When we talk about aging, what are we afraid of?

250904 科普讲堂

组织者：王红蕾
组员：　陆彤
　　梁艺鸽

The global population is aging at an unprecedented rate

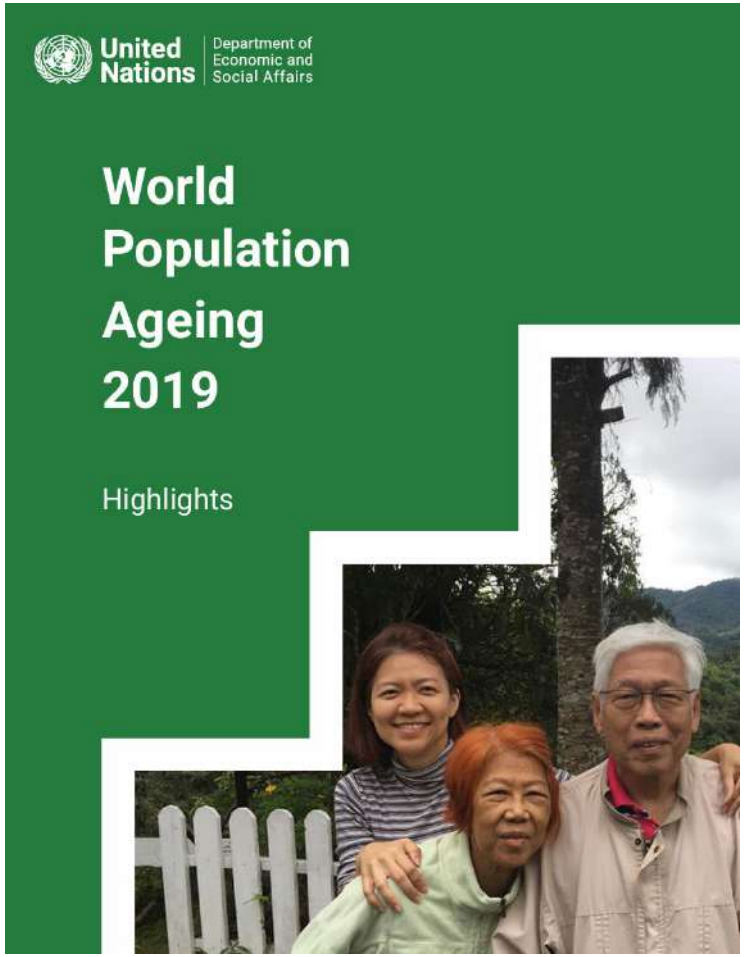


Table 1.
Number of persons aged 65 years or over by geographic region, 2019 and 2050

Region	*Number of persons aged 65 or over in 2019 (millions)*	*Number of persons aged 65 or over in 2050 (millions)*	*Percentage change between 2019 and 2050*
World	**702.9**	**1548.9**	**120**
Sub-Saharan Africa	31.9	101.4	218
Northern Africa and Western Asia	29.4	95.8	226
Central and Southern Asia	119.0	328.1	176
Eastern and South-Eastern Asia	260.6	572.5	120
Latin America and the Caribbean	56.4	144.6	156
Australia and New Zealand	4.8	8.8	84
Oceania, excluding Australia and New Zealand	0.5	1.5	190
Europe and Northern America	200.4	296.2	48

Source: United Nations, Department of Economic and Social Affairs, Population Division (2019). *World Population Prospects 2019.*

*Excluding Australia and New Zealand.

It scared people to realize we are getting old.

Aging is characterized by a gradual decline in physiological function, resulting in increased susceptibility to diseases and eventual mortality.

C. Lopez-Otin, et al., *Cell*, 2023

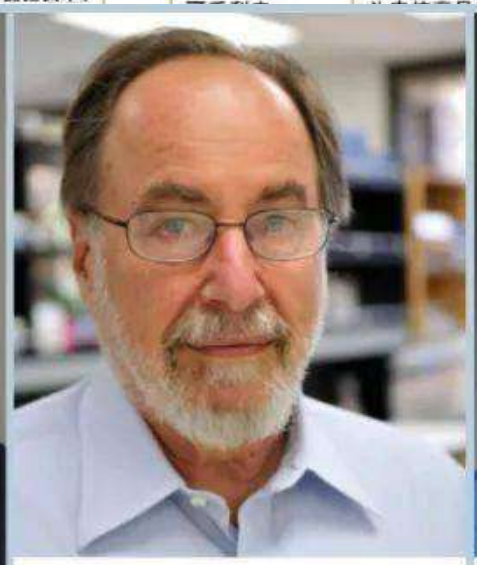
Anti-aging: A trillion-yuan investment "gold mine"

2022 年以来，抗衰老一级市场融资事件

企业简称	简介	融资时间	融资金额	融资轮次	投资机构
Rejuvenation Technologies	mRNA 疗法抗衰产品研发商	2023-09	1060 万美元	种子轮	Khosla Ventures，Shanda Ventures，Asymmetry Ventures，Merchant Adventures，Longevity Tech Fund，Y Combinato
美央创新科技	医美抗衰人工智能平台	2023-09			博远资本、金鼎资本、复健资本、
艾凯生物	细胞治疗药物研发企业	2023-08			
芙迈蕾	国产高端医美器械平台	2023-08			
海南乐孕	生殖抗衰品牌	2023-08			
Clock.bio	抗衰老技术研发商	2023-08			
帧元国际	抗衰技术产品研发企业	2023-07			
雅光医疗	光电医美研发商	2023-06			
Qaadu	抗衰护肤品牌	2023-06			
RAS	DTC 抗衰护肤品牌	2023-04			
至善唯新	布局衰老等领域的基因疗法公司	2023-02			
海创生物	生态性抗老科学护肤品牌	2023-02			
非凡生物科技	SOD 厂商	2023-01			
芙迈蕾	国产高端医美器械平台	2022-12			
青杆生物	抗衰产品研发企业	2022-11	数千万元	天使轮	顺福资本、海南承家继业资本
Arey	头皮抗衰品牌	2022-11	2854 万元	种子轮	Greycroft PartnersFemale Founders Fund
雅光医疗	光电医美研发商	2022-09	未披露	B 轮	乾道基金
维泰瑞隆	衰老相关退行性疾病创新企业	2022-08	2 亿美元	B 轮	云锋基金、高榕资本、和玉资本（MSA Capital）、康桥资本、江远投资、中发展领创/生命园创投基金、超弦基金、Future Innovation Fund 等
森美 SEIMEI	营养抗衰生物科技品牌	2022-08	255 万美元	种子轮+天使轮	嘉程资本、普曼资本、川至创投、多位个人天使投资人
				战略融	
Bio	台企业	2022-01	8200 万美元	C 轮	Alpha Wave Ventures
Altos Labs	抗衰老技术研发商	2022-01	30 亿美元	天使轮	Yuri Milner，Jeff Bezos，Tr

Shinya Yamanaka
Senior Scientific Advisor

iPSCs

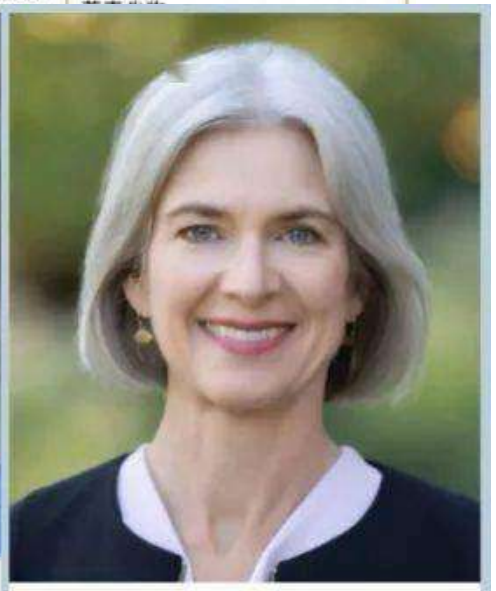


David Baltimore
Lead Independent Director

Reverse transcriptase

Frances Arnold
Director

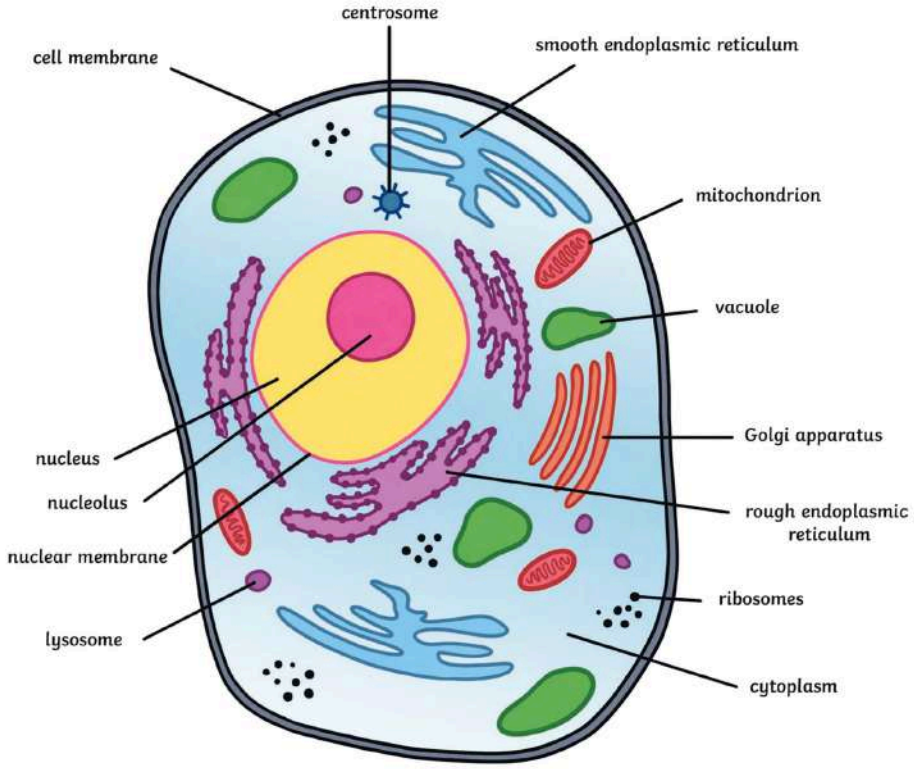
Directed evolution



Jennifer Doudna
Director

CRISPER-Cas9

Understanding senescence at microscopic view



When we talk about aging, what are we afraid of?

1. The underlying logic of aging——陆彤
2. The connection between aging and diseases——王红蕾
3. Strategies for delaying aging——梁艺鸽

TECHNOLOGY

Peter Thiel Is Very, Very Interested in Young People's Blood The contrarian venture capitalist believes transfusions may hold the key to his dream of living forever.

彼得·蒂尔（Peter Thiel）盯上年轻人的血：
这位逆向投资人相信，输血或许是通往永生之路

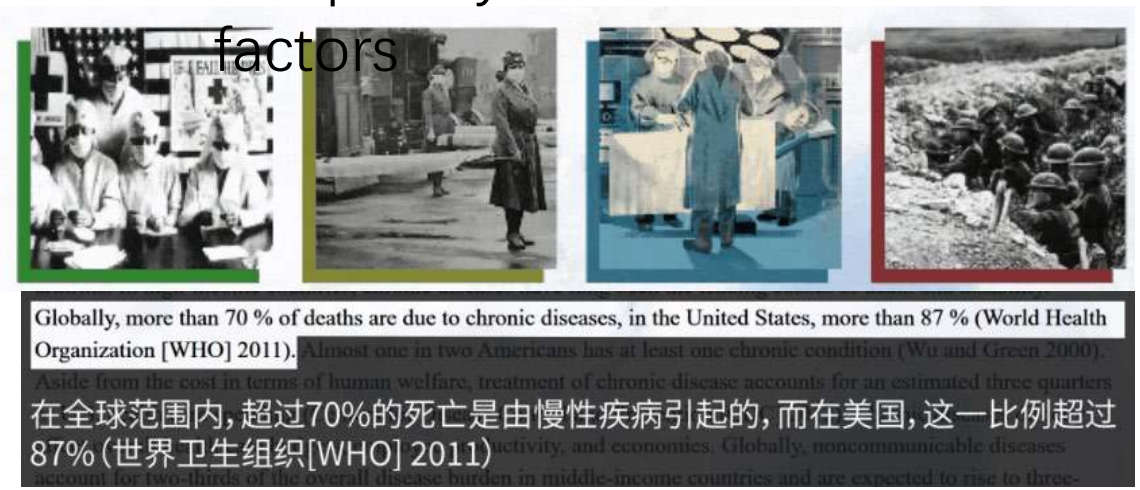
EXCLUSIVE STAT+

扎克伯格和陈述宣布将在纽约建立生物中心，开发能够对抗疾病的细胞技术或“细胞机器”

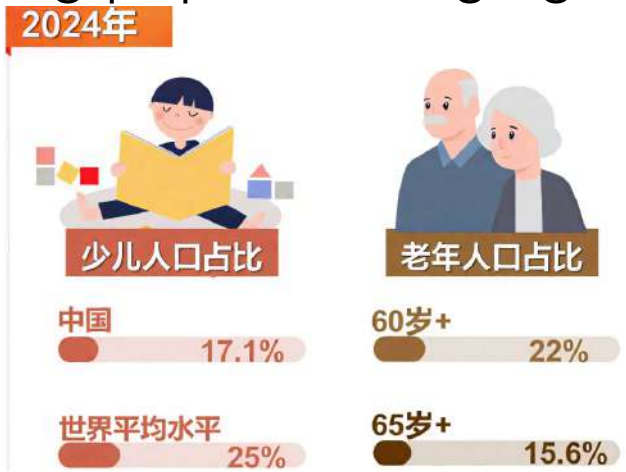
By Jason Mast

Why do humans desire to Never Age ?

Contemporary factors



Accelerating population aging



Increased social

Continuous technological advancemer

The Underlying Logic of Aging

- Identification of fourteen hallmarks of aging.
- The theoretical foundations of aging.

Diverse Interpretations of Aging

Physiology

Progressive loss of physiological integrity
Impaired function
Increased risk of death

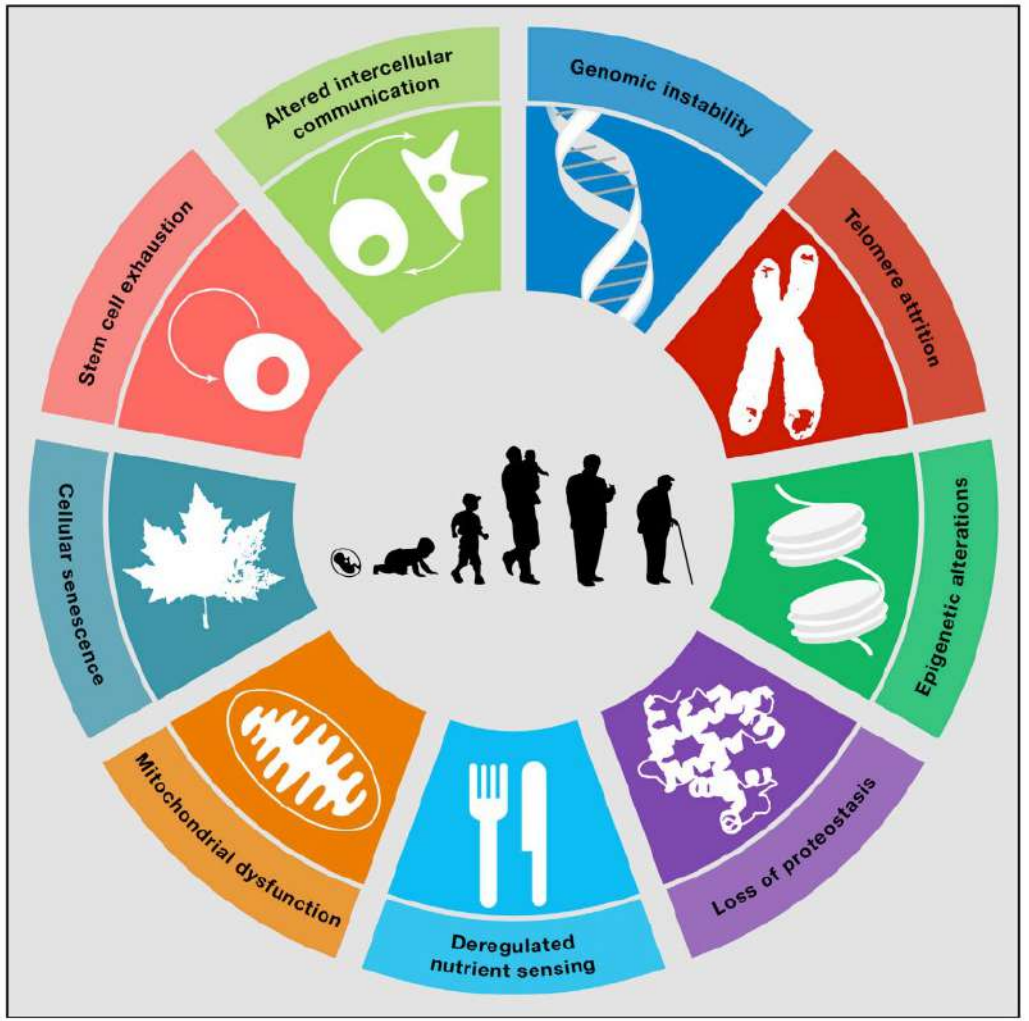
Pathology

Stress and strain
Injury and infection
Decline in immune response

Sociology

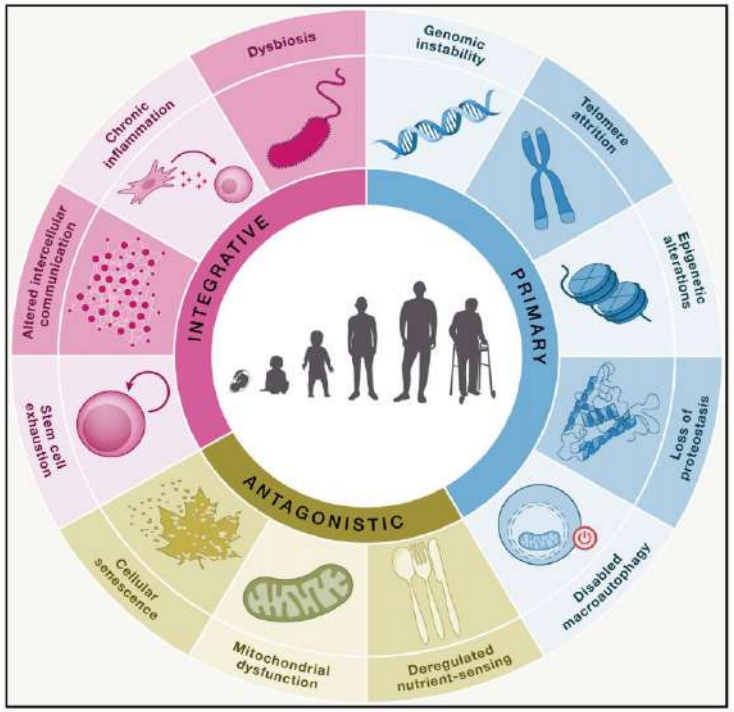
Loss of interest
Detachment from reality
Nostalgia

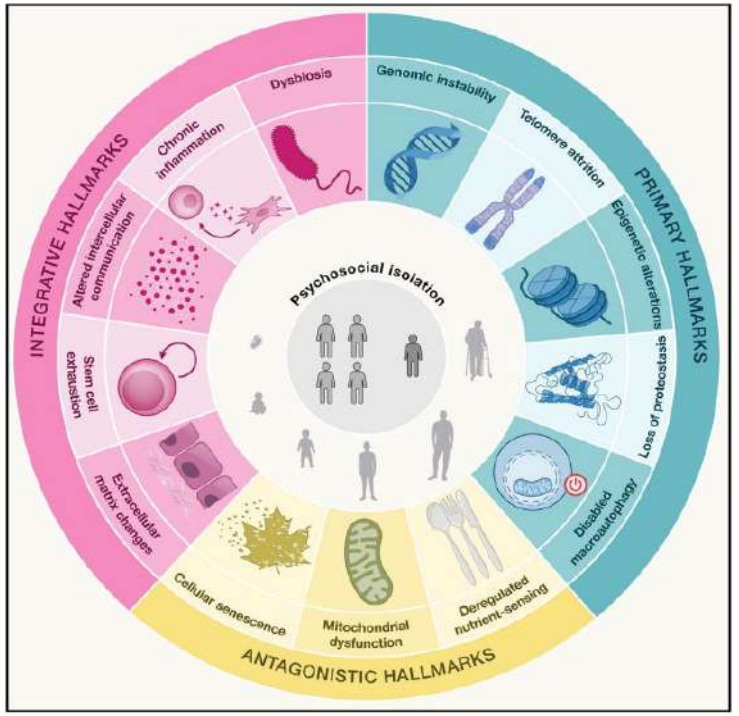
The Hallmarks of Aging



Carlos López-Otín,et al.,*Cell*,2013

Research on hallmarks of aging: from 9 to 14





\+ Disabled macroautophagy
Chronic inflammation
Dysbiosis

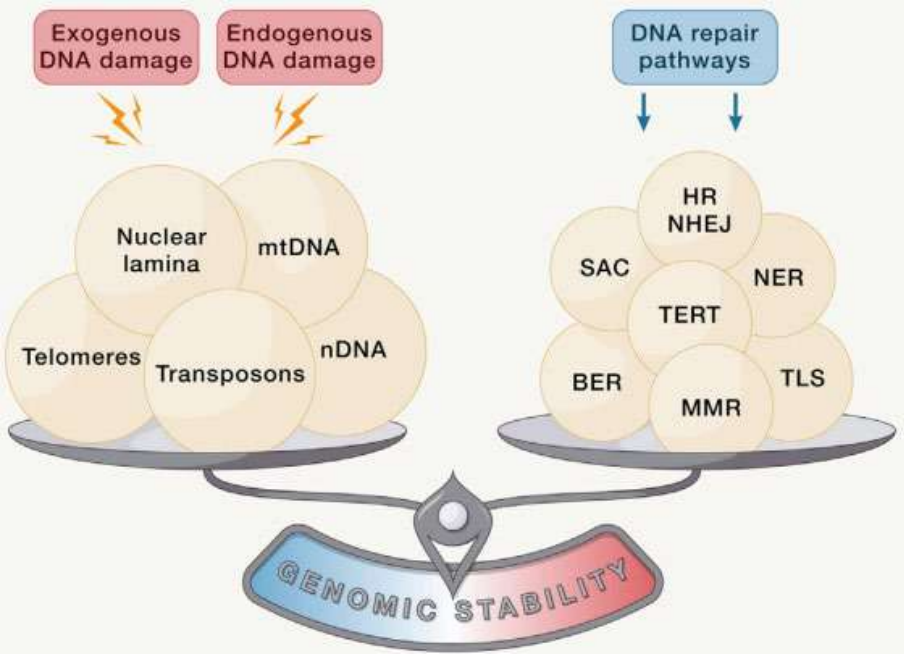
\+ Extracellular matrix changes
Psychosocial isolation

Three Criteria

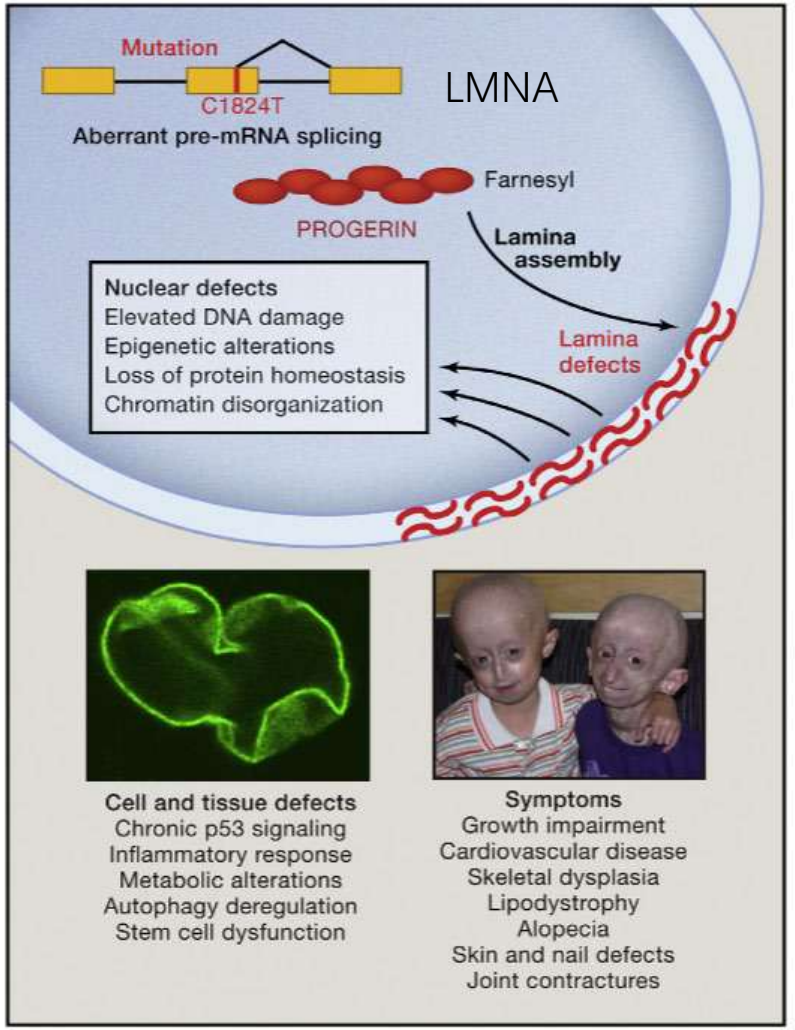
- Time-dependent & age-related
- Experimental accelerability via hallmark accentuation
- Therapeutic modifiability

Carlos López-Otín,et al.,*Cell*,2022
Guido Kroemer, et al.,*Cell*,2025

01 Genomic instability

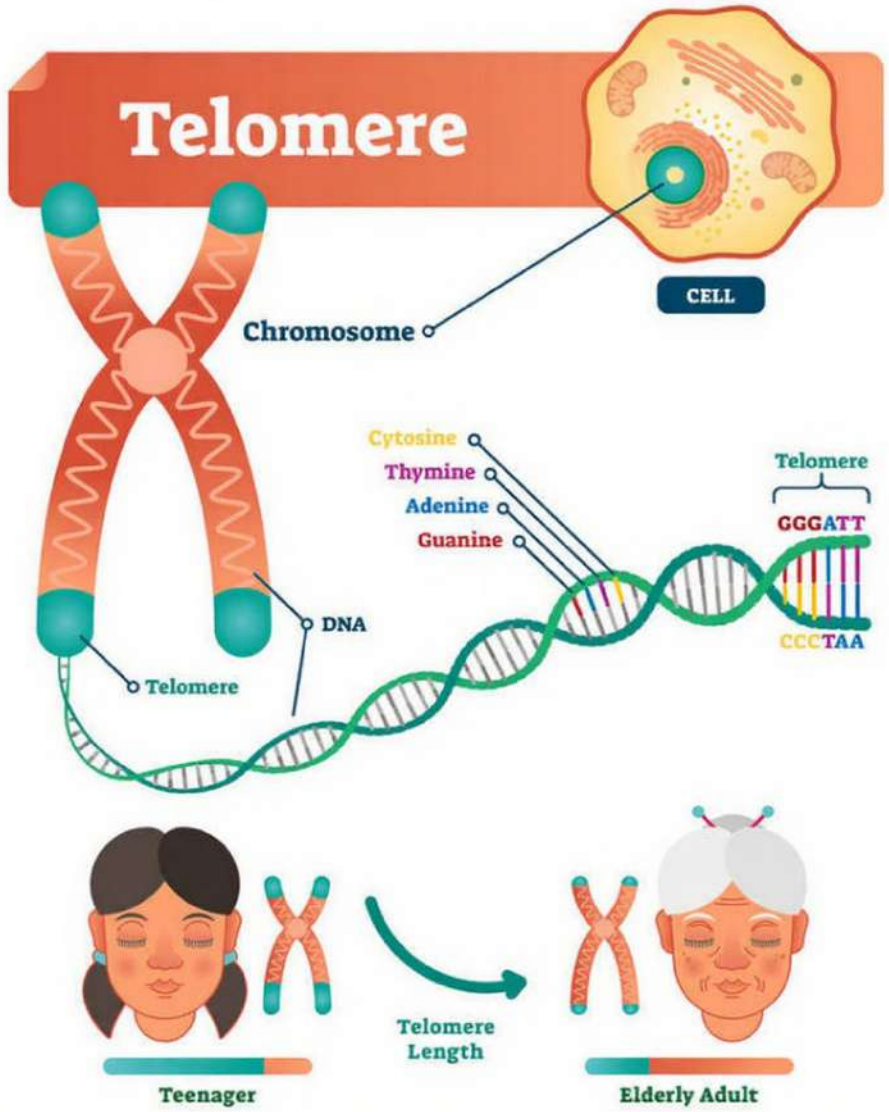


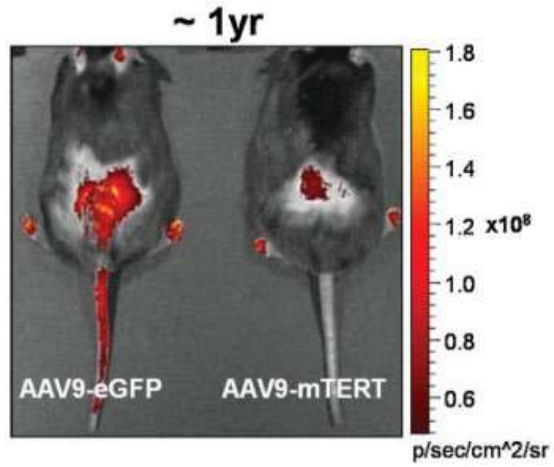
Hutchin-son-Gilford progeria syndrome (**HGPS**,or progeria)

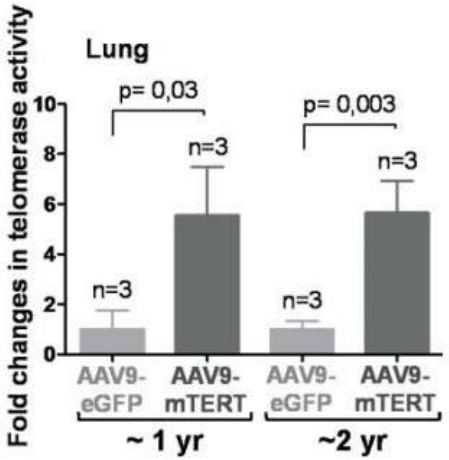


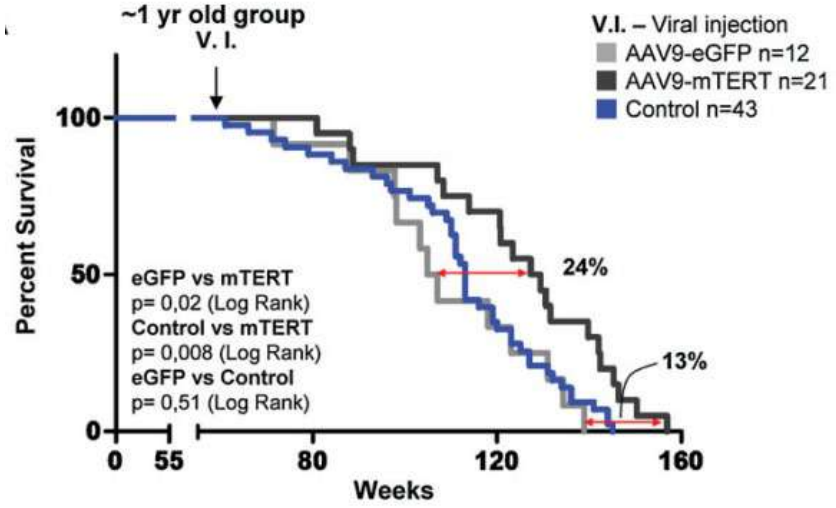
Carlos López-Otín,et al.,*Cell*,2022
Gordon, L.B.,et al,*Cell*,2008

