Attività fisica e aging

Antonio Paoli

Director - Nutrition and Exercise Laboratory

nutex

Department of Biomedical Sciences
University of Padova Italy

Lo sport fa bene...

The Complete Book of Running
by James F. Fixx

Running or jogging has become not just a habit but an indispensable way of life to millions of Americans, and their numbers are increasing at a startling rate. In every state of the union, and at any hour of the day or night, men, women and children are running. This is no fad; it is a phenomenon that is not going to disappear for its benefits and rewards are so immediate and so striking that almost anyone who tries it for a week is apt to be smitten for life.

But though running's popularity is easy to confirm, what is less obvious-and only partially understood-is that its psychological benefits are at least as important as its physical ones. The Complete Book of Running is virtually an encyclopedia that covers every aspect of running.

ISBN 4-87187-317-X
978-4-87187-317-8

When he started running several years ago, Jim Fixx weighed nearly 220 pounds and breathed hard just thinking about exercise. Today, at 180 pounds, he has been declared medically fitter than most college athletes, has competed in—and finished—six Boston Marathons, has won the Connecticut 10,000-meter championship in his age category and has run the equivalent of once around the equator.

It includes chapters on

What Happens to your Mind
The Longevity Factor
Getting Thin
Running for Women
Running Wen you're Over Forty
Running for Kids
Gear

ISHI PRESS INTERNATIONAL

History and Philosophy

Research Quarterly for Exercise and Sport
©2002 by the American Alliance for Health, Physical Education, Recreation and Dance
Vol. 73, No. 1, pp. 38–46

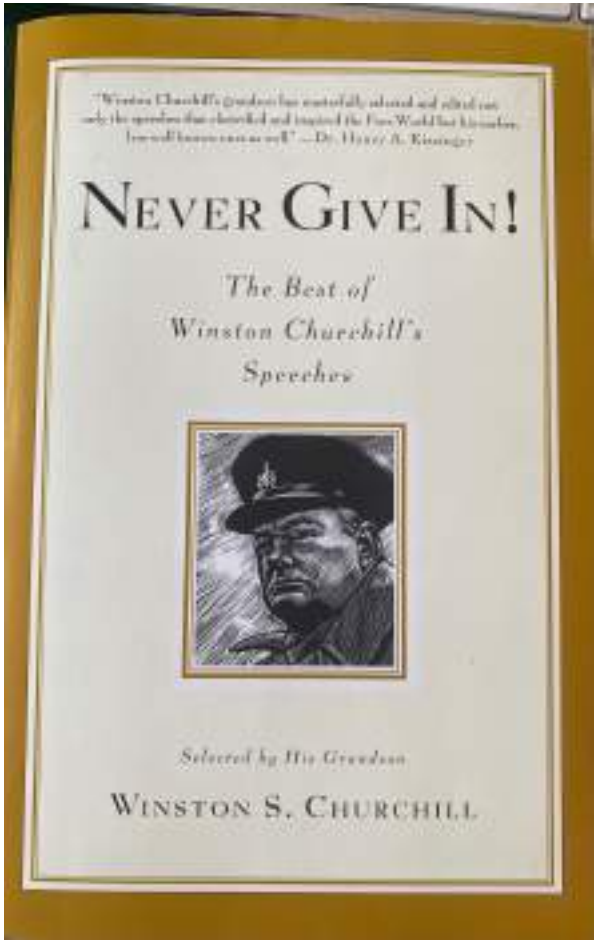
James F. Fixx (1932-1984)

Running, Heart Disease, and the Ironic Death of Jim Fixx

Darcy C. Plymire

Jim Fixx was one of millions of Americans who started running in the 1960s, 1970s, and 1980s. Unlike other runners, however, Fixx wrote a best-selling book about running and, ironically, died of a heart attack at the age of 52 years while running. Fixx and the authors of other running books believed heart disease resulted from overcivilization and recommended running as a cure. Running was not merely a physical exercise, according to those authors, but also a way of life. Moreover, these running authors, who were often doctors themselves, advised their readers to listen to their bodies, instead of their doctors. Fixx's adherence to that philosophy offers an explanation for his seemingly irrational behavior—running through chest pain and discomfort.

Bere, fumare ed essere sedentari fa male



Winston Churchill (1874-1965)

Quanto
vorreste vivere?

ג וַיֹּאמֶר יְהוָה, לֹא-יָדוֹן רוּחִי בָאָדָם לְעֹלָם, בְּשַׁגַּם, הוּא בָשָׂר; וְהָיוּ יָמָיו, מֵאָה וְעֶשְׂרִים שָׁנָה.

3 And the LORD said: 'My spirit shall not abide in man for ever, for that he also is flesh; therefore shall his days be a hundred and twenty years.'

ז וּמֹשֶׁה, בֶּן-מֵאָה וְעֶשְׂרִים שָׁנָה--בְּמֹתוֹ; לֹא-כָהֲתָה עֵינוֹ, וְלֹא-נָס לֵחֹה.

7 And Moses was a hundred and twenty years old when he died: his eye was not dim, nor his natural force abated.

Biogerontology (2009) 10:65–71
DOI 10.1007/s10522-008-9156-4

RESEARCH ARTICLE

Theoretical estimation of maximum human lifespan

Byung Mook Weon · Jung Ho Je

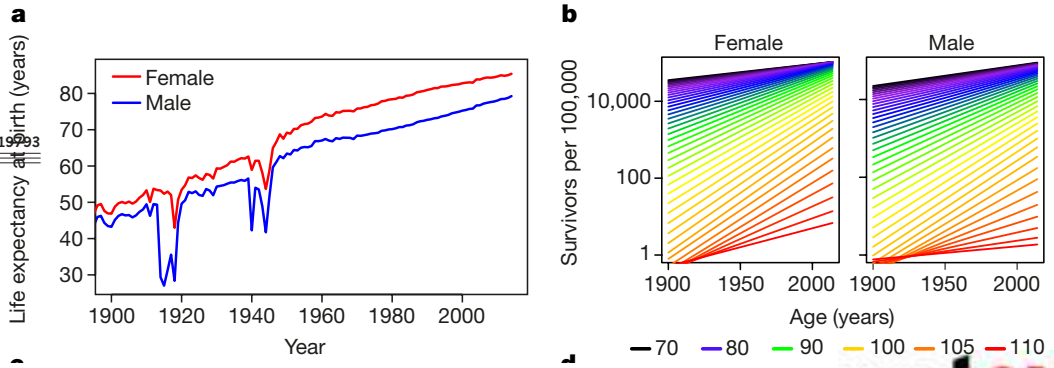
Based on such tendency, we develop an estimation method for maximum human lifespan and indeed obtain about 126 years from periodic life tables for Swedish female between 1950 and 2005. Despite uncertainty from available mortality data, our approach may offer quantitative biodemographic opportunities linking aging and survival kinetics.

LETTER

doi:10.1038/nature19793

Evidence for a limit to human lifespan

Xiao Dong[1]*, Brandon Milholland[1]* & Jan Vijg[1,2]



Quanto
vorreste vivere?

Come
vorreste vivere?

NON È SOLO QUESTIONE DI ANNI

"Così poi Eos dai fiori d'oro rapì Titone,
della vostra stirpe, simile agli immortali;
e si avviò per chiedere a Zeus dalle nere nubi
che egli fosse immortale e vivesse in eterno;
a lei Zeus assentì con un cenno ed esaudì il suo desiderio.
Stolta, e non pensò nella sua mente, Eos veneranda,
a chiedere la giovinezza e tener lontana la vecchiaia
rovinosa."

