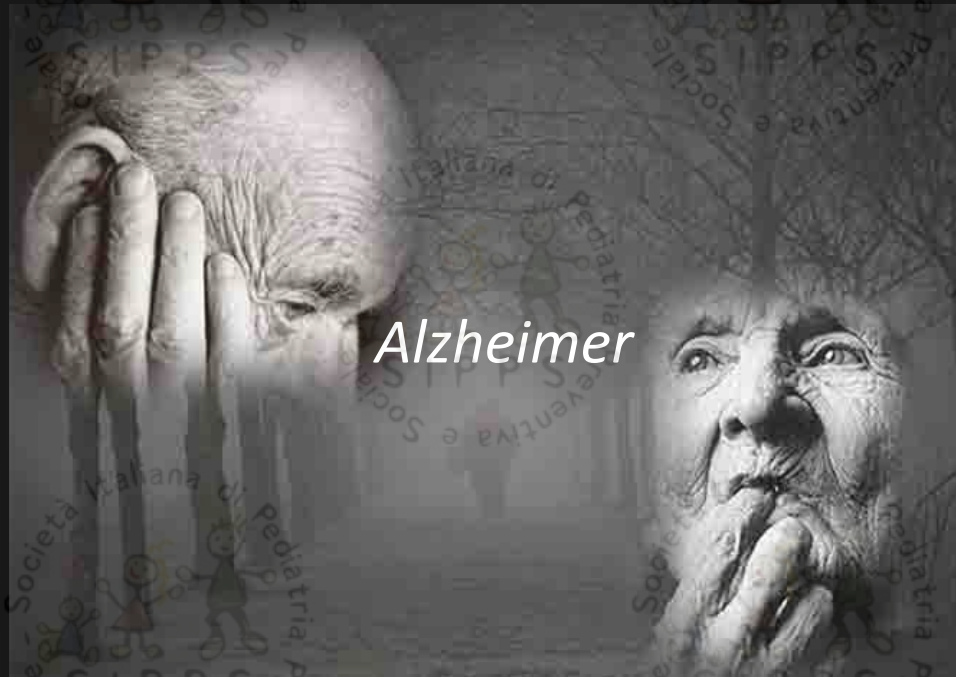


Concentration of male MC



Le cellule "MC maschili" sono presenti prevalentemente nelle donne (67%)

Sono o statisticamente inferiori nelle donne affette da Alzheimer



Alzheimer

Se non riesci a ricordare dove hai messo le chiavi, non pensare subito all'Alzheimer. Inizia invece a preoccuparti se non riesci a ricordare a cosa servono le chiavi.”

Rita Levi Montalcini



Una cosa buona dell'Alzheimer...
incontri ogni giorno gente nuova.

Woody Allen

Il cervello delle donne

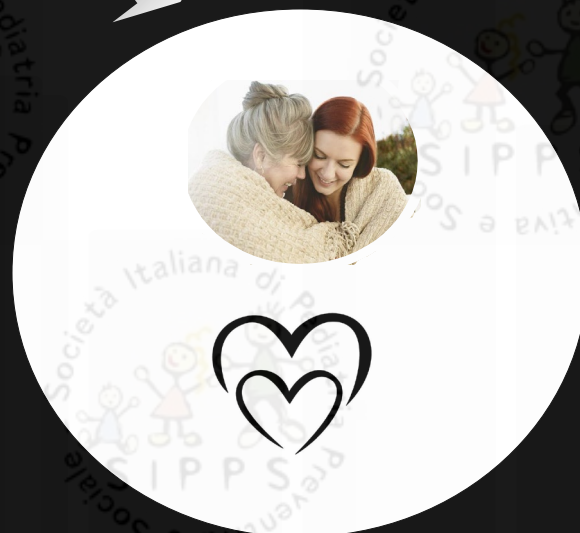




Segreti
trans-generazionali



Contrasti
adolescenziali



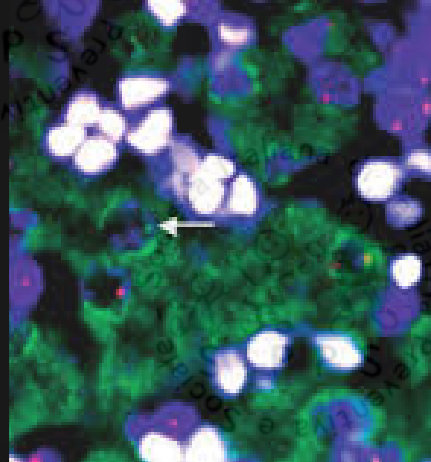
Condivisione
istintiva

Microchimerism

What did they leave behind in your body?



MISTERO



I giocattoli più semplici
quelli che anche il bambino più piccolo
riesce ad usare
vengono chiamati nonni.

I nonni sono coloro che
vengono da lontano
e vanno via per primi
ad indagare oltre la vita...

MiSTERO

Vi ringraziamo per l'attenzione



che avete dedicato a nostro nonno
Giulia e Jozio

MISTERO

To be continued...