How blood(products) influence ageing

@Age

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NUHS National University Health System

NUS National University of Singapore

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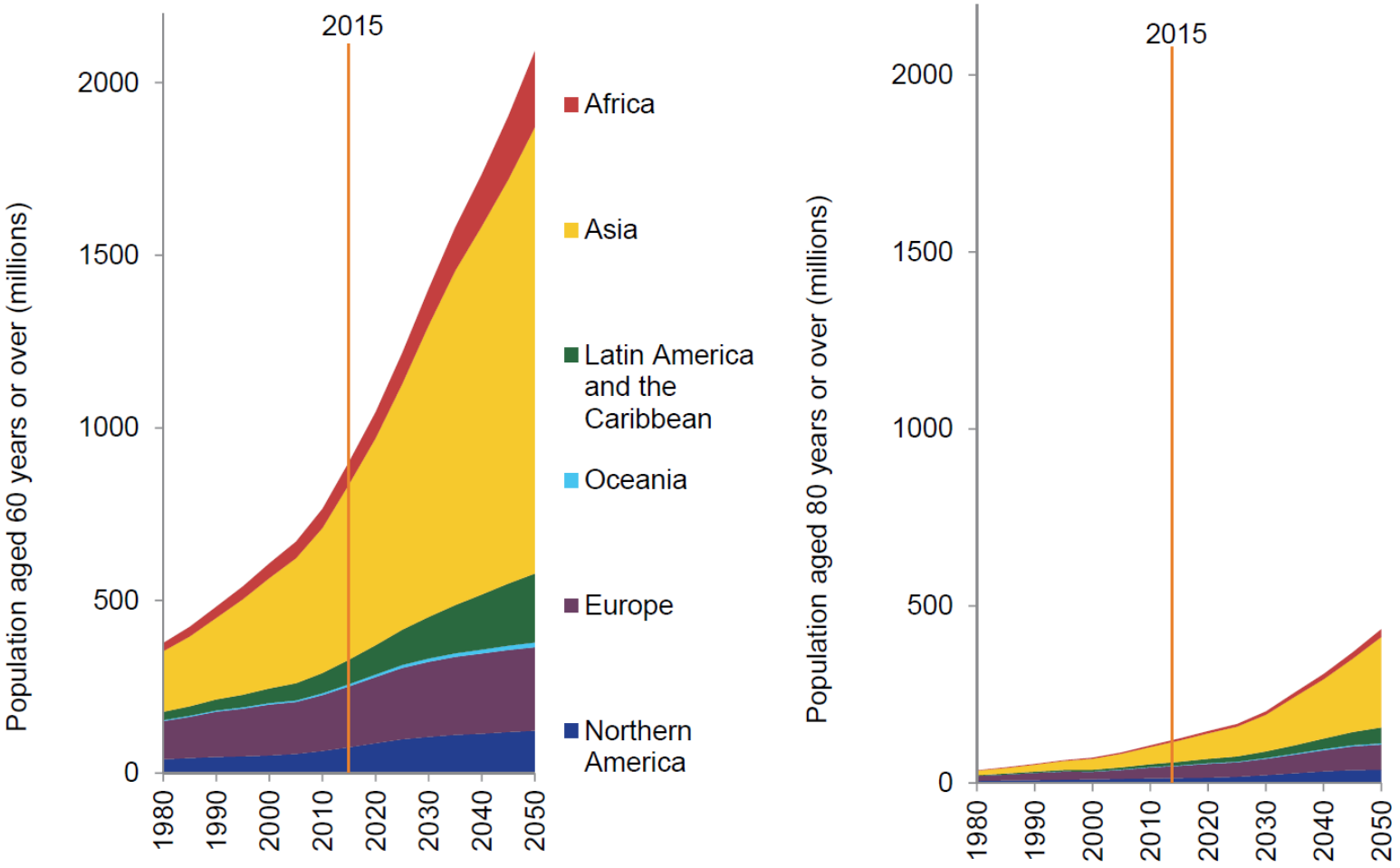
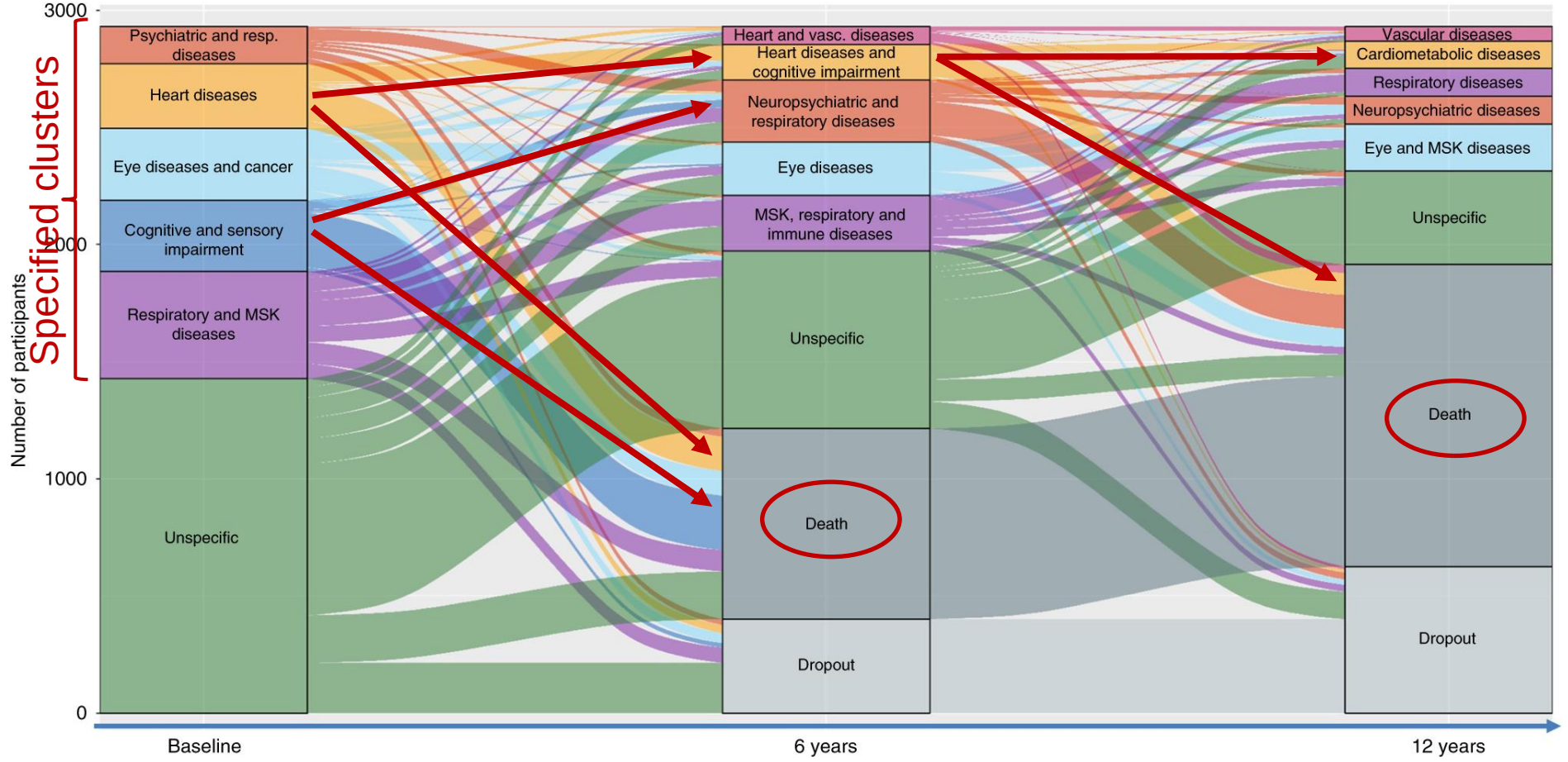
Population changes



Data source: United Nations (2015). *World Population Prospects: The 2015 Revision*.

