

# Vieillissement du système immunitaire

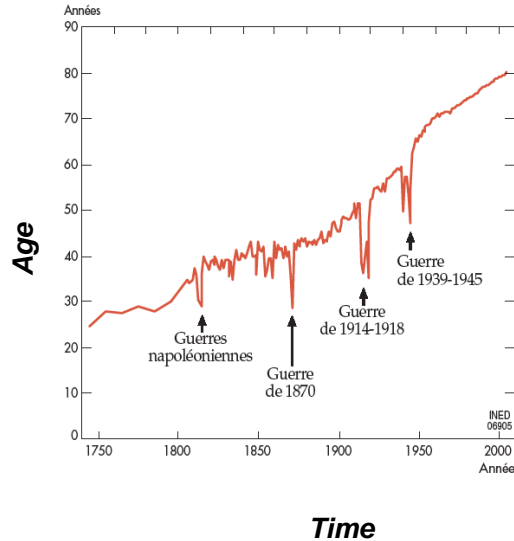
***Victor Appay***

***Team Vulnerability and Ageing of the Immune System***



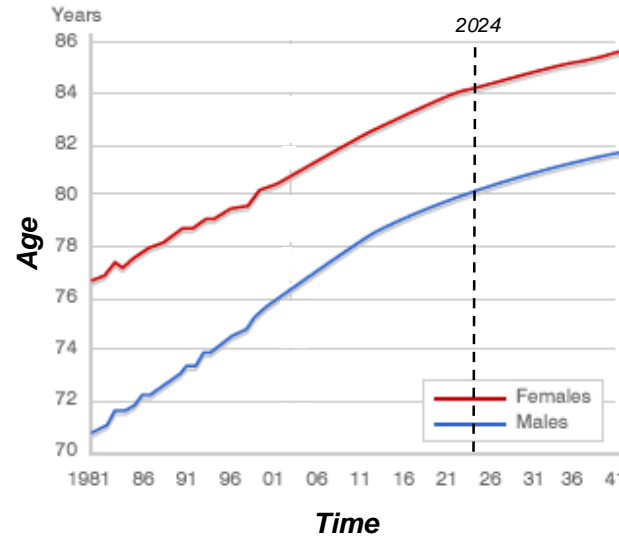
# Changes in life expectancy at birth

## From 1740 to 2004 in Europe

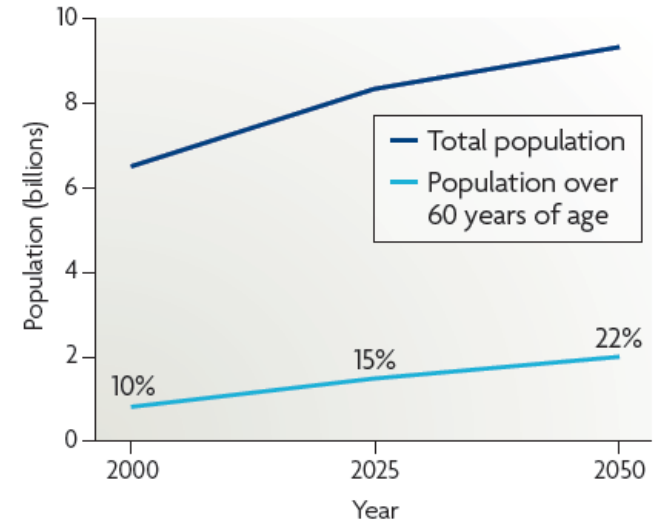


## Some estimates for the years to come ...

### Life expectancy



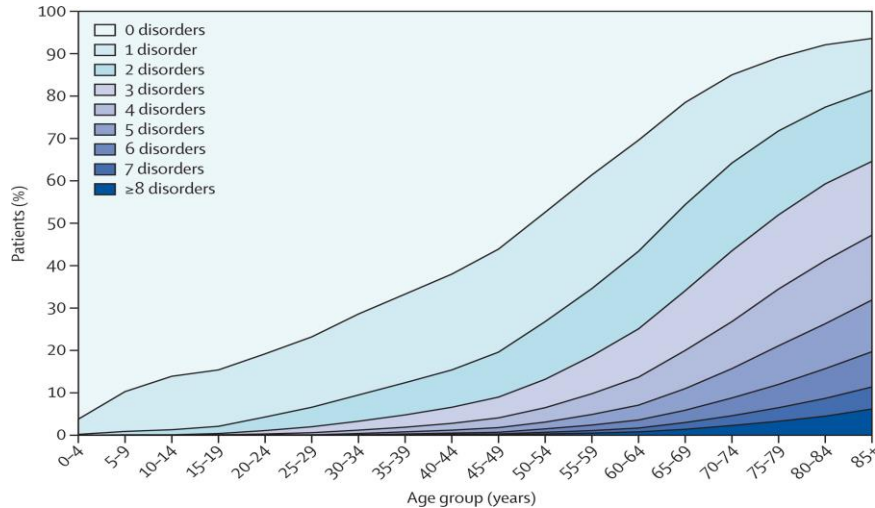
### The world population



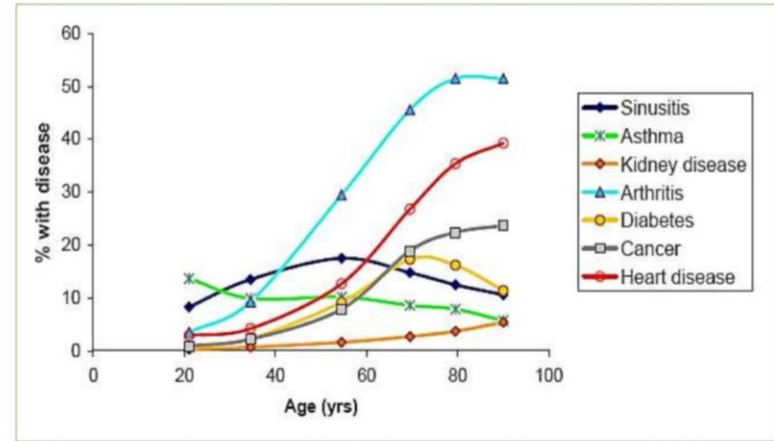
Adapted from Dorshkind et al, Nat Rev Imm, 2009

