Enhancing and Restoring Immunity As We Age
Immune Senescence
Immune Resilience
Immune Restoration

Promoting Health Span and Life Span

Dr. Nalini Chilkov, Founder

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Healthy Aging SUMMARY NOTES

www.aiiore.com/nanp23

IMMUNITY and AGING

Promoting Health Span and Life Span

- Caloric Restriction
- NAD+ Precursors
- SIRT 1 Activation
- mTOR Inhibition
- Autophagy & Mitophagy

LIFE SPAN vs HEALTHSPAN

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LIFE-SPAN vs HEALTH-SPAN

HEALTH SPAN

- **HealthSpan** is the length of time in one's life during which an individual is **in reasonably good health** A revolutionary increase in life span has already occurred. A corresponding increase in health span, the **maintenance of full function** as nearly as possible to the end of life, should be the next gerontological goal.

- **Healthy aging involves both delaying the physiological consequences of aging and maintaining functioning as aging progresses.** Interventions thus need to focus on preventing frailty and disability.

IMMUNE AGING and SENESCENCE

Immune Aging: results from genetic and epigenetic events accumulating throughout the lifespan
Decline in both innate and adaptive immune responses PLUS
increase in inflammation= **INFLAMMAGING**

Immuno-senescence
Senescent cells secrete inflammation-associated factors including IL-6 and IL-8, referred to as **senescence-associated secretory phenotypes (SASP)**
Changes in innate and adaptive immunity with age contribute to decreased efficiency of responses to new infections, poorer immunity to previously encountered pathogens and the development of chronic, low-grade inflammation and autoimmunity.

An aged, senescent immune system has a causal role in driving systemic ageing and therefore represents a key therapeutic target to extend healthy ageing.

Yousefzadeh, M.J., Flores, R.R., Zhu, Y. *et al.* An aged immune system drives senescence and ageing of solid organs. *Nature* (2021). https://doi.org/10.1038/s41586-021-03547-7

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Baby Boomers are Aging

According to the projections of World Population Prospects 2019
from the United Nations' Department of Economic and Social Affairs (DESA)

The number of

people aged over 80 will triple in the next 30 years

https://population.un.org/wpp/Publications/Files/WPP2019_Highlights.pdf

FRAILTY

Images and titles courtesy of Clinical Frailty Scale Geriatric Medicine Research, Dalhousie University, Halifax, Canada

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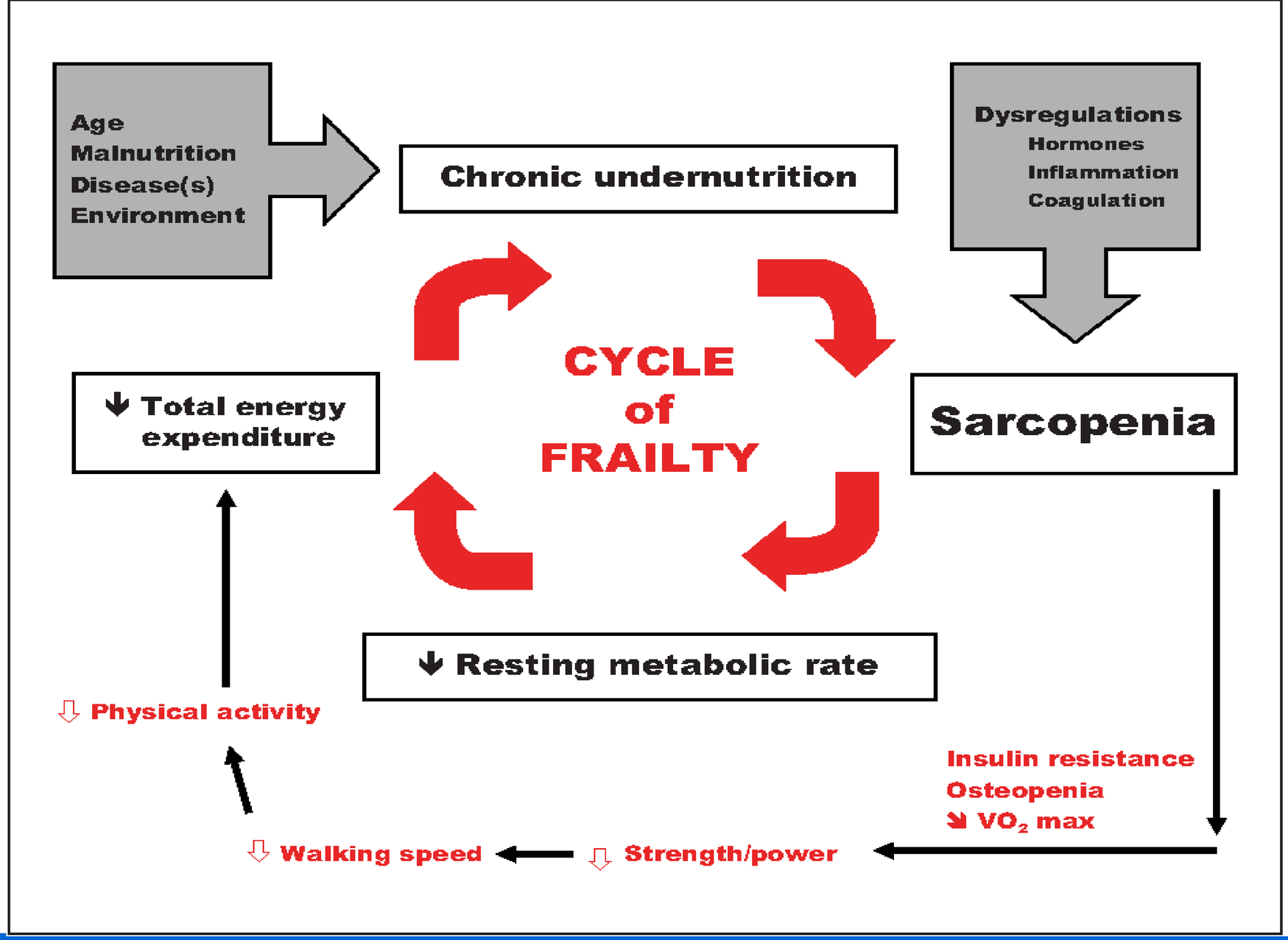
Inspiring Minds

FRAILTY

The syndrome of geriatric frailty reflects impairments in the regulation of multiple physiologic systems, embodying a lack of resilience to physiologic challenges and thus elevated risk for a range of deleterious endpoints: disability, falls, hospitalization, institutionalization, mortality

Abnormal Weight Loss
Sarcopenia
Osteopenia
Anemia
Autonomic Dysfunction
Cognitive Decline
Impaired Motor Function
Impaired Sensory Function

Fatigue-Exhaustion
Activation of Inflammation
Activation of Coagulation
Hypovitaminosis
Hypochlorhydria
Malnutrition



Color version available online

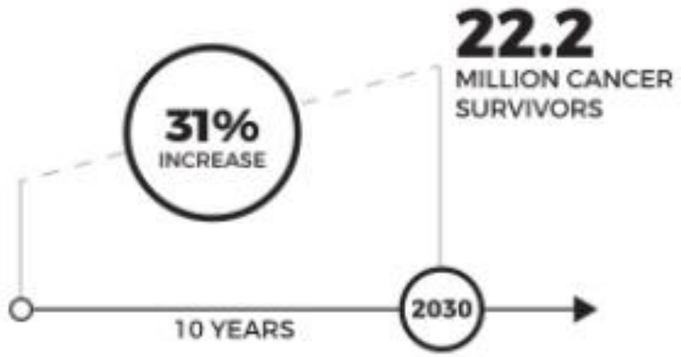
WHY is CANCER a DISEASE of AGING?

The process of aging is a central component of cancer evolution and progression

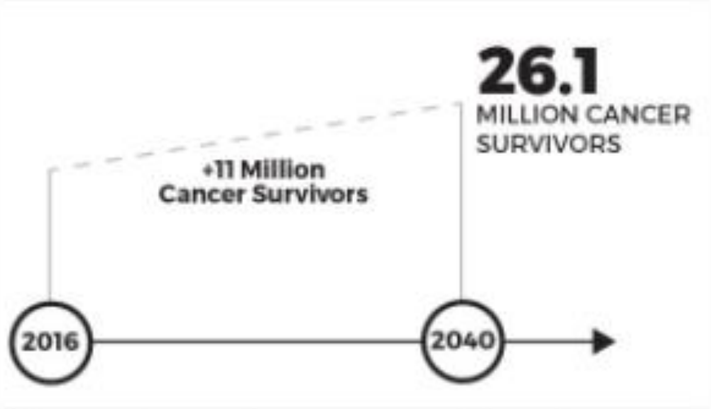
FRAILTY INFLAMMATION IMMUNITY

- Inflammation
- Oxidative Stress
- Cellular senescence
- Immuno-senescence
- DNA Methylation
- Somatic Mutations in Normal Cells
- Telomere Length
- Mitochondrial Dysfunction

Age is the most important risk factor for tumorigenesis. More than 60% of new **cancers** and more than 70% of **cancer** deaths occur in elderly subjects >65 years. The immune system plays an important role in the battle of the host against **cancer** development.



The number of cancer survivors is projected to increase by 31.4%, to 22.2 million, by 2030.[1]



The number of cancer survivors is projected to grow to 26.1 million by 2040.[1]

Over the next decade, the number of people who have lived 5 or more years after their cancer diagnosis is projected to increase approximately 33%, to 15.1 million.[1]

https://cancercontrol.cancer.gov/ocs/statistics

In 2019, **67%** of survivors (10.3 million) have survived 5 years or more after diagnosis; **45%** have survived 10 years or more; and **18%** have survived 20 years or more.[1]

https://cancercontrol.cancer.gov/ocs/statistics

64% of survivors are currently age 65 or older.[1]

It is estimated that by 2040, 73% of cancer survivors in the United States will be age 65 or older.[2]

