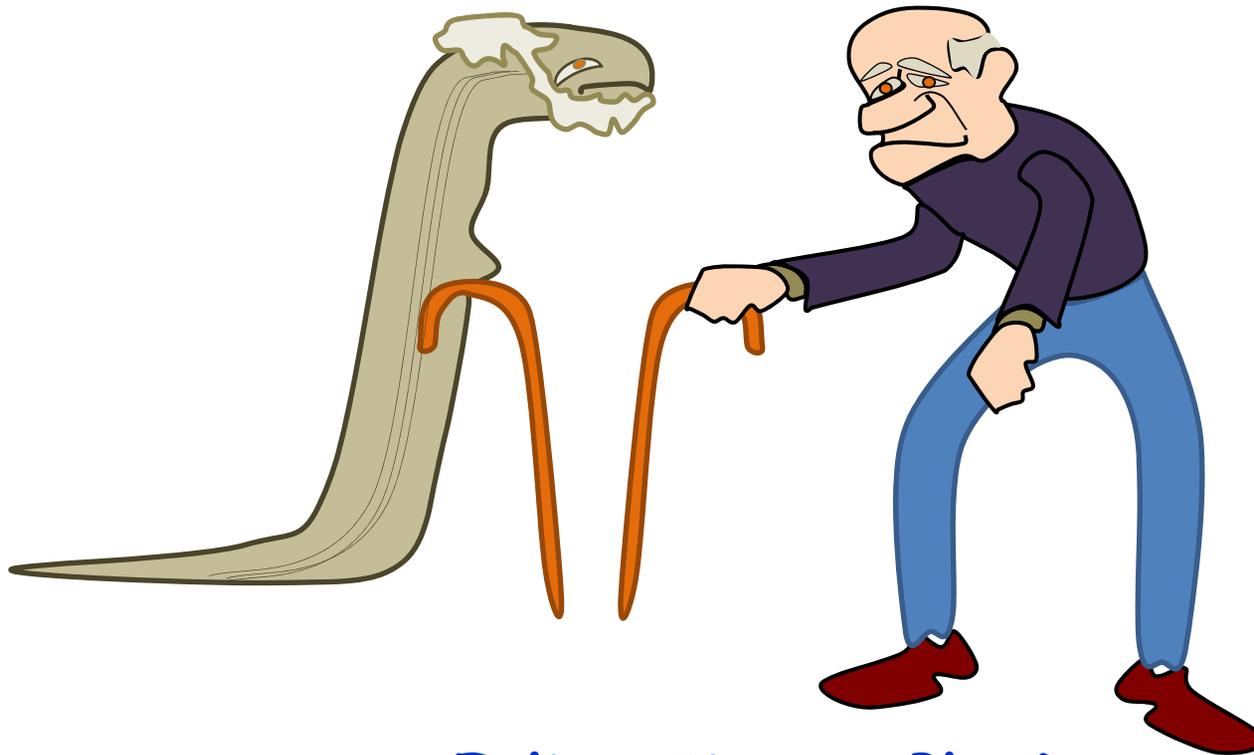


# Opportunities for Biological and Physiological Studies

- The GeroScience Interest Group -

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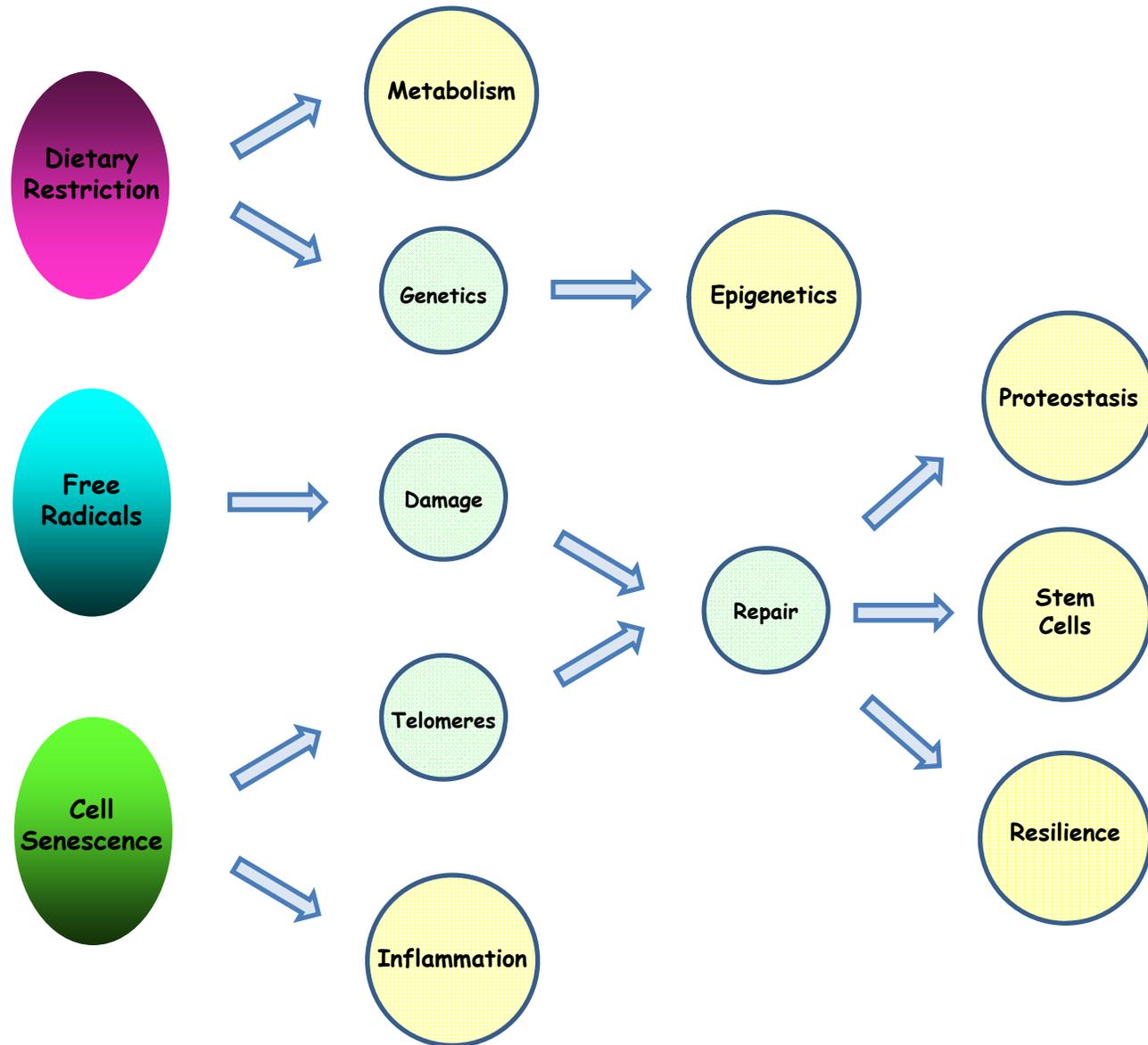
Felipe Sierra, Ph. D.,  
March 2015

# Today's menu

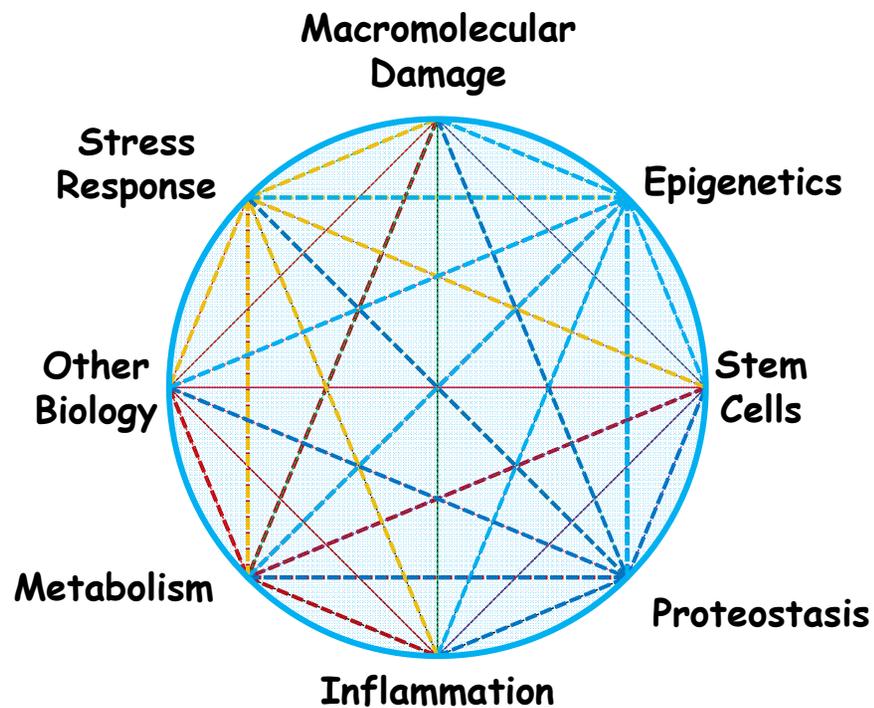
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- ✓ *From the old guard to current paradigms and trends*
- ✓ *Geroscience*
- ✓ *Some ideas on translation*
- ✓ *Is there anything we can translate?*

# Conceptualizations



# Conceptualizations



Sierra & Kohanski  
*J Gerontol* June 2014

Kennedy *et al.*  
*Cell* Nov 2014



López-Otín *et al.*  
*Cell* 153:1194 (2013)

# Today's menu

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- ✓ *From the old guard to current paradigms and trends*
- ✓ ***Geroscience***
- ✓ *Some ideas on translation*
- ✓ *Is there anything we can translate?*