OMERO, Inno ad Afrodite, vv. 218-276, in Inni omerici, a cura di F. Càssola, Milano, Fondazione Lorenzo Valla/Arnoldo Mondadori, 1991

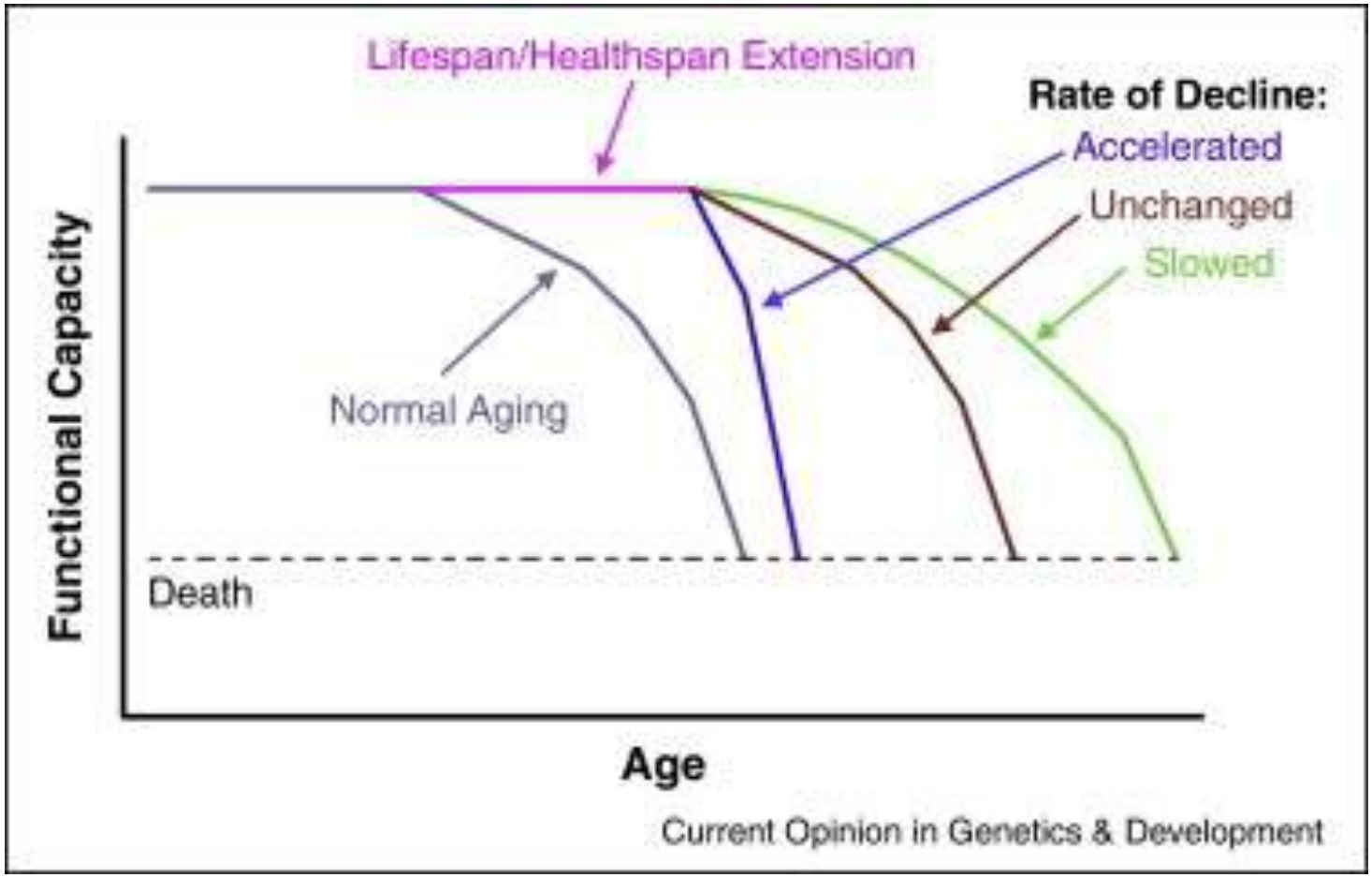
Non è solo questione di anni

Ruggero Bacone, inglese, filosofo naturale del 13° secolo tentò degli approcci Alchemici per perseguire la ricerca della giovinezza eterna.

Al tempo di Bacone si riteneva che i giovani fossero in possesso di una maggior quantità di "respiro vitale" e gli uomini anziani speravano di assorbirlo con "frequentazioni strette" con donne giovani.


THE
Mirror of Alchimy,
LONDON

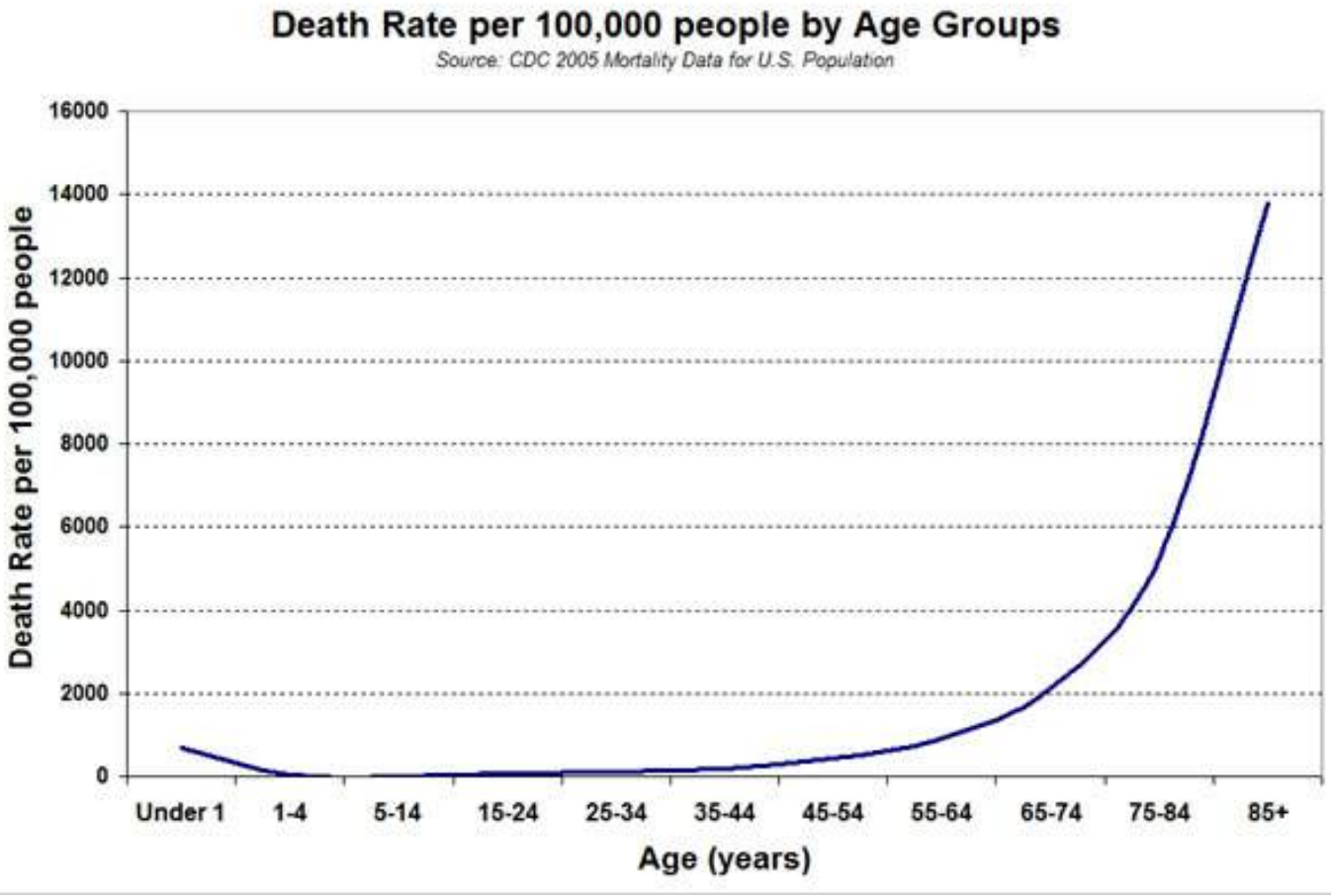
Non è solo questione di anni



Non è solo questione di anni

BENJAMIN GOMPERTZ, 1779–1865

Non è solo questione di anni



Nel 1825 il matematico britannico Benjamin Gompertz osservò che il rischio di morte aumenta esponenzialmente con il passare degli anni. Per l'uomo, raddoppia *ogni 8 anni dopo i 30 anni*. La legge sembra valere per tutti i mammiferi in età adulta, ma non per la talpa nuda: dopo aver raggiunto la maturità a 6 mesi di età, ogni Heterocephalus glaber corre un rischio di morte giornaliero *di poco superiore a 1 su 10 mila*. Questo rischio rimane invariato per tutta la durata della vita, e anzi sembra diminuire leggermente.

Non è solo questione di anni

eLIFE elifesciences.org

RESEARCH ARTICLE

Naked mole-rat mortality rates defy Gompertzian laws by not increasing with age

J Graham Ruby, Megan Smith, Rochelle Buffenstein*

Calico Life Sciences LLC, South San Francisco, United States

Abstract The longest-lived rodent, the naked mole-rat (*Heterocephalus glaber*), has a reported maximum lifespan of >30 years and exhibits delayed and/or attenuated age-associated physiological declines. We questioned whether these mouse-sized, eusocial rodents conform to Gompertzian mortality laws by experiencing an exponentially increasing risk of death as they get older. We compiled and analyzed a large compendium of historical naked mole-rat lifespan data with >3000 data points. Kaplan-Meier analyses revealed a substantial portion of the population to have survived at 30 years of age. Moreover, unlike all other mammals studied to date, and regardless of sex or breeding-status, the age-specific hazard of mortality did not increase with age, even at ages 25-fold past their time to reproductive maturity. This absence of hazard increase with age, in defiance of Gompertz's law, uniquely identifies the naked mole-rat as a non-aging mammal, confirming its status as an exceptional model for biogerontology.

