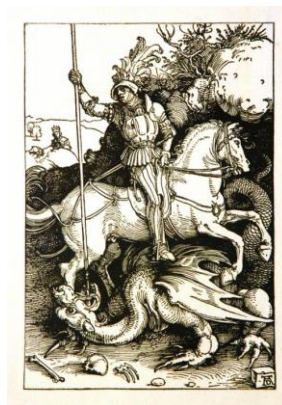


Biology of Aging as a Basis for Future Treatment of Non-communicable Diseases and Health Care for the Aged

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Aging – the Main Risk Factor of Non-Communicable Diseases

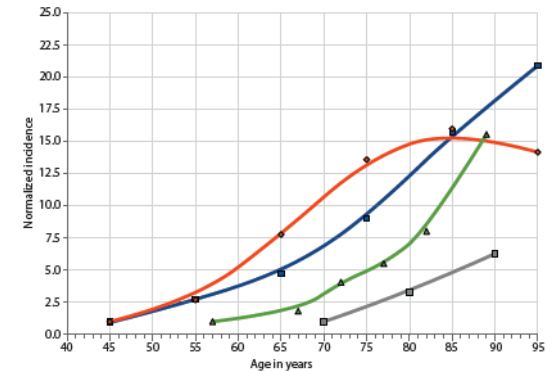
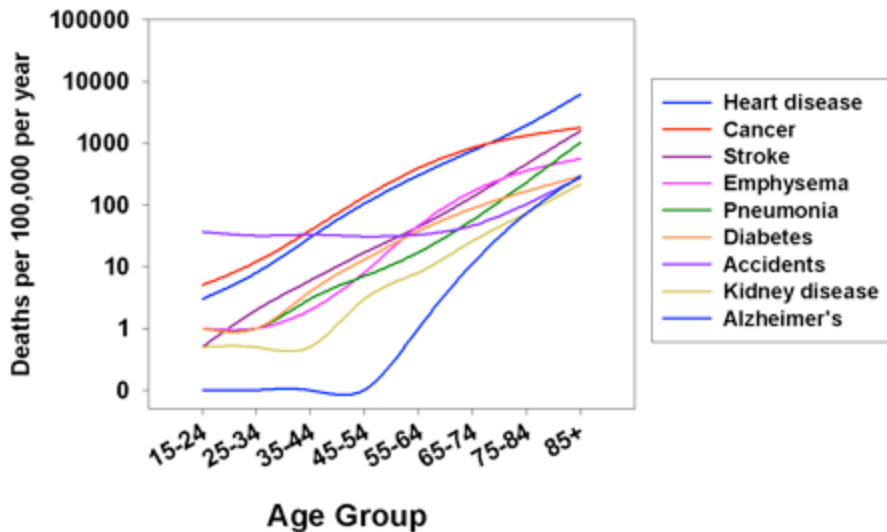


Fig. 1. Chronic diseases and aging. The incidence of major chronic diseases rises exponentially with age, as shown: cardiovascular disease (blue squares) [data from (32)], cancer (red diamonds) [data from (32)], AD (gray squares) [data from (33)], and influenza-associated hospitalization (green triangles) [data from (34)]. Incidence rates are normalized to the first data point.

www.ScienceTranslationalMedicine.org 14 July 2010 Vol 2 Issue 40 40cm21 1

<http://www.stanford.edu/group/brunet/background.html>

The Demographic and Biomedical Case for Late-Life Interventions in Aging

Michael J. Rae,¹ Robert N. Butler,^{2*} Judith Campisi,³ Aubrey D. N. J. de Grey,¹ Caleb E. Finch,⁴ Michael Gough,⁵ George M. Martin,⁶ Jan Vijg,⁷ Kevin M. Perrott,⁸ Barbara J. Logan^{8††}. *Science Translational Medicine*.

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Information theoretical analysis of aging as a risk factor for heart disease (David Blokh and Ilia Stambler, *Aging and Disease*, in press).