# GEROSCIENCE

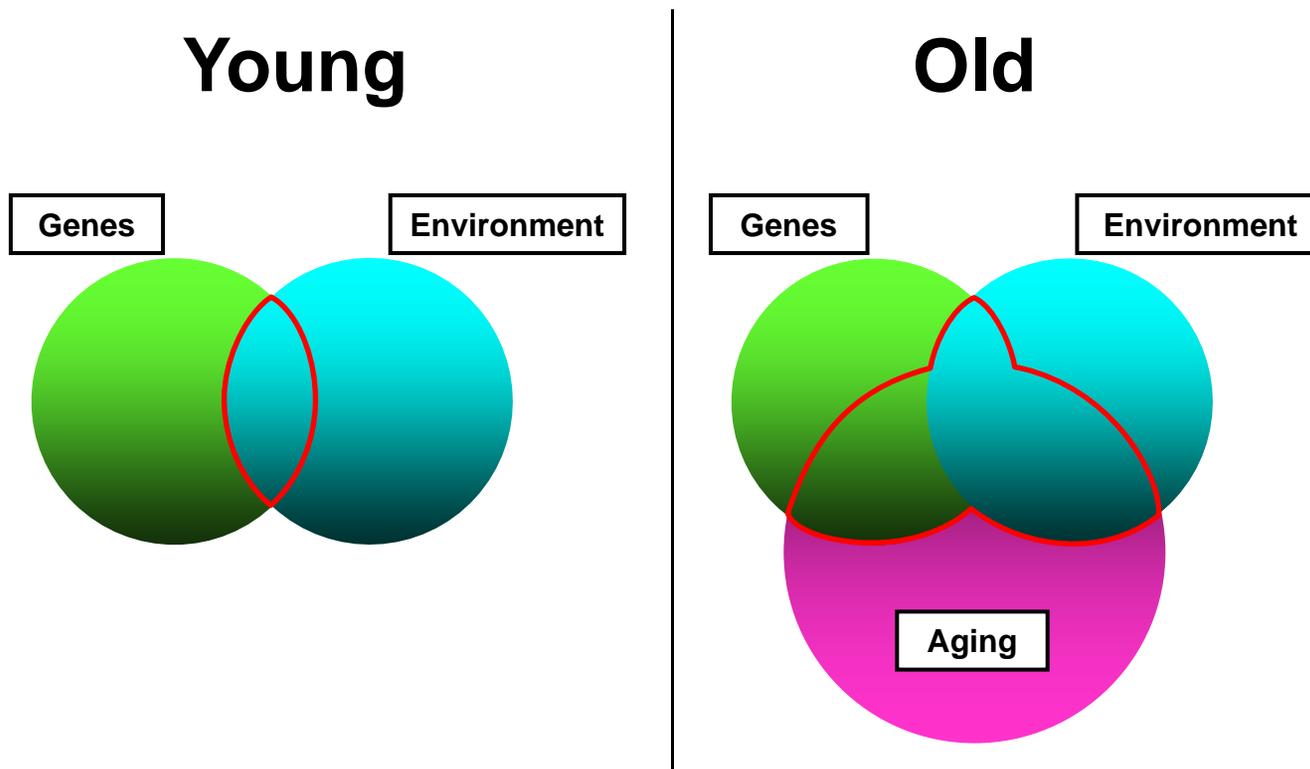
## Rationale

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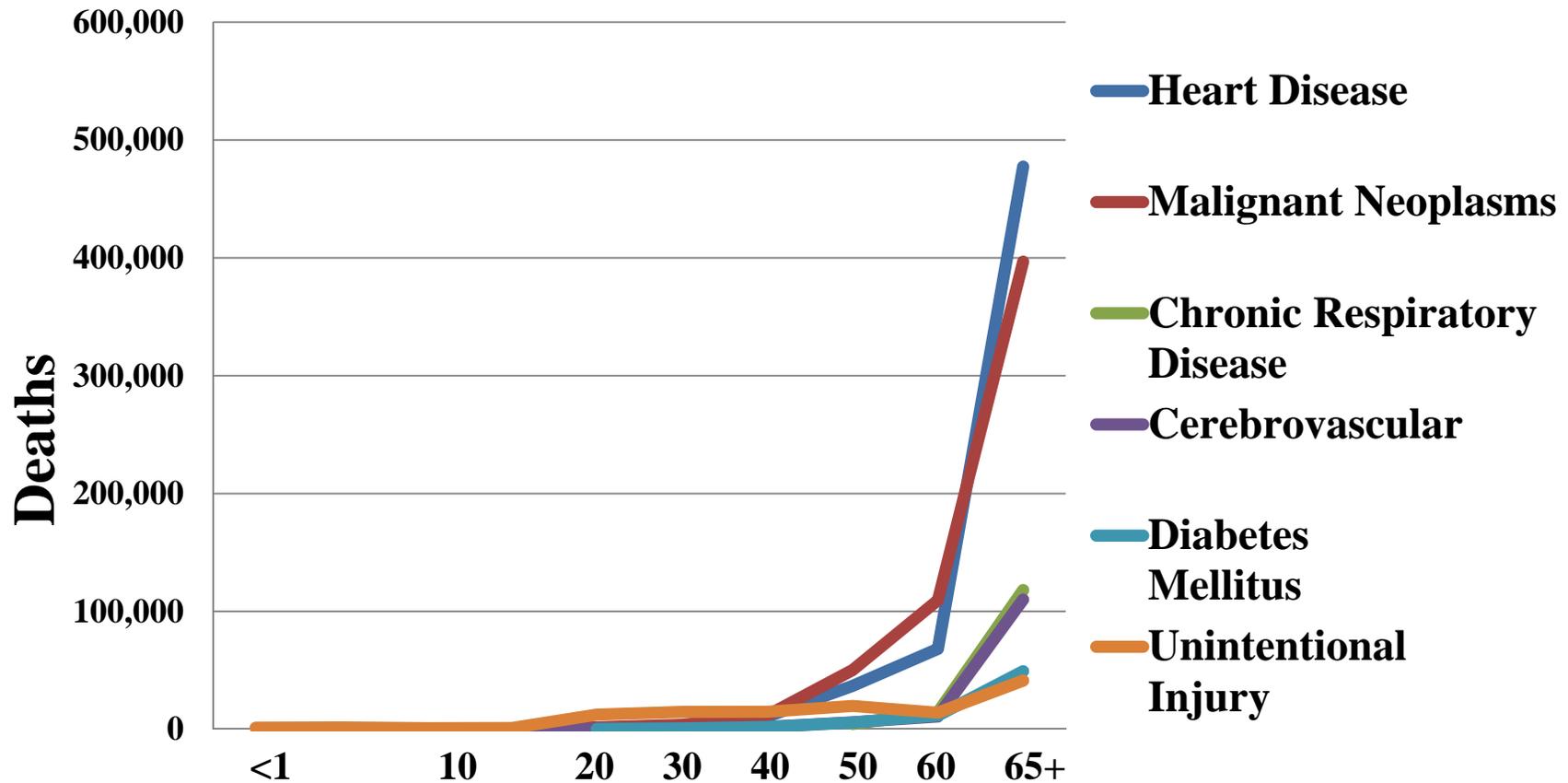
- The goal of biomedical research is to increase the quality of human life.
- Chronic diseases of the elderly are currently the main limitation to achieving that goal.
- Aging biology is the major risk factor for most of these diseases.

# Major elements affecting disease risk

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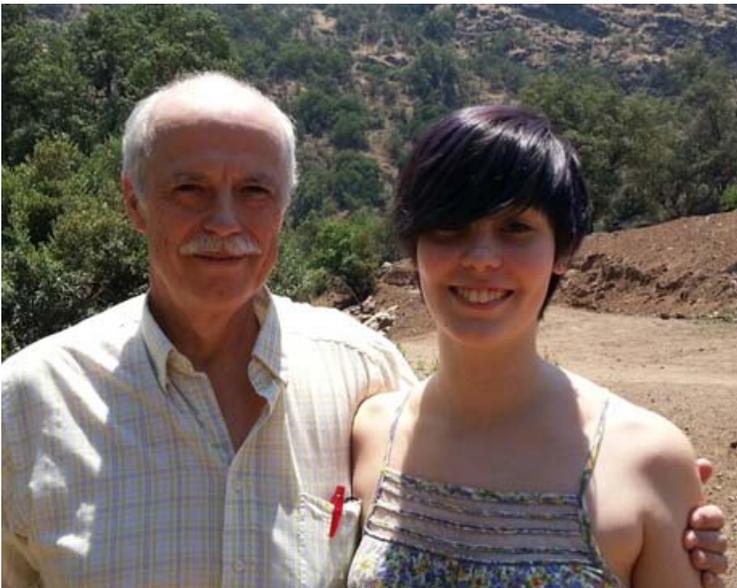
# Death causes as a function of age US - 2010



[Adapted from www.cdc.gov/injury/wisqars/leadingCauses.html](http://www.cdc.gov/injury/wisqars/leadingCauses.html)

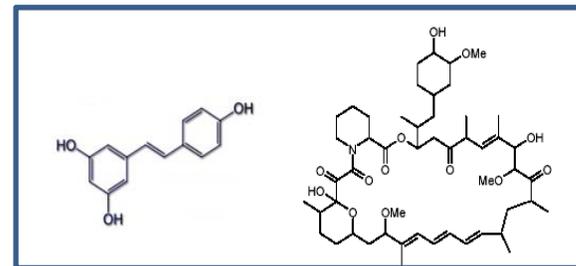
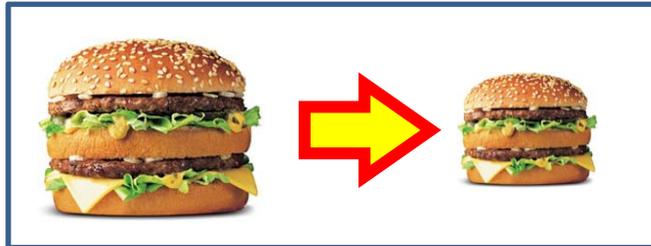
# Risk factors for Cardiovascular Disease

Cholesterol, obesity and the usual suspects (smoking, exercise, diet...)