DOI: https://doi.org/10.7554/eLife.31157.001

I figli di centenari sono in una forma migliore rispetto a figli di di genitori che non longevi

Prole di centenari: per la maggior parte hanno entrambi i genitori che hanno vissuto a lungo

Lower	Weight	Higher
Lower	Waist circumference	Higher
Lower	BMI	Higher
Lower	N° of drug assumed	Higher
Lower	N° of subjects taking drugs	Higher
Lower	N° of subjects with lipid-lowering therapy	Higher
Lower	Myocardial Infarction	Higher
Lower	Stroke, cerebral thrombosis	Higher
Lower	Cancer	Higher
Lower	Irregular heart failure	Higher
Lower	Hypertension	Higher
Lower	Osteoporosis	Higher
Lower	More than 2 pathologies	Higher
Lower	IGF-1	Higher
Higher	Handgrip strength	Lower
Higher	N° of subjects able to perform chair stand	Lower
Higher	N° of subjects able to climb stairs w/o aid	Lower

Prole di non longevi: entrambi i genitori non longevi

Courtesy by C. Franceschi

Quanto
vorreste vivere?

Come
vorreste vivere?

Non è solo questione di anni

9 HALLMARKS OF AGING

López-Otín et al. Cell *153*, 1194–1217, 2013

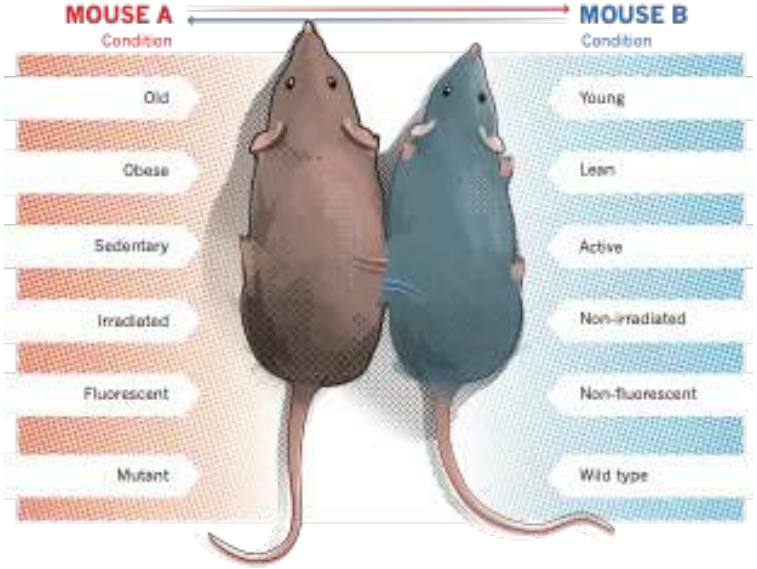
Tra mito e scienza…

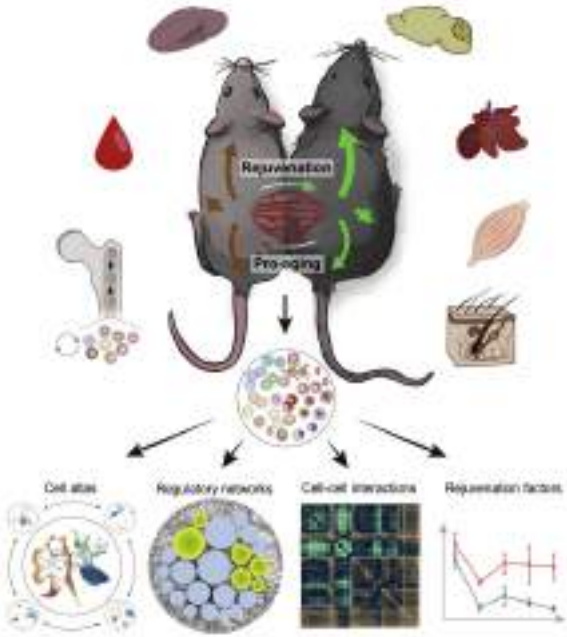
P. BERT. — EXPÉRIENCES ET CONSIDÉRATIONS. 69

EXPÉRIENCES
ET
CONSIDÉRATIONS
SUR LA GREFFE ANIMALE

PAR LE Dr PAUL BERT,

1864

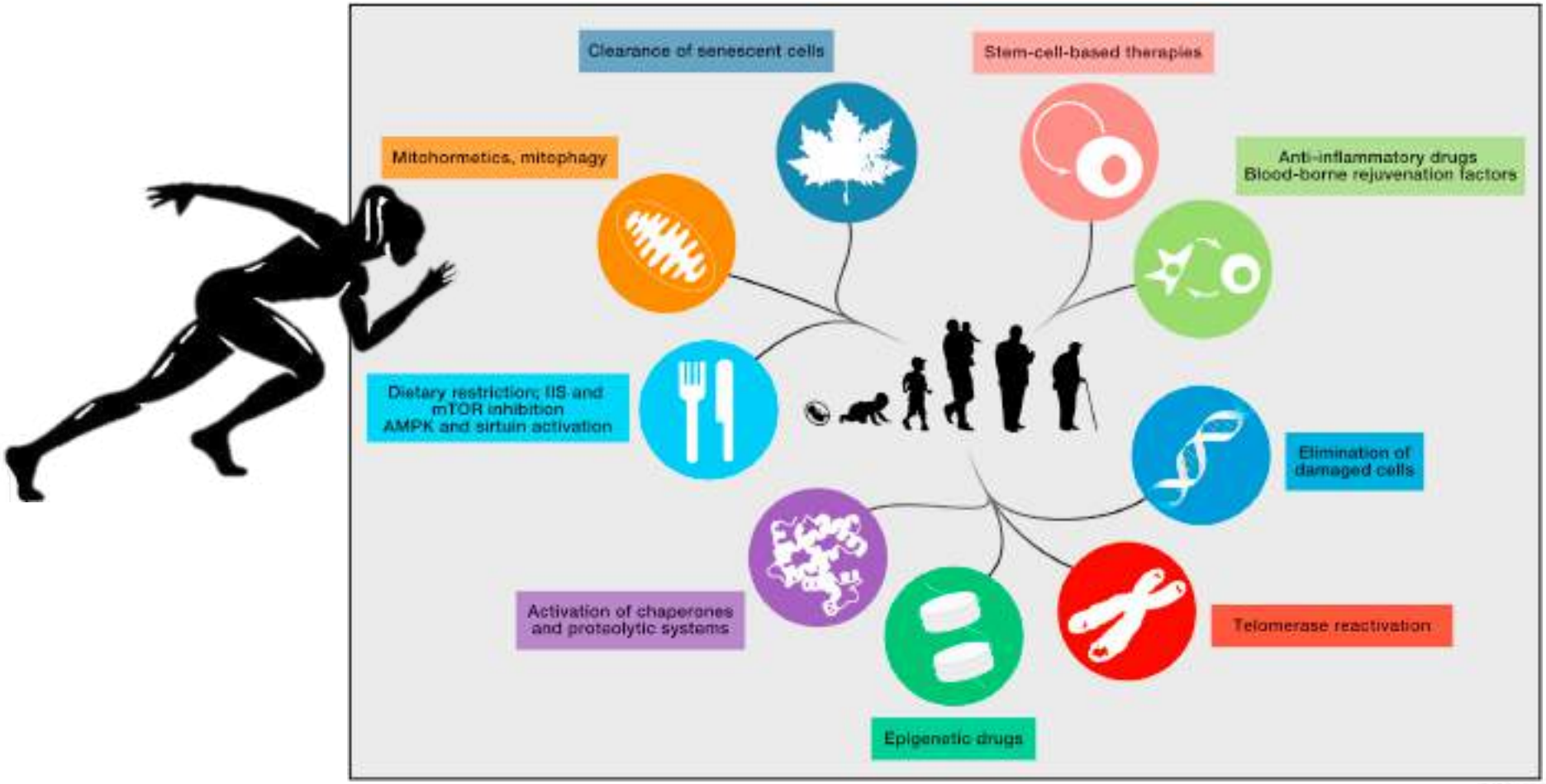




Ma et al. Cell Stem Cell. 2022 Jun 2;29(6):990-1005.e10.