Multimorbidity trajectories

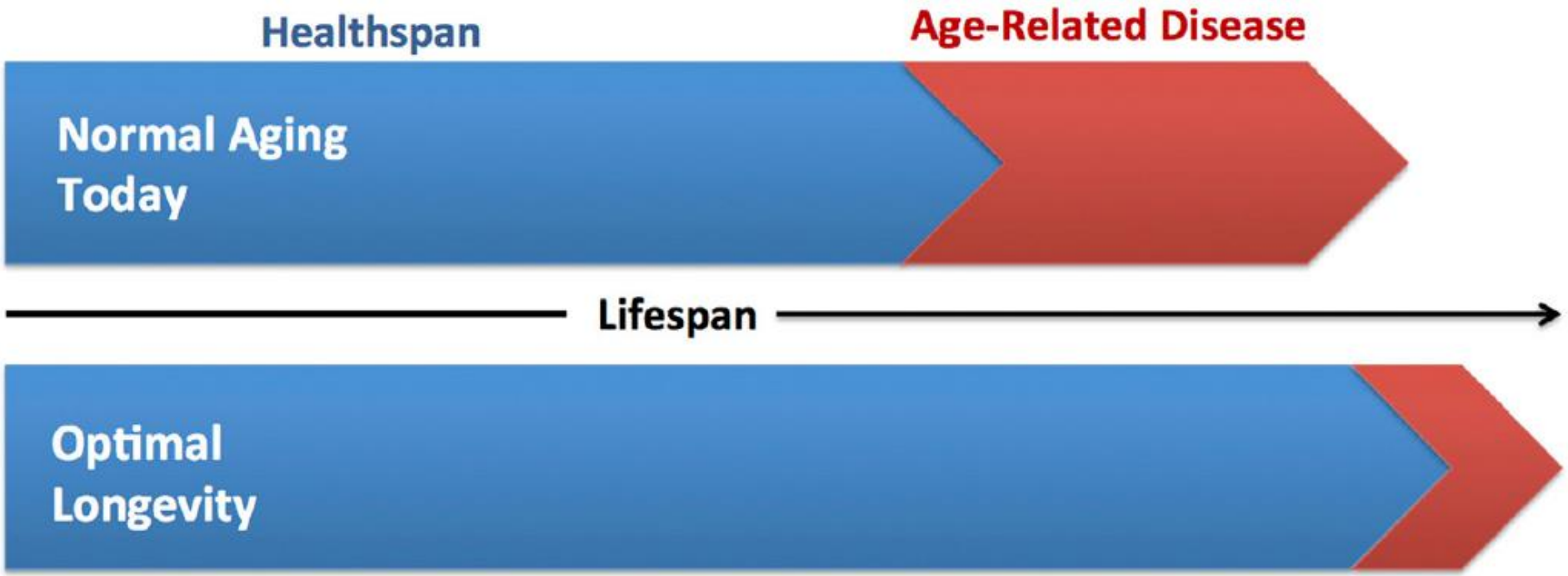
70 years: 70% multimorbidity



Vetrano et al., Nature Communications 2020

Swedish National Study on Aging and Care in Kungsholmen
76.1 ± 11.0 years
Excluded N = 432 <2 chronic disease

Aim of Geroscience



Seals & Melov, Aging 2014

NIA 2018

Feature » Health and Ageing

Geroscience's coming of age

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The search for a fountain of youth endures across cultures. But the time is coming when we treat ageing as a disease, not an inevitability, reports **Bob Roehr**

Lack of knowledge!

The lifespan of worms can be increased 10-fold through a single mutation to the insulin signaling pathway. The lifespan of a mouse can be upped by 50%. As for humans, however, "There is still this notion among physicians and the public in general that ageing is an inevitable universal process, that there's not much you can do about it," says Joao Pedro de Magalhães, a professor at the Institute of Ageing and Chronic Disease at the University of Liverpool, UK. "And that's not true."

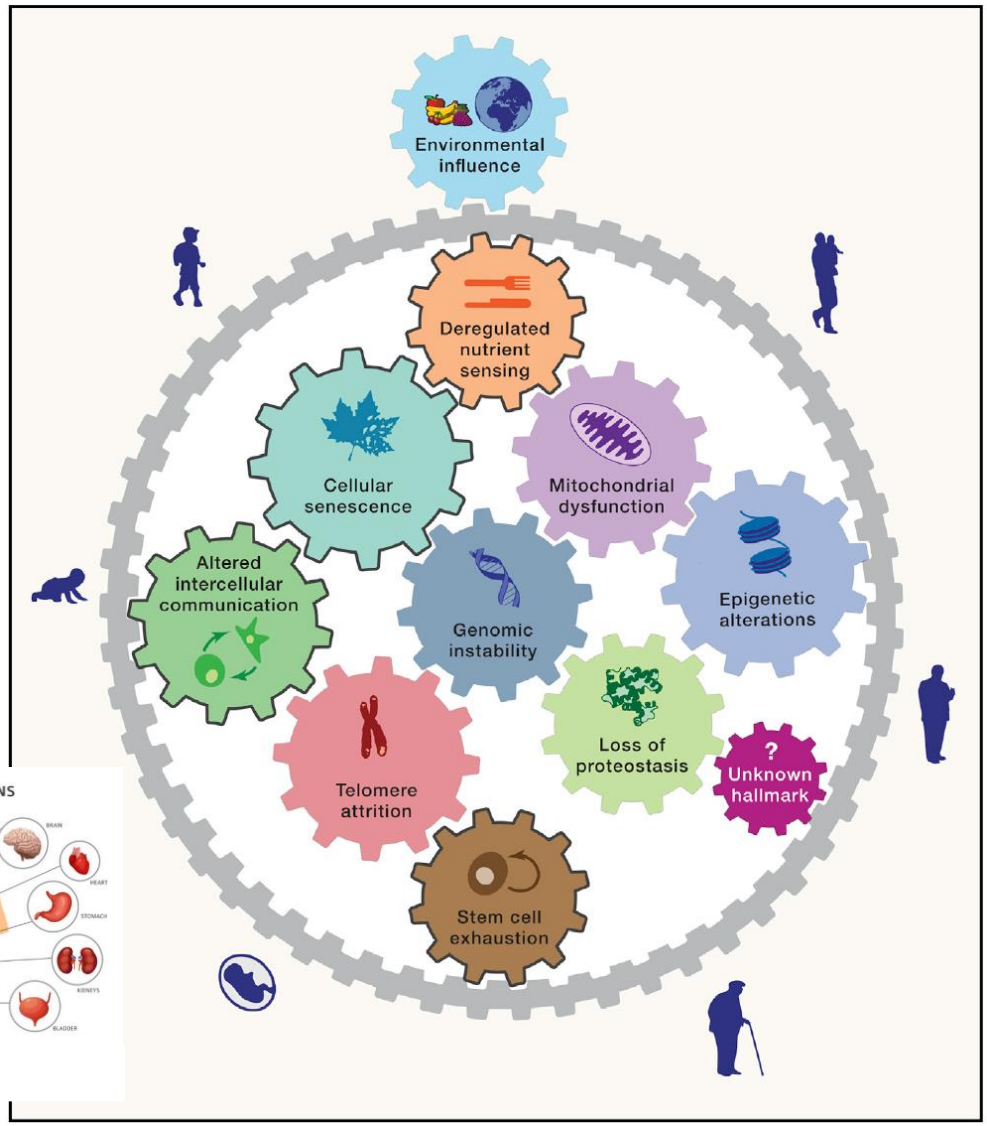
Enter geroscience: a discipline that first emerged in the 1990s as "a fundamentally different approach" to thinking about ageing, says Linda Partridge, a leader in the field with appointments to the Max Planck Institute in Cologne, Germany, and University College London, UK. In geroscience, she tells *The BMJ*, the appearance of one chronic condition associated with ageing predicts the emergence of another, and another, and so on. Many of these diseases share common signaling pathways and biological mechanisms such as inflammation.[1]

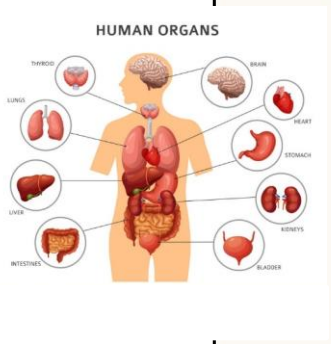
Opportunity!