# Aging and Disease

- So... aging is the major risk factor for chronic diseases... **WE KNEW THAT!**
- But I can't change my age!
- Yet... aging is plastic



And healthspan is also improved

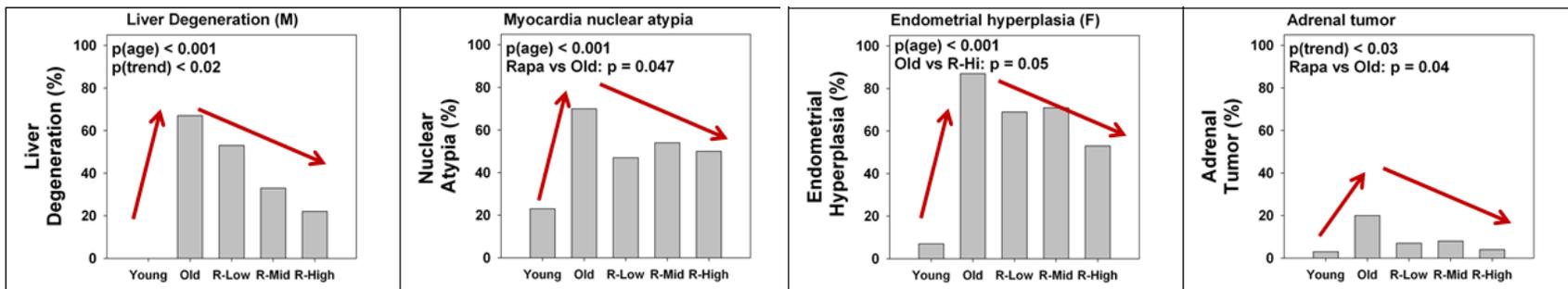
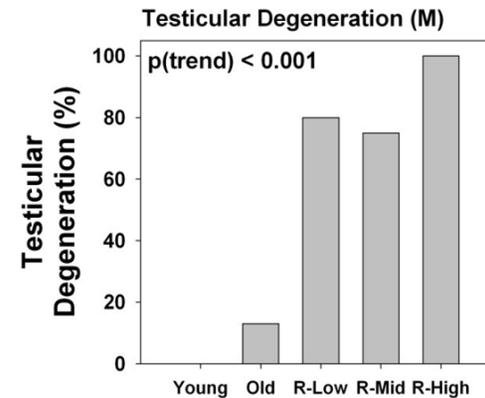
# An example: Rapamycin

## Rapamycin improves:

- Liver degeneration
- Endometrial hyperplasia
- Adrenal tumors
- Tendon aging
- Myocardial nuclear atypia
- Adrenal telangiectasia
- Ovarian cysts
- Thyroid cold follicles
- Lung tumors

## But not all is good

- Cataracts
- Testicular degeneration
- Glucose metabolism



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SO WE CAN INTERVENE

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Should we?

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**WE CAN'T WAIT !**

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... to address the major risk  
factor for most chronic  
diseases: **aging!**

# The World is Aging... Fast!

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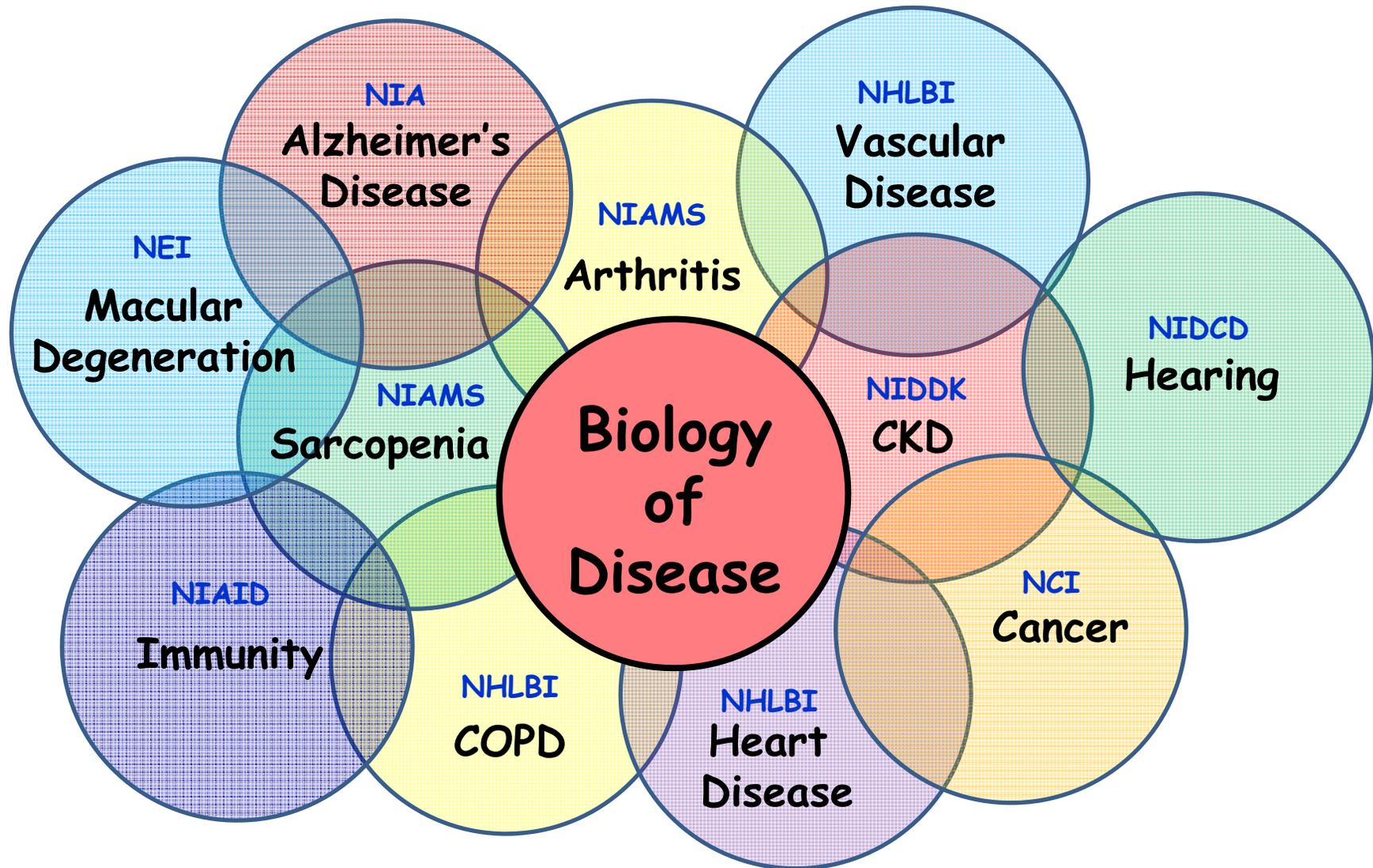
- ✓ As a species, we are not prepared for this onslaught.
- ✓ Our social and economic systems can't handle it either.

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**Where do we start?**

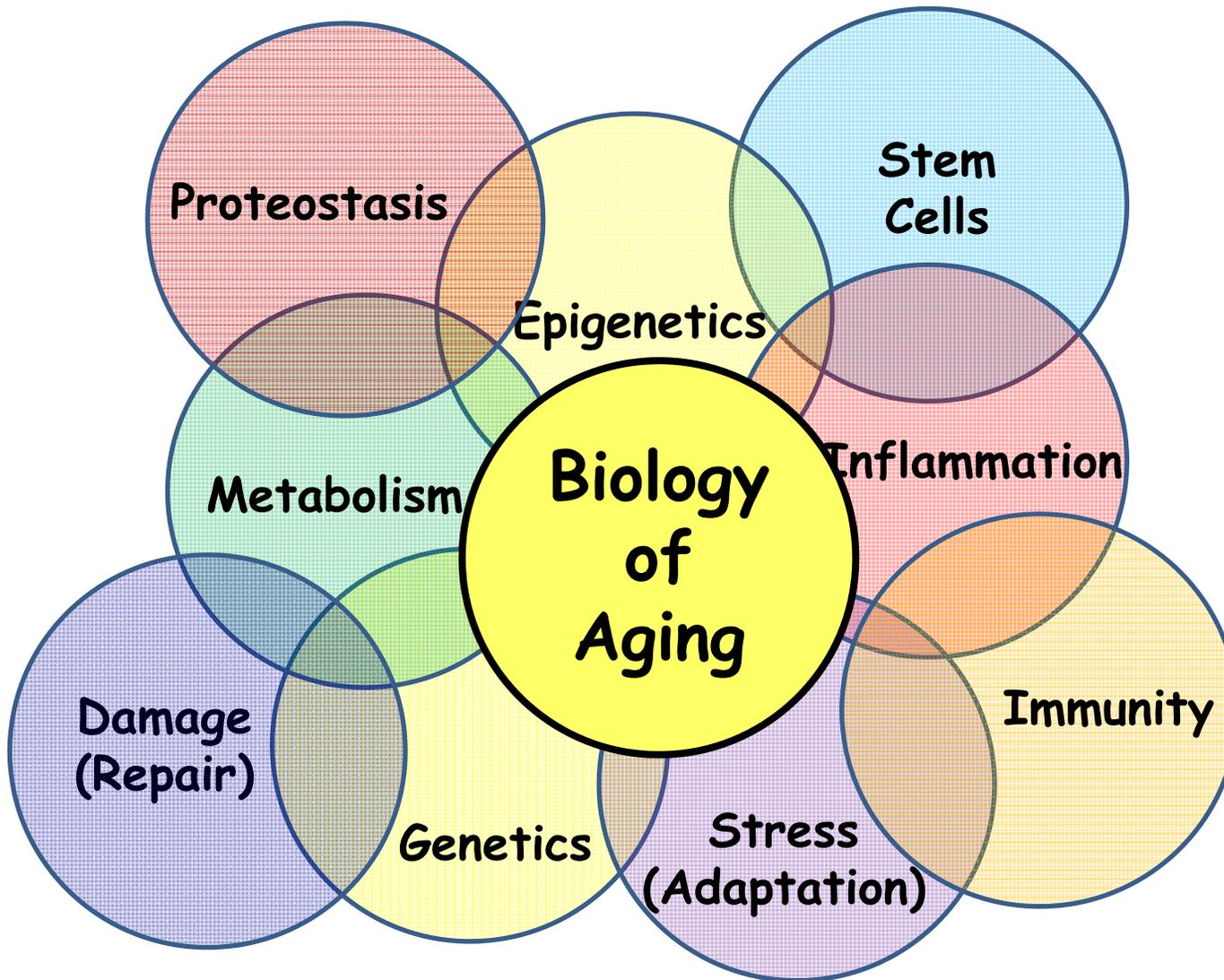
# Many chronic diseases are studied individually

