

# Konzepte für das ewige Leben

IFIMP2011

105—na und ?! Anästhesie-,  
Intensiv- und Notfallmedizin  
im Alter

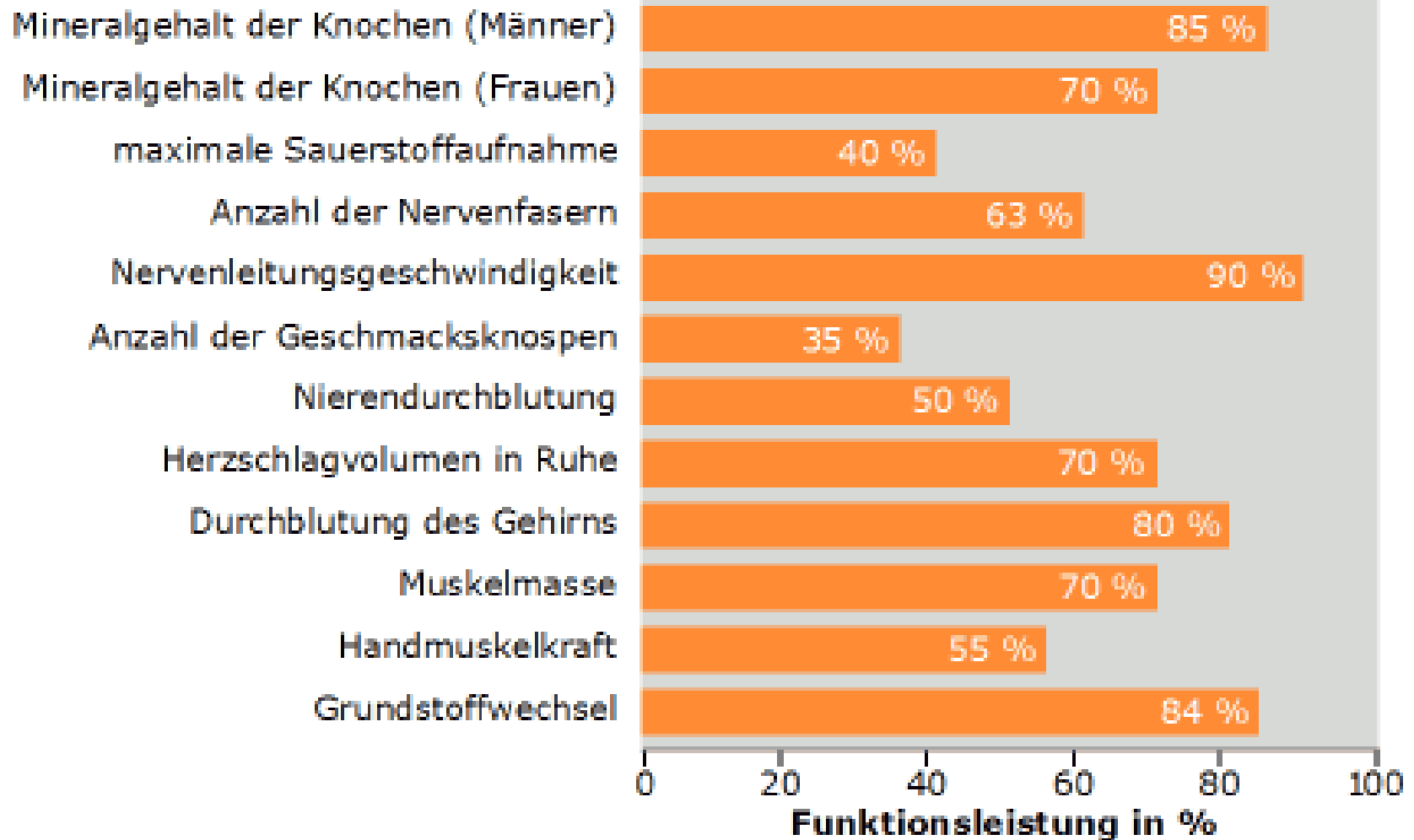


**Günter Lepperdinger**

Institut für Biomedizinische Altersforschung  
Österreichische Akademie der Wissenschaften

