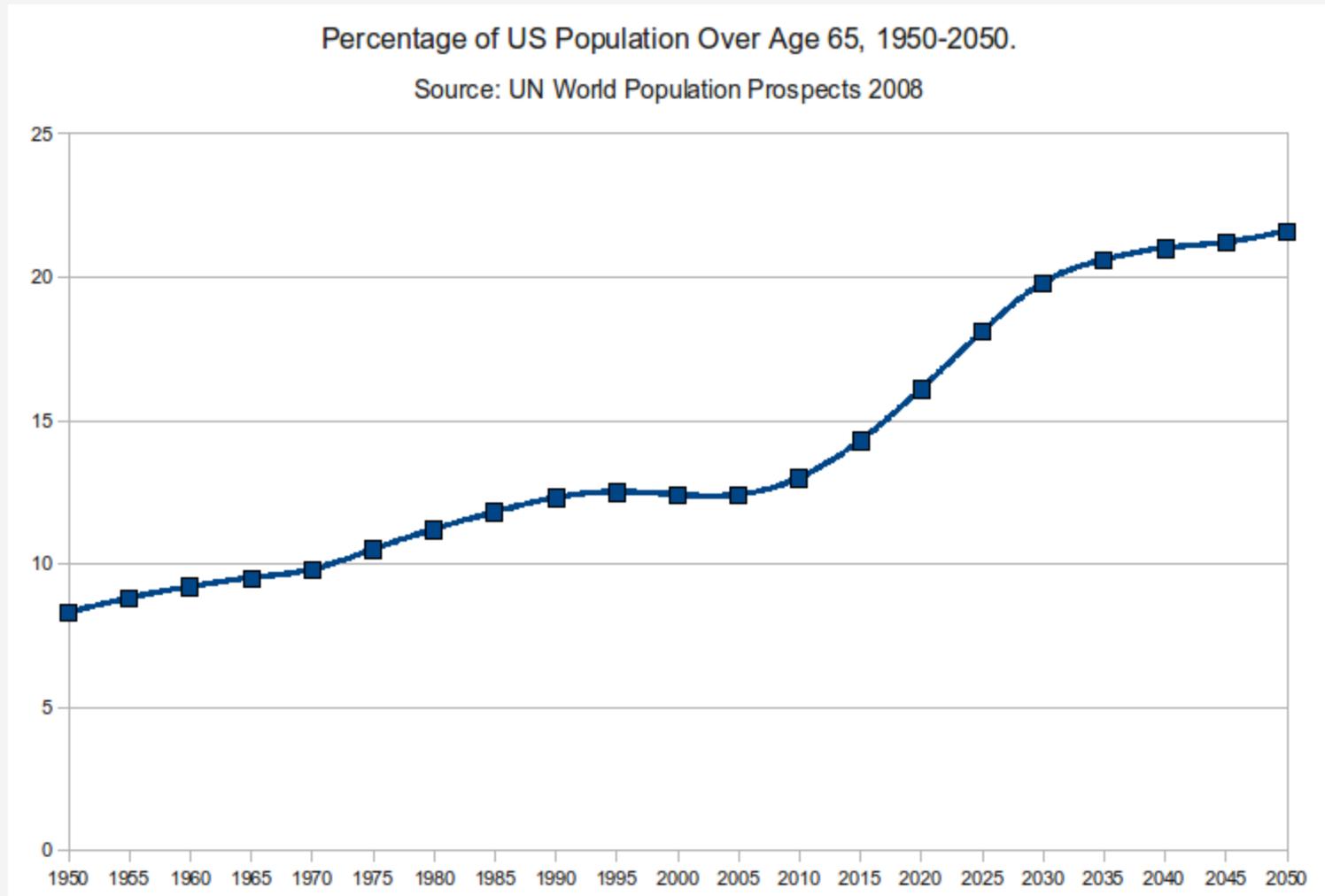


# Rejuvenation biotechnology:

why the longevity “problem” is going to get worse – well, different

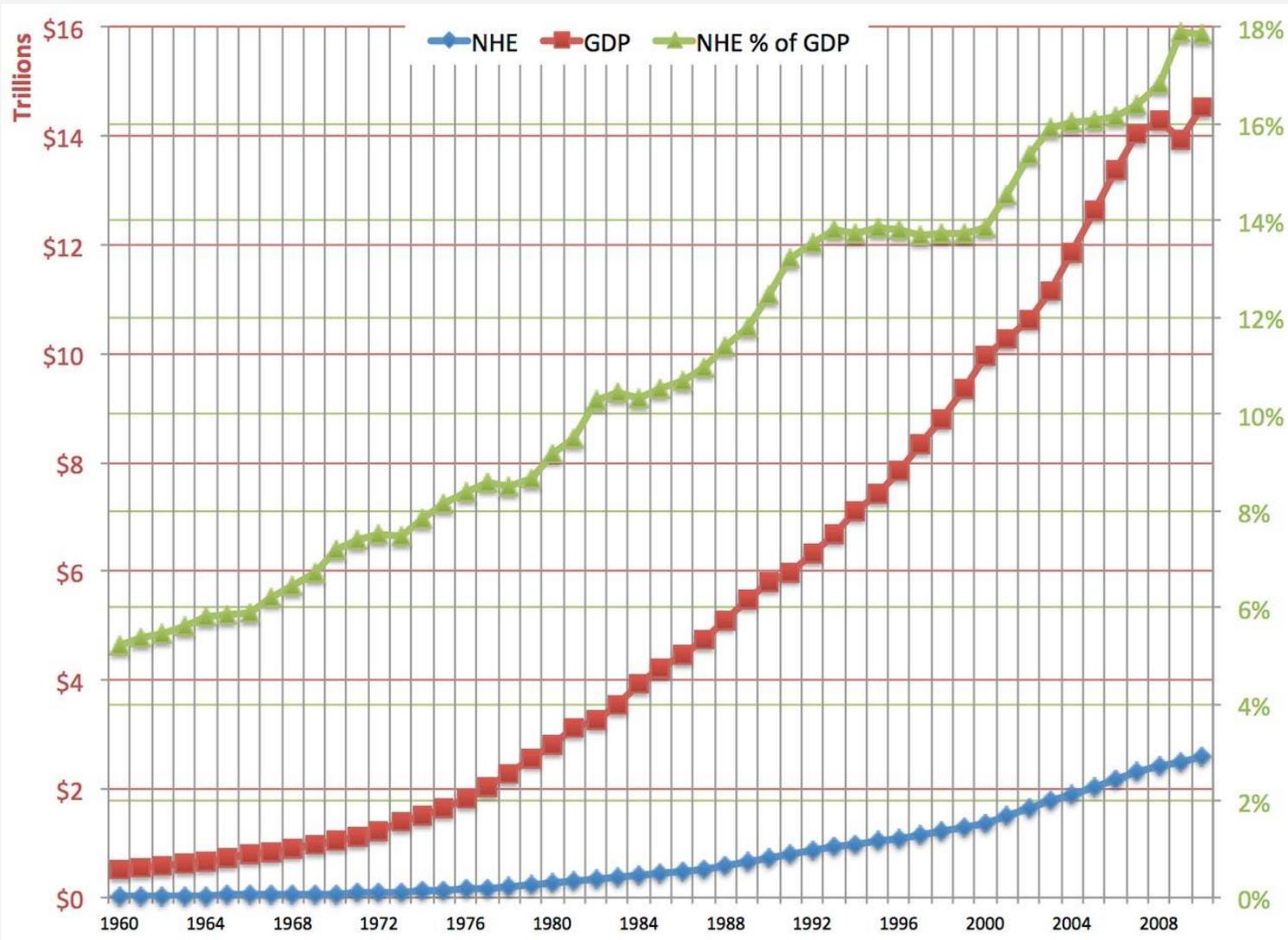
*Aubrey D.N.J. de Grey, Ph.D.*  
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<http://www.sens.org/>

# The aging population



\* Source: [http://esa.un.org/wpp/unpp/panel\\_population.htm](http://esa.un.org/wpp/unpp/panel_population.htm)

# The economics of aging



Source: <http://sambaker.com/econ/classes/nhe10/>

If historical rates continue, US healthcare spending will be 34% of GDP by 2040. Source: <http://www.whitehouse.gov/administration/eop/cea/TheEconomicCaseforHealthCareReform>

In 2010, the US spent \$1.186 trillion on healthcare for people 65+ Source: [http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us\\_dchs\\_2012\\_hidden\\_costs\\_112712.pdf](http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us_dchs_2012_hidden_costs_112712.pdf)

# Age-related vs. infectious diseases

- Most infectious diseases have been easily prevented
  - Sanitation
  - Vaccines
  - Antibiotics
  - Carrier control
- Age-related diseases have not. Why not?

# Targeting pathology: tricky

presbycusis  
osteoporosis  
osteoarthritis  
autoimmunity  
greying hair  
presbyopia  
cataract  
glaucoma  
temporal arteritis  
polymyalgia rheumatica  
wrinkling  
Alzheimer's disease  
Pick's disease  