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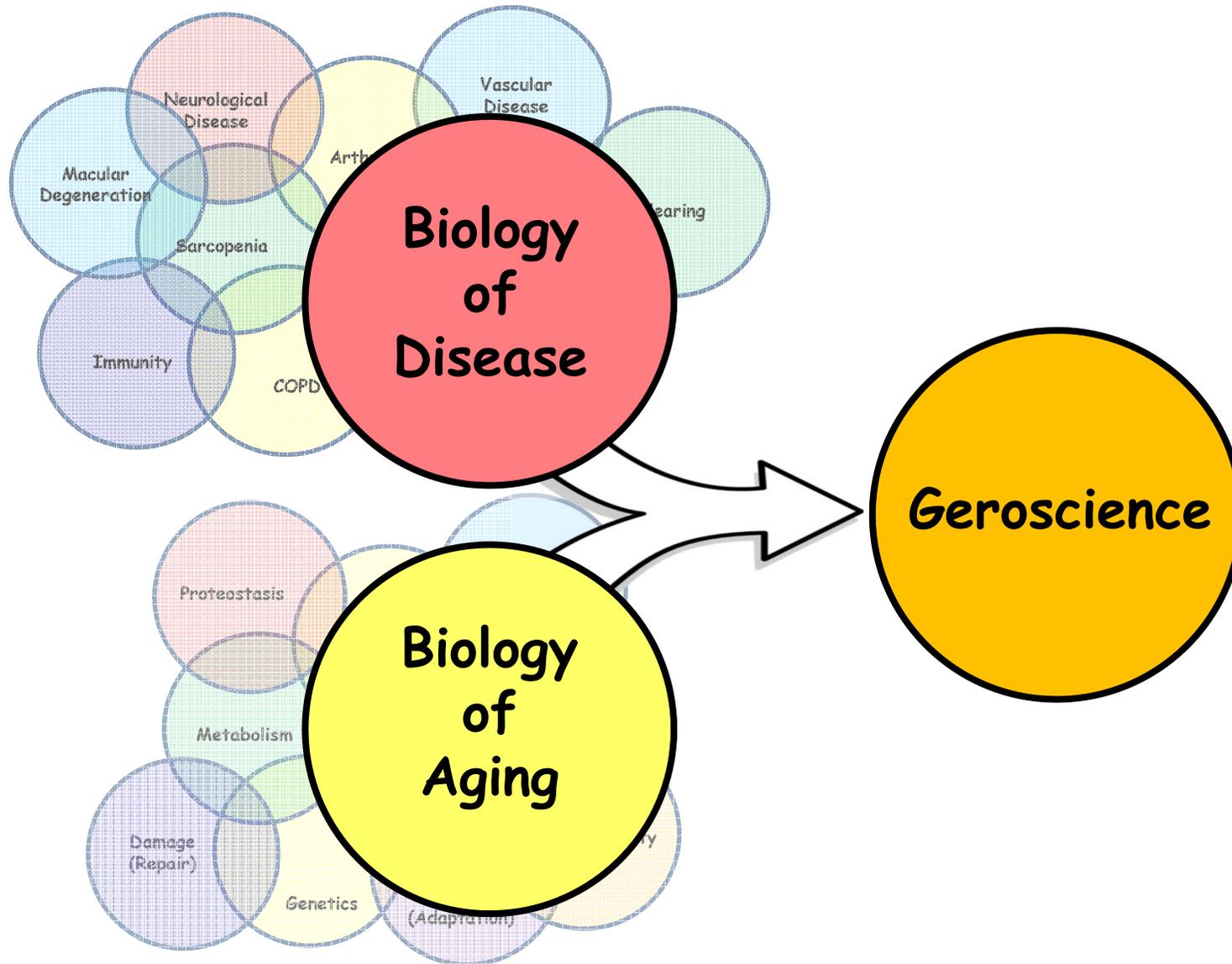


# Aging is the major risk factor for most chronic diseases

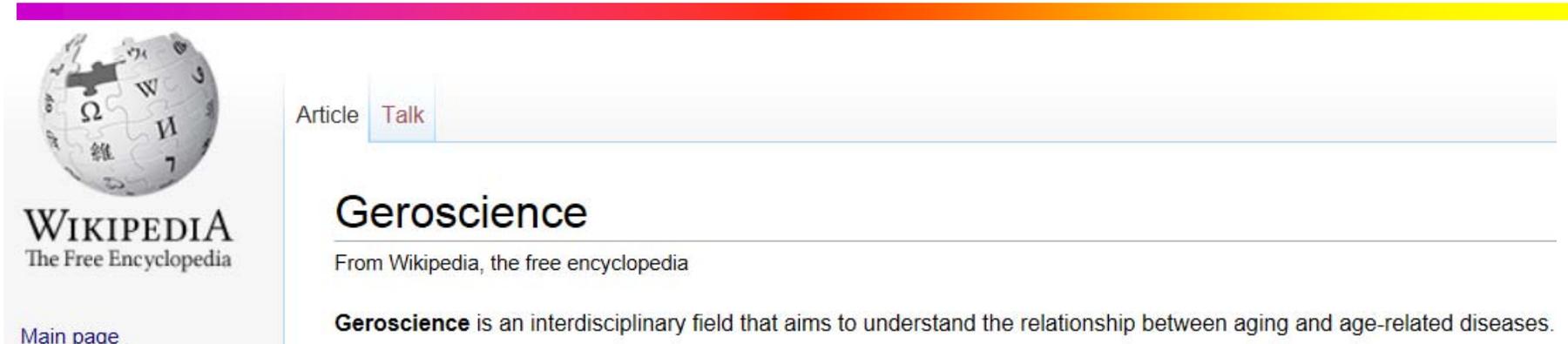
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# Convergence

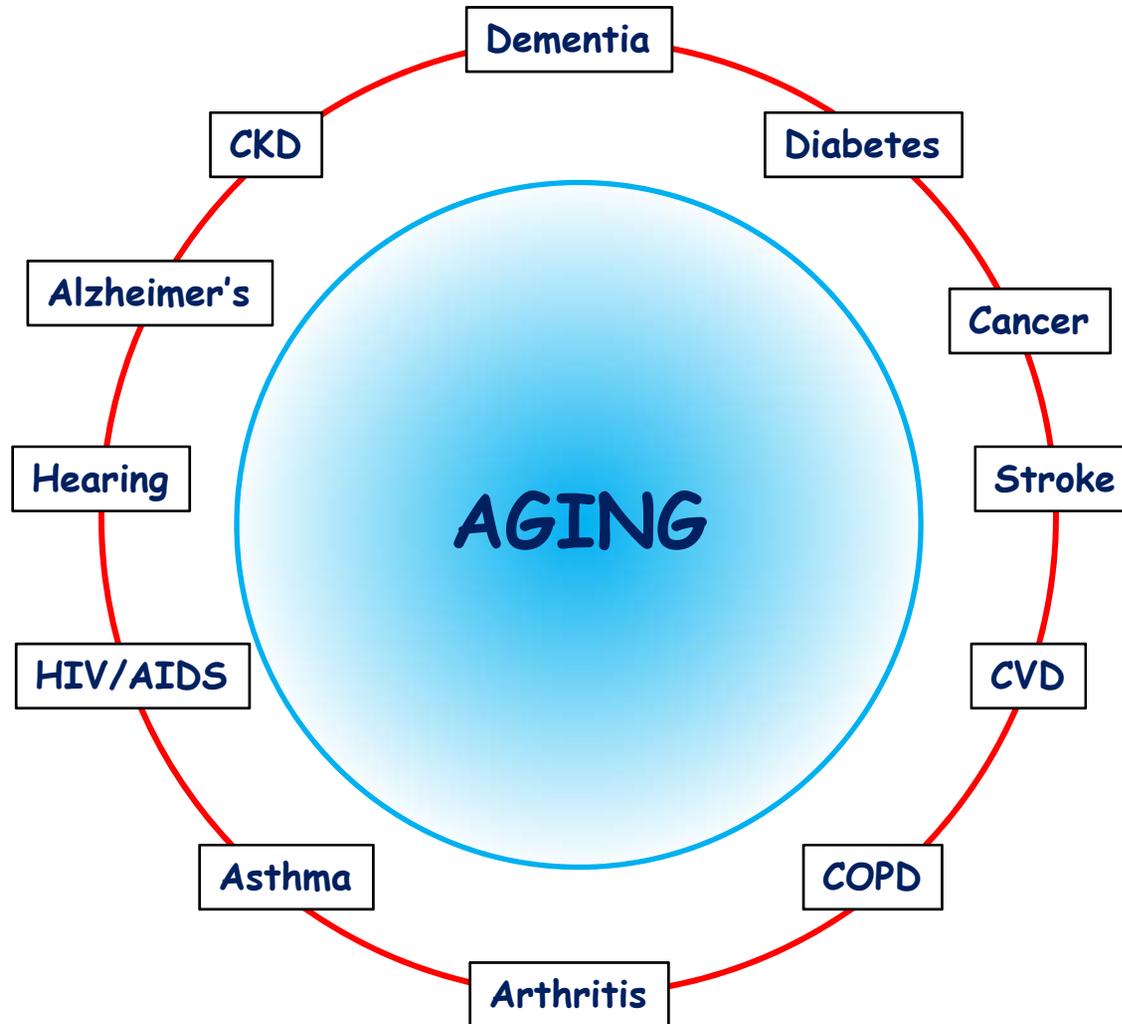


# GEROSCIENCE



**Geroscience** is an interdisciplinary field that aims to understand the relationship between aging and age-related diseases. Because aging is the major risk factor for most non-genetic chronic diseases, an understanding of the role of aging in the onset of disease should open up new avenues for disease prevention and cures. This term describes the interrelated activities of molecular biologists, neuroscientists, protein chemists, cell biologists, geneticists, endocrinologists, pharmacologists, mathematicians, and others. They have the common goal of explaining and intervening in age-related disease.