# Organalterung

## Funktionsleistung zwischen 30 / 75 Jährigen



# Nature – Nurture - Epigenetics

## Epigenetic revolution



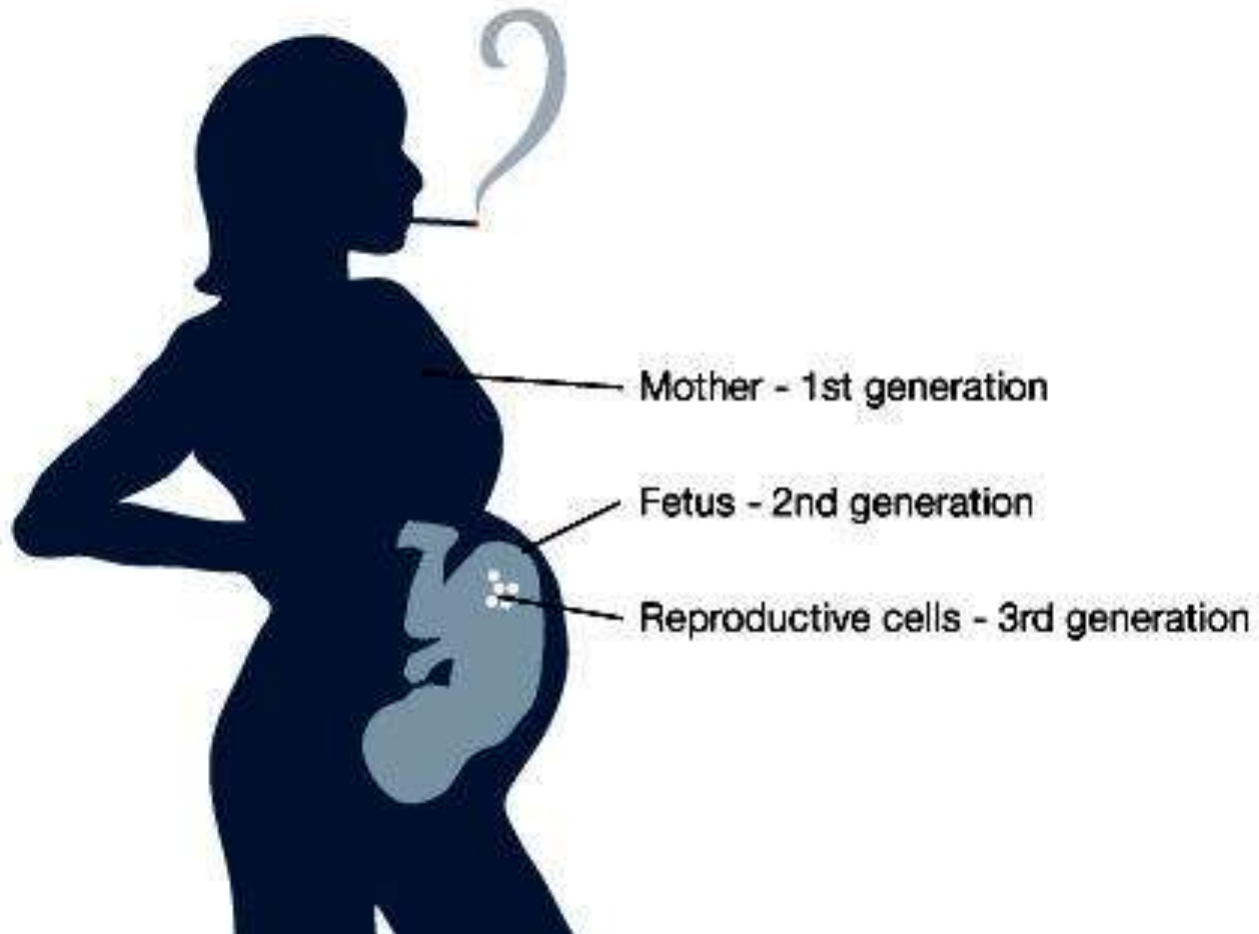
# Nature – Nurture

you are what you eat



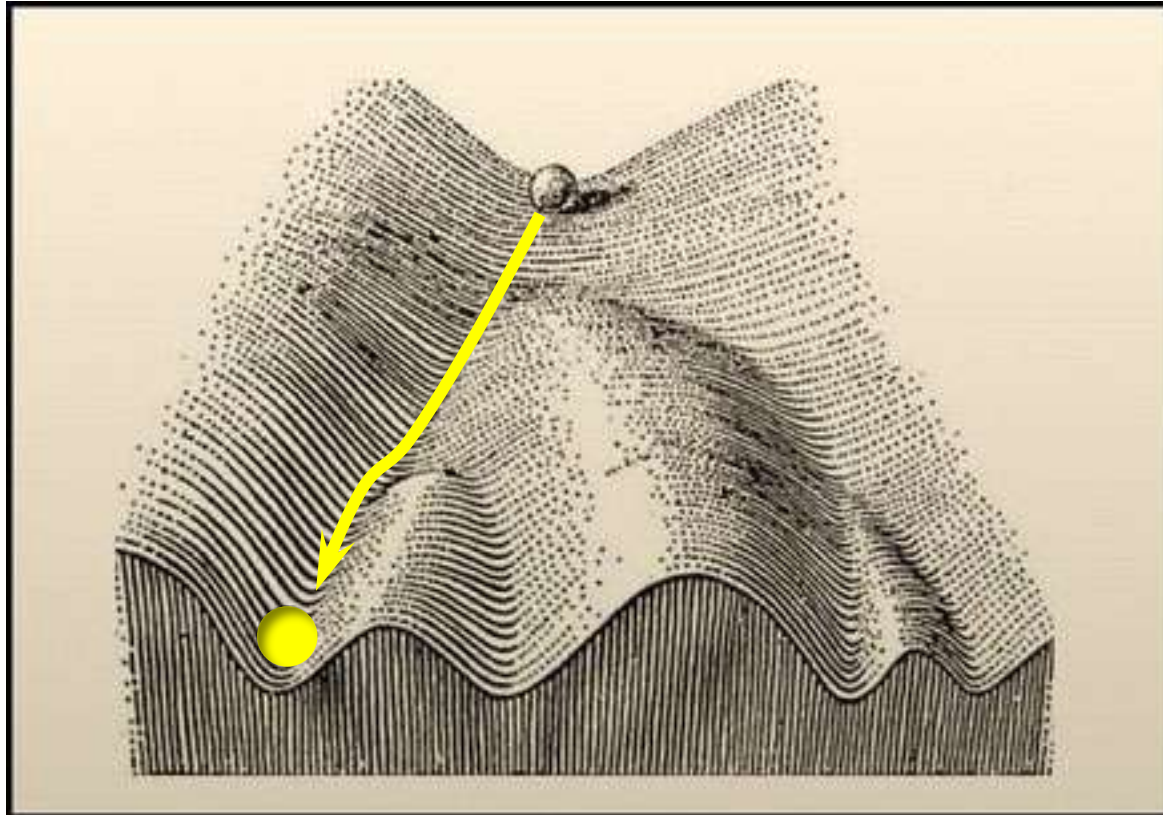
# Nature – Epigenetics

## The genome's dark matter - Lamarck revisited



# Epigenetics

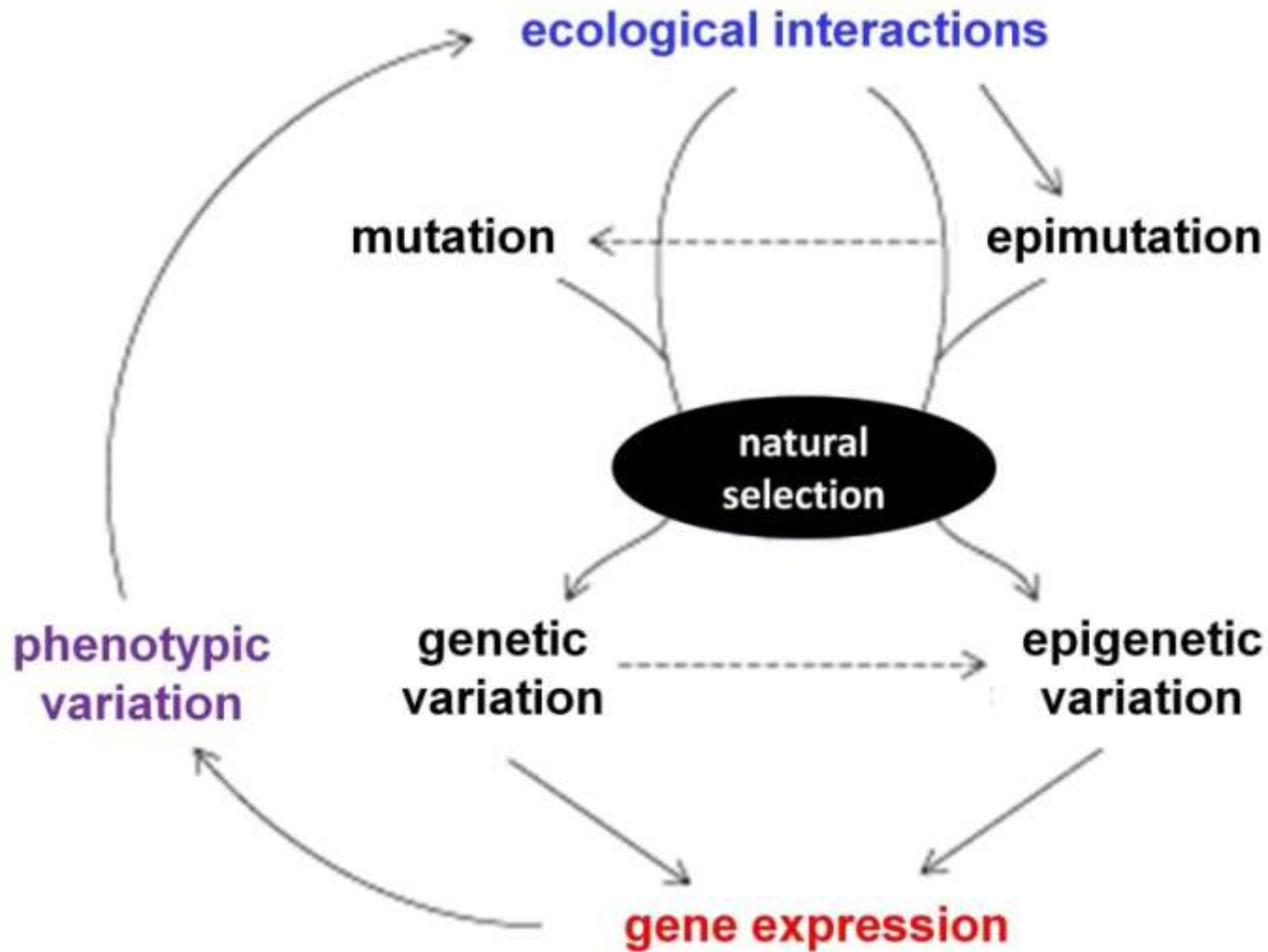
## Waddington's landscape



*Waddington's epigenetic landscape, from C.H. Waddington. The strategy of genes: a discussion of some aspects of theoretical biology (Allen & Unwin, 1957)*