Among today's survivors, the most common cancer sites represented include female breast (23%, 3.9 million), prostate (22%, 3.7 million), colorectal (9%, 1.5 million), melanoma (8%, 1.4 million), and gynecologic (8%, 1.3 million).* [1]

https://cancercontrol.cancer.gov/ocs/statistics

HALLMARKS of AGING

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HALLMARKS of AGING

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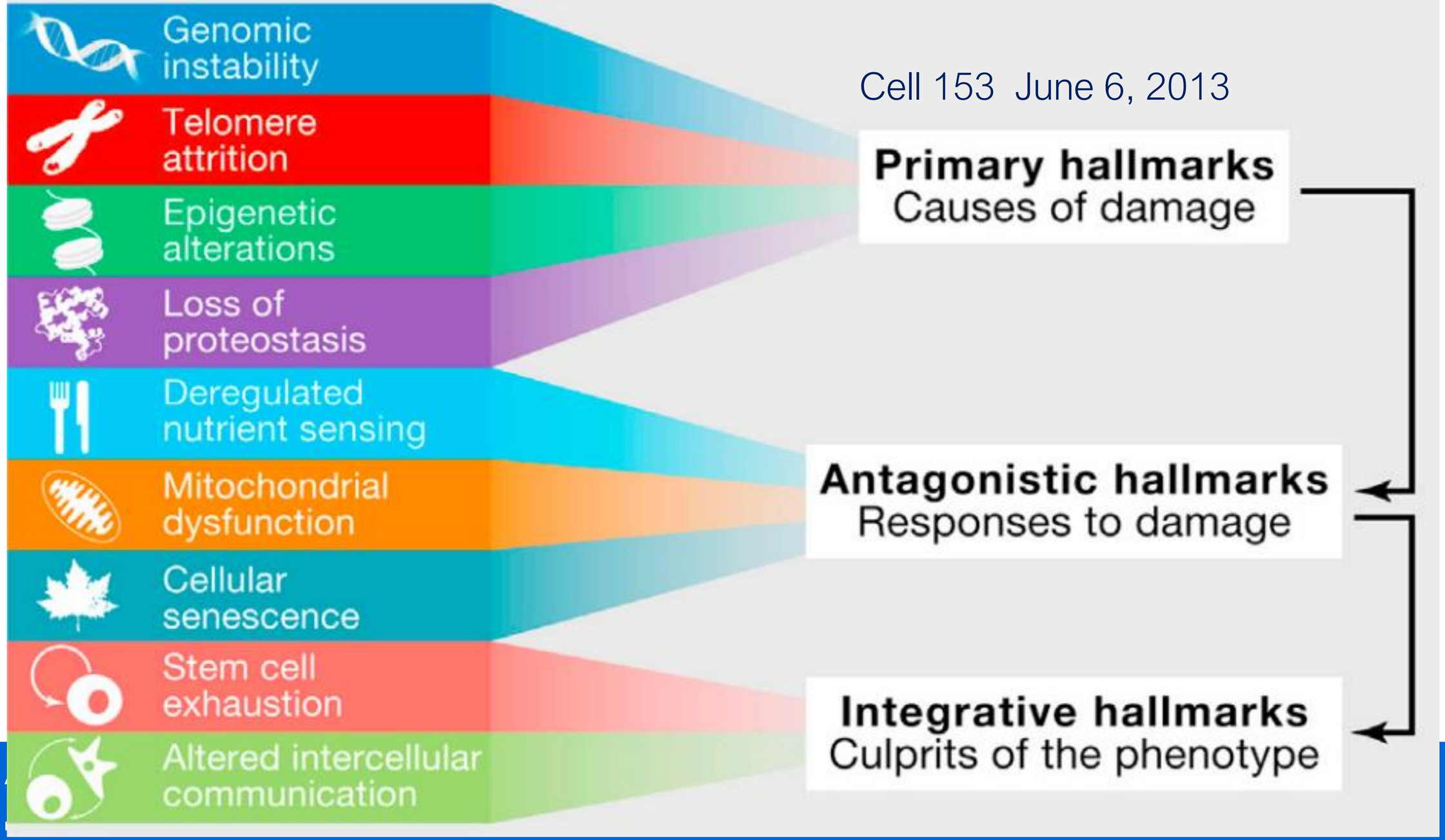
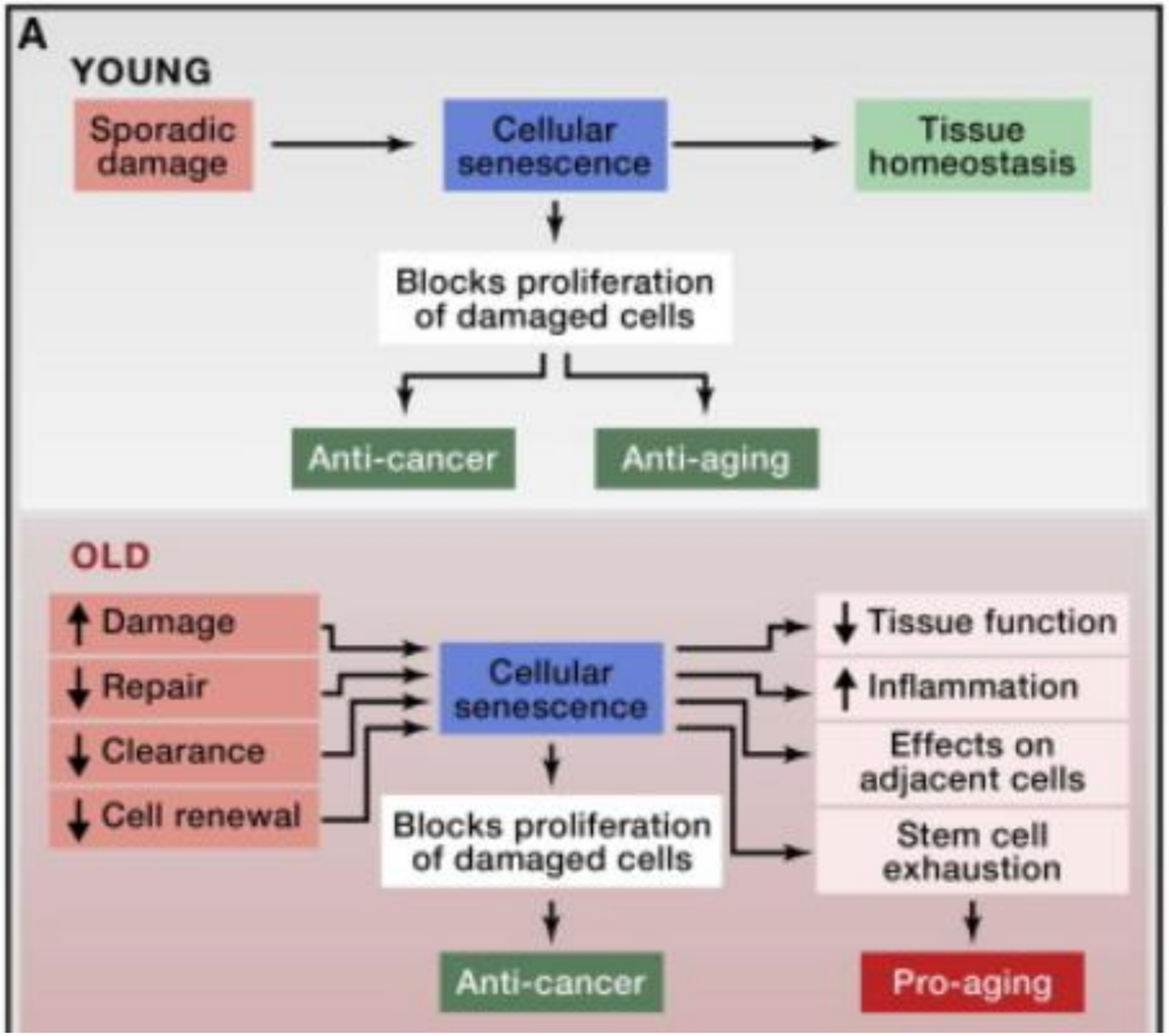
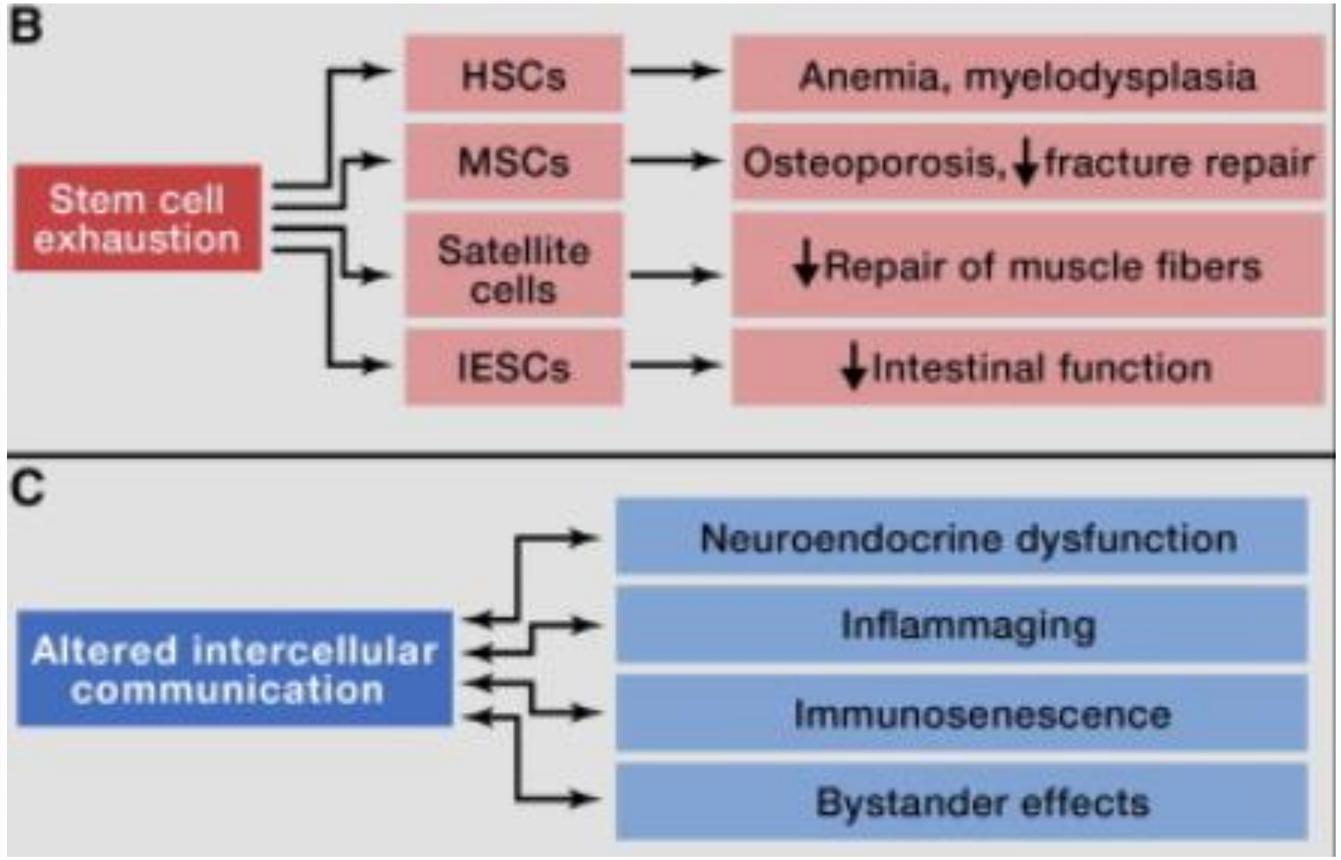
Functional Interconnections between HALLMARKS of Aging



Cellular Senescence, Stem Cell Exhaustion and Altered Intercellular Communication





CALORIC RESTRICTION, AGING and LONGEVITY

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Caloric Restriction Extends Lifespan

Caloric restriction (CR) is the most effective intervention into the aging process and maximum life span and it is mediated in part by epigenetic mechanisms
(Sinclair 2005; Weindruch et al. 1986).

The restriction of total calories by 25–60% relative to normally fed controls wihle providing essential nutrients can lead to a 50% increase in lifespan (Colman et al. 2009; Cruzen and Coleman 2009; Holloszy and Fontana 2007, Li et al. 2011).