Age is best correlated with heart disease among non-specific parameters:

No.	Clusters. Correlation with Disease	Parameters	Sum of ranks
1	Cluster 1. Highest Correlation (Specific diagnostic parameters)	Cp – Chest Pain Type	25
2		Exang – Exercise Induce Angina	24
3		Oldpeak – ST Depression Induced by Exercise (Ischemia)	23
4	Cluster 2. Good Correlation (Non-specific parameters)	AGE	15
5		Thalach – Maximum Heart Rate Achieved	14
6	Cluster 3. Weak Correlation (Non-specific parameters)	Restecg - Resting electrocardiographic results	10
7		Trestbps - Resting blood pressure	9
8		Chol - Serum cholesterol	8
9		Fbs - Fasting blood sugar	7

Estimation of heterogeneity in diagnostic parameters of age-related diseases. *Aging and Disease*, 5, 2014 (Blokh D and Stambler I).

Aging and disease show the same pattern of Variability in Diabetes Patients:

Subjects	Disease Status	Age	Heterogeneity (Entropy)
53	Healthy	21-25	0.527
22	Healthy	26-29	0.592
41	Healthy	30-39	0.583
18	Healthy	40-49	0
24	Patients	21-25	0
18	Patients	26-29	0
34	Patients	30-39	0
26	Patients	40-49	0

**If the Degenerative Aging Processes are the Main Risk Factors for Disease
– They should be addressed preferentially!**

Can we postpone, or even reverse those processes? Yes. We Can!

Basic Aging Process	Disease	Potential Treatment
Inflammation ("Inflammaging")	Heart Disease, Cancer	Anti-inflammatory substances
Cross-linkage	Atherosclerosis	Enzymatic hydrolysis, Oxido-reductive depolymerization, immunoclearance
Demineralization	Osteoporosis	Supplementation
Loss of DNA Repair	Cancer	DNA Repair Enhancement
Stem cell depletion	Neurodegenerative diseases	Stem cell therapy
Beta Cell senescence	Diabetes	Cell therapy, elimination of senescent cells
Naïve T cell depletion	Susceptibility to infectious diseases	Thymus regeneration

Genetic engineering

- **Subtraction**
- **Gene Inhibition for “Aging Accelerating Genes”:**

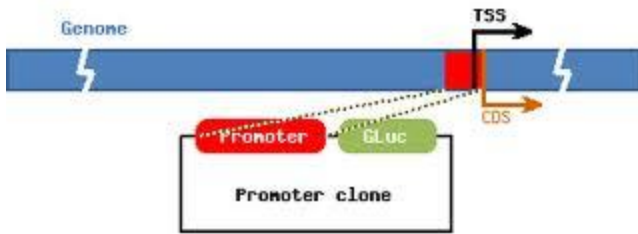
DAF, mTOR, IGF, NF-κB

- RNA Interference

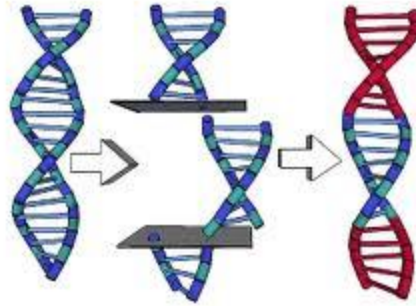
- **Addition**

- **Gene Stimulation for “Longevity Genes”:**

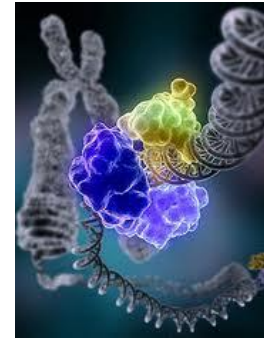
Sirtuins, FOXO, Klotho, cholesteryl ester transfer protein (CETP),
Telomerase



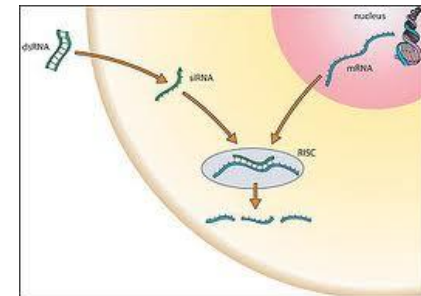
Gene Inhibition/Stimulation



Gene Splicing



DNA Repair



RNA Interference

Geroprotectors

- **Subtraction/ Detoxification**

- Chelation
- Enterosorbents
- Statins
- Anti-inflammatory
- Anti-glycemic
- Anti-oxidant
- Anti-coagulants

