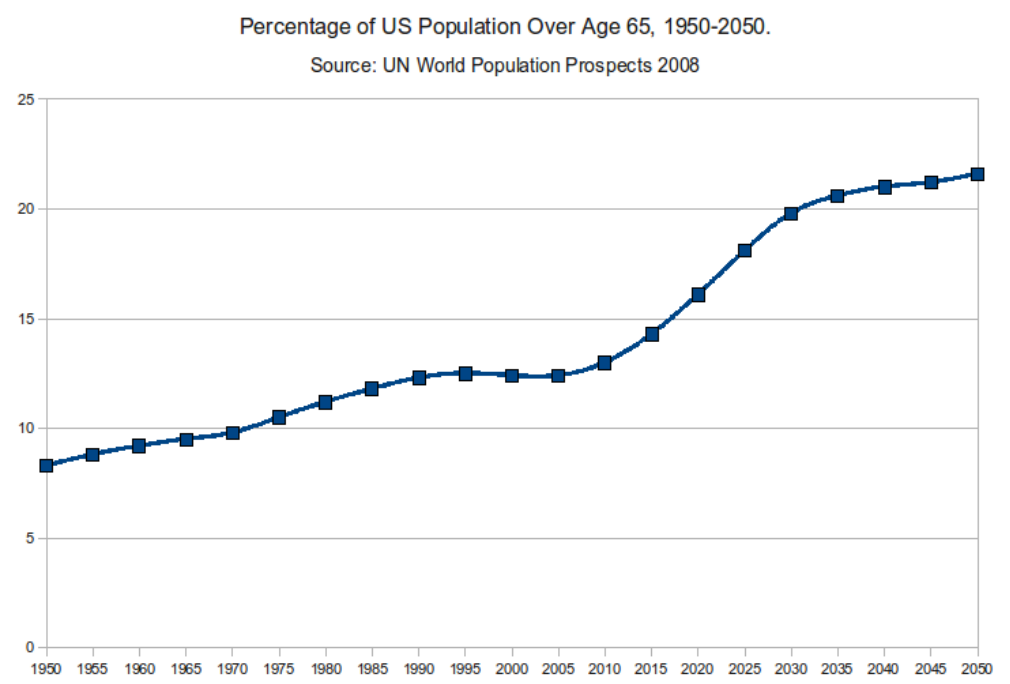
Rejuvenation biotechnology:

why age may soon cease to mean aging

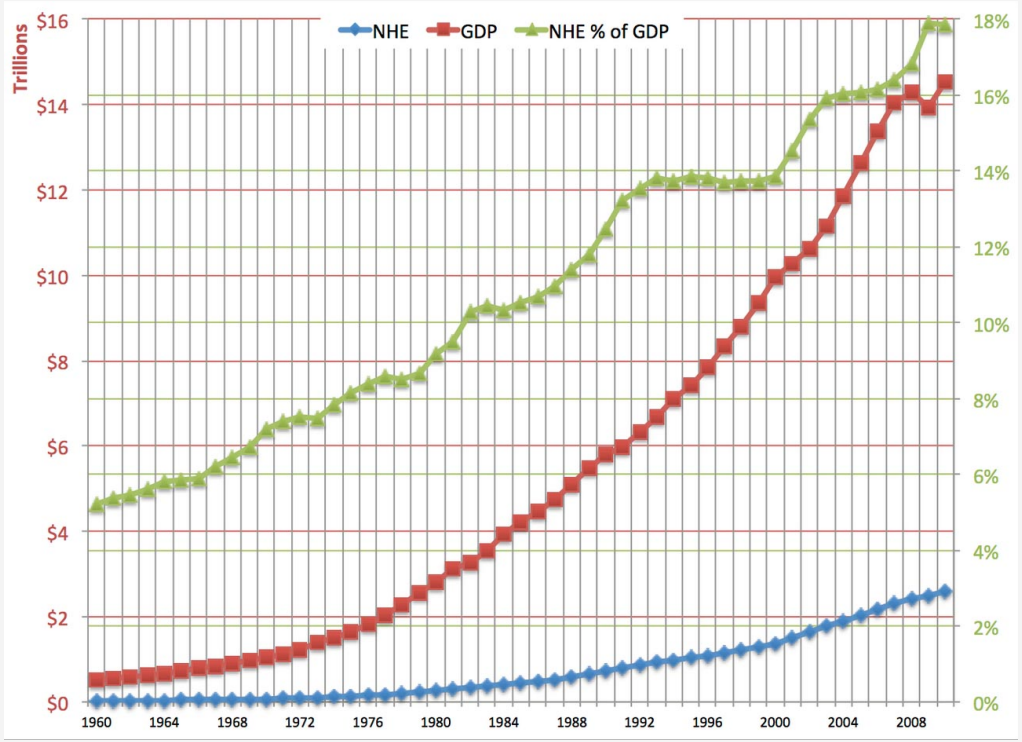
Aubrey D.N.J. de Grey, Ph.D.
Chief Science Officer, SENS Research Foundation
VP New Technology Discovery, AgeX Therapeutics
aubrey@sens.org
http://www.sens.org/
http://www.agexinc.com