# AGING BIOLOGY IS AT THE CORE OF CHRONIC DISEASES

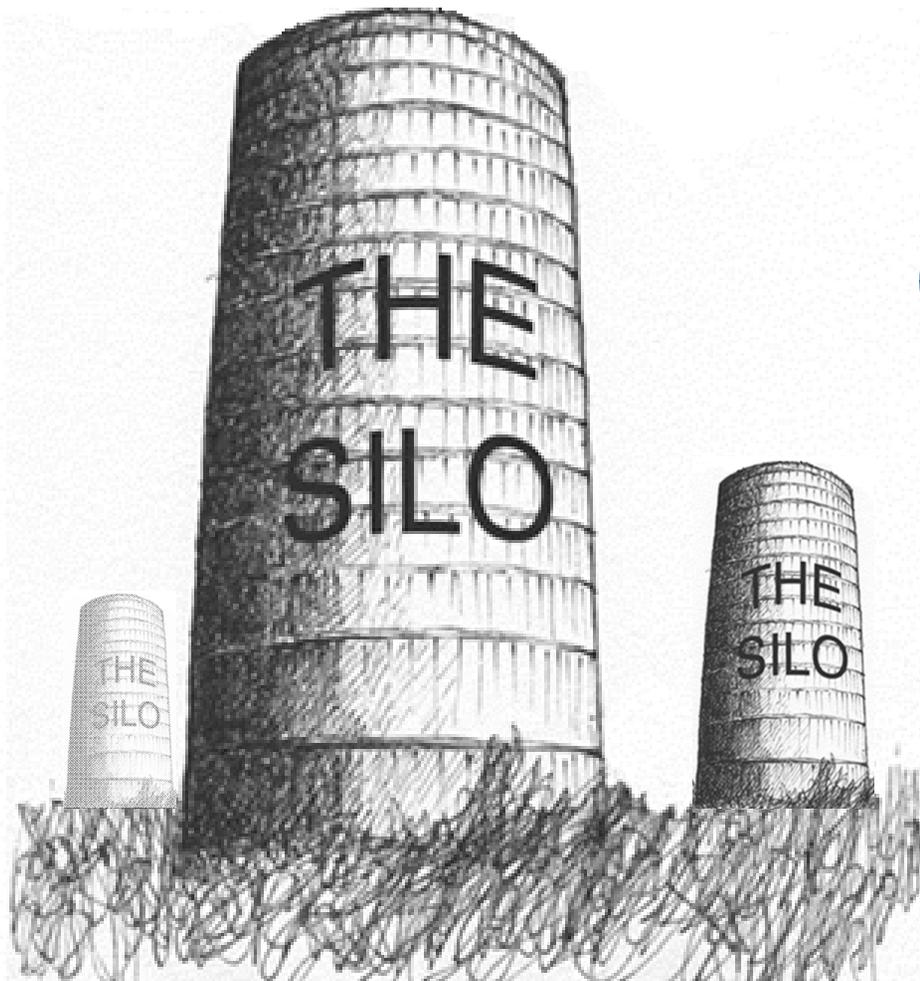


# Today's menu

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- ✓ *From the old guard to current paradigms and trends*
- ✓ *Geroscience*
- ✓ *Some ideas on translation*
- ✓ *Is there anything we can translate?*

# WE NEED TO BREAK THE "WAR ON DISEASE X" MODEL



In an aging world,  
the single disease  
model may have come  
close to running its  
course - the time has  
arrived for a new  
model.

NINDS  
Neurological  
Disease

NHLBI  
Vascular  
Disease

NEI  
Macular  
Degeneration

NIAMS  
Arthritis

NIDCD  
Hearing

NIAID  
Immunity

NIDDK  
CKD

NHLBI  
COPD

NCI  
Cancer

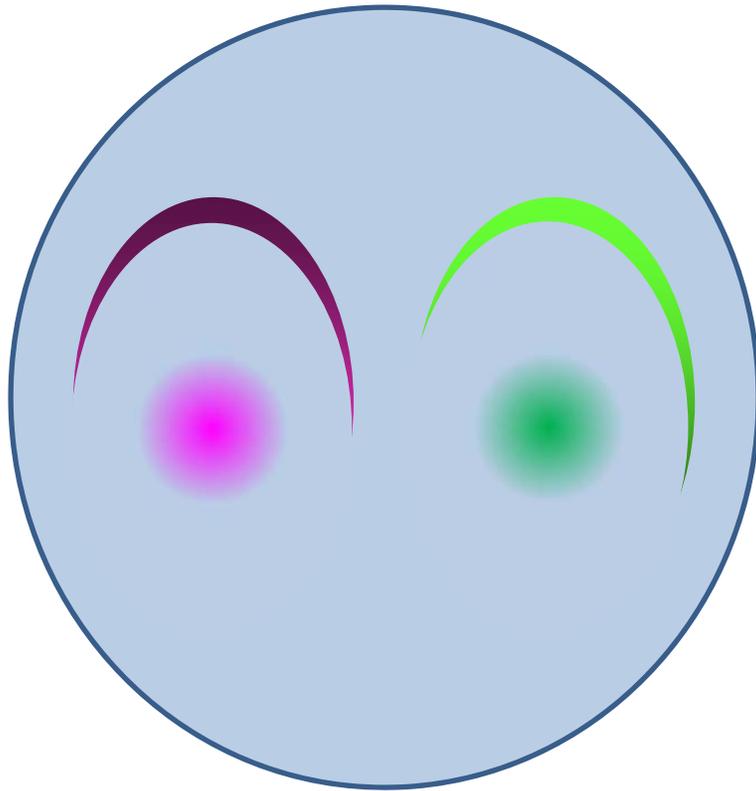
NHLBI  
Heart  
Disease

Jay Olshansky

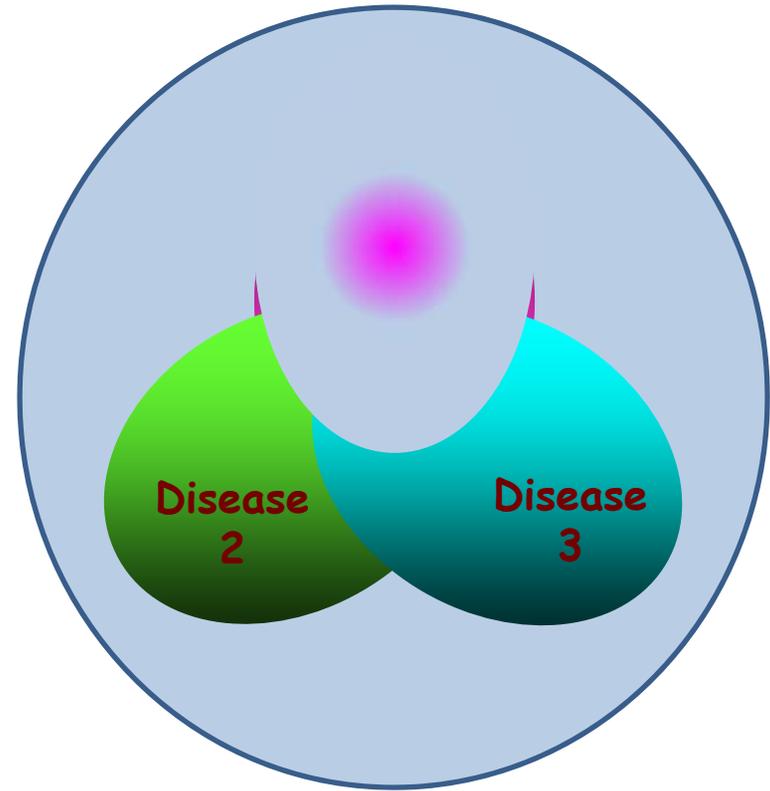
# Perhaps 'curing' one disease at a time is not a good idea