DNA methylation may be altered in response to CR through its effects on specific gene loci leading to increased longevity (Hass et al. 1993).

SIRT1, an important HDAC in the aging process, is strongly linked to CR. For example, many studies have shown that its activity is affected by CR both in vitro and in vivo (Cohen et al. 2004; Lin et al. 2000; Guarente and Picard 2005; Leibiger and Berggren 2006).
The longevity-extension effects of sirtuin were originally discovered in yeast (Guarente and Picard 2005) and activation of SIRT1 is often observed in various tissues of animals subjected to CR while inactivation of SIRT1 may lead to ablation of the lifespan extending effects of CR. It is therefore apparent that

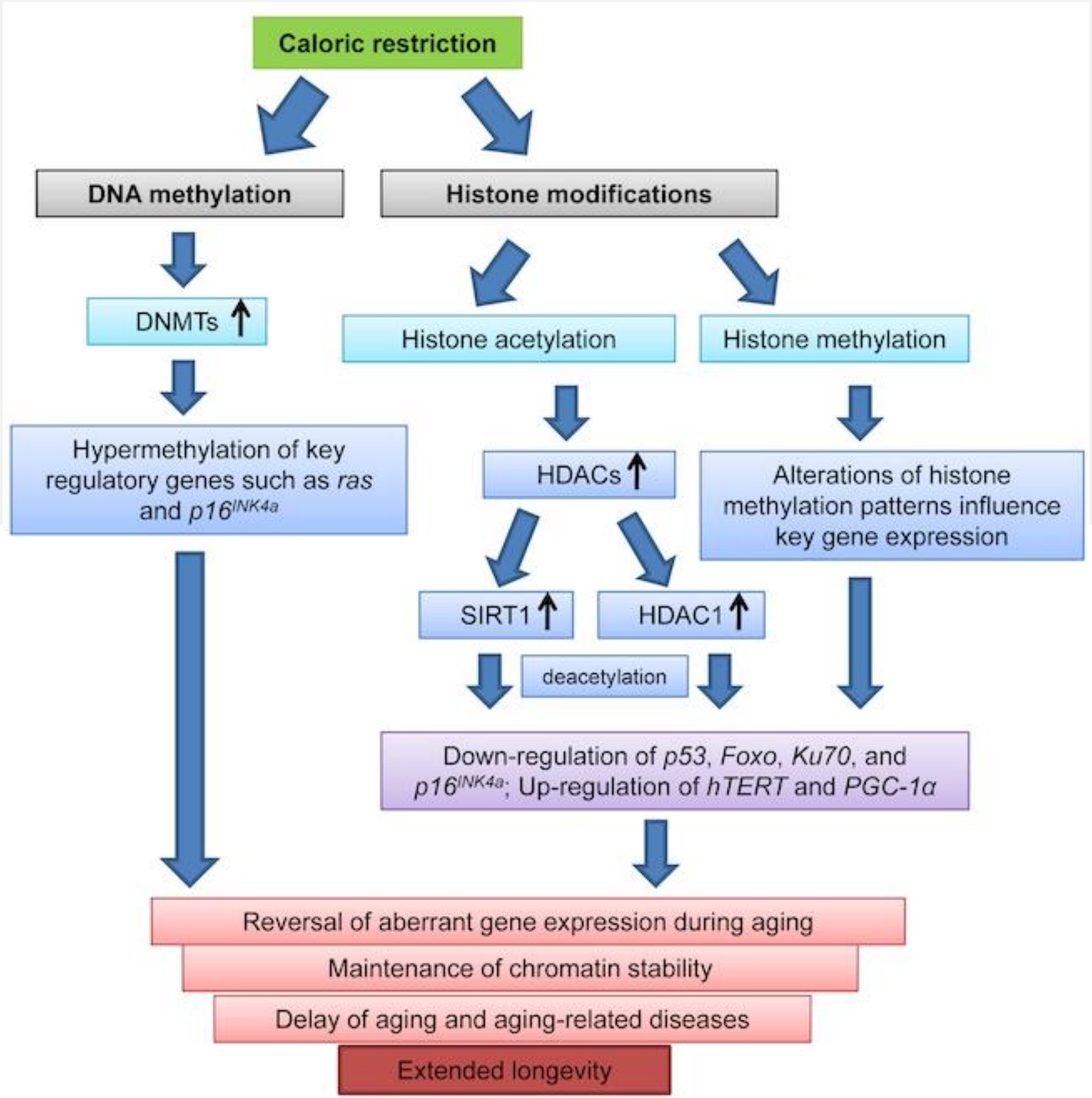
Epigenetic processes are not only central to the aging process, but that they are involved with key mediators of aging such as DNA methylation and SIRT

CALORIC RESTRICTION

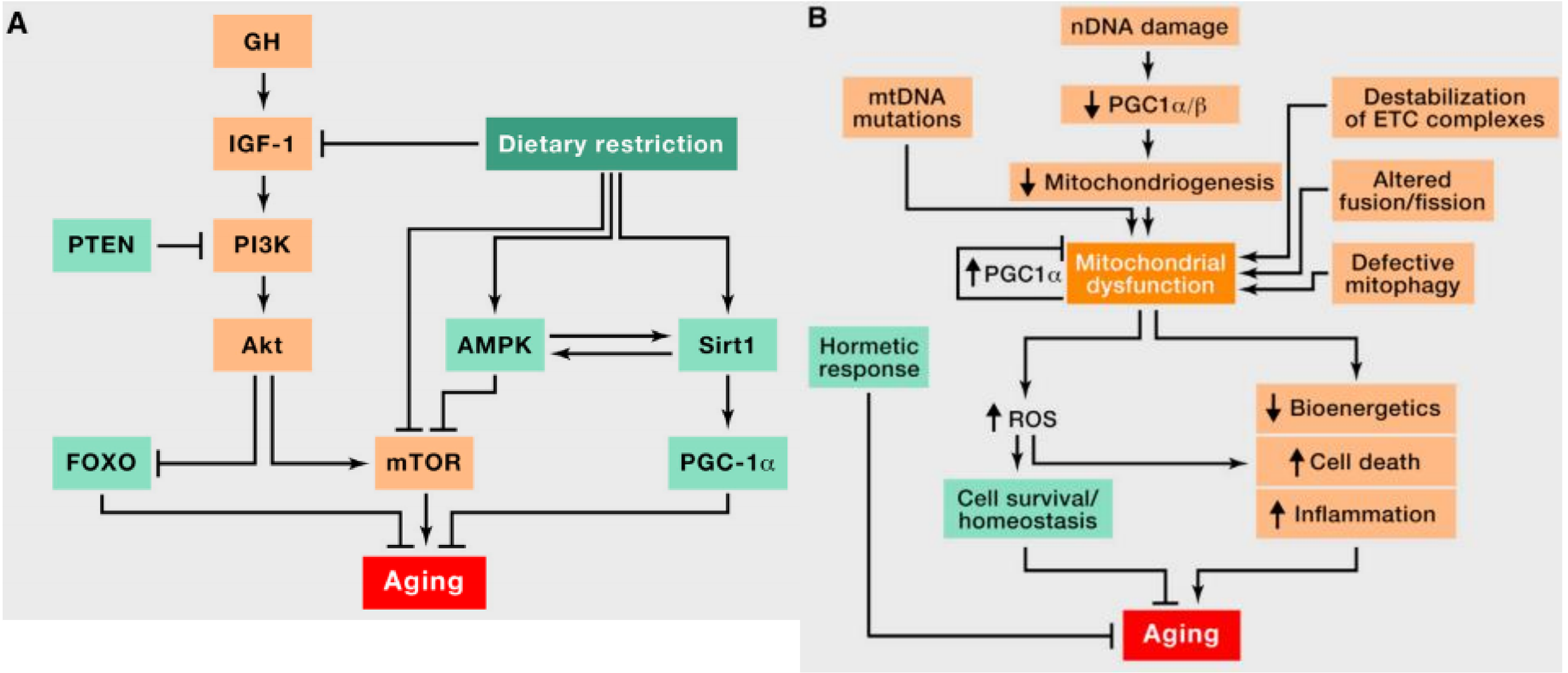
Delaying
Aging Processes
Extending Longevity

Epigenetic changes

in gene expression



CALORIC RESTRICTION and AGING



Summary of aging-related diseases affected by caloric restriction in experimental animal models and clinical trials

Diseases	Findings	Rodents	Nonhuman primates	Humans
Cancer	CR prevents a broad range of cancer incidences, including breast and gastrointestinal cancer.	Y	Y	Y/?
Diabetes	CR improves glucose homeostasis and prevents diabetes.	Y	Y	Y
Cardiovascular diseases	CR lowers blood pressure and favorably alters lipid profile, resulting in significantly reducing the risk of cardiovascular disease and related complications.	Y	Y	Y
Neurodegenerative diseases	CR reduces aging-associated neuronal loss and neurodegenerative disorders such as Parkinson's disease and Alzheimer's disease.	Y	Y	Y/?
Immune deficiencies	CR delays the onset of T-lymphocyte-dependent autoimmune diseases.	Y	Y/?	Y/?

*Li, Y., Daniel, M. & Tollefsbol, T.O. **Epigenetic regulation of caloric restriction in aging.** BMC Med 9, 98 (2011). https://doi.org/10.1186/1741-7015-9-98*

Recent studies have shown that intermittent fasting, protein restriction, and an epigenetic diet can have similar effects to those of CR.

Restraining insulin/IGF-1 signaling is the most effective and efficient intervention applicable to extend lifespan and prevent age-related diseases

The other mechanism that plays a role in CR-mediated anti-aging benefits is autophagy.

Mechanism pathway involved in calorie restriction effect.