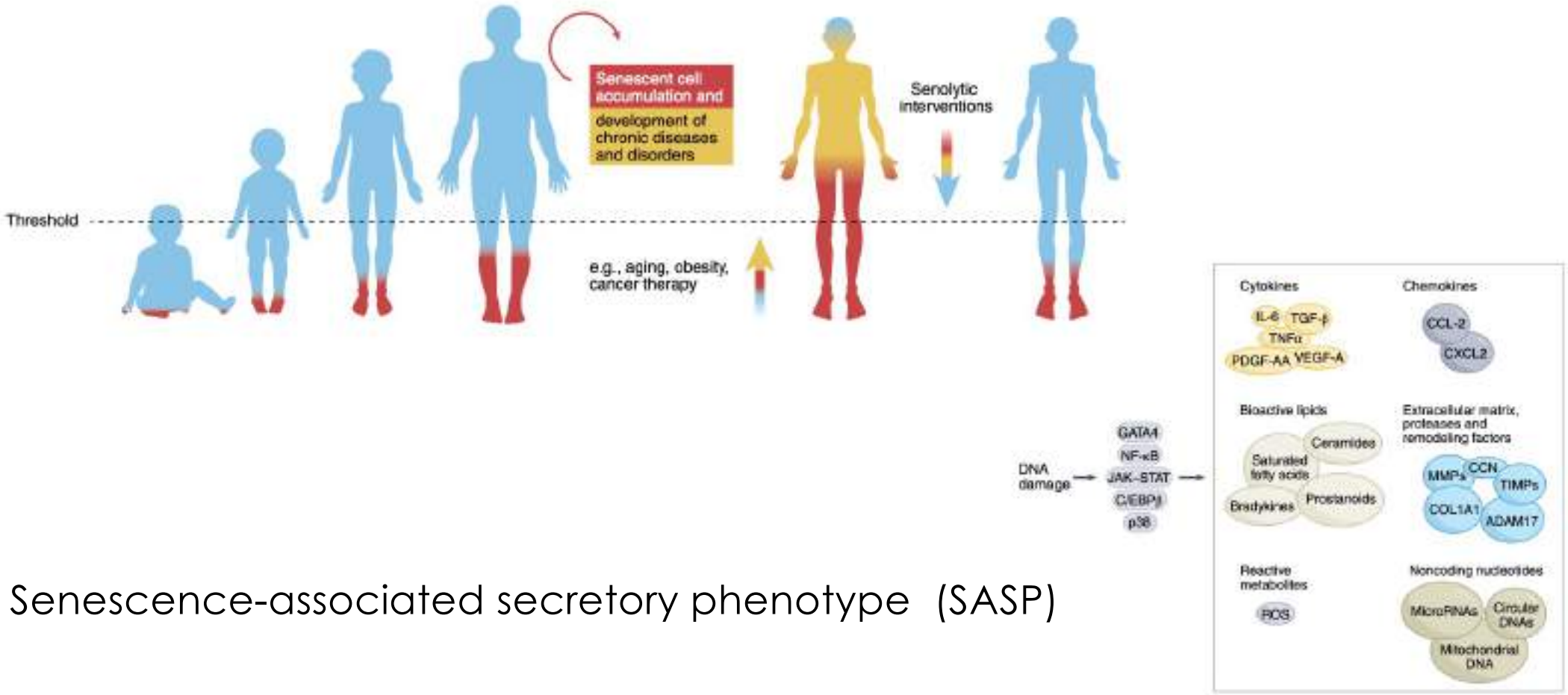
Scudellari M. Nature. 2015 Jan 22;517(7535):426-9

INVECCHIAMENTO (SENESCENZA)



López-Otín et al. Cell *153*, 1194–1217, 2013

Senescenza

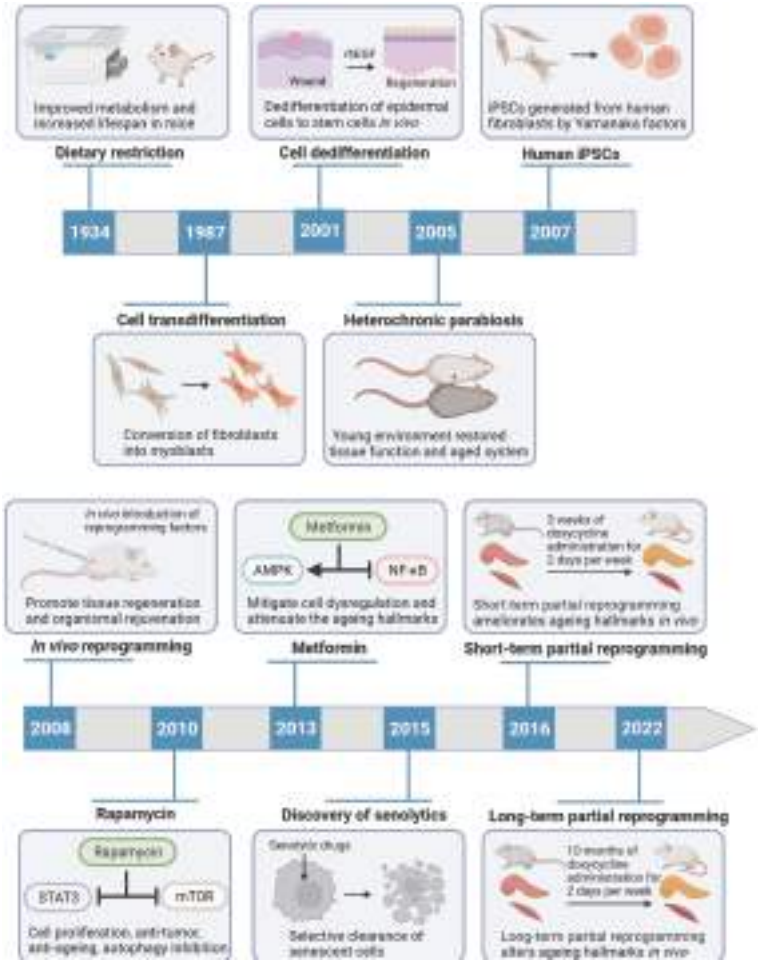


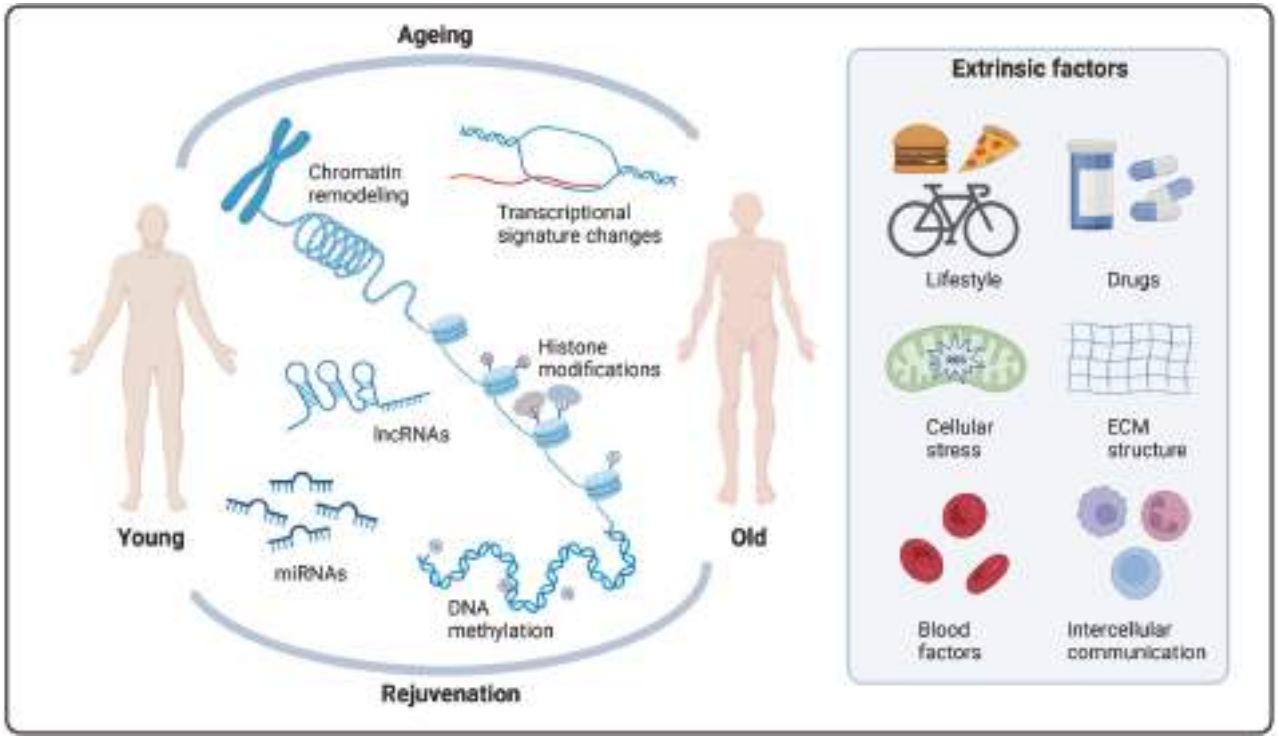
Senescence-associated secretory phenotype (SASP)

Chaib et al. Nat Med. 2022 Aug;28(8):1556-1568

nutex

Senescenza





Ji S, et al. Signal Transduct Target Ther. 2023 Mar 14;8(1):116.

