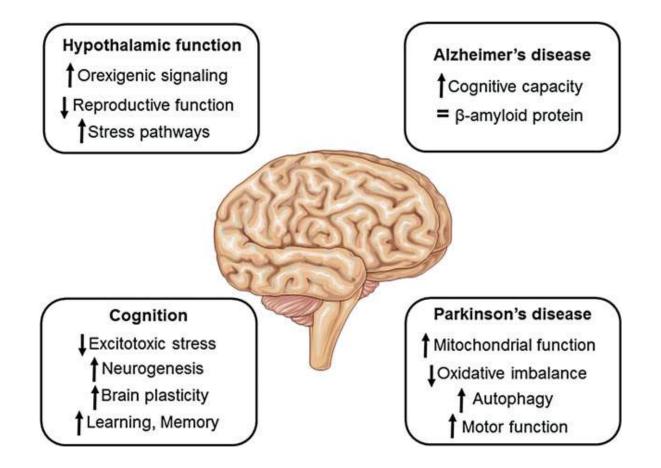
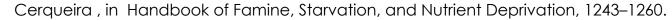
Digiuno intermittente e invecchiamento

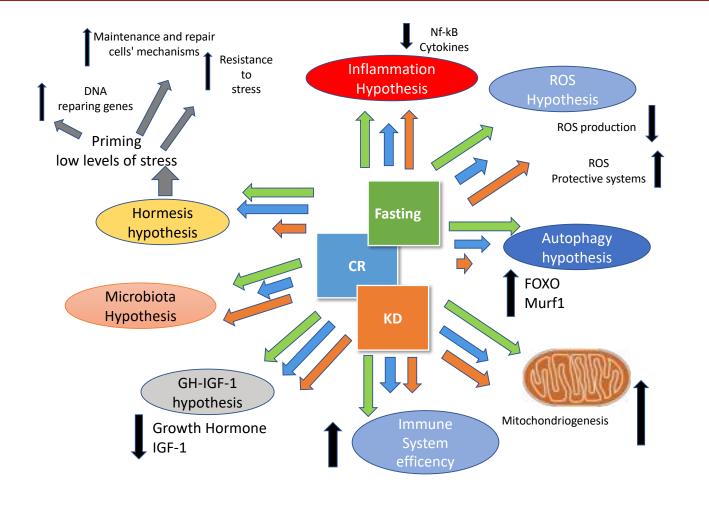








Digiuno intermittente e invecchiamento





Paoli et al. Nutrients 2019, Mar 28;11(4)



Tipi di TRE



Skipping breakfast

1 2 3 4 5 6 7 8 9 10 11 12 <mark>13 14 15 16 17 18 19 20</mark> 21 22 23 24

Skipping dinner –early breakfast

 1
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Skipping dinner –late breakfast

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24



"L'invenzione dell'agrigoltura, la rivoluzione industriale e le nuove tecnologie che riducono la fatica fisica hanno portato ad una drammatica riduzione o eliminazione dell'esercizio fisico intenso e del digiuno lasciando il compito di stimolare il cervello solo alle sfide intellettive. In aggiunta alla riduzione delle risposte adattive cerebrali l'attuale l'indulgente stile di vita sedentario promuove obesità, diabete e CVD che a loro volta aumentano il rischio di AD.

Bisogna affrontare la realtà: c'è necessità di esercizio, periodi di digiuno e cahllenges intellettive per mantenere la salute del cervello."