02 Telomere attrition



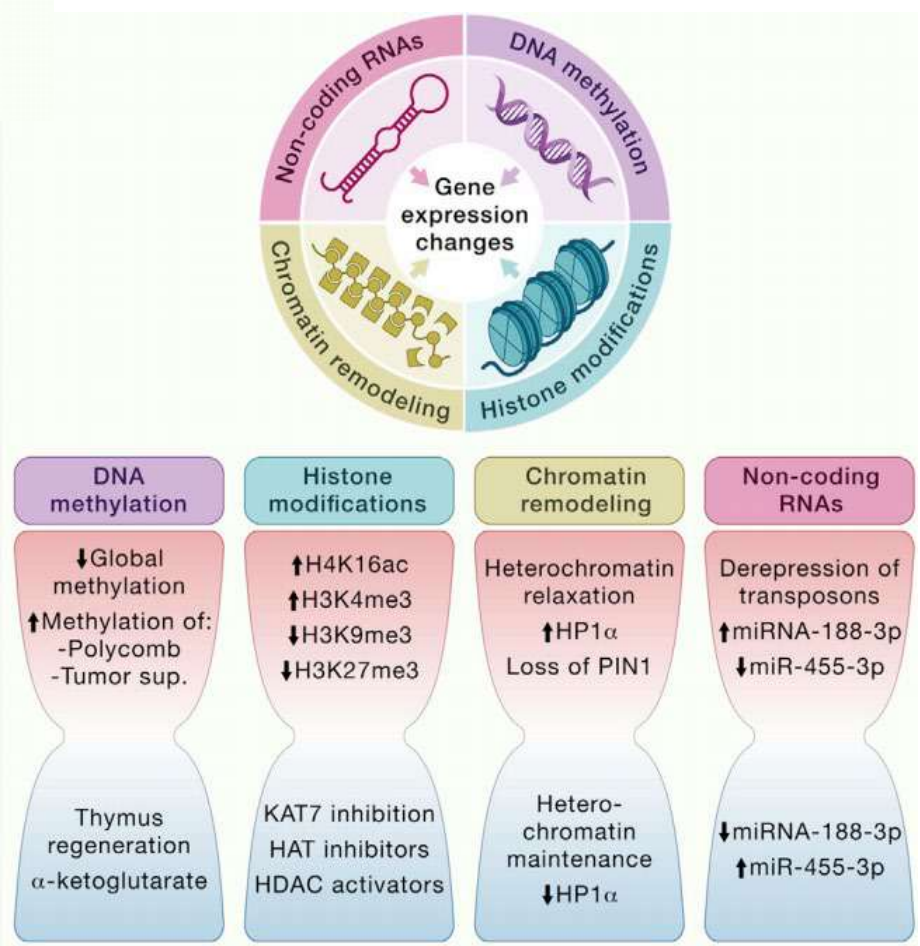




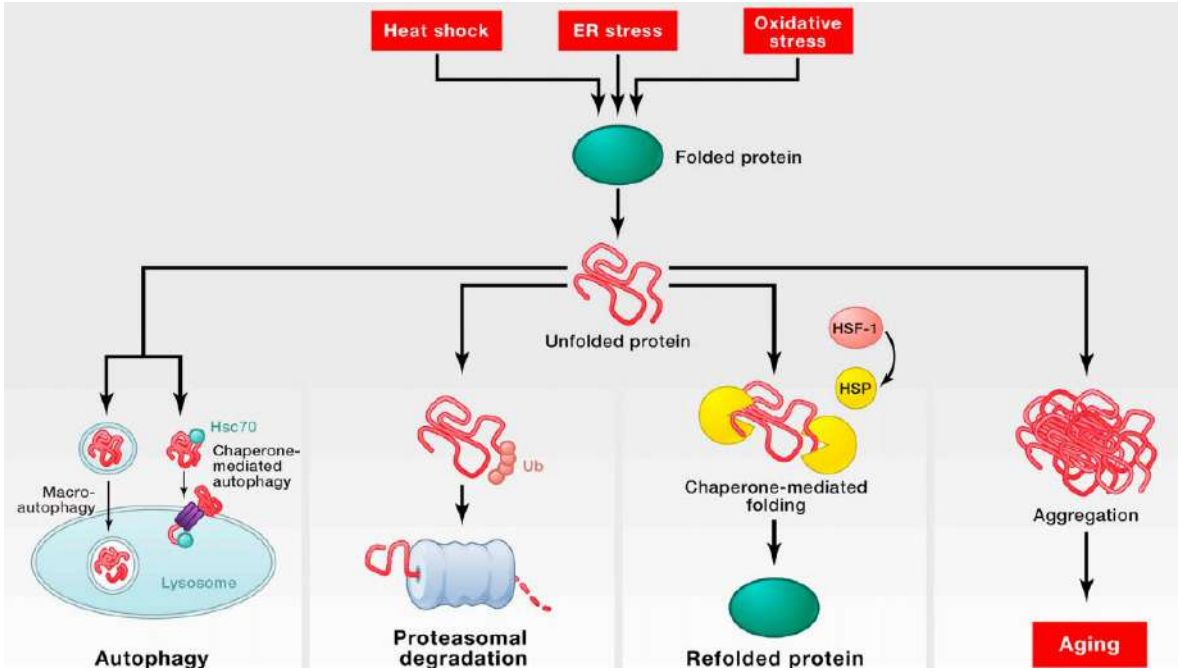


Bruno Bernardes de Jesus,et al.,*EMBO Molecular Medicine*,2012

03 Epigenetic alterations

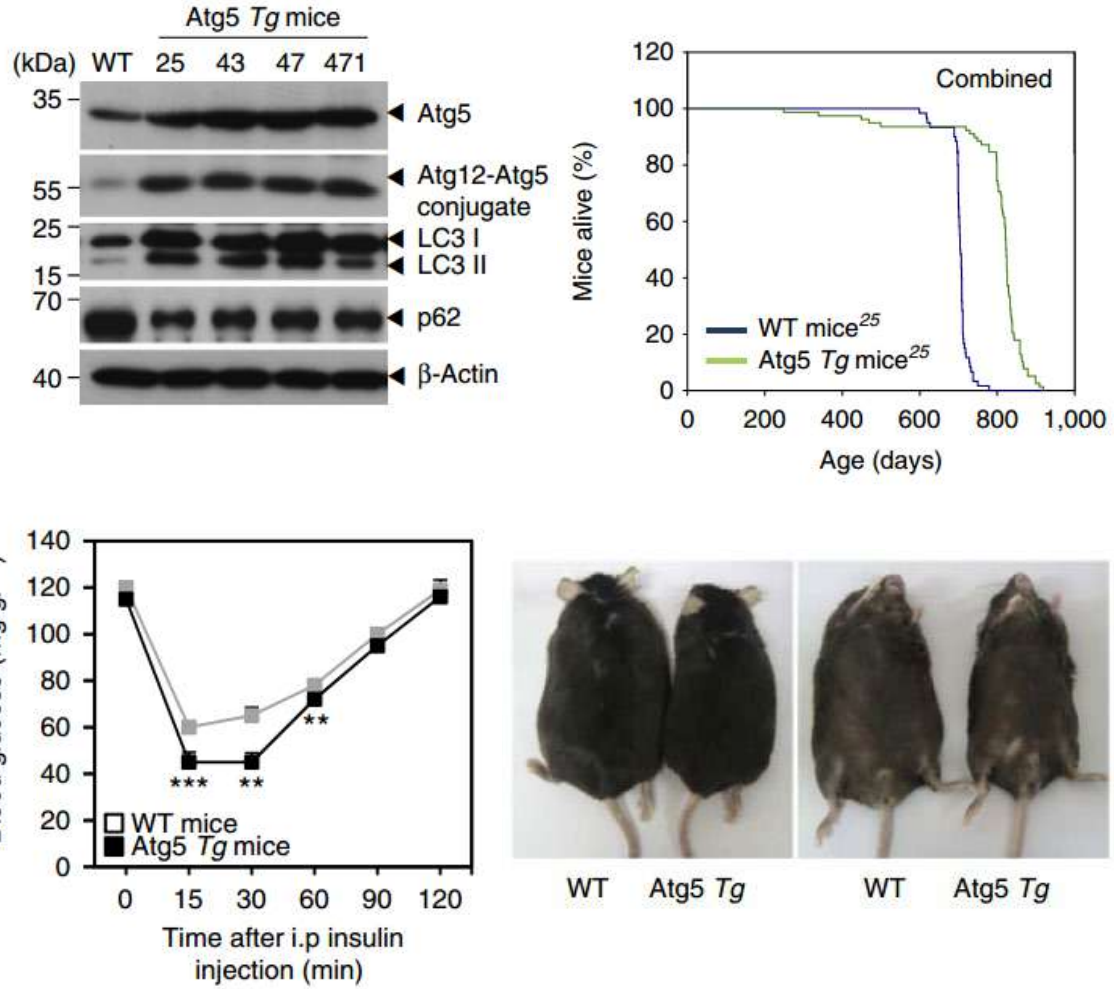


04 Loss of proteostasis

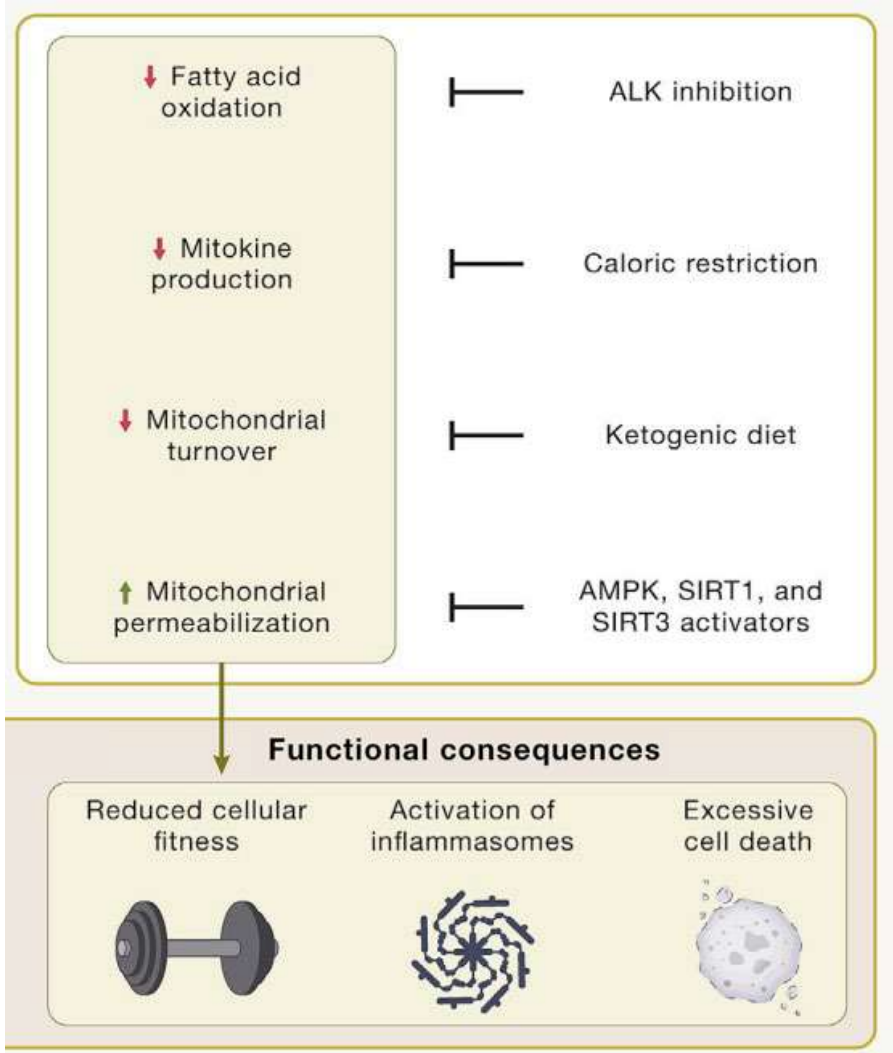


Carlos López-Otín,et al.,*Cell*,2013

05 Disabled macroautophagy

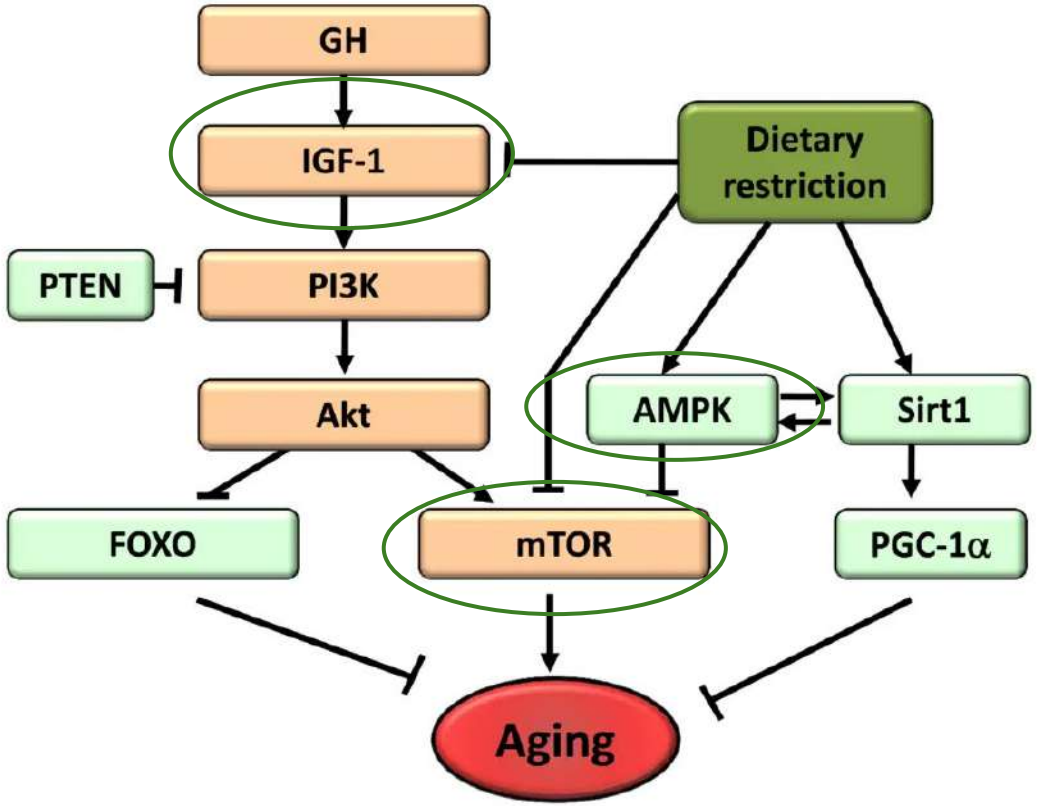


06 Mitochondrial dysfunction

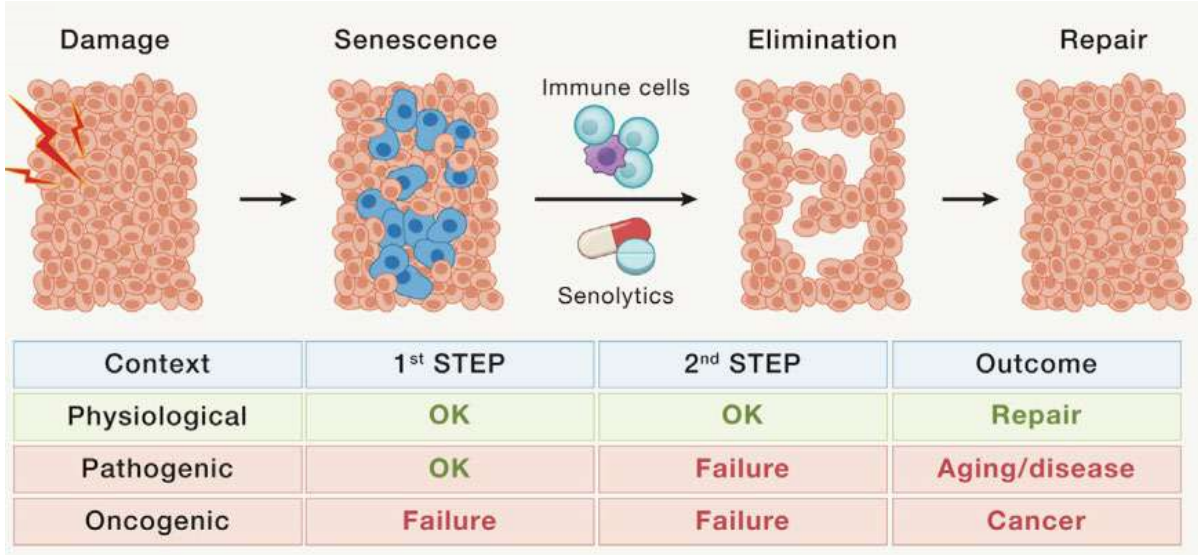


Jong-Ok Pyo ,et al.,*Nature Communications*,2013
Carlos López-Otín,et al.,*Cell*,2022

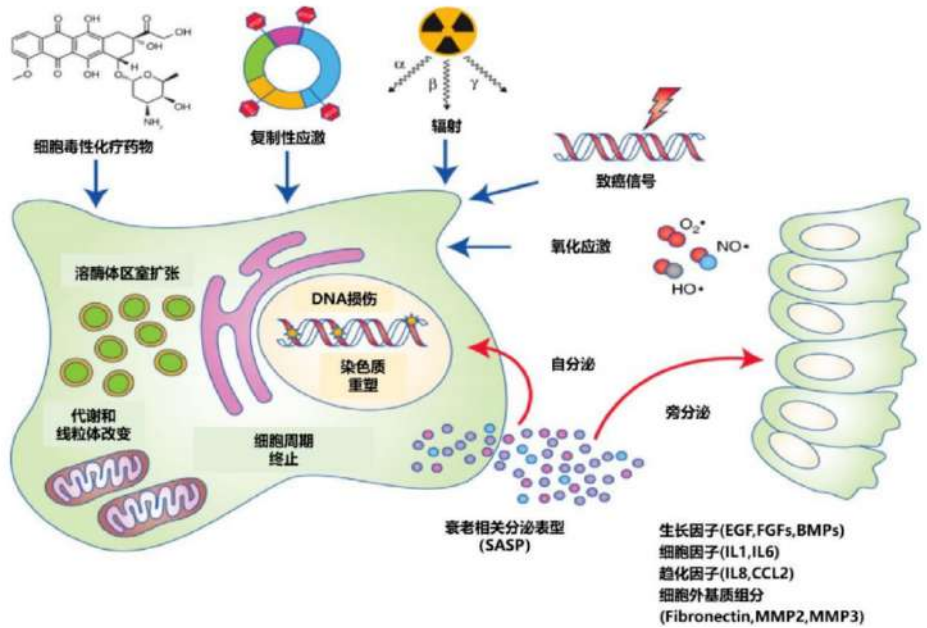
07 Deregulated nutrient-sensing



08 Cellular senescence

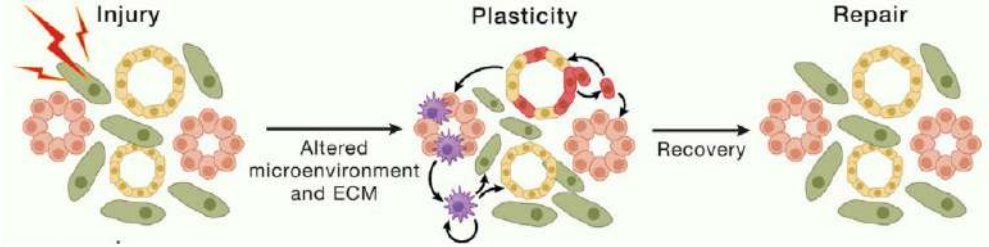


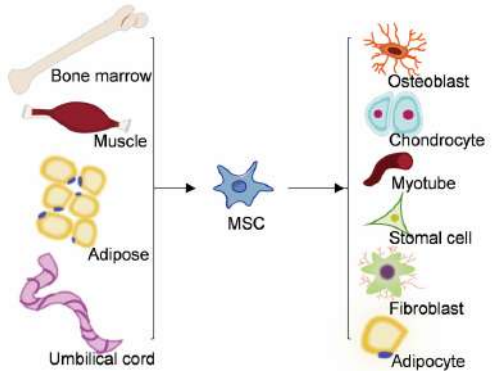
Context	1st STEP	2nd STEP	Outcome
Physiological	OK	OK	Repair
Pathogenic	OK	Failure	Aging/disease
Oncogenic	Failure	Failure	Cancer

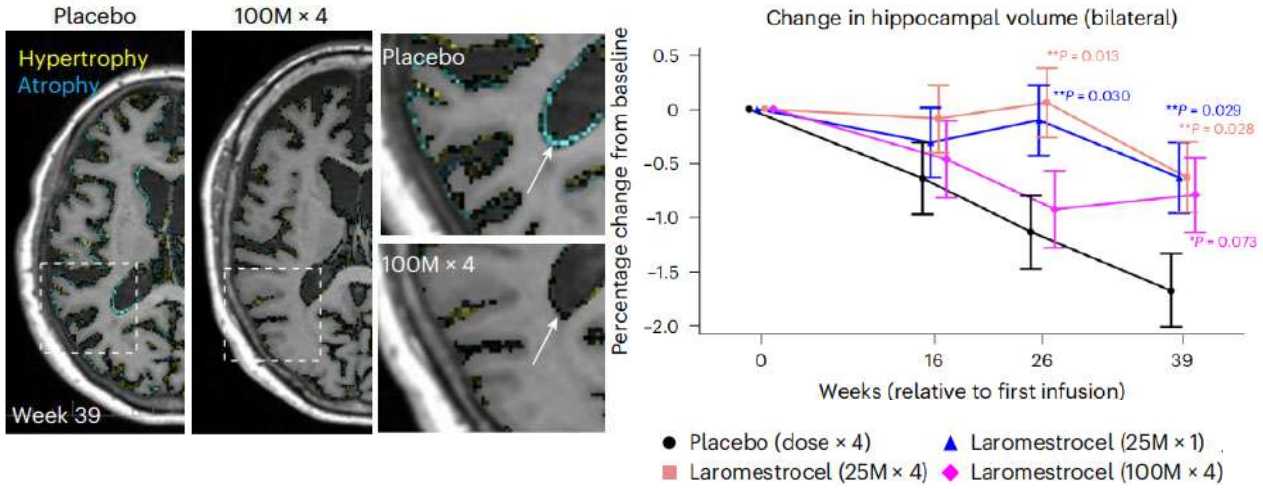


Carlos López-Otín,et al.,*Cell*,2022

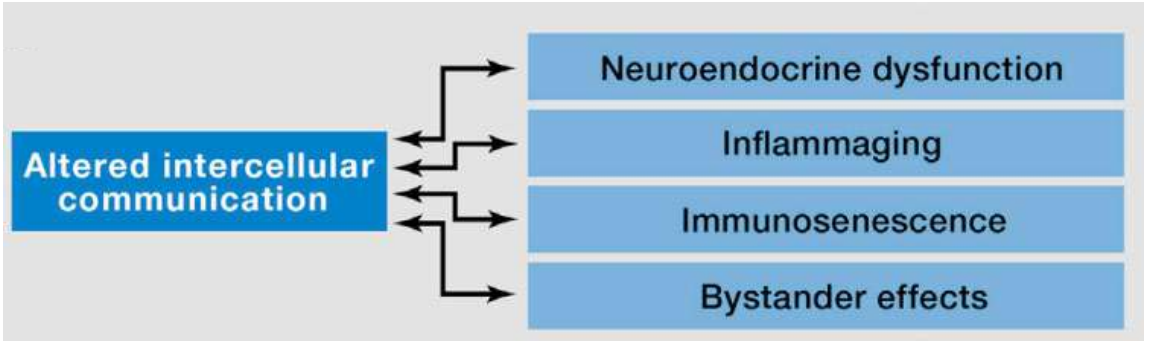
09 Stem cell exhaustion



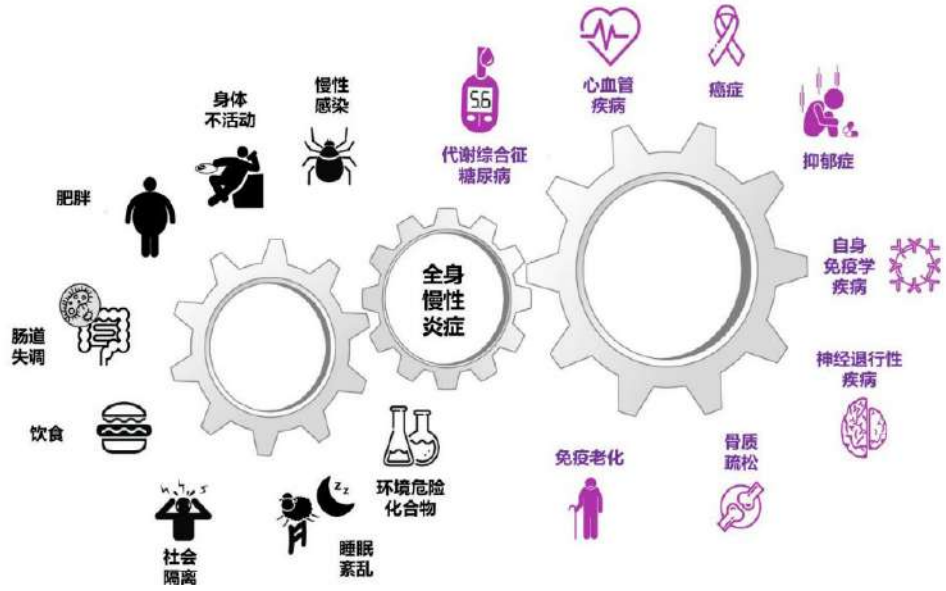




10 Altered intercellular communication



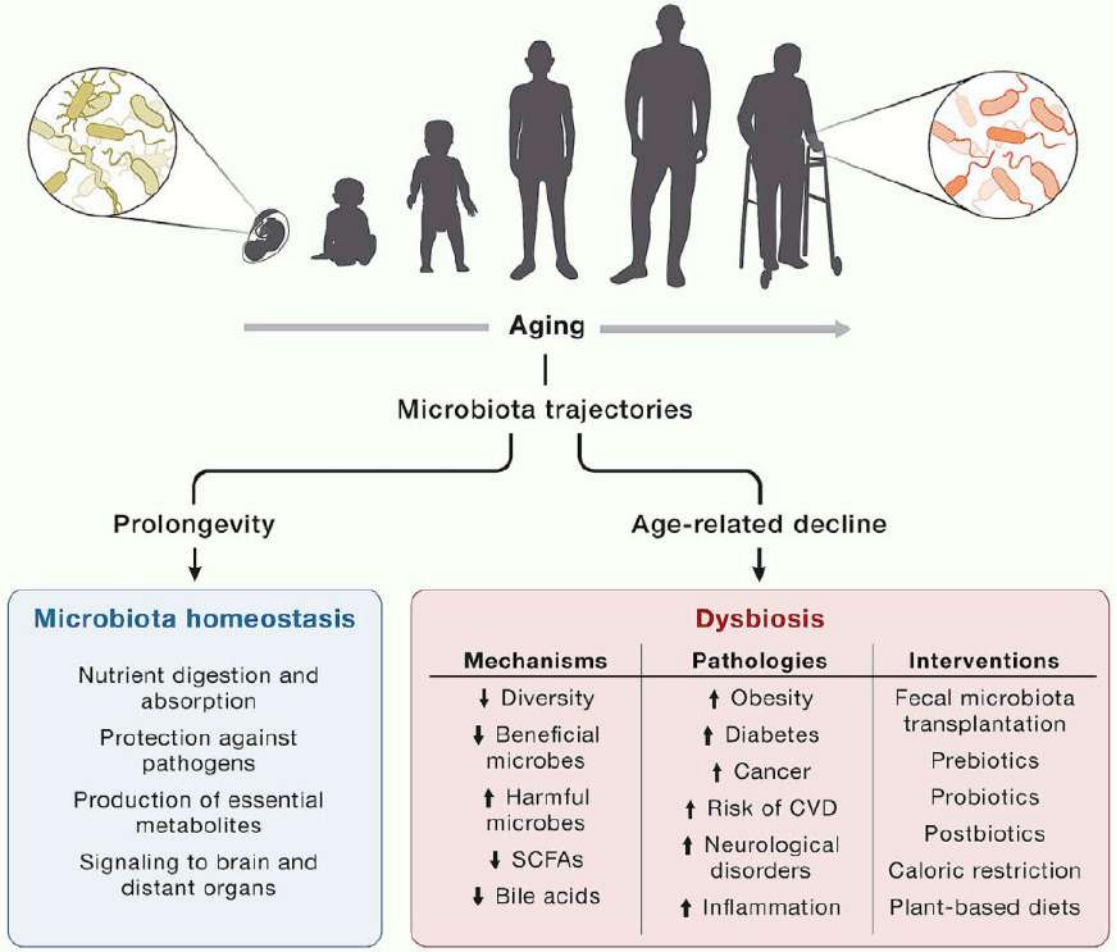
11 Chronic inflammation



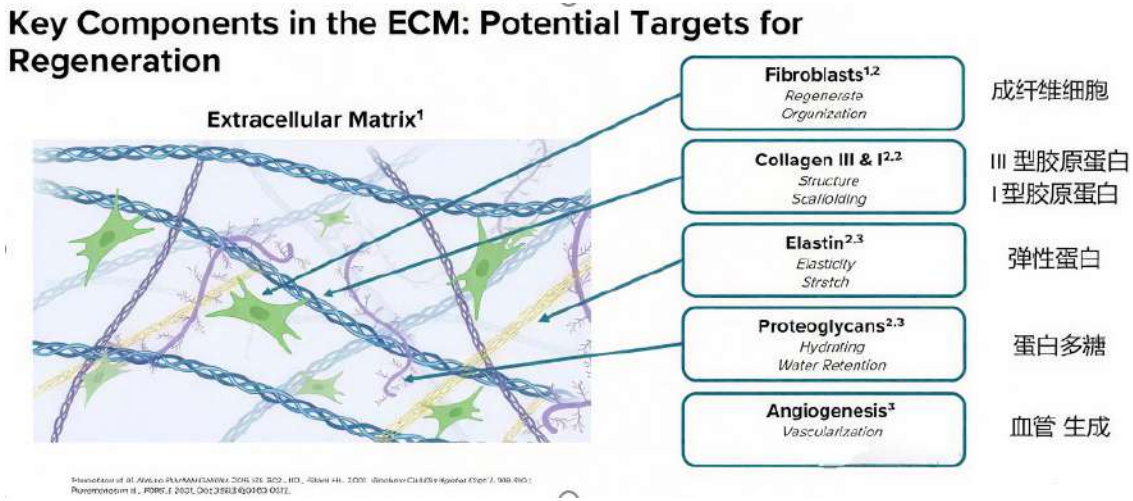
Brian G. Rash ,et al.,*Nature Medicine*,2025
Ruiyan Mei,et al.,*Frontiers in Immunology*,2024

Carlos López-Otín,et al.,*Cell*,2013

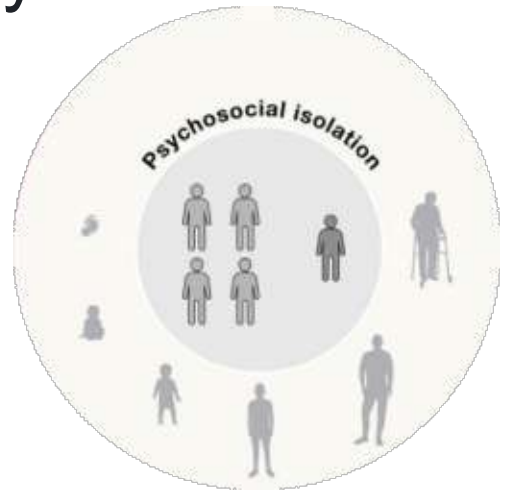
12 Dysbiosis



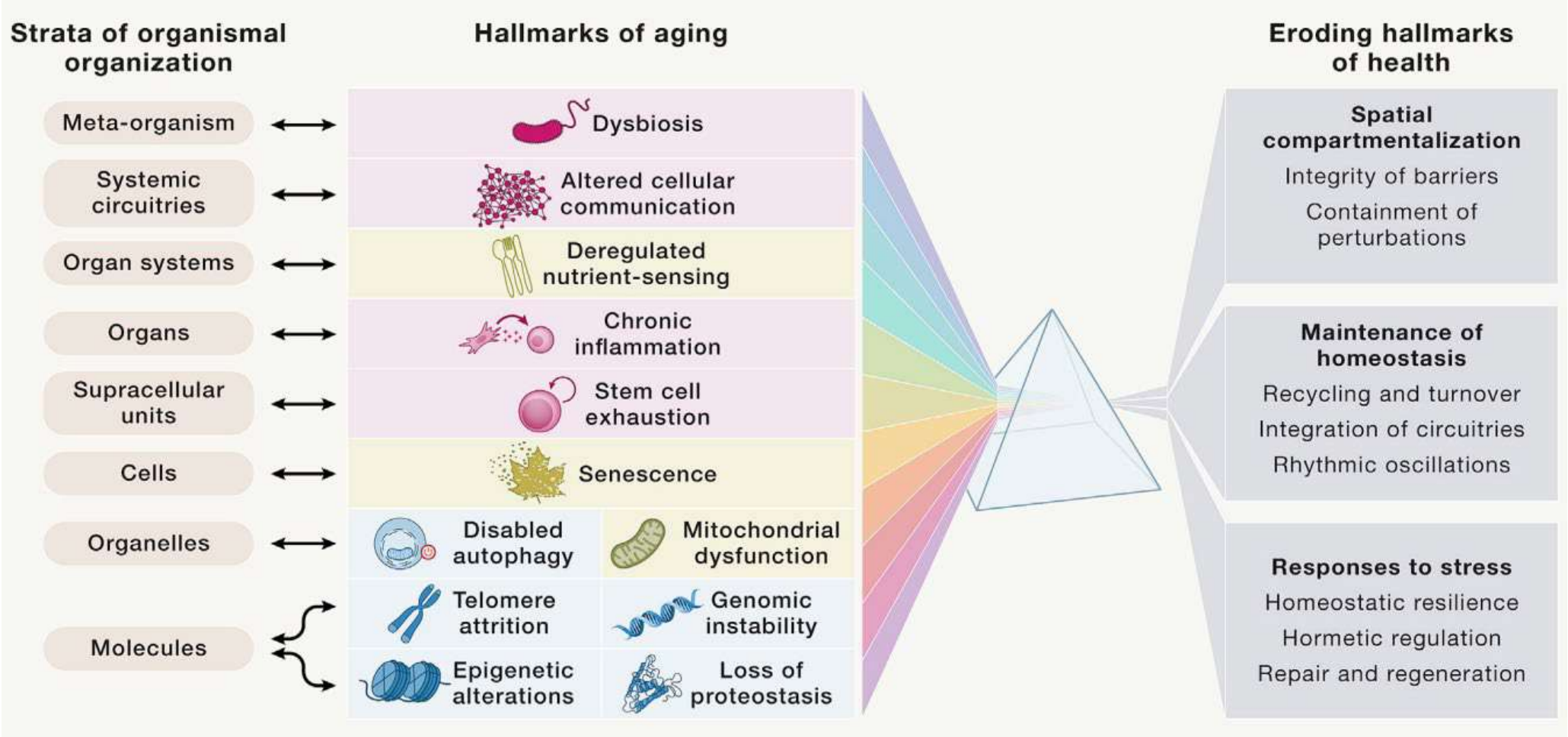
13 Extracellular matrix changes



14 Psychosocial isolation



Integration of hallmarks

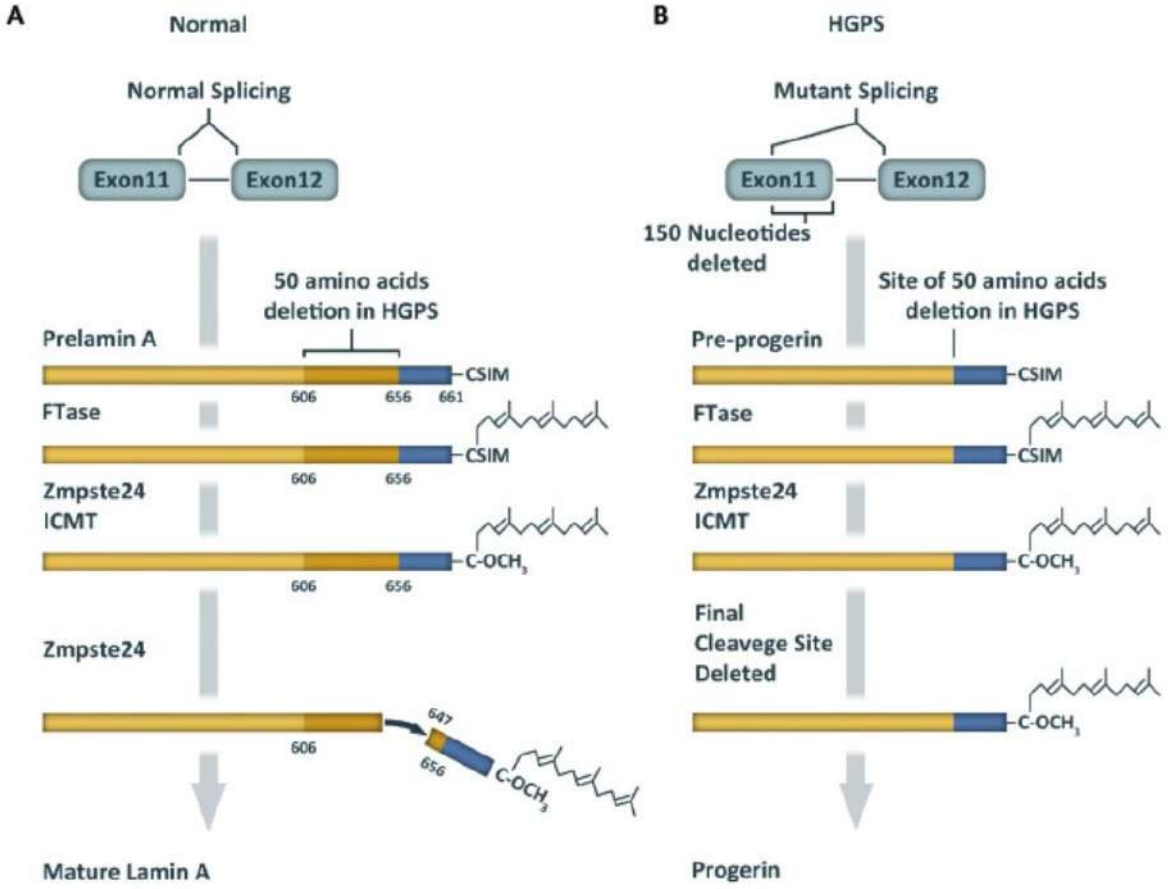


Carlos López-Otín,et al.,*Cell*,2022

- ✓ **When aging is regarded as a kind of diseases.**
- ✓ **When aging becomes a factor that contributes diseases.**
- ✓ **When aging is a normal physiological phenomenon.**