# Problem: the quality of life

## Increased number of chronic disorders with age



Barnett et al, The Lancet, 2012



Prevalence of selected chronic conditions, expressed in percentages, as a function of age for the US population (2002-2012 dataset). All forms of cancer and heart disease are featured. Source: CDC/NCHS, National Vital Statistics System, Mortality

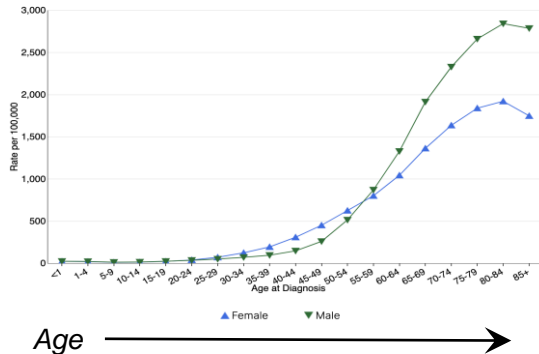
***Role of inflammation ... immune system...?***

# OLDER PEOPLE

## *Vulnerability to malignant and emerging infectious diseases and reduced vaccine efficacy*

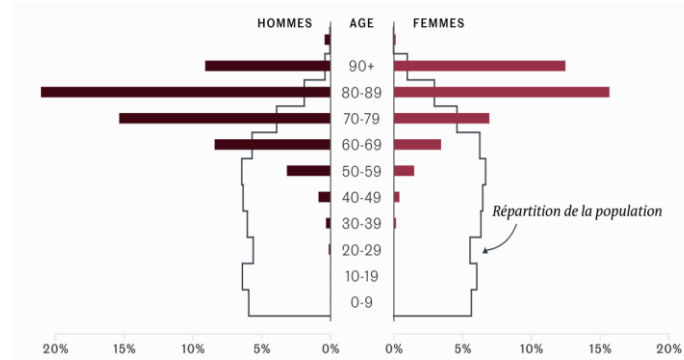
### Cancer:

Rate of death according to age and gender in the US



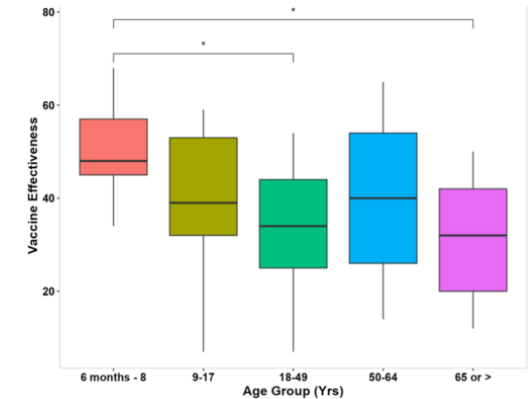
### COVID-19:

Percentages of death according to age and gender in France



### Influenza:

Vaccine effectiveness by age for Influenza A/B viruses between 2011-2020 in the US

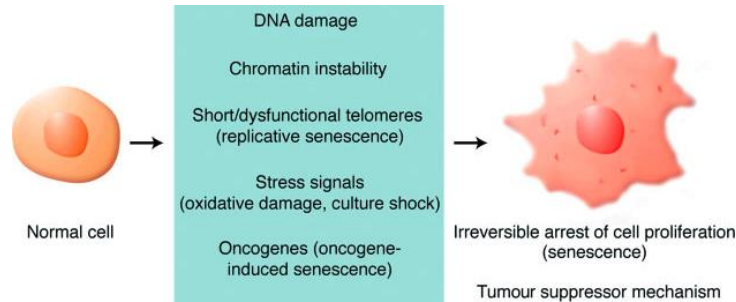


***Role of ageing related immune alterations?***

# What is "immunosenescence" / immune ageing?

**= *Alteration of the immune system competence with time / age***

## Immune ageing $\neq$ Cellular senescence

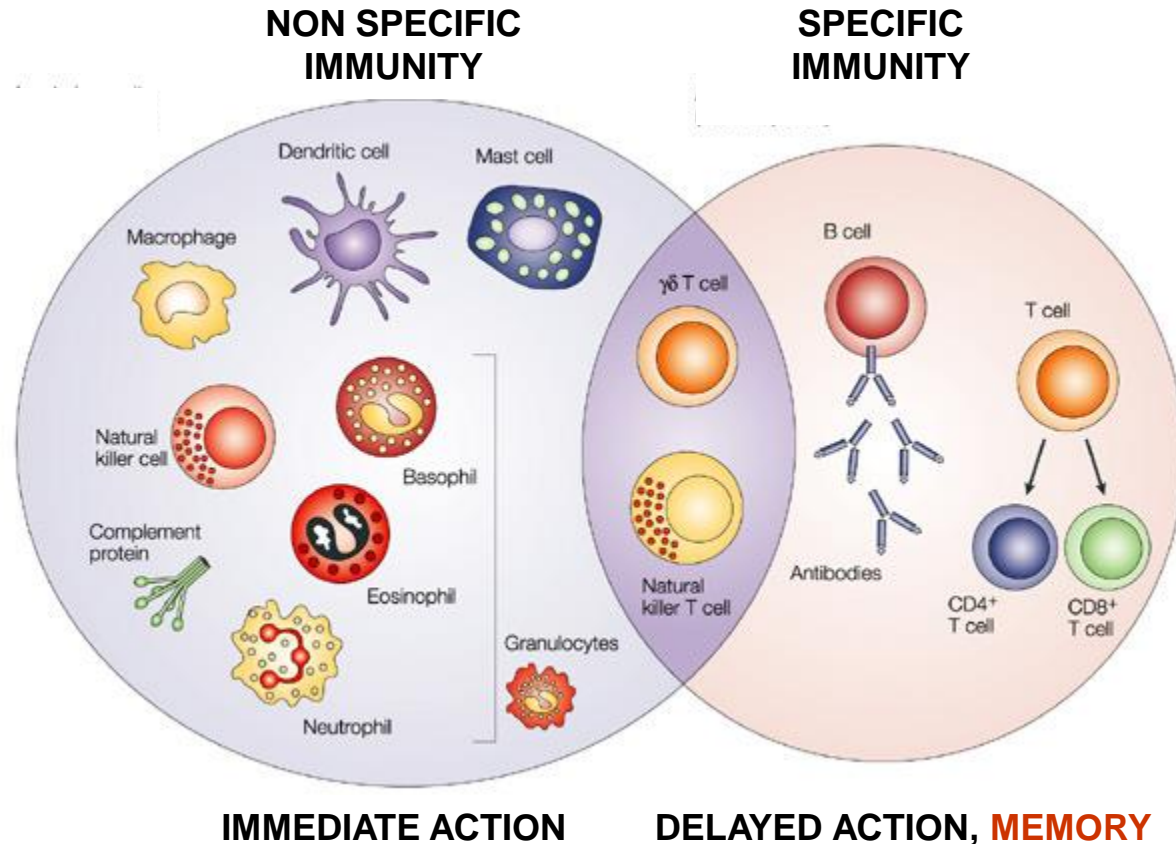


**=> Immune ageing**

**= *Changes of quantity, distribution, phenotype and function of cells (and organs) of the immune system associated to advanced age***