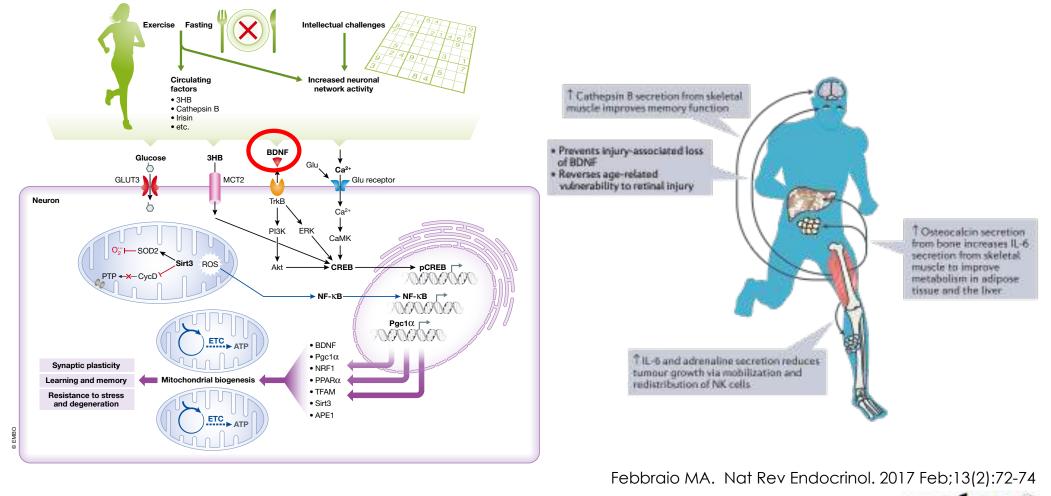


Mark P Mattson

Professor of Neuroscience at Johns Hopkins University Former Chief of the Laboratory of Neurosciences at the National Institute on Aging.

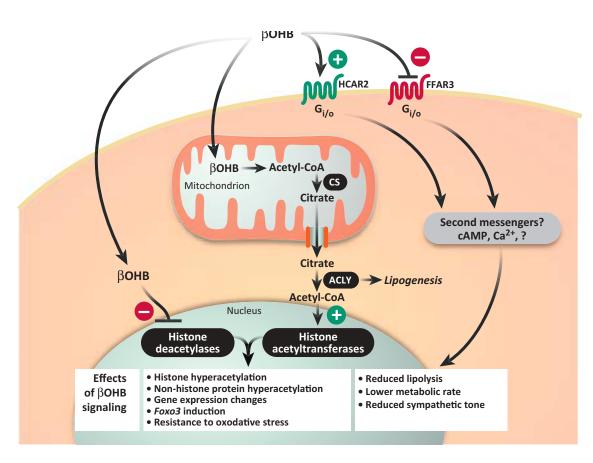


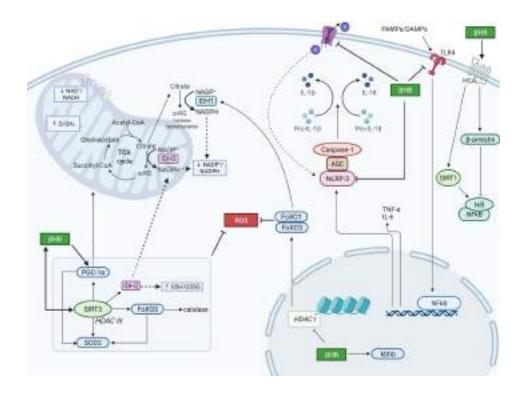






Paoli A. Camandola & Mattson The EMBO Journal (2017) 36: 1474–1492





Paoli et al. Trends Endocrinol Metab. 2024 Feb; 35(2): 125-141.



Paoli A. Newman & Verdin Trends Trends Endocrinol Metab. 2014 Jan;25(1):42-52

Exercise

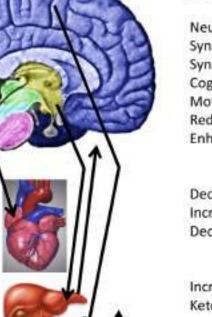
Neurogenesis Synaptogenesis Synaptic plasticity Cognitive function Motor function DNA repair Mitochondrial biogenesis Reduced inflammation

Decreased resting heart rate Increased heart rate variability Decreased blood pressure

Increased insulin sensitivity Ketone body production

Increased insulin sensitivity

Fatty acid mobilization Reduced inflammation



Intermittent Fasting

Neurogenesis Synaptogenesis Synaptic plasticity Cognitive function Motor function Reduced inflammation Enhanced autophagy

Decreased resting heart rate Increased heart rate variability Decreased blood pressure