- ✓ **When aging is regarded as a disease.**
- ✓ **When aging becomes a factor that contributes diseases.**
- ✓ **When aging is a normal physiological phenomenon.**

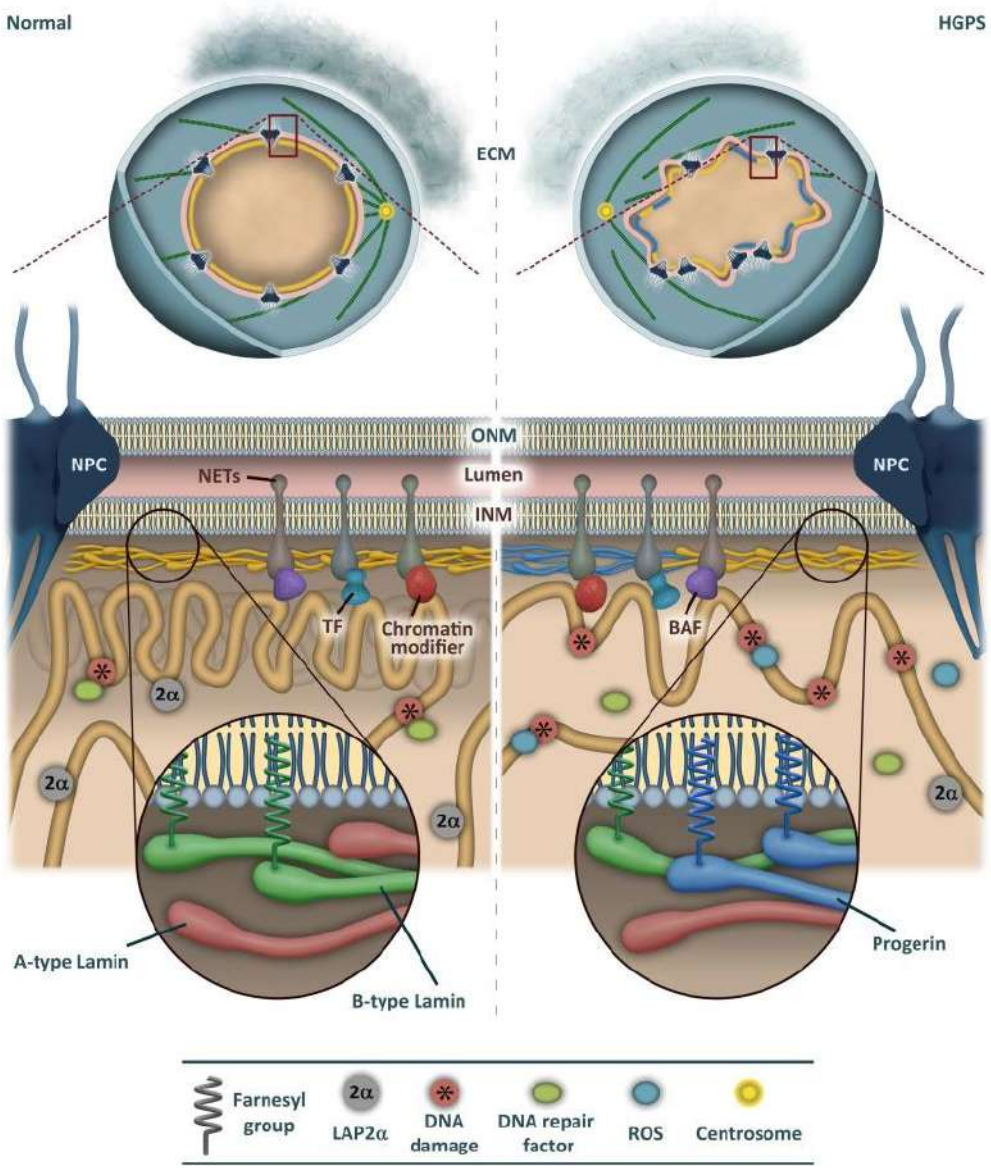
Hutchinson-Gilford Progeria Syndrome(HGPS，哈钦森-吉尔福德综合症): A premature aging disease

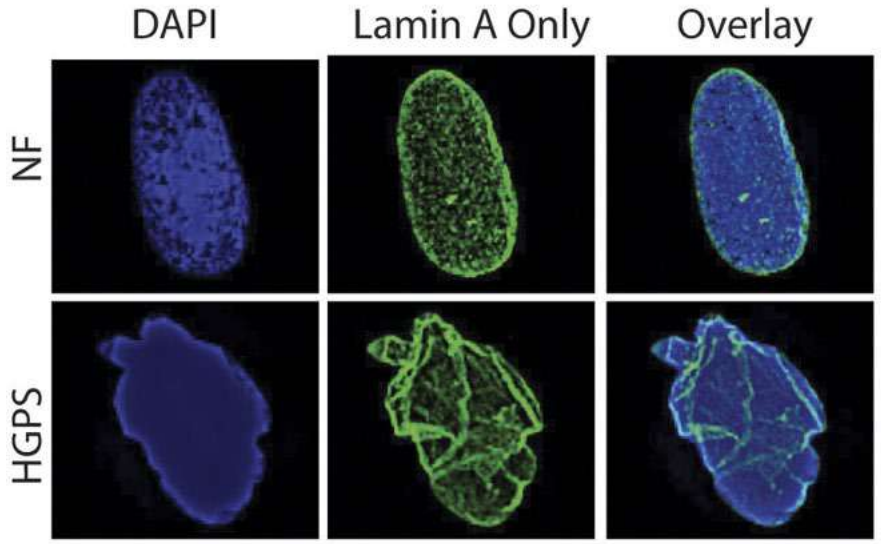


- **Symptom**: Onset by 12-18 months old, sclerotic skin, lipodystrophy, altered skin pigmentation, alopecia, bone and growth defects, cardiovascular complications, death in mid-teens.
- **Causes**: A mutation in ***LMNA*** gene exon 11 activates a cryptic splice site leading to deletion of 50 amino acid residues from the precursor protein.

Foo MXR, Ong PF, Dreesen O., *J Dermatol Sci*. 2019
Gonzalo S, Kreienkamp R, Askjaer P., *Ageing Res Rev.*, 2017

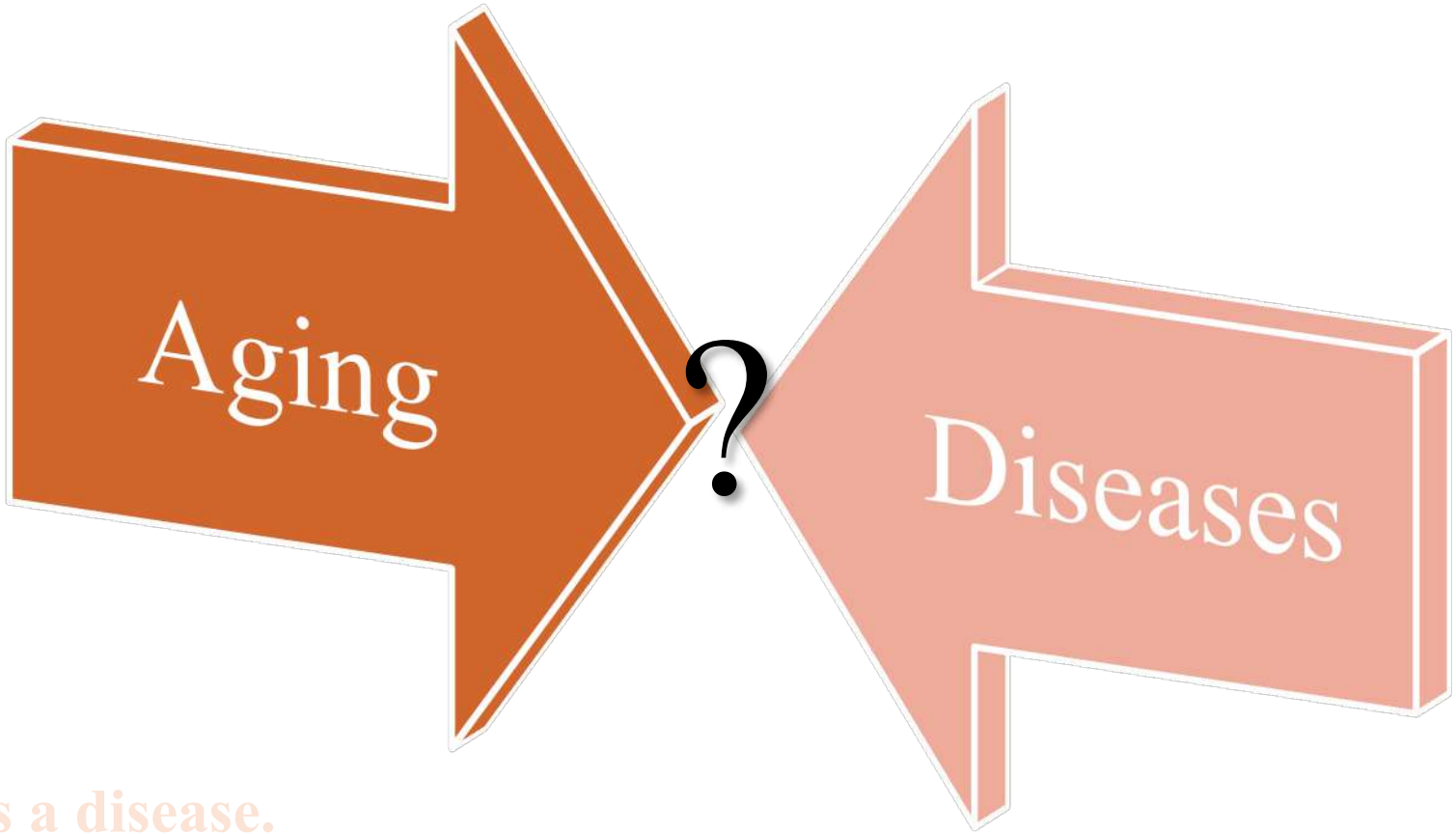
Hutchinson-Gilford Progeria Syndrome(HGPS，哈钦森-吉尔福德综合症): A premature aging disease



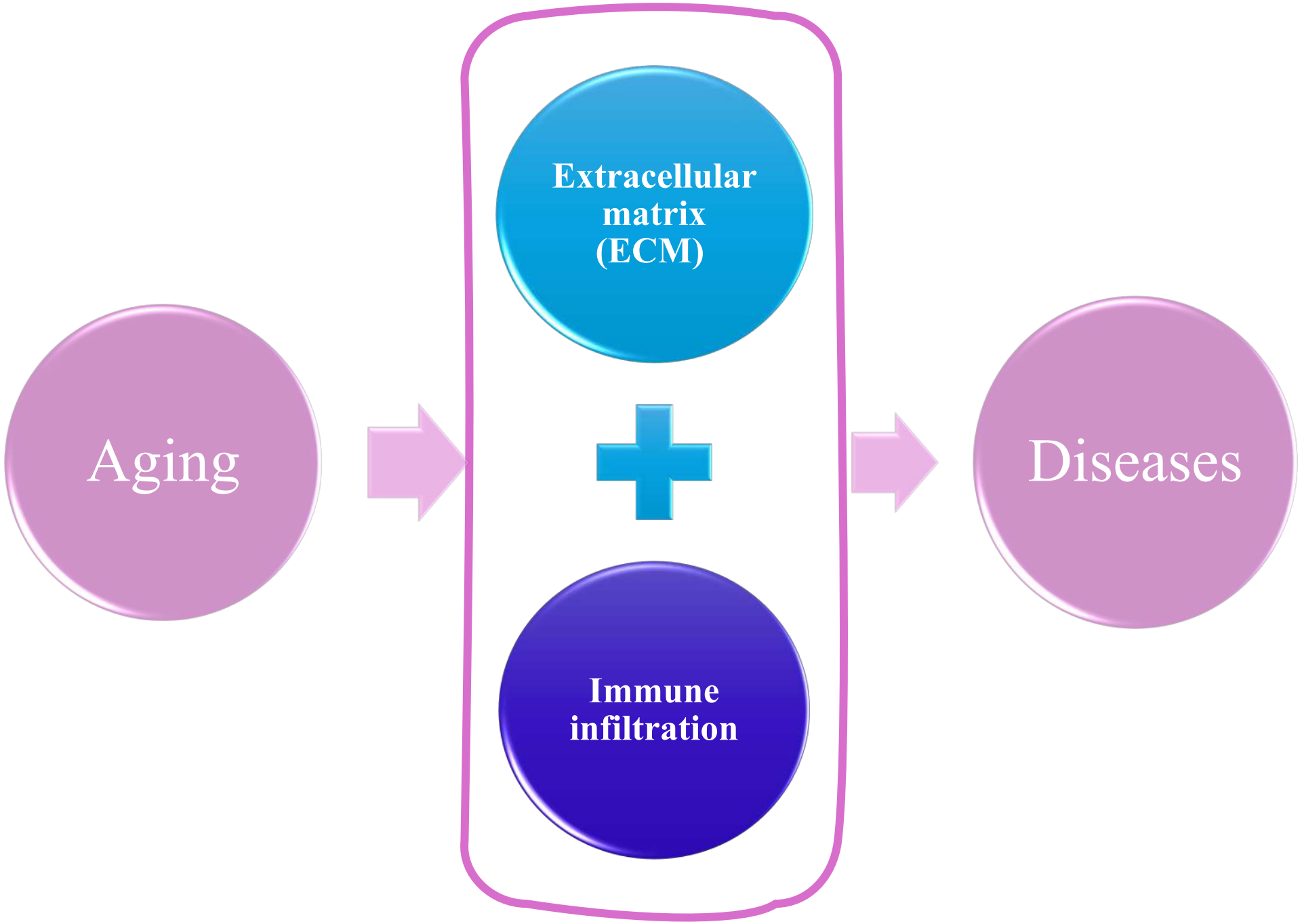


HGPS cells show nuclear defects.

Gonzalo S, Kreienkamp R, Askjaer P., *Ageing Res Rev.*, 2017



- ✓ When aging is regarded as a disease.
- ✓ **When aging becomes a factor that contributes diseases.**
- ✓ When aging is a normal physiological phenomenon.


Aging
Extracellular matrix (ECM)
Immune infiltration
Diseases

ECM composition diversity across organs

Soft tissues

Elastic

‘Looser’ connective tissue environment

Brain

Breast

Lung

……

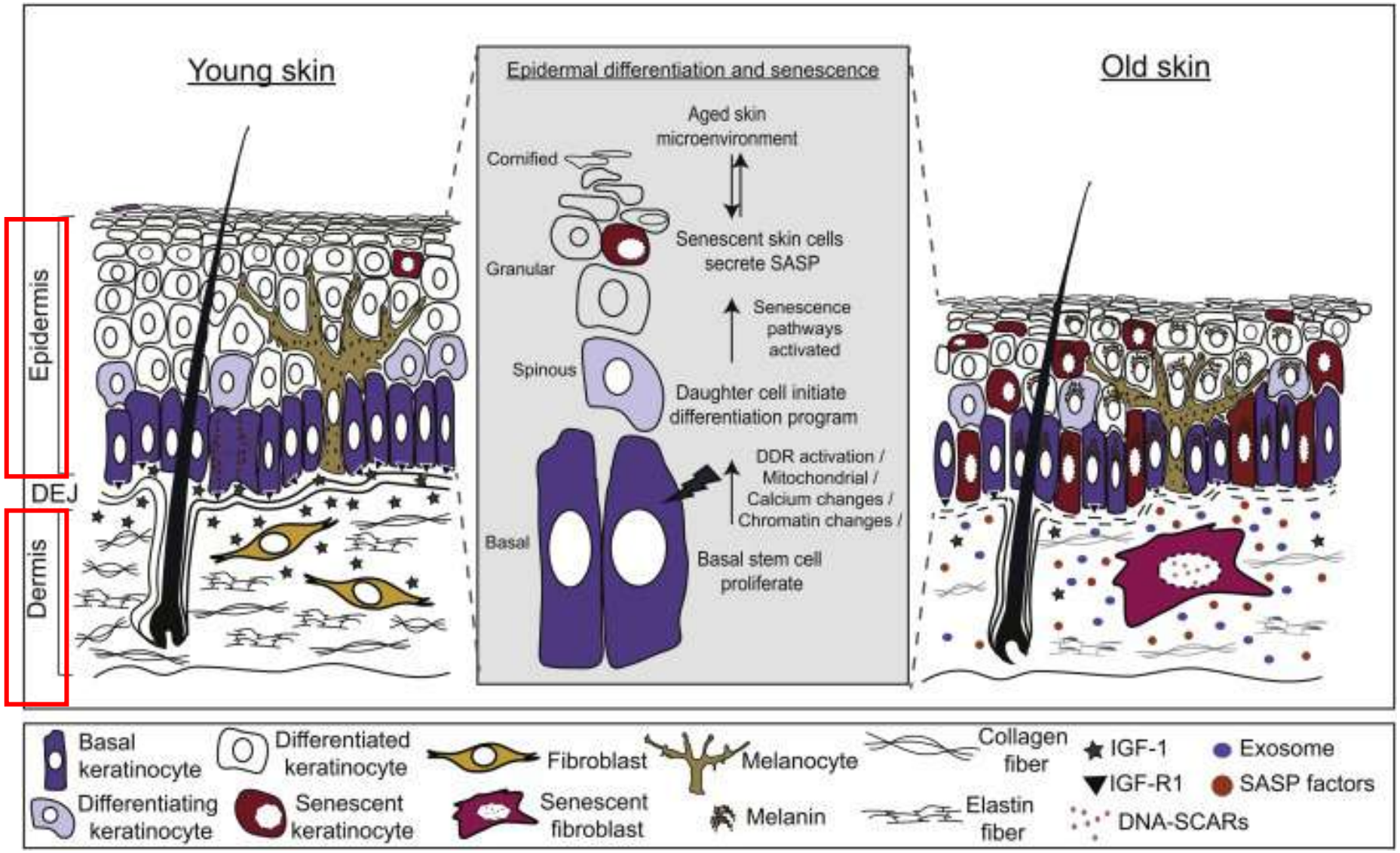
Hard tissues

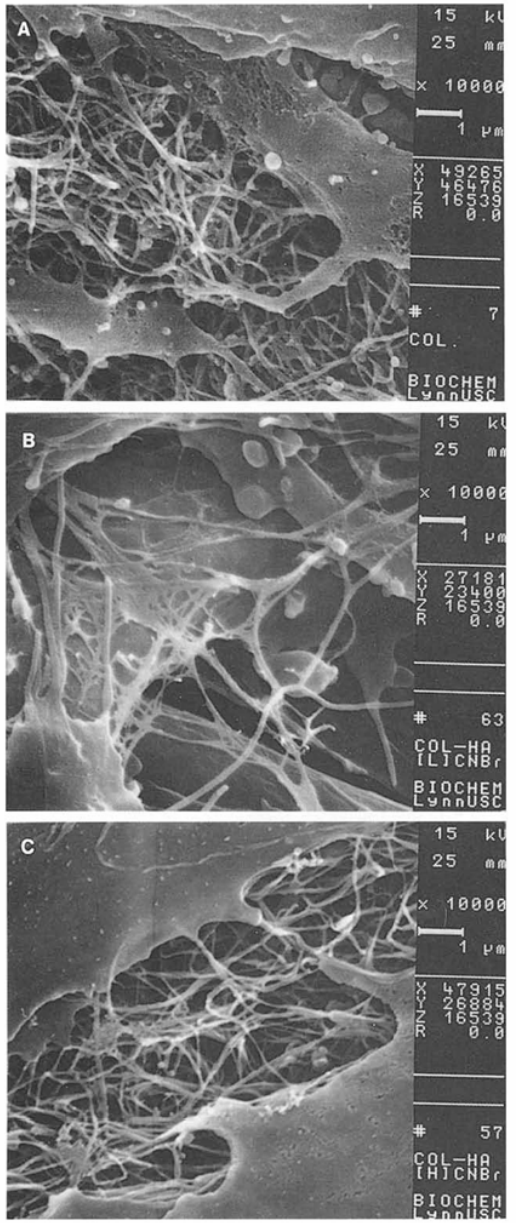
Stiffer structures

Skin

Bone

The structural and functional differences of young and aged skin.

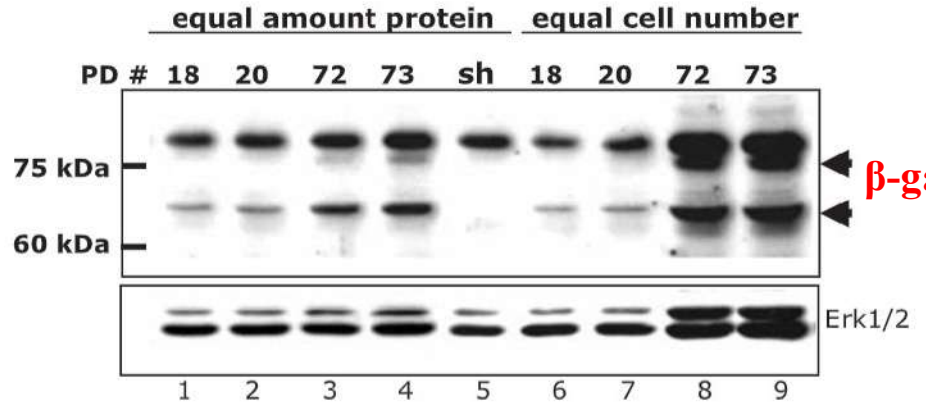




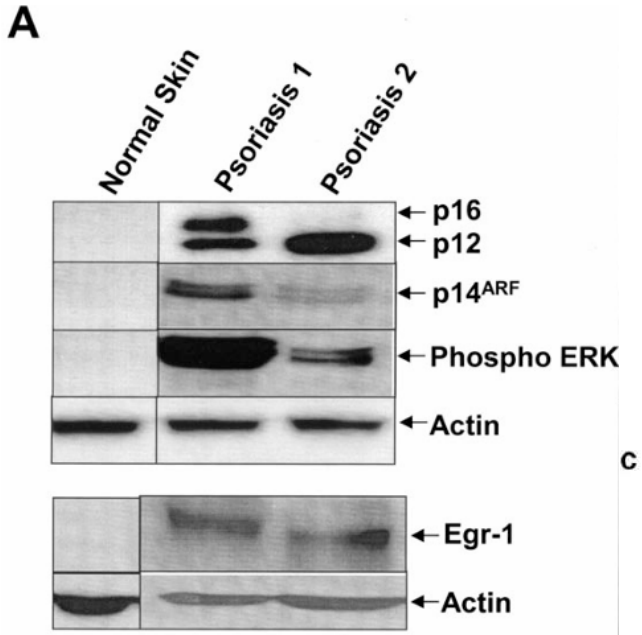
Chin Yee Ho and Oliver Dreesen, *Mechanisms of Ageing and Development*, 2021

LYNN L. H. HUANG-LEE* and MARCEL E. NIMNI, Matrix Biology., 1994

Senescent skin cells have been reported in various age-related skin pathologies based on biomarkers.



β-galactosidase (β-gal)

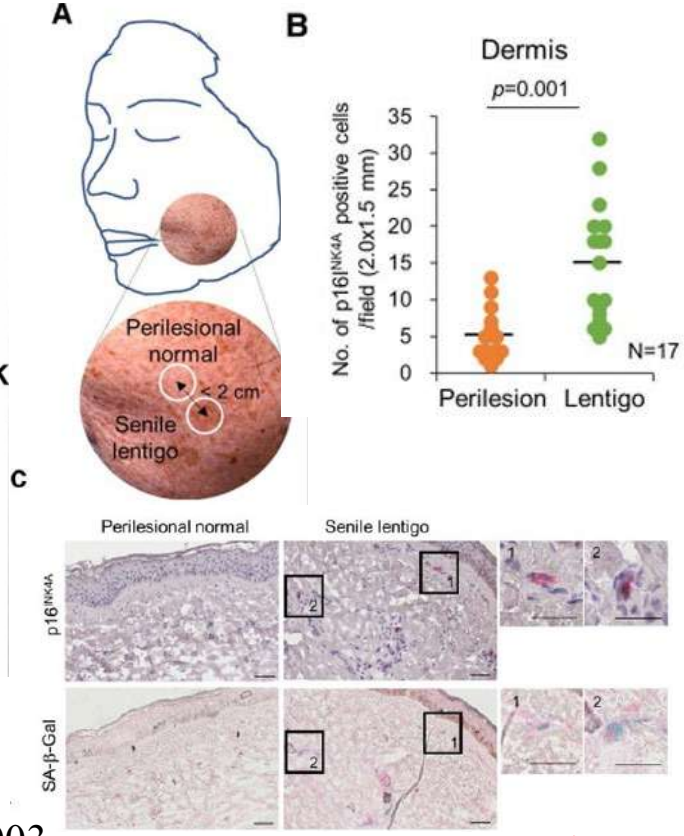


Psoriasis (牛皮癣):
p16/p12/p14^{ARF}

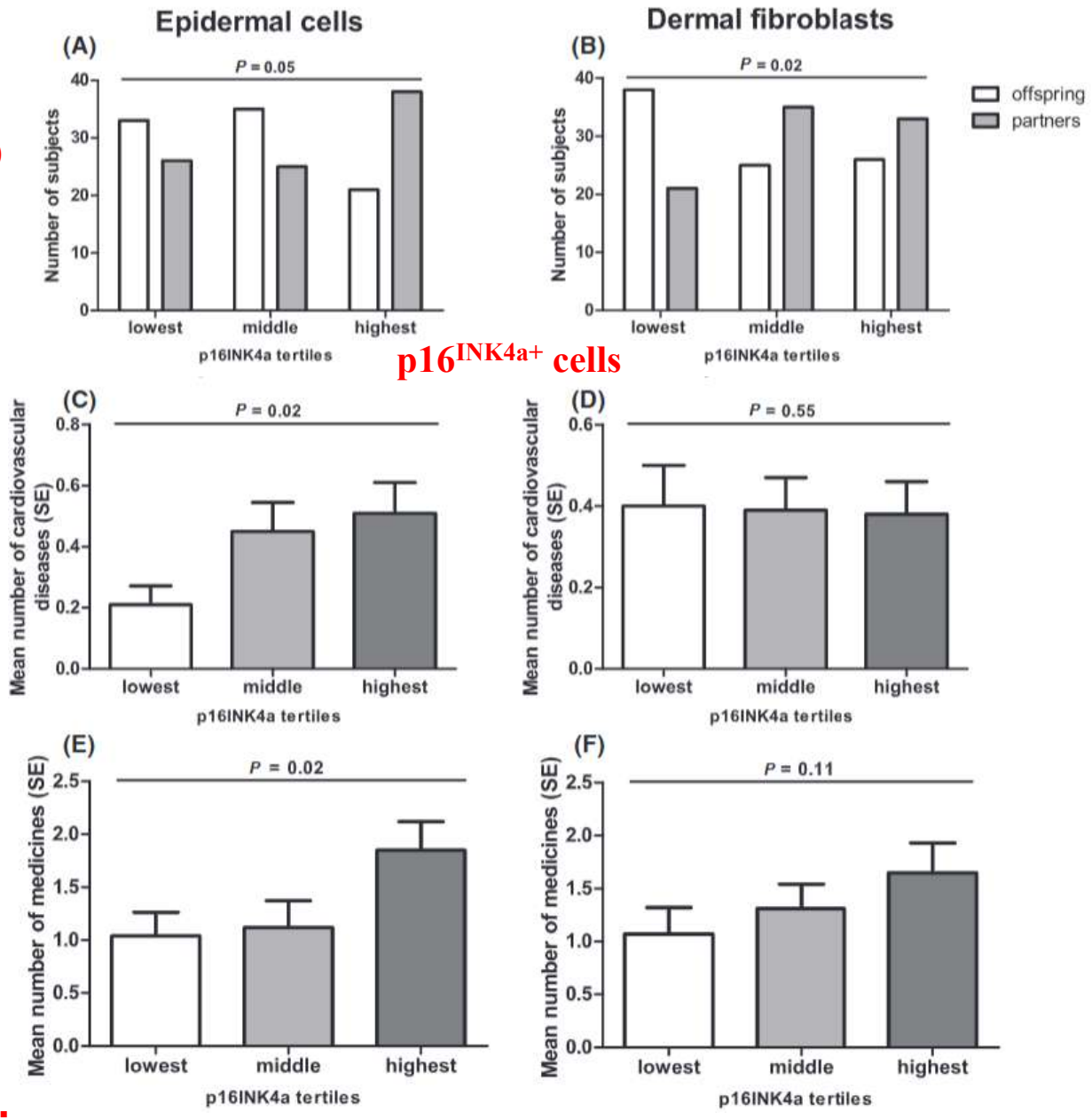
B.Y. Lee, et al., *Aging Cell*, 2006

Chaturvedi *et al.*, *Am. J. Pathol.*, 2003

J.E. Yoon, et al., *Theranostics*, 2018



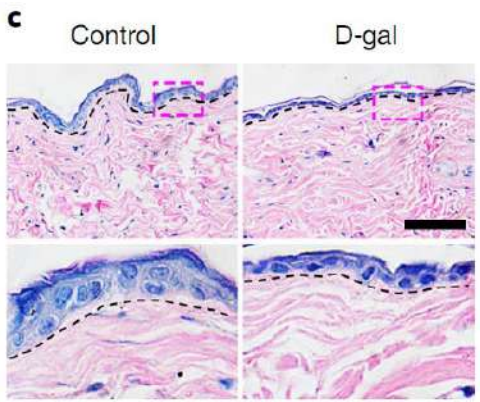
hyperpigmented lesions (色素沉积):
p16^{INK4A}/SA-β-galactosidase