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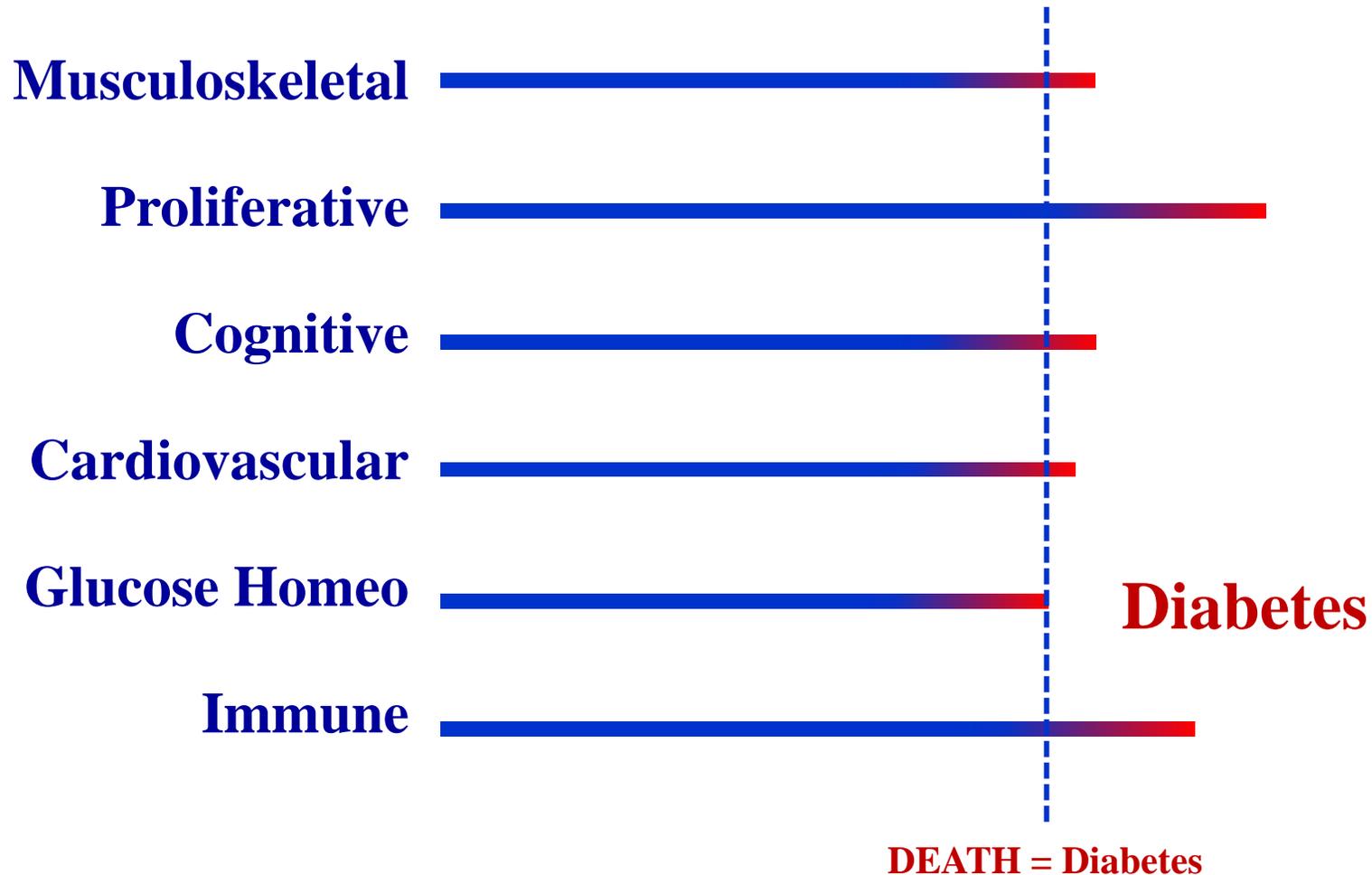
Young



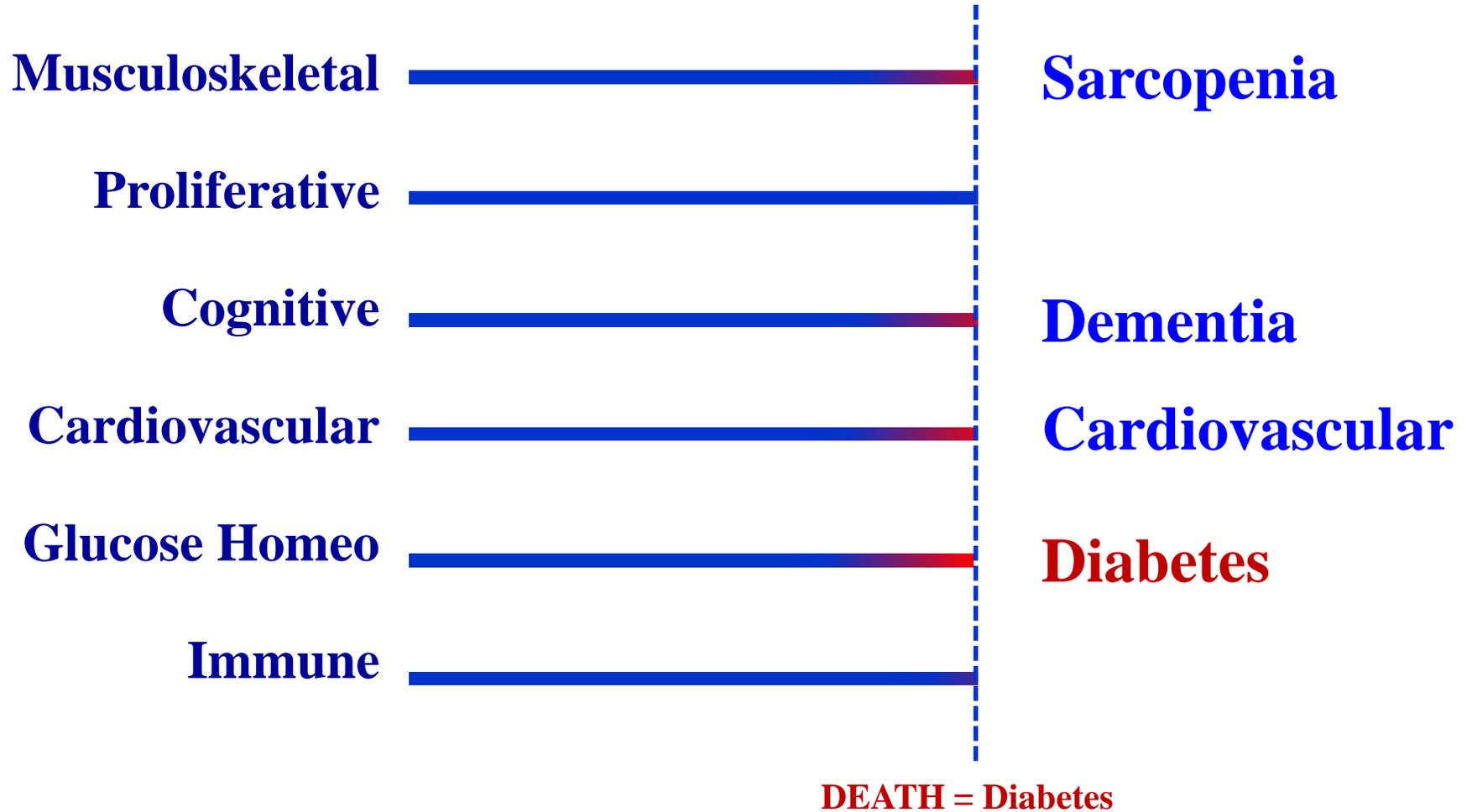
Old



# Aging results in functional decline Cause-of-Death as main focus in multiple organs

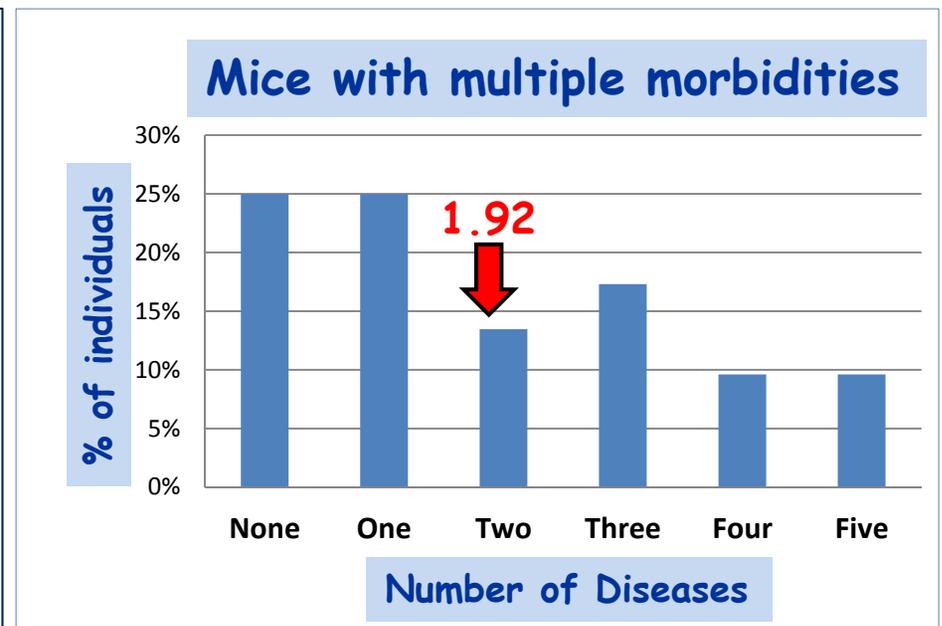
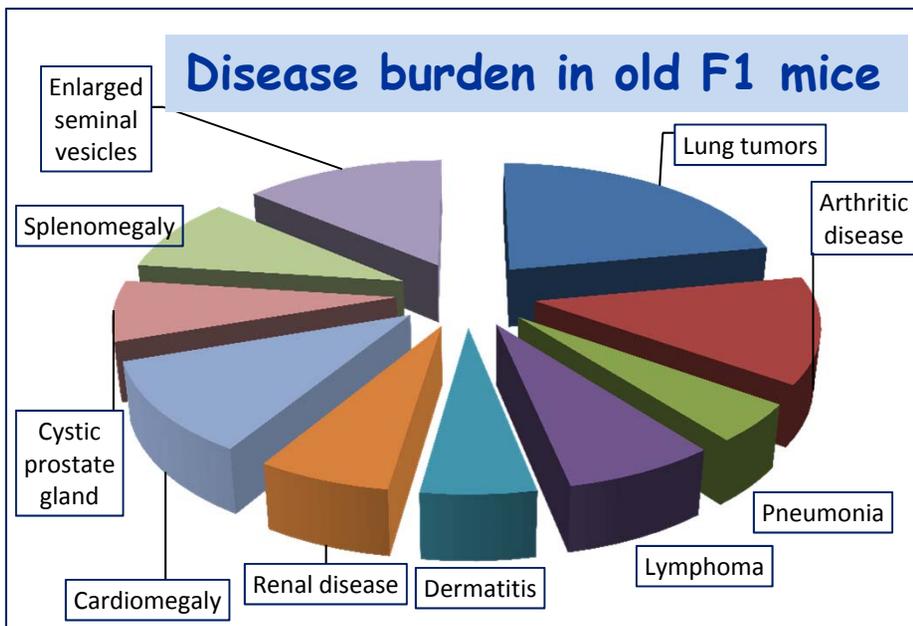