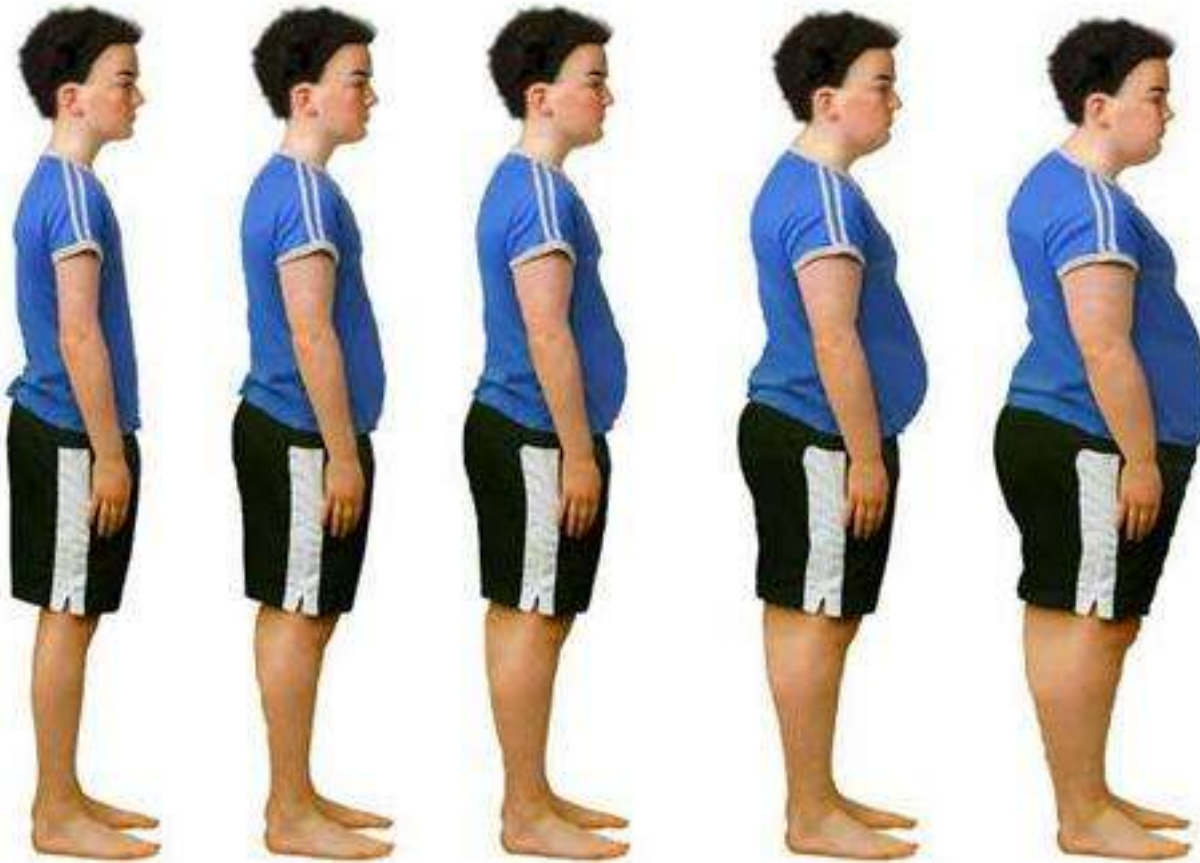
# Epigenetics 2

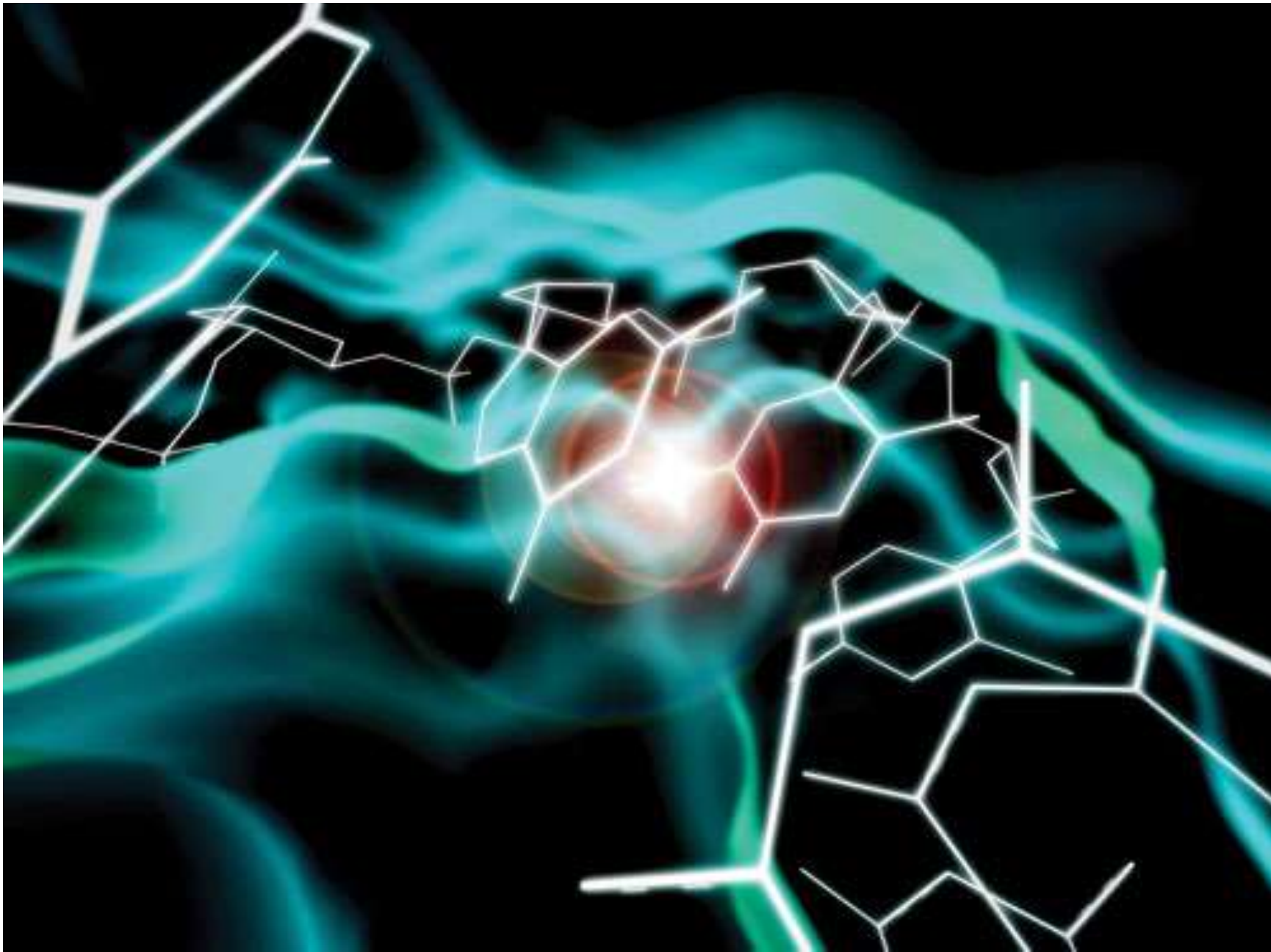
## The genome's hidden agenda



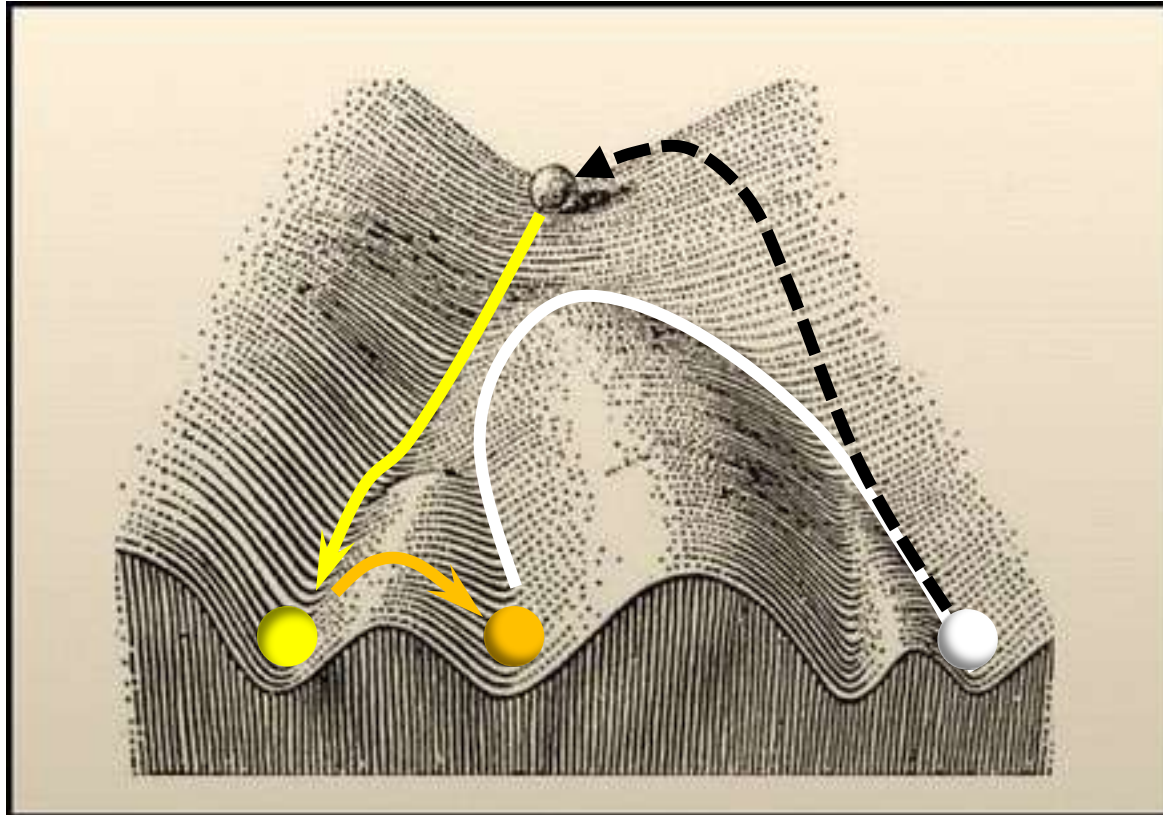
# Nature – Nurture – Epigenetics

is there a choice...





# Epigenetics back into future



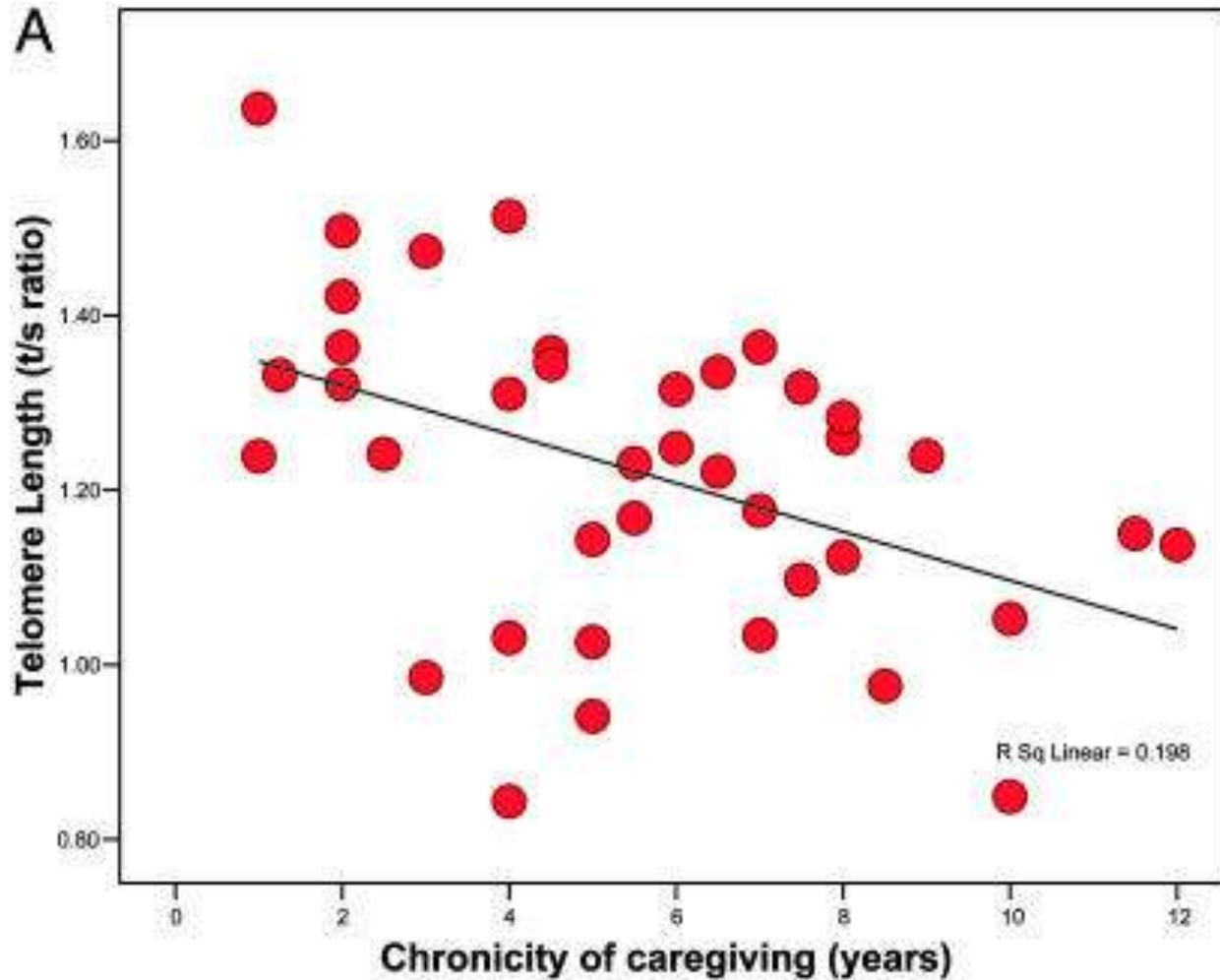
- **Age**
- **Memory**
- **Fitness**
- **Immunity**
- ...