The aging population



* Source: 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_costs112712.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?

Well, if not impossible, at least intractable?

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 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 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

Aging in three words

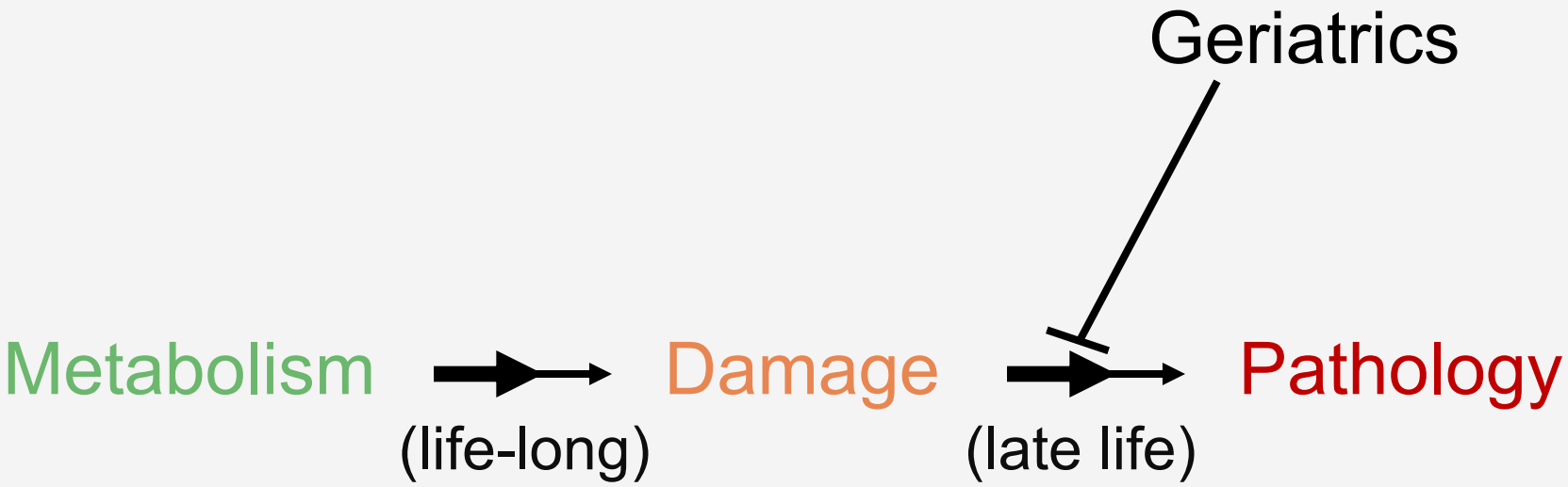
What is ‘aging’, exactly?