Increased insulin sensitivity Ketone body production

Increased insulin sensitivity

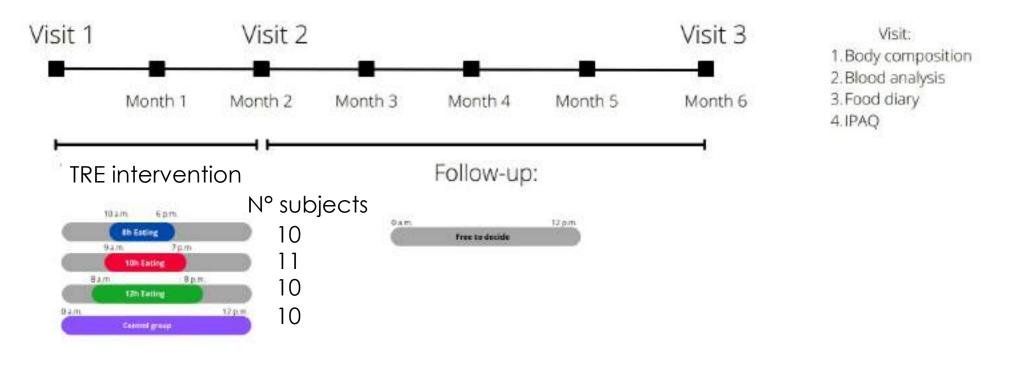
Fatty acid mobilization Reduced inflammation





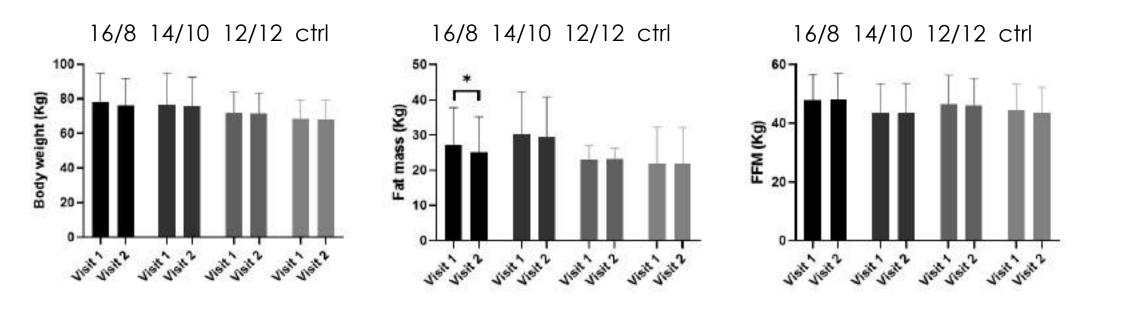
van Praag et al. J Neurosci. 2014 Nov 12;34(46):15139-49

Sedentary subjects





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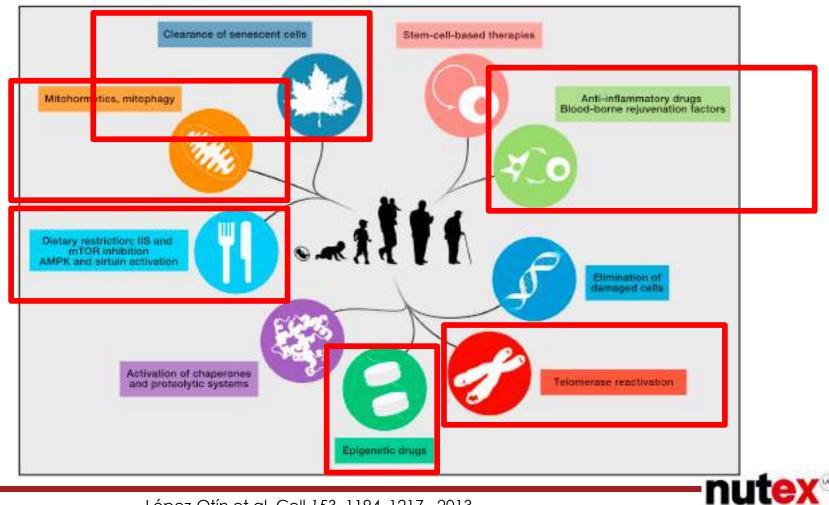