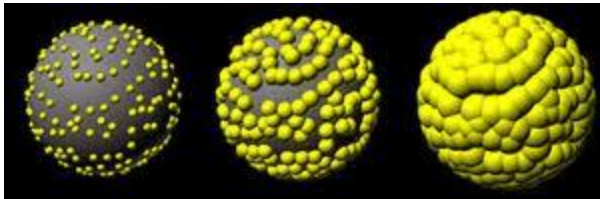
- **Addition /Supplementation**

- Hormone Replacement Therapy
- Hyaluronan
- Vitamins
- Microelements
- Macroergics
- Mitochondrial modulators



Nanomedicine

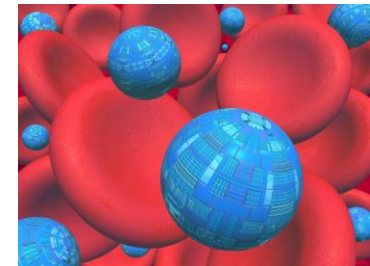
- Subtraction
 - Carbon and Gold nano-shells
 - Targeted Drug Delivery
 - “Artificial immune cells” – in Research and Development
- Addition
 - Artificial Cells such as:
 - “Nanobots” for molecular repair
 - “Artificial respirocytes” for oxygen delivery - in Research and Development



Gold nano-shells



Artificial Immune Cells



Artificial Respirocytes
(Oxygen Delivery)

Strategies for Engineered Negligible Senescence (SENS) “The 7 Deadly Things”

- **Subtraction:**

- 1) Death-resistant cells to be removed by targeted ablation (ApoptoSENS)
- 2) Tissue stiffening to be prevented by compounds breaking Advanced Glycation End-products – AGE-breakers (GlycoSENS)
- 3) Extracellular aggregates to be cleaned up by immunotherapeutic clearance (AmyloSENS)
- 4) Intracellular aggregates to be dissolved by novel lysosomal hydrolases (LysoSENS)
- 5) Nuclear (epi-)mutations leading to cancer to be neutralized by the removal of telomere-lengthening machinery (OncoSENS)

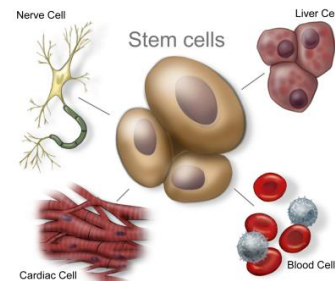
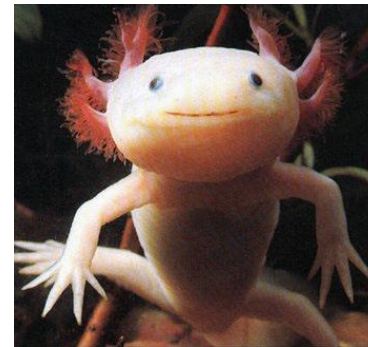
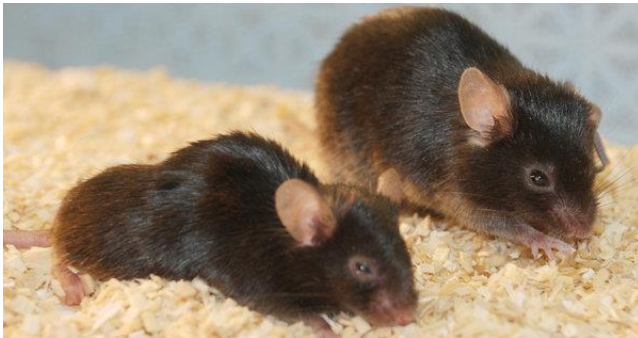
- **Addition:**

- 6) Cell loss and tissue atrophy to be replenished by adding stem cells and tissue engineering (RepleniSENS)
- 7) Mutant mitochondria to be backed up by allotopic expression of 13 proteins in the nucleus (MitoSENS);



Regenerative Medicine

- Subtraction
 - Cell removal
 - Apoptosis
 - Tumor Suppression
 - Removal of senescent cells
- Addition
 - Cell replenishment
 - Induction of regeneration
 - Stem cells and their products
 - Tissue engineering (bioreactors/scaffolds/tissue printing)