Aging is a consequence of physics, not biology

It is the life-long accumulation of “damage” to the body that occurs as an intrinsic side-effect of the body’s normal operation

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

What we do these days against aging



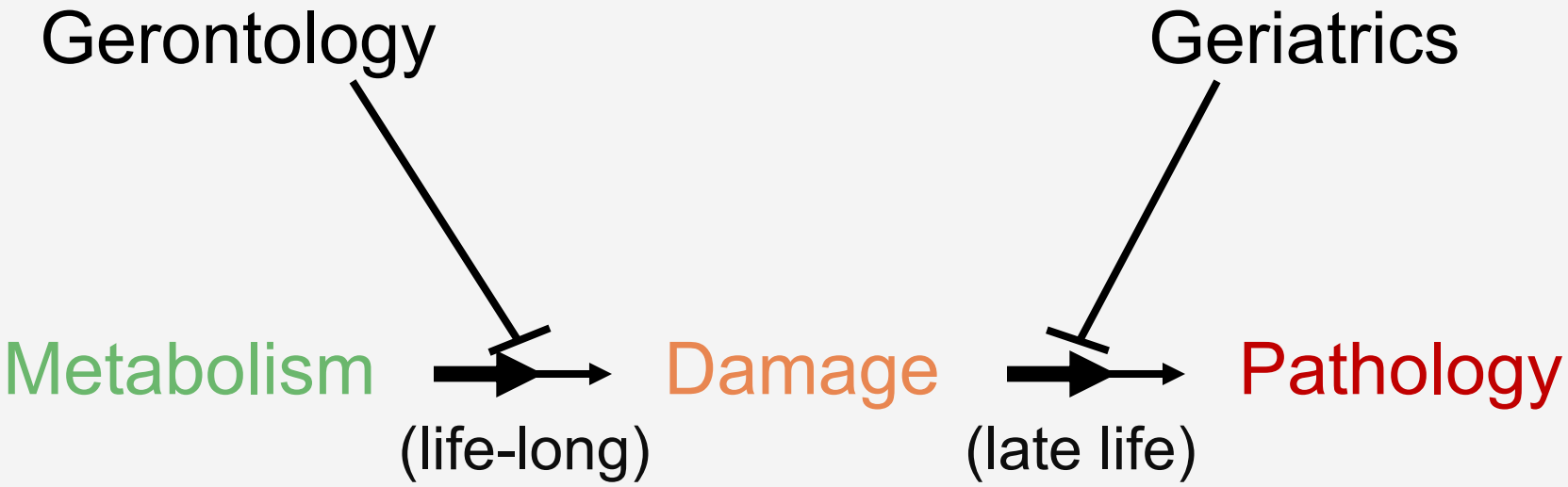
Diseases and aging: popular view

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

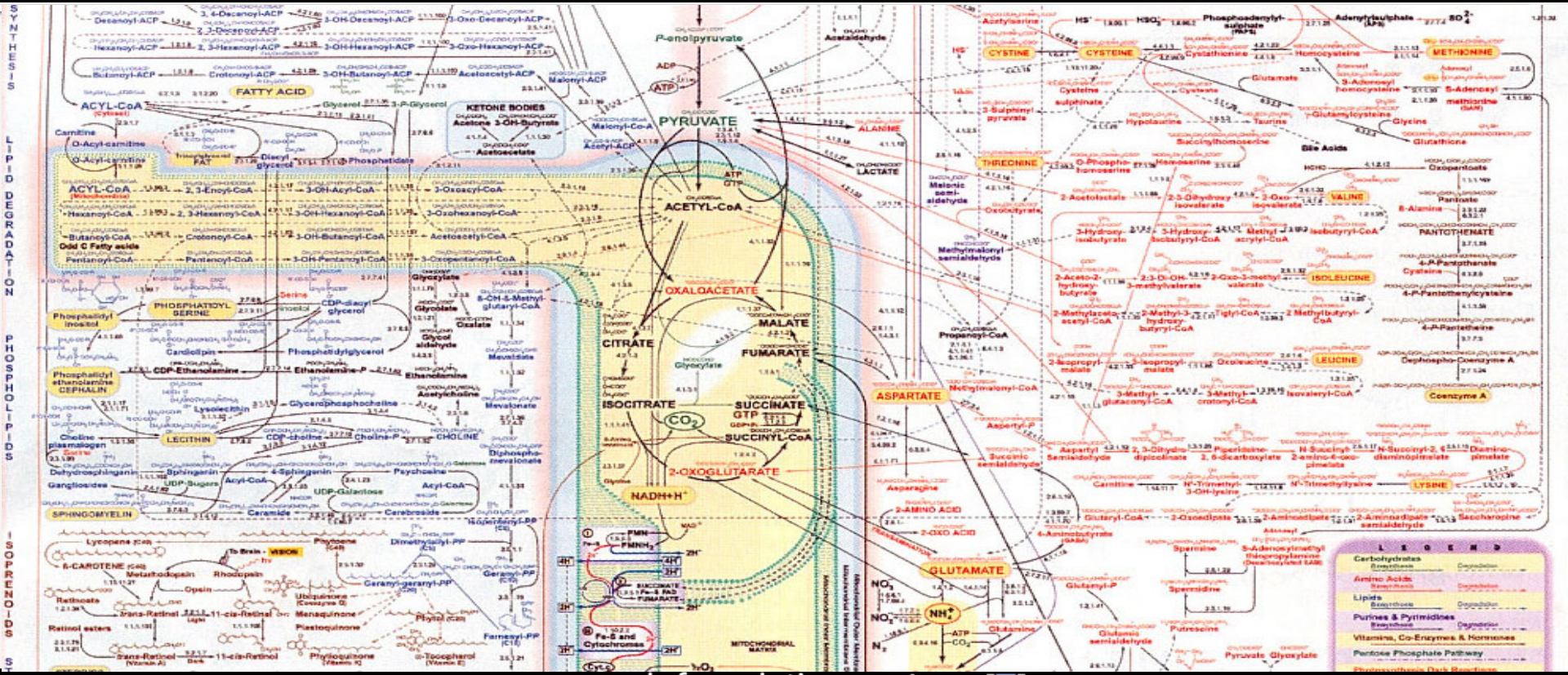
Diseases and aging: correct view

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

A more promising alternative?