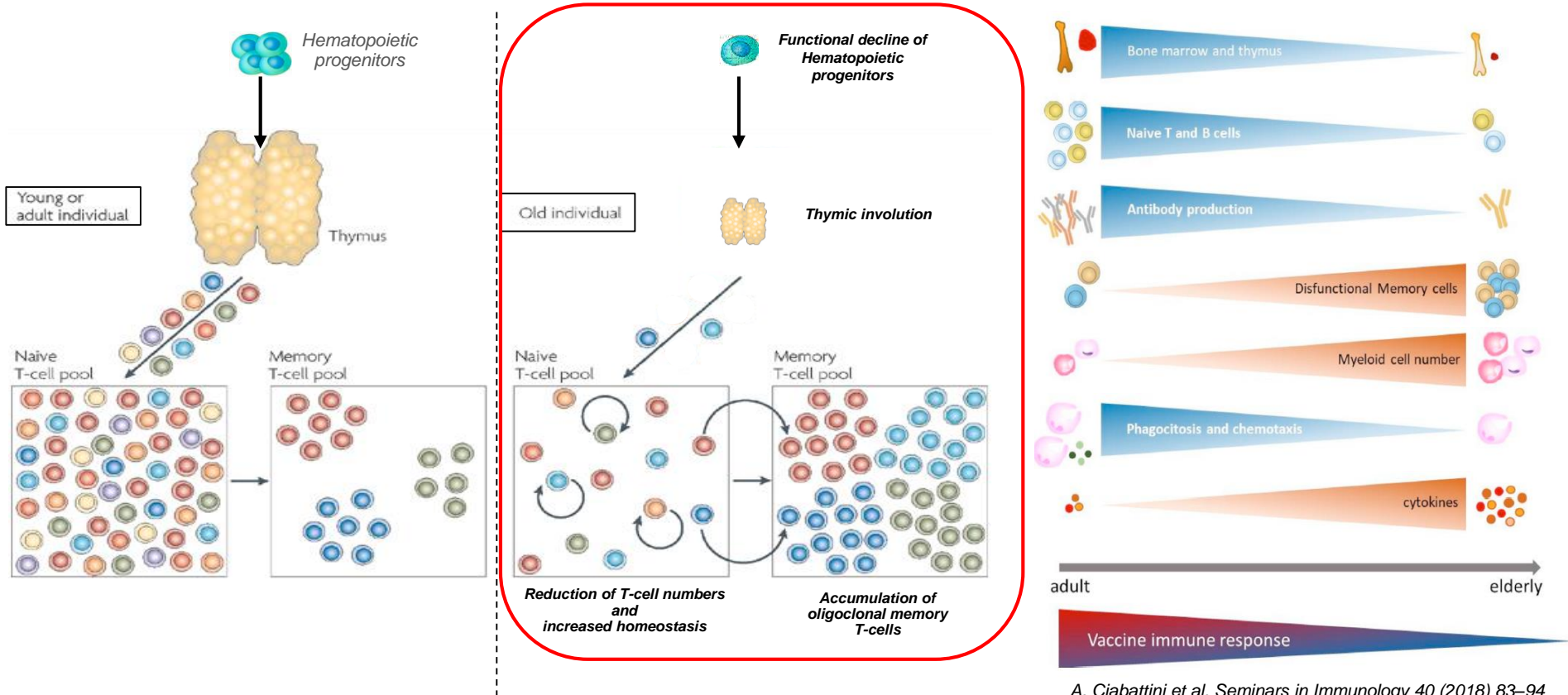
**=> Biological age**

# Immunocompetent cells



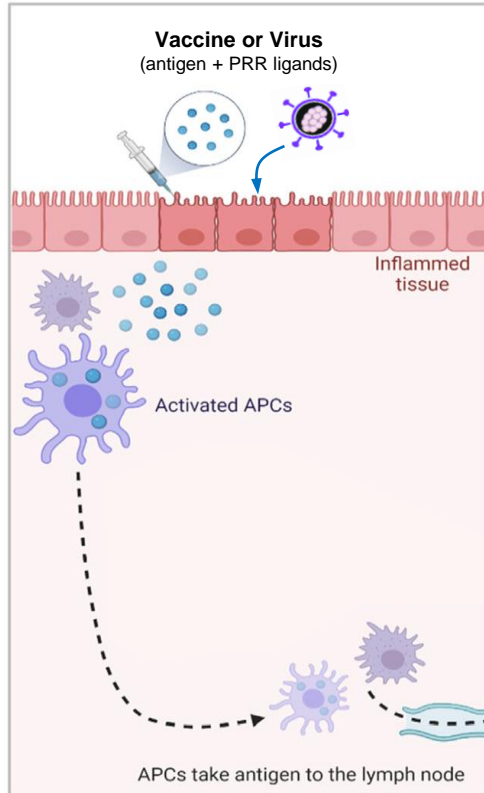
=> ALL CELLS OF THE IMMUNE SYSTEM ARE EFFECTED WITH AGE!