corticobasal degeneration  
progressive supranuclear palsy  
Parkinson's disease  
multiple system atrophy  
dementia with Lewy bodies  
sarcopenia  
glomerulonephritis  
senile cardiac amyloidosis  
atherosclerosis  
arteriosclerosis  
age-related macular degeneration  
cardiomyopathy  
diastolic heart failure  
cancer  
systemic inflammation  
oxidative stress  
reduced coronary blood flow  
loss of cardiac reserve  
andropause  
thymic involution  
reduced plasma renin activity  
reduced aldosterone  
reduced melatonin diurnal rhythm

reduced light adaptation  
reduced ethanol metabolism  
altered drug pharmacokinetics  
somatopause  
loss of cardiac adaptability  
incontinence  
impaired wound healing  
idiopathic axonal polyneuropathy  
autonomic neuropathy  
arrhythmia  
chronic obstructive pulmonary disorder  
benign prostatic hypertrophy  
menopause  
leukoaraiosis  
stroke  
vascular dementia  
frontotemporal dementia  
immunosenescence  
anosmia  
cachexia  
anorexia of aging  
systolic hypertension  
ageusia  
erectile dysfunction  
orthostatic hypotension  
impaired adaptive beta-cell proliferation  
fibroblast collapse  
anergic T-cell clones  
cellular senescence  
vascular calcification  
impaired transdermal absorption  
impaired thermoregulation  
reduced tactile acuity  
impaired vasoconstriction  
loss of neuromuscular junctions  
delayed withdrawal reflex