Senescenza… misurarla…

Received: 15 June 2020 | Revised: 21 August 2020 | Accepted: 13 September 2020
DOI: 10.1111/acel.13256

ORIGINAL ARTICLE

Aging Cell WILEY

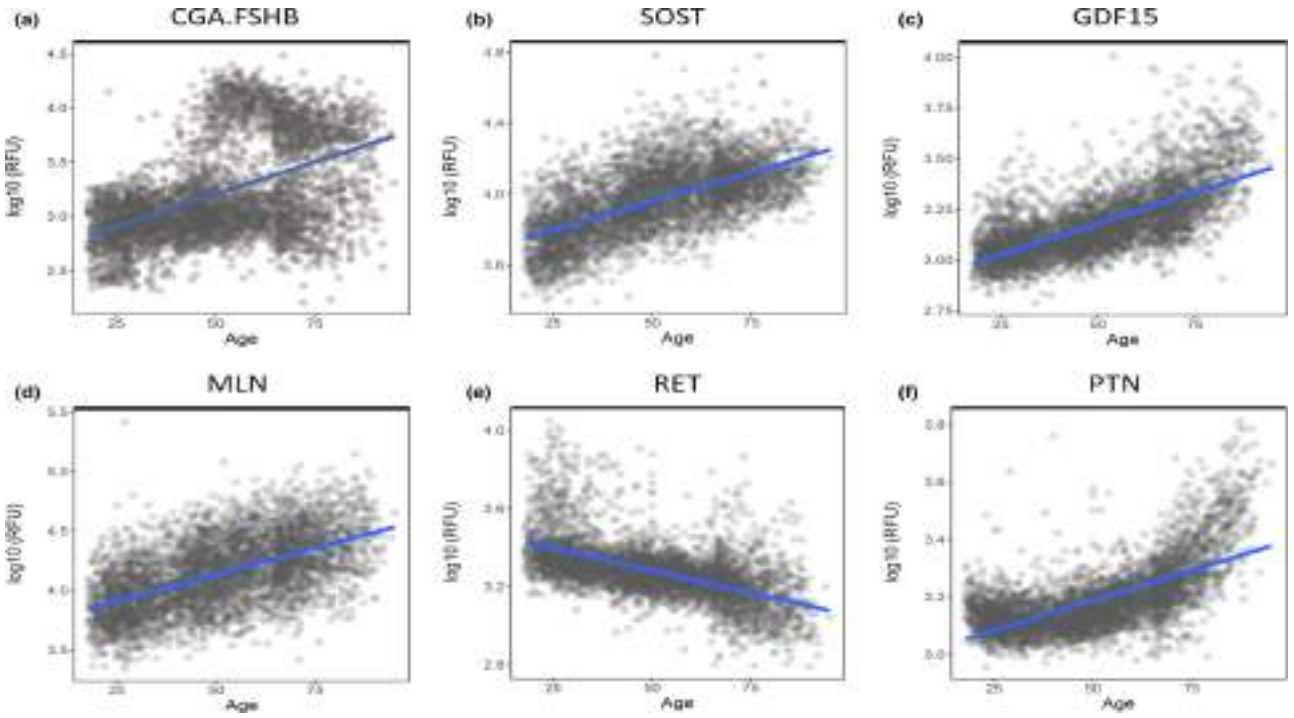
Data mining of human plasma proteins generates a multitude of highly predictive aging clocks that reflect different aspects of aging

Benoit Lehallier[1,2,3] | Maxim N. Shokhirev[4] | Tony Wyss-Coray[1,2,3,5] | Adiv A. Johnson[6]

CGA-FSHB Glycoprotein Hormones, Alpha Polypeptide FSH

MLN Small peptide hormone that is secreted by cells of the small intestine to regulate gastrointestinal contractions and motility

GDF15 strong prognostic protein in patients with different diseases such as heart diseases and cancer.



nutex

INVECCHIAMENTO e EPIGENETICA

PRINCIPALI MECCANISMI EPIGENETICI

- **Metilazione del DNA:**

Coinvolge l'aggiunta di gruppi metile (-CH3) a specifiche regioni del DNA.
Solitamente si verifica sulla citosina, creando la 5-metilcitosina.
Può influenzare l'accessibilità del DNA ai fattori di trascrizione e all'apparato trascrizionale.

- **Modificazioni degli istoni:**

Gli istoni sono proteine attorno alle quali il DNA si avvolge formando la struttura nucleosomale.
Le modificazioni includono metilazione, acetilazione, fosforilazione e ubiquitinazione delle istone.
Queste modificazioni possono influenzare la struttura della cromatina e quindi l'accesso al DNA.

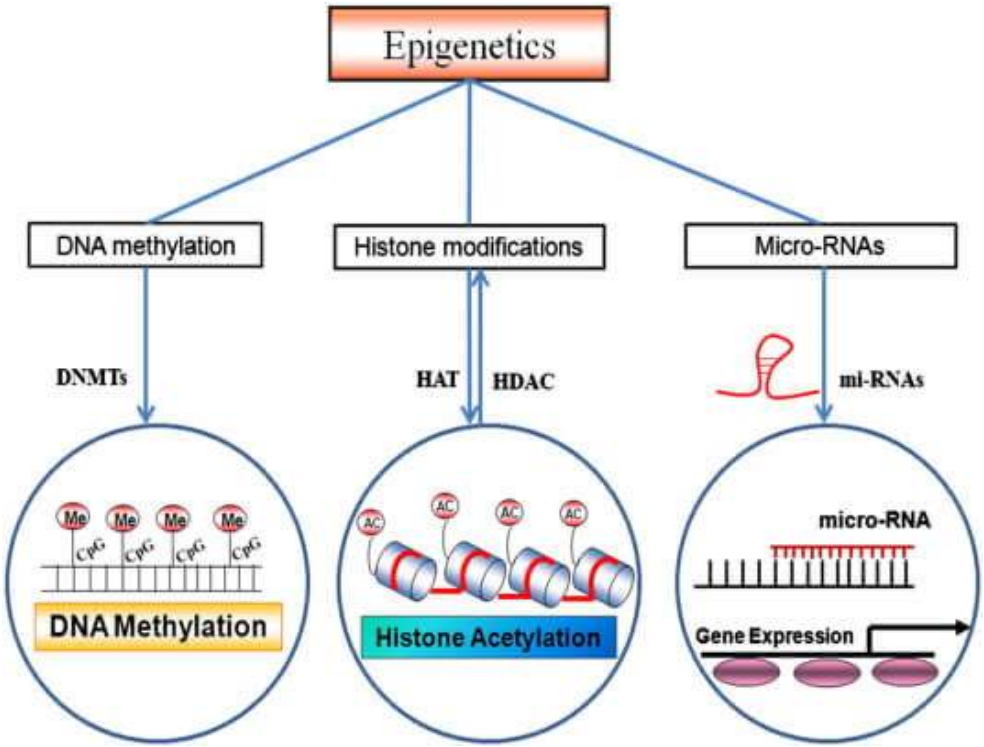
- **RNA interference (RNAi):**

Coinvolge l'azione di piccoli RNA (come siRNA e miRNA) non codificanti per regolare l'espressione genica.
Gli RNAi possono causare silenziamento genico post-trascrizionale bloccando la traduzione o promuovendo la degradazione dell'mRNA bersaglio.