# Immune alterations associated with age

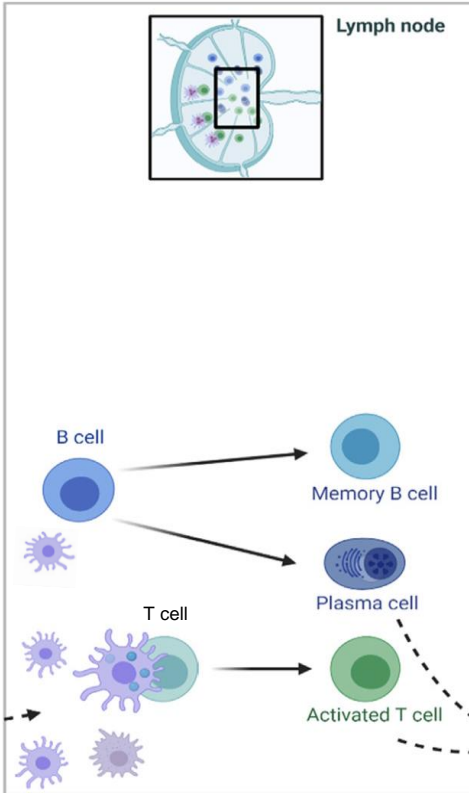


# Consequences of ageing on immune responsiveness

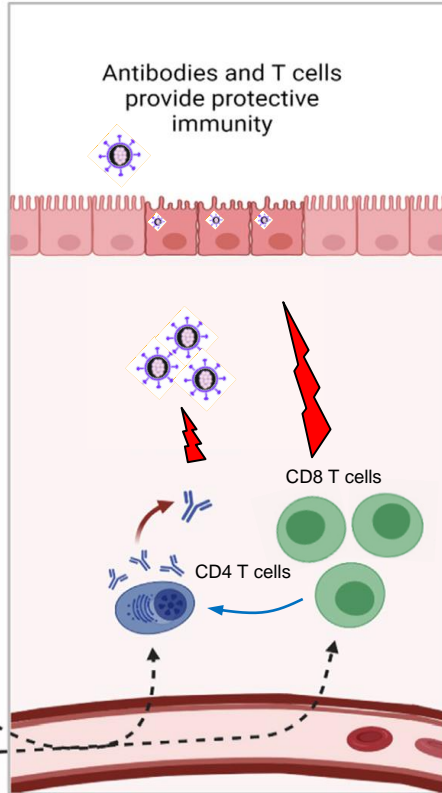
## ① Activation of APCs and draining to DLN



