

Check Against Delivery.
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Can Human Life Expectancy Rise Dramatically?

by Aubrey de Grey
SENS Foundation, Cambridge, United Kingdom

Session 10, Keynote Lecture
Our Common Future, Essen, November 6th, 2010

Our Common Future, Hannover/Essen, 2-6 November 2010 (www.ourcommonfuture.de)

Can human **healthy**
(and total) life expectancy
rise dramatically?

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SENS Foundation

SENS Foundation is a US-registered charity that works to develop, promote and enable widespread access to **regenerative medicine** solutions to the disabilities and diseases of...

AGING

Who dies of aging?

Death from aging is not only “natural causes”

It's anything that mainly kills older people

About **150,000** people die per day worldwide

Two thirds of them die of aging: **100,000/day**

In the USA, the proportion is over 90%

Why are we doing this?



Fun



Not fun

What is aging?

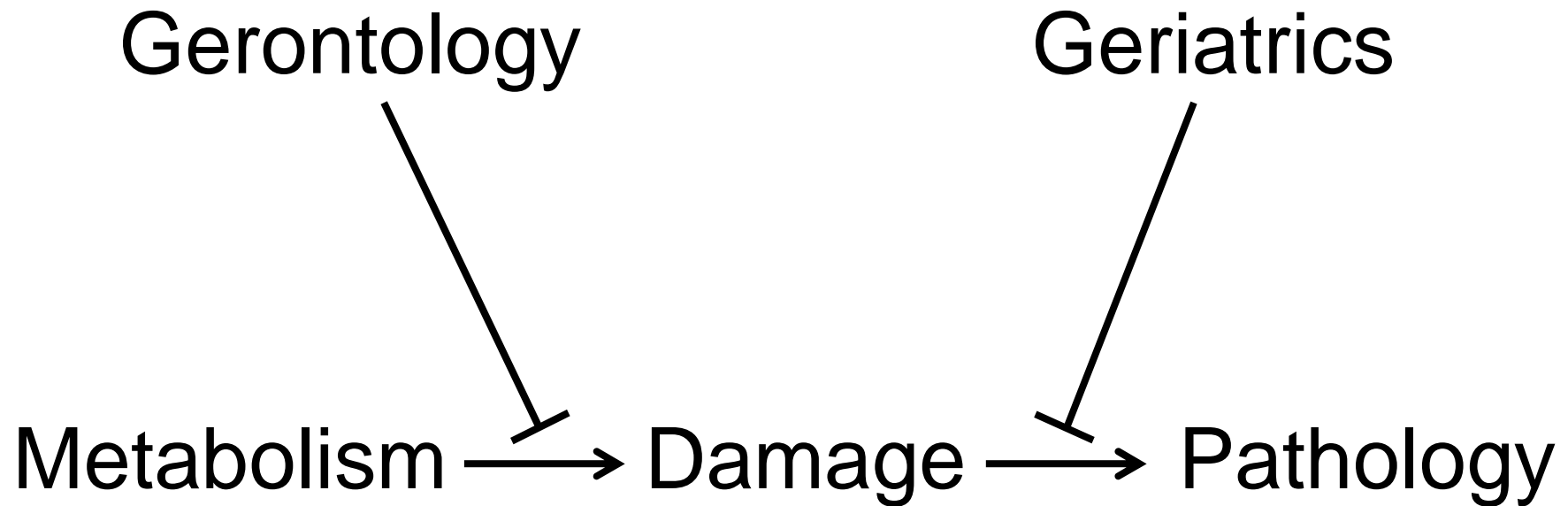
Metabolism

ongoingly causes “*damage*”.

Damage

eventually causes pathology.