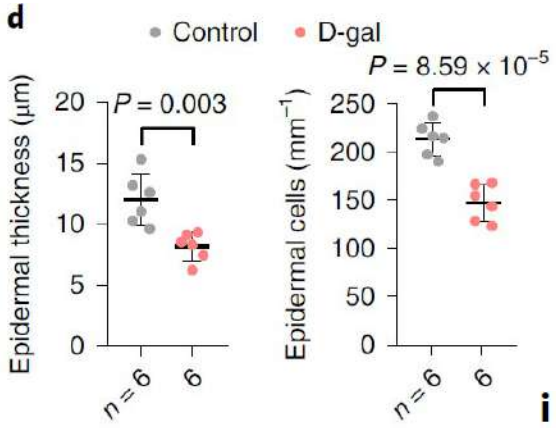


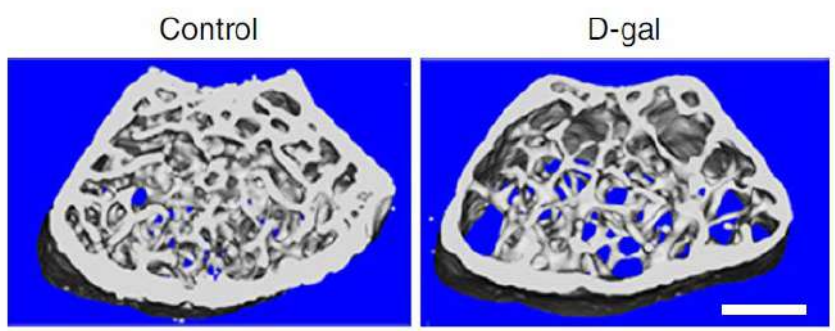
p16^{INK4a+} cells

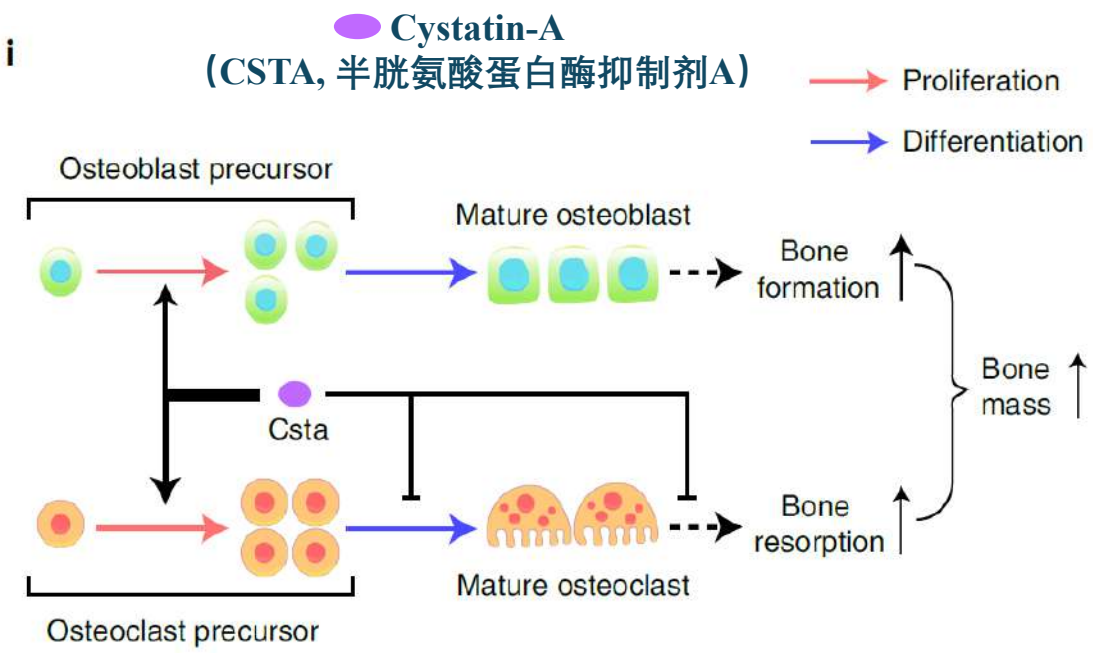
Waaijer, M.E.C., *et al.*, *Aging Cell.*, 2012

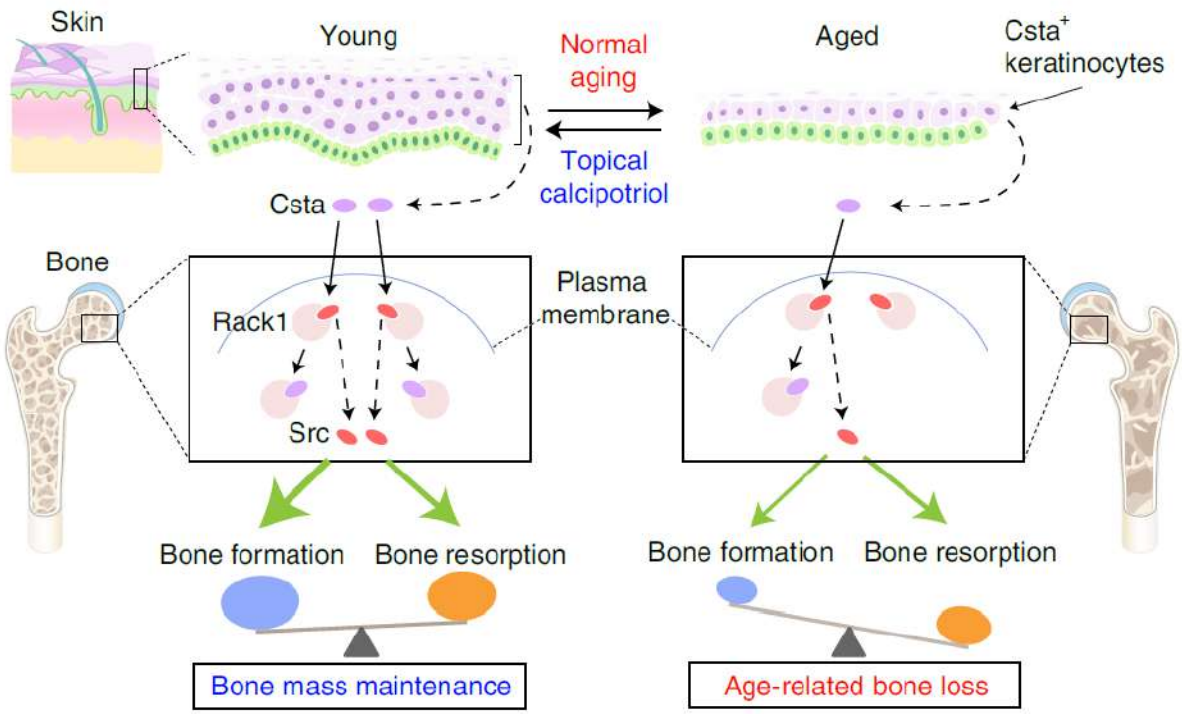
Skin chronological aging drives age-related bone loss via secretion of cystatin-A





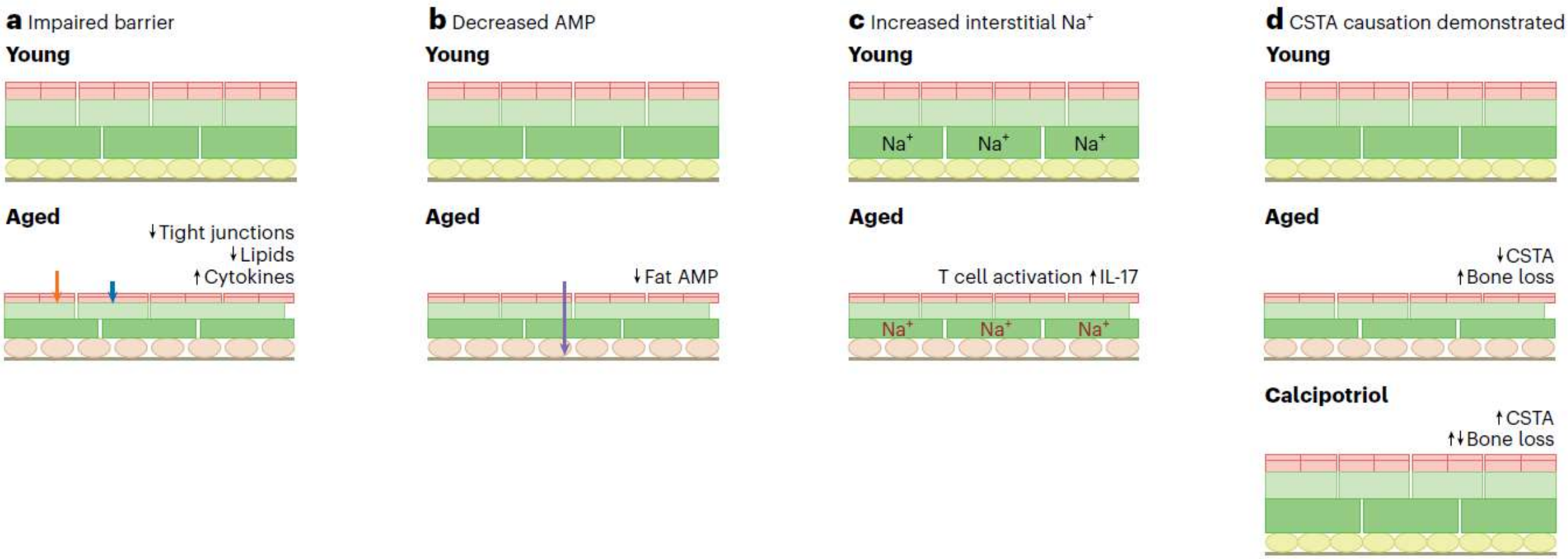






Liang, W. *et al., Nat. Aging,* 2022

Changes associated with skin aging and possible mechanisms linking them with systemic age-related disease.



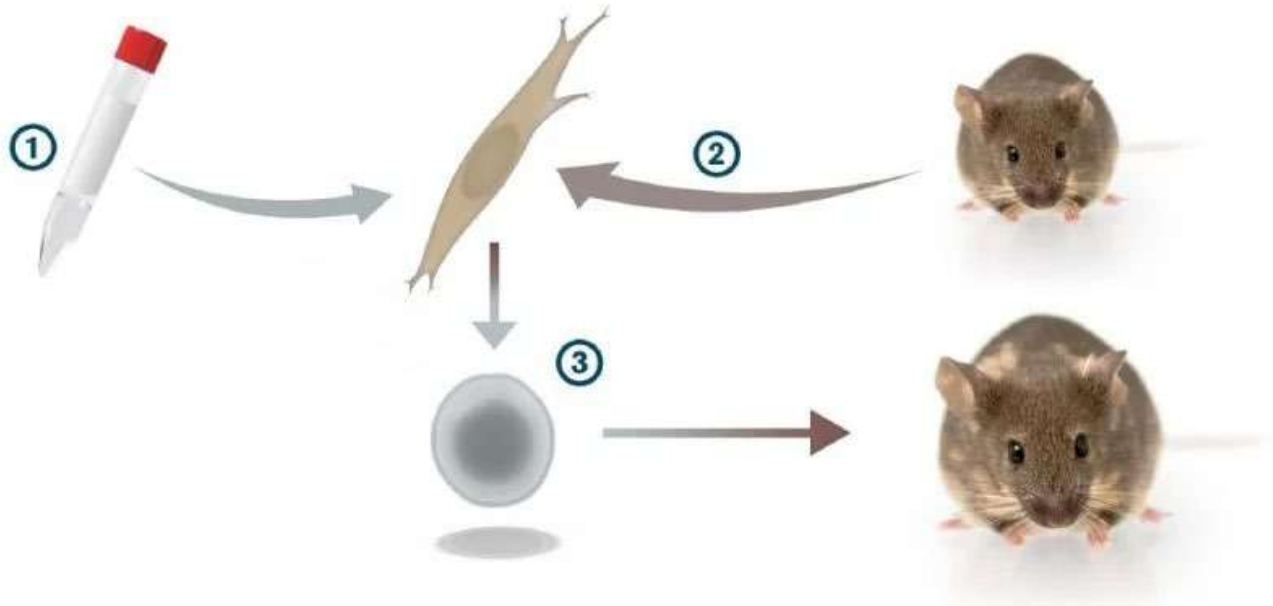
Troy, T. C., Arabzadeh, A., Larivière, N. M., Enikanolaiye, A. & Turksen, K. *PLoS ONE*, 2009
Choi, E. H. et al. *J. Invest. Dermatol*., 2007
Elias, P. M. & Ghadially, R. *Clin. Geriatr. Med*., 2002
Zhang, L. J. et al. *Immunity*., 2019
Maifeld, A. et al. *J. Invest. Dermatol*.,2022
Liang, W. et al., *Nat. Aging,* 2022
Theodora Mauro and Daniel Bikle, *Nat. Aging*., 2022

Cell

Shinya Yamanaka
山中伸弥
Nobel Prize in Physiology or Medicine 2012

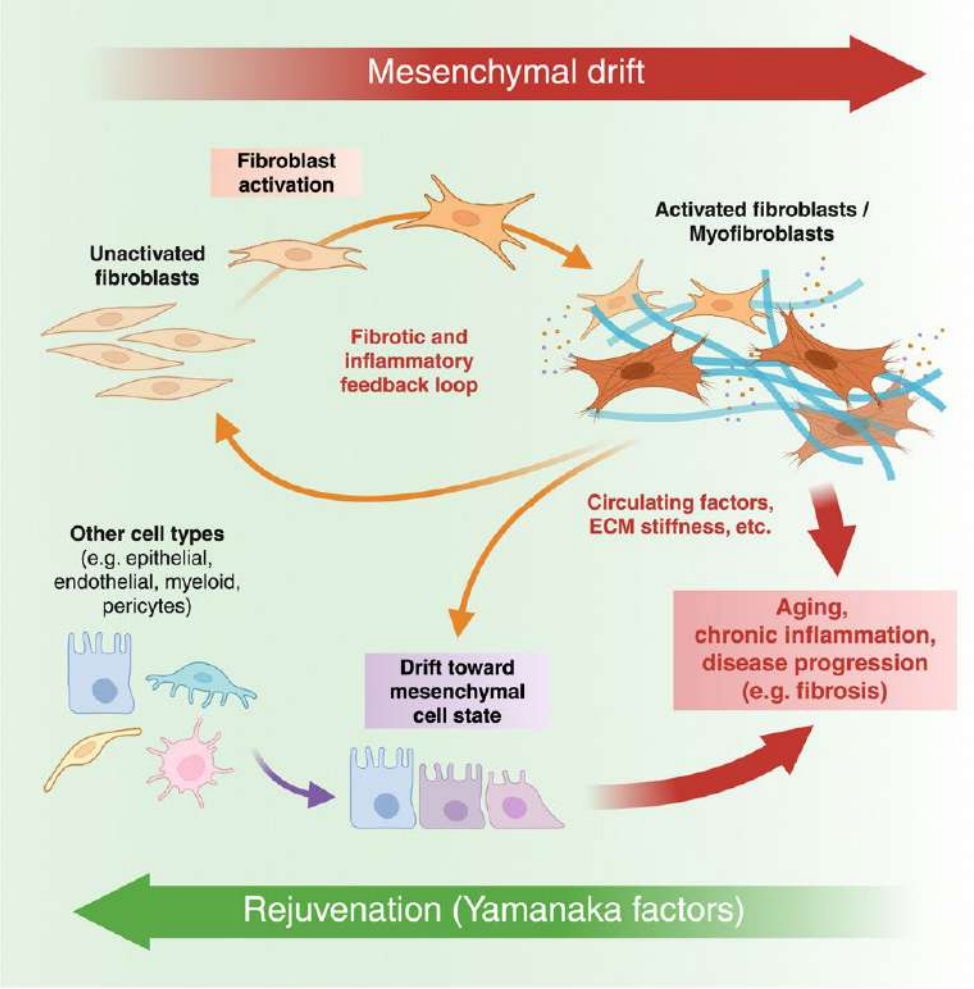
Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors

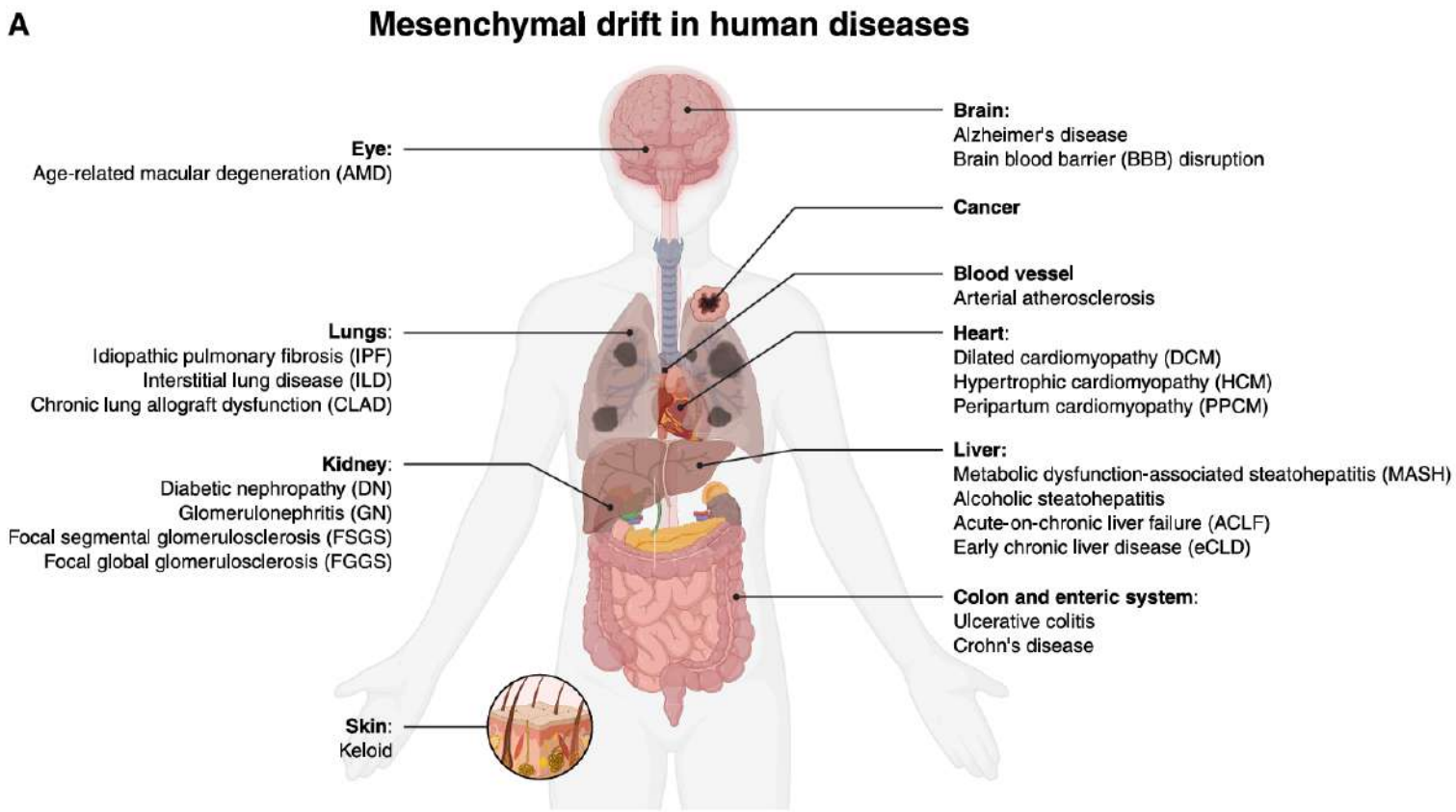
Kazutoshi Takahashi[1] and Shinya Yamanaka[1,2,*]
[1]Department of Stem Cell Biology, Institute for Frontier Medical Sciences, Kyoto University, Kyoto 606-8507, Japan
[2]CREST, Japan Science and Technology Agency, Kawaguchi 332-0012, Japan
*Contact: yamanaka@frontier.kyoto-u.ac.jp
DOI 10.1016/j.cell.2006.07.024



① Yamanaka factors: Oct3/4, Sox2, c-Myc, Klf4

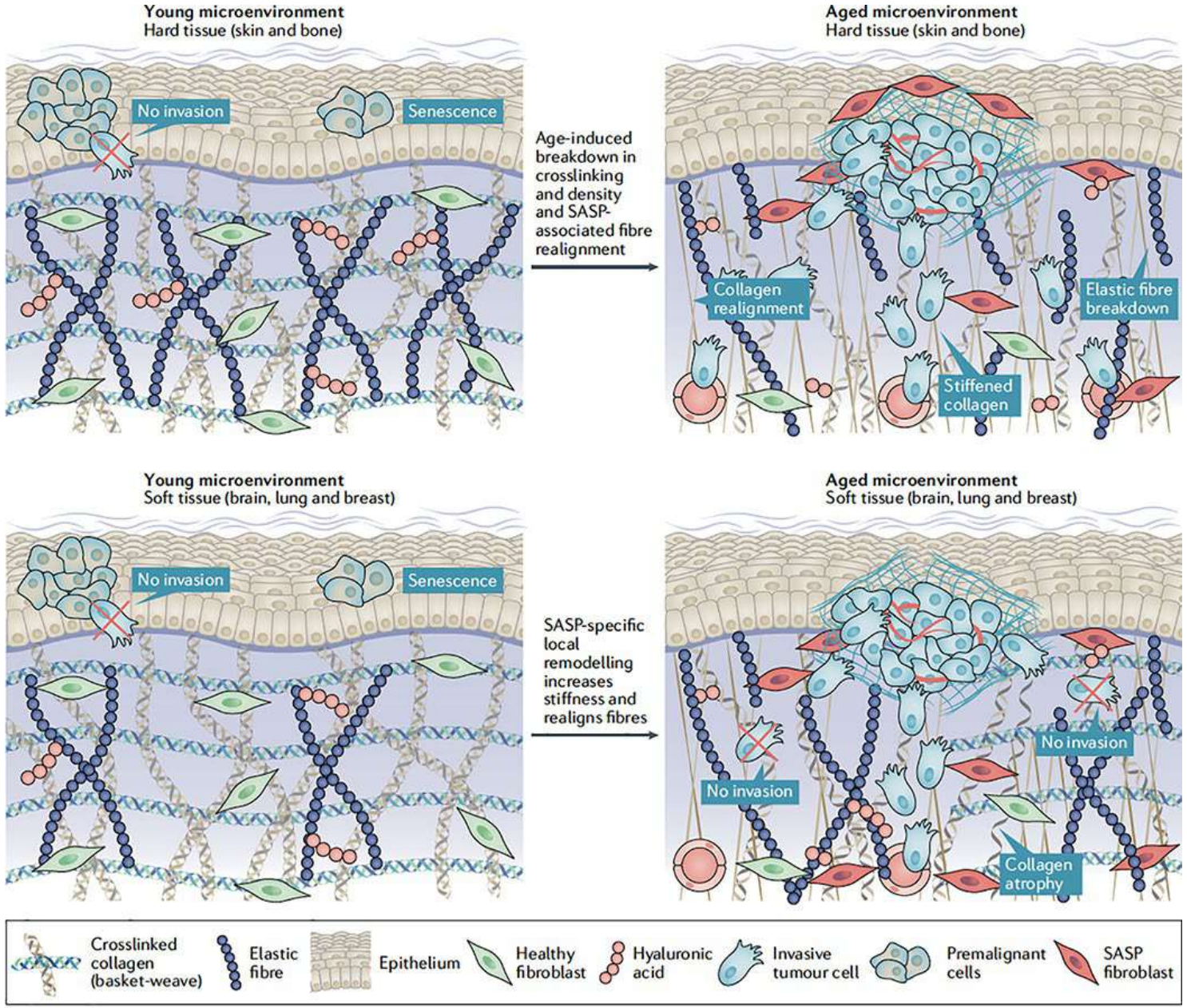
Mesenchymal drift is a bridge connected aging and diseases.





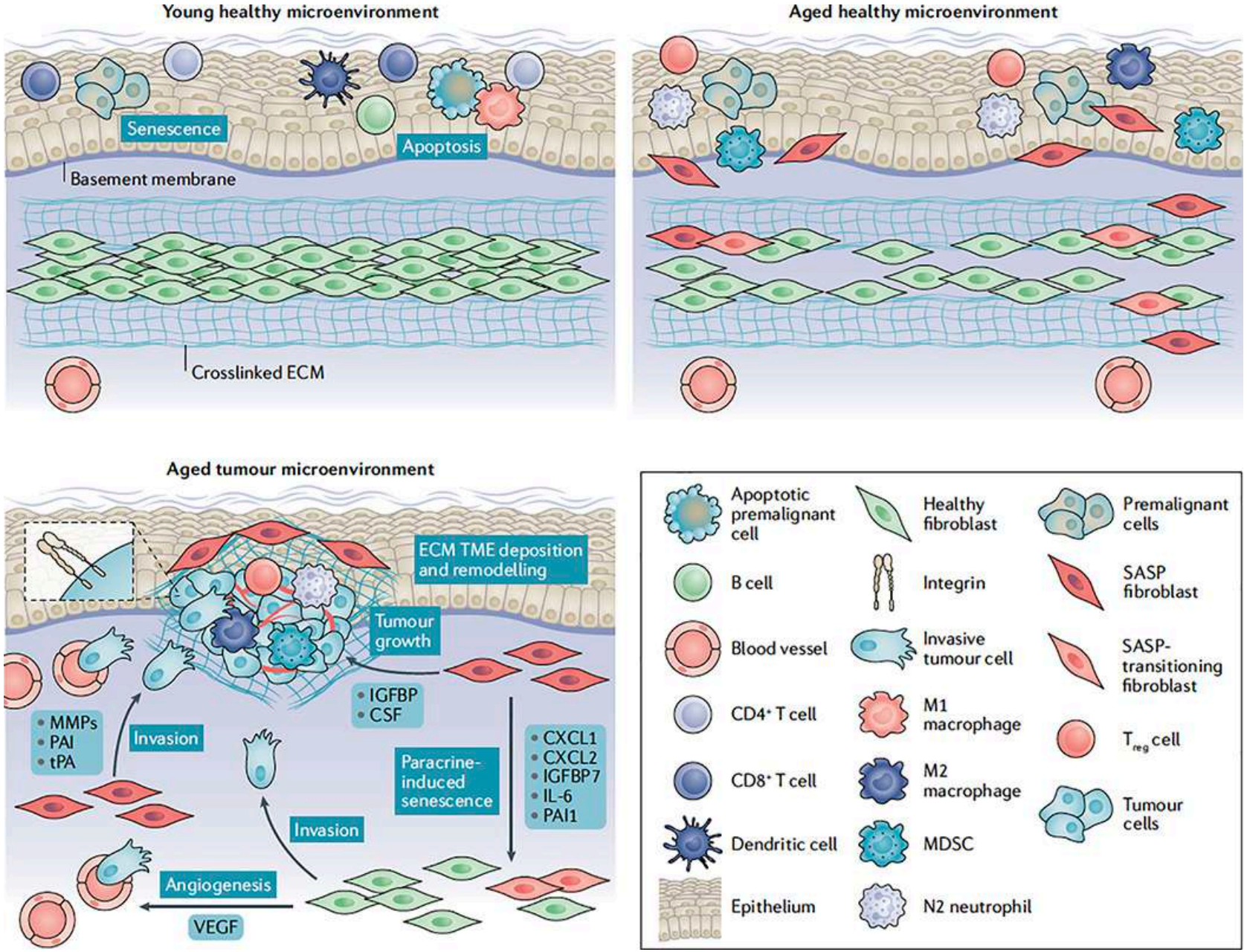
Lu, et al., *Cell*, 2025

Age-induced contextual changes in extracellular matrix structure and function



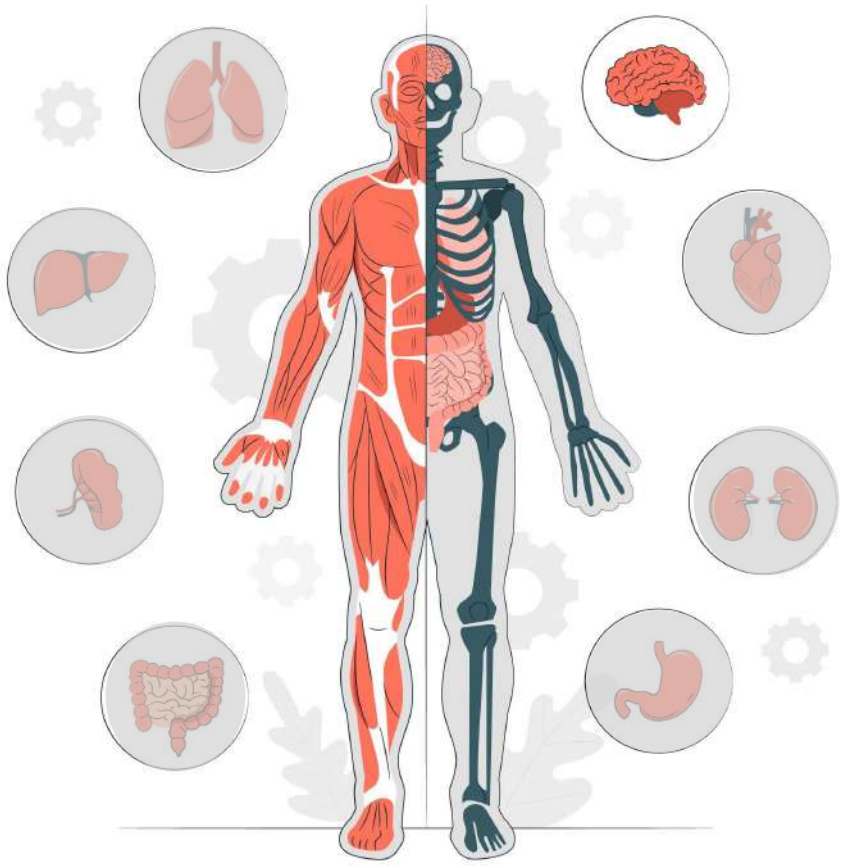
Fane M, Weeraratna AT., *Nat Rev Cancer*. 2020

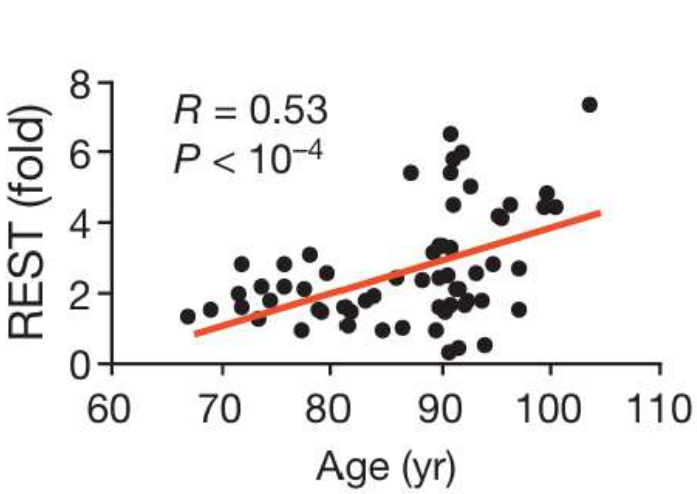
Stromal (基质的) deregulation in the aged microenvironment drives tumorigenesis and progression.