Unpublished data



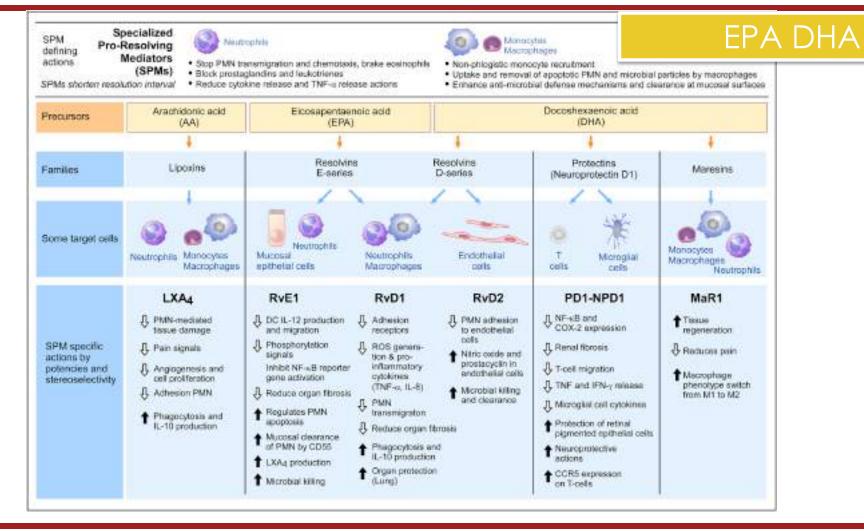
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NUTRACEUTICA E INVECCHIAMENTO



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

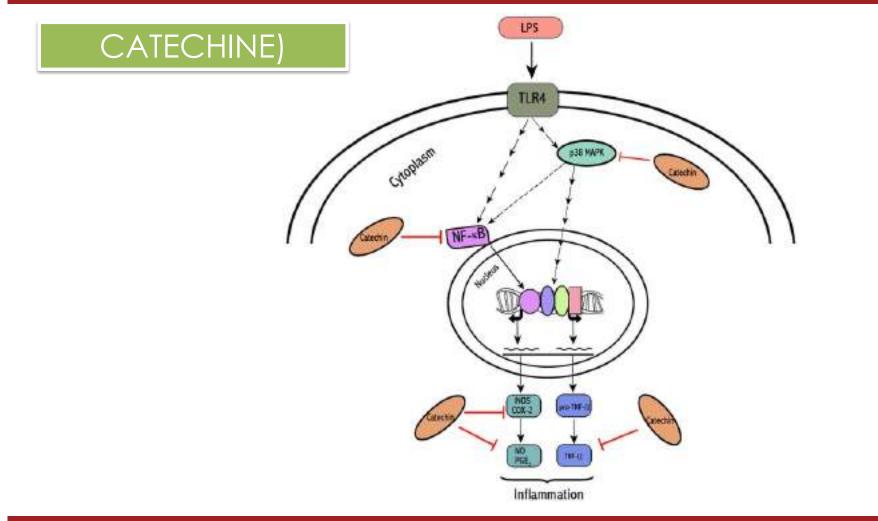






Barnig et al. Front Immunol. 2019 Jul 23;10:1699

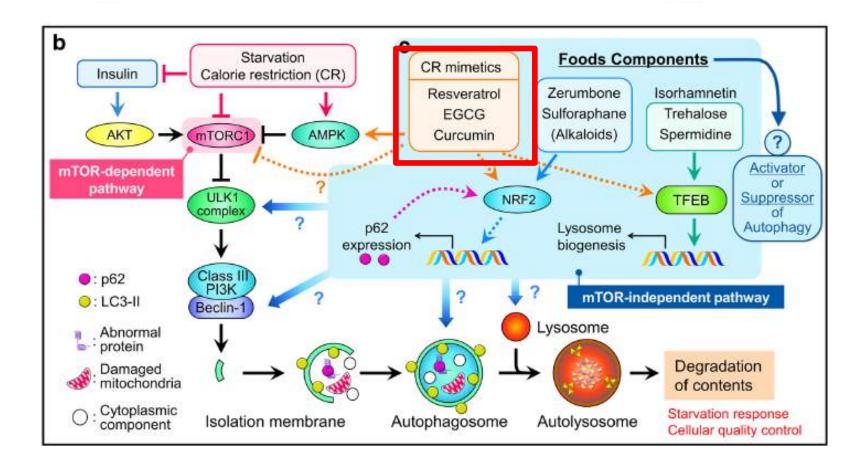






Sunil et al. Inflammopharmacology. 2021 Aug;29(4):1139-1155.