Options for intervention



Problem 1: this is pathology

Cancer

Heart Disease

Diabetes

Incontinence

Osteoporosis

Macular

Degeneration

Stroke

Sarcopenia

Osteoarthritis

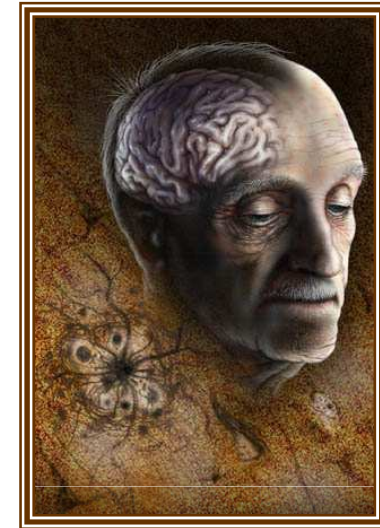
Hormonal
Imbalance

Kidney Failure

Parkinson's

Pneumonia

Emphysema

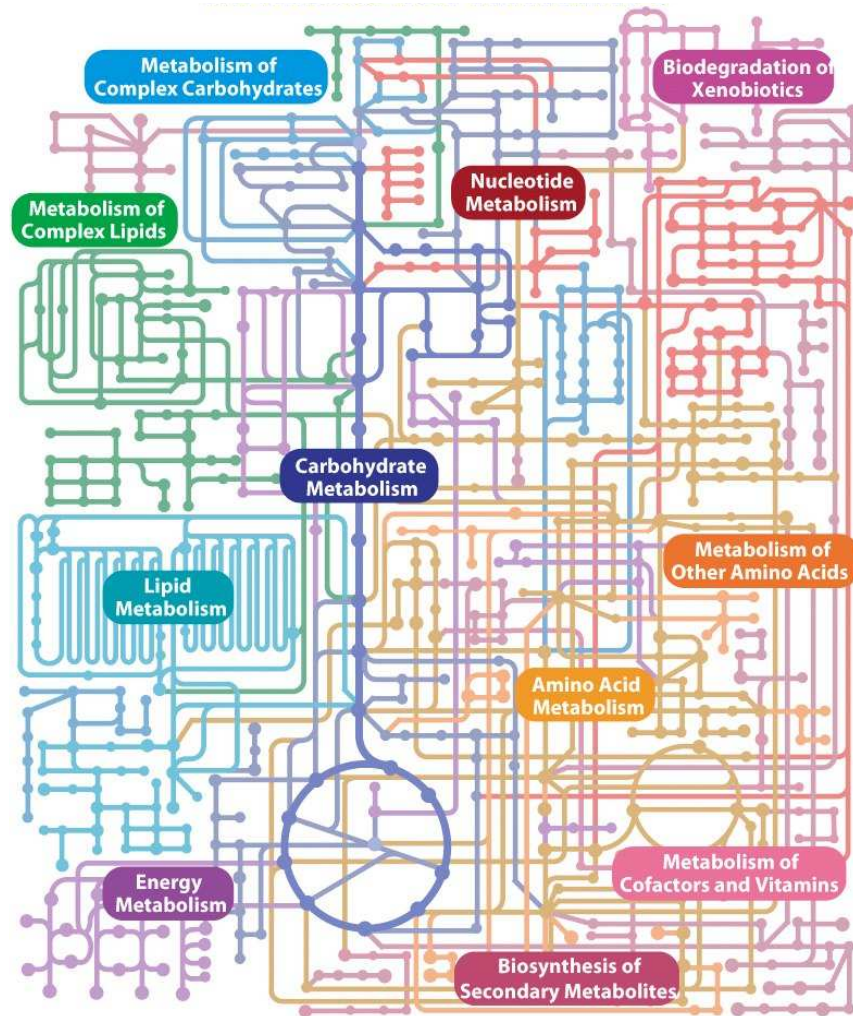


Alzheimer's

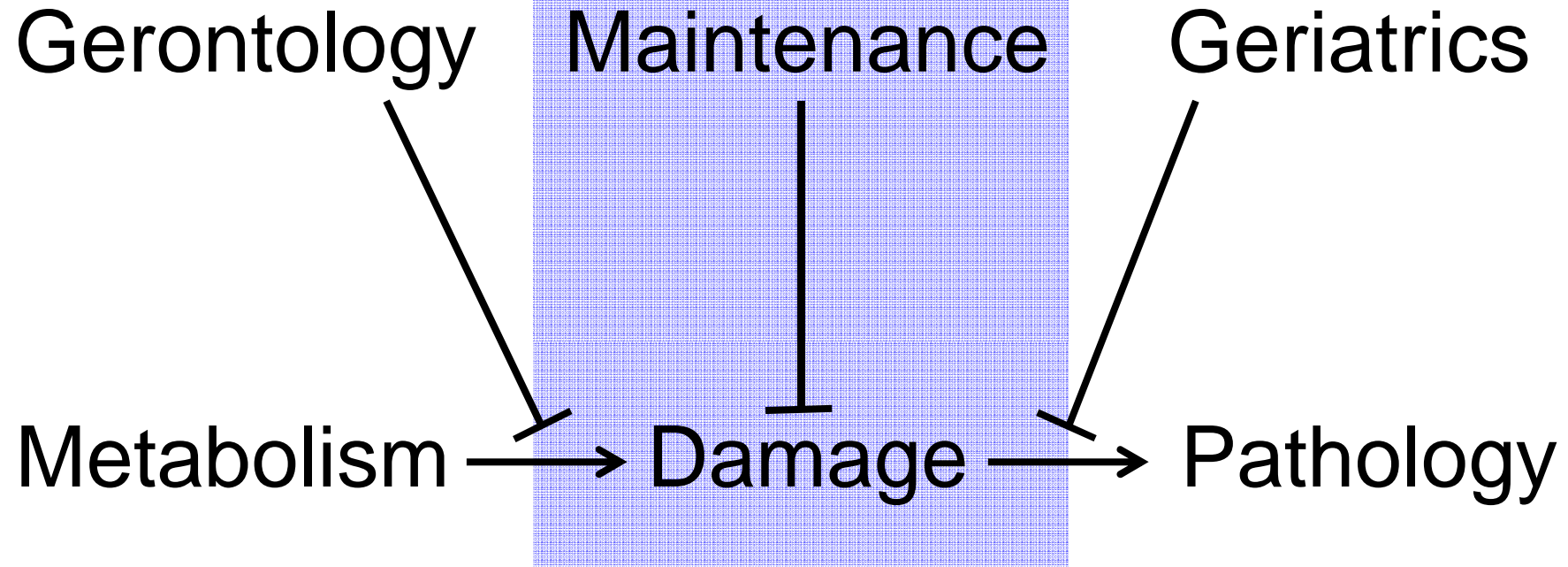
Sex Drive

...and LOTS more

Problem 2: this is metabolism



Options for intervention



Claim: unlike the others, the maintenance approach may achieve a big extension of human healthy lifespan quite soon.

Reasons for the maintenance approach

It targets initially inert
intermediates (“damage”).

Reasons for the maintenance approach

It targets initially inert intermediates (“damage”).

Damage is simpler than metabolism or pathology.

This is the damage

Seven Deadly Things

1. **Junk** - Inside Cells
2. **Junk** - Outside Cells
3. **Cells** - Too Few
4. **Cells** - Too Many
5. **Mutations** - Chromosomes
6. **Mutations** - Mitochondria
7. **Protein Crosslinks**

No new type of damage confirmed since 1982.

Giving the middle-aged 30 years of extra healthy life:

Robust Human Rejuvenation

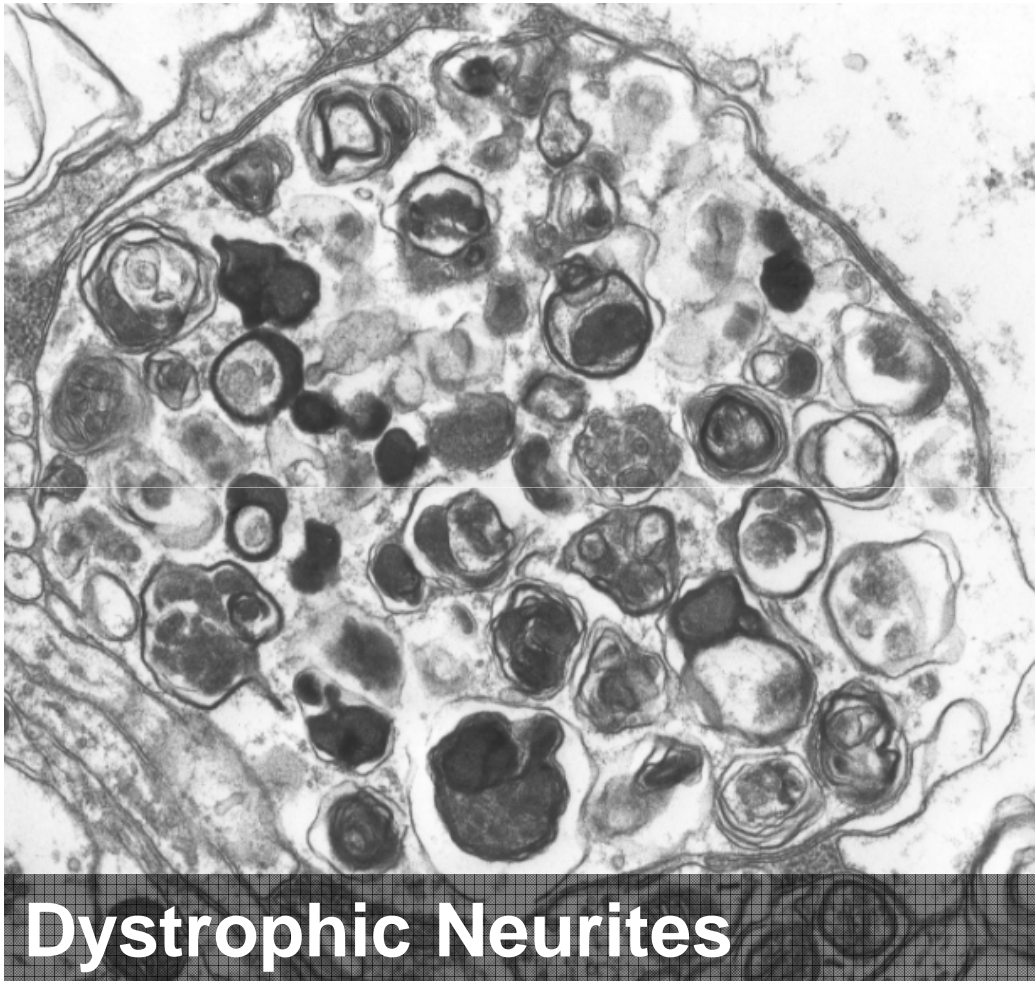
Damage rising with age	It or its effects reversible by
Cell loss, cell atrophy	Cell therapy, mainly
Extracellular junk	Phagocytosis by immune stimulation
Extracellular crosslinks	AGE-breaking molecules/enzymes
Death-resistant cells	Suicide genes, immune stimulation
Mitochondrial mutations	Allotopic expression of 13 proteins
Intracellular junk	Transgenic microbial hydrolases
Nuclear [epi]mutations (only cancer matters)	Telomerase/ALT gene deletion plus periodic stem cell reseedling

Giving the middle-aged 30 years of extra healthy life:

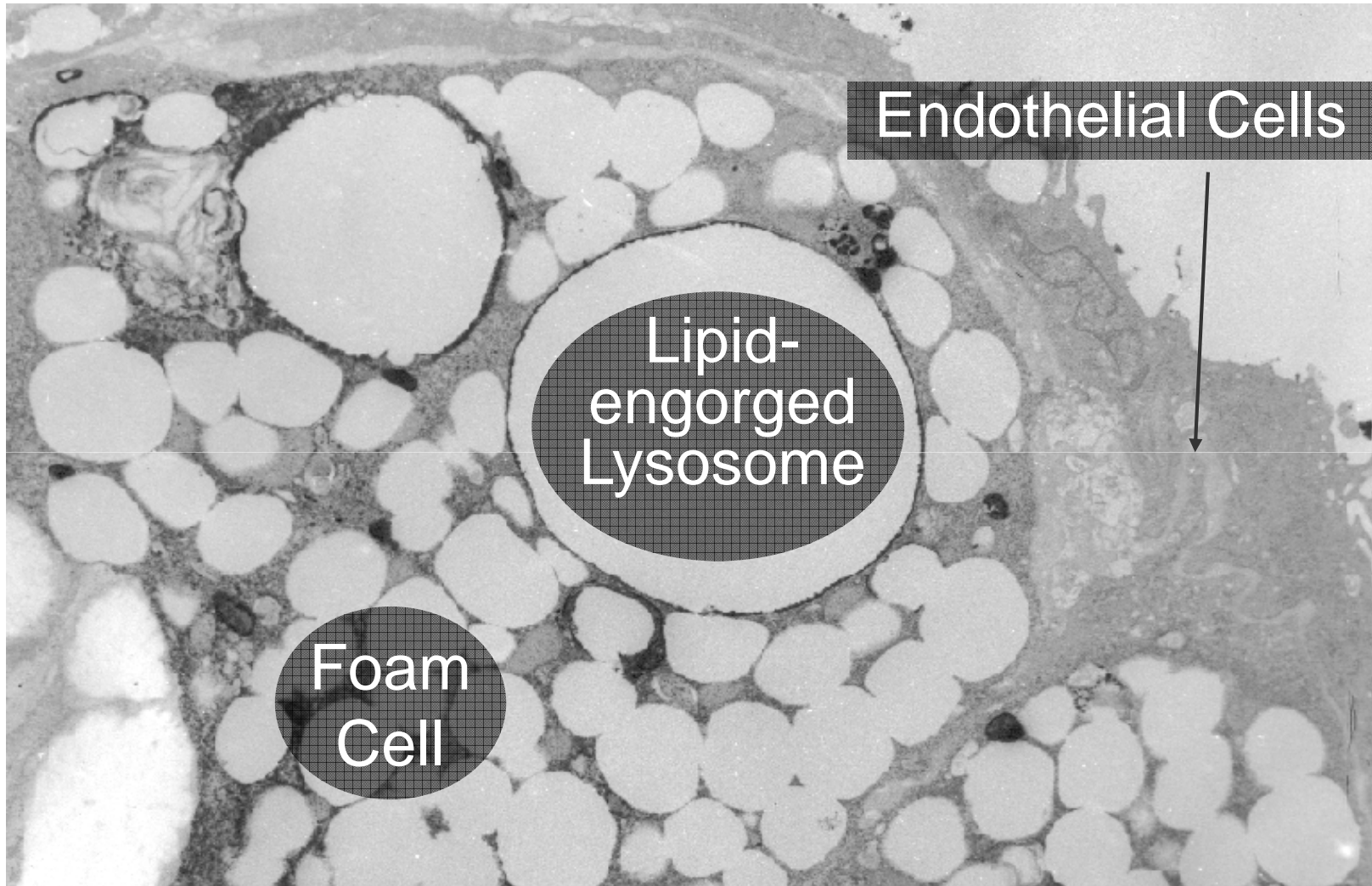
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Intracellular junk in Alzheimer's



Intracellular junk in the artery



Bioremediation: the concept

Microbes, like all life, need an ecological niche.

Some get it by brawn (growing very fast)...

...some by brain (living off material that others can't).

Any **abundant, energy-rich** organic material that is hard to degrade thus provides selective pressure to evolve the machinery to degrade it.