impaired pH maintenance  
reduced chemical clearance  
altered dermal immune cell residence and function  
aberrant allergic and irritant reactions  
loss of skin elasticity  
impaired vitamin D synthesis  
reduced renal reserve  
renal cortex atrophy  
gut dysbiosis  
loss of jejunal villus height  
impaired response to vaccination  
impaired thirst  
lentigo senilis  
thinning hair  
impaired proprioception  
impaired balance  
reduced vital capacity  
reduced cardiorespiratory endurance  
impaired sweat response  
impaired blood distribution  
nutrient malabsorption  
diverticular disease  
presbyphagia  
increased reflux  
alveolar loss  
neuronal loss  
senile emphysema  
degenerative disc disease  
joint calcification  
pineal calcification  
aberrant differentiation  
gait instability  
frontal demyelination  
axonal atrophy  
impaired functional connectivity  
impaired working memory

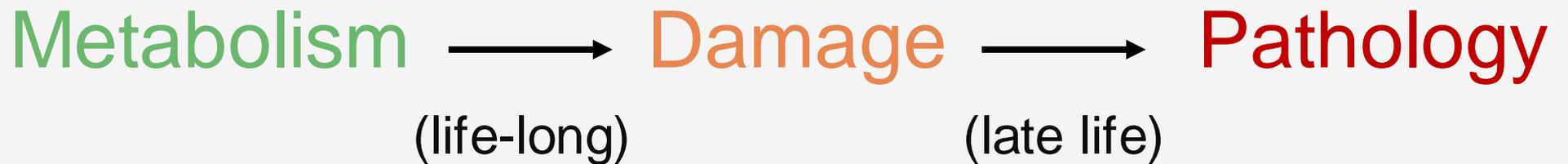
# What is 'aging', exactly?

Aging is the life-long accumulation of “damage” to the body that occurs as intrinsic side-effects of the body’s normal operation.

Damage: changes in structure & composition that the body cannot automatically reverse.

The body can tolerate some damage, but too much of it causes disease and disability.

# Aging in three words



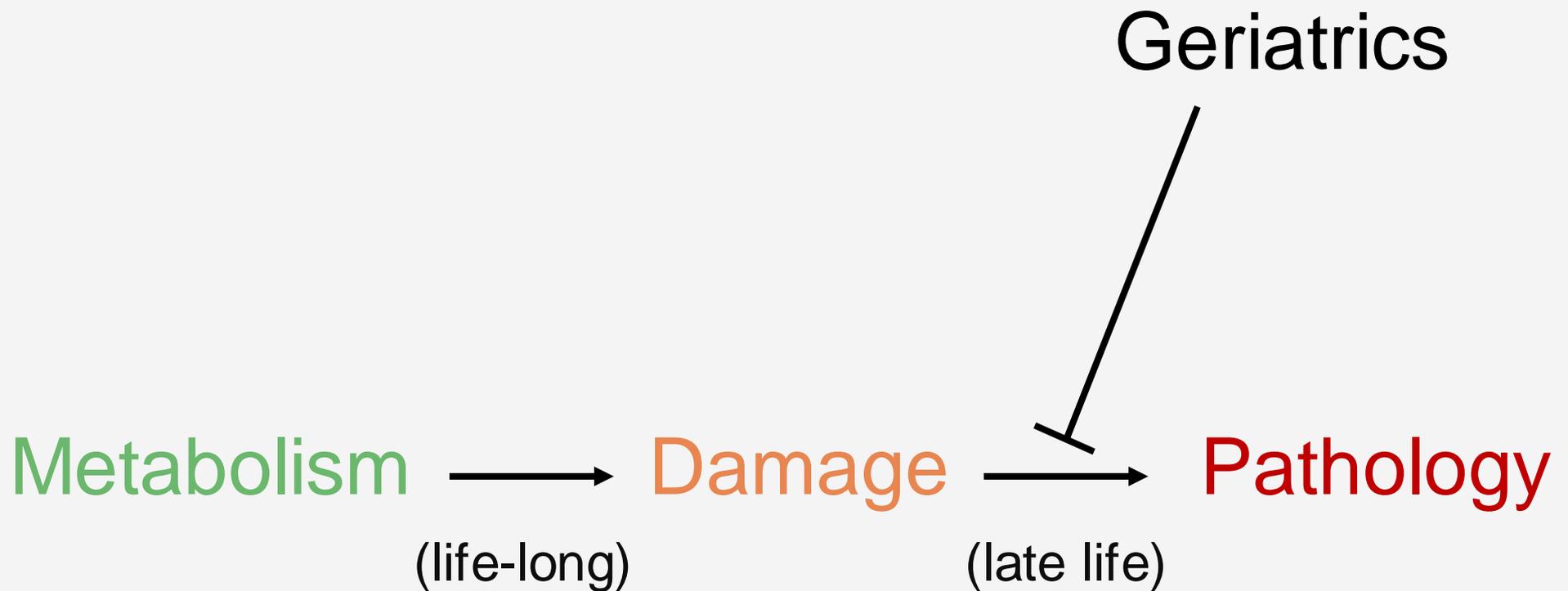
# Diseases and aging: popular view

Diseases			Aging
Communicable	Congenital	Chronic	
Tuberculosis Malaria HIV ...	Tay-Sachs MELAS Li-Fraumeni ...	Alzheimer's Cancer Atherosclerosis ...	Frailty Sarcopenia Immunosenescence ...