*irreversible - convertible*





# Telomerverkürzung in Beziehung zu Pflegestress



Epel et al., Proc Natl Acad Sci U S A. 2004 December 7; 101(49): 17312–17315.

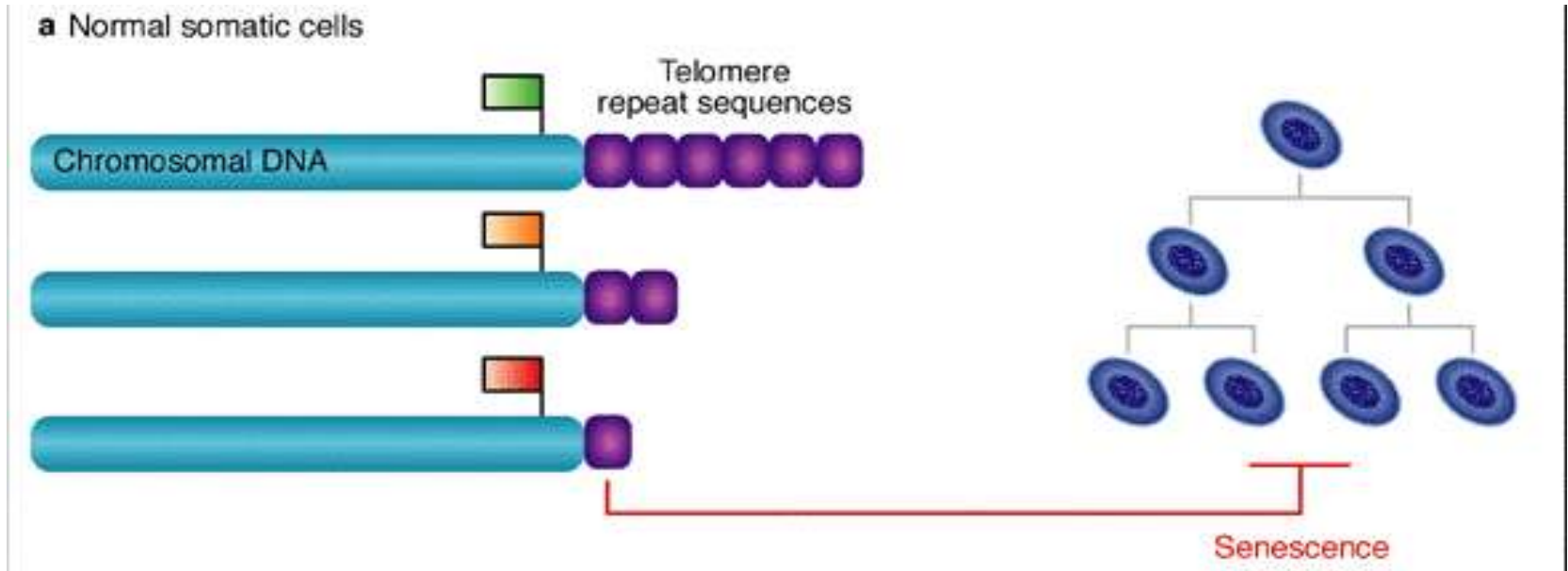
# Alters-assozierte Pathologien mit kurzen Telomeren

- Heart failure
- Immunosenescence
- Digestive tract atrophies
- Infertility
- Viability of stem cells, reduced
- Angiogenic potential, reduced
- Wound healing, reduced
- Body mass, reduced

infections  
ulcers

# Telomer Verkürzung

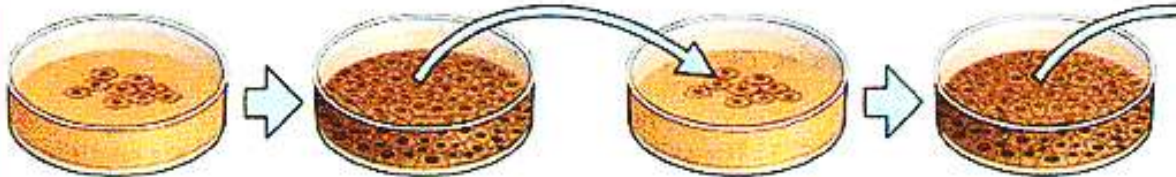
## ... replikative Seneszenz



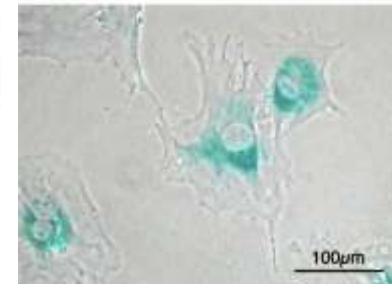
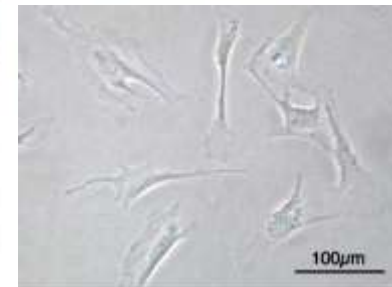
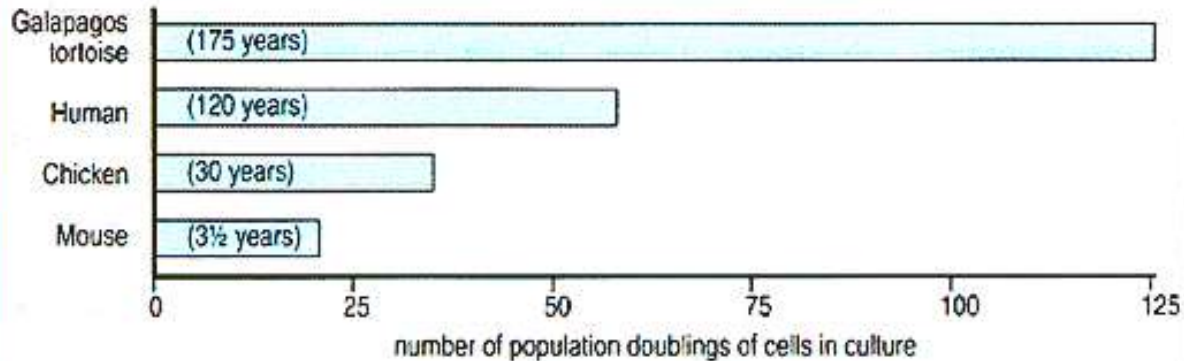
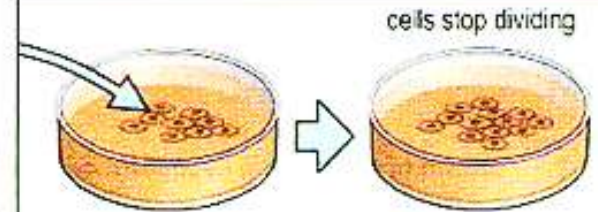
Kurze Telomere signalisieren der Zelle: Wachstumsstopp

# Zelluläre Seneszenz

Cells divide until they completely cover the dish and continue to divide when placed in fresh culture medium

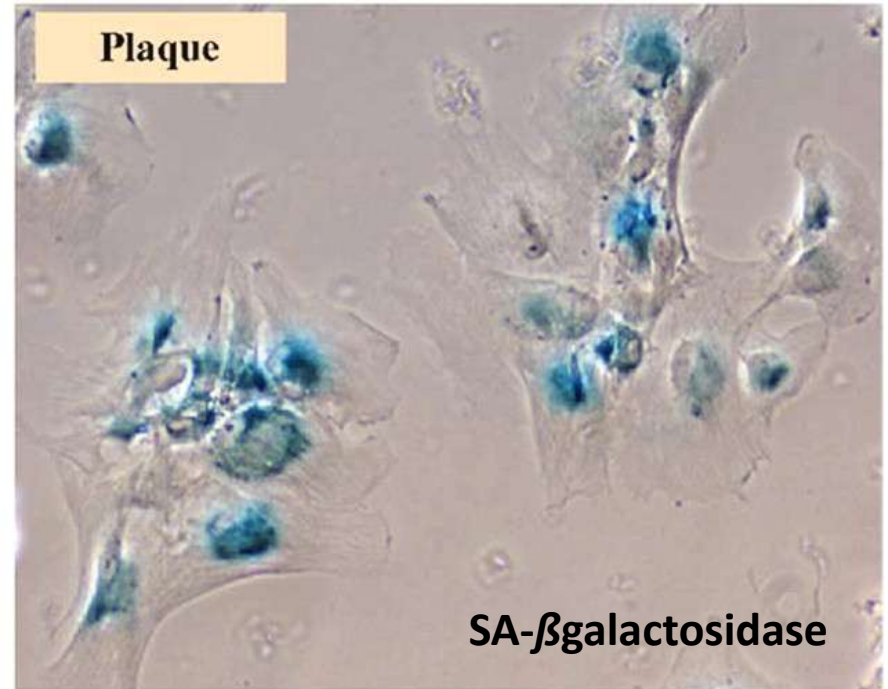
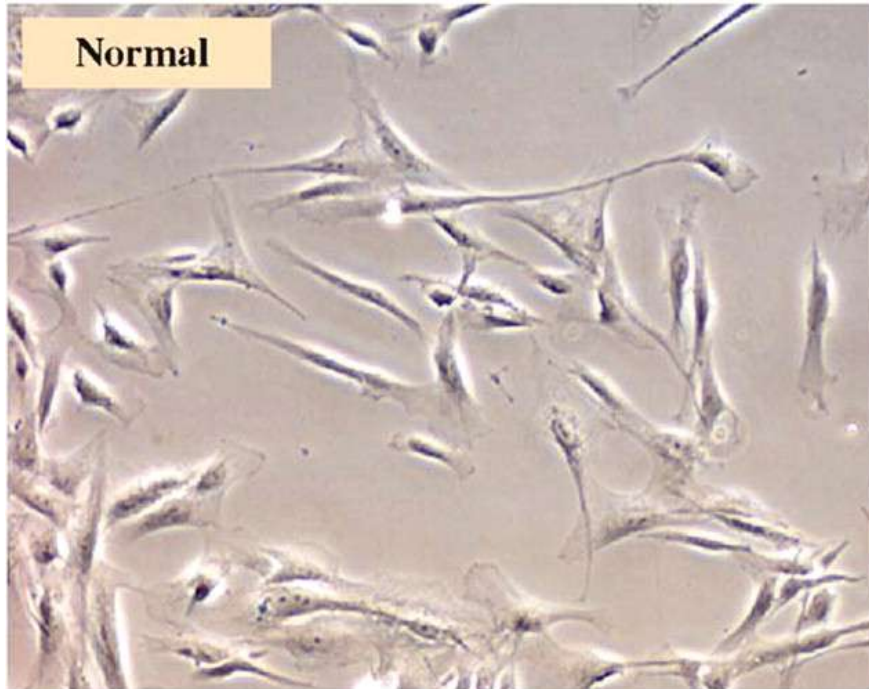