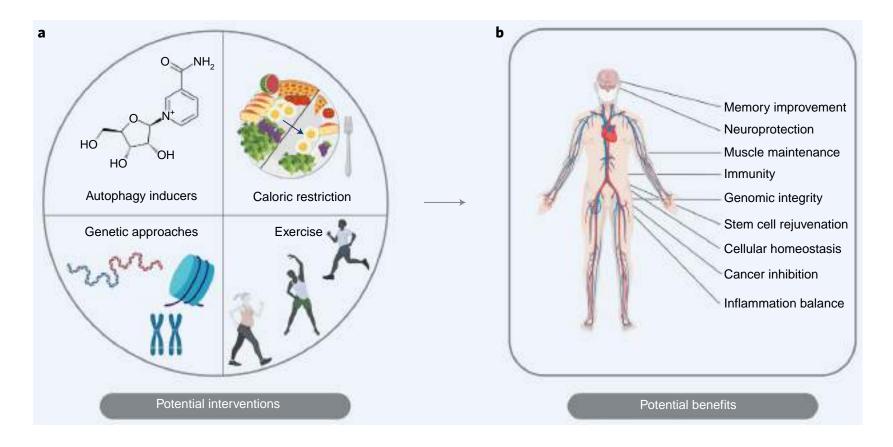
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Yano et al. Curr Pharmacol Rep 2020, dec; 5: 335–345







Aman et al. Nat Aging. 2021 Aug;1(8):634-650



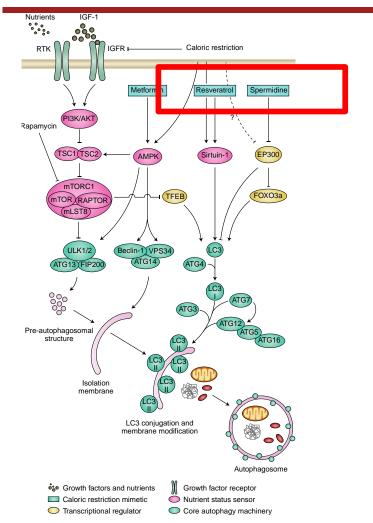


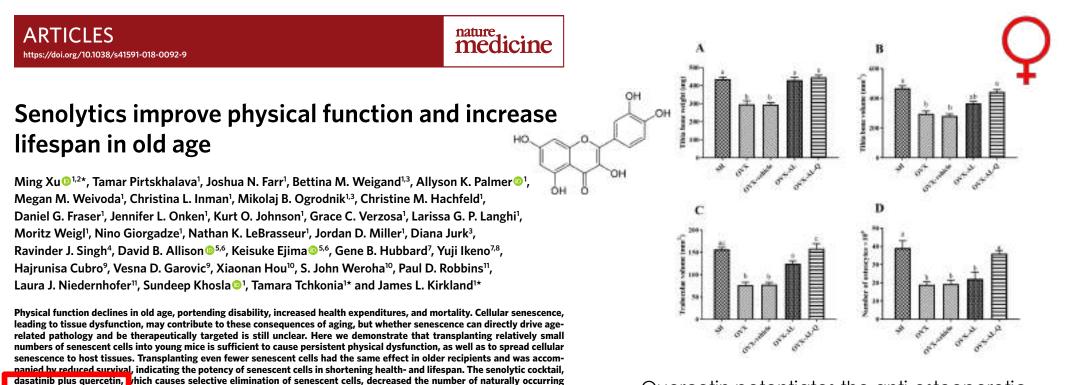
Table 2 | Select compounds that induce autophagy