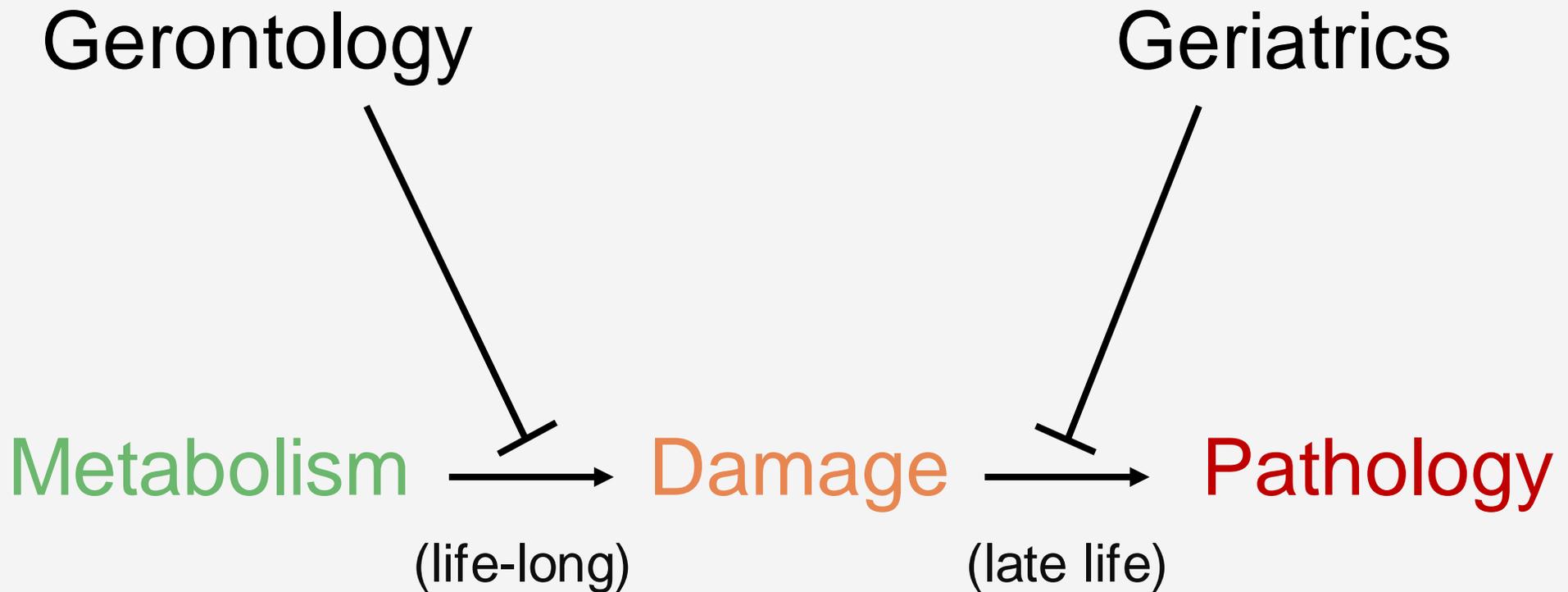
# Diseases and aging: correct view

Diseases		Aging	
Communicable	Congenital	Specific	General
Tuberculosis Malaria HIV ...	Tay-Sachs MELAS Li-Fraumeni ...	Alzheimer's Cancer Atherosclerosis ...	Frailty Sarcopenia Immunosenescence ...