## ② T and B cell priming in the DLN



## ③ Adaptive immunity

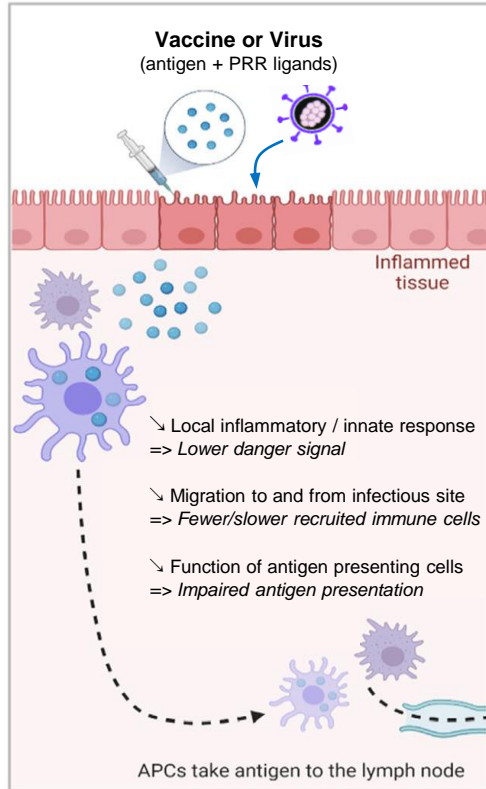


Adapted from Bell and Kutzler, *Advanced Drug Delivery Reviews*, 2022

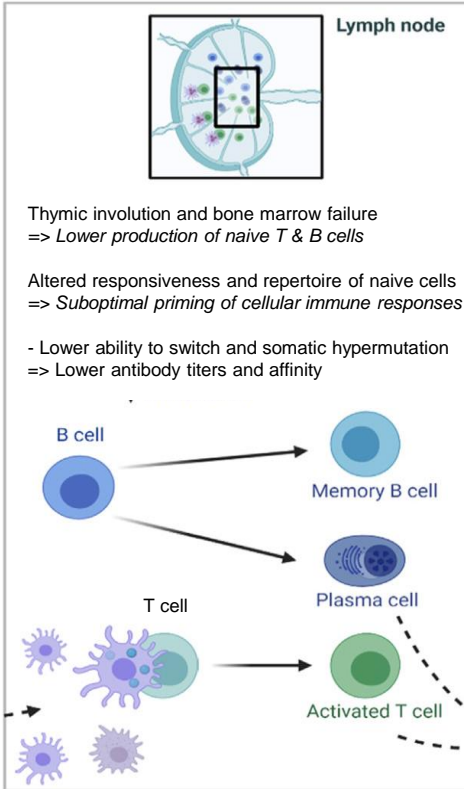


# Consequences of ageing on immune responsiveness

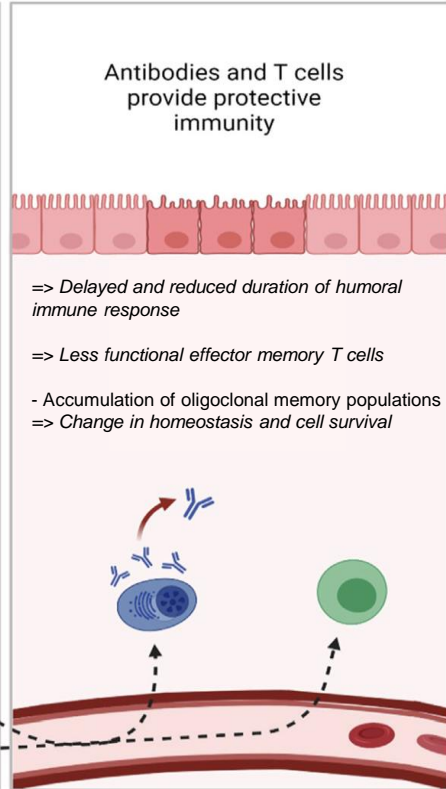
## ① Activation of APCs and draining to DLN



## ② T and B cell priming in the DLN



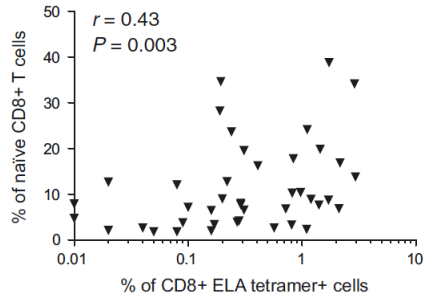