De Magalhães tells *The BMJ*, "We can retard ageing as a whole [by treating] multiple ageing diseases as one. Given that we can do it in so many different species, there is no reason to think that we cannot do it in humans."

Mechanisms of ageing

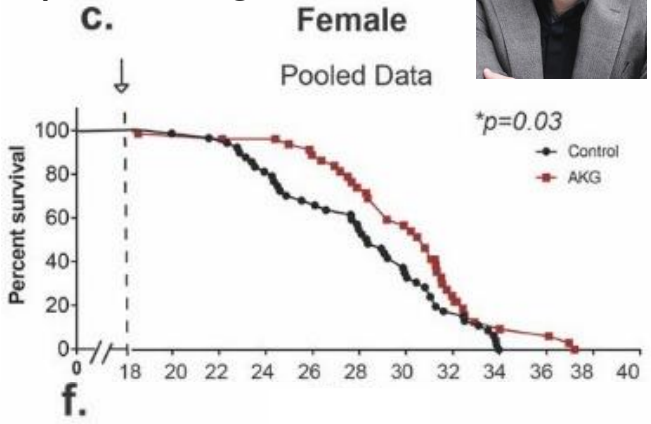
Identification

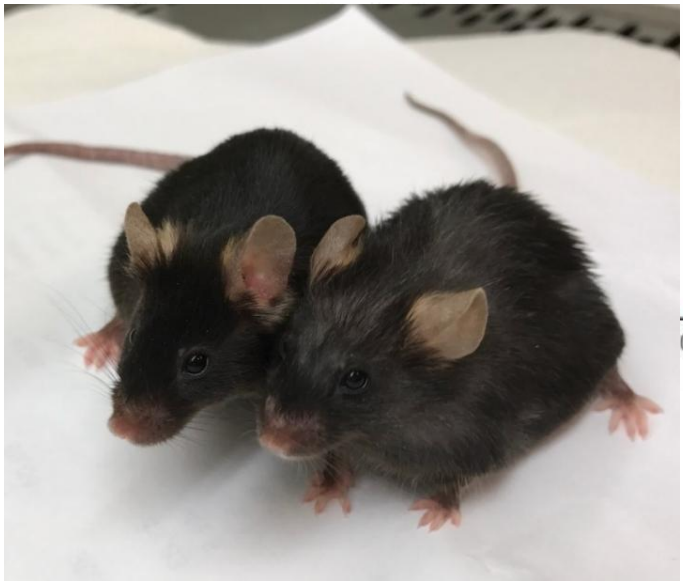




Intervention

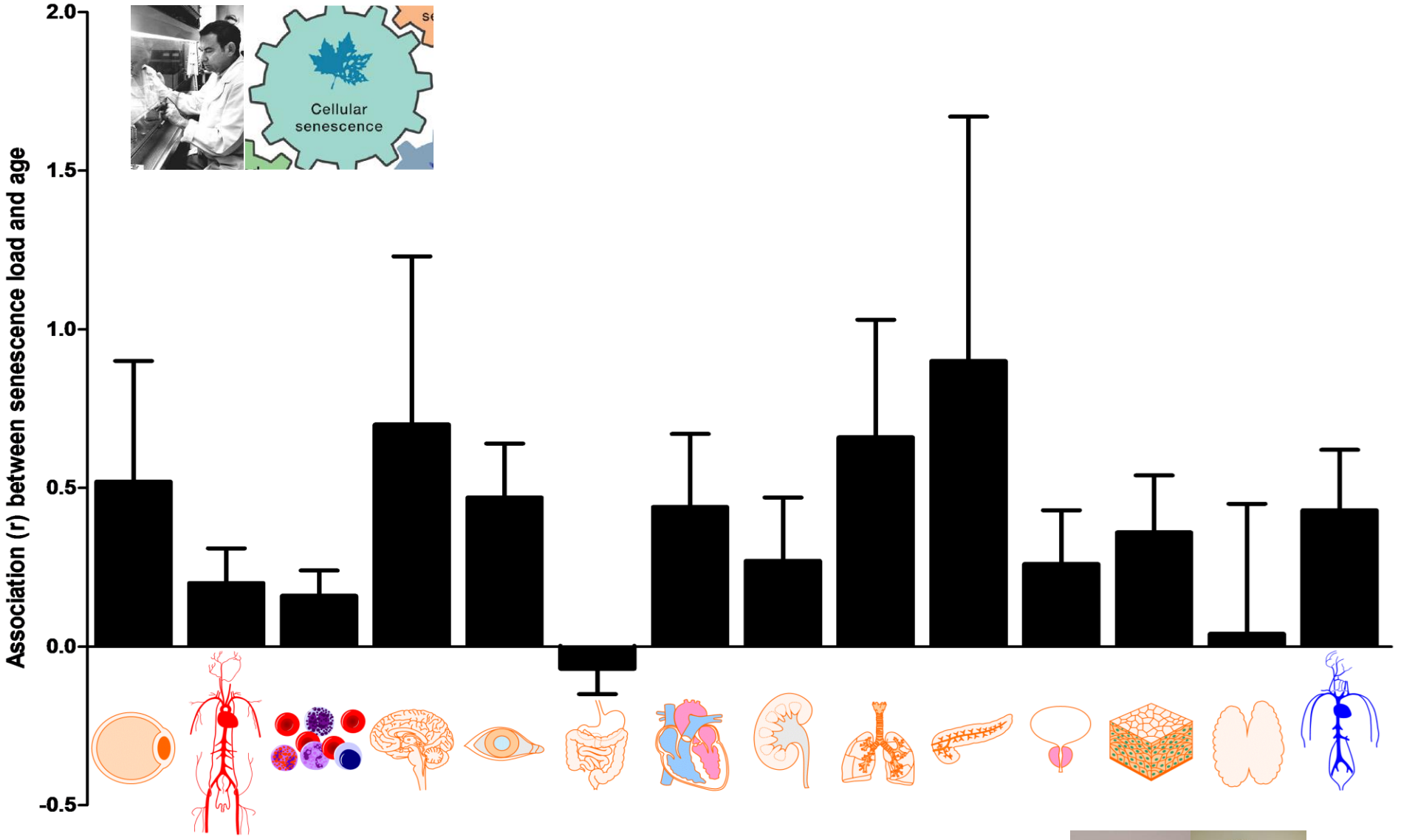
Alpha-ketoglutarate





Tuttle et al., Exp Gerontol 2018; Singh et al., Cell 2019; Shahmirzadi et al., Cell Metabolism 2020