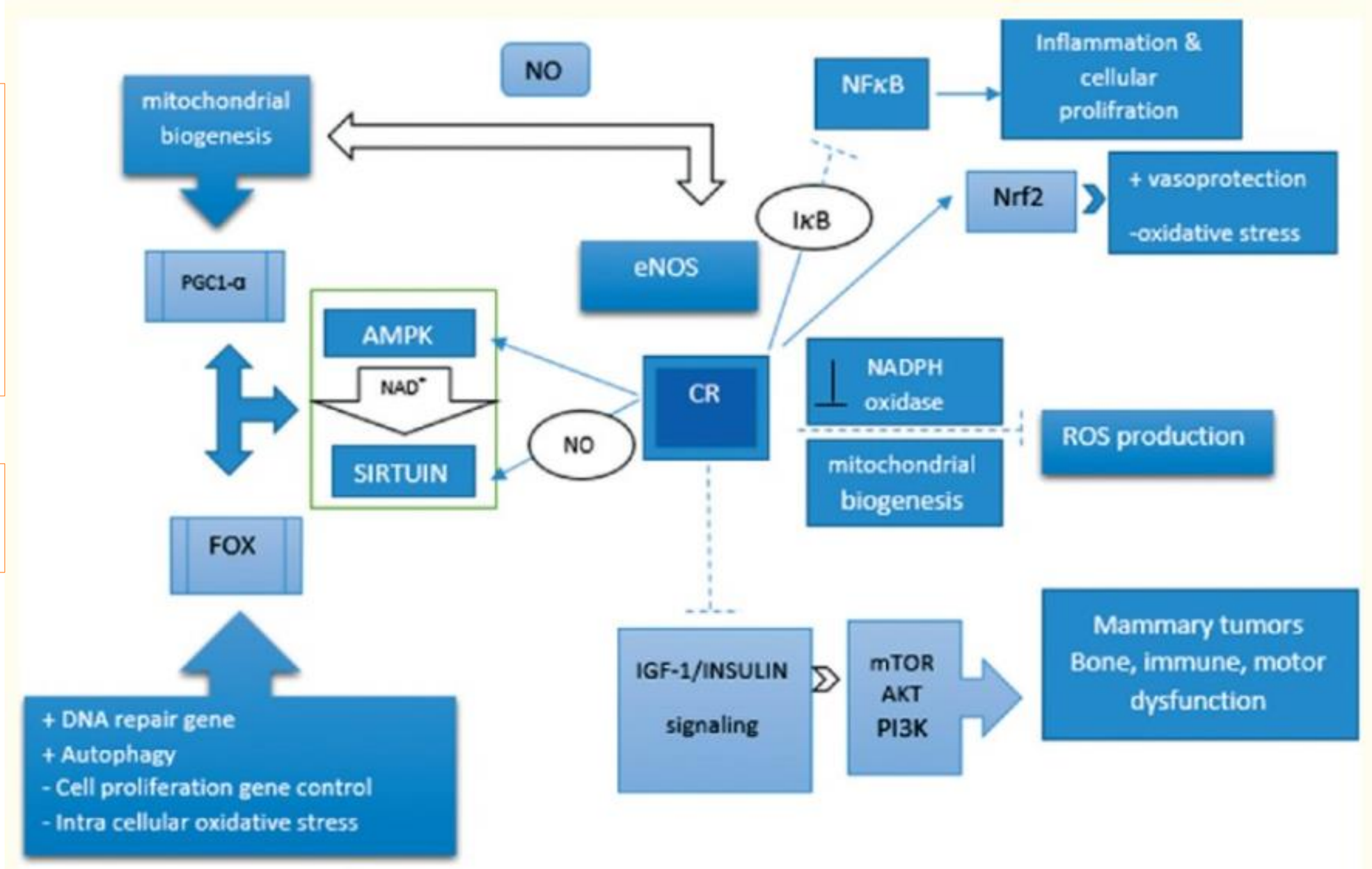
Calorie restriction upregulates activated protein kinase (AMPK) and sirtuin pathways and downregulates (IGF-1)insulin-like growth factor 1/insulin pathway.

Generally, calorie restriction activates a pathway that reduces inflammation, reactive oxygen species production, and oxidative stress by improving mitochondrial biogenesis and detoxifying enzyme activity.

Moreover, it can regulate cell proliferation and differentiation by regulating nuclear factors

Mechanism pathway involved in calorie restriction effect.

induce: --->
inhibit: ---|



Contraindications to Fasting and Calorie Restriction

- Children & Teenagers under 18 who are still growing
- Pregnant Women and Breast-Feeding Mothers
- Recovering from Surgery
- Eating Disorders
- Insulin dependent Type 1 Diabetes
- Sarcopenia
- Underweight
- Active Infection
- Mental Illness
- Medications: Insulin and Diabetes Drugs, Anti-coagulants, Anti-hypertensives, Psychiatric medications, thyroid medications, diuretics, cardiovascular medications, seizure medications

NEURO-IMMUNO-INFLAMMAGING

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Neuro-Immuno-INFLAMMAGING

Corbi G, Conti et al

Dietary Phytochemicals in Neuroimmunoaging: A New Therapeutic Possibility for Humans?

Front Pharmacol. 2016 Oct 13;7:364.
doi: 10.3389/fphar.2016.00364.
PMID: 27790141; PMCID: PMC5062465.

Phytochemicals Effects on Neuro-Immuno-Inflammaging.

Neuro-immuno-inflammaging is characterized by reduced SIRT1 and Nfr2 activity with consequent increased NF-κB activation. The increased NF-κB activation, also trough Toll Like Receptors (TLR), induces in turn raised proinflammatory factors such as TNFa, IL1b, IL6, iNOS.

The disequilibrium between anti- (IL10) and pro-inflammatory molecules determines increased inflammation, and a vicious circle is established that sustains neuroinflammaging. The phytochemicals (like curcumin, resveratrol, sulforphane, etc.) inducing increase in Nrf2 and SIRT1 activity could be able to inhibit the NF-κB activation and then to break the vicious circle ending the progression of the brain aging.

NEURO-INFLAMMATION 2-4g/day

H. Green Tea Catechins	NFkB,TNFa,IL1B,COX-2
Rz. Curcuma longa	COX 2, NFkB, TNFa, IL6, IL1
Curcuminoids	LOX5, CRP, IL8
O-3 FA EPA DHA	COX 2, LOX5, PGE2, IL1, IL6, TNFa, CRP
Probiotics	TNFa, IL6, IL 10, NFkB
Rx. Scutellaria baicalensis	TNFa IL-6 IL-1 NFkB
Baicalein polyphenol	COX-2
Berberine alkaloid	IL-6 TNFa IL1
Ganoderma polysaccharide	TNFa, IL1B1,IL6
Resveratrol stilbene	COX1, COX2, NFkB, IL1, IL6, IL8
Boswellia serrata-AKBA	IL1, IL2, IL6,IFN,TNFa, NFkB, IL10,PGE2

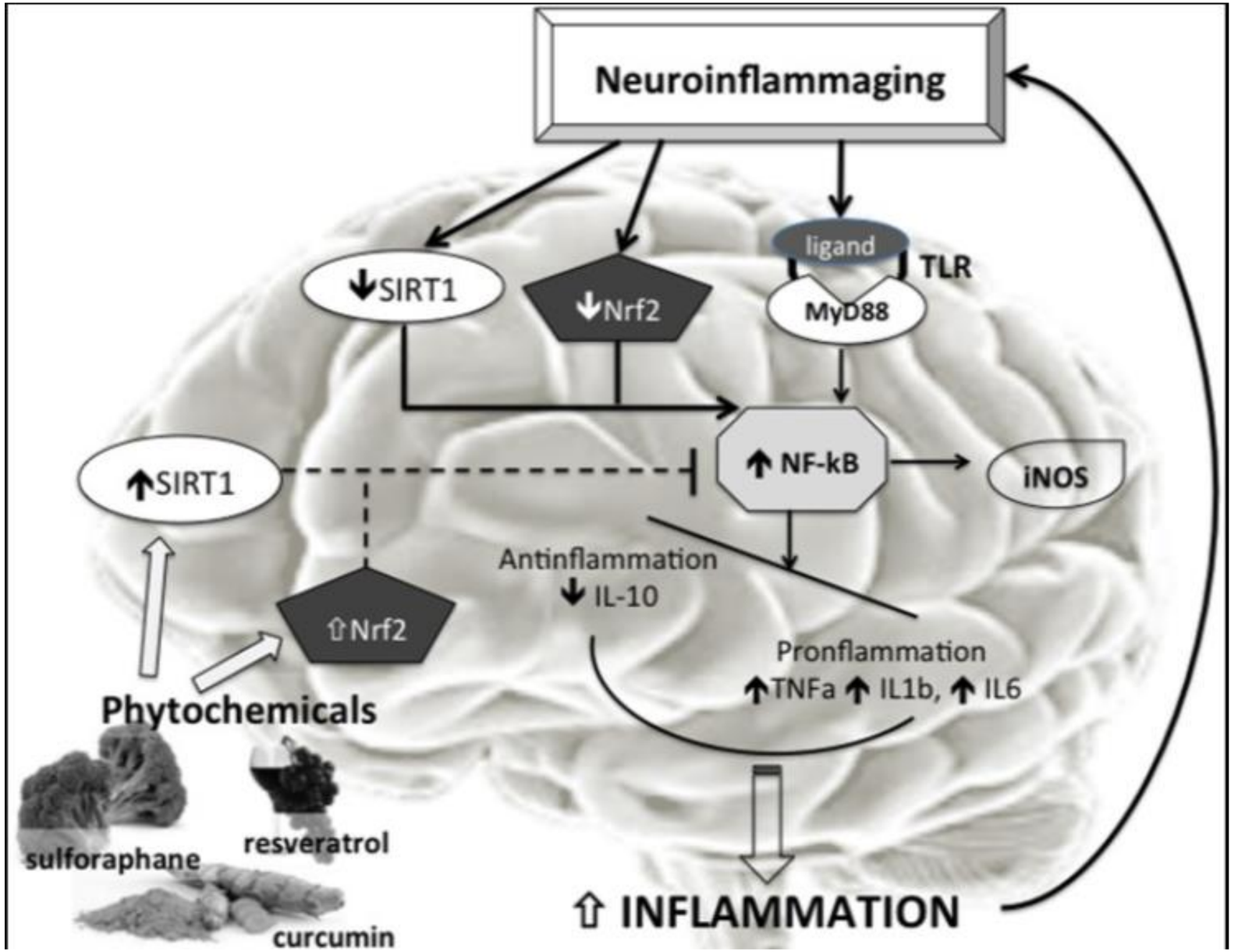






Phytochemicals effect on Neuro-inflammaging.

Ferulic Acid
Pterostilbene
Resveratrol
Curcumin
Sulforaphane
EGCG
O3-FA



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Dietary Phytochemicals in Neuroimmunoaging: A New Therapeutic Possibility for Humans?
Front Pharmacol.
2016 Oct 13;7:364.
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PMID: 27790141

MICROBIOME + Epithelial Barrier of GI Tract in Elderly

Barriers of the gastrointestinal tract are more permeable in the elderly due to the presence of low-grade inflammation, and gut microbiota-related substances have been found in the circulation and tissues

Growing evidence has shown that the microbiota and their metabolites can modulate immune cells and cytokines through epigenetic modifications

One particular metabolite that has been associated with immune system function are the short-chain fatty acids (SCFAs), produced mainly by the gut microbiome from undigested complex carbohydrates in the host colon. **SCFAs have been shown to modulate inflammation**

Ray, D., & Yung, R. (2018). Immune senescence, epigenetics and autoimmunity. *Clinical immunology (Orlando, Fla.)*, *196*, 59–63. https://doi.org/10.1016/j.clim.2018.04.002

