Miss Marple and the Hidden Secrets of Ageing

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Reinhart and Kirkegaard
Retiring Government
Ageing as a new phenomenon
- US life expectancy

![Graph showing US life expectancy over time, indicating a steady increase from approximately 40 years in 1895 to around 80 years in 2015.](Image)
Hygiene
Decline in death from CVD

Nabel & Braunwald, NEJM 2012
Life expectancy

men

women

Bron: CBS

Bruggink, CBS 2011
‘Geriatric giants’

dementia

depression

proprioceptive, visual, hearing impairment

falls, mobility impairment

incontinence

A NEW DISEASE!
Life expectancy increases = years with diseases.
Ageing

Phantom V

Alpha sud

year
a. 1951
b. 1959
b. 1968

driving
a. 30%

b. 60%
c. 90%

year
a. 1959
b. 1971
b. 1985

driving
a. 3%
b. 15%
c. 30%
Age related diseases/syndroms

Cellular damage

Molecular damage

Stress
Chronological age ≠ biological age

cognition + mobility + social participation

Rowe, Gerontologist, 2007
Senescence

Senescence stimuli

DNA damage foci (DNA-SCARS/TIF)

Heterochromatin foci (SAHF)

SA-Bgal

growth arrest

SASP

Campisi, 2011
Measuring senescence

Senescence stimuli → growth arrest

- SA-Bgal
- p16INK4a
- DNA damage foci (DNA-SCARS/TIF)
- Heterochromatin foci (SAHF)

SASP
Senescence associated ...

Universal aging traits
- Impaired wound healing
- Weak immune system
- Reduced hearing
- Osteoporosis
- Sarcopenia
- Hair graying
- Skin wrinkling
- Poor vision

Age-related diseases
- Alzheimer’s disease
- Parkinson’s disease
- Cataracts
- Macular degeneration
- Glaucoma
- Atherosclerosis
- Hypertension
- IPF
- COPD
- Osteoarthritis
- Type 2 diabetes (obesity, fat dysfunction)
- Cancer
- Treatment-related disability

Naylor et al., Clin Pharm Ther 2013
Senescent cells and medication

Number of medication

<table>
<thead>
<tr>
<th>Level</th>
<th>Number of Medication</th>
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<tbody>
<tr>
<td>low</td>
<td>~1.0</td>
</tr>
<tr>
<td>middle</td>
<td>~1.5</td>
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<tr>
<td>high</td>
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</tbody>
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p = 0.02

‘Senescence load’

Waaijer et al., Aging Cell, 2012
Life expectancy increases = years with diseases.

Heterogeneity at old age, biological age.

Identification of pathways involved in ageing.
Caloric restriction

30% decrease ad libitum feeding without malnutrition (mech via oxidative damage, mitochondrial function)
18 years caloric restriction

= no increase in lifespan
= increase in healthspan → 20% decrease in age associated diseases (DM, CVD, cancer)

Mattison et al., Nature 2012
Heterochronic parabiosis

Regeneration capacity muscle / heart

pre  +  +  +  +  -  -  -

Loffredo et al., Cell 2013, Conboy et al., Nature 2007
Target: senescent cells

Elimination of senescent cells

Aging stopped

Baker et al., Nature 2011
Anno 2030: Applied gerontology = ‘Gero’care

understanding ageing

‘gero’care based on geroscience

prevention of age-related diseases

‘minimal’ prolongation of lifespan,
lifespan = healthspan
Life expectancy increases = years with diseases.

Heterogeneity at old age, biological age.

Identification of pathways involved in ageing.

Holistic approach to antagonize ageing = geroscience.
DON'T BE AFRAID OF CHANGE.