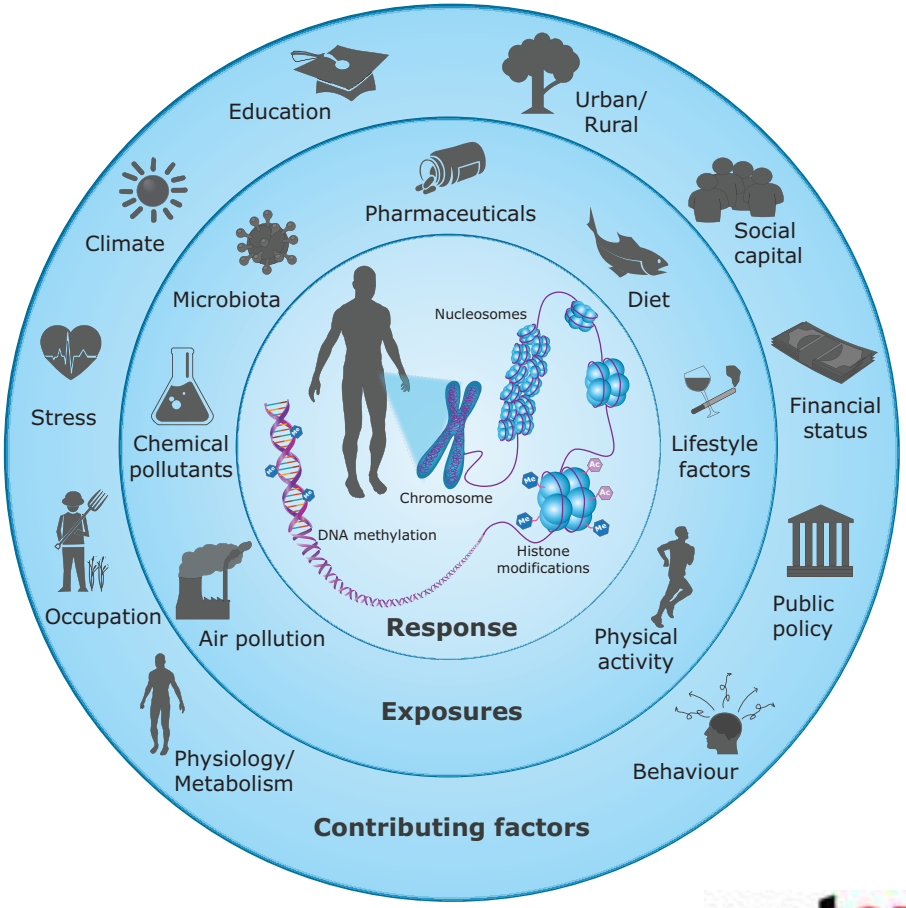
- **Modificazioni dell'architettura della cromatina:**

Questo include cambiamenti nella struttura tridimensionale del DNA all'interno del nucleo.
Ad esempio, la formazione di loop di cromatina o cambiamenti nella posizione dei cromosomi può influenzare l'accessibilità del DNA e la sua espressione genica.

Ruolo dell'epigenetica

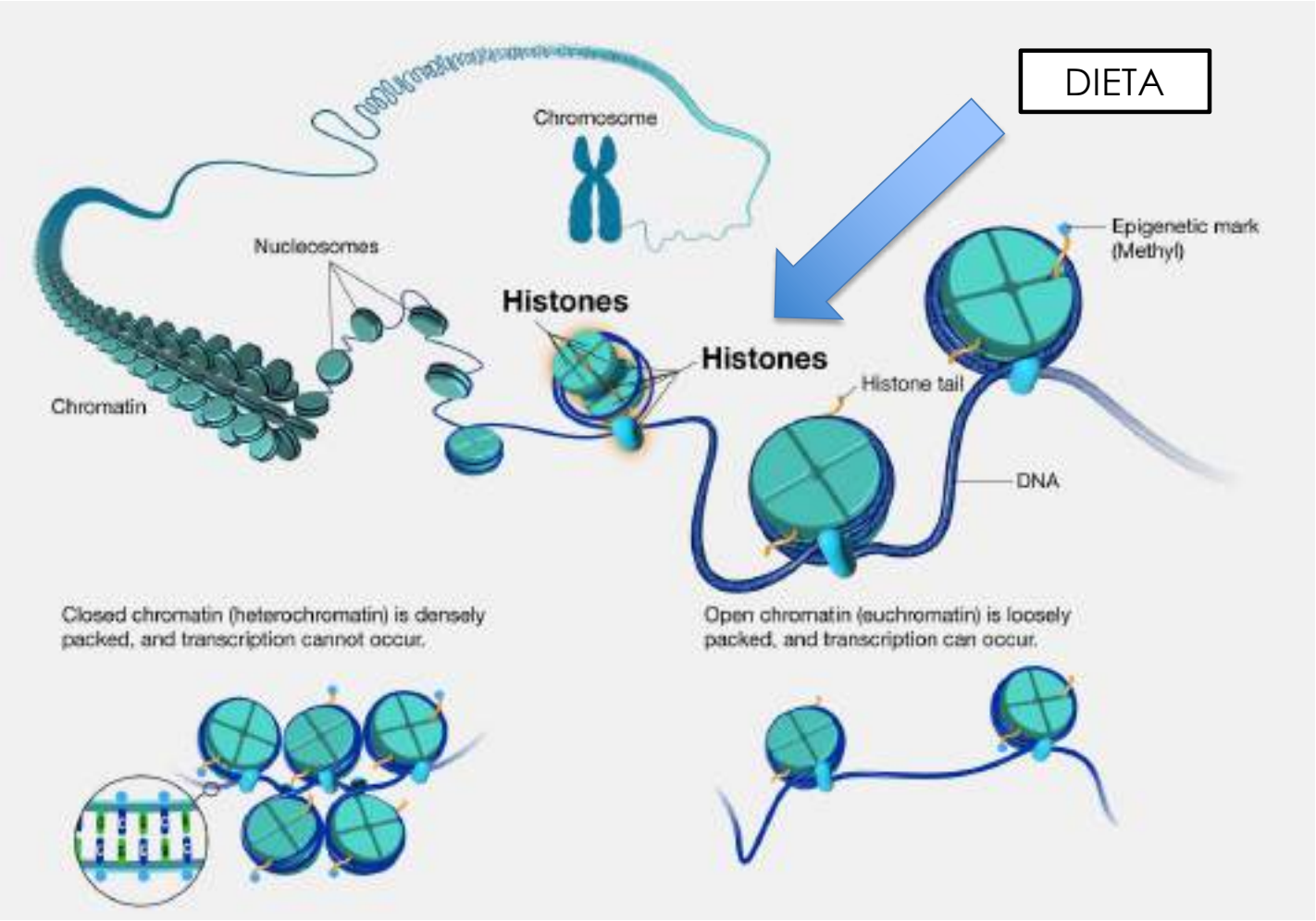


The human exposome and health in the Anthropocene



Karlsson et al. Int J Epidemiol. 2021 May 17;50(2):378-389

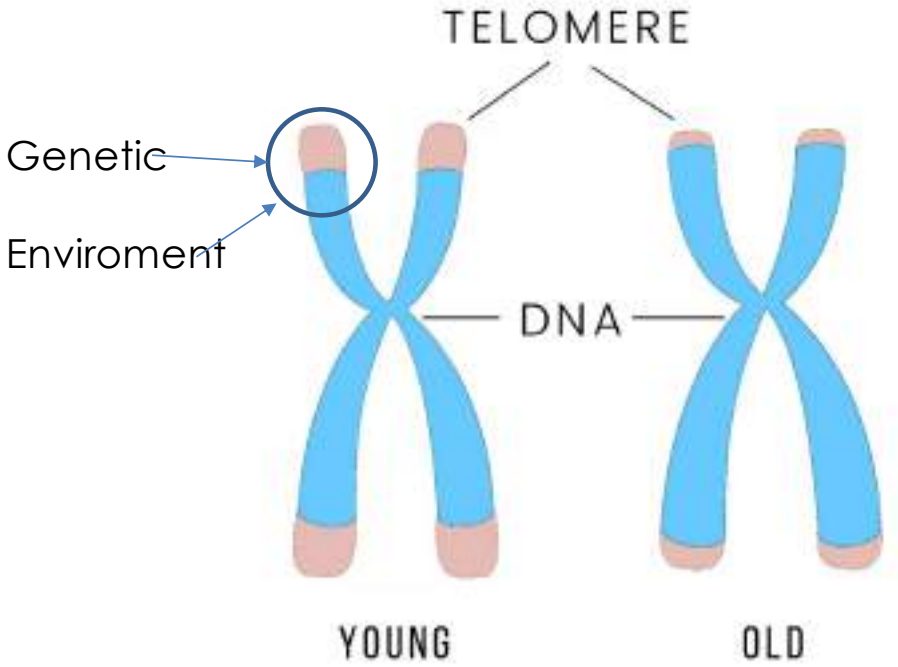
Ruolo dell'epigenetica



I telomeri

telomeri sono formati da ripetizioni TTAGGG in tandem del DNA alle estremità dei cromosomi.

Anello protettivo contro la fusione e la degradazione dei cromosomi.



TELEROMERE shortening causes:

Dysfunctional cells;
Apoptosis;
Cell senescence;
Death.