Senescence and chronological age



Tuttle et al., Aging Cell 2020

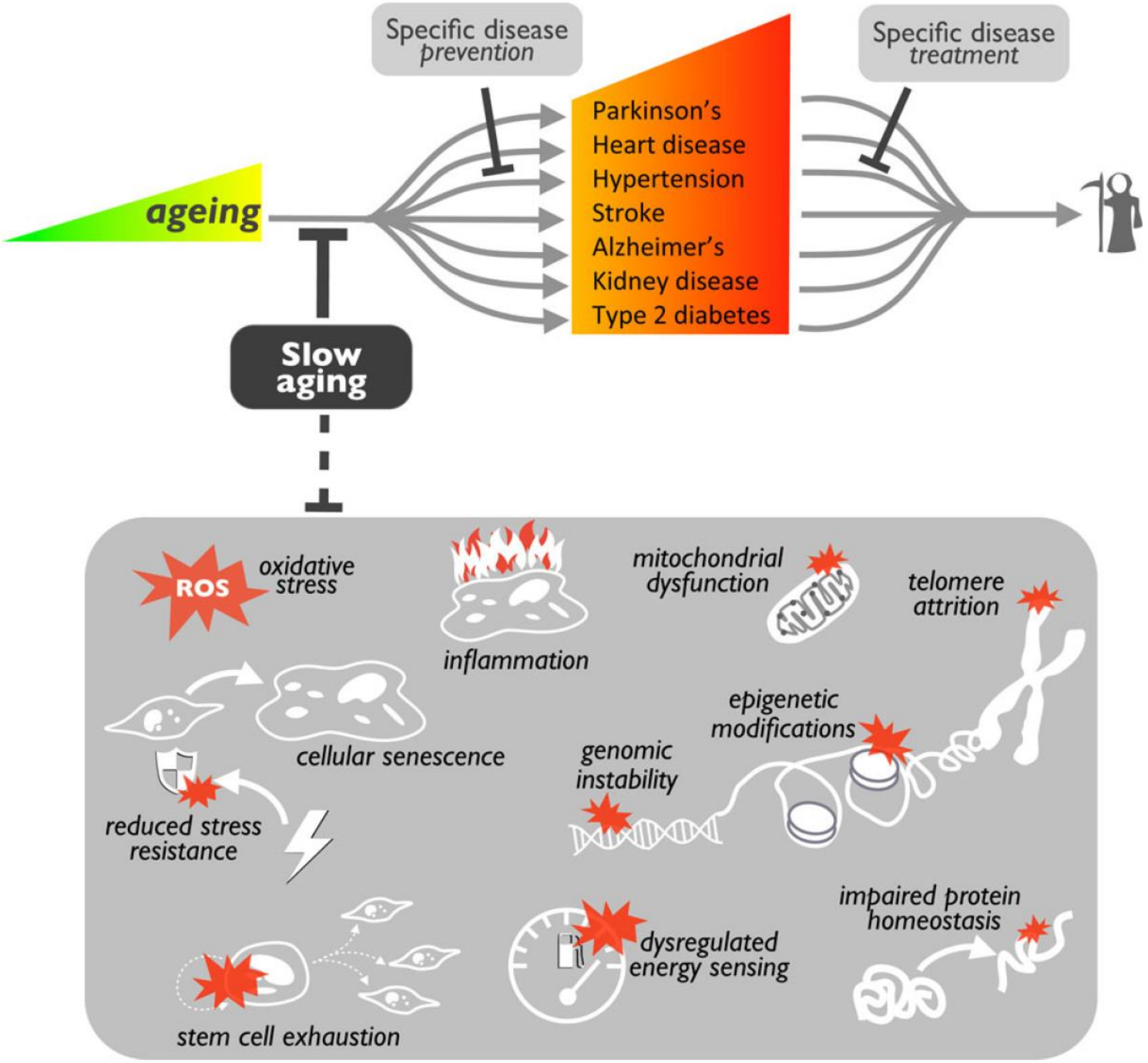
Senescence and age-related diseases

Marker

Disease	Articles	p14 p16	p19 p21	p27	p53	Cyclin D γH2Ax	53BP1 Bmi-1 p-HP1γ	Saβ-Gal	Ki67	IL-6	IL-8	IL1α	MMP3	TGFβ-1	TNFα	MCP-1	ICAM1	Laminin	LMα4	SAHF	SACA	Clusterin
Brain																						
Cognitive Impairment	2																					
Alzheimer's Disease	4																					
Dementia	2																					
PSP	1																					
MND	2																					
Multiple Sclerosis	1																					
Eye																						
ECD	2																					
Glaucoma	2																					
Cataract	1																					
Retinal Microaneurysm	1																					
Endocrine																						
Obesity/Metabolic	2																					
Type 2 Diabetes	5																					
Diabetes Nephropathy	5																					
Respiratory																						
COPD	13																					
IPF	5																					
Heart																						
Hypertension	2																					
Atherosclerosis	8																					
Aortic Valve Stenosis	1																					
Aneurysm	5																					
Coronary Artery Disease	7																					
Heart Failure	4																					
Liver																						
NAFLD	3																					
ARLD	1																					
Infectious Hepatitis	5																					
Liver Cirrhosis	9																					
Hepatic Encephalopathy	1																					
Kidney																						
Chronic Kidney Disease	6																					

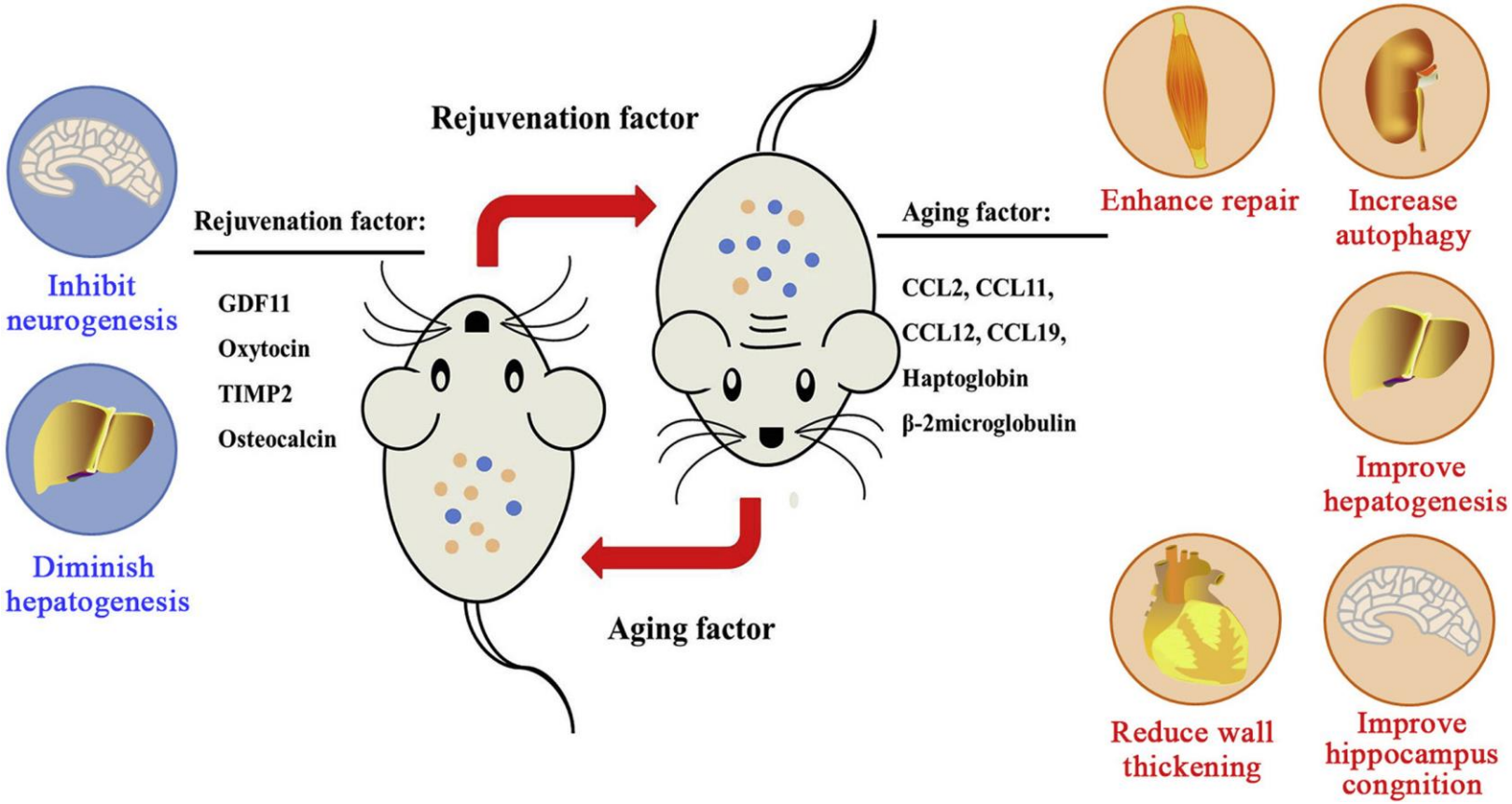
Key	p<0.05	Expect direction	0.051>p<0.20	Expect direction	p>0.20	Inconclusive	0.051>p<0.20	Opposite direction	p<0.05	Opposite direction