Table 2 Select compounds that induce autophagy		
Agent	Developmental status	Mechanism of autophagy induction
ABT-199 (also known as Venetoclax)	Approved for the treatment of chronic lymphocytic leukaemia (CLL)	BH3 mimetic and Beclin-1 activator
ABT-263 (also known as Navitoclax)	Phase I/II clinical trials for cancer	BH3 mimetic and Beclin-1 activator
ABT-737	In preclinical development	BH3 mimetic and Beclin-1 activator
Alvespimycin (also known as 17-DMAG)	Discontinued from clinical tests (hepatotoxicity)	HSP90 inhibitor and inhibition of Akt/ mTOR/p70S6K signalling?
Beclin-1-derived peptide	In preclinical development	Beclin-1 activator
Carbamazepine	Approved for treatment of seizures and bipolar disorders	Reduction in Ins(1,4,5)P $_3$ and inositol levels
Clonidine and Rilmenidine	Approved for the treatment of hypertension	Reduction in cAMP levels
Caloric restriction	Not available	Multiple
Everolimus (also known as KADUUI)	Approved for cancer therapy	Inhibition of m I OKC I
Geldanamycin	Discontinued from clinical tests (hepatotoxicity)	Inhibition of Akt/mTOR/p70S6K signalling?
Hydroxycitrate	Nutritional supplement	CRM and AMPK activation
Lithium	Approved for treatment of bipolar disorders	Reduction in Ins(1,4,5)P $_3$ and inositol levels
Metformin	Approved for type II diabetes	CRM and AMPK activation
Perhexiline	Approved for angina	CRM, AMPK activation and Acetyl-CoA reduction
Physical exercise	Not available	Multiple
Rapamycin (also known as sirolimus)	Approved for immunosuppression and cancer therapy	Inhibition of mTORC1
Resveratrol	Nutritional supplement	CRM and SIRT1 activation
Statins	Approved for obesity	Depletion of geranylgeranyl disphosphate AMPK activation and mTORC1 inhibition
Spermidine	Nutritional supplement	CRM and EP300 deacetylase inhibitor
Fanespimycin (also known as 17-AAG)	Discontinued from clinical tests	HSP90 inhibitor and inhibition of Akt/ mTOR/p70S6K signalling?
Temsirolimus (also known as CCI-779)	Approved for cancer therapy	Inhibition of mTORC1
Forins	Experimental agent	Inhibition of mTORC1
Trehalose	Nutritional supplement, Phase I/II clinical trials for bipolar disorder and vascular aging	Glucose transporter inhibition and AMPK activation
Trifluoperazine	Approved for schizophrenia	Dopamine agonist and unknown

Paoli A. Leidal et a

Leidal et al. Nat Cell Biol. 2018 Dec;20(12):1338-1348





cretion of frailty-related proinflammatory cytokines in explants of human adipose tissue. Moreover,

intermittent oral administration of senolytics to both senescent cell-transplanted young mice and naturally aged mice allevi-

ated physical dysfunction and increased post-treatment survival by 36% while reducing mortality hazard to 65%. Our study provides proof-of-concept evidence that senescent cells can cause physical dysfunction and decreased survival even in young

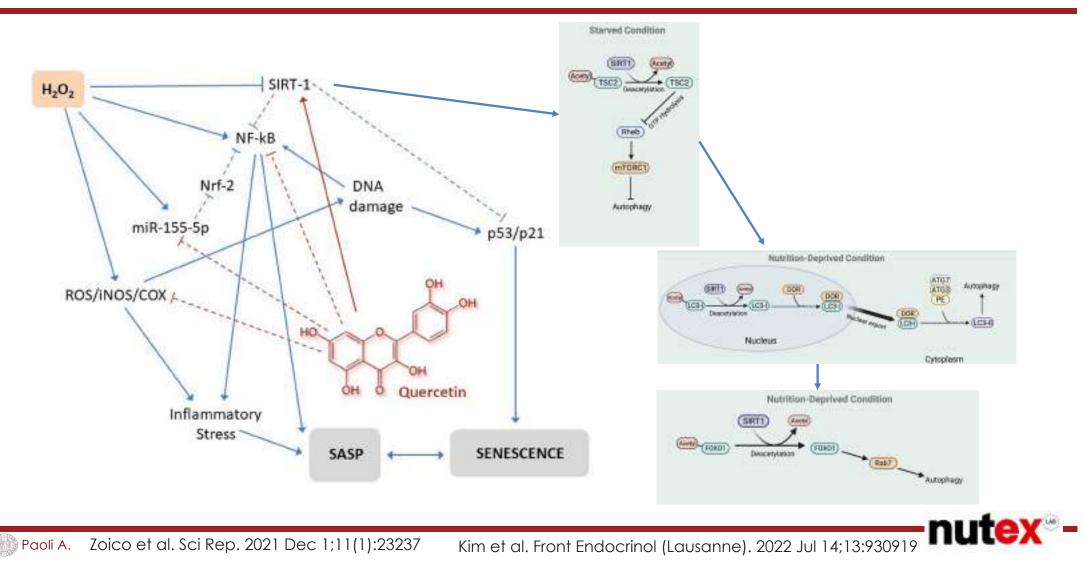
mice, while senolytics can enhance remaining health- and lifespan in old mice.

Paoli A.

Quercetin potentiates the anti-osteoporotic effects of alendronate through modulation of autophagy and apoptosis mechanisms in ovariectomy-induced bone loss rat model



Mousavi et al. . Mol Biol Rep. 2023 Feb 2





CONCLUSIONI 1

Se fossimo in grado di fornire a ciascuno la dose giusta di nutrimento ed esercizio fisico, né in difetto né in eccesso, avremmo trovato la strada per la salute.