Factors associated with TELEROMERE shortening:

Oxidative stress
Inflammation
Psychosocial, environmental, and behavioral factors

Starkweather et al., Nurs Res. 2014 ; 63(1): 36–50.

nutex

Stile di vita ed aging clocks

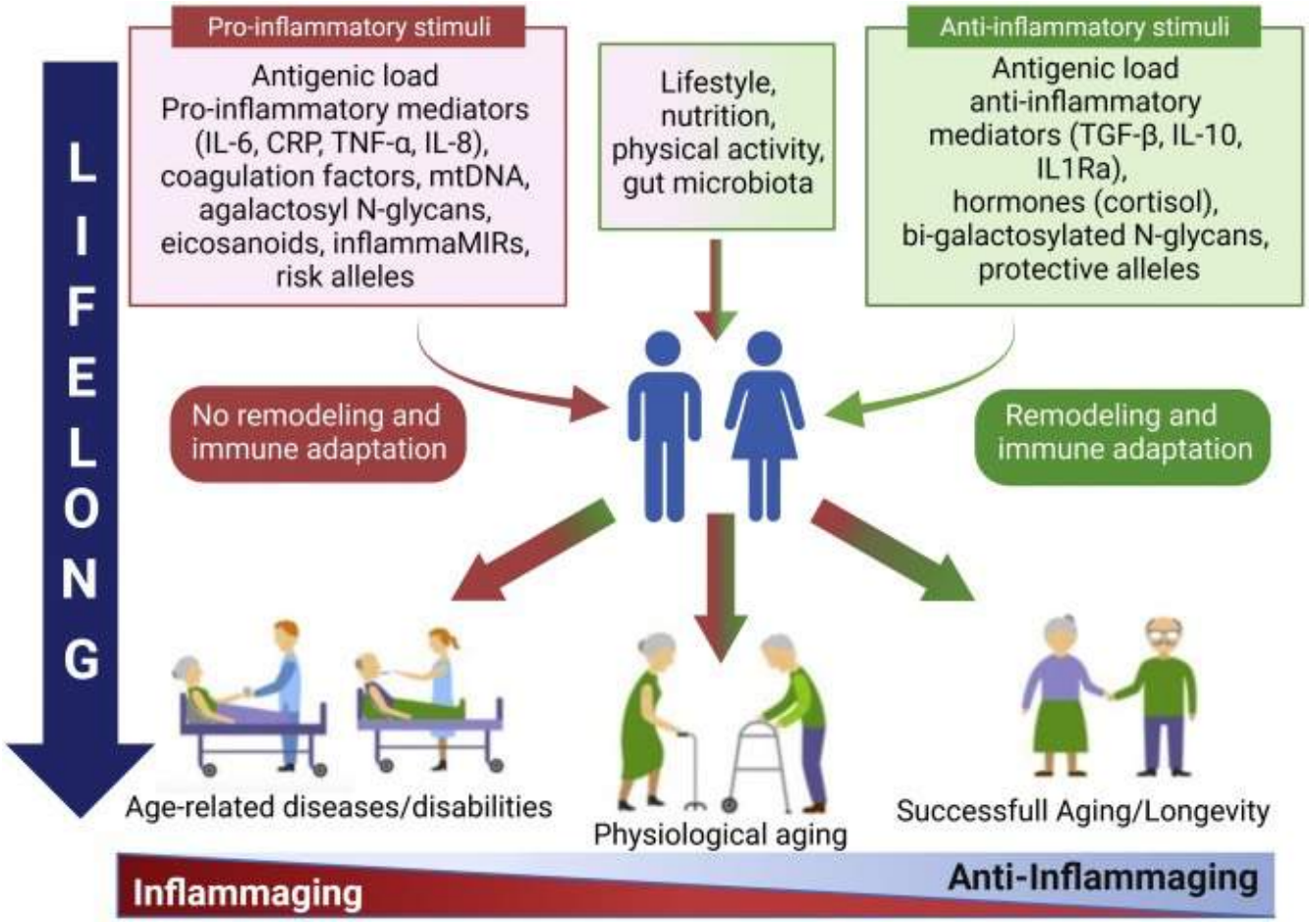
TABLE 2 Factors associated with a slower aging clock in humans

Factor(s)	Aging clock(s) used	Cohort size	Age information (years)	Tissue/data analyzed	Study reference
Fatty fish consumption, coffee consumption, exercise	Enroth et al. (2015)	976	14–94	Plasma	Enroth et al. (2015)
Smoking cessation	Horvath (2013) and Hannum et al. (2013)	22	46.77 ± 6.99	Blood	Lei et al. (2017)
Poultry intake, fish intake, markers of vegetable/fruit consumption, education, income, exercise, alcohol consumption	Horvath (2013) and Hannum et al. (2013)	4575	30–100	Blood	Quach et al. (2017)
Markers of vegetable/fruit consumption, nut consumption, education, income, exercise, alcohol consumption	PhenoAge (M. E. Levine et al., 2018)	4207	50–79	Blood	M. E. Levine et al. (2018)
Omega-3 supplementation, carbohydrate intake, dairy intake, whole grain intake, markers of vegetable/fruit consumption, education, income, exercise, alcohol consumption	GrimAge (A. T. Lu, Quach, et al., 2019)	2174	59–73*	Blood	A. T. Lu, Quach, et al. (2019)
Aerobic exercise	Lehallier (Lehallier et al., 2020)	47	19–77	Plasma	Lehallier et al. (2020)
Calcium alpha-ketoglutarate	TruAge (Demidenko et al., 2021)	42	43–72	Saliva	Demidenko et al. (2021)
Leisure-time physical activity	GrimAge (A. T. Lu, Quach, et al., 2019)	1040	21–74	Blood	Kankaanpää et al. (2021)
Docosanoic, fiber intake, magnesium intake, vitamin E intake	MoveAge (McIntyre et al., 2021)	5139	18–85+	Accelerometer data	McIntyre et al. (2021)
Lifestyle factors, including physical activity, intake of vegetables and fruits, and moderate drinking	LIQI (Li et al., 2018)	286	48.9 ± 10.6	Blood	Peng et al. (2021)
Cardiovascular health factors, including diet, smoking status, and physical activity	Horvath (Horvath, 2013) and Hannum (Hannum et al., 2013)	2170	64.19 ± 7.06	Blood	Pottinger et al. (2021)
Mediterranean diet, Dietary Approaches to Stop Hypertension diet	Esposito (Esposito et al., 2022)	4510	≥35	Blood	Esposito et al. (2022)
Sleep quality	Klemera-Doubal Method (Klemera & Doubal, 2006) and PhenoAge (M. E. Levine et al., 2018)	363,886	56.5 ± 8.1	Blood	Gao et al. (2022)
Higher diet quality	DunedinPoAm (Belsky et al., 2020), GrimAge (A. T. Lu, Quach, et al., 2019), and PhenoAge (M. E. Levine et al., 2018)	1995	67 ± 9	Blood	Y. Kim et al. (2022)
Higher diet quality	Hannum (Hannum et al., 2013), PhenoAge (M. E. Levine et al., 2018), and GrimAge (A. T. Lu, Quach, et al., 2019)	2694	56 ± 9	Blood	Kresovich et al. (2022)
Light alcohol consumption	MonoDNAmAge (Liang et al., 2022), Horvath (Horvath, 2013), Hannum (Hannum et al., 2013), PhenoAge (M. E. Levine et al., 2018), and GrimAge (A. T. Lu, Quach, et al., 2019)	2242	18–83	Monocytes, blood, and peripheral blood mononuclear cells	Liang et al. (2022)
Serum zinc levels	Horvath (2013)	10	37.83 ± 12.05	Blood leukocytes	Noronha et al. (2022)
Vitamin D supplementation	Horvath (2013) and Vetter et al. (2019)	1036	68.28 ± 3.49	Blood	Vetter et al. (2022)

*Self-reported omega-3 intake data was available for 2174 members of a larger cohort composed of 2356 people. The age range provided is for the full cohort (n = 2356).