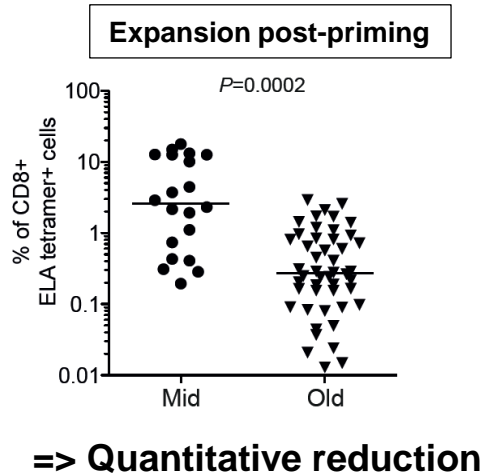
## ③ Adaptive immunity



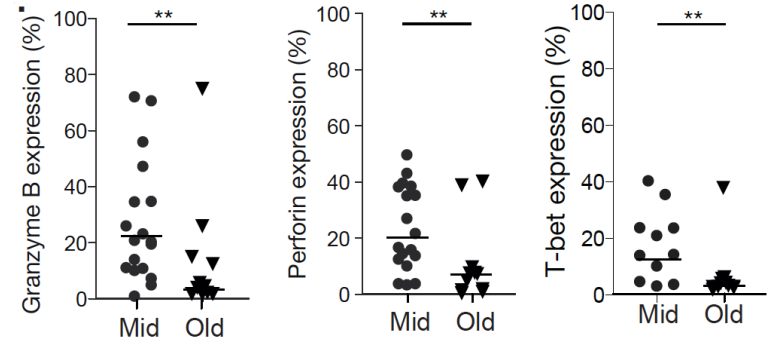
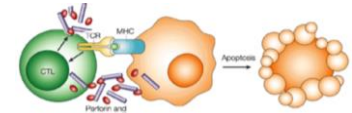
=> Reduced protection

# Reduced naive CD8<sup>+</sup> T cell priming efficacy in older people

In vitro priming of antigen specific CD8<sup>+</sup> T cell in older (>70y) vs middle aged people