After a finite number of cell multiplications, cells stop dividing



# Seneszente Zellen

... es gibt sie in vivo - 1

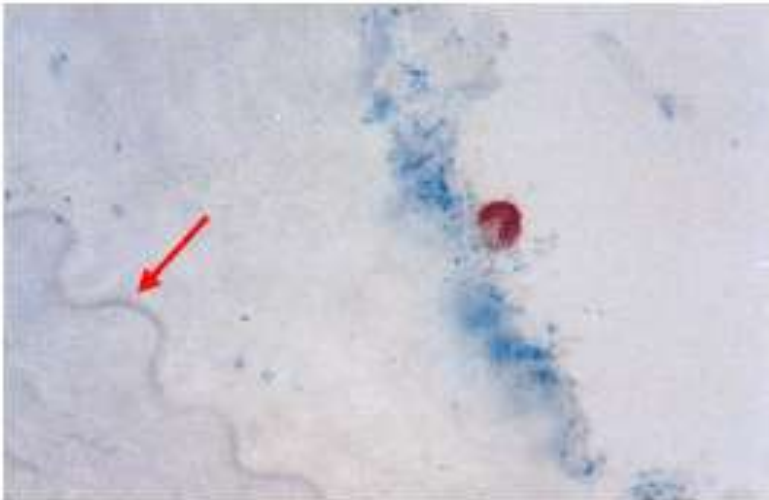


Evidence of senescence in human plaque VSMCs. (A) Human normal or (B) plaque VSMCs in culture, showing typical morphological features of senescence, including large flattened shape and SA $\beta$ G activity as shown in blue in the perinuclear region of the plaque cells.

# Seneszente Zellen

## ... es gibt sie in vivo - 2

### SA- $\beta$ galactosidase



The images show senescence-associated  $\beta$ -galactosidase staining (blue) in neointimal lesions that develop following balloon denudation of the endothelium.

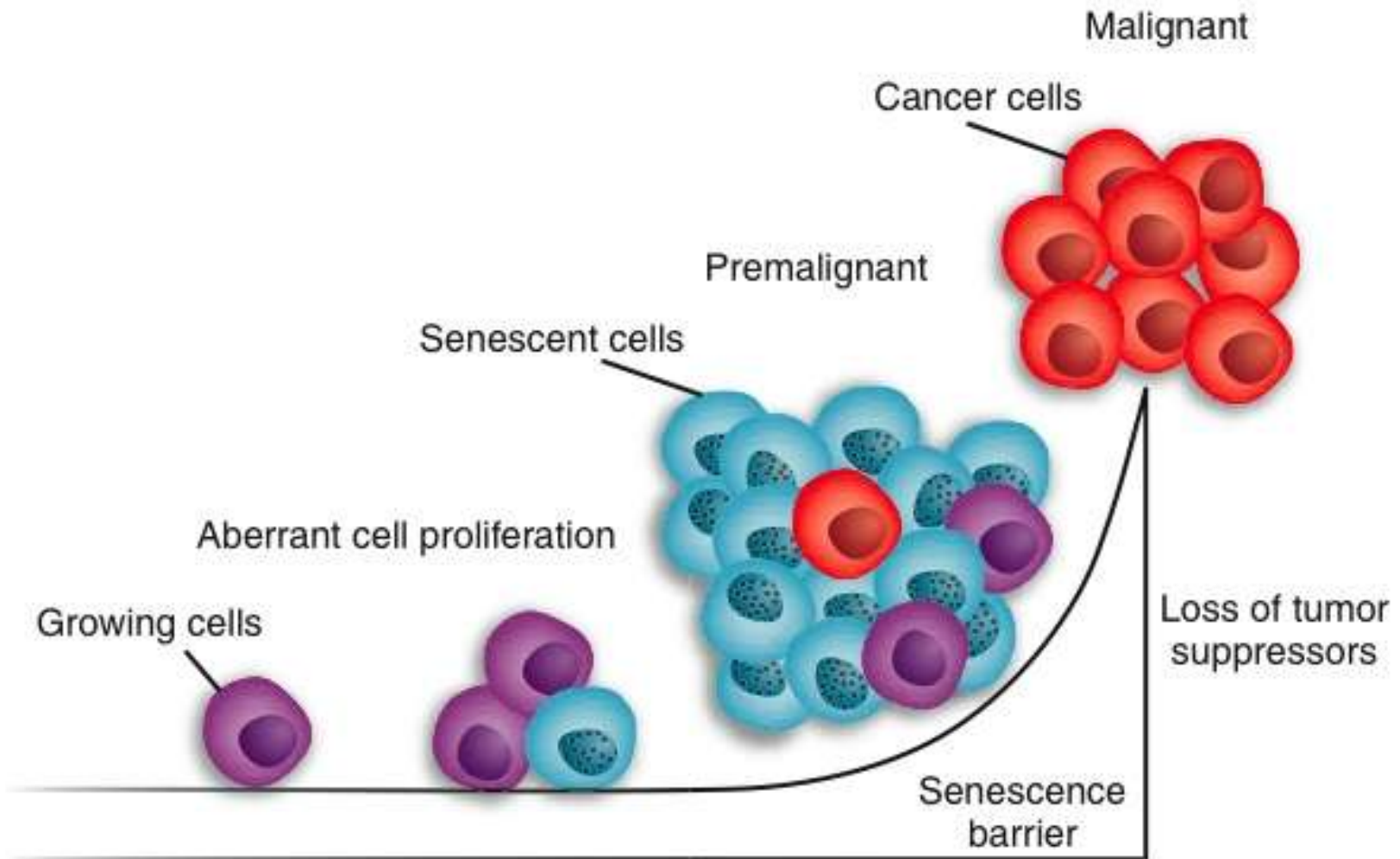
(Top panel) Re-grown endothelial cells are stained brown. Note that some endothelial cells are senescent. The underlying blue cells are senescent vascular smooth muscle cells.

(Bottom panel) A leukocyte (stained red) is adhering to the surface of the neointima where senescent smooth muscle cells have emerged. The red arrow points to the internal elastic lamina

[www.ucl.ac.uk/wibr/research/mito/sm/senescence-mechanisms/](http://www.ucl.ac.uk/wibr/research/mito/sm/senescence-mechanisms/)