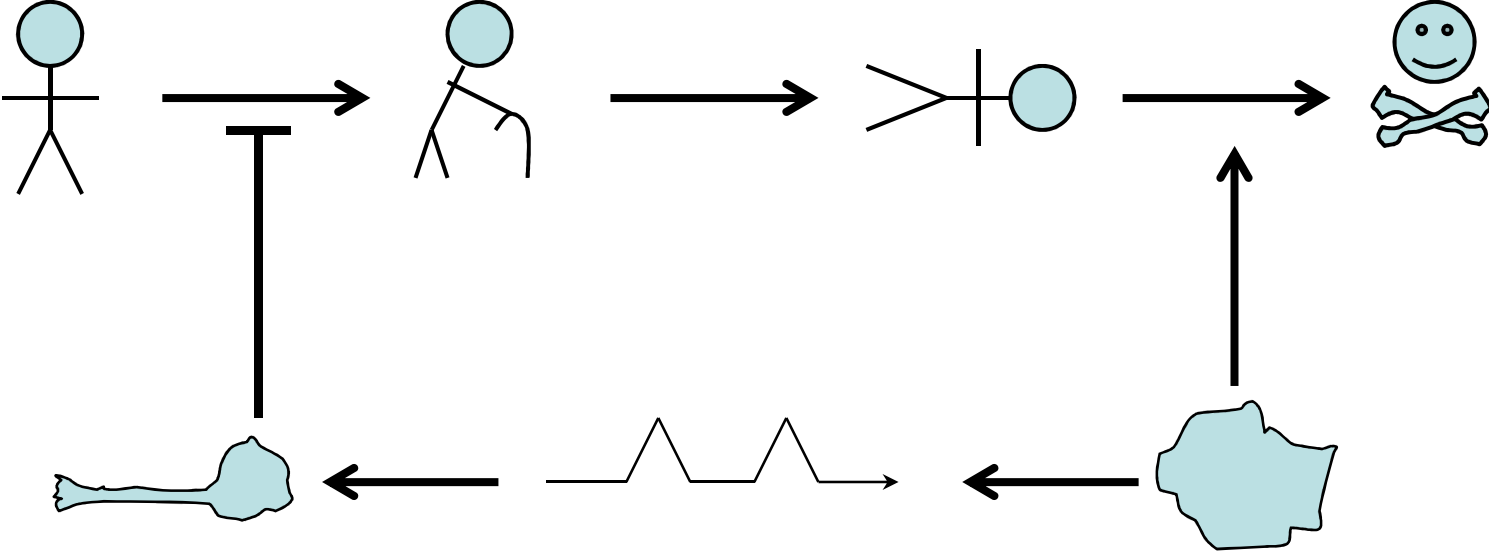
That selective pressure **works**. Even TNT, PCBs...

Xenocatabolism: the concept

Graveyards

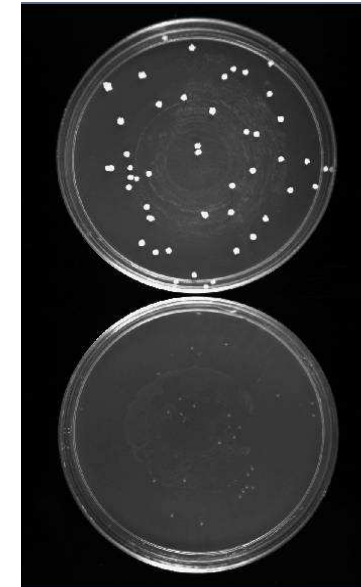
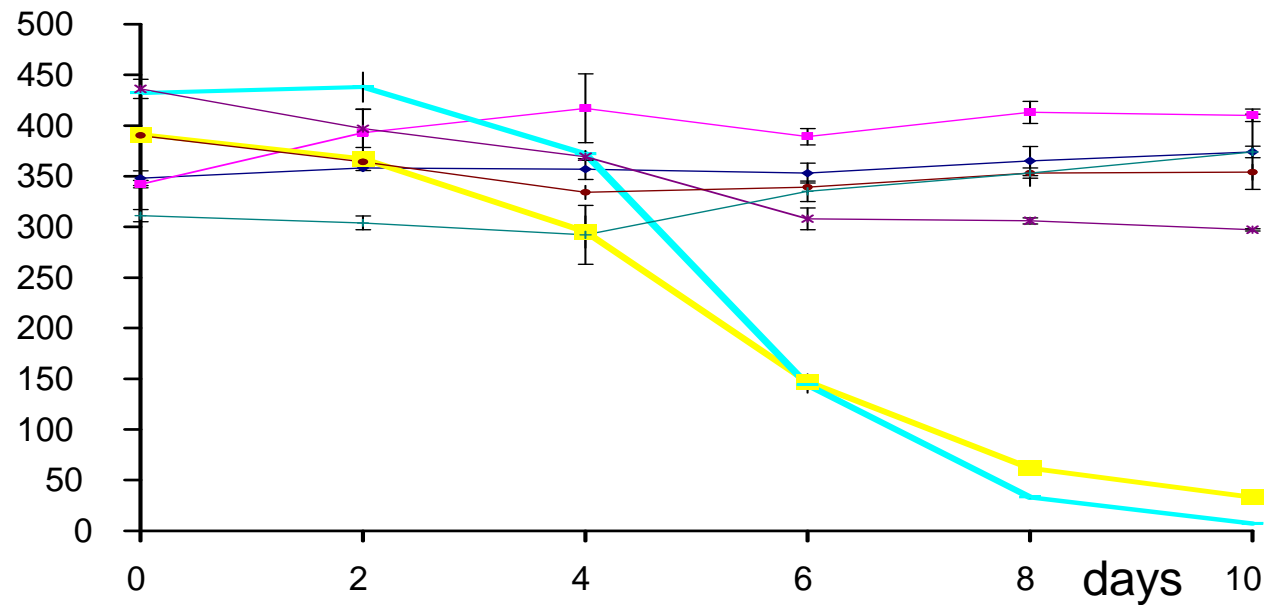
are abundant in human remains,
accumulate bones (which are not energy-rich),
do not accumulate oxysterols, tau etc.,
so, should harbour microbes that degrade them...
...whose catabolic enzymes could be therapeutic