# The tragic result of that popular view



# Is prevention better than cure?



# Targeting metabolism: also tricky

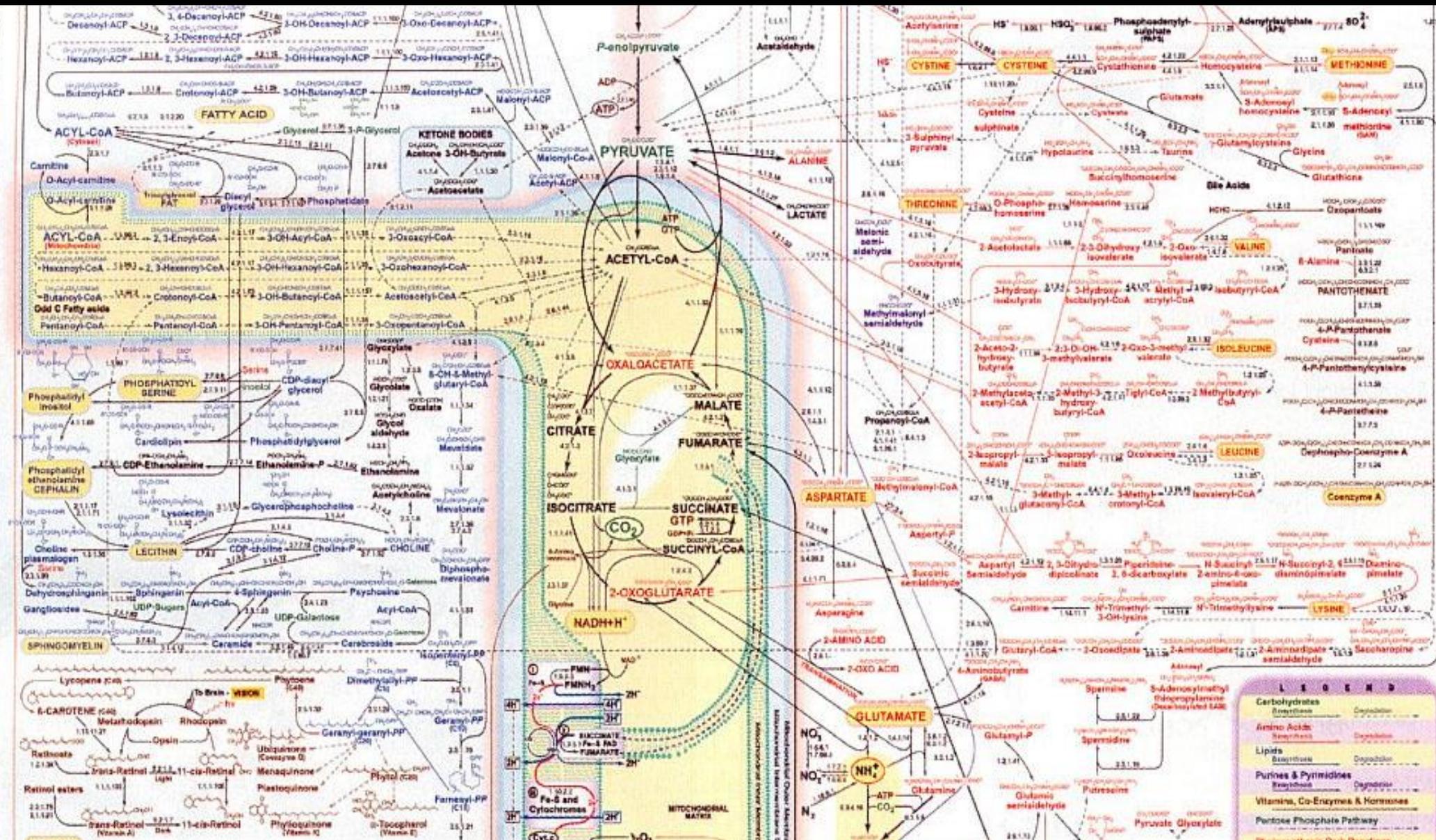
SYNTHESIS

LIPID DEGRADATION

PHOSPHOLIPIDS

ISOPRENOIDS

S



LEGEND	
Carbohydrates	Carbohydrate
Amino Acids	Amino Acid
Lipids	Lipid
Purines & Pyrimidines	Nucleotide
Vitamins, Co-Enzymes & Hormones	Vitamin
Pentose Phosphate Pathway	