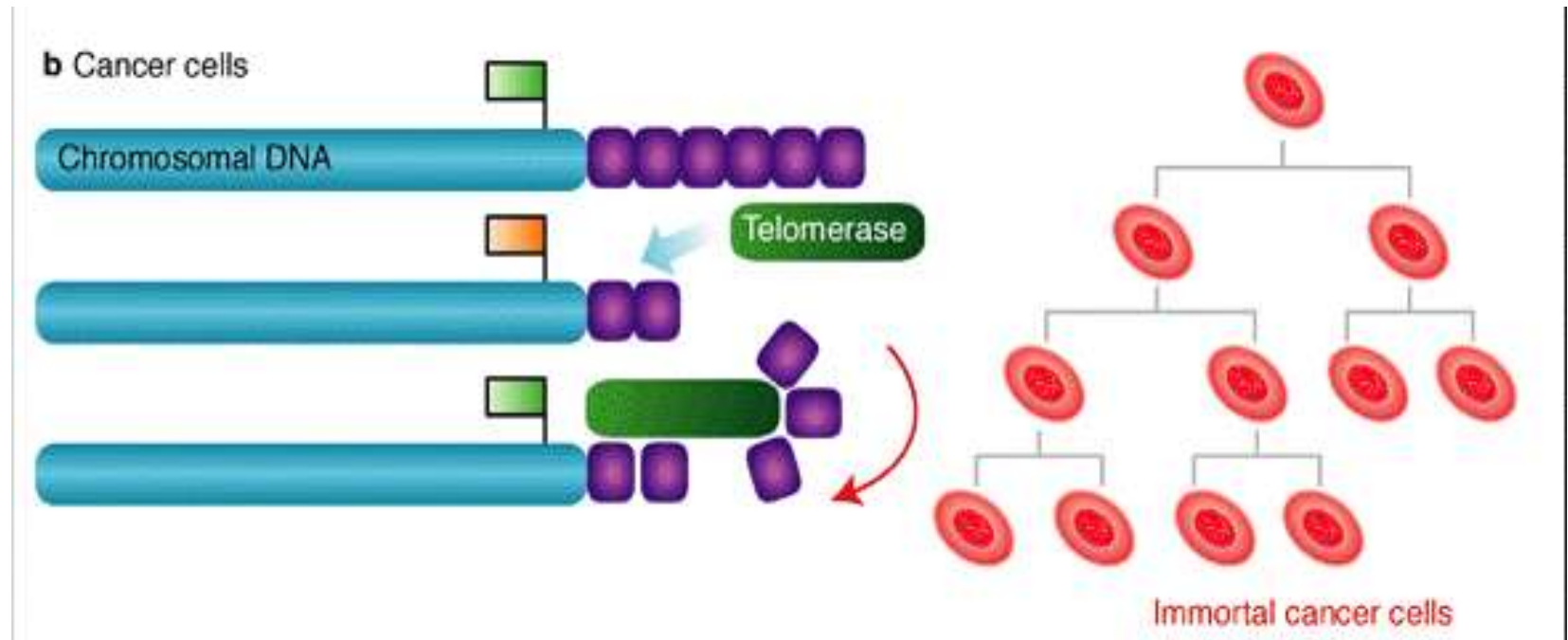
# Seneszenz

## ... ein Tumorsuppressor Mechanismus



# Telomerase

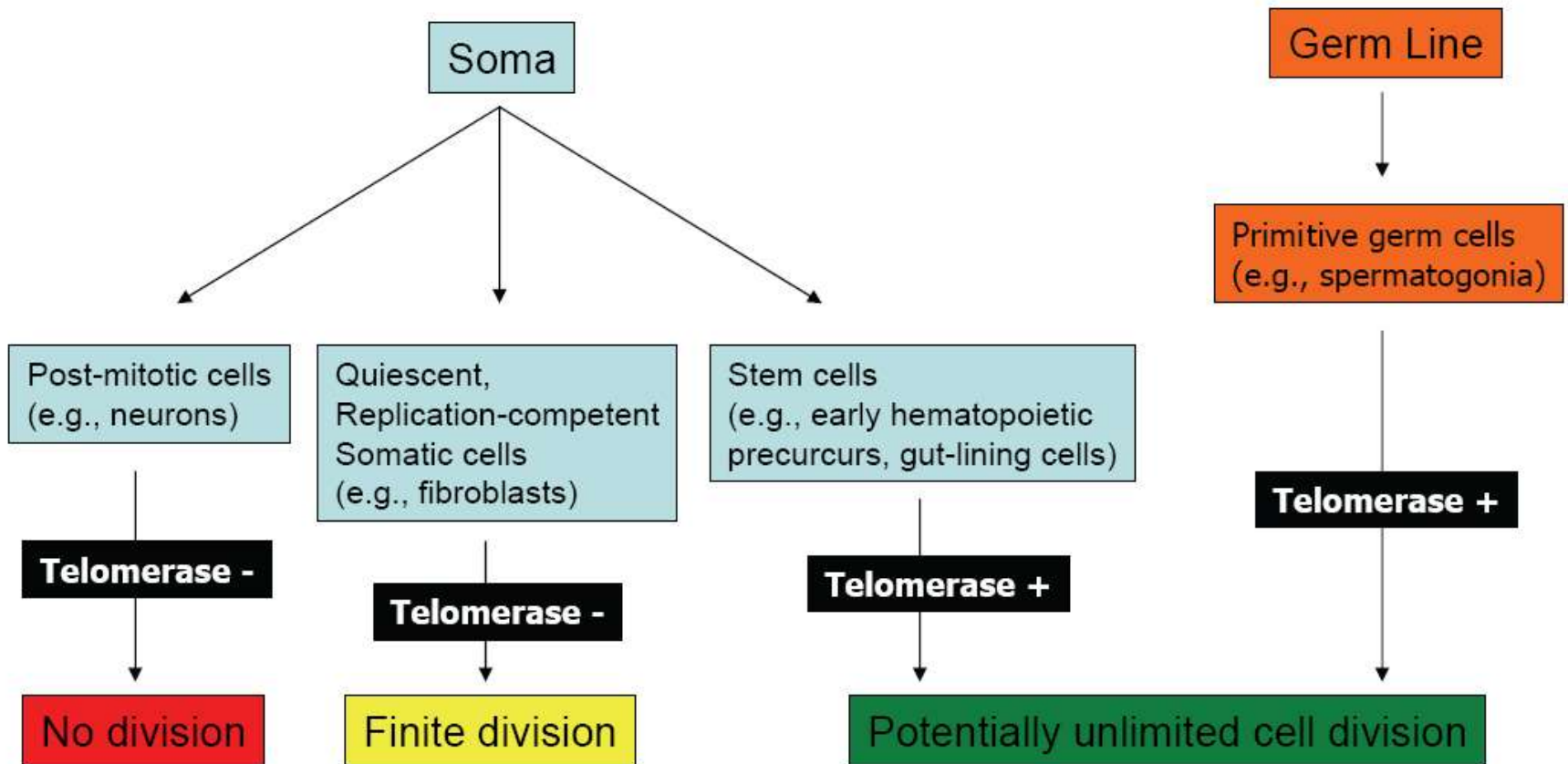
## ... Krebspromotion



The presence of telomerase in cancer cells allows them to maintain telomere length while they proliferate

# Telomerase

... replikatives Zellteilungspotential



# Biomedical ageing research ,inevitable consequences'

- Genotoxic scarification – **cancer & neoplasia**
- Molecular damage – **cellular dysfunction**
- Cellular dysfunction – **organ derailment**
- Endocrine lapse – **hyper/neoplasia**
- Immune fade – **chronic infection**
- Somatic decay – **frailty**

# Biomedical ageing research 2

## natural programmes for compensation

- Genotoxic scarification – **cellular senescence**
- Molecular damage – **aggregates**
- Cellular dysfunction – **encapsulation**
- Endocrine lapse – **organ remodelling**
- Immune fade – **anti-autoimmunity**
- Somatic decay – **retirement**

# Biomedical ageing research 3

## Putative de-ageing measures

- Genotoxic scarification – DNA repair/telomerase
- Molecular damage – proteasome / autophagy
- Cellular dysfunction – apoptosis / replacement
- Endocrine lapse – exocrine reprogramming
- Immune fade – haematopoietic fitness
- Somatic decay – stem cell protection

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## Biomedical ageing research 2

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# Biomedical ageing research 3

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# Stammzellen

... „Jungbrunnen“ oder die Antithese des Alterns

“backup-Zellen”

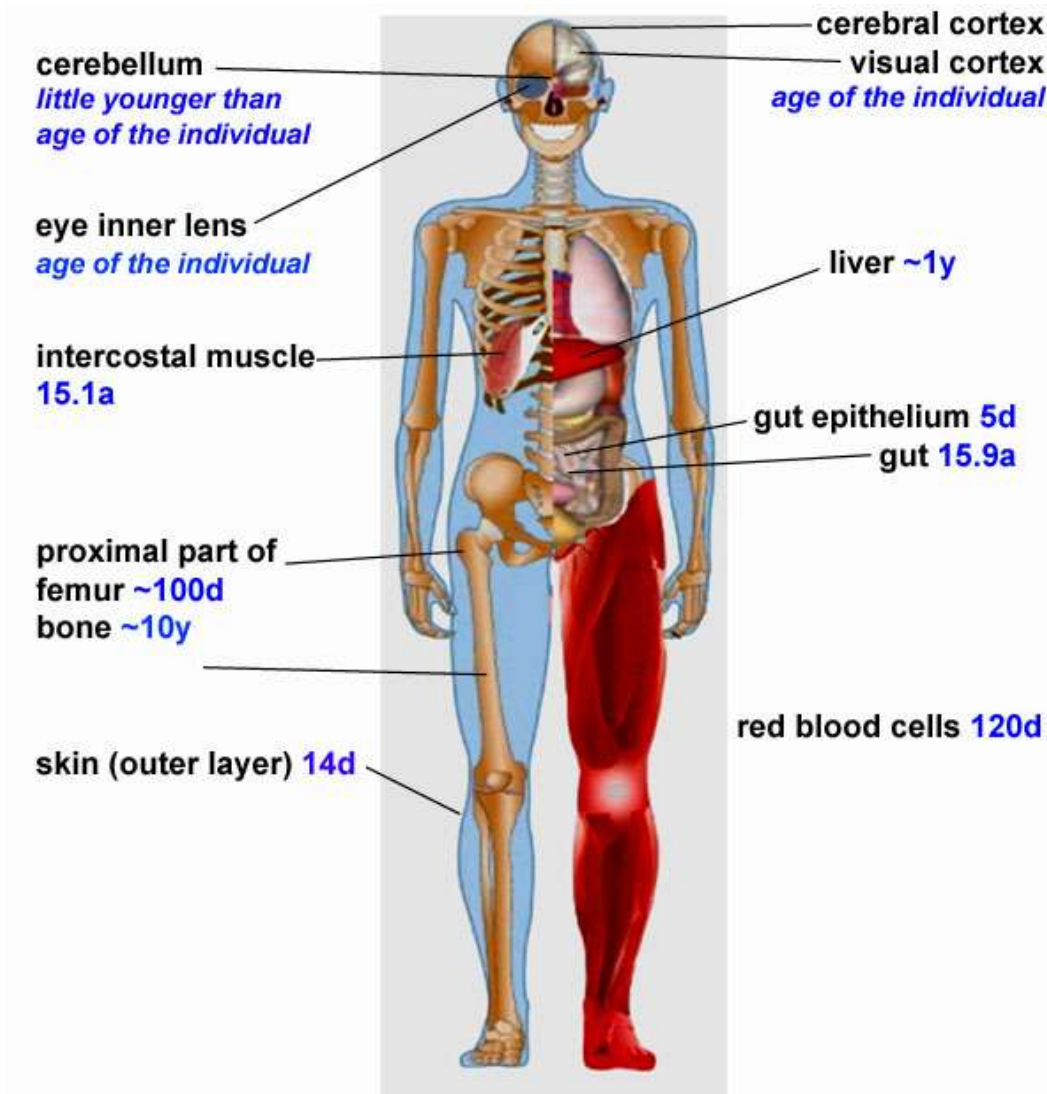
Stammzellen ergänzen  
und erneuern  
kontinuierlich  
Gewebe und Organe  
und erneuern  
gleichzeitig die eigene  
Zellpopulation