Rx: Prebiotics + Probiotics

SIRTUINS

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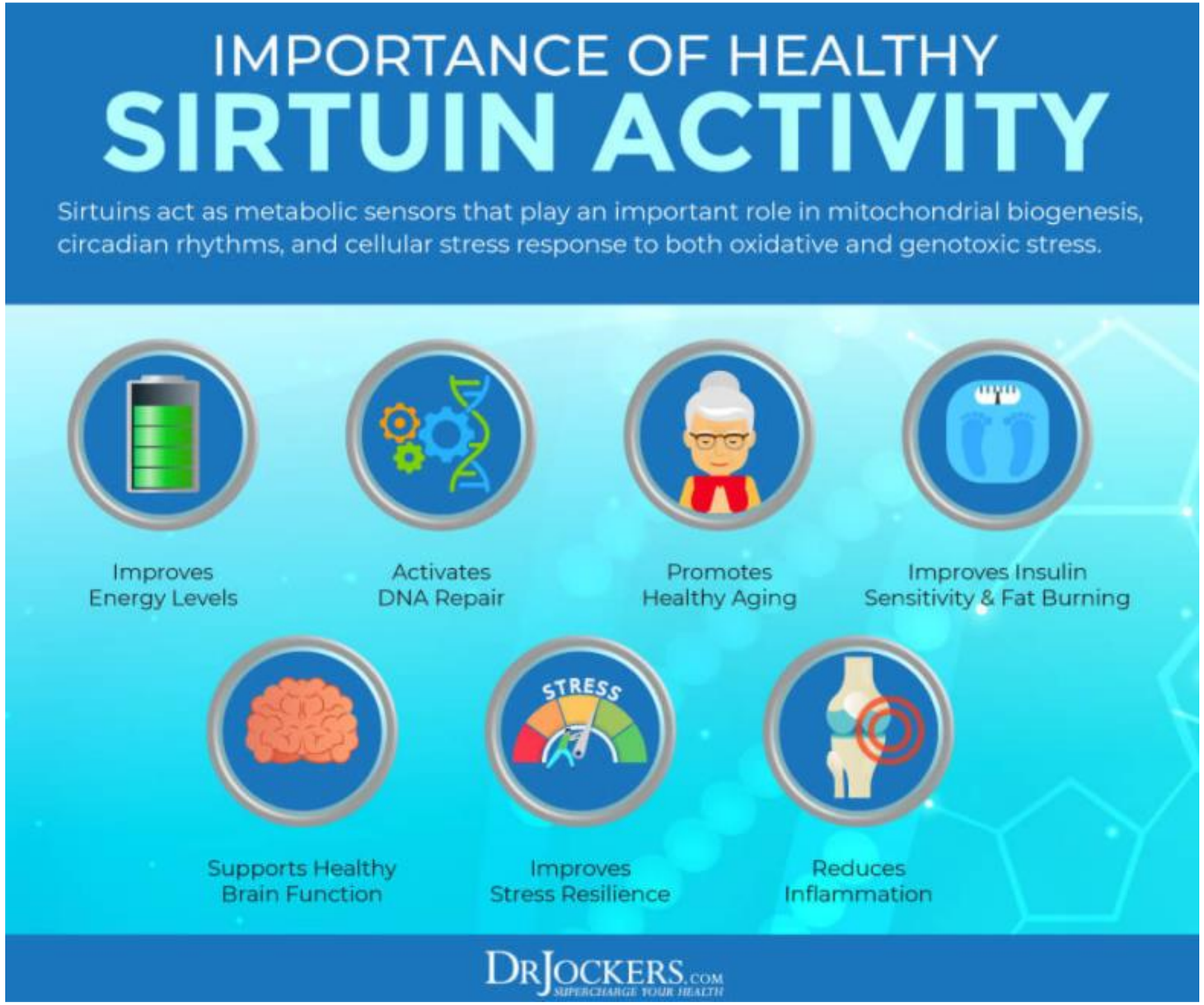


SIRTUINS

A family of NAD-dependent deacetylases
Regulators of Lifespan

Both nuclear and cytoplasmic targets

IMPACT
- Energy Metabolism (ATP)
- Oxidative Stress
- Inflammation
- Tumorigenesis
- Aging
- Diabetes II
- Stress Response

HUMAN SIRTUINS
SIRT1- 7

Nucleus: 1,6,7
Cytosol 1,2
Mitochondria 3,4,5

- Cardioprotective
- Neuroprotective
- Anti-Tumor
- Anti-Aging
- Promote Health span
- Promote Lifespan

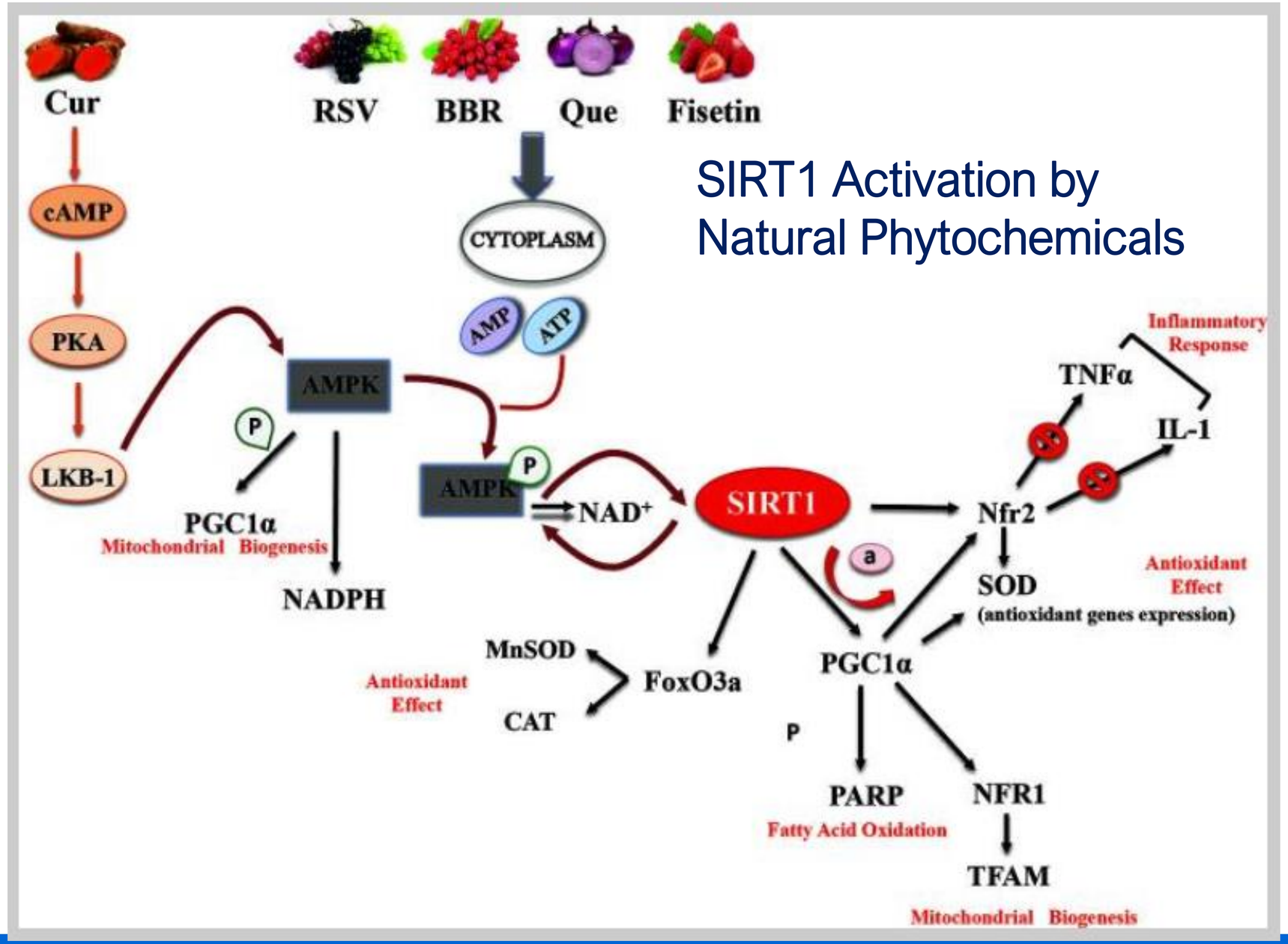
SIRTUIN ACTIVATORS

- Ginsenosides
- Salidroside
- Berberine
- Quercetin
- Curcumin
- Fisetin

- Co-Factors -> NAD+
- NMN
- NR

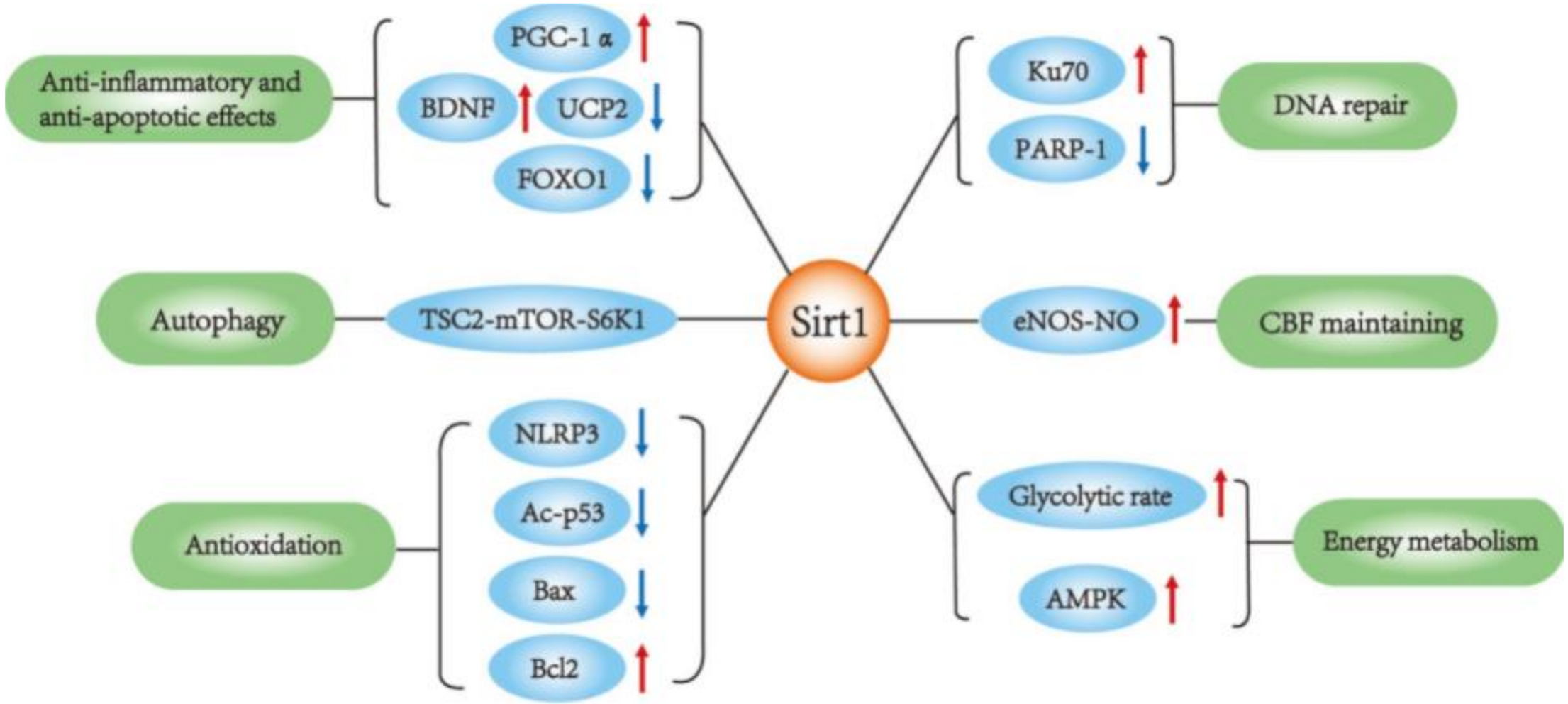
- Caloric Restriction
- Fasting/Intermittent Fasting
- Exercise

Basic mechanisms and effects of SIRT1 activation by polyphenol and non-polyphenol molecules.



