



**GOUVERNEMENT**

*Liberté  
Égalité  
Fraternité*



# IHU HealthAge 1st SAB

## September 5-7, 2024

**T-cell program**

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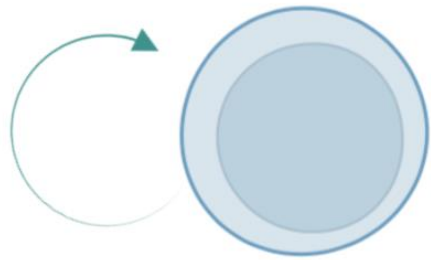
Toulouse Institute for Infectious and Inflammatory Diseases  
Infinity



# T-cell immunosenescence

- **At the organism level:** Involution of primary lymphoid organs & environmental stimuli lead to memory inflation within the T-cell compartment
- **At the cellular level:** Ageing leads to cellular senescence, participating in inflammaging through acquisition of the SASP phenotype

## Physiological immunosenescence

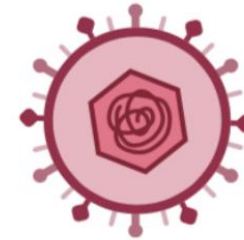


Reduced self-renewal capacity from HSC



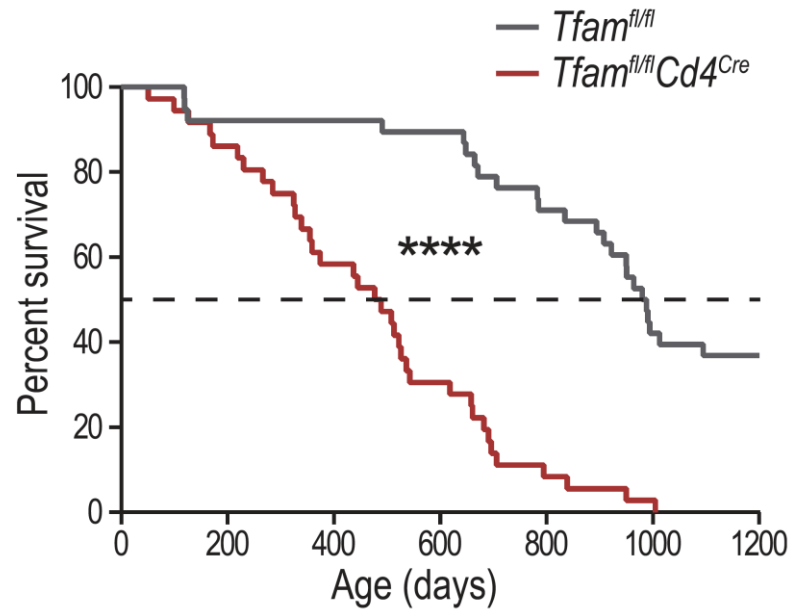
Thymic involution leading to decreased naïve T cells output

## Accelerated immunosenescence



Chronic antigenic stimulation from persistent viruses

# T-cells with dysfunctional mitochondria induce multimorbidity & premature senescence



**T-cell dysfunction is sufficient to induce premature whole body aging**



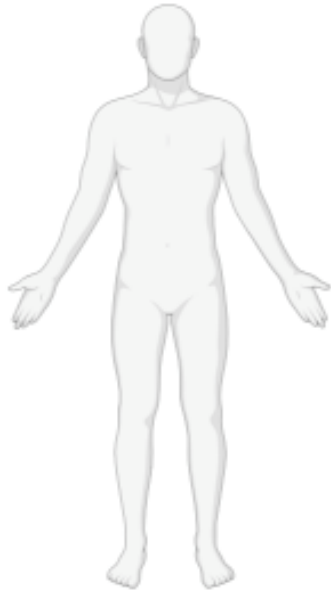
- **Energy metabolism of T-cells might serve as an early warning of failing health, functional decline and aging**
- **An aging clock based on T-cell parameters ?**

**T-cell dysfunction leads to premature death**

# T-Clock, an aging clock based on T-cell parameters



## *INSPIRE-T cohort*



**1000 individuals aged from  
20 to 100 years old**



### Clinical datas

- Frailty score
- Morbidity



### Biobank

- PBMCs
- 1 sample/year/individual
- T cell phenotyping (26 parameters)  
heterogeneity/function/senescence

Guyonnet S et al. J Frailty Aging 2021

# From in-depth exploration of basic mechanisms to rejuvenation



- A comprehensive analysis will be performed to evaluate T-cell phenotype, function, signaling activity, metabolic status, and transcriptional and epigenetic profiles.
- This data will be integrated and examined in the context of each subject's resilience capacity.
- Molecular markers in T-cells that can predict hyper- versus hypo-resilience responses will be identified and validated experimentally. Furthermore, the most promising T-cell pathways for drug development will be evaluated for their therapeutic potential in preclinical studies using primary human T-cells and murine models.