# Comparison: car maintenance

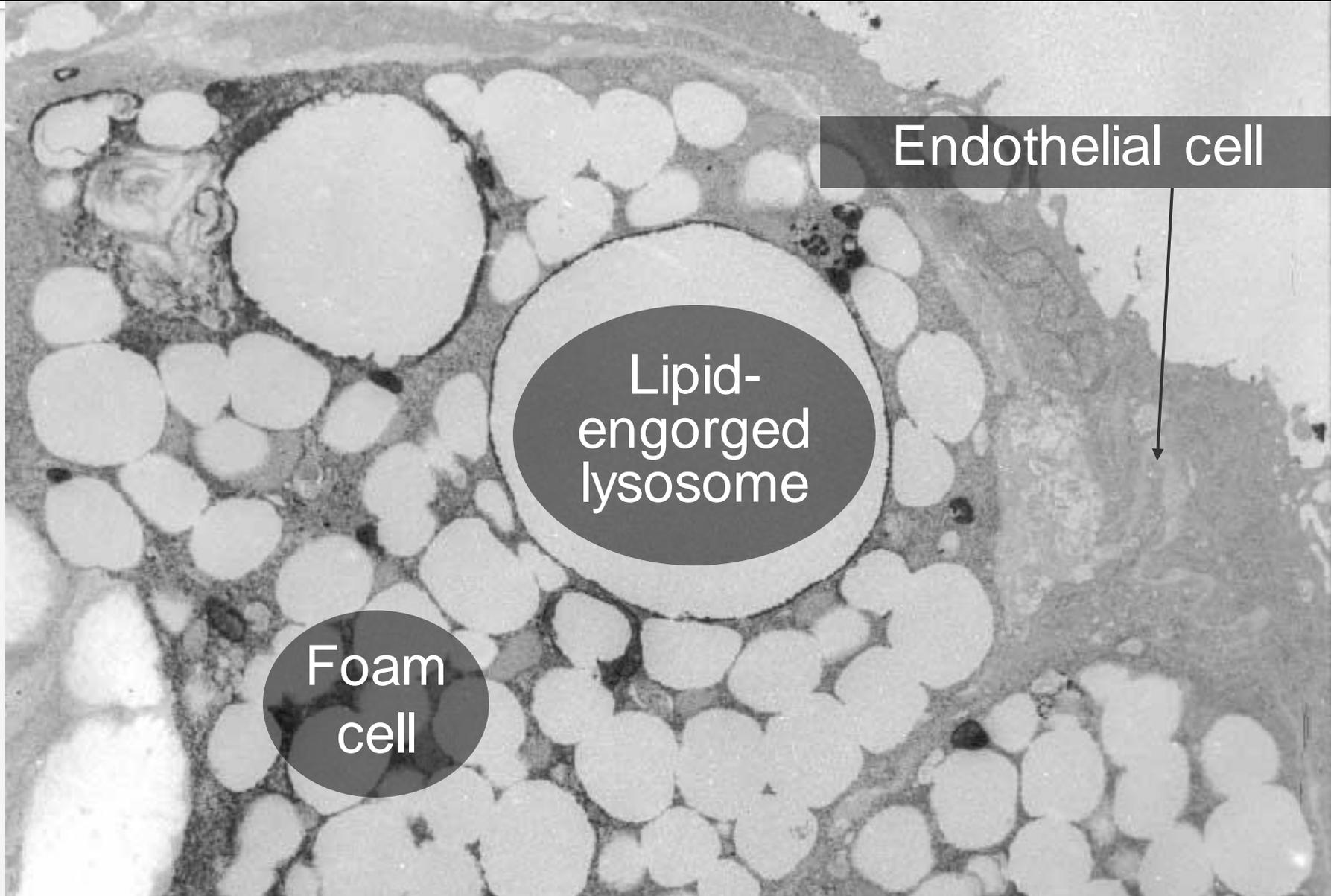


# The “seven deadly things” & their fixes

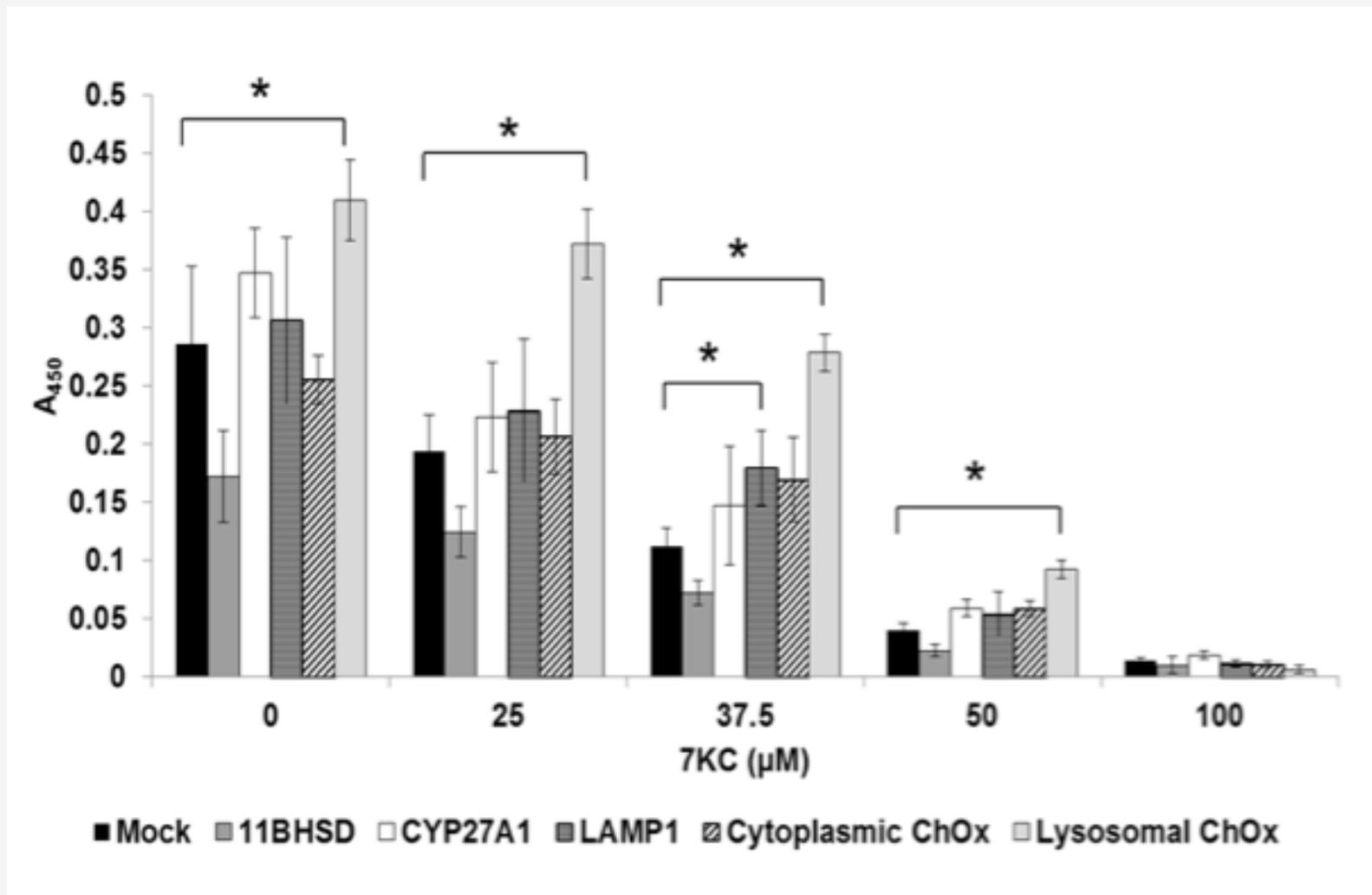
Damage type	The maintenance approach
Cell loss, cell atrophy	Replace, using stem cells
Division-obsessed cells	Reinforce, using telomere control
Death-resistant cells	Remove, using suicide genes etc
Mitochondrial mutations	Reinforce, using backup copies
Intracellular waste products	Remove, using foreign enzymes
Extracellular waste products	Remove, using immune system
Extracellular matrix stiffening	Repair, using crosslink-breakers