Front Pharmacol. 2020; 11: 1225.
Published online 2020 Aug 7. doi: 10.3389/fphar.2020.01225
SIRT1 Activation by Natural Phytochemicals: An Overview
Concetta Iside, et al

SIRT1 interacts with multiple targets of regulation of apoptosis, autophagy, DNA repair, inflammation, metabolism and oxidative stress, cerebral blood flow



NAD+ PRECURSORS

Nicotinamide Adenine Di-Nucleotide

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Increasing NAD levels may aid Healthy Aging

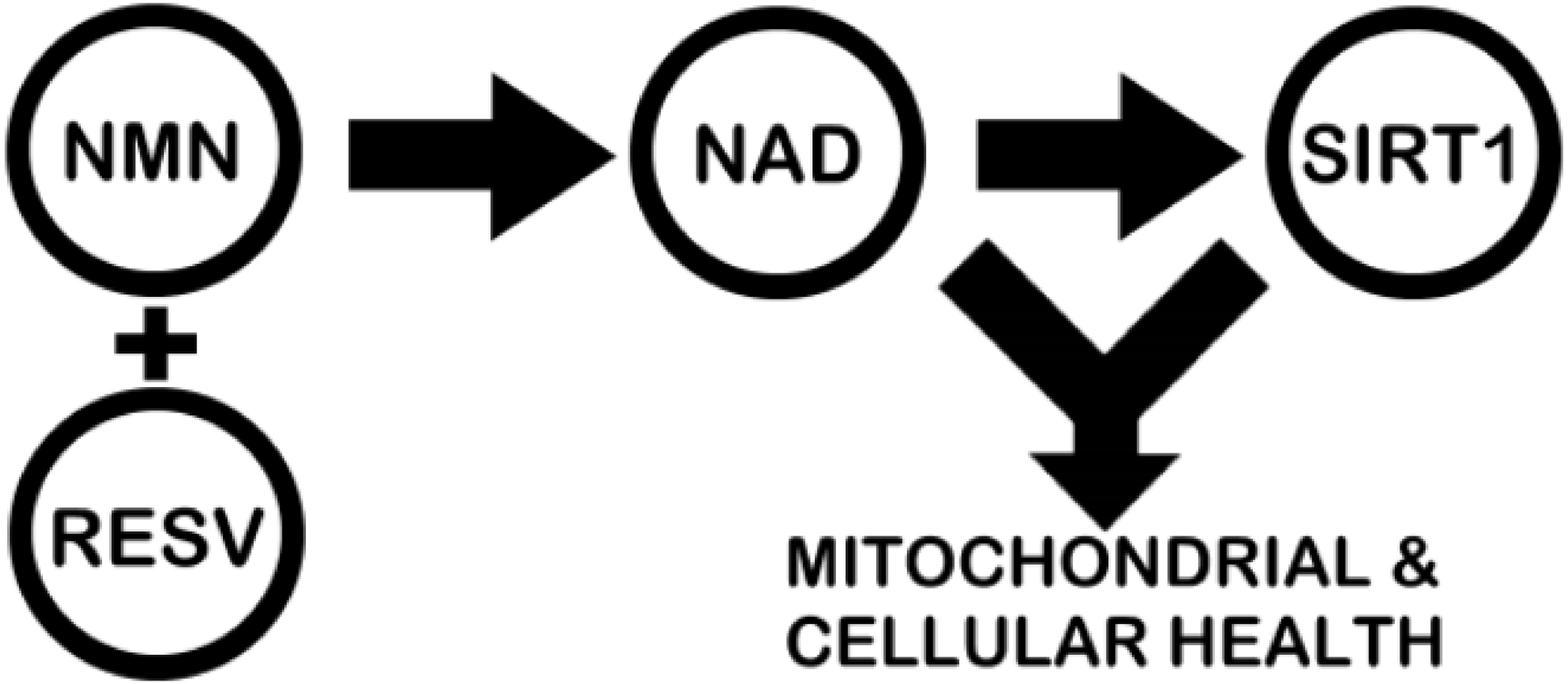
NAD levels are lower with advanced age

Deficiency may increase risk of

- Oxidative damage
- Diabetes II/Glucose metabolism dysfunction
- Neurodegenerative disorders
- Disrupted Circadian Rythyms

Aging: Declining levels of NAD and SIRT1

Declining levels of both NAD and SIRT1 contribute to mitochondrial dysfunction and the aging process



Nicotinamide Adenine Dinucleotide (NAD+) is an essential coenzyme found in all living cells.

NAD+ precursors: B3 vitamins niacin (NA), nicotinamide (NAM), nicotinamide riboside (NR).

NICOTINAMIDE RIBOSIDE (NR):
NR has a dose-response effect on blood NAD+ levels,

NR shows improvements in cardiovascular health, liver health, body composition, and mitochondrial function.

Safety profile is established, validated, and vetted, numerous additional studies in humans are ongoing or have recently completed.

Nicotinamide Ribonucleoside (NR)
NAD+ Precursor

- Supports healthy NAD+ levels, and thus ATP production in all cells of the body and plays a role in cellular repair and protects against DNA damage and oxidative stress.*

- Supports the number and health of mitochondria for ATP (cellular energy) production.*

- Supports sirtuin activity – which, in turn, supports numerous functions associated with aging and cellular metabolism.*

- Supports healthy metabolic function – including fat and glucose metabolism.
  Supports exercise efficiency and healthy lean body composition.*

- Supports healthy methylation, which is necessary for the production of neurotransmitters and DNA, as well as healthy homocysteine levels.*

Nicotinamide Mononucleoside (NMN)

NMN is a SIRT Activator

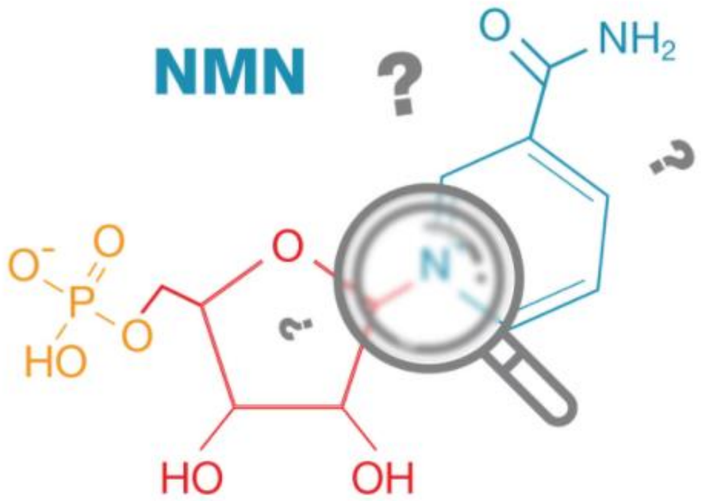
Sirtuins Govern

- Homeostasis
- Cell cycle
- Apoptosis

And Mediate

- Mitochondrial Function
- Inflammation
- Stress Response
- Cardiovascular Function
- Neurological Function
- Life Span

NMN: Nicotinamide Mononucleoside
Mostly Murine Studies



Benefits,

- Promotes Vascular Health/Circulation
- Protects against CVD
- Improves Muscle Endurance/Strength
- Improves Insulin sensitivity, Reduces risk of Obesity
- Reduces risk of Diabetes
- Enhances Mitochondrial Function

Side Effects: No adverse effects at recommended doses in one human study and multiple murine studies

Dosing 250 -500mg daily (best combined WITH resveratrol)

Nicotinamide Mononucleotide (NMN)
NAD+ Precursor

NMN is a direct and stable precursor to nicotinamide adenine dinucleotide (NAD+), a widely studied coenzyme present in all living cells and critical for energy production, DNA repair, and cell survival.

Impacts

- Energy production (mitochondrial ATP)
- Metabolism
- Aging/Telomere Length
- Gene expression/Methylation
- Stress response
- DNA repair
- Brain and Cognitive Function

NAD_Selected References

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mTOR Inhibition and Healthy Longevity

The TOR pathway regulates cell growth and proliferation, development, metabolism and aging in response to 4 major signaling cues
Growth Factors, Nutrients, Energy and Stress.

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mTOR and AGING

Ageing, the lifelong accumulation of damage to molecules, cells and tissues, is often associated with increased vulnerability to disease, such as cancer, cardiovascular and neurodegenerative diseases

Aging is a process subjected to regulation by classical signaling pathways and transcription factor, nutrient and stress sensors or reduced availability of growth factors alarm eukaryotic cells to **reduce their metabolic activity in order to survive**

One of the central regulators of cellular and organismal metabolism in eukaryotes is the target of rapamycin (TOR). TOR is an evolutionarily conserved nutrient-sensing Ser/Thr kinase

Inhibition of the mechanistic target of rapamycin (mTOR)

Extends life span and ameliorates aging-related pathologies including declining immune function

Phase 2a randomized, placebo-controlled clinical trial to determine whether low-dose **mTOR inhibitor therapy enhanced immune function and decreased infection rates in 264 elderly subjects** given the study drugs for 6 weeks.

mTOR inhibition was associated with a significant (P = 0.001) **decrease in the rate of infections reported by elderly subjects for a year after study drug initiation.**

In addition, we observed an **up-regulation of antiviral gene expression and an improvement in the response to influenza vaccination in this treatment grou**p. **Selective TORC1 inhibition has the potential to improve immune function and reduce infections in the elderly.**

Joan B. Mannick, Melody Morris et al. Sci Transl Med Volume 10(449):eaaq1564 July 11, 2018
TORC1 inhibition enhances immune function and reduces infections in the elderly