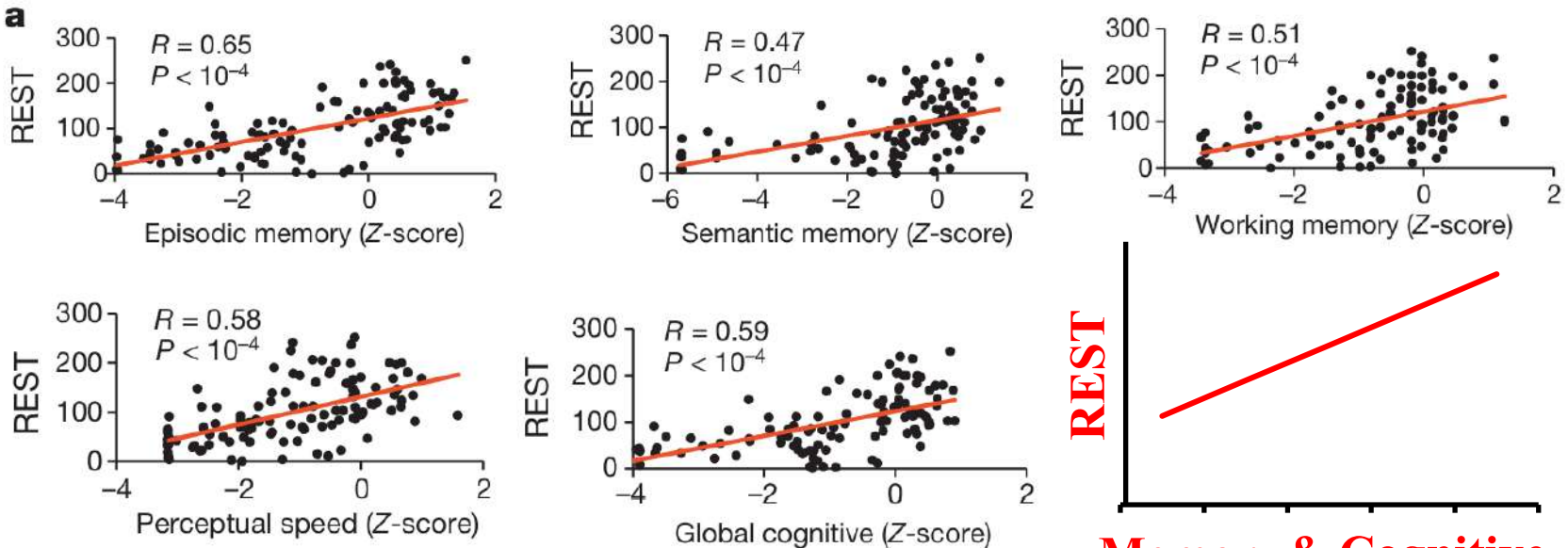


Fane M, Weeraratna AT., *Nat Rev Cancer*. 2020

During physiology aging, the repressor element-1 silencing transcription factor(REST)/ neuron-restrictive silencer factor (NRSF) preserves neuron function





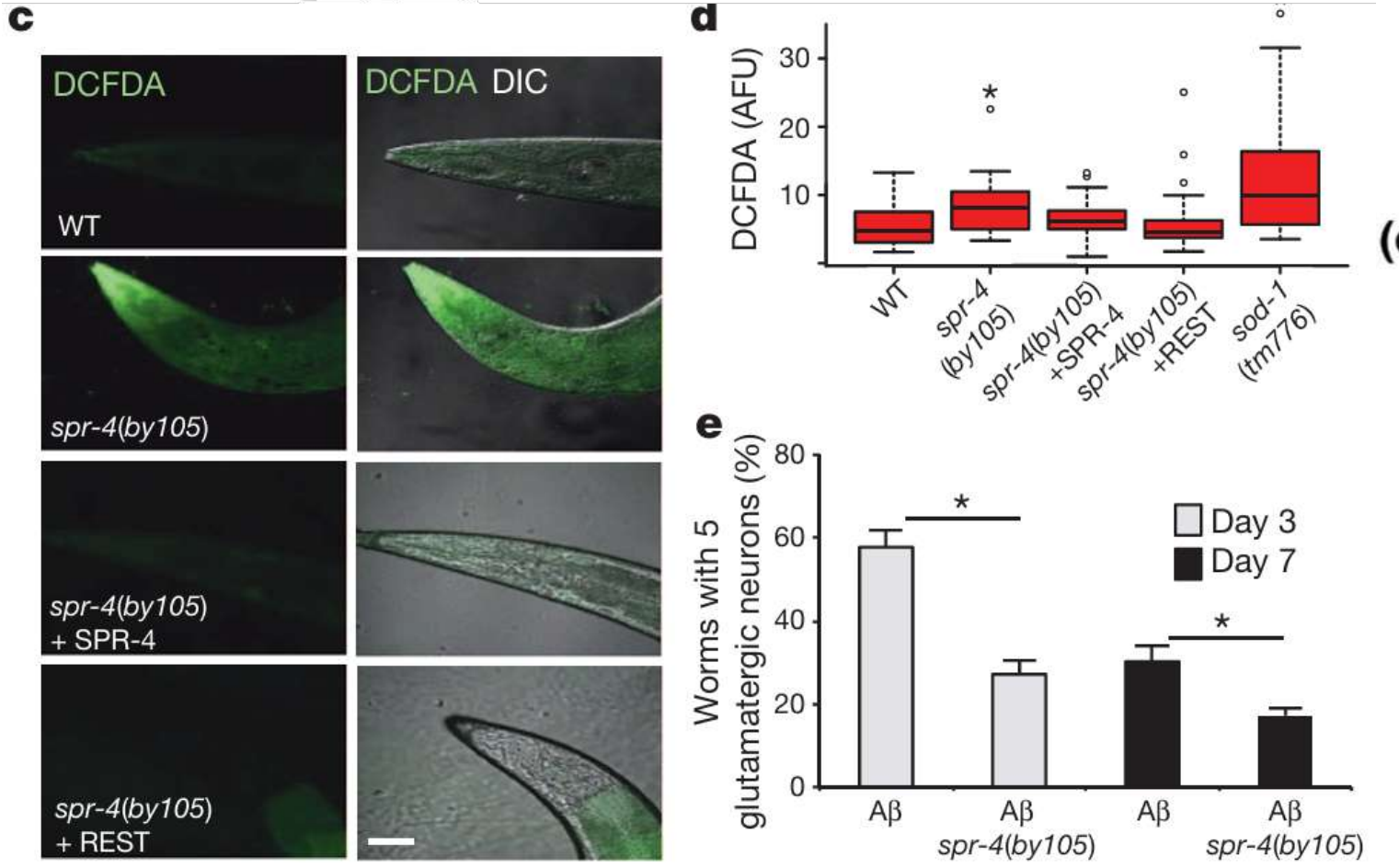


Memory& Cognitive

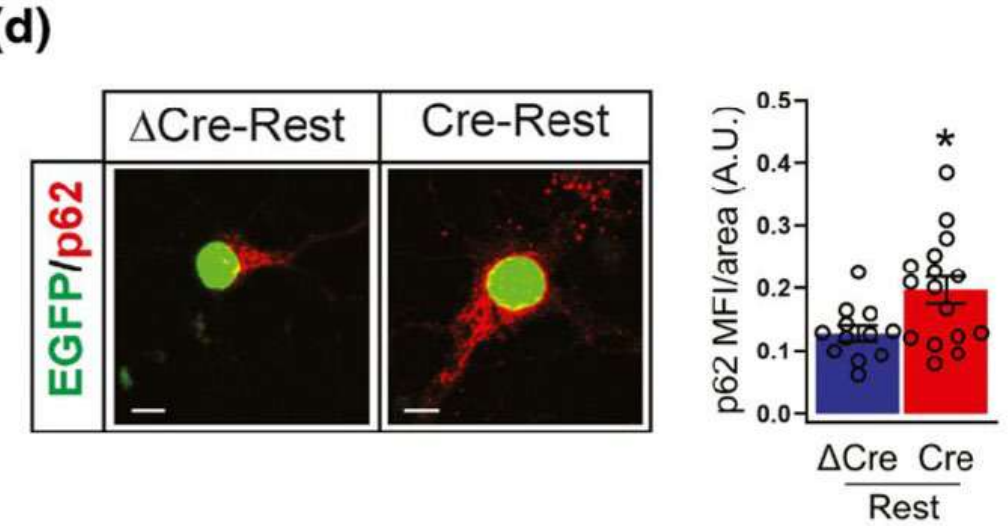
Tao Lu, et al., *Nature*, 2014

REST is essential to promote stress resistance and autophagy.

Oxidative stress & Aβ toxicity

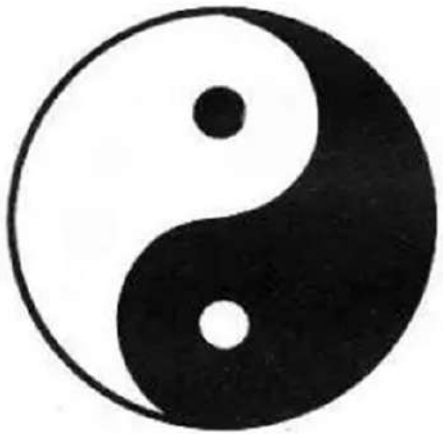


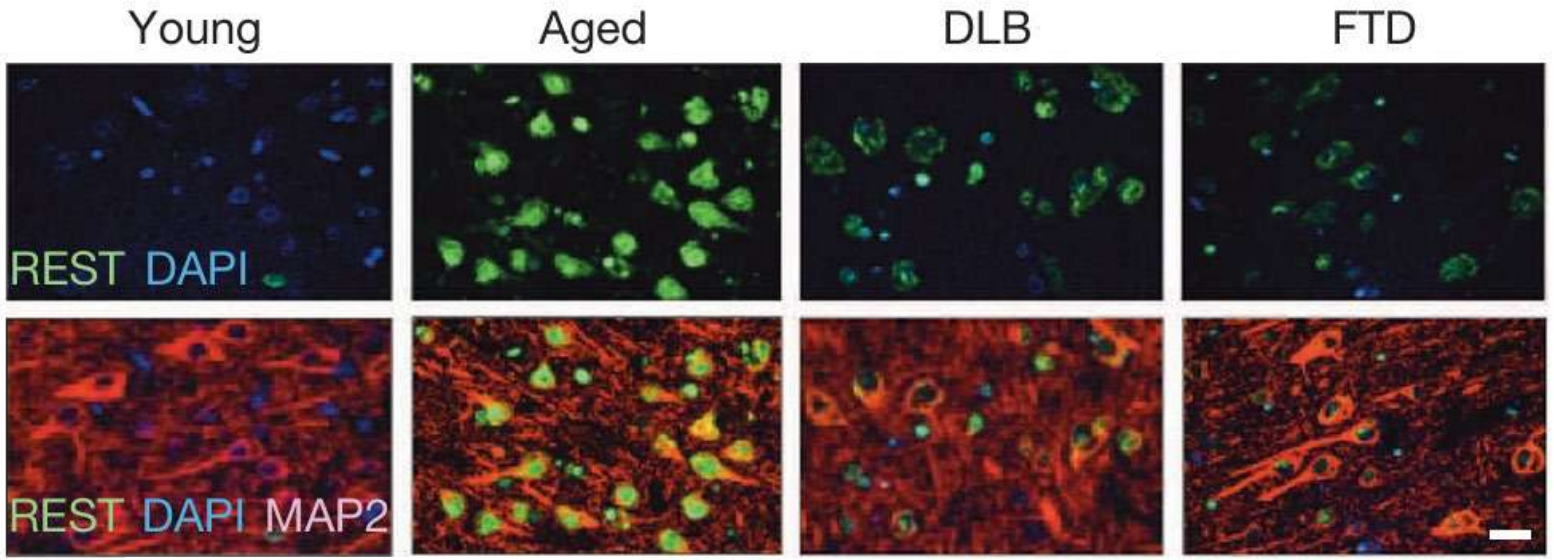
Autophagy

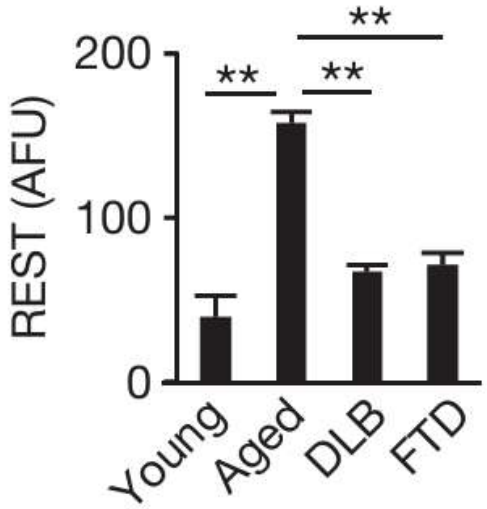


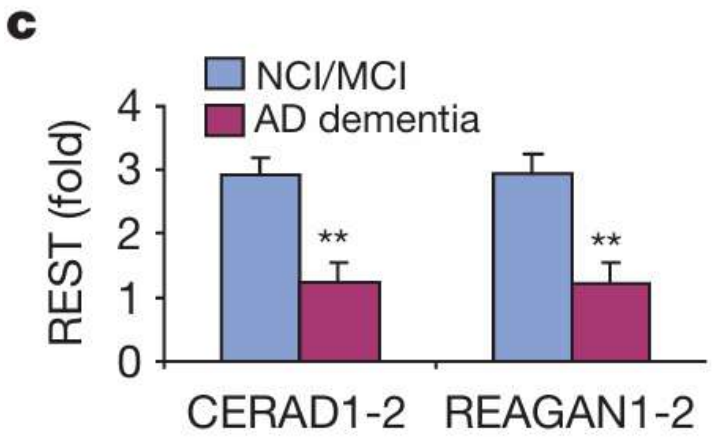
Tao Lu, et al., *Nature*, 2014
Rocchi, A. et al., *Aging Cell*, 2020

REST is depleted in neurodegenerative disorders.

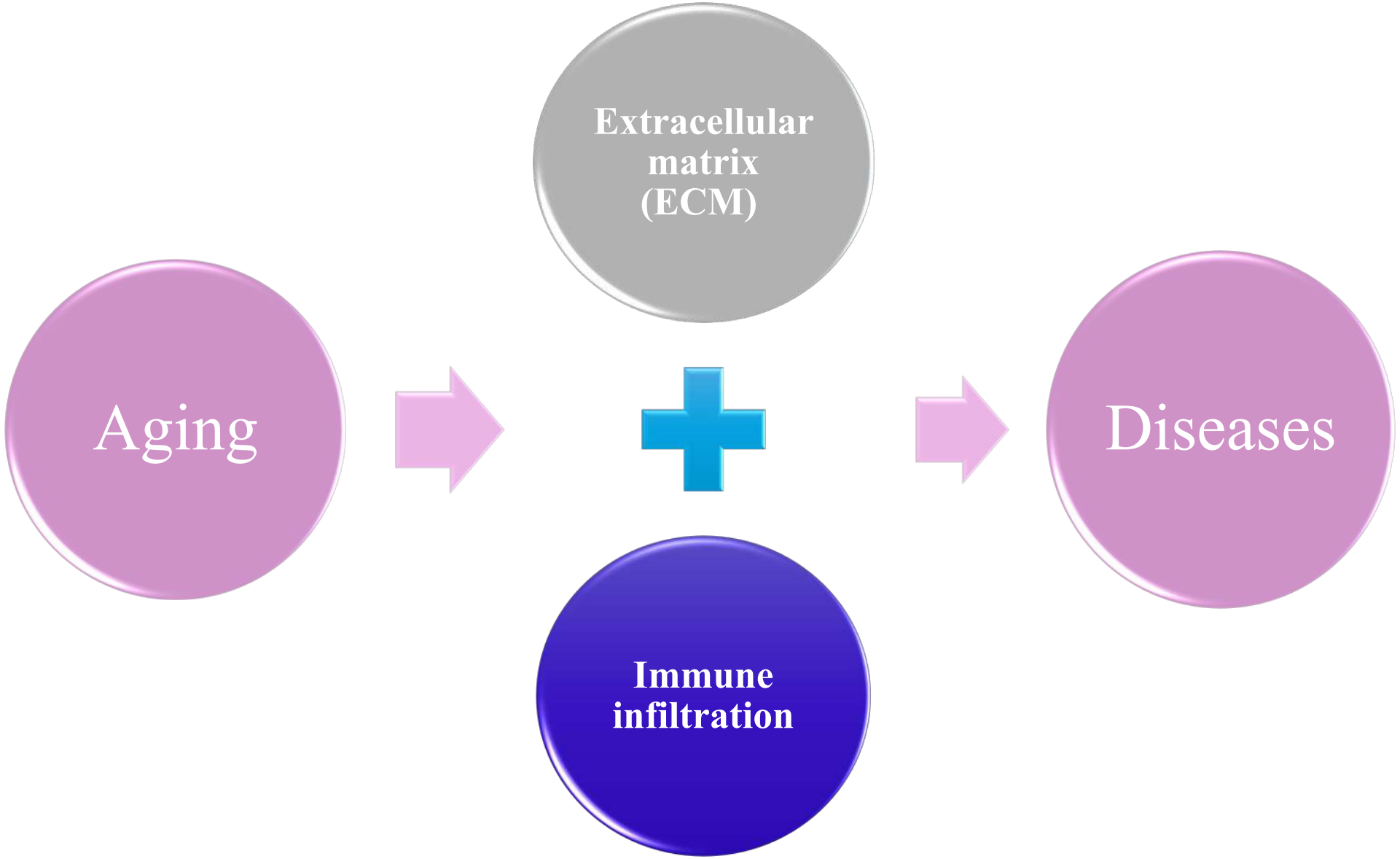




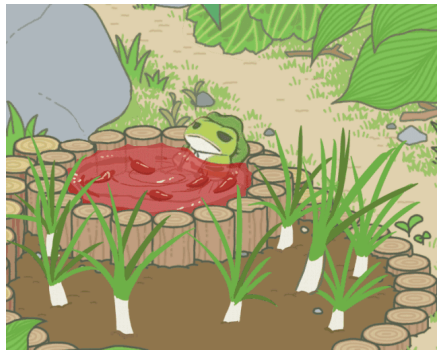




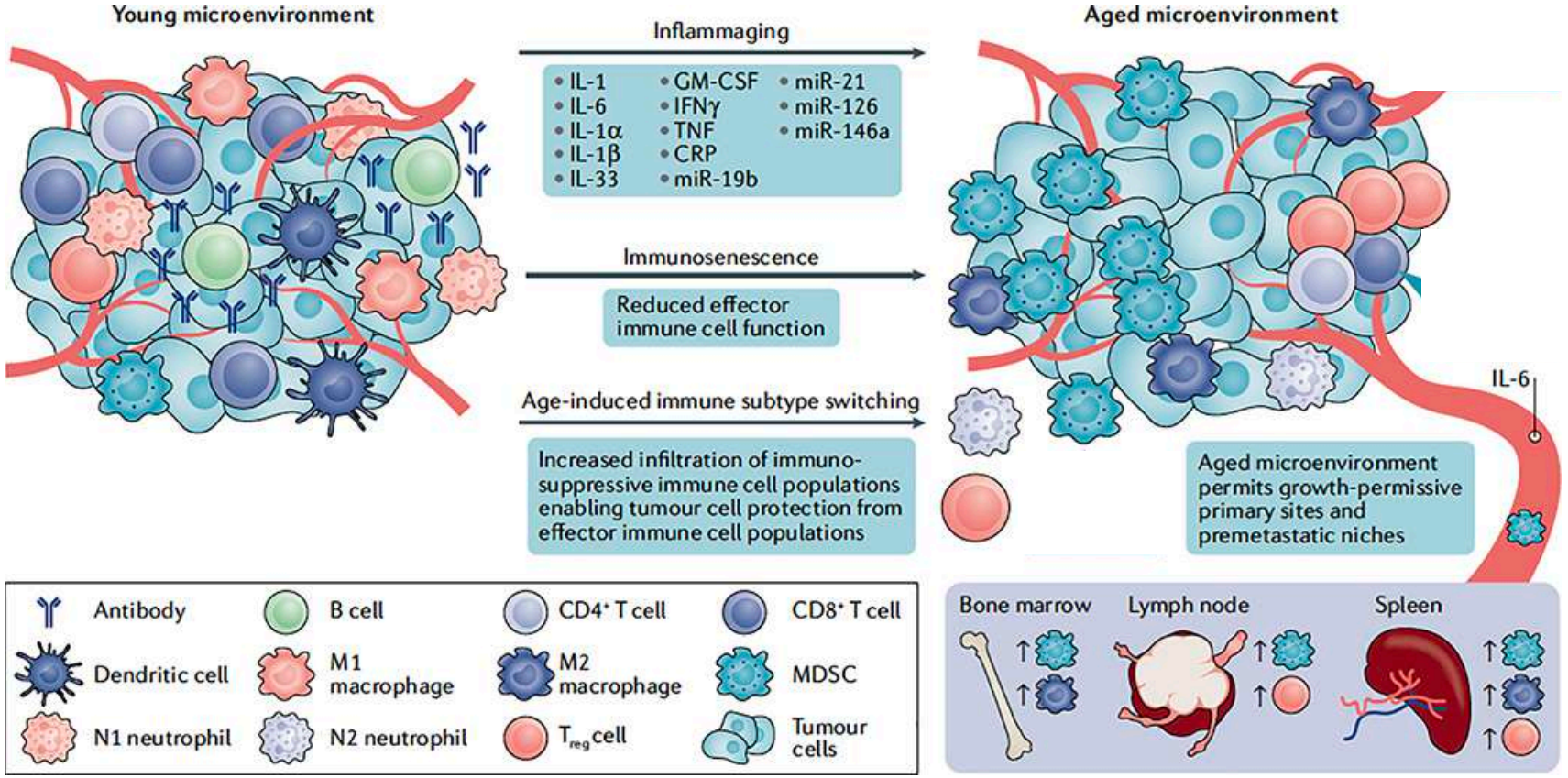
Tao Lu, et al., *Nature*, 2014


Extracellular matrix (ECM)
Aging
Diseases
Immune infiltration

Inflammaging is an age-related driver of cancer progression

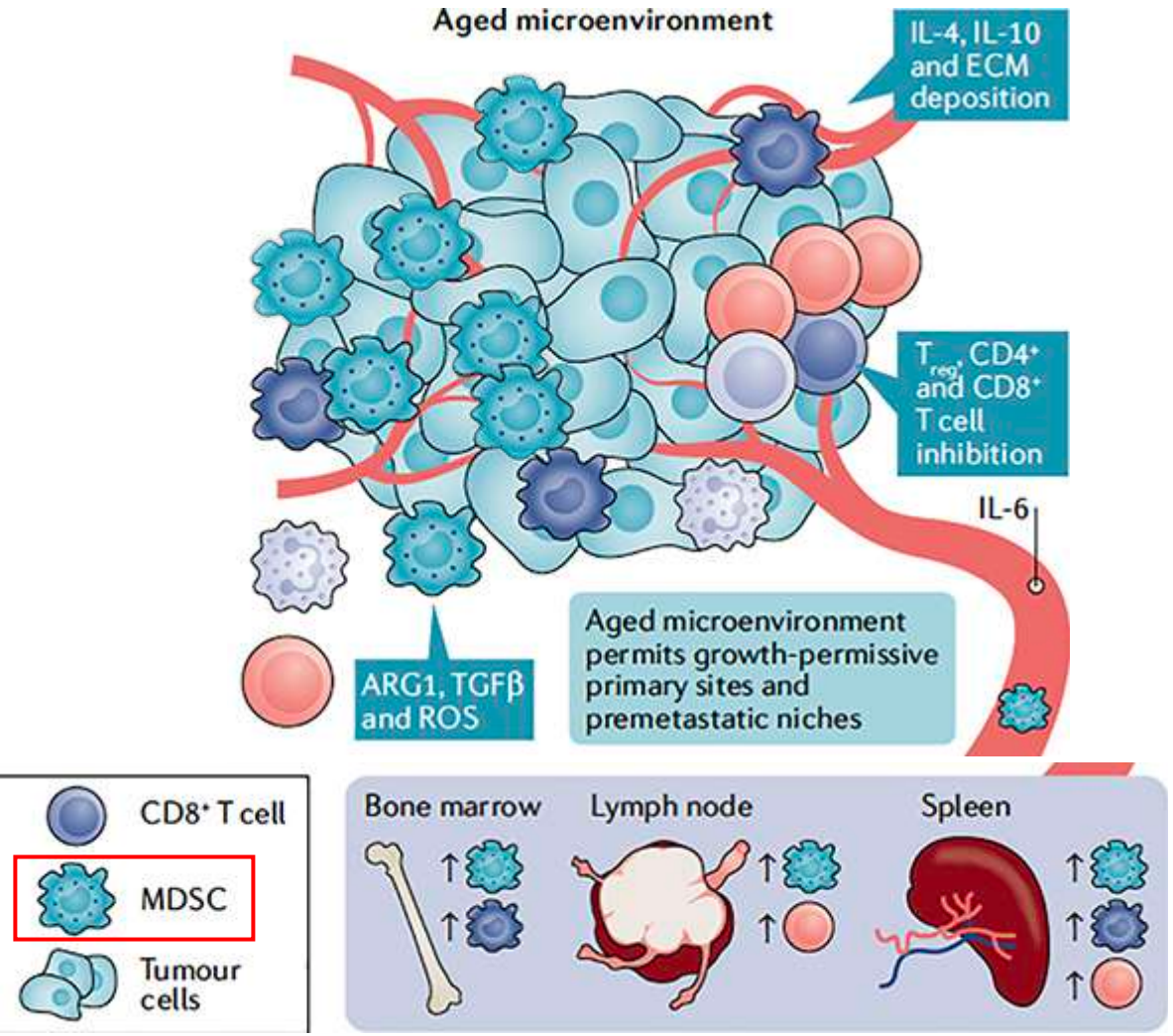


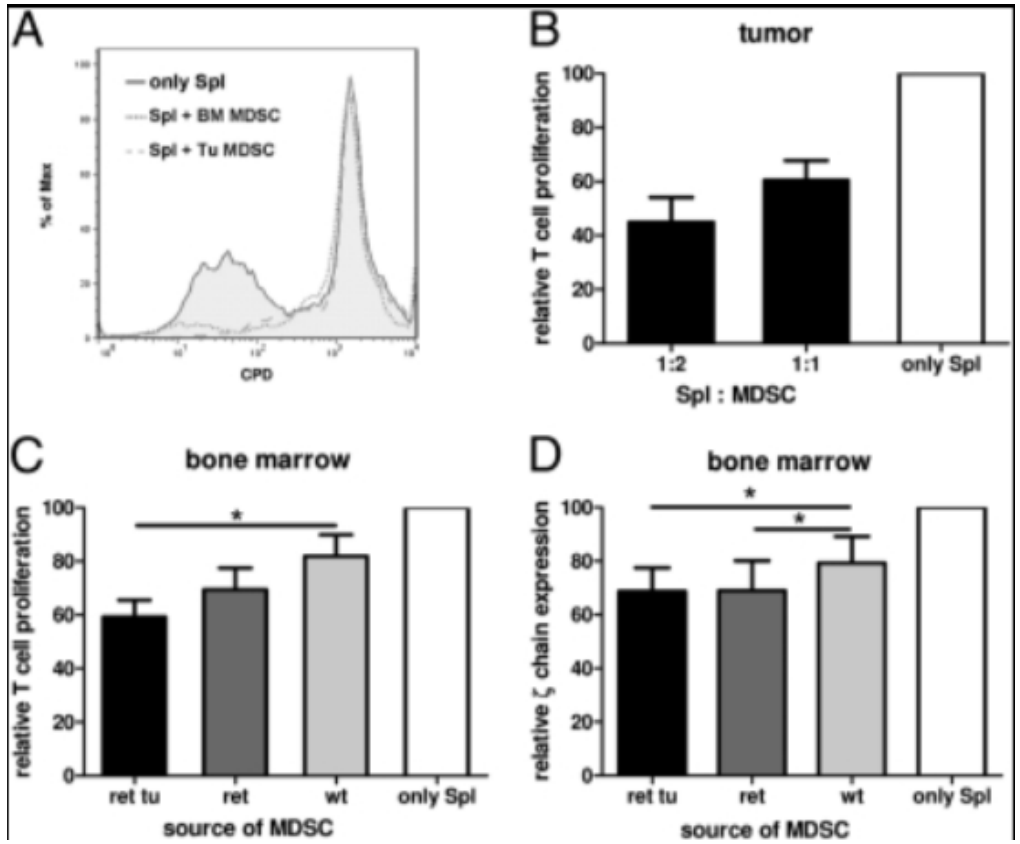
Inflammaging: an increase in systemic low-grade chronic inflammation.



Fane M, Weeraratna AT., *Nat Rev Cancer*. 2020

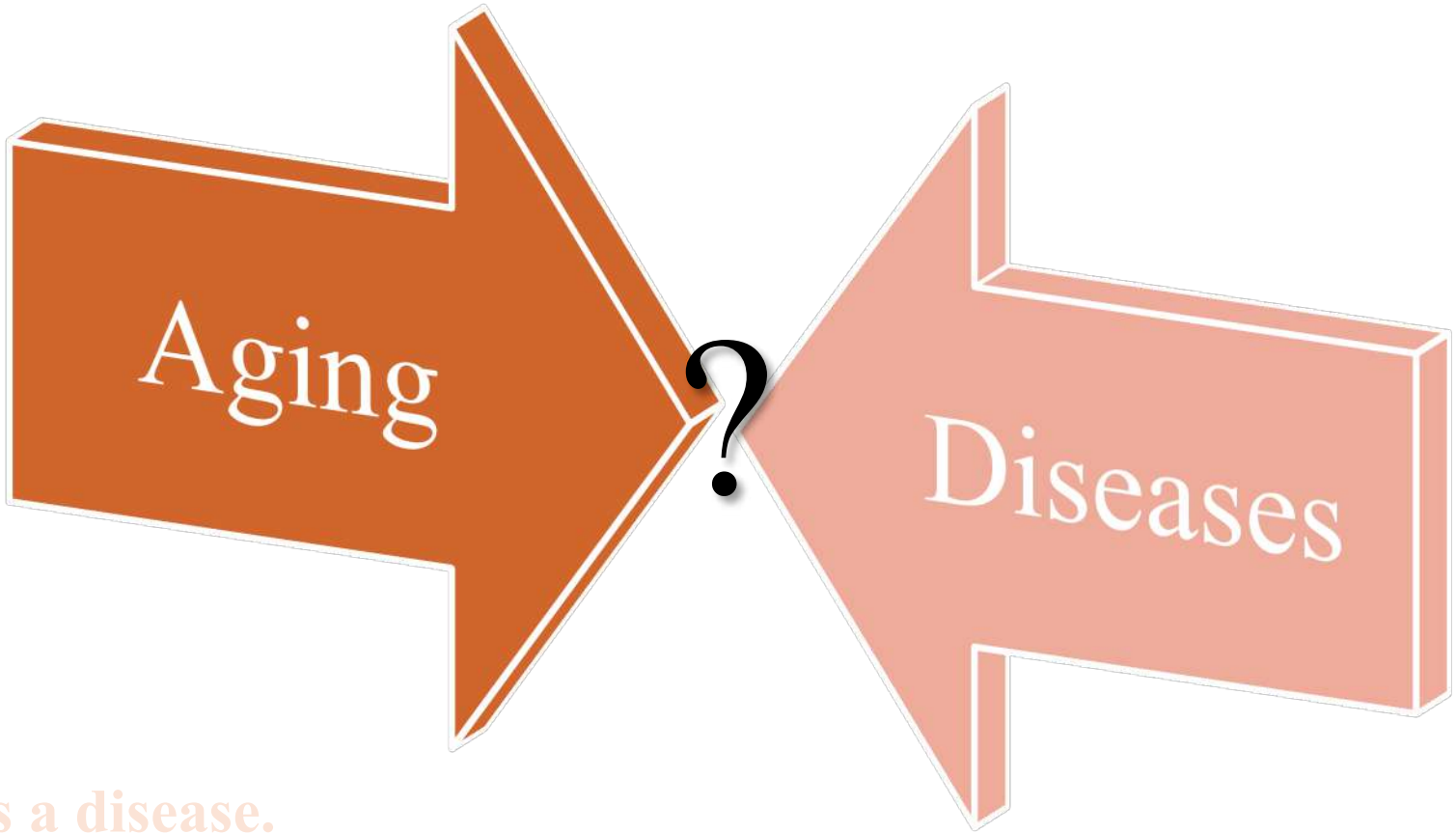
The recruitment of myeloid-derived suppressor cells (MDSCs) is one of the key elements that appear to link inflammaging to many types of cancer





MDSC (髓源性抑制细胞):potent repressors of T cells

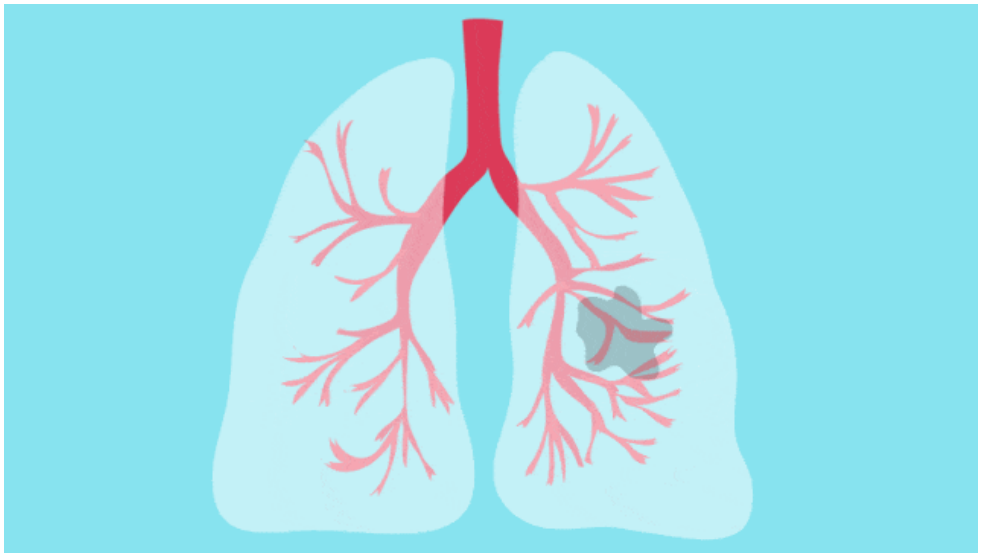
Fane M, Weeraratna AT., *Nat Rev Cancer*. 2020
LOU Yixia, et al., *Journal of Army Medical University*, 2023
Meyer C. et.al., *PNAS*, 2011



- ✓ When aging is regarded as a disease.
- ✓ When aging becomes a factor that contributes diseases.
- ✓ **When aging is a normal physiological phenomenon.**

If these are found on your physical examination report, don't be worried.