Reservezellen, die auf Stressoren/Stresssituationen  
spezifisch reagieren

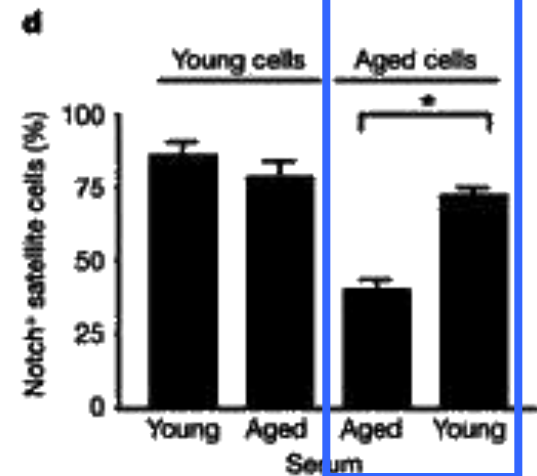
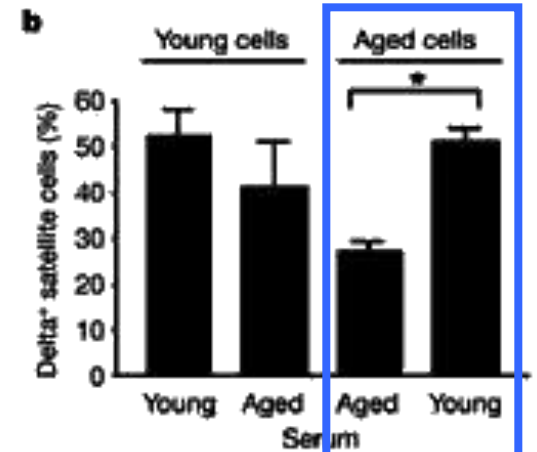
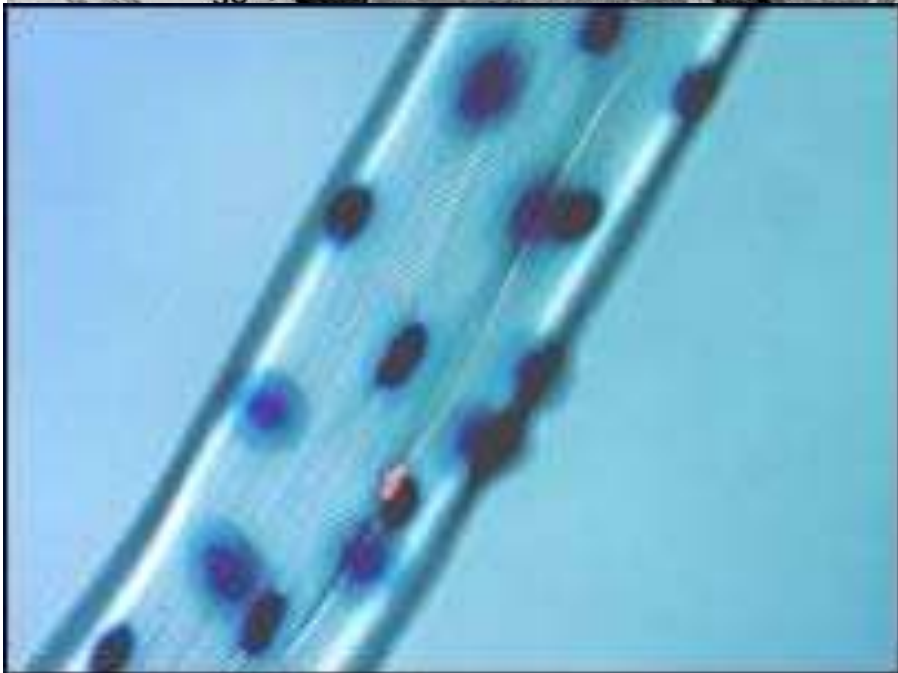
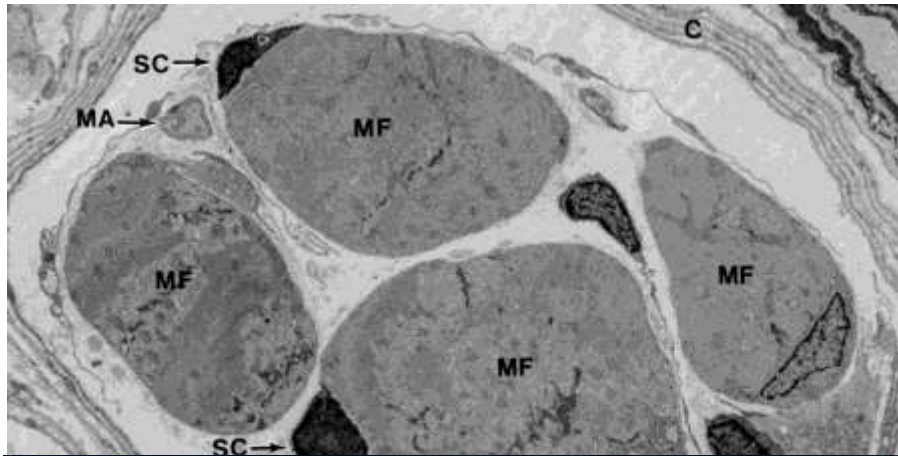
# Biological Tissue Age

... rejuvenation - regeneration - repair



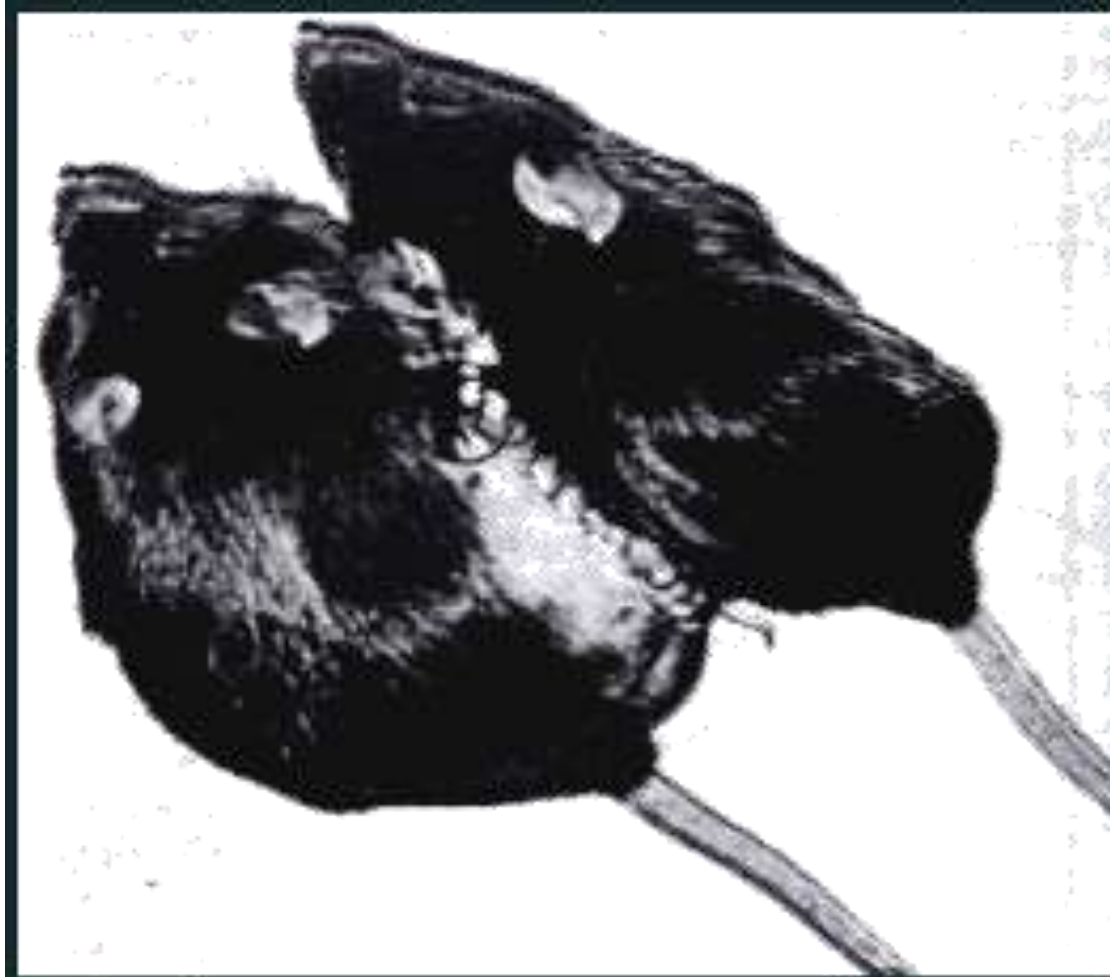
# Muskelstammzellen

## ... Funktionsbeeinträchtigung durch Serumkomponenten



# Parabiose

... „Doppelorganismus“



Haessler HA Ann. NY Acad. Sci. 131: 476-84 (1965)