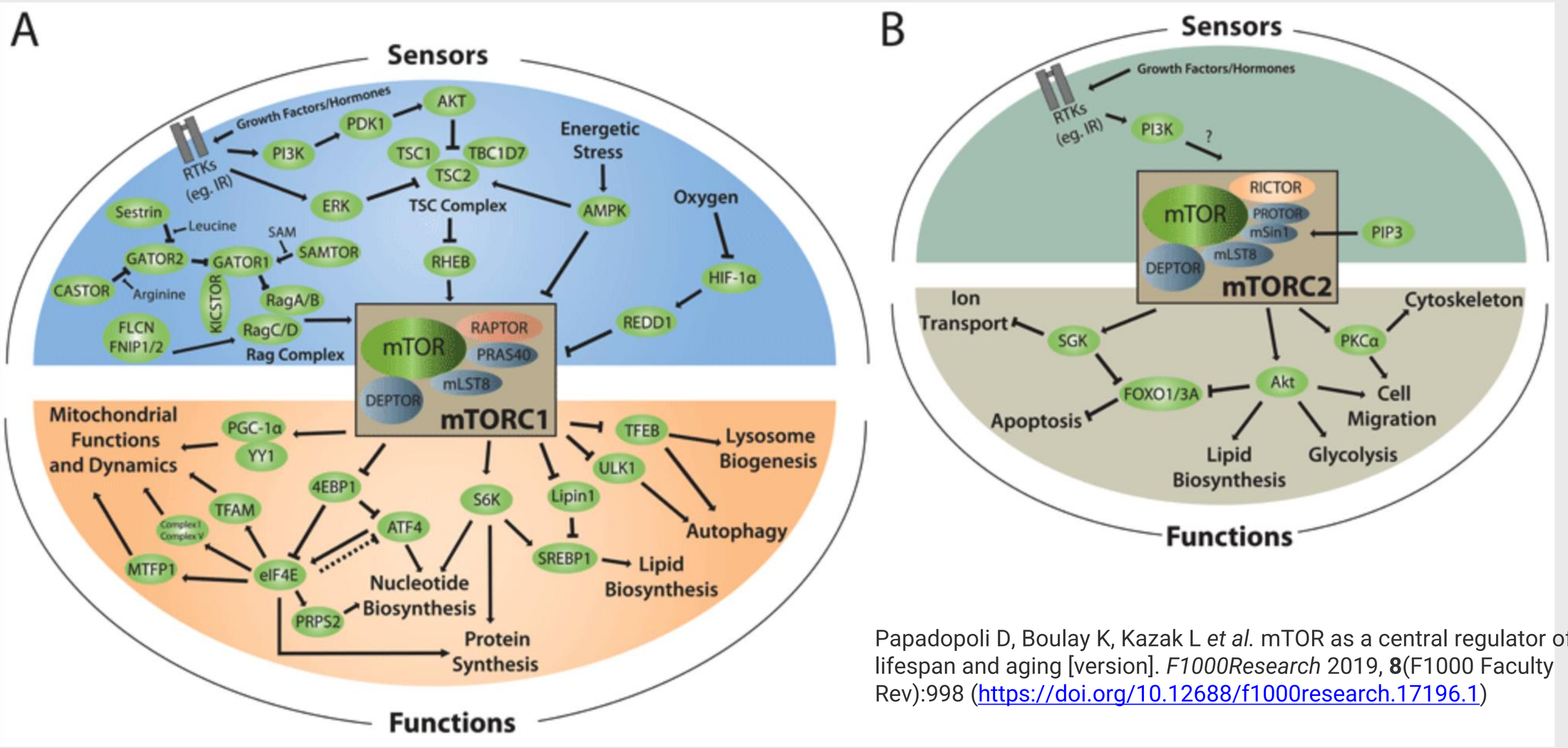
Dialing down mTORC1 dials up immunity

Aging may be regulated by a discrete set of intracellular proteins including the mechanistic target of rapamycin (mTOR) kinase.

mTOR has **extended life span in every species studied to date and ameliorated multiple aging-related pathologies including declining immune function.**

Mannick *et al*. now show that **low-dose TORC1 inhibitor therapy in elderly humans decreased the incidence of all infections, improved influenza vaccination responses, and up-regulated antiviral immunity.** Thus, targeting the TORC1 pathway that regulates aging may have clinical benefits for elderly humans including **improvement in immune function and decreased infection rates.**

Joan B. Mannick, Melody Morris et al. Sci Transl Med Volume 10(449):eaaq1564 July 11, 2018
TORC1 inhibition enhances immune function and reduces infections in the elderly

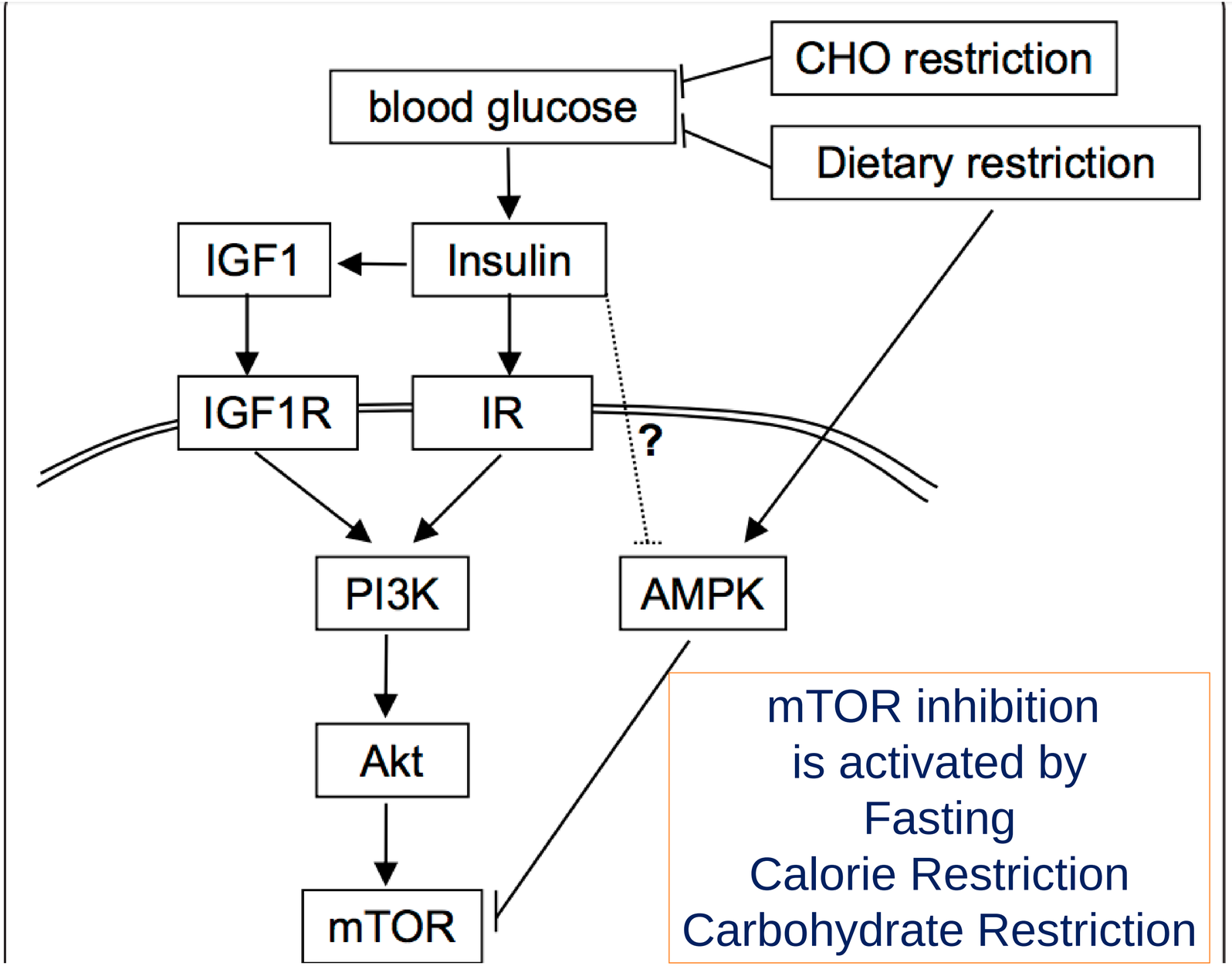


Papadopoli D, Boulay K, Kazak L *et al.* mTOR as a central regulator of lifespan and aging [version]. *F1000Research* 2019, **8**(F1000 Faculty Rev):998 (https://doi.org/10.12688/f1000research.17196.1)

Figure 1. mTOR acts as a nutrient sensor coordinating cellular functions linked to proliferation, growth, and survival.

Effects of short-term fasting on cancer treatment

de Groot et al.
Journal of Experimental & Clinical Cancer Research (2019) 38:209
https://doi.org/10.1186/s13046-019-1189-9



mTOR inhibition
is activated by
Fasting
Calorie Restriction
Carbohydrate Restriction

Selected Phytochemical mTOR Inhibitors

PHYTOCHEMICAL + SOURCE. (3-6 g day = Therapeutic dose)

- EGCG: Green Tea
- Ginsenoside Rg1: Rdx Panax ginseng
- Astragaloside: Rdx Astragalus membranaceus
- Curcumin: turmeric rhizome
- Reservatrol: Polygonum cuspidatum, red/purple grapes
- Genisten: soy isoflavone
- DIM 3,3-Diindolylmethane : cruciferous vegetables
- Honokiol :Chinese Magnolia Bark Cortex Magnolia Hou Po
- Caffeine
- Vitamin D3

Pharmaceutical:
Rapamycin
Everolimus
Sirolimus

The mTOR Signaling Pathway in Cancer and the Potential mTOR Inhibitory Activities of Natural Phytochemicals APJP_Volume 15_Issue 16_Pages 6463-6475

Phytochemicals That Inhibit mTOR

Phytochemical	Type of Neoplasm	Reference
Curcumin Curcuma Longa	Colorectal	Anticancer Res. 2009 August; 29(8): 3185
Curcumin Curcuma Longa	Multifocal	Cancer Res 2009;69(3):1000–8
Curcumin Curcuma Longa	Prostate	Cancer Ther. 2008 Sep;7(9):2609-20.
Curcumin Curcuma Longa	Leiomyosarcoma	Gynecol Oncol. 2011 Jul;122(1):141-8. Epub 2011 Mar 29.
Curcumin +EGCG Curcuma longa+ Camelia sinensis	Leiomyosarcoma	Int J Clin Oncol. 2012 Feb 15.
EGCG Camelia sinensis	Breast	Br J Cancer. 2008 Oct 7;99(7):1056-63. Epub 2008 Sep 16.
Isoliquiritigenin Glycyrhhiza spp	Adenoid Cystic Carcinoma	Apoptosis. 2012 Jan;17(1):90-101.