Tuttle et al., Ageing Res Rev 2021



Seals et al., J Physiol 2015

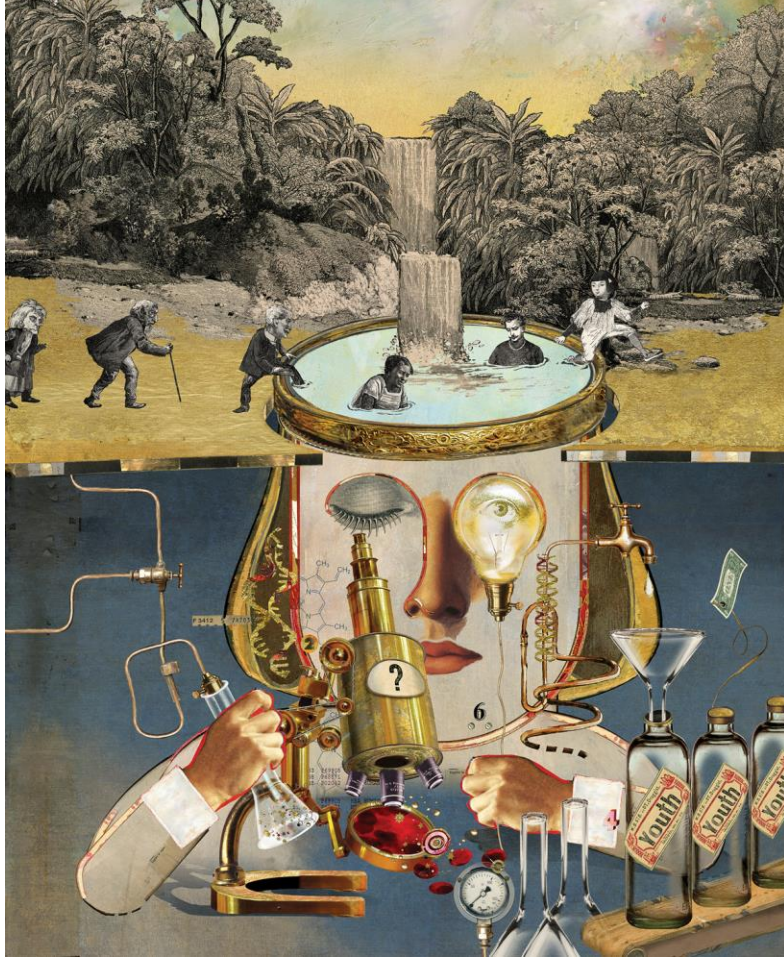
‘Blood’ factors influencing health



Wei et al., J Formosan Med J 2020

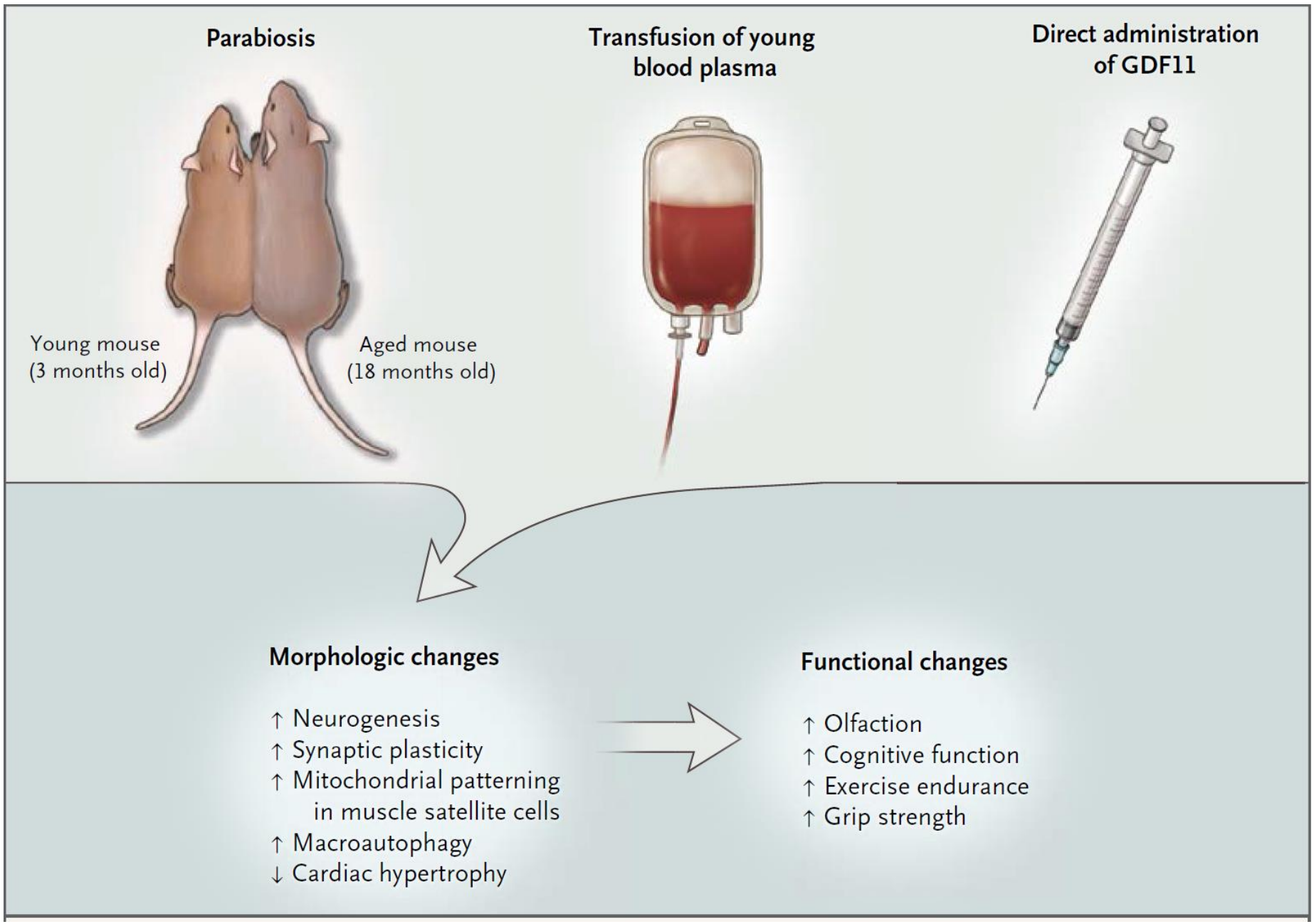
Scientist Robert Boyle *1627:
‘*replacing the blood of the elderly with that of the young would be beneficial’*

Doctor Alexander Bogdanov 1920:
underwent young blood transfusions
‘more energetic and better looking’



Bruno Mallart

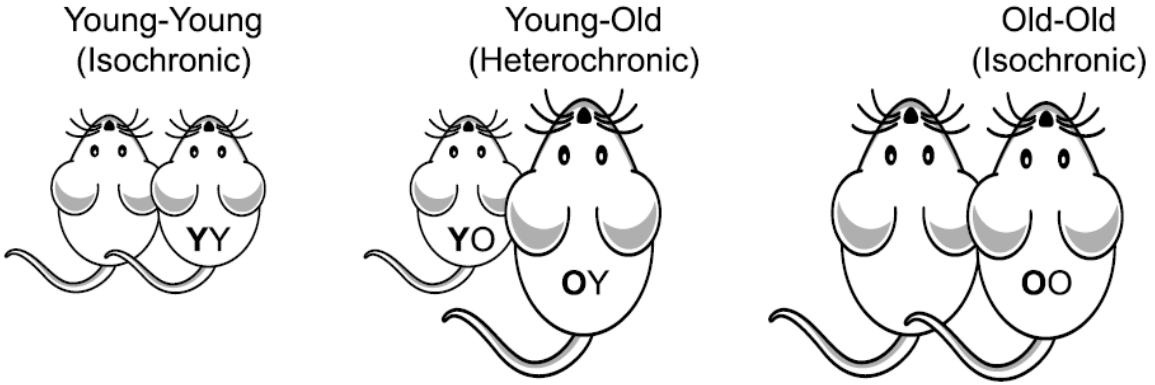
Parabiosis:
two living organisms are surgically joined,
→ develop single, shared circulatory systems