Environmental decontamination *in vivo*



7-ketocholesterol degradation a promising start

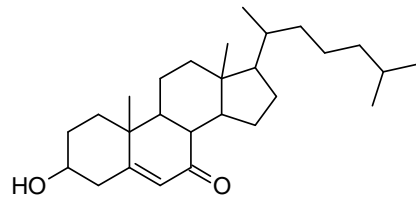
7Kc over time in enrichment cultures



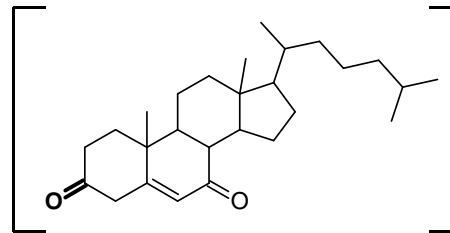
Biodegradation 2008; 19(6):807-813

Stable isotope labelling and LC/MS reveal 7-ketocholesterol metabolites in the culture supernatant

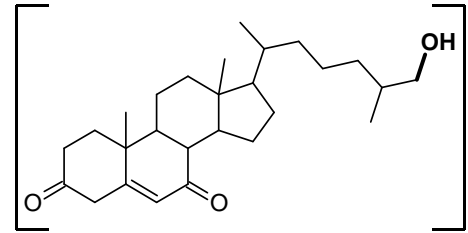
7-ketocholesterol
 $M = 400$, $M_{13C} = 401$



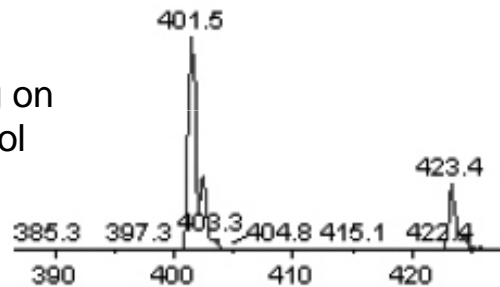
Dione metabolite(?)
 $M = 398$, $M_{13C} = 399$