**Existence of any 8<sup>th</sup> is looking increasingly unlikely**

# Intracellular junk in the artery



# Our enzyme protects cells from 7KC



*Mathieu et al., Biotechnol. Bioeng. 2012; 109(9):2409-2415*

# Things you may be thinking right now

- This guy looks crazy; what do “credentialed” people think about these ideas?
- Even if he’s right, are the consequences for longevity big/near enough to affect my work?
- Even if they are, will society let it happen?

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# What do other experts think?



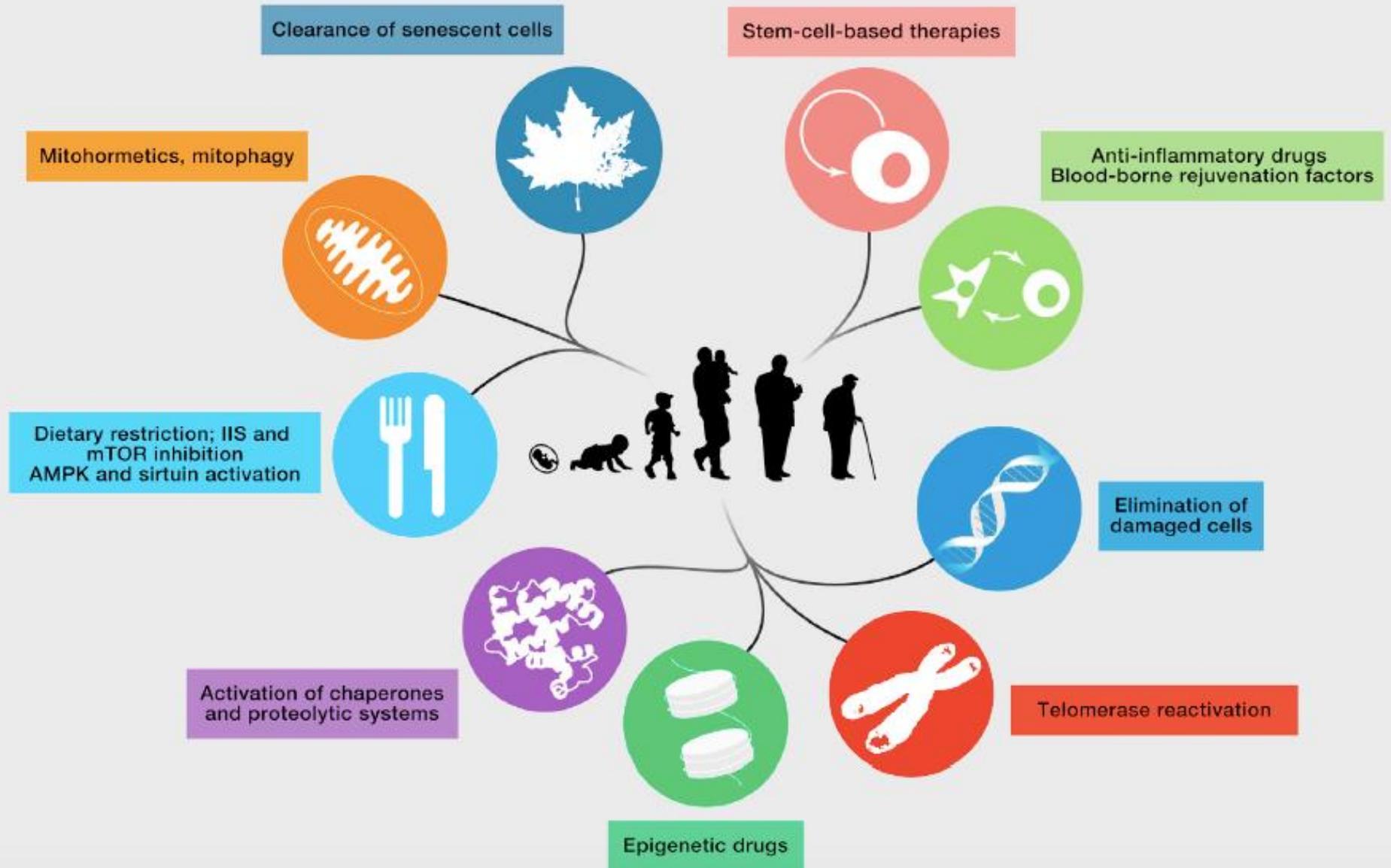
See their names, their awesome credentials and their hard-hitting endorsement of our research approach at