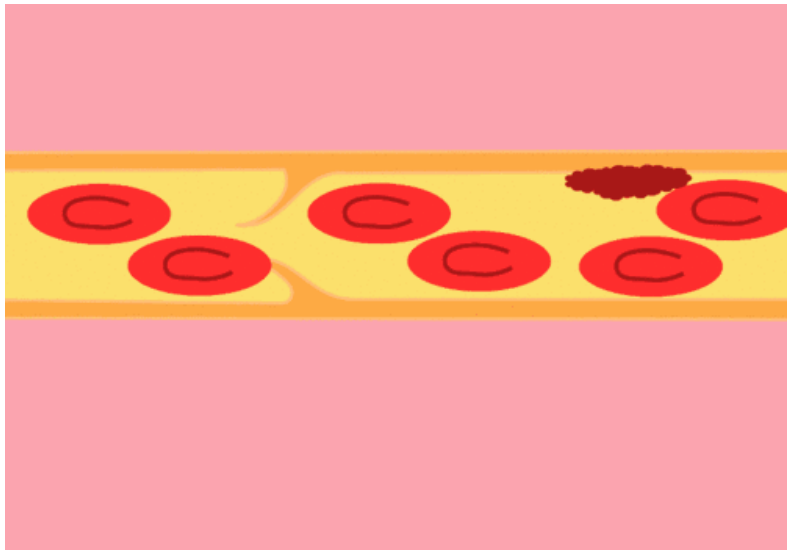
Nodules
结节



- The smaller the nodule, the more likely it is to be benign.
- 80% of benign nodules: ≤ 2 cm in diameter.

Feragalli B, et al., *Radiol Med*. 2005

Carotid atherosclerosis
动脉粥样硬化

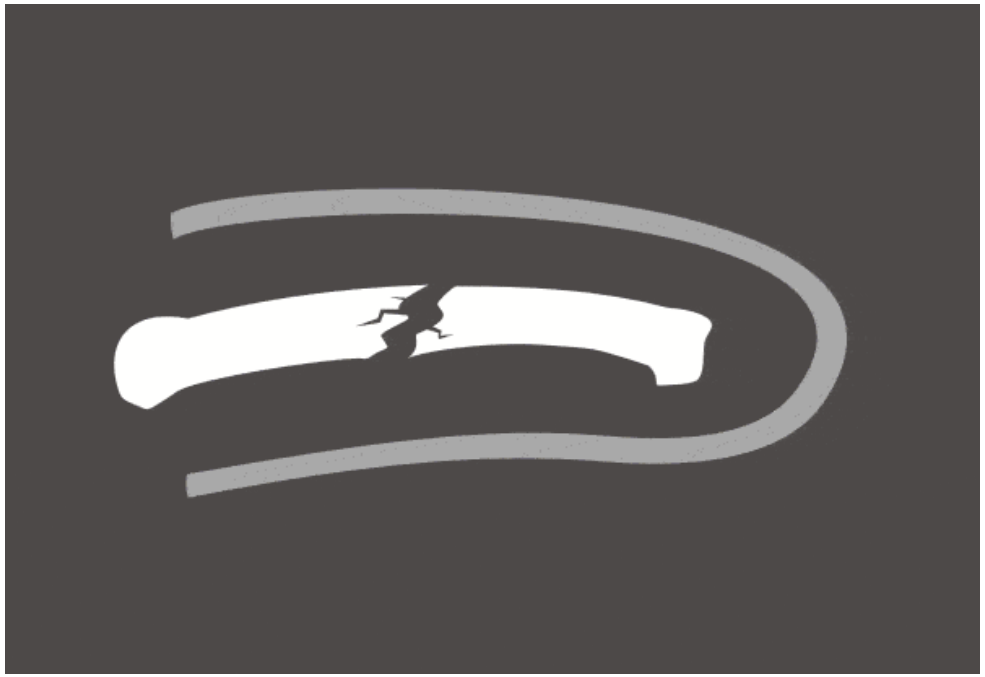


The prevalence of increased carotid intima-media thickness, carotid plaque, and carotid stenosis increased consistently with age and was higher in men than in women.

Song P, et al., *Lancet Glob Health*. 2020

If these are found on your physical examination report, don't be worried.

Osteoporosis
骨质疏松症



- Postmenopausal（绝经后） osteoporosis is a frequent clinical condition which affects nearly 1 in 3 women.
- Osteoporosis is a chronic disease that cannot be cured.

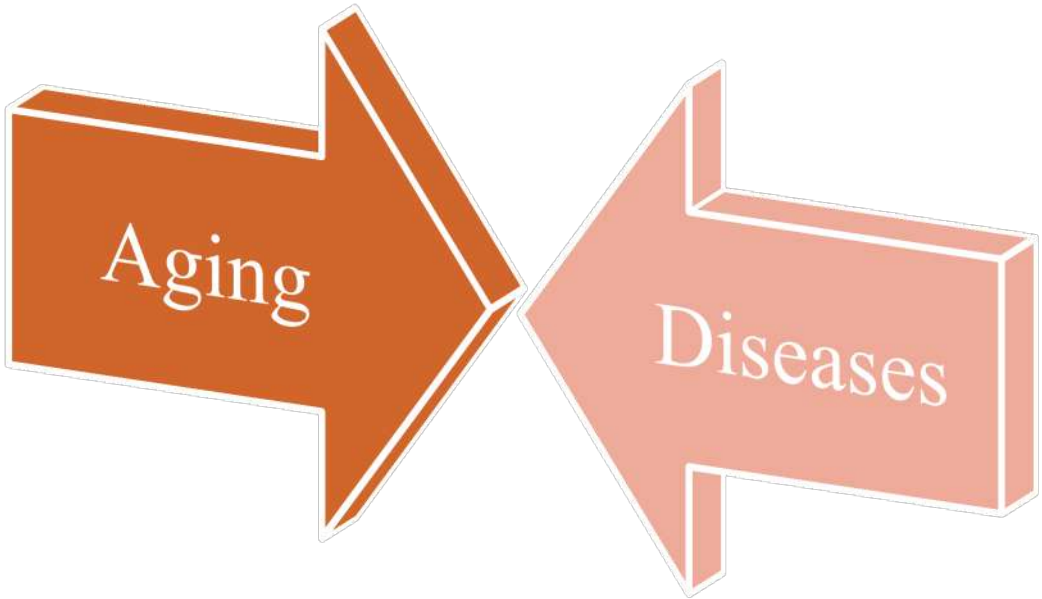
Gosset A, Pouillès JM, Trémollieres F. *Best Pract Res Clin Endocrinol Metab.* 2021

Benign prostatic hyperplasia (BPH)
良性前列腺增生

Age-related changes associated with metabolic disturbances, changes in hormone balance, and chronic inflammation may cause BPH development.

Kim EH, Larson JA, Andriole GL. *Annu Rev Med.* 2016

Take home message



✓ When aging is regarded as a disease.

Hutchinson-Gilford Progeria Syndrome

A mutation in ***LMNA*** leading to deletion of 50 amino acid residues from the precursor protein caused premature aging.

✓ When aging becomes a factor that contributes diseases.

- **Stromal(基质的) deregulation and inflammaging in the aged microenvironment drives diseases progression.**
- **Repressor element 1-silencing transcription factor (REST) preserves function and protects against neurodegeneration during ageing.**

✓ When aging is a normal physiological phenomenon.

Nodules, Carotid atherosclerosis, Osteoporosis, Benign prostatic hyperplasia

Strategies for delaying aging

Part1: Classic strategies
Part2: For reference only
Part3: New theoretical framework of aging

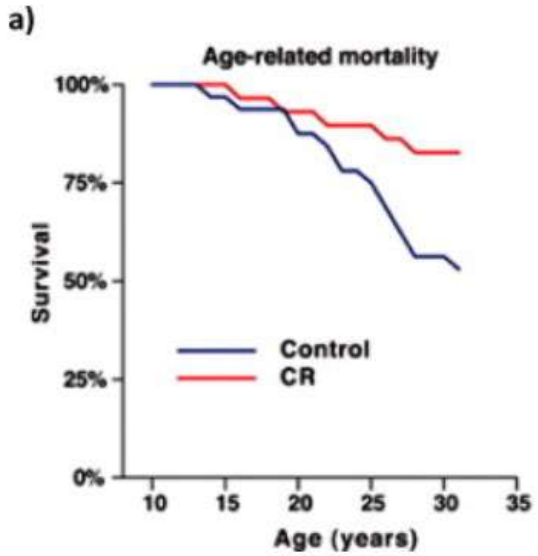
lyg

Francis Bacon
(1561-1624)

“发育、性成熟过程迟缓、漫长，
是个体长寿的标志之一”

Caloric/Dietary Restriction(CR/DR) is the most classic way to delay aging

THESE TYPICAL RATS ARE BOTH 900 DAYS OLD



	Life-span increase	
	Dietary restriction	Mutations/ drugs
Yeast	3-fold	10-fold (with starvation/ DR)
Worms	2- to 3-fold	10-fold
Flies	2-fold	60–70%
Mice	30–50%	30–50% (~100% in combination with DR)
Monkeys	Trend noted	Not tested

Fontana, L. *et al. Science* **328**, 321–326 (2010)

Insulin-like signaling pathway

LETTERS TO NATURE

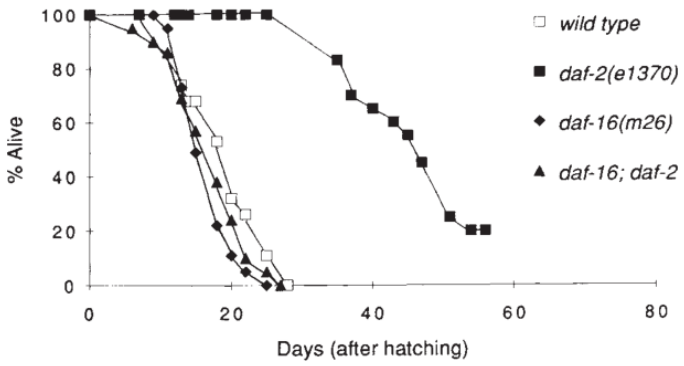
A *C. elegans* mutant that lives twice as long as wild type

Cynthia Kenyon, Jean Chang, Erin Gensch, Adam Rudner & Ramon Tabtiang

Department of Biochemistry and Biophysics, University of California at San Francisco, San Francisco, California 94143–0554, USA

We have found that mutations in the gene *daf-2* can cause fertile, active, adult *Caenorhabditis elegans* hermaphrodites to live more than twice as long as wild type. This lifespan extension, the largest yet reported in any organism[1], requires the activity of a second gene, *daf-16*. Both genes also regulate formation of the dauer larva, a developmentally arrested larval form that is induced by crowding and starvation and is very long-lived[2–4]. Our findings raise the possibility that the longevity of the dauer is not simply a consequence of its arrested growth, but instead results from a regulated lifespan extension mechanism that can be uncoupled from other aspects of dauer formation. *daf-2* and *daf-16* provide entry points into understanding how lifespan can be extended.

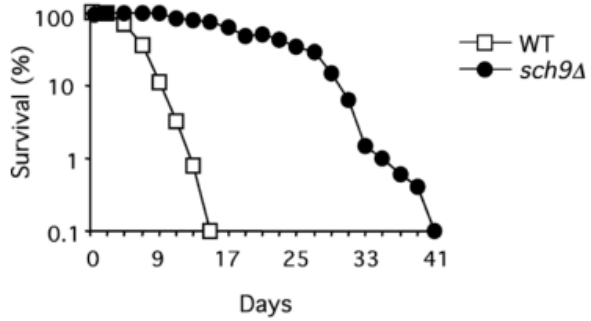
daf: dauer larvae formation



Regulation of Longevity and Stress Resistance by Sch9 in Yeast

Paola Fabrizio,[1] Fabiola Pozza,[1] Scott D. Pletcher,[2] Christi M. Gendron,[2] Valter D. Longo[1]*

The protein kinase Akt/protein kinase B (PKB) is implicated in insulin signaling in mammals and functions in a pathway that regulates longevity and stress

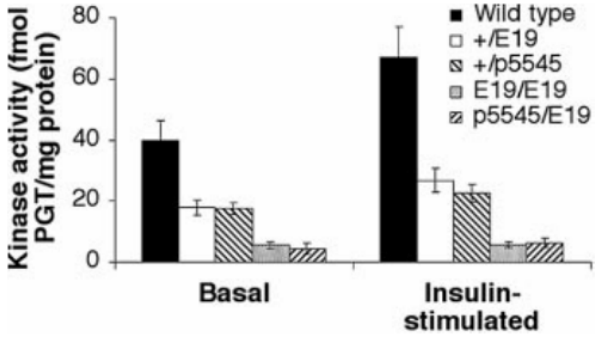


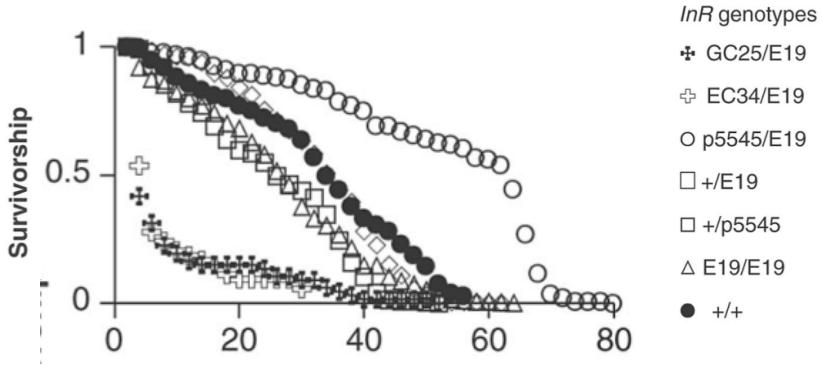
Fabrizio, P. *et al. Science* **292**, 288–290 (2001)

A Mutant *Drosophila* Insulin Receptor Homolog That Extends Life-Span and Impairs Neuroendocrine Function

M. Tatar,[1]* A. Kopelman,[1] D. Epstein,[1] M.-P. Tu,[1,2] C.-M. Yin,[2] R. S. Garofalo[3]

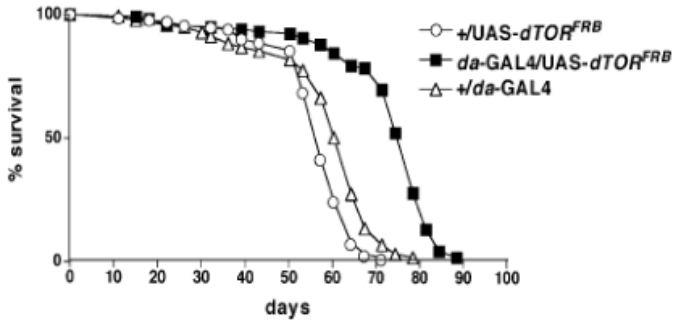
The *Drosophila melanogaster* gene *insulin-like receptor* (*InR*) is homologous to mammalian insulin receptors as well as to *Caenorhabditis elegans daf-2*, a signal transducer regulating worm dauer formation and adult longevity. We describe

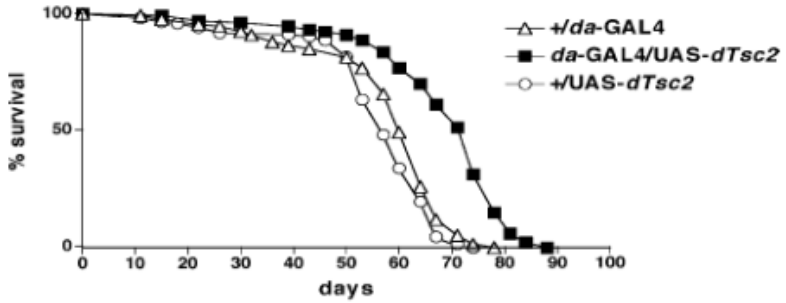




Tatar, M. *et al. Science* **292**, 107–110 (2001)

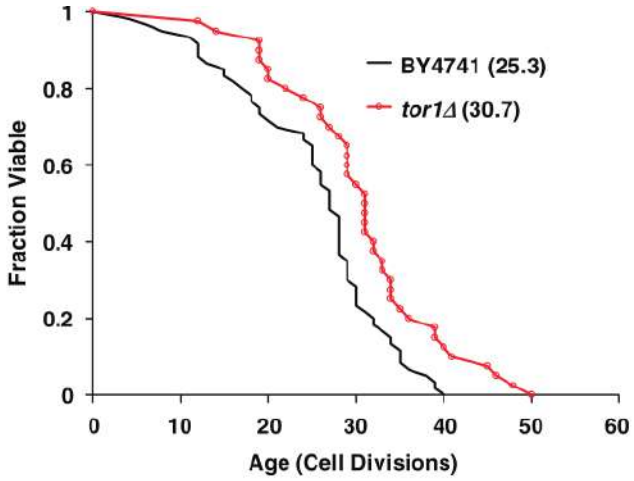
Target of Rapamycin (TOR)

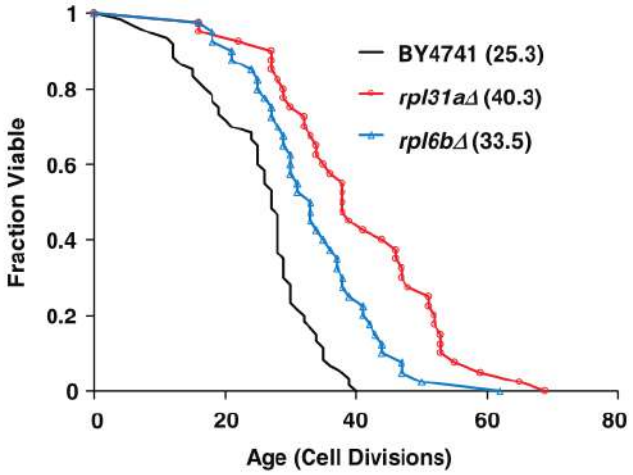




In Drosophila:

Inhibition of dTOR pathway led to a mean lifespan increase



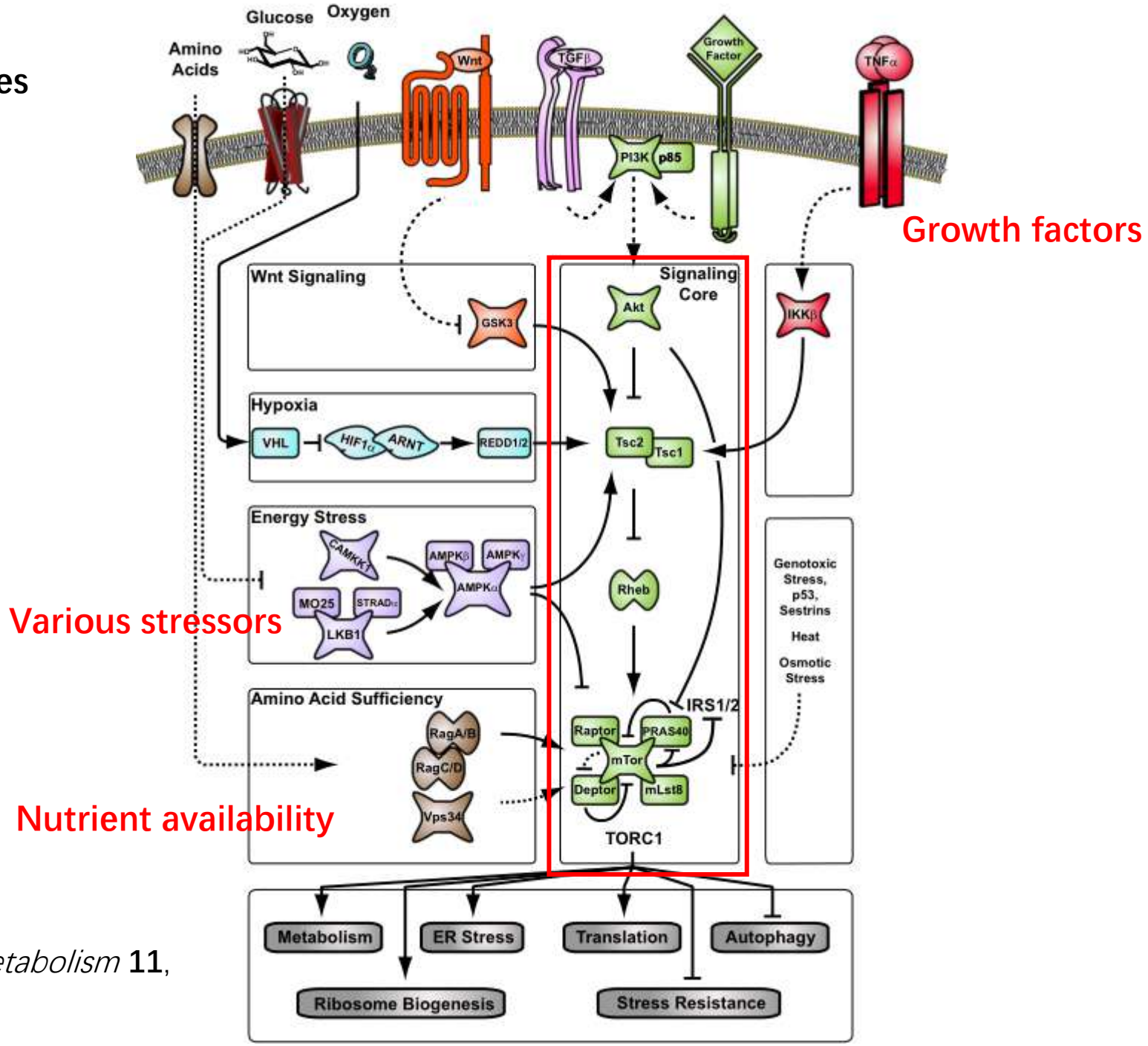


In yeast:

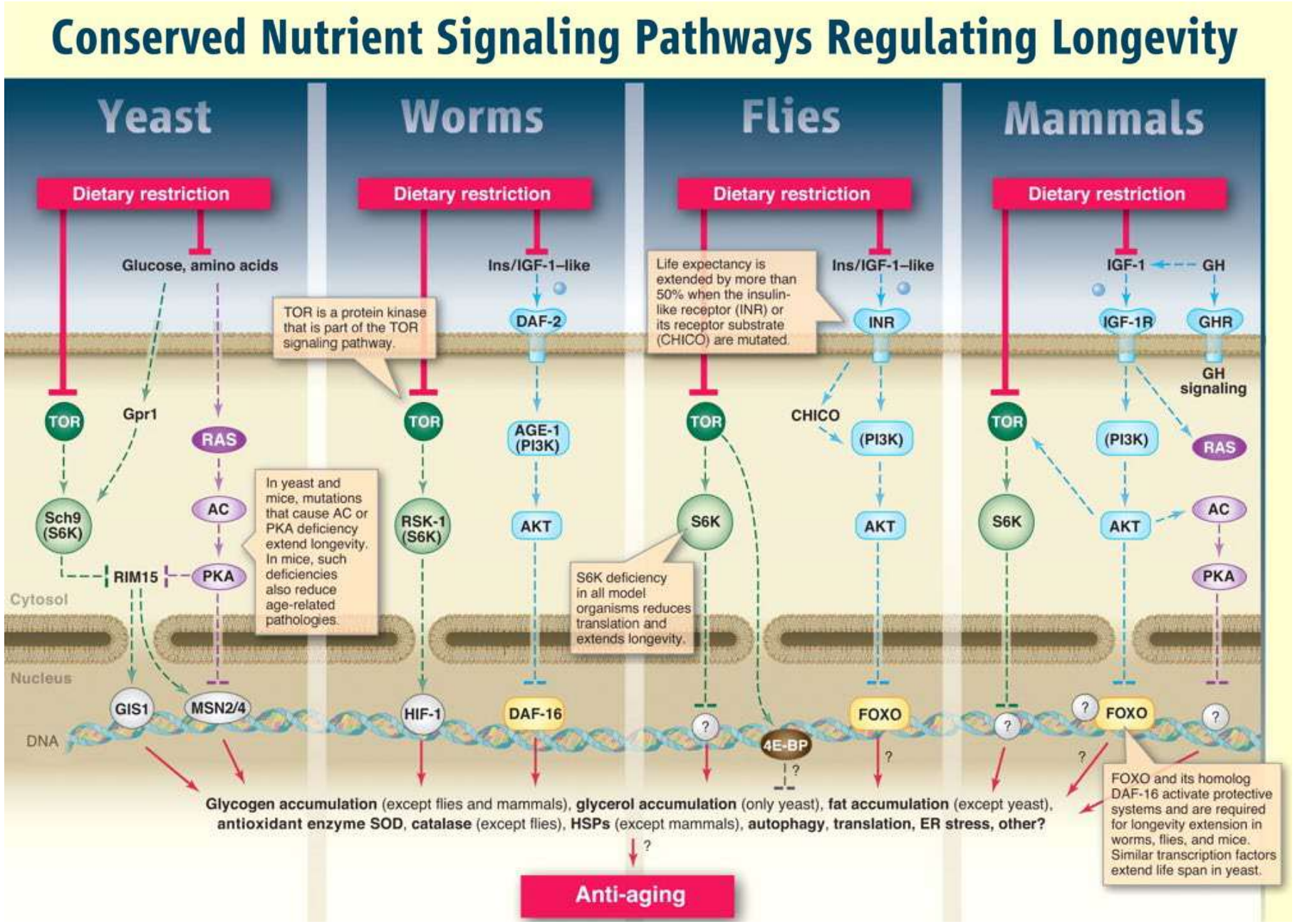
Deletion of TOR1 and **RPL31A or RPL6B**, ribosomal proteins transcriptionally regulated by TOR, increases life span

Kaeberlein, M. *et al. Science* **310**, 1193–1196 (2005)

- **TOR acts as a major hub that integrates signals and regulate several outputs**

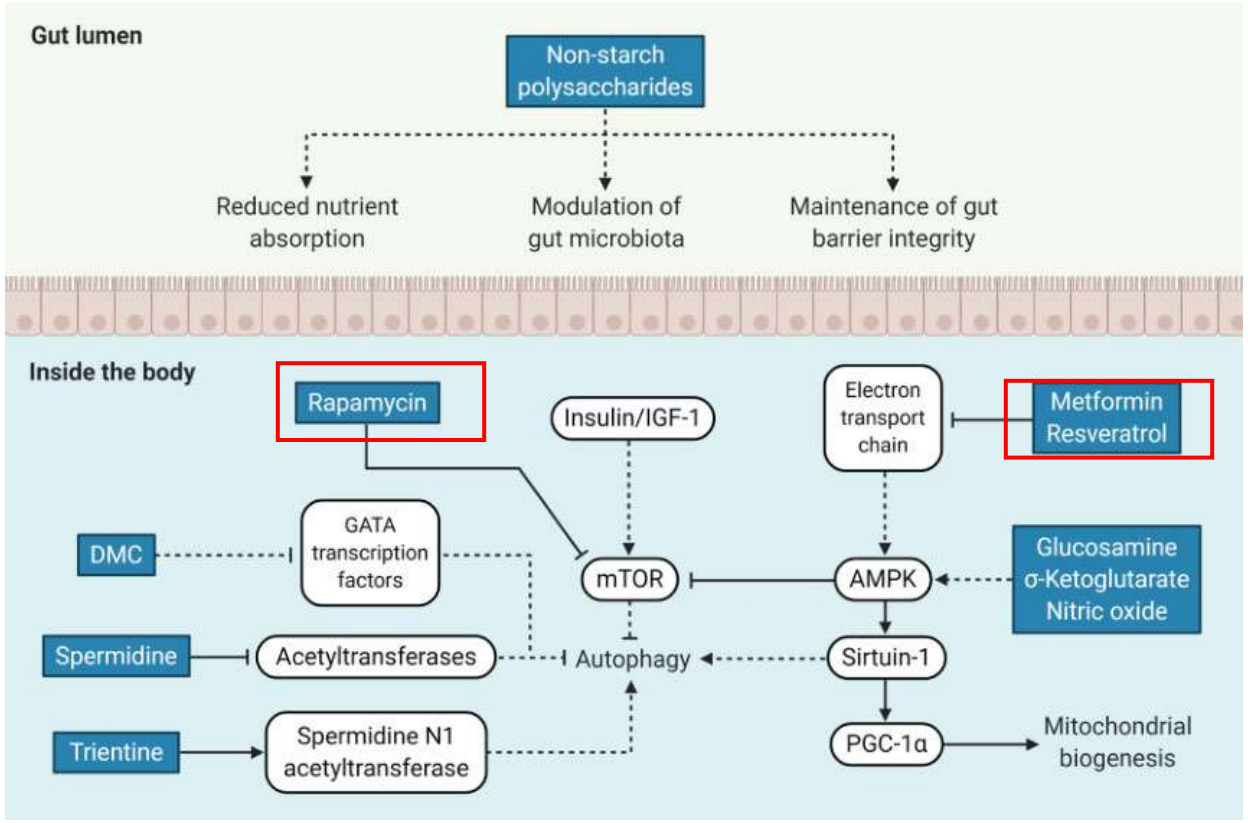


Kapahi, P. *et al. Cell Metabolism* **11**, 453–465 (2010)



Fontana, L. *et al. Science* **328**, 321–326 (2010)

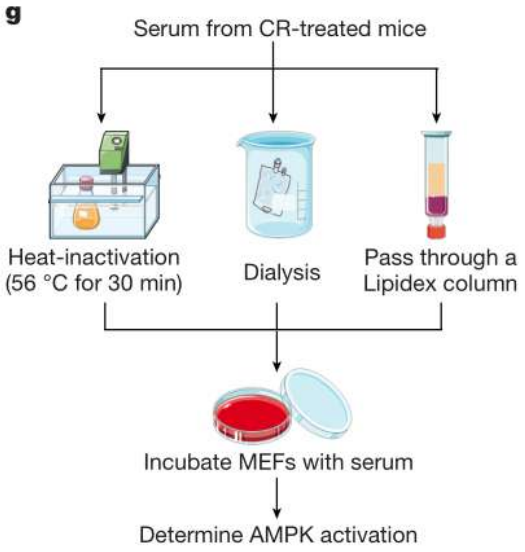
Finding “CR mimetics”

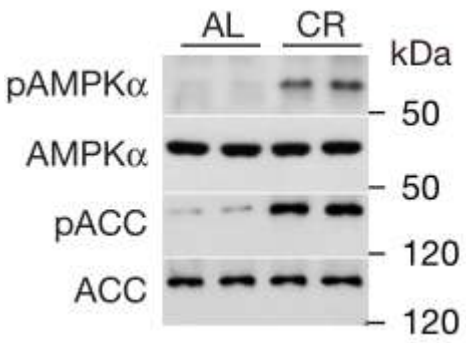


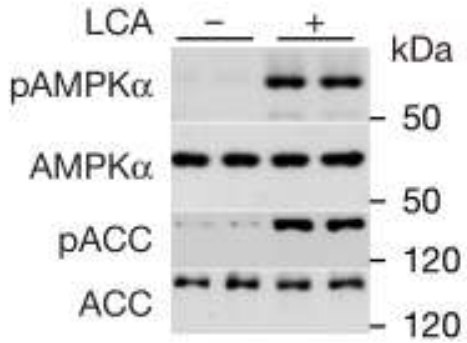
Martel, J. *et al. Ageing Research Reviews* **66**, 101240 (2021)

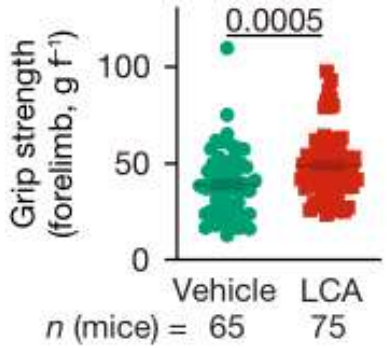
Finding “CR mimetics”

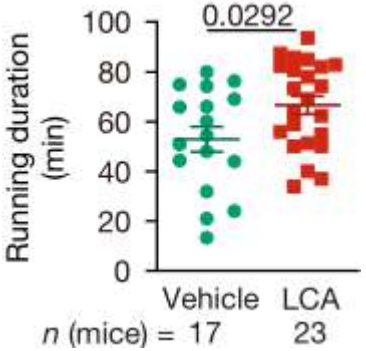
Lithocholic acid (LCA) is one of the metabolites that alone can recapitulate the effects of CR in mice