Laviano et al., NEJM 2014

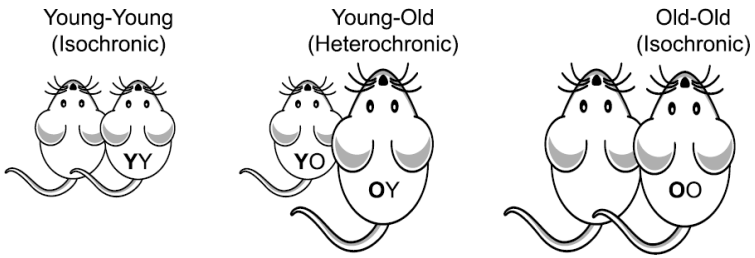
Loffredo et al., Cell 2013; Conboy et al., Nature 2007;
Andersen et al., Cell Res 2014; Sinha et al., Science 2014

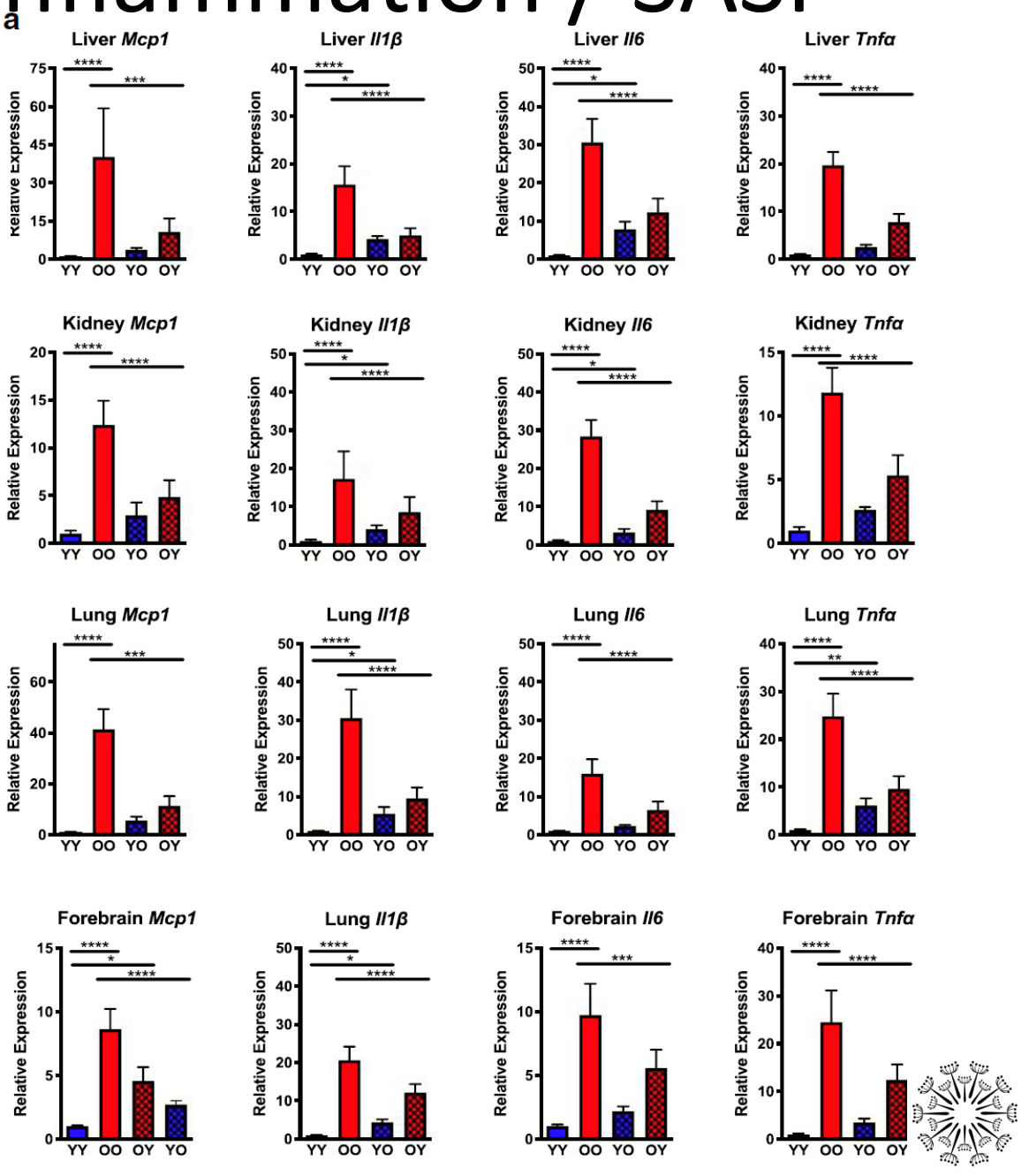
Parabiosis and cellular senescence



Yousefzadeh et al., GeroScience 2021

Parabiosis and inflammation / SASP

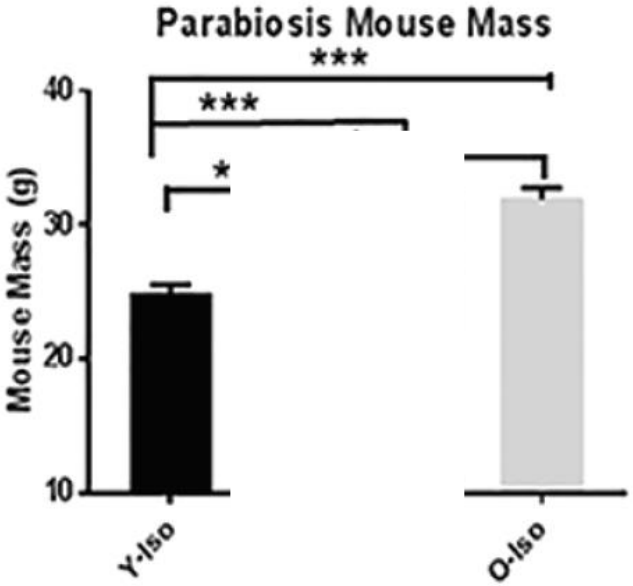