**Cytotoxic factors**  
(Granzyme B, Perforin, T-bet)

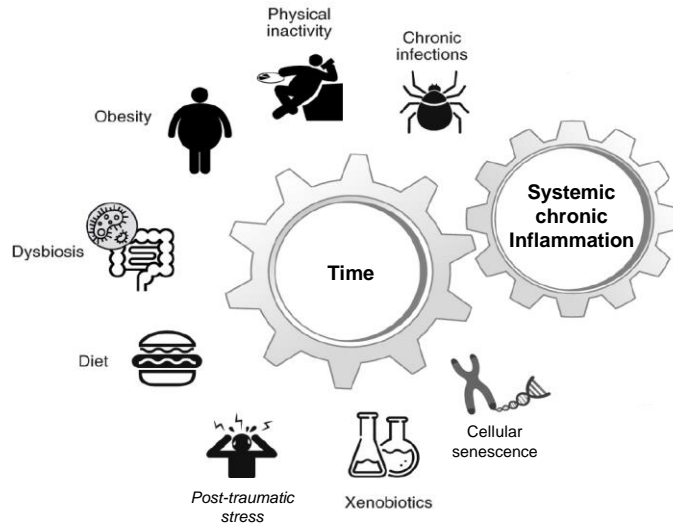


**=> Qualitative reduction (functional capacity)  
of CD8<sup>+</sup> T cell priming efficacy**

**=> Reduced *de novo* T responsiveness  
with old age**

# Hyper-Inflammatory status with advanced age

- Increase in serum or tissue levels of inflammatory cytokines with age:  
IL-6, IL-1b, TNF, PGE2, acute phase proteins

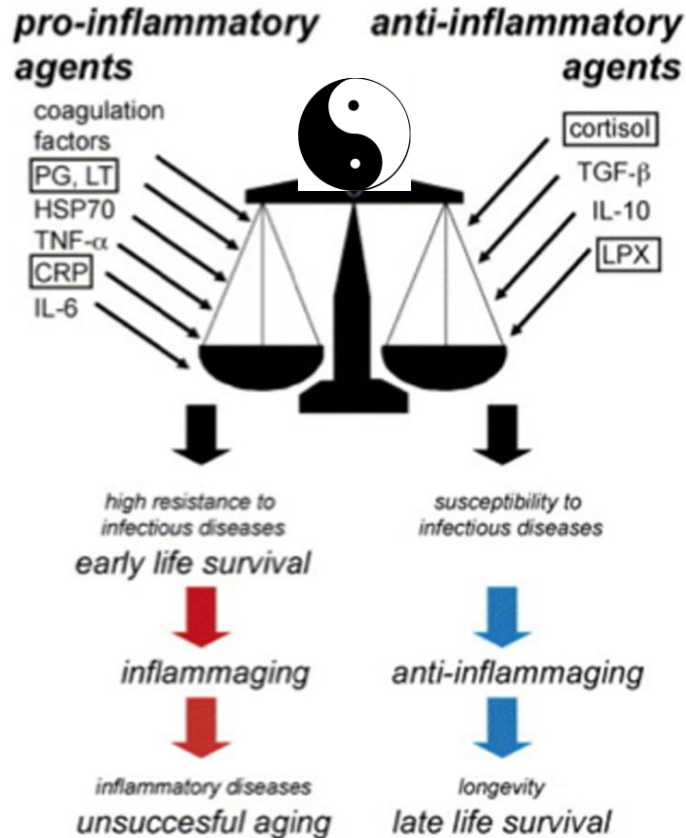


Adpated from Furman et al, Nat Med, 2019

**=> Increased risk and severity of inflammatory diseases**

**= Inflamm-ageing**

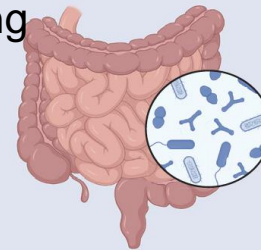
# Healthy ageing: the right inflammatory balance



## Causes of inflammation

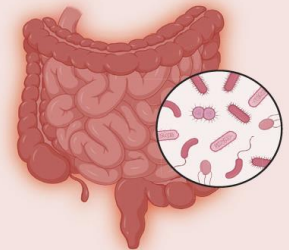
- Comorbidities
- Persistent viral infections
- Senescent cells (SASP)
- Gut dysbiosis

Young



- ↓ Gut inflammation
- ↑ Short chain fatty acids
- ↑ Microbial diversity
- ↑ Bile acids
- ↑ Beneficial microbes

Old



- ↑ Gut inflammation
- ↓ Short chain fatty acids
- ↓ Microbial diversity
- ↓ Bile acids
- ↓ Beneficial microbes

# How to improve immunity in older people?



**Anti-aging medicine...**

- e.g. extract / inducer of telomerase
- Resveratrol (Red wine)
- Caloric restriction



**+ Meditation...**

**+ Physical activity**