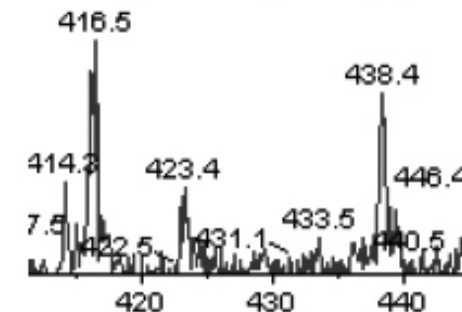
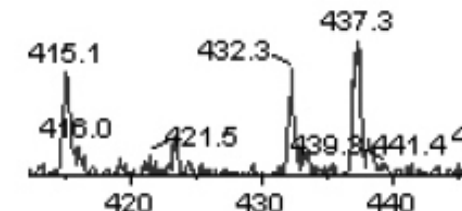
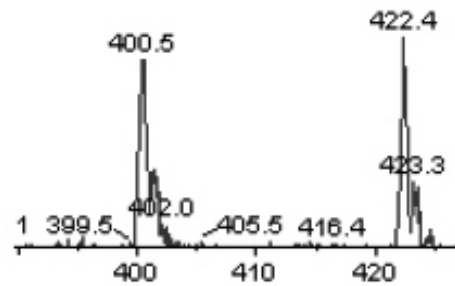
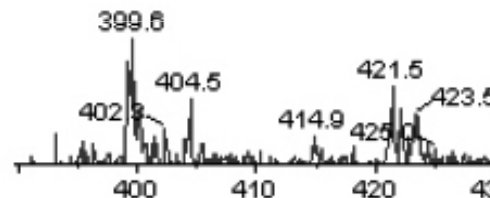
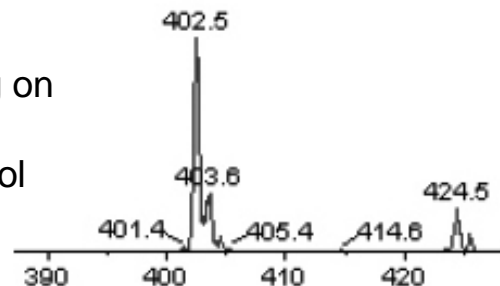
Hydroxylated dione(?)
 $M = 414$, $M_{13C} = 415$



Culture growing on
7-ketocholesterol



Culture growing on
 ^{13}C -labeled
7-ketocholesterol



Steps to biomedical application

- 1) Isolate competent strains; select by starvation.
- 2) Identify the enzymes (mutagenesis, chemistry, genomics).
- 3) Make lysosome-targeted transgenes; assay cell toxicity.
- 4) Assay competence *in vitro* (more mutagenesis/selection).
- 5) Construct transgenic mice; assay toxicity *in vivo*.
- 6) Assay competence in disease mouse models.
- 7) Test in humans as for lysosomal storage diseases.

Learn more

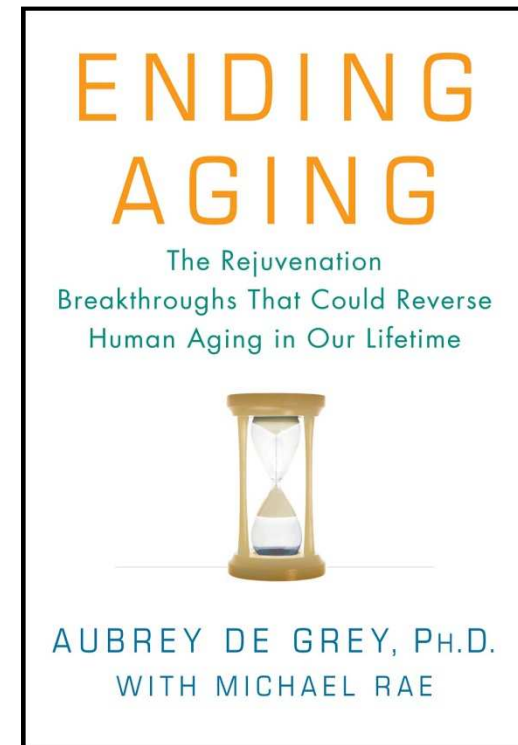
Read the (semi-technical) book.

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



Support SENS Foundation

SENS Foundation works to develop, promote and enable widespread access to regenerative medicine solutions to the disabilities and diseases of aging.

To be successful in our mission we need your support.

Time - On our website you will find details of how your skills can be used to accelerate our progress, and help us to make these audacious ideas into a reality.

Money - You may also wish to **make a donation**. Any amount, no matter how small, helps to fund essential research, education and outreach initiatives.

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human regenerative engineering

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