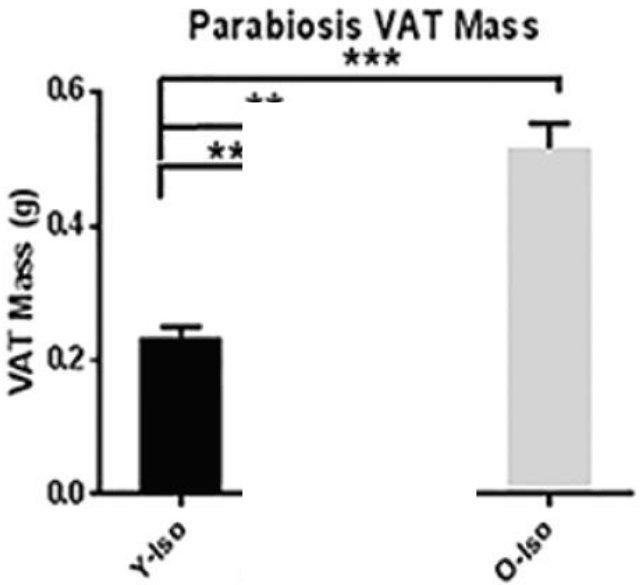


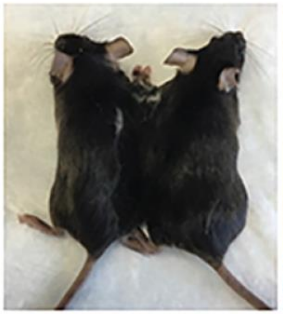
Yousefzadeh et al., GeroScience 2021

Parabiosis, visceral tissue, inflammation

Visceral adipose tissue





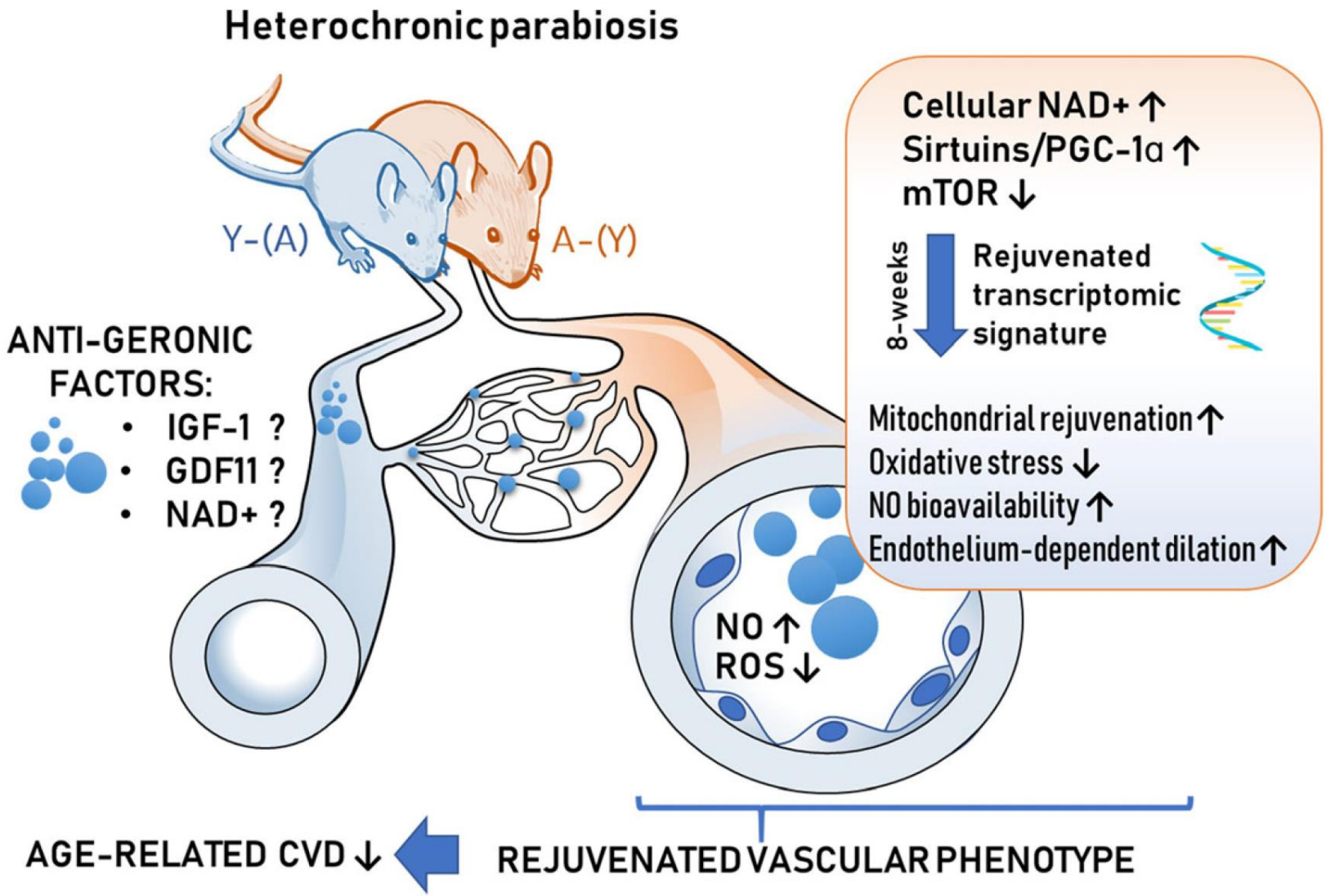


Dorsal

Ventral

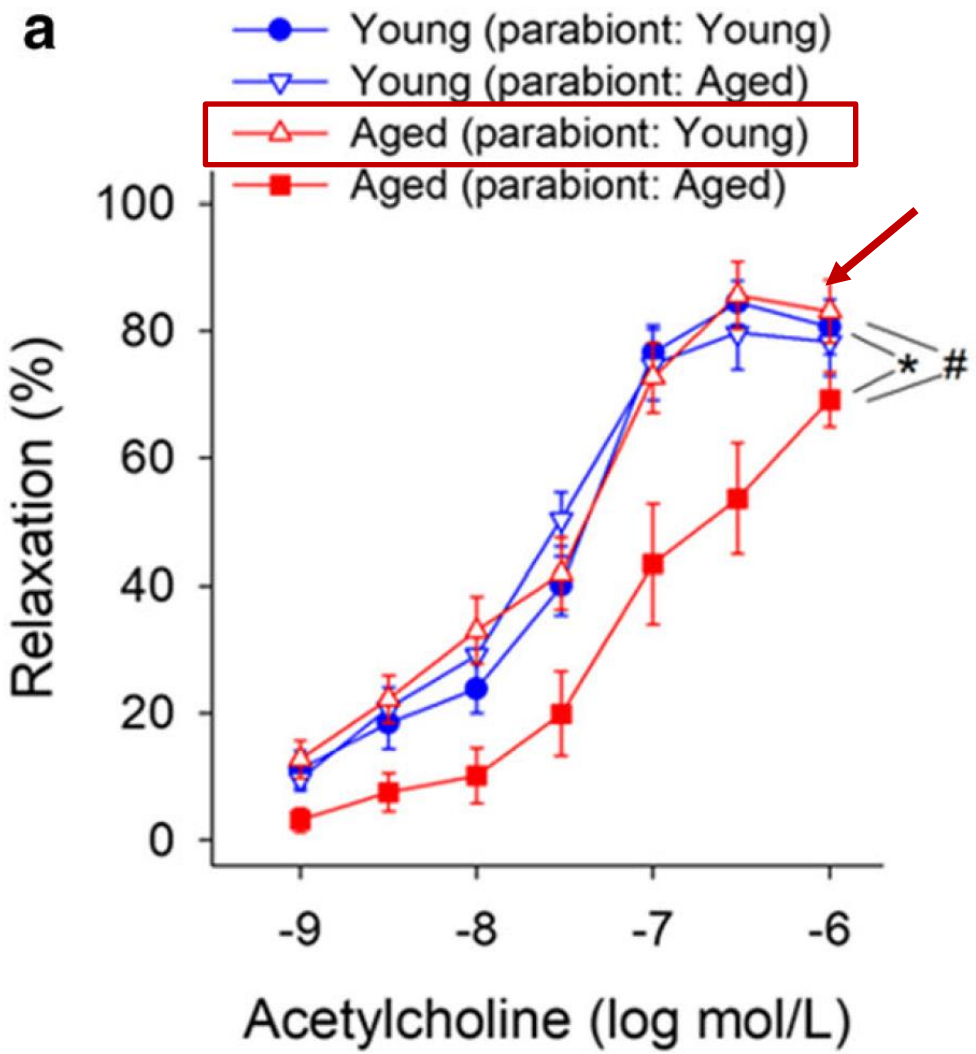
Ghosh et al., J Gerontol A Biol Sci Med Sci 2019