Ippocrate (460-377 a.C.)

UNIVERSITA

- L'attuale stile di vita, pur prolungando l'aspettativa di vita, ha influenzato negativamente alcuni aspetti
- Per mantenere un cervello sano è importante mantenere anche un corpo efficiente
- TUTTO MUSCOLI E NIENTE CERVELLO È UNA "FAKE NEWS"
- Un approccio attento all'alimentazione (quantitativo e qualitativo) è fondamentale per il benessere dell'organismo







INIVERSED.

DI PADOVA

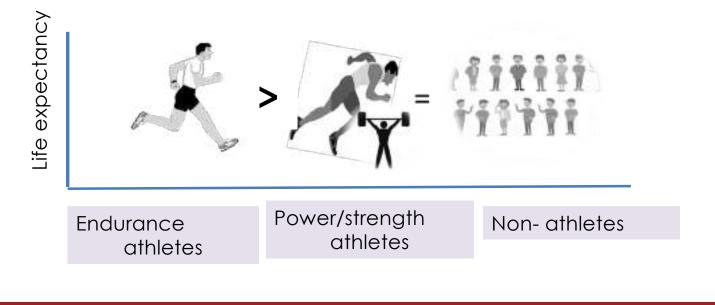
CONCLUSIONI 2

- Il digiuno intermittente e la caloric reduction si sono dimostrati un'arma efficace per il mantenimento della salute fisica e cognitiva
- Il digiuno intermittente lavora in sinergia dell'esercizio
- Vi sono alcuni attivi che agiscono migliorando alcuni aspetti legati all'invecchiamento e quindi, di fatto, MIGLIORANDO il processo di invecchiamento
- Infiammazione, stress ossidativo, riduzione dell'autofagia sono alcuni tra gli Hallmarks of aging
- Catechine, Omega 3, Resveratrolo, Quercetina agiscono su questi fenomeni









nut



Teramoto & Bungum. J Sci Med Sport. 2010 Jul;13(4):410-6.



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Gerontology

Non è finita... finché non è finita...

Behavioral Science Section: Research Article

Gerontology DOI: 10.1159/000524885

Received: December 1, 2021 Accepted: April 25, 2022 Published online: May 25, 2022

Feeling Younger, Rehabilitating Better: Reciprocal and Mediating Effects between Subjective Age and Functional Independence in Osteoporotic Fracture and Stroke Patients

Daphna Magda Kalir^a Amit Shrira^b Yuval Palgi^c Carmel Batz^b Aya Ben-Eliezer^d Noemi Heyman^e Devora Lieberman^f Irena Seleznev^e Inna Shugaev^{d, g} Oleg Zaslavsky^h Evgeniya Zikrin^f Ehud Bodner^{b, i}



Rehabilitation outcomes following osteoporotic fractures or strokes could improve if subjective age and an optimistic outlook are taken into consideration





SAPETE A CHE VELOCITÀ CAMMINA LA MORTE...?

A CHE VELOCITÀ DOVETE CAMMINARE PER SFUGGIRLE?



LA VELOCITÀ DELLA TRISTE MIETITRICE... 1600 persone ultrasettantenni Misurata la velocità di marcia Dopo 5 anni 266 deceduti... camminavano a meno di 2,9 Km/h

Di chi camminava a più di 4,9 Km/h non era morto nessuno!

How fast does the Grim Reaper walk? Receiver operating characteristics curve analysis in healthy men aged 70 and over



BMJ 2011;343:d7679 doi: 10.1136/bmj.d7679



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POST DOC

Giuseppe Cerullo PhD Alex Rizzato PhD

Research Assistant Matteo Bozzato MSc

PhD STUDENTS

Alessandro Sampieri MSc Gioi Spinello MSc Luca Simoni PharmD Davide Charrier MSc

Lab Technician Marta Canato PhD



antonio.paoli@unipd.it

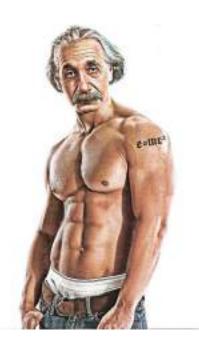


Antonio Paoli



@antoniopaoliMD

THANKS FOR YOUR ATTENTION!





antonio.paoli