





## IHU HealthAge 1<sup>st</sup> SAB

### September 5-7, 2024