# But what about HEALTH?

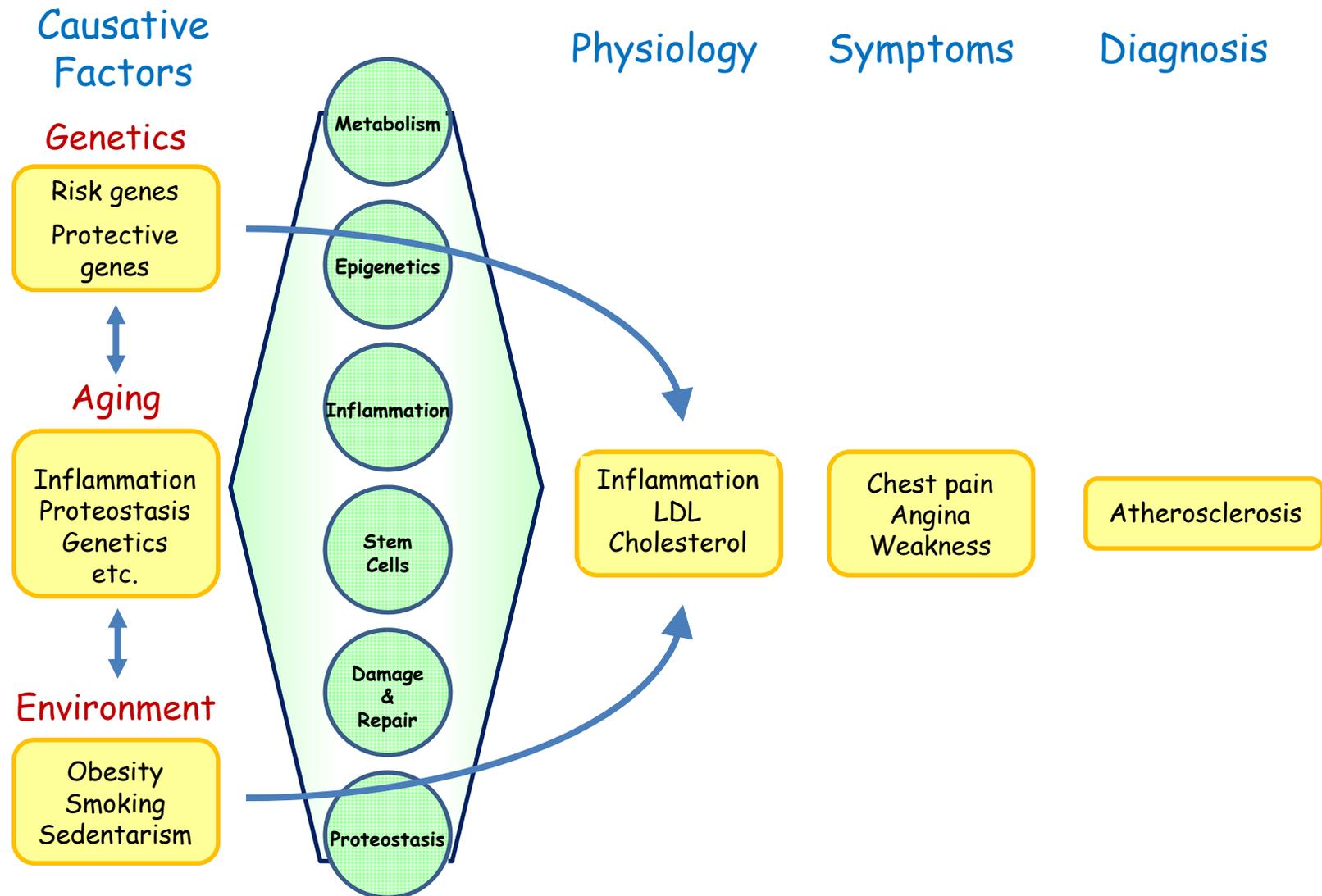


# Net Disease as a metric of "Successful Aging"

Most existing laboratory animals acquire multiple chronic diseases with age



# From Biology to Disease



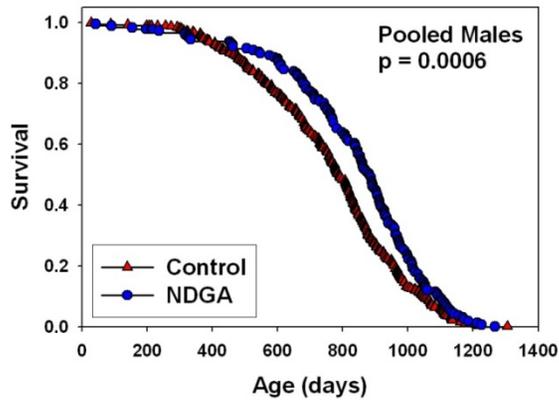
# Today's menu

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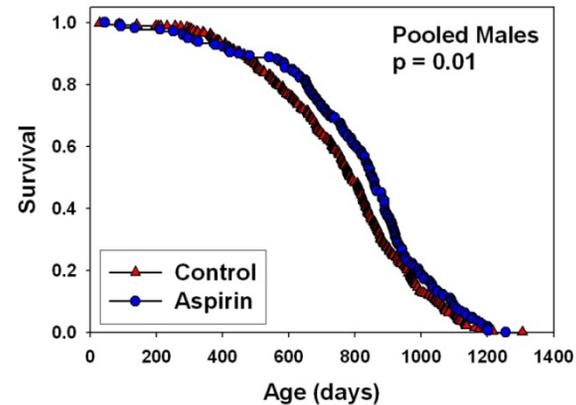
- ✓ *From the old guard to current paradigms and trends*
- ✓ *Geroscience*
- ✓ *Some ideas on translation*
- ✓ *Is there anything we can translate?*

# Intervention Testing Program (ITP)

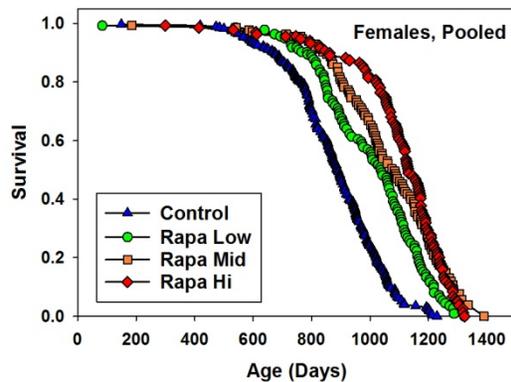
5 de los 17 compuestos estudiados han mostrado un efecto positivo



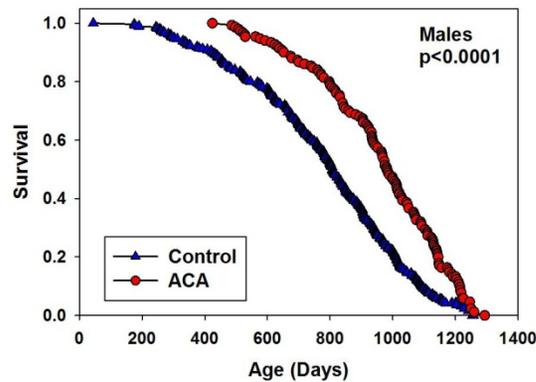
NDGA



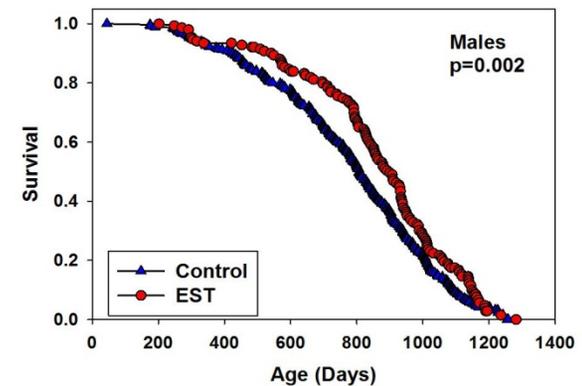
Aspirin



Rapamycin



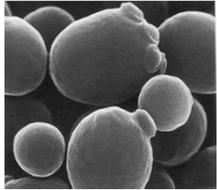
Acarbose



17- $\alpha$  estradiol



# We have some advantages



*Saccharomyces cerevisiae*



*Caenorhabditis elegans*



*Drosophila melanogaster*



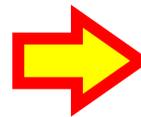
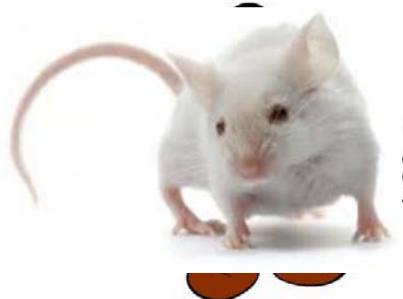
*Mus musculus*