Parabiosis and CVD



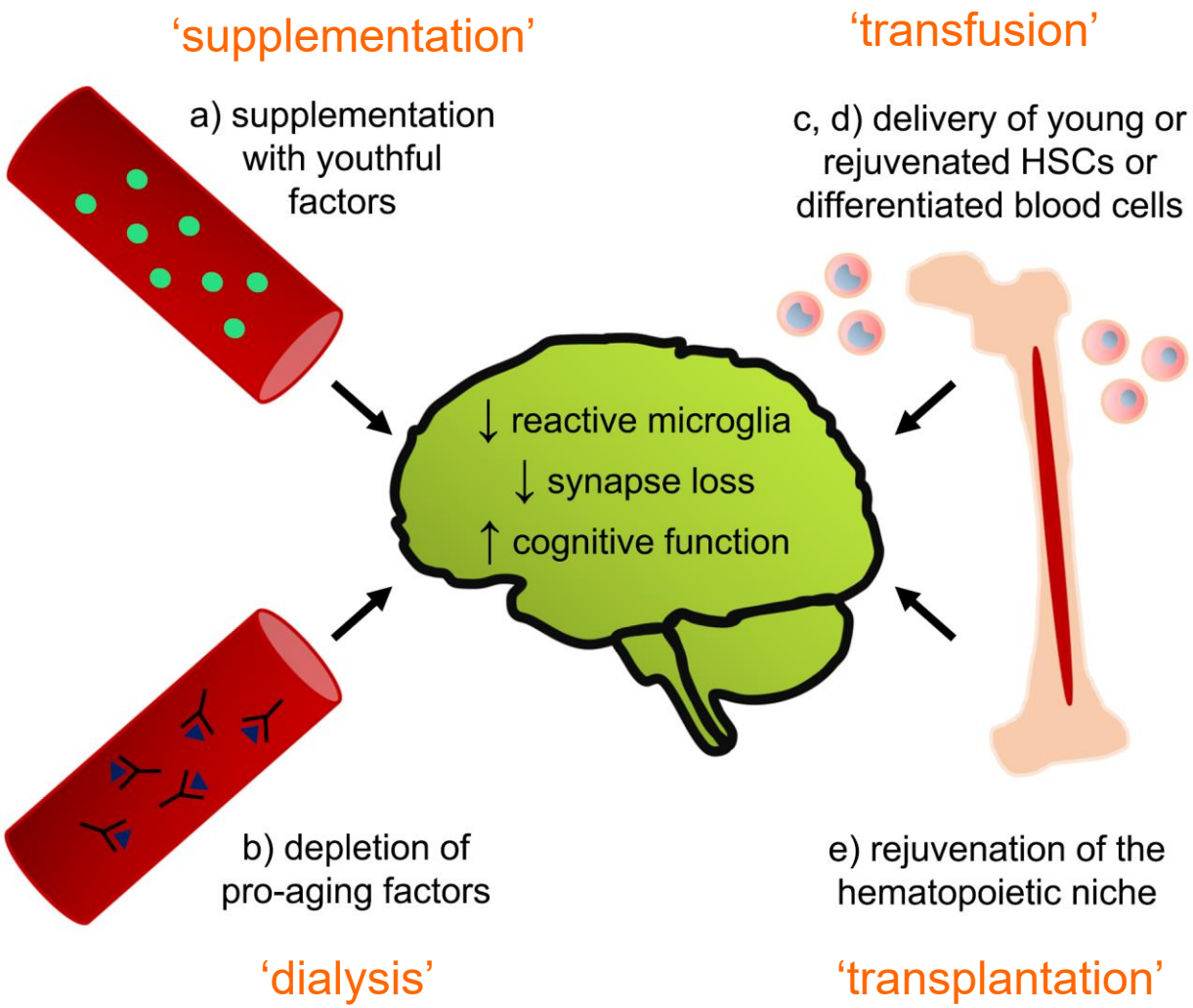
Kiss et al., GeroScience 2020

Parabiosis and vasorelaxation



Kiss et al., GeroScience 2020

Rejuvenation blood and bone marrow



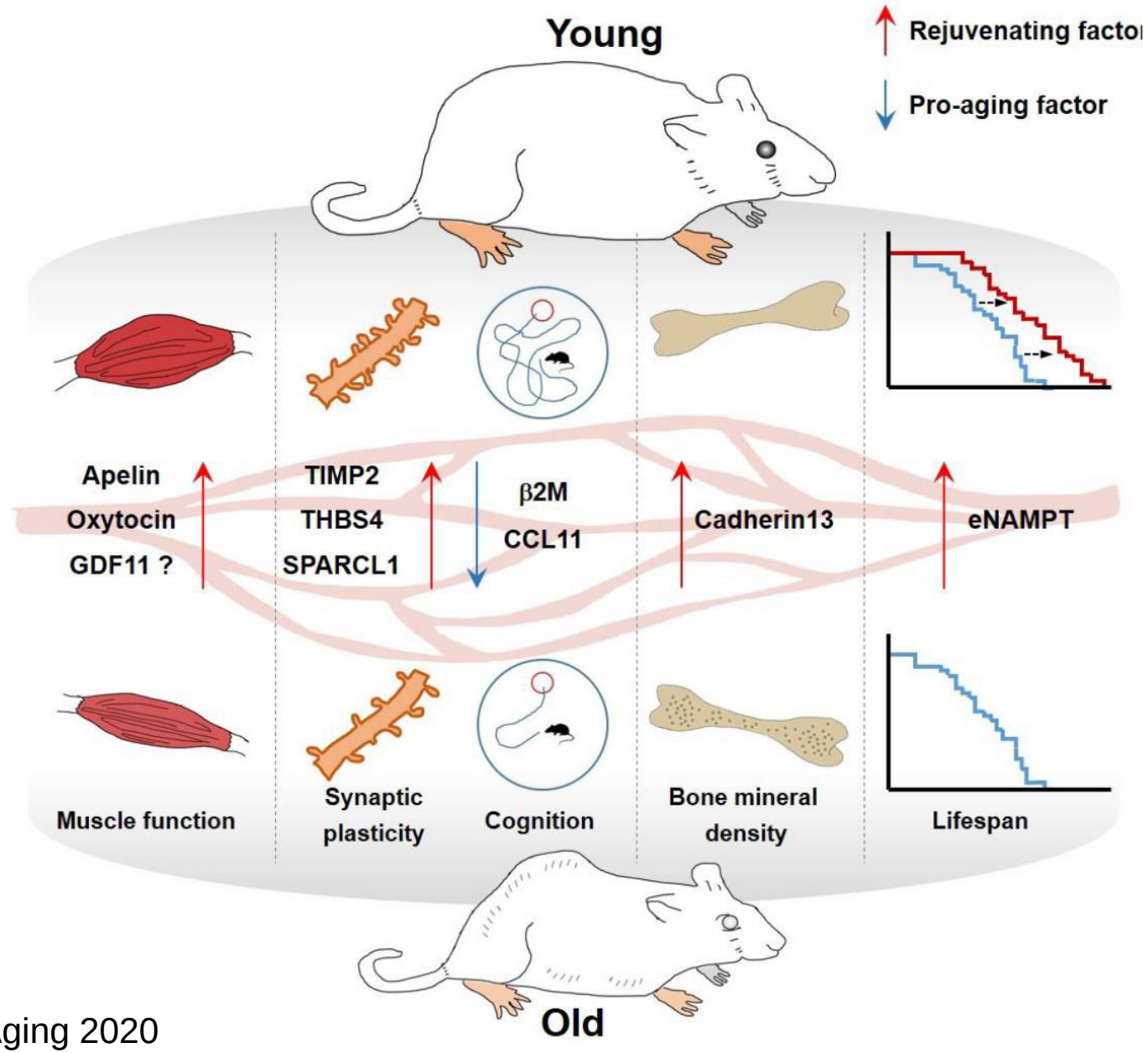
Clinical trials in humans:
young plasma (4 weekly 250ml) infusion

AD
PD
stroke
postoperative recovery
joint replacement

Cord blood
iPSC

Kang et al., Communications Biology 2020

Circulating plasma factors



Kang et al., Aging 2020

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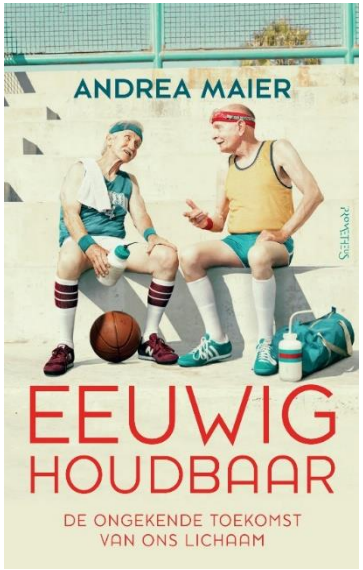
Medical Research Future Fund

Australian Government
National Health and Medical Research Council
NHMRC

HORIZON 2020



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