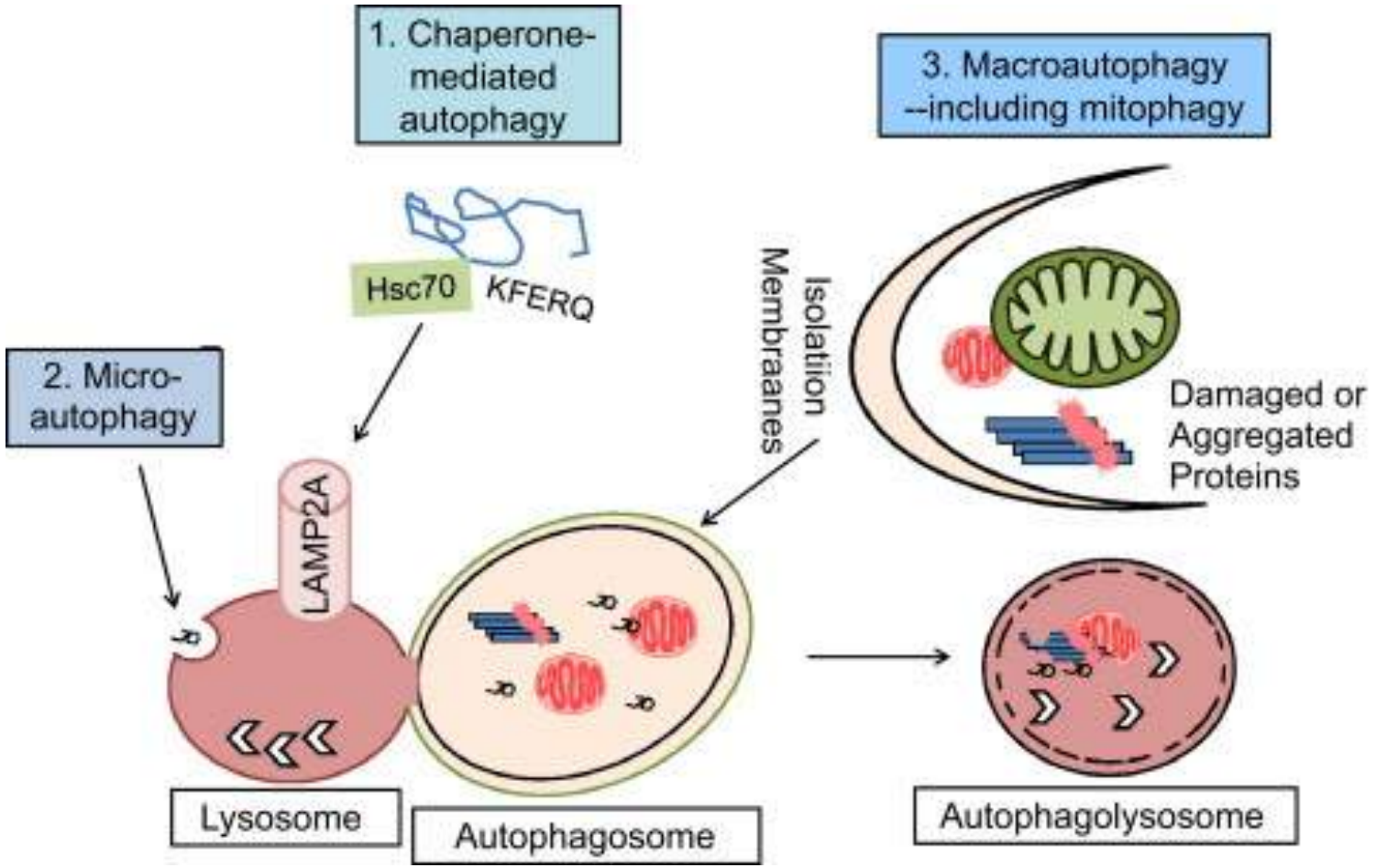
Johnson et al. Aging Cell. 2022 Aug;21(8):e13664.

Invecchiamento e infiammaizone



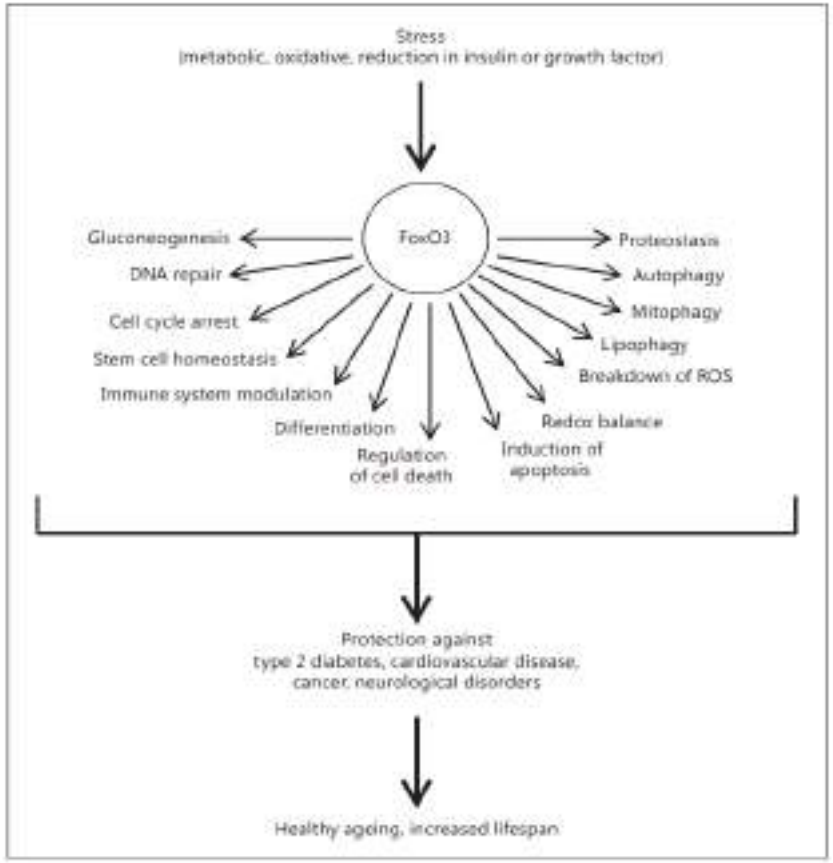
Santoro et al. Ageing Res Rev. 2021 Nov;71:101422

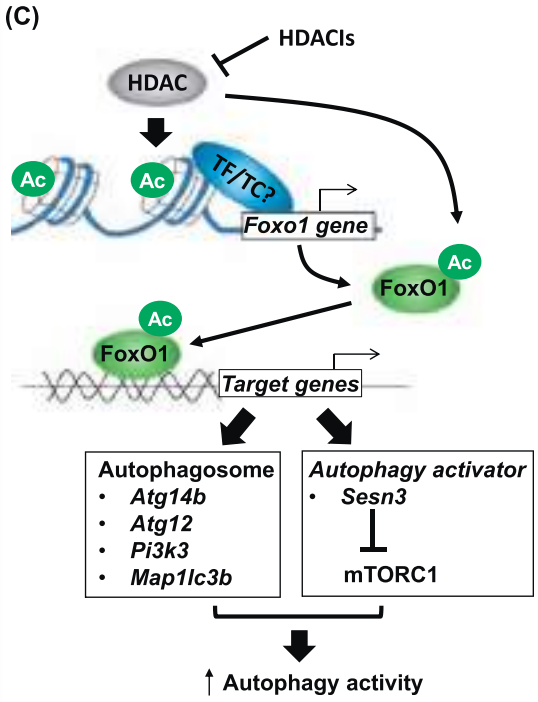
Invecchiamento e autofagia

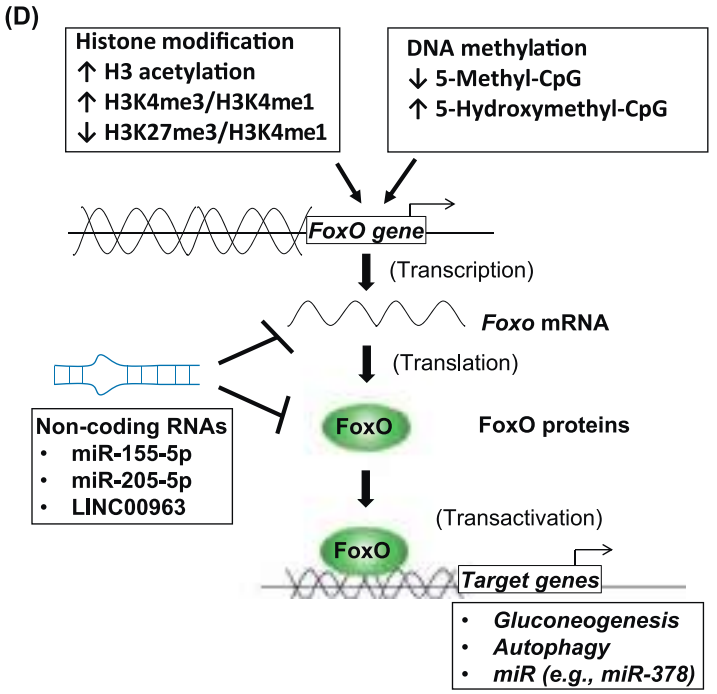


Zhang J. Redox Biol. 2013;1(1):19-23.

Invecchiamento e autofagia







Morris et al., Gerontology 2015;61:515–525

Cheng Z.. Trends Endocrinol Metab. 2019 Sep;30(9):658-671