[www.sens.org/about/leadership/research-advisory-board](http://www.sens.org/about/leadership/research-advisory-board)

# Cell 153:1194 (2013)



# Cell 153:1194 (2013)



# Our work is respected by experts

- Total synthesis of glucosepane, allowing identification of antibodies and degraders (*Science*, 2015)
- Modified bacterial enzyme protects cells from atherogenic oxysterols (*Biotech Bioeng*, 2012)
- Catalytic antibodies cleave cardiotoxic amyloid (*J Biol Chem*, 2014)
- Much more ongoing in our research centre and funded labs

# Things you may be thinking right now

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# So... longevity?

- We ***DON'T WORK ON LONGEVITY***, whatever the media may like to tell you
- However, we know that this medicine may increase longevity a lot, I mean really a lot
- We think this is a good thing, even though it will put people like you out of business 😊

# How BIG is the longevity side-benefit?

- Rejuvenation therapies may never be perfect; first-generation version may give “only” ~30y extra life
- However, that would buy us time to develop better ones with which to re-rejuvenate the same people, and so on (“**longevity escape velocity**”)
- So...?

# How BIG is the longevity side-benefit?

- Western mortality rate in the 20s is under  $10^{-3}/y$
- If it didn't rise with age (and in fact it will surely fall with time), most people would live to over 1000
- Period (i.e. "headline") life expectancy will very suddenly become incalculable (literally!)

# How NEAR is the longevity side-benefit?

- This is pioneering technology, so we don't know
- Guess: 50% chance in 20-25y if funding rises soon
- At least 10% chance it'll take >100y
- That's for the therapies I've mentioned today
- They will probably give around 30yr extra life
- LEV thenceforth seems inevitable to me...
- **Everyone will understand the above this decade**

# Things you may be thinking right now

- This guy looks crazy; what do “credentialed” people think about these ideas?
- Even if he’s right, are the consequences for longevity big/near enough to affect my work?
- Even if they are, will society let it happen?

# Sociological considerations

- Overpopulation?
- Inequality of access?
- Immortal dictators?
- Boredom?
- Pensions collapse?

# Sociological considerations

- ~~Overpopulation?~~
- ~~Inequality of access?~~
- ~~Immortal dictators?~~
- ~~Boredom?~~
- ~~Pensions collapse?~~

# Sociological considerations

- No age-related ill-health
- Elderly *contribute* wealth
- Energy to explore novelty
- Flexible career structure
- Not a burden on your kids

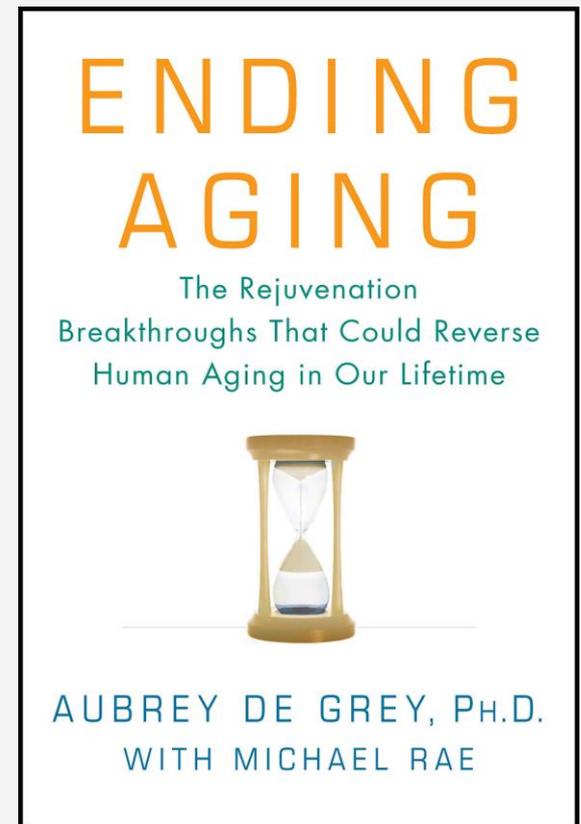
# Learn more

Read the (semi-technical) book.

Available at Amazon and all good book stores.  
Paperback is cheaper, and has an extra chapter!

Visit us on the web at  
<http://www.sens.org/>

Drop us a line at  
[foundation@sens.org](mailto:foundation@sens.org)





sens research foundation

reimagine aging

[www.sens.org](http://www.sens.org)

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