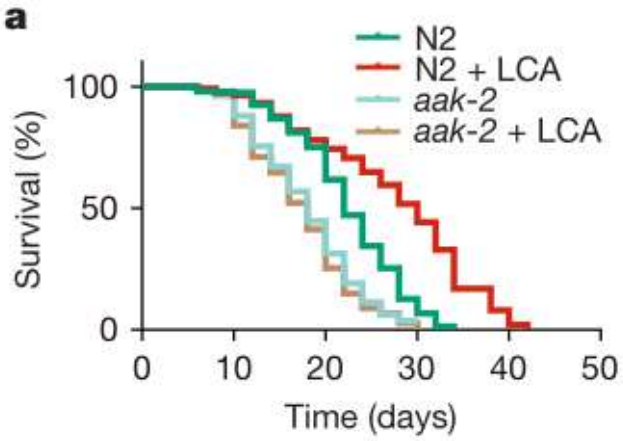


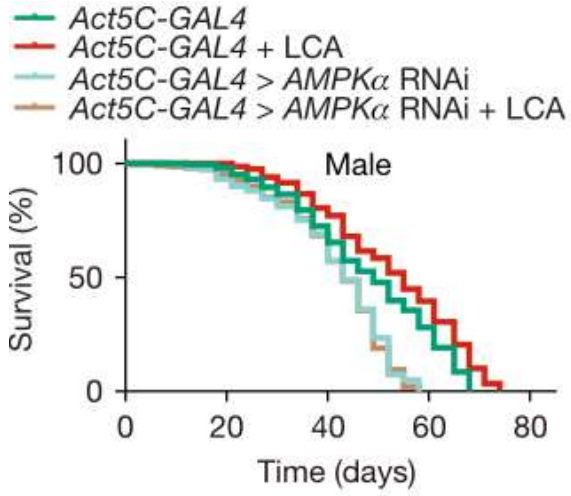


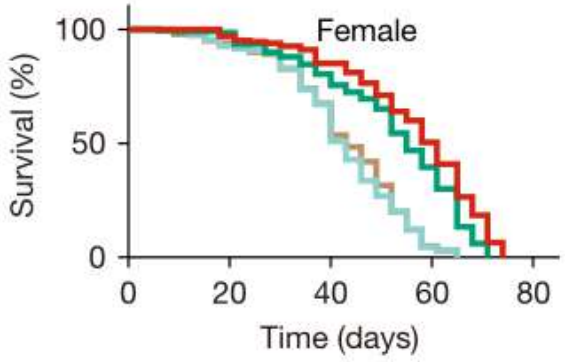








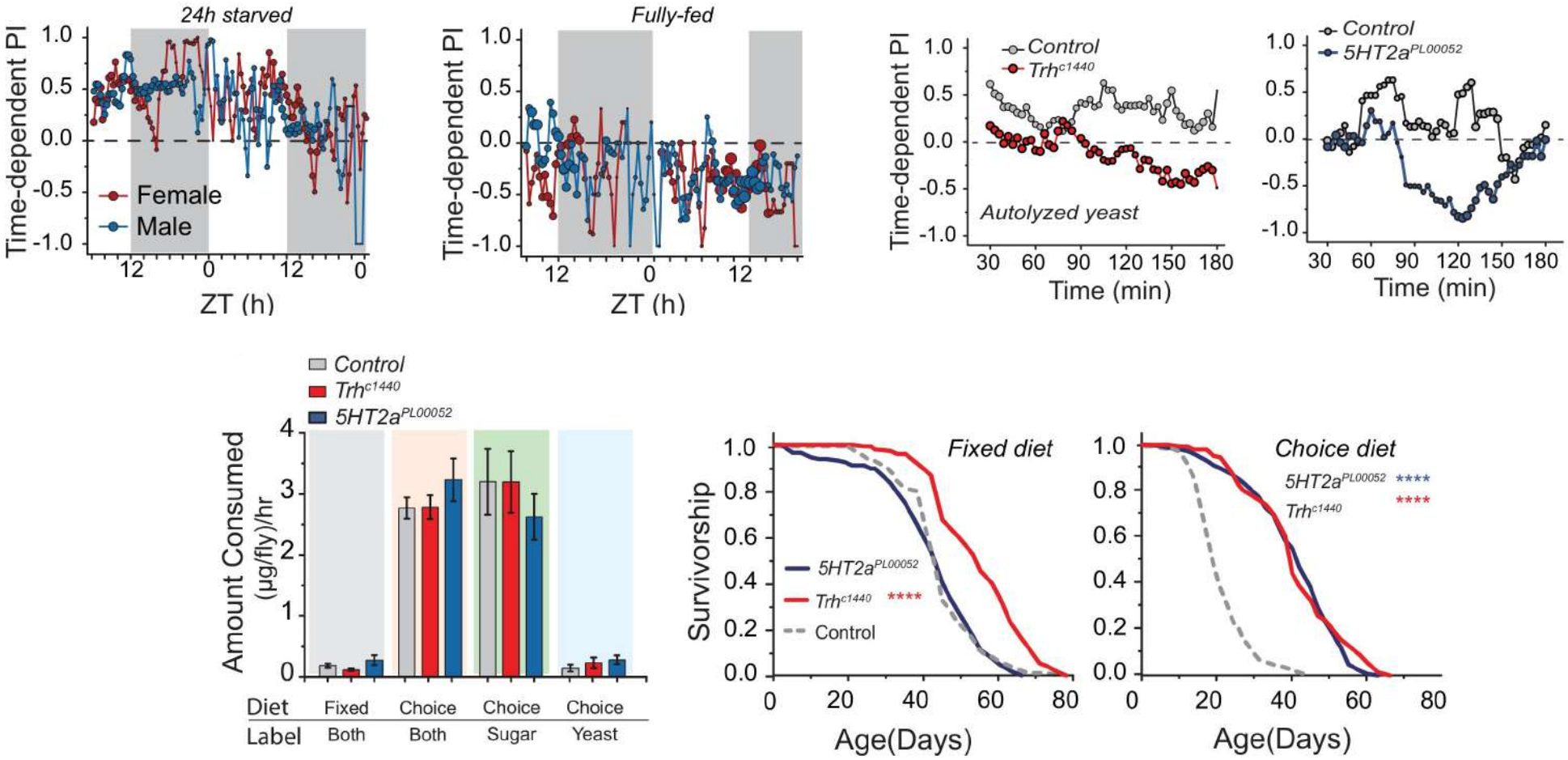




Qu, Q. *et al. Nature* **643**, 192–200 (2025)

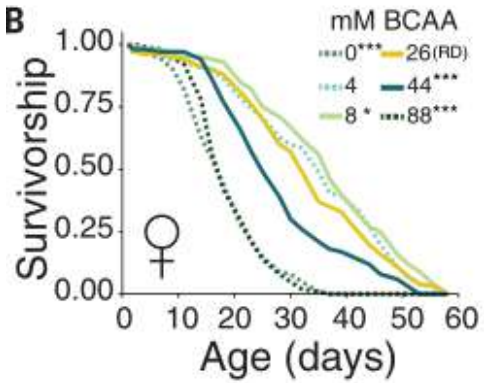
Finding “CR mimetics”—— Fool the brain

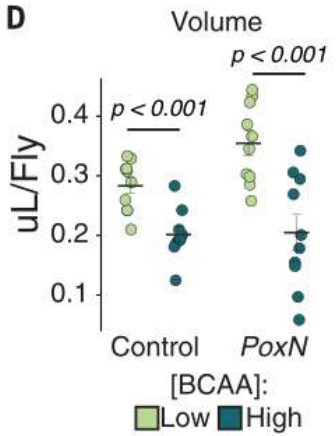
Perceived value of dietary protein is a critical determinant of its effect on lifespan

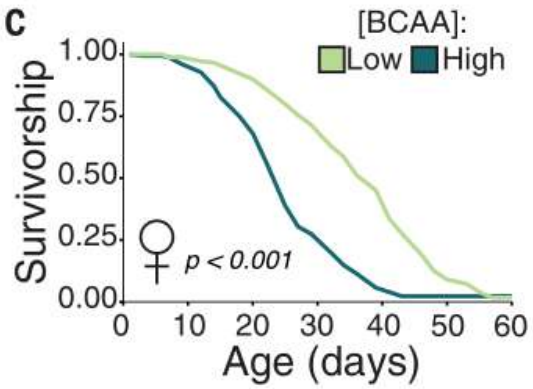


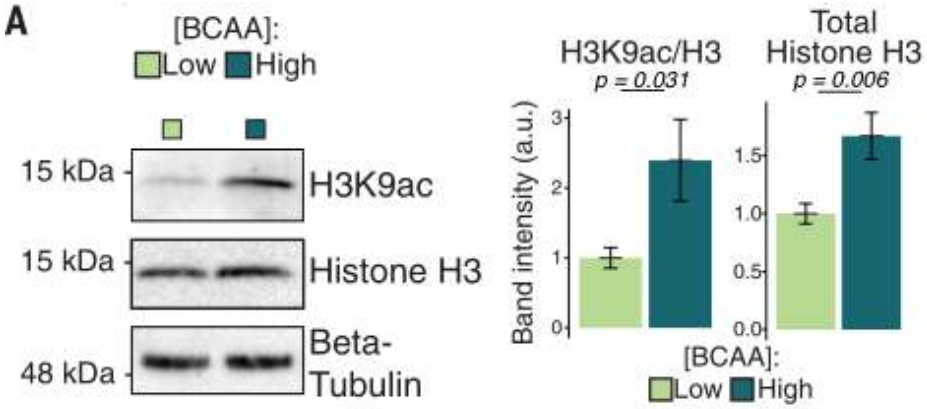
Ro, J. *et al. eLife* **5**, e16843 (2016)

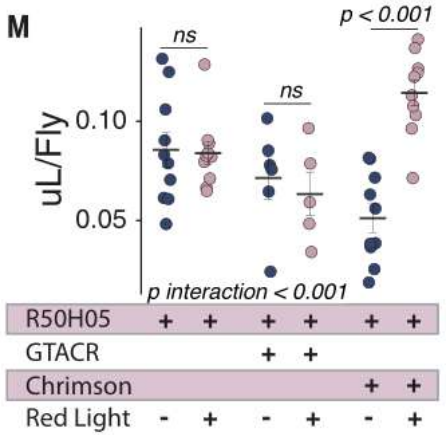
Neural states that encode the motivation to seek food are sufficient to slow aging

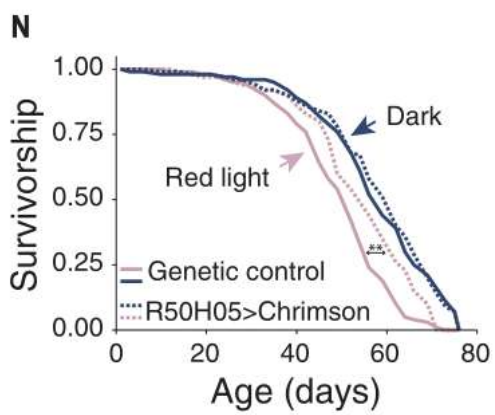


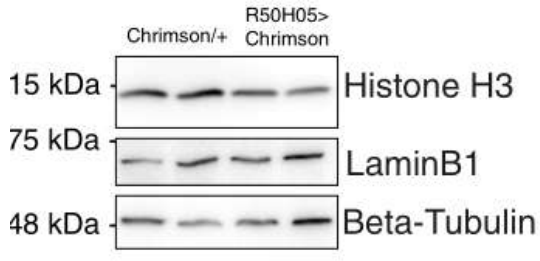


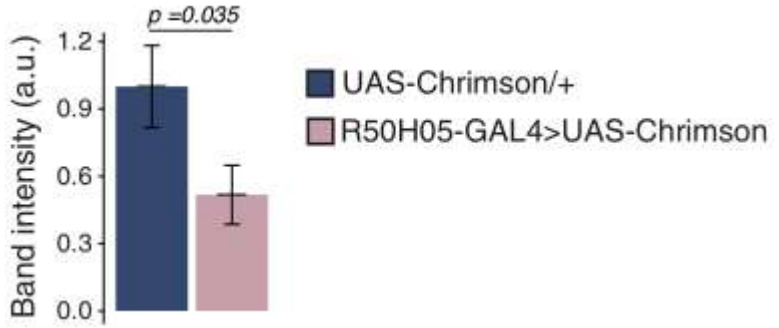












Weaver, K. J. *et al. Science* **380**, 625–632 (2023)

Antiaging diets

- the cyclic KDs increased life span, memory function and metabolic parameters
- KDs VS ketone itself effect?

Ketogenic diets (KDs)

Time-Restricted Feeding (TRF)

Protein Restriction(PR)

- Improves several metabolic parameters
- Promote and maintain intrinsic circadian rhythms in mice
- Effect on life span and age-related health outcomes in was limited to male mice

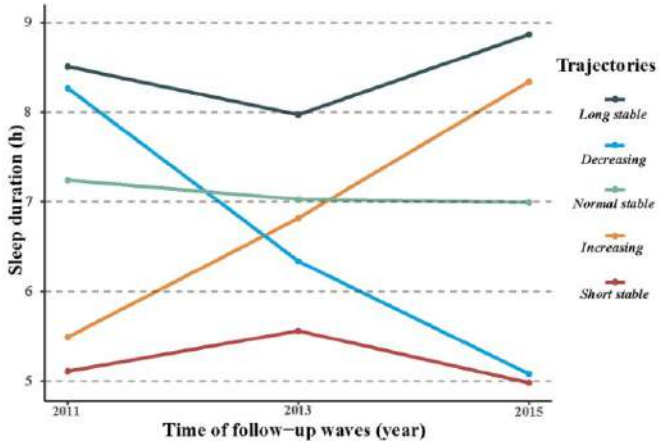
- the effects of reduced caloric intake VS protein itself ?

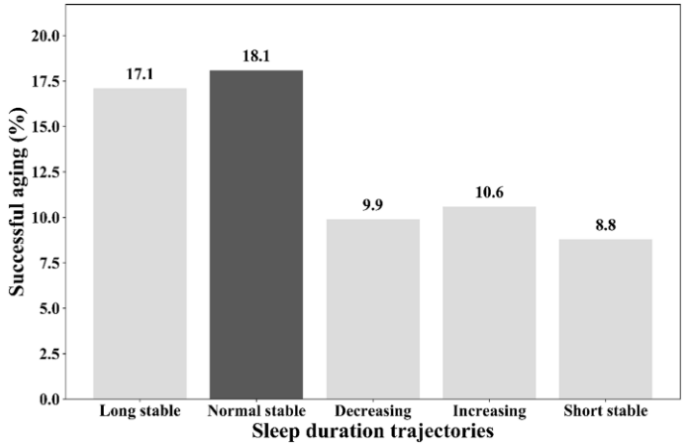
Lee, M. B. *et al. Science* **374**, eabe7365 (2021)

Part2: For reference only

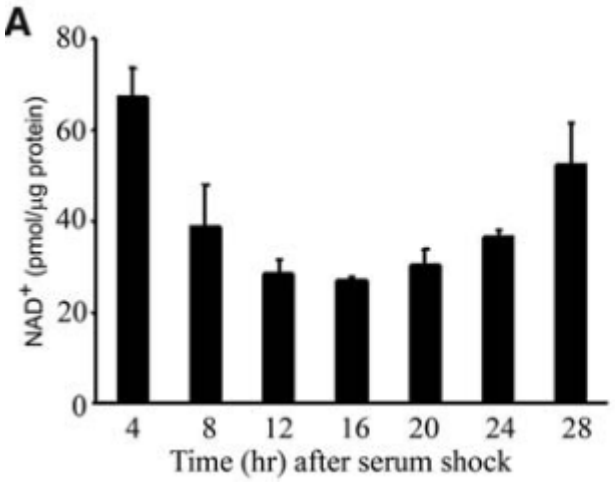
- A cliché
- Food for thought

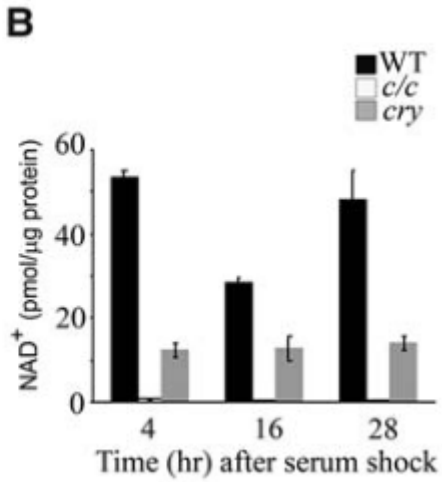
Sleep matters



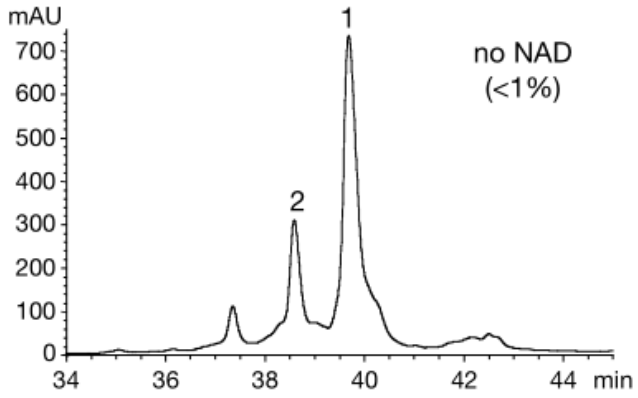


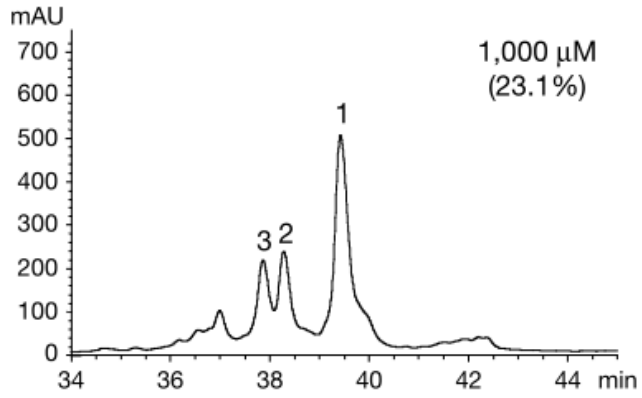
Tian, L. *et al. BMC Public Health* **24**, 3029 (2024)





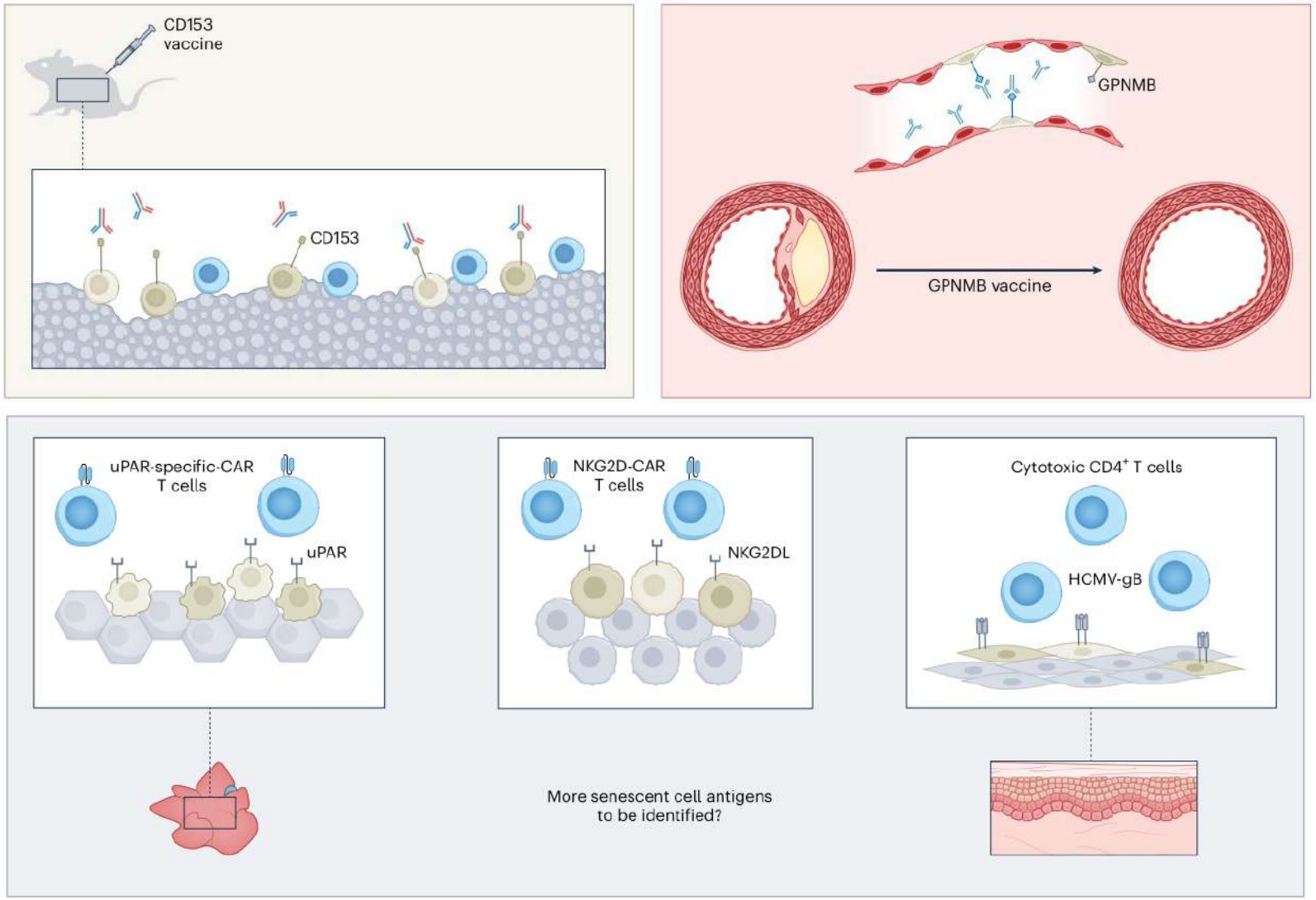
Nakahata, Y. *et al. Science* **324**, 654–657 (2009)





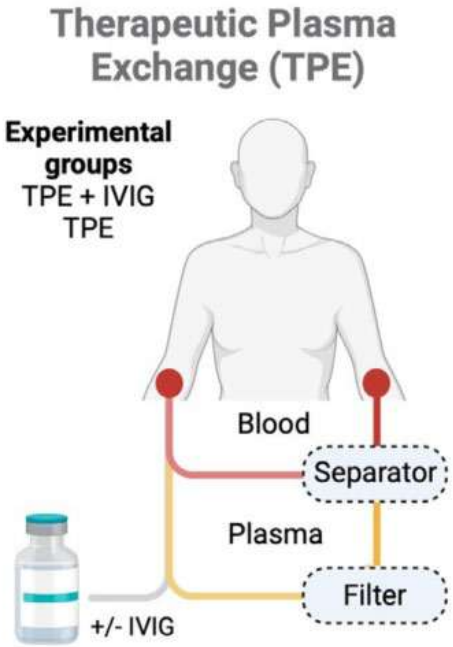
Imai, S. *et al. Nature* **403**, 795–800 (2000)

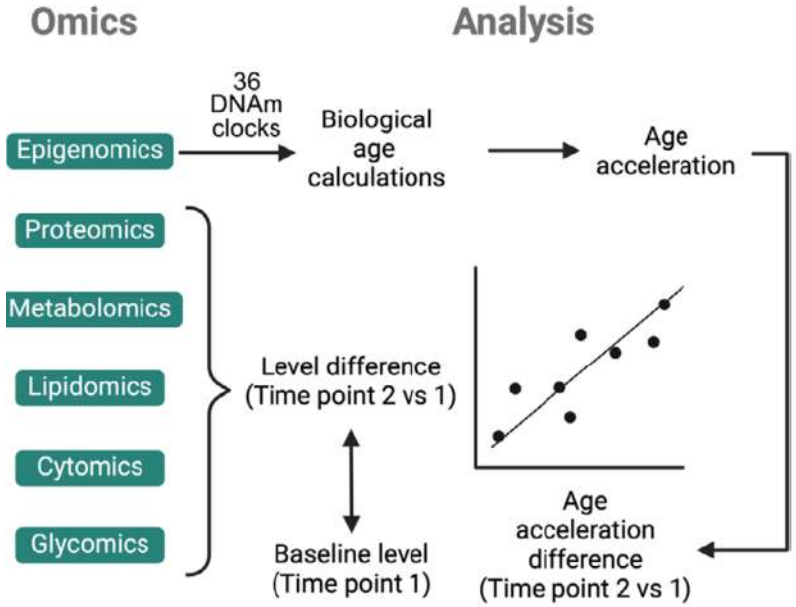
Senolytic vaccines

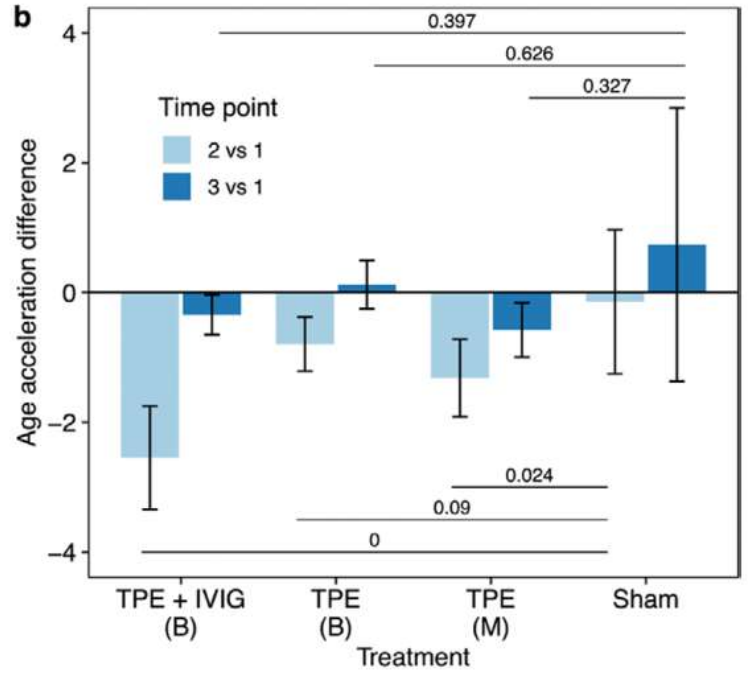


Wu, R. *et al. Nat Aging* **4**, 464–482 (2024)

Therapeutic plasma exchange (TPE)

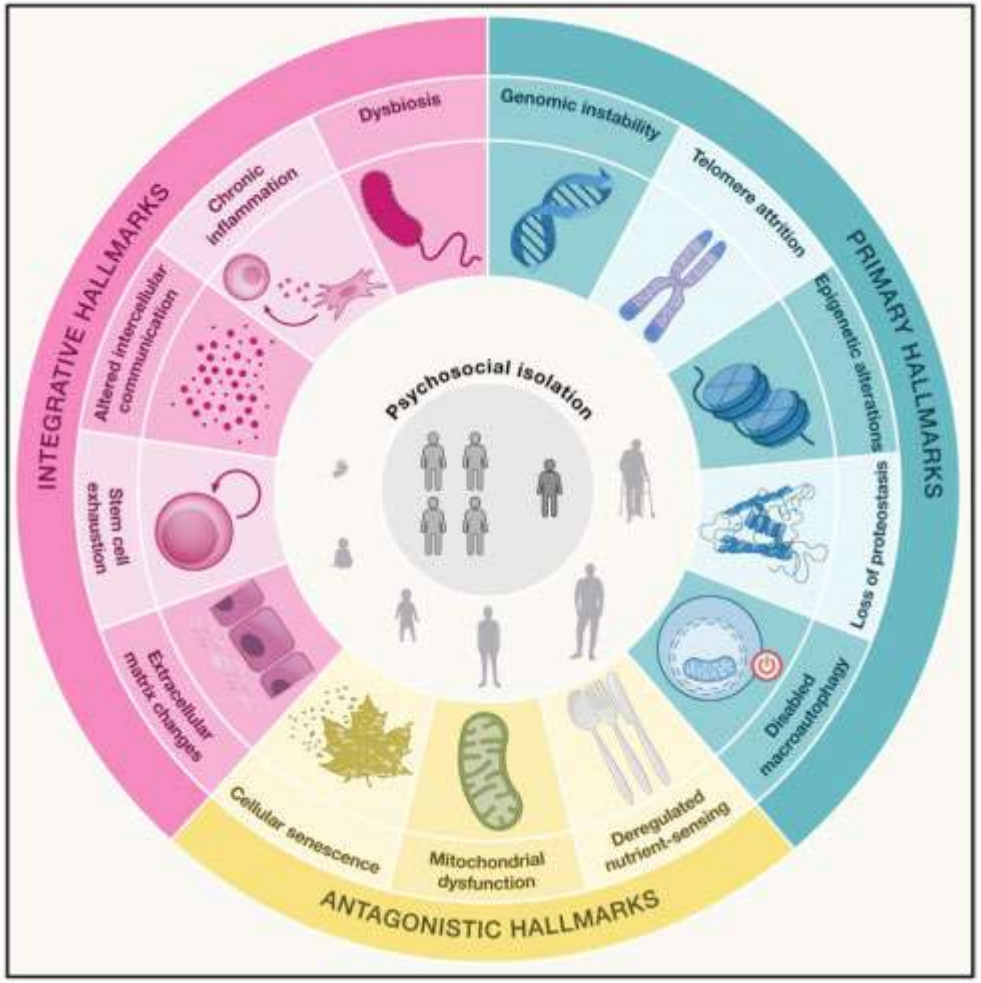






Fuentealba, M. *et al. Aging Cell* **24**, e70103 (2025)

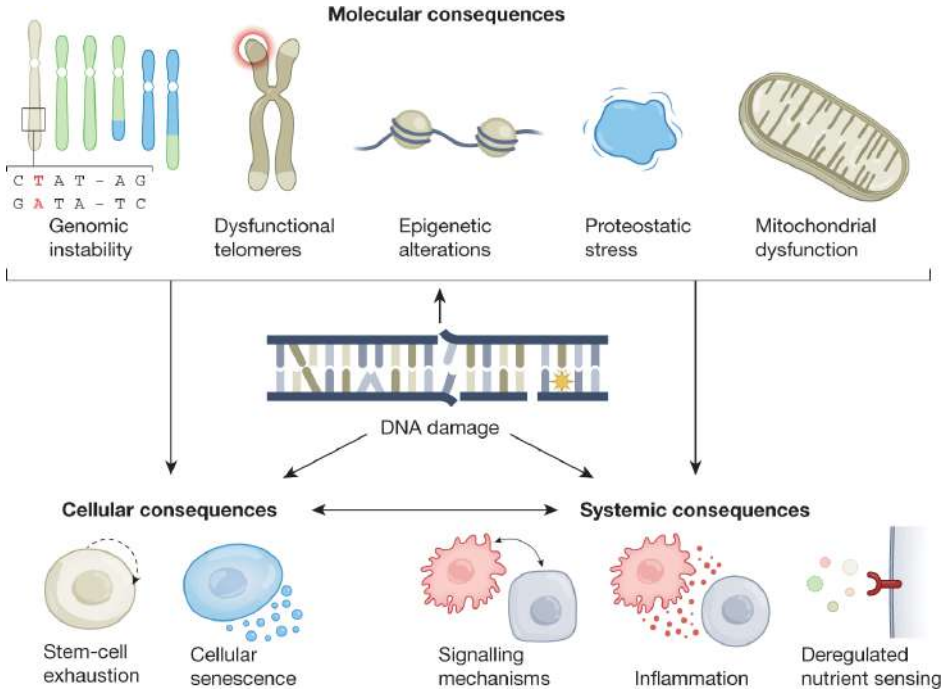
Part3: New theoretical framework of aging



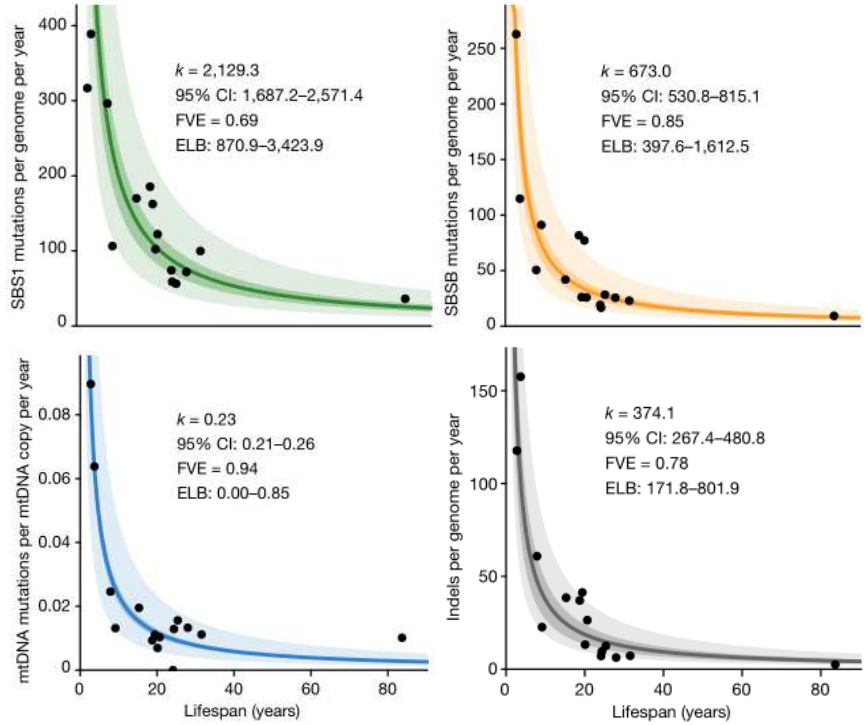
But what causes these changes to happen in the first place?

Is there an upstream process that drives them?