Robotics/Bionics

- Subtraction:
- Robotic Surgery



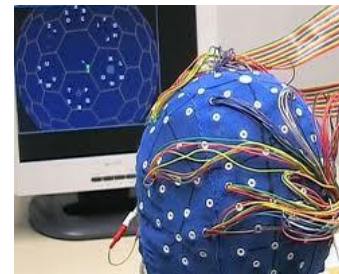
- Addition:
- Artificial Limbs
- Artificial Organs
- Exoskeletons
- Brain-Computer Interfaces/Neuro-prosthetics



Artificial Heart



Robotic Arm



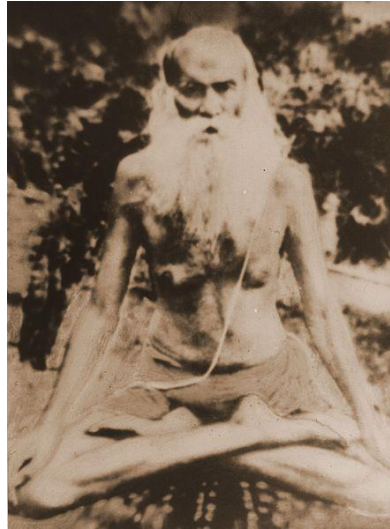
Brain-Computer Interface
Neuro-prosthetics



Exoskeleton

Holistic Treatments for Life-extension

Moderation - Rest - Meditation



Exercise



Natural Nutrition



Electromagnetic Therapy

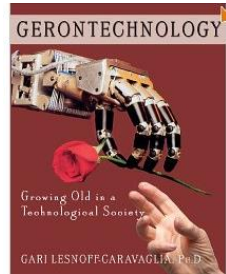


**Program for the pursuit of
Healthy Longevity
By ameliorating Degenerative
Aging Processes
is needed**

Program for the pursuit of longevity

From the outside:

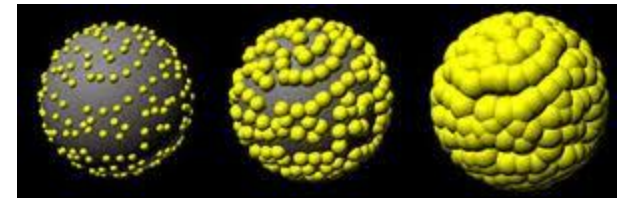
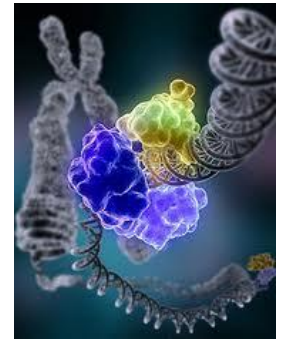
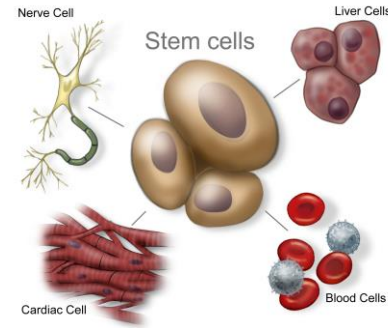
- Gerontotechnologies
- Preventive geriatrics
- Cognitive and psychological techniques
- Environmental technologies
- Improving conditions of daily life, means of access and convenience for the aged
- Social, educational and occupational integrative frameworks for the aged



Program for the pursuit of longevity

From the inside:

- Regenerative medicine: stem cells and their products, regeneration and cell death
- Tissue engineering
- Gene therapy: activation of sirtuins, telomerase, other “longevity genes”
- Geroprotectors
- Nanomedicine
- Artificial organ replacement
- Quantified self



Program for the Pursuit of Longevity: Health Policy and Research Policy

- What's the plan?
- Who decides?
- Who pays?
- How can we accelerate progress in biology of aging and healthy longevity?
- How do we make the results of this research rapidly and universally accessible?
- **Possible Initial Recommendations:** Providing increased *funding, incentives and coordination* for academic, commercial and public organizations involved in Research and Development *to ameliorate degenerative aging processes* as the basis for future treatment of non-communicative diseases and health care for the aged.