*Callithrix jacchus*

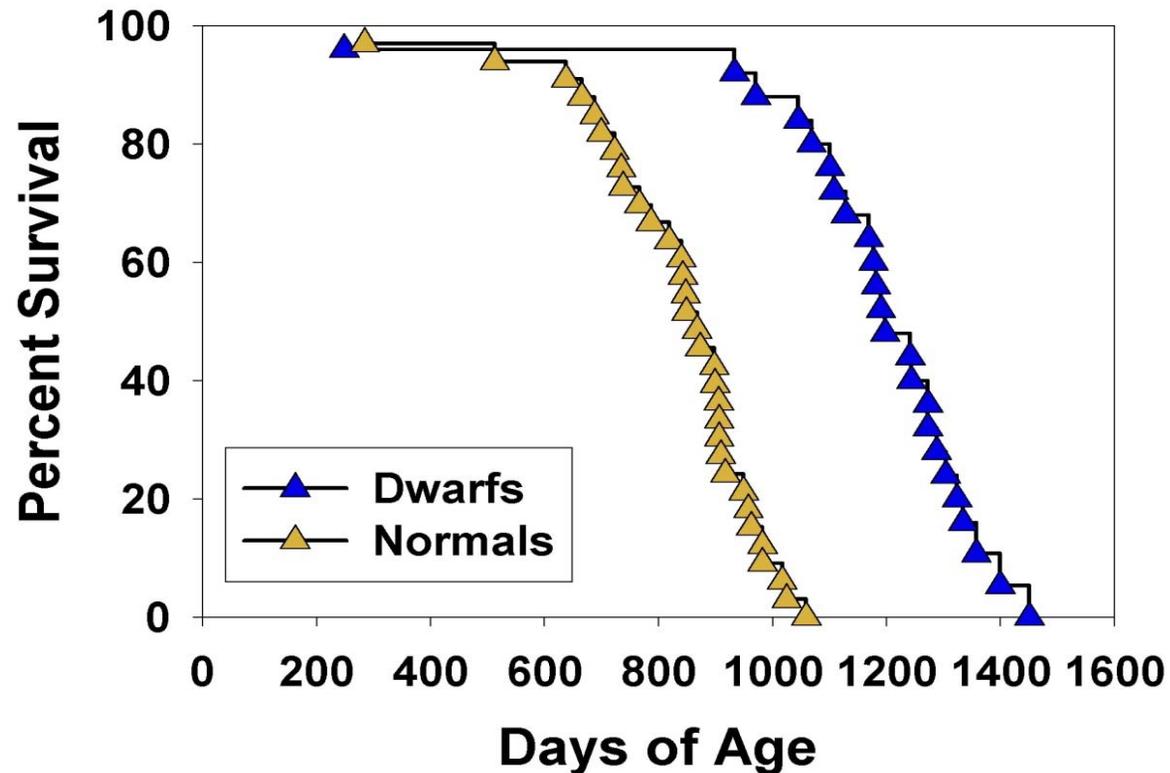


*Canis lupus*



# We have some disadvantages

## CLASSICAL APPROACH: LIFESPAN



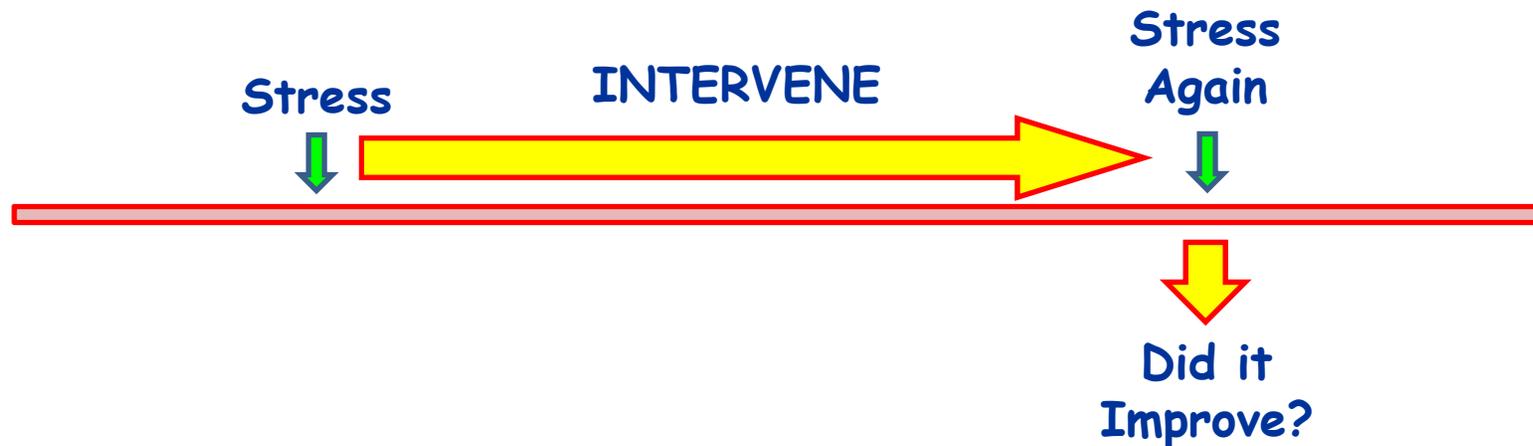
IT WON'T WORK VERY WELL IN HUMANS

# How will we test efficacy of interventions against aging?

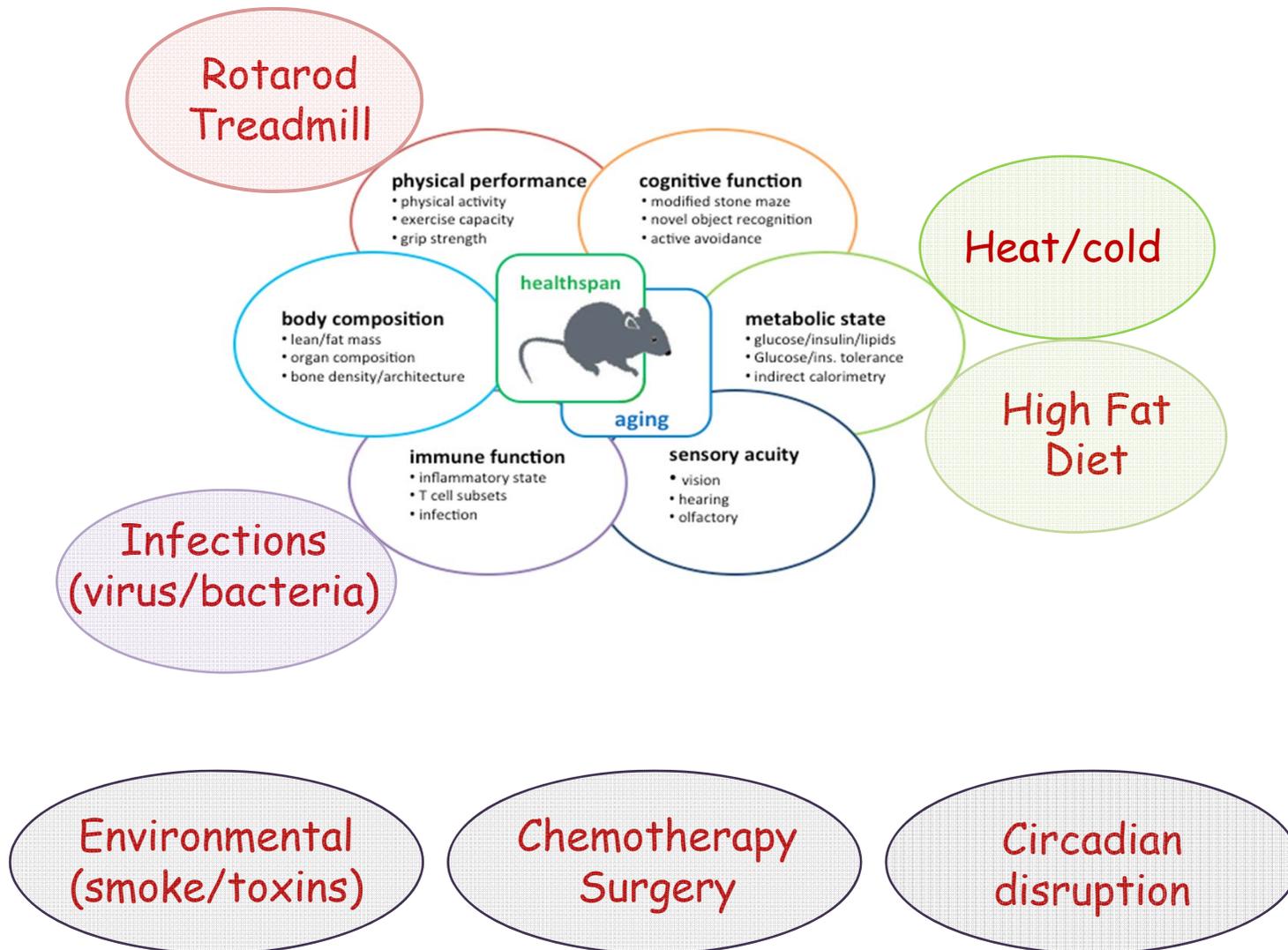
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**So... we need proxies**  
(but don't call them biomarkers)

- **Resilience**



# Measures of Resilience - Mice



# Today's discussions

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- ✓ *From the old guard to current paradigms and trends*

Major hallmarks identified, need to develop them into biomarkers.

- ✓ *Geroscience*

Basic concepts: aging is at the heart of chronic diseases, and it is malleable.

- ✓ *Some ideas on translation*

Findings are robust and the field is poised for translation. Resilience might be a useful surrogate.

- ✓ *Is there anything we can translate?*

Not quite, but some approaches appear promising.