Phytochemicals That Inhibit mTOR

Phytochemical	Type of Neoplasm	Reference
Salidroside Rhodiola rosea	Bladder	Mol Carcinog. 2011 Apr 22. doi: 10.1002/mc.20780.
Ursolic Acid Salvia spp, Heydotis/Oldenlandia	Breast	Nutr Cancer. 2010;62(8):1074-86.
Withaferin A Withania somnifera	Colorectal	Mol Cancer Ther. 2010 Jan ; 9(1): 202–210
Silibinin Silybium marianum	Breast, Prostate	Mol Cancer Ther. 2009 Jun;8(6):1606-12. Epub 2009 Jun 9.
Apigenin Matricaria, Petroselinum,	Breast, Prostate, Colon, Cervical, Lung, Ovary, Skin Liver, Pancreas, Hematologic,	Anticancer Agents Med Chem. 2013 Sep; 13(7): 971–978 Biomed Pharmacother. 2018 Jul;103:699-707. doi: 10.1016/j.biopha.2018.04.072. Epub 2018 Apr 24.
Genistein Soy	Breast	Genome Med. 2010; 2(12): 90.
Honokiol Magnolia spp	Breast, Prostate, Renal, Brain	J Immunother. 2009 Jul-Aug; 32(6): 585–592. doi: 10.1097/CJI.0b013e3181a8efe6

Inhibition of mTOR

Phytochemical	Type of Neoplasm	Reference
Resveratrol Polygonum cuspidatum	Multifocal	.Ann N Y Acad Sci. 2015 Aug;1348(1):116-23. doi: 10.1111/nyas.12829. Epub 2015 Jul 22. Anticancer Agents Med Chem. 2013 Sep;13(7):1032-8.
Baicailein Scutellaria baicelensis	Prostate, Breast, Hepatic, multi	Int J Mol Sci. 2016 Oct; 17(10): 1681. Pub online 2016 Oct 9. doi: 10.3390/ijms17101681 Cancer Lett. 2015 Mar 28;358(2):170-179. doi: 10.1016/j.canlet.2014.12.033. Mol Cell Biochem. 2015 Aug;406(1-2):111-9. doi: 10.1007/s11010-015-2429-8.
Quercetin-Isoquercitrin Camelia sinensis, Cruciferae spp, Allium spp, Rubus spp, +	Renal, Prostate, Colon, multi	PLoS One. 2016; 11(6): e0157251. Pub online 2016 Jun 10. doi: 10.1371/journal.pone.0157251 PLoS One. 2012; 7(10): e47516. Pub 2012 Oct 18. doi: 10.1371/journal.pone.0047516 Molecules. 2016 Jan; 21(1): 108. Publ online 2016 Jan 19. doi: 10.3390/molecules21010108
Urolithin Punica granatum	Pancreatic	**Mol Cancer Ther DOI:** 10.1158/1535-7163.MCT-18-0464 Vol 8 (2) February 2019. AACR
Vitamin D Cholecalciferol	Breast	Int J Mol Sci. 2017 Oct 19;18(10). pii: E2184. doi: 10.3390/ijms18102184. J Nutr Biochem. 2018 Mar;53:111-120. doi: 10.1016/j.jnutbio.2017.10.013.
Calorie Restriction **Carbohydrate restriction**	Multifocal	Oncotarget. 2015 Oct 13;6(31):31233-40. doi: 10.18632/oncotarget.5180. Cell. 2017 Feb 23; 168(5): 775–788.e12.doi: 10.1016/j.cell.2017.01.040
Omega 3 Fatty Acid DHA	Prostate	Biomed Res Int. 2013;2013:568671. doi: 10.1155/2013/568671

AUTOPHAGY-MITOPHAGY

A dynamic recycling system contributing to cellular renovation and homeostasis, Autophagy is an anti-aging function.

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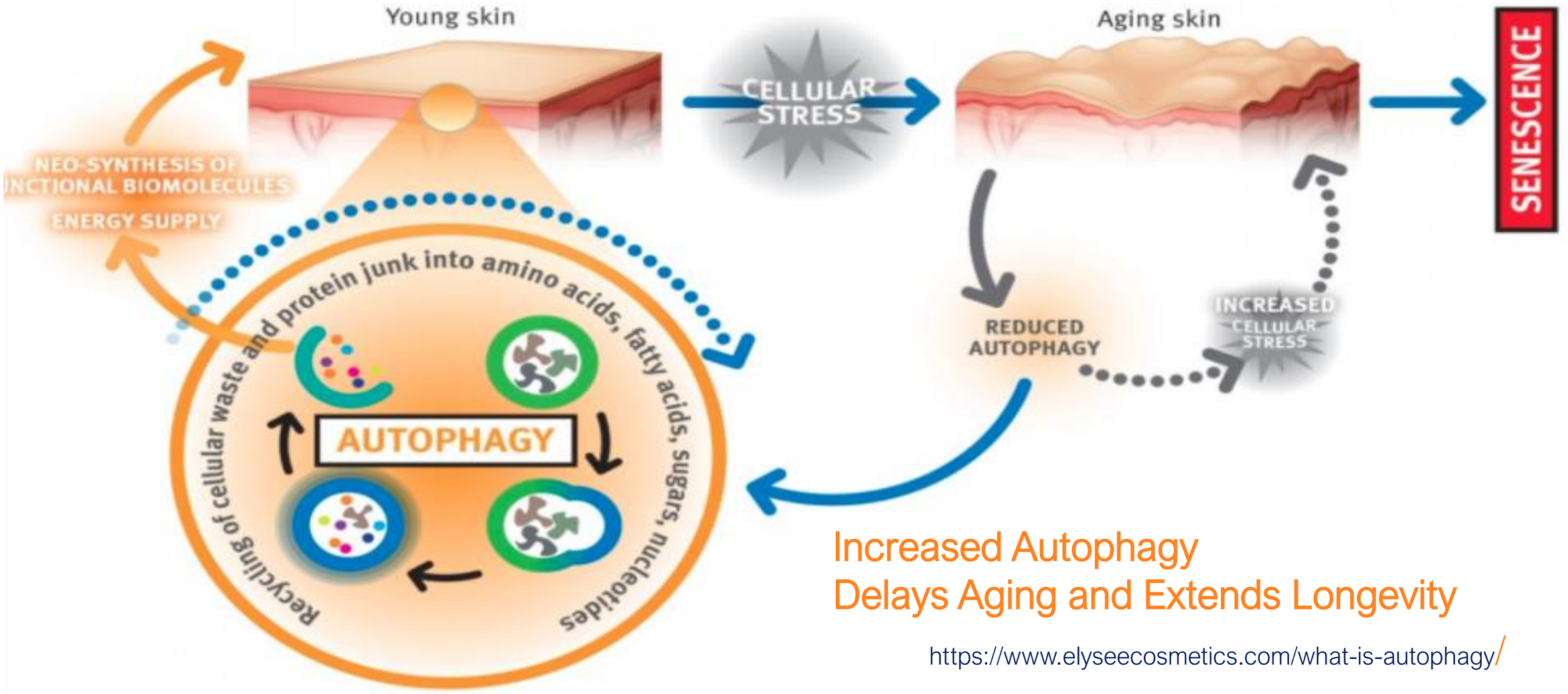
QUALITY CONTROL AUTOPHAGY and MITOPHAGY

Autophagic Cell Death:
Catabolic Process
degrades cellular contents and recycles damaged organelles

During autophagy, cells form autophagosomes that capture cellular contents and target them for degradation

By blocking growth signaling and promoting autophagosome formation, autophagy typically regulates protein levels and promotes survival in cells experiencing nutrient insufficiency and other types of stress

Generic autophagy processes



Increased Autophagy
Delays Aging and Extends Longevity

https://www.elyseecosmetics.com/what-is-autophagy/

QUALITY CONTROL AUTOPHAGY and MITOPHAGY

MITOPHAGY (Mitochondrial Autophagy). MEDIATED BY SIRT1

Mitochondrial quality, which is facilitated by coordination of degradation of defective mitochondria and their replacement by biogenesis, is one critical factor in keeping the levels of reactive oxygen species (ROS) low; therefore, it plays key roles for health and longevity of cells as well as tissues

However, under oxidative stress or during senescence or aging of cells, mitochondrial autophagy (mitophagy), a major mechanism for the removal of damaged mitochondria, is frequently impaired, and therefore mitochondrial quality deteriorates

Cells. 2021 Mar; 10(3): 612.
Published online 2021 Mar 10. doi: 10.3390/cells10030612 PMCID: PMC7999186PMID: 33802063
Nicotinamide Treatment Facilitates Mitochondrial Fission through Drp1 Activation Mediated by SIRT1-Induced Changes in Cellular Levels of cAMP and Ca^{2+} Seon Beom Song,

QUALITY CONTROL AUTOPHAGY and MITOPHAGY

Autophagy requires low protein and low carbohydrate intake

Caloric Restriction

- Fasting-Fasting Mimicking Diet
- Ketogenic diet

- TONIC LONGEVITY HERBS
- Panax ginseng
- Astragalus memranaceus
- Schizandra chinensis
- Rehmannia glutinosa
- Withania somnifera

- PHTYOCHEMICALS
- Resveratrol
- EGCG
- Curcumin
- Quercetin
- Silibinin

Mariño G, Pietrocola F, Madeo F, Kroemer G. Caloric restriction mimetics: natural/physiological pharmacological autophagy inducers .*Autophagy*. 2014;10(11):1879-1882. doi:10.4161/auto.36413

Caloric Restriction Caloric Restriction Mimetics

Mariño G, Pietrocola F, Madeo F, Kroemer G. Caloric restriction mimetics: natural/physiological pharmacological autophagy inducers. *Autophagy*. 2014;10(11):1879-1882. doi:10.4161/auto.36413

Autophagy and Caloric Restriction

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SUMMARY
IMMUNE RESTORATION
Promotion of Health Span and Life Span

- Caloric Restriction
- SIRT 1 Activation
- NAD+ Precursors
- mTOR Inhibition
- Autophagy_Mitophagy Activation

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IMPORTANT NUTRICEUTICALS

Omega 3 Fatty Acids
Vitamin D3

PHYTOCHEMICALS
Curcumin (curcuminoid)
EGCG (catechin)
Resveratrol (stilbene)
Ginsenoside Rgb1 (ginsenoside)
Astragaloside (polysaccharide)
Salidroside aka Rhodioloside (glucoside)
Berberine (isoquinoline alkaloid)
NAD Precursors:
- Nicotinamide Riboside (NR) David Sinclair
- Nicotinamide Monenucleotide (NMN)

LIFESTYLE INTERVENTIONS

The Blue Zones: regions of the world where a higher than usual number of people live much longer than average

Food/Diet Epigenetic Effects

- Intermittent Fasting: Valter Longo
- Calorie Restriction: David Sinclair

Hydration

Sleep

Exercise-Body Composition, Insulin Sensitivity,

Parasympathetic Regulation: Heart Rate Variability (oura ring)

- Nature
- Meditation-Relaxation
- Stress Modulation

Family-Community- Avoiding Isolation

Golden Pearls of Chinese Longevity Medicine

PhytoMedicine:

Rdx Panax Ginseng, Rdx Astragalus membranaceus, Rdx Rehmannia

Kidney Yin Tonics/ Restore Left/Zuo Gui Yin

Kidney Yang Tonics/Restore Right/You Gui Yin

MycoMedicine: Ganoderma lucidum, Coriolus versicolor

Acupuncture : Su San Li (St 36) Point of Longevity,

Qi Hai (CV 6) Gate of Qi. Tai Xi (Kid 3) Great Stream

Tai Chi/Chi Gung

Selected Dietary Phytochemicals with Epigenetic Effects:

EGCG, Resveratrol, Sulforaphane, Genistein, Curcumin, Ginsenosides,
Polyphenols: Baicalin, Baicalein, Alkalioids:Berberine

Dietary Epigenetics in Cancer and Aging Cancer Treat Res. 2014 ; 159: . doi:10.1007/978-3-642-38007-5_15.

Healthy Aging SUMMARY NOTES

www.aiiore.com/nanp23

Dr. Nalini Chilkov, L.Ac. OMD support@aiiore.com

IMMUNITY and AGING

Promoting Health Span and Life Span

- Caloric Restriction
- NAD+ Precursors
- SIRT 1 Activation
- mTOR Inhibition
- Autophagy & Mitophagy

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