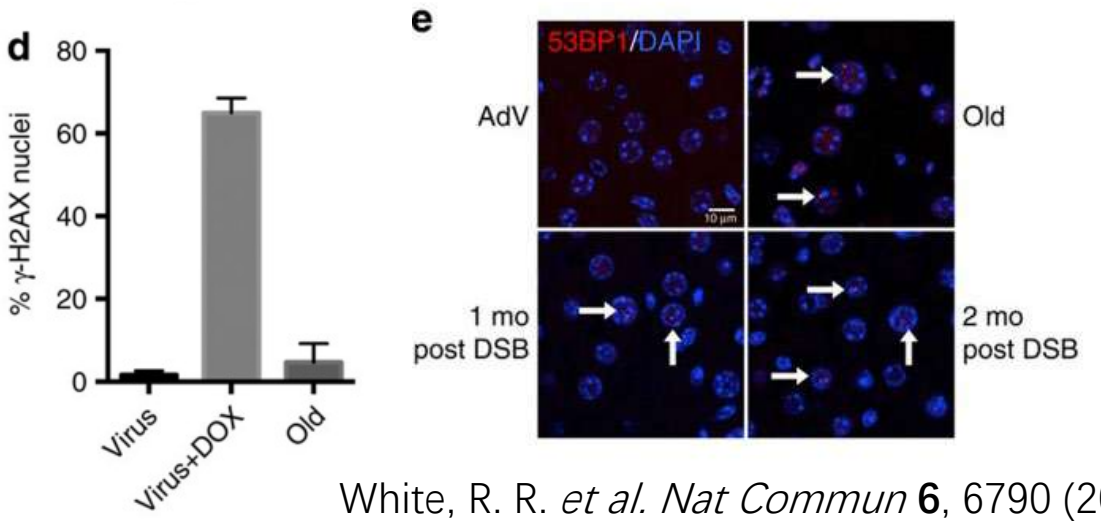
The mutation theory of aging (TOTA)



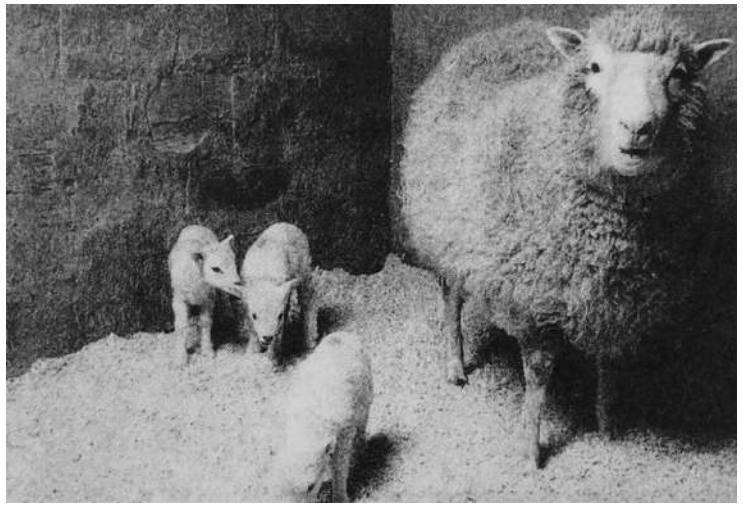
Schumacher, B. *et al. Nature* **592**, 695–703 (2021)

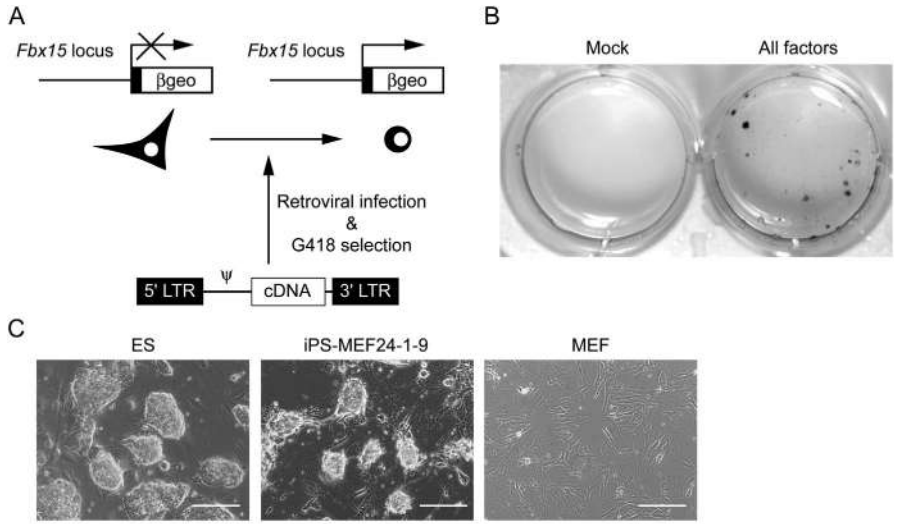


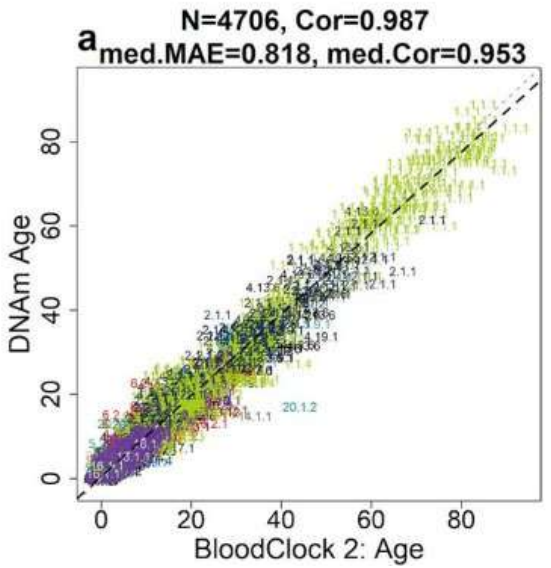
Cagan, A. *et al.* *Nature* **604**, 517–524 (2022)



White, R. R. *et al. Nat Commun* **6**, 6790 (2015)



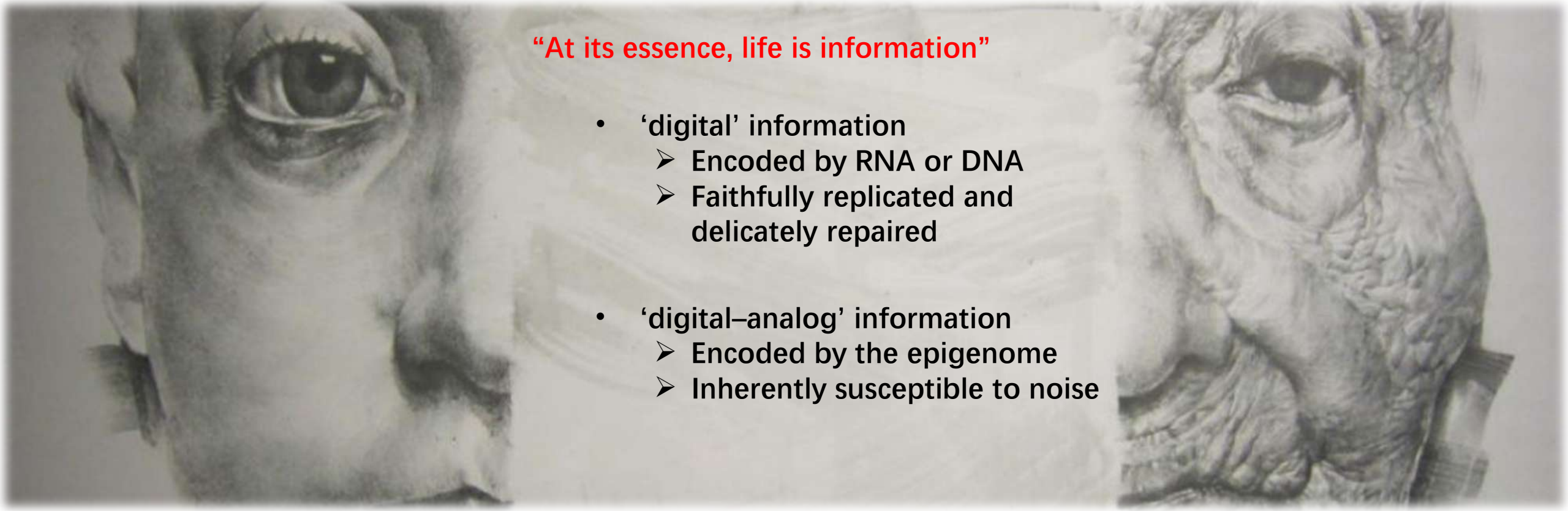




Takahashi, K. *et al. Cell* **126**, 663–676 (2006)

Lu, A. T. *et al. Nat Aging* **3**, 1144–1166 (2023)

Aging has a nongenetic origin ?

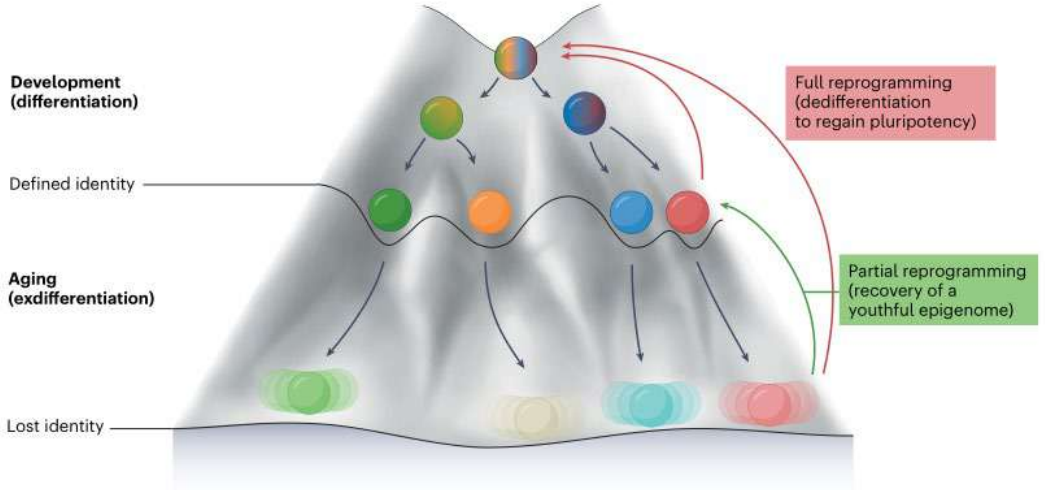


"At its essence, life is information"

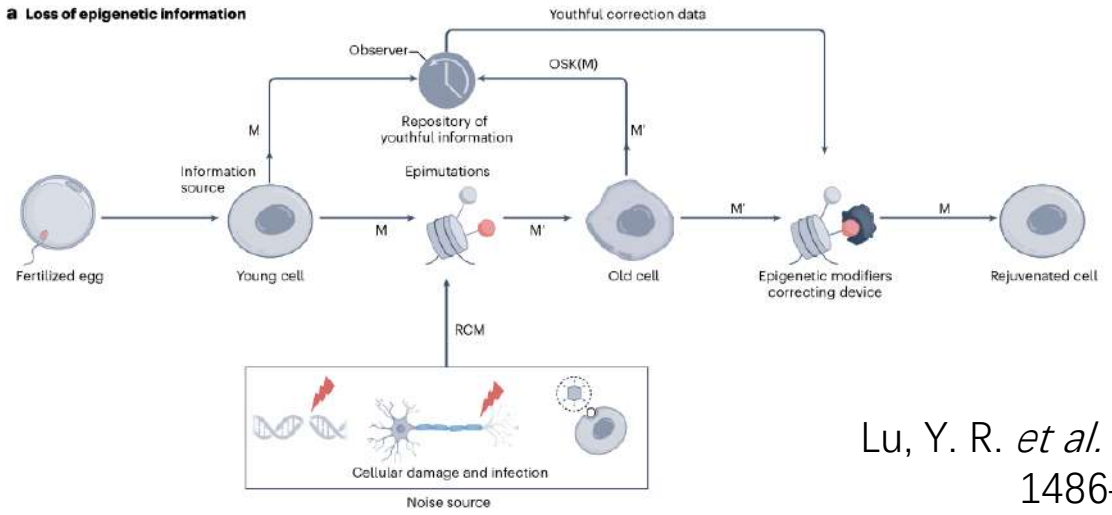
- 'digital' information
  - Encoded by RNA or DNA
  - Faithfully replicated and delicately repaired

- 'digital–analog' information
  - Encoded by the epigenome
  - Inherently susceptible to noise

The information theory of aging

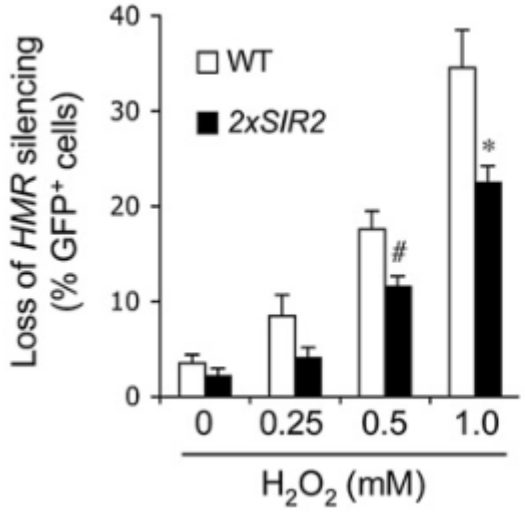


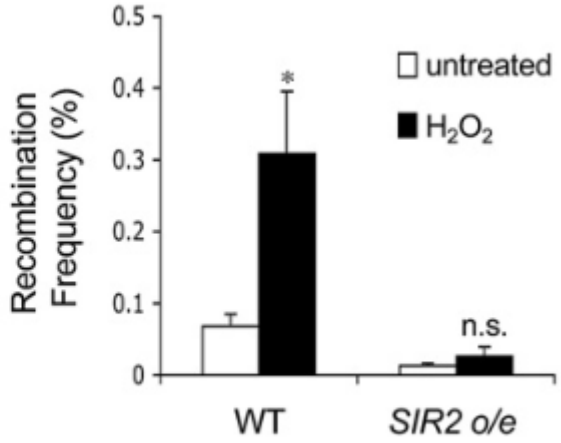
Waddington landscape metaphor

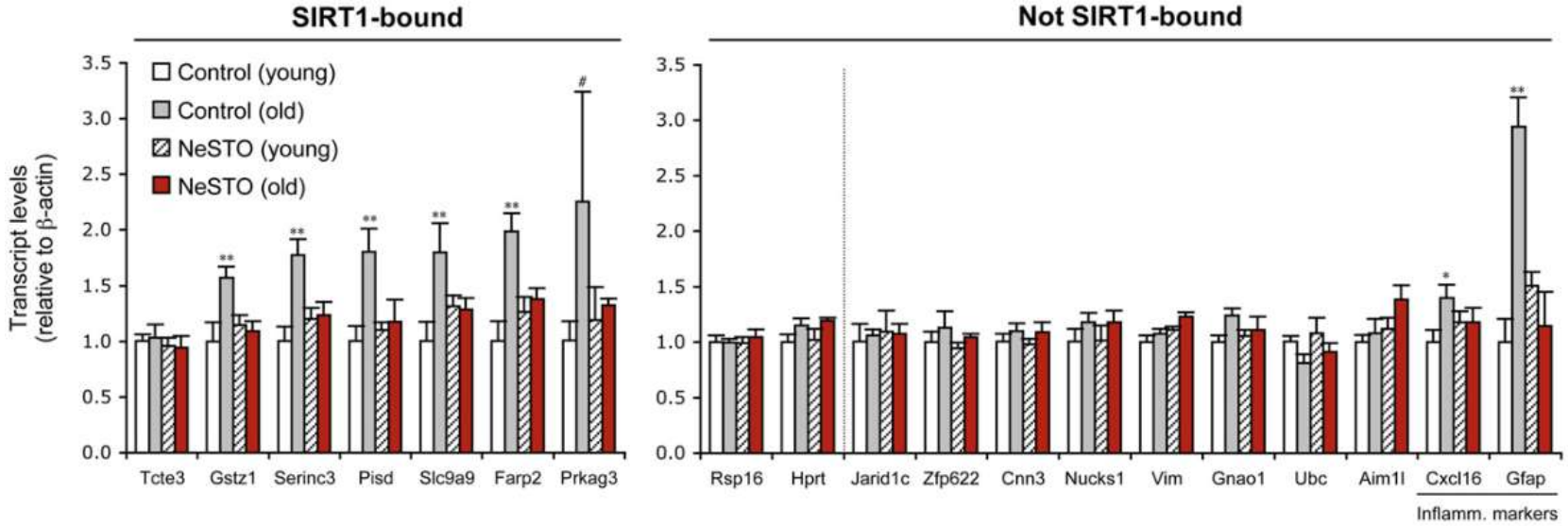


Lu, Y. R. *et al. Nat Aging* **3**, 1486–1499 (2023)

‘Relocalization of chromatin modifiers (RCM) hypothesis’

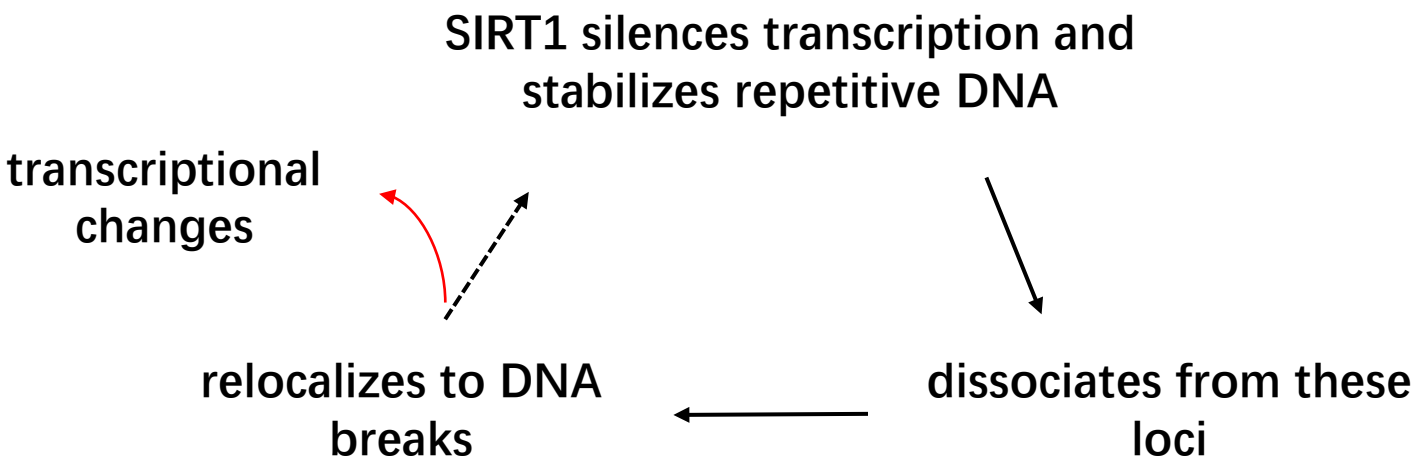




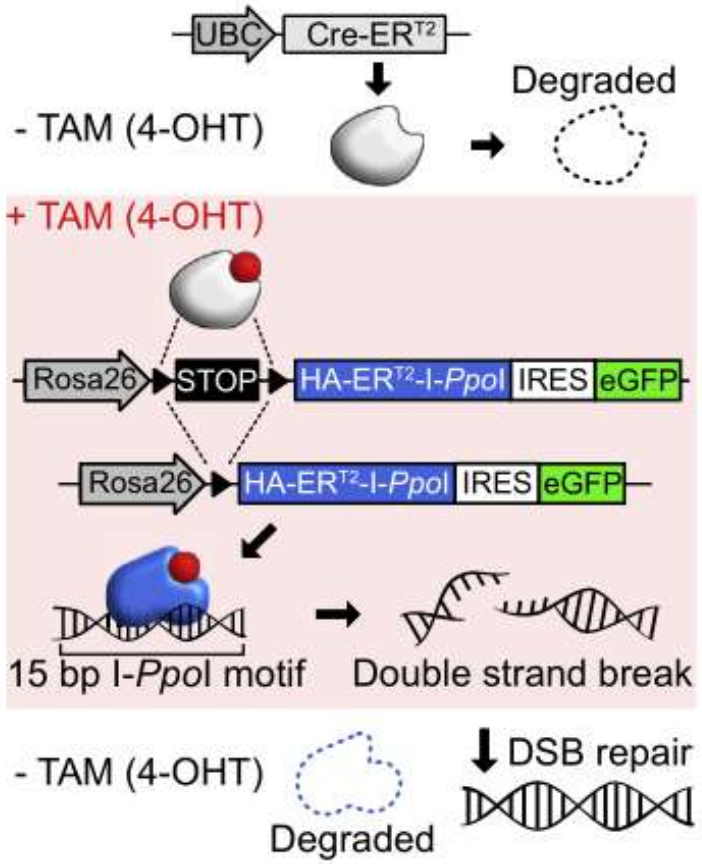


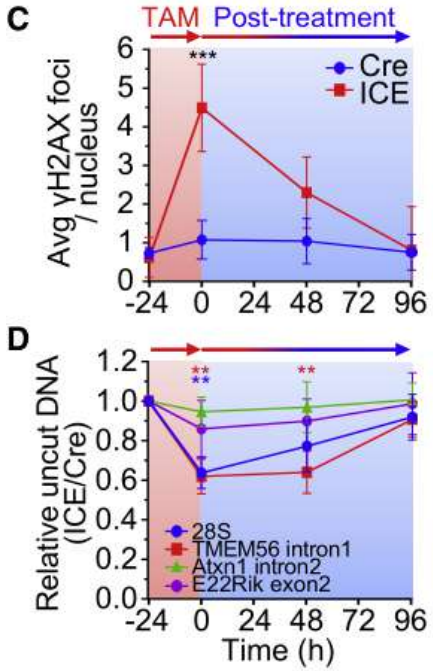
Oberdoerffer, P. *et al. Cell* **135**, 907–918 (2008)

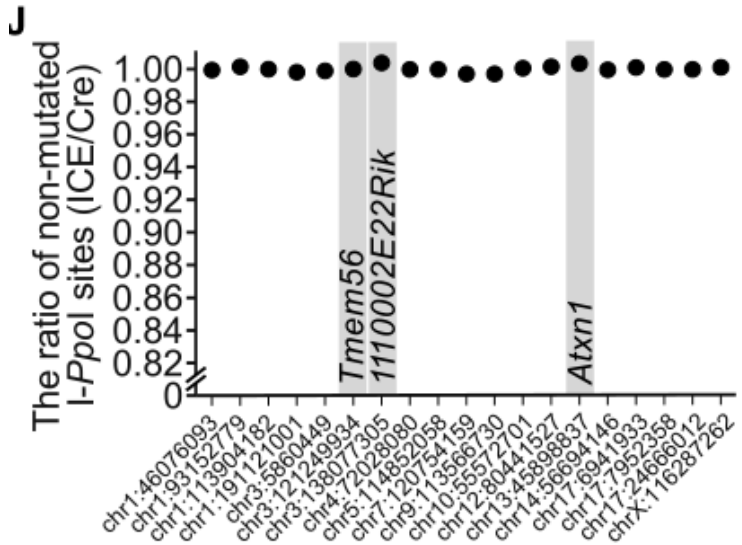
‘Relocalization of chromatin modifiers (RCM) hypothesis’



“ICE” Mice (Inducible changes to the epigenome)

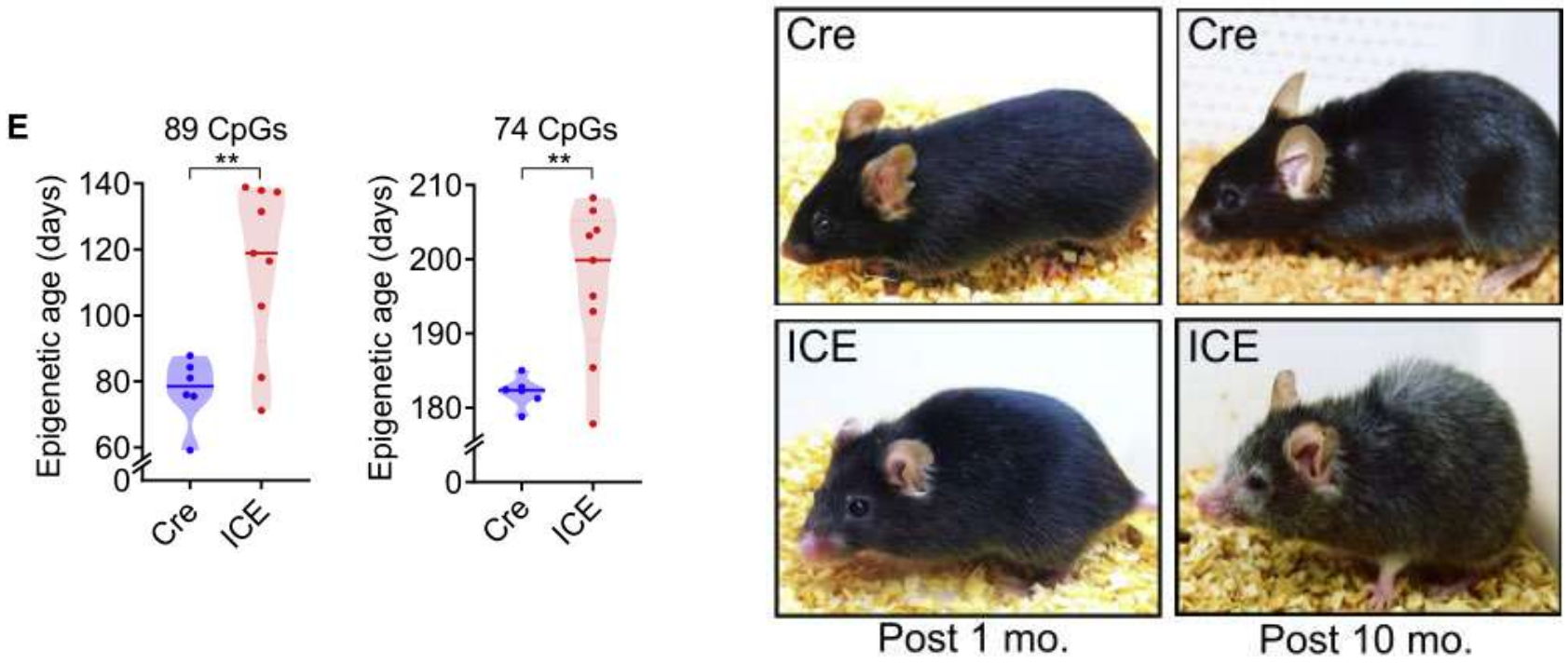






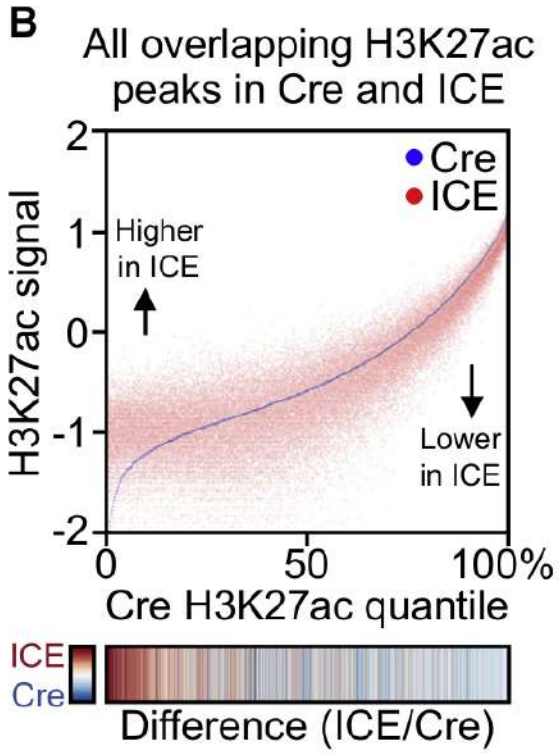
Yang, J.-H. *et al. Cell* **186**, 305-326.e27 (2023)

The ICE system phenocopies aging in vivo

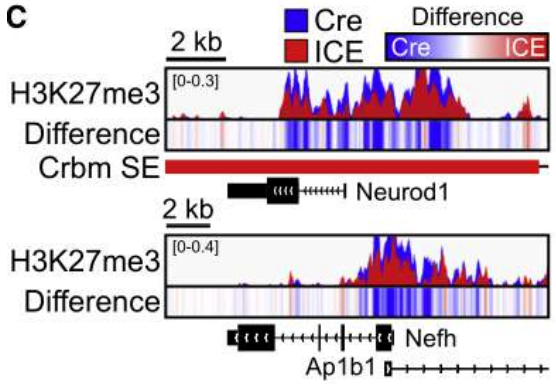


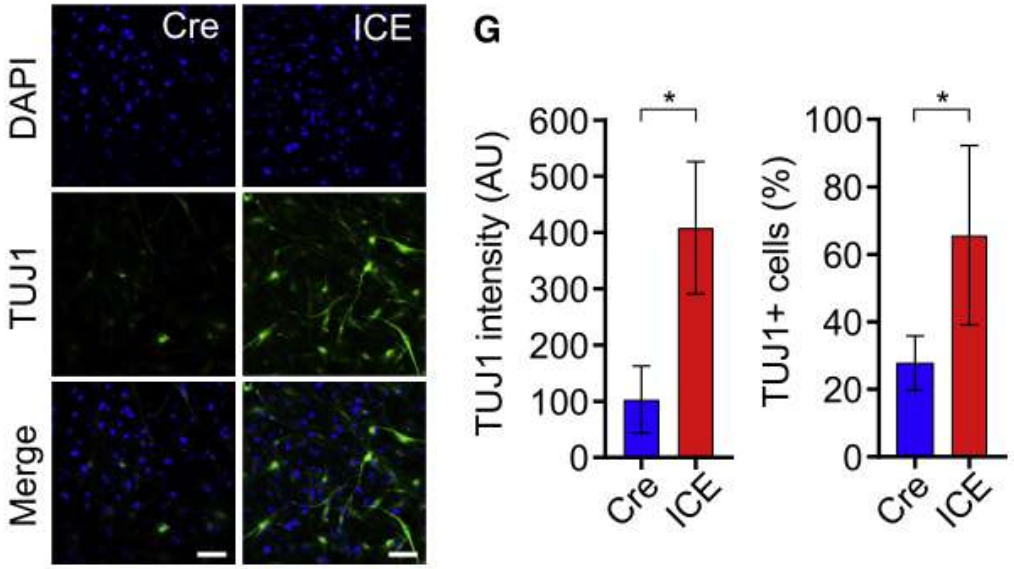
Yang, J.-H. *et al. Cell* **186**, 305-326.e27 (2023)

Erosion of the epigenetic landscape



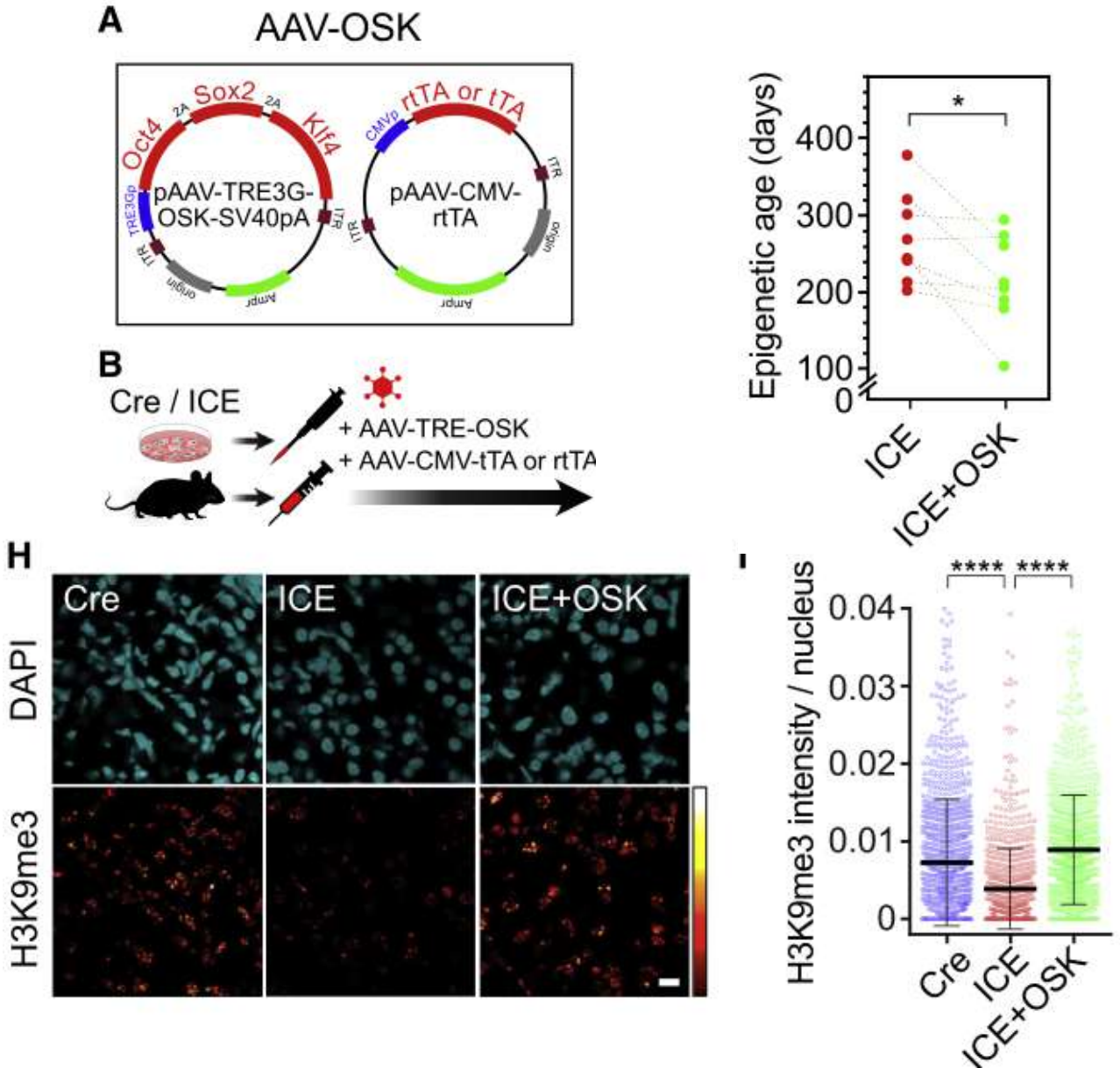
Cells lose the ability to maintain cellular identity





Yang, J.-H. *et al. Cell* **186**, 305-326.e27 (2023)

Epigenetic reprogramming restores a youthful epigenome in ICE mice



Yang, J.-H. *et al. Cell* **186**, 305-326.e27 (2023)

Take home messages:

1. Caloric/Dietary Restriction(CR/DR) is the most classic way to delay aging and the genetics of ageing research has revealed a complex network of interacting intracellular signaling pathways and higher-order processes

2. Conventional CR mimetics such as metformin, rapamycin and spermidine have effect on life-span by targeting nutrient-sensing pathways

3. Evolutionarily conserved neuromodulatory systems sufficient to control aging and physiology independent of food consumption

4. A loss of epigenetic information is a reversible cause of aging