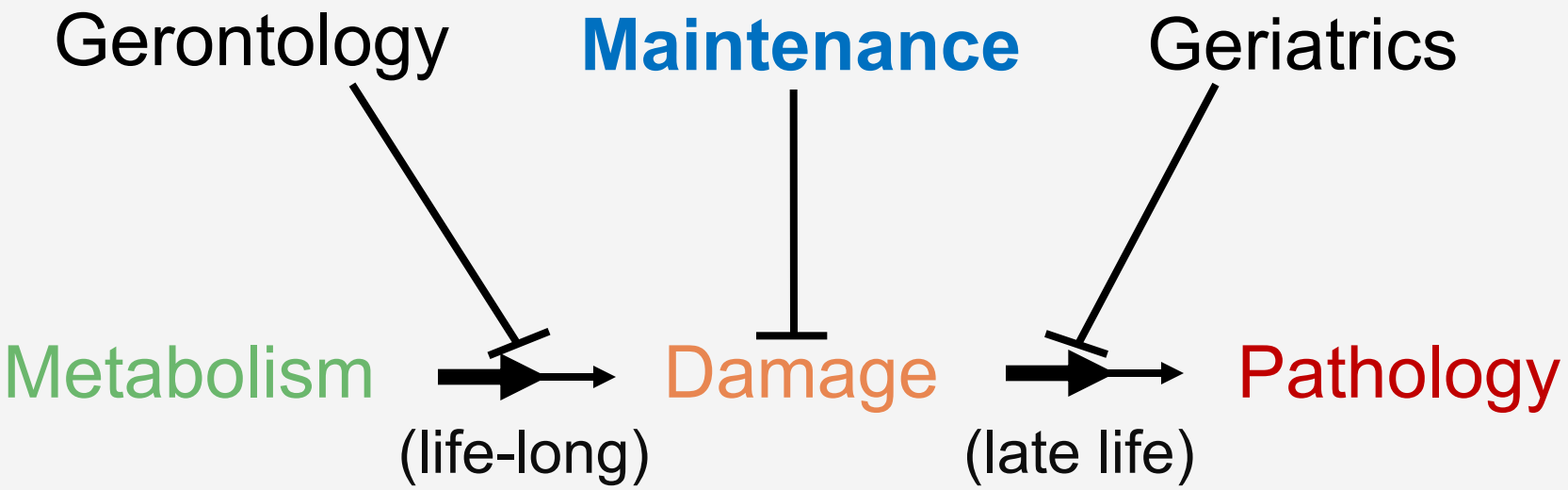
Unfortunately…



sens research foundation
reimagine aging

AGEX THERAPEUTICS
The Leader in Precision Gerontology

A common-sense alternative



Comparison: car maintenance

sens research foundation
reimagine aging

AGEX THERAPEUTICS
The Leader in Precision Gerontology

Why is rejuv. biotech so promising?

Aging is a consequence of physics, not biology!

Comprehensive preventative maintenance is how we already keep simple machines working as well as when they were built, long beyond their designed lifespan.

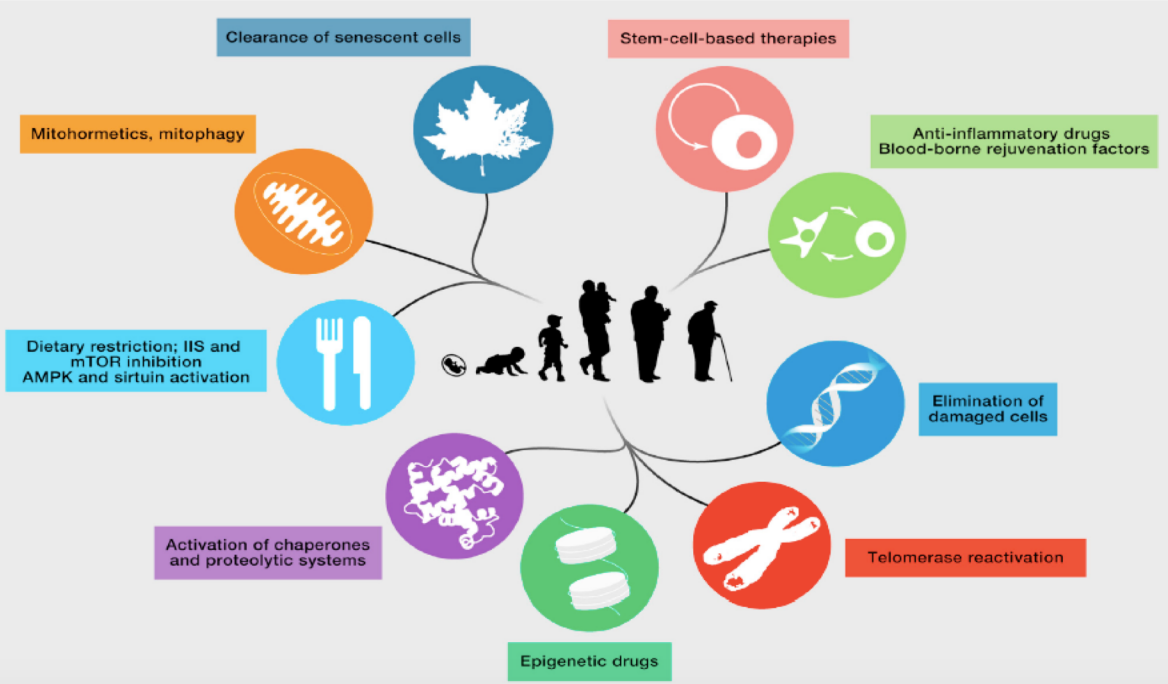
The body is far more complex. But wait: how much more complex is its **damage**?