Generate  
parabiotic mice



Young Young

Injure  
leg muscle



Dry ice



Regenerated  
muscle



Young Old



Regenerated  
muscle



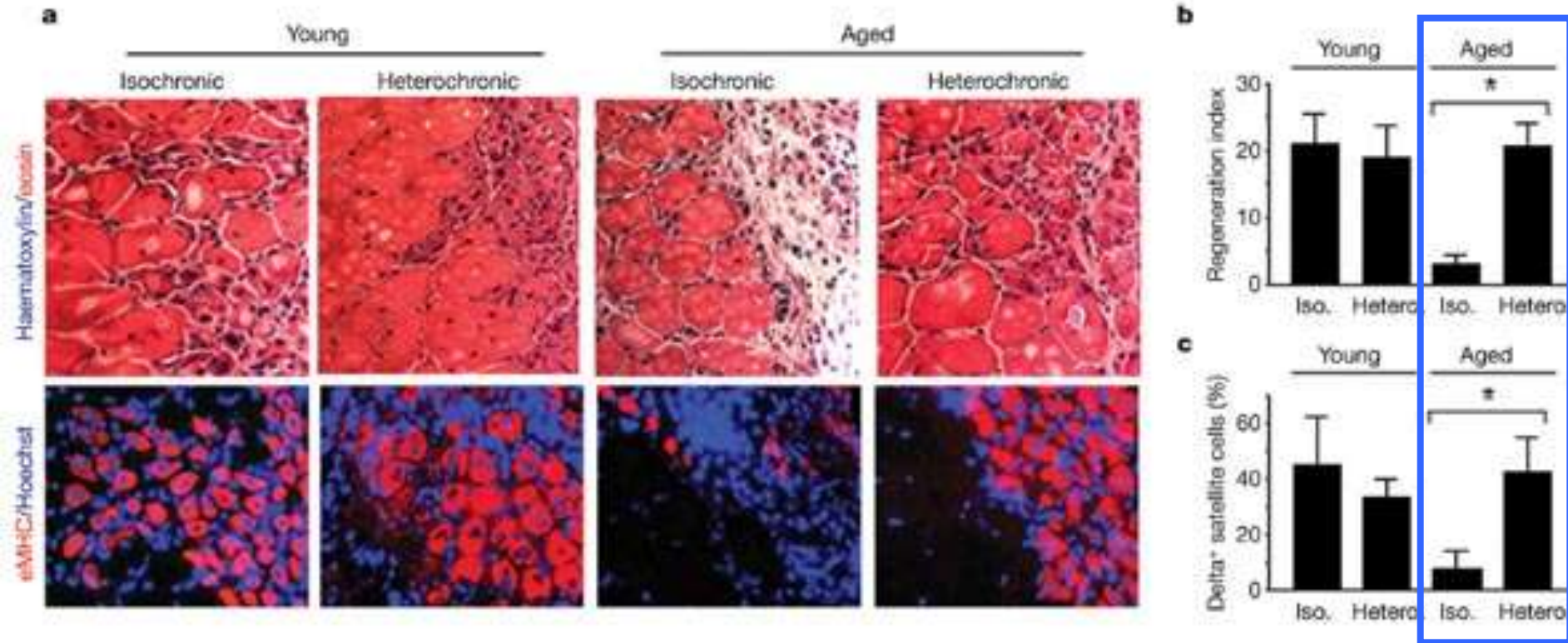
Old Old



Impaired  
regeneration

# Serumbestandteile

## ... Muskelheilung



**Externes Milieu bzw Umweltfaktoren etc**



# Mesenchymal Stem Cell (**MSC**)

Proliferation

Commitment

Lineage  
Progression

Differentiation

Maturation

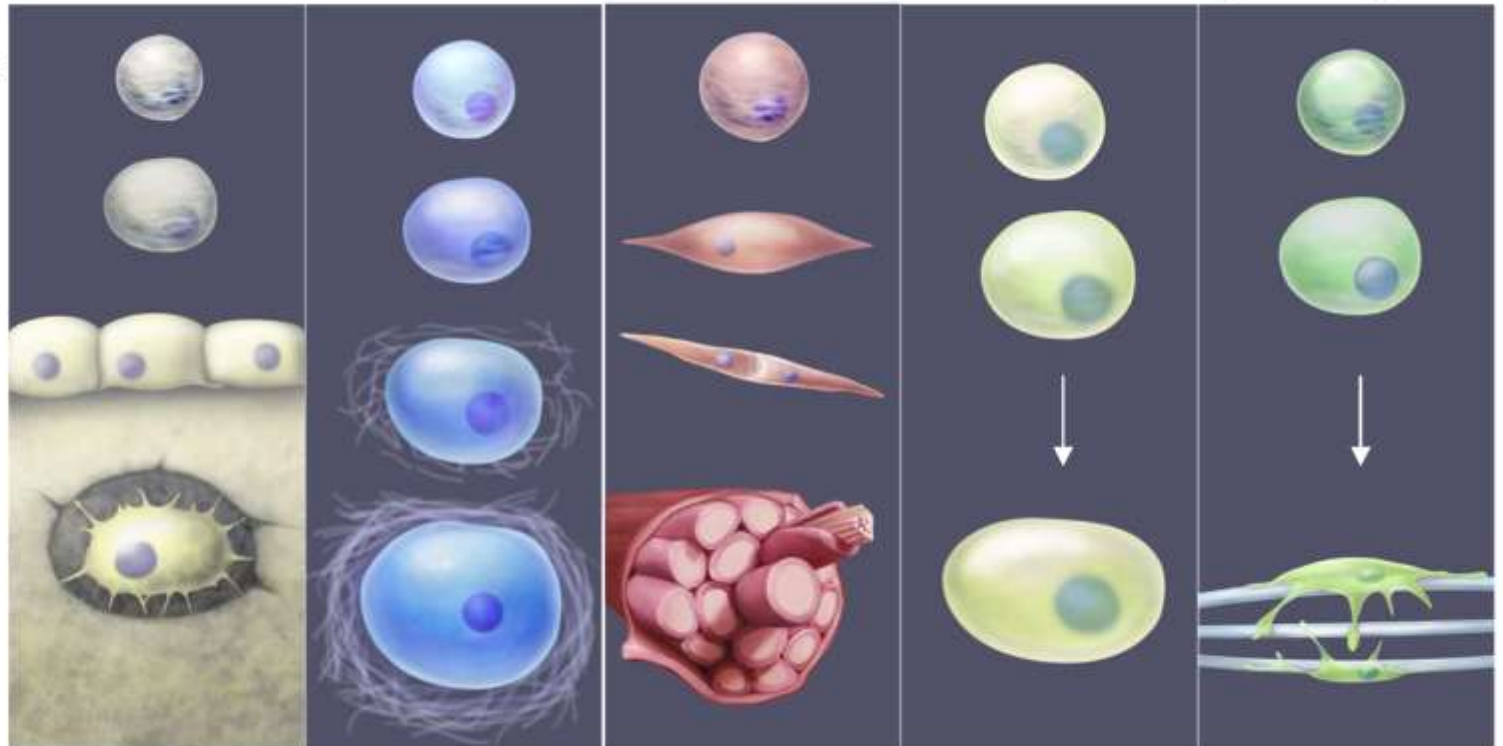
Osteogenesis

Chondrogenesis

Myogenesis

Marrow  
Stroma

Tendogenesis/  
Ligamentogenesis



**Bone**

**Cartilage**

**Muscle**

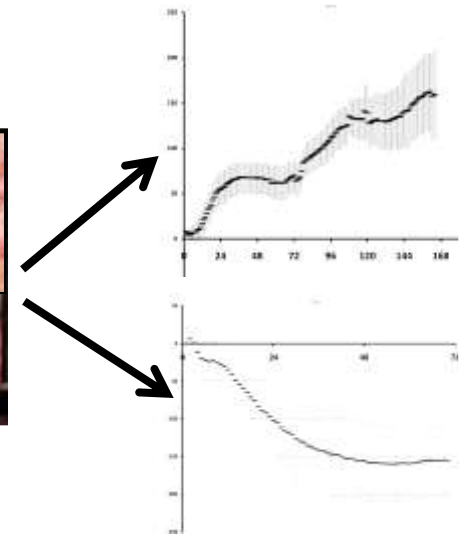
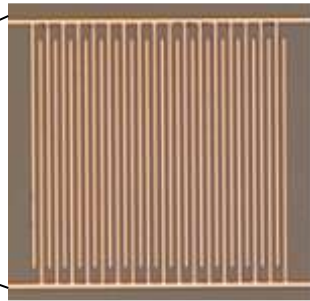
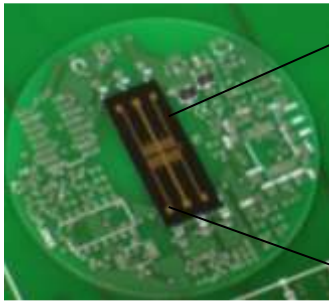
**Marrow**

**Tendon**

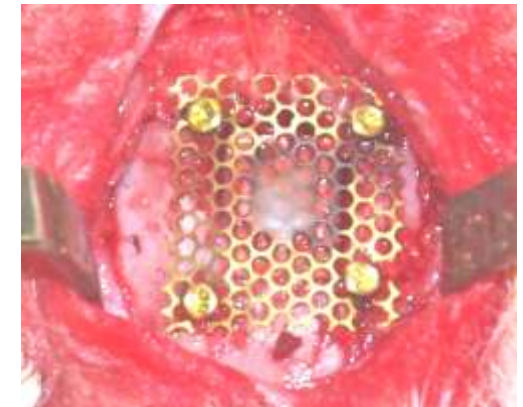
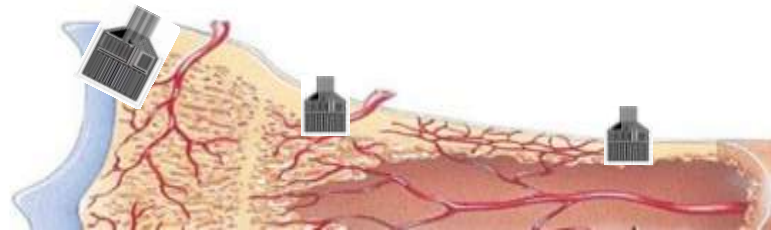
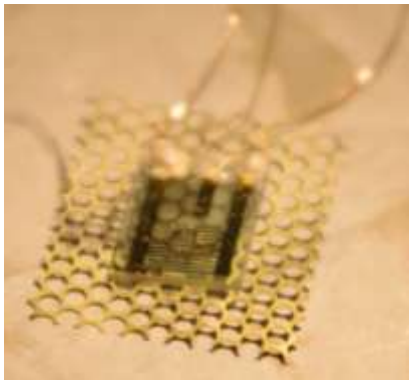
# Age-online Monitoring

... Stem Cell fate / Physiological Fitness

in vitro



in vivo



...

# perception matters