The “7 deadly things” (Ann. NYAS 2002 etc)

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 8th is looking increasingly unlikely

Cell 153:1194 (2013) – over 2000 citations



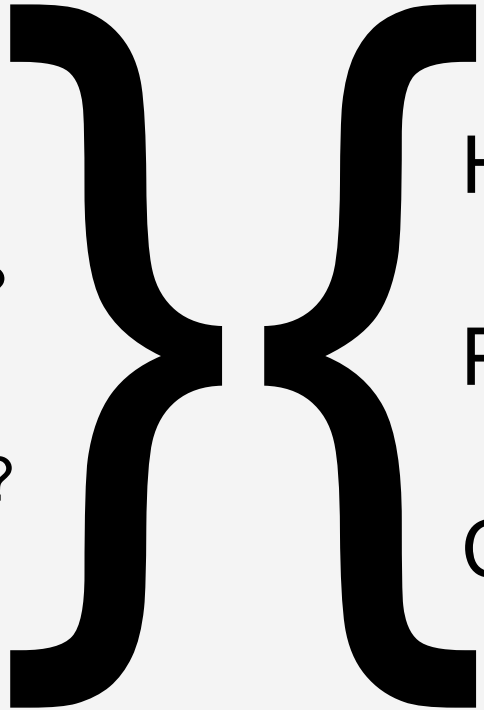
So… longevity?

- 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
- And yes, we think this is a good thing

“Ethical” considerations

- Overpopulation?
- Unequal access?
- Immortal dictators?
- Boredom?
- Pensions collapse?
- Etc, etc, etc

won’t happen



Health

Proportion

Choice

Probably

Our implementation progress

- Total synthesis of glucosepane, allowing identification of antibodies and degraders (*Science*, 2015)
- Modified bacterial enzyme protects cells from atherogenic oxysterols (*Biotech Bioeng*, 2012)
- Antibodies cleave cardiotoxic amyloid (*J Biol Chem*, 2014)
- Two out of 13 mitochondrial genes successfully relocated to the nucleus (*Nucleic Acids Res*, 2016)

Recent spin-outs from SRF

- LysoClear: reversing macular degeneration
- Antoxerene: clearing senescent cells
- Covalent: clearing transthyretin amyloid
- Arigos: cryopreserving organs for transplant
- Revel: breaking AGE crosslinks vs hypertension

Other SENS-aligned startups

- AgeX – funded by Juvenescence and Kizoo among others
- Insilico Medicine – mostly funded by Juvenescence
- Lygenesis – funded by Juvenescence
- BioAge – funding from Andreessen Horowitz
- Repair Biotechnologies – mostly self-funded so far
- Revel – funding from Juvenescence and Kizoo
- Rejuvenation Tech – funded by YCBio (Y Combinator)
- Elevian – funding from BOLD and others
- Nanotics, AgeCurve, Nuchido, Elastrin, Retrotope, Leucadia, Cleara, Senolytx…
- Oh and that little company Unity

Long timeline? So what?

- Unity raised >$300M before even STARTING its FIRST clinical trial
- Exit via acquisition will be on a totally normal timeframe
- Size of the RB industry soon? Think about it…
- Who needs an exit anyway?

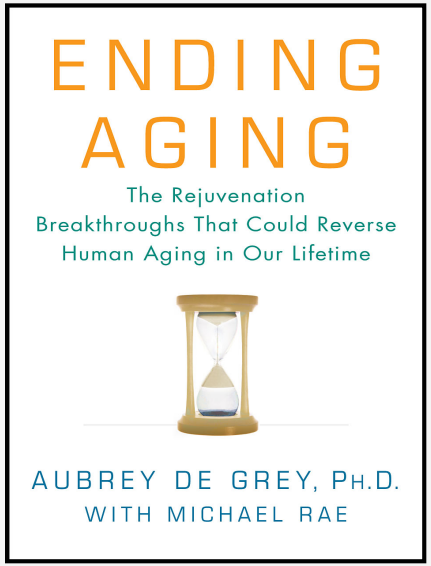
Project 21: Get SENS mostly in the clinic ASAP

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

www.sens.org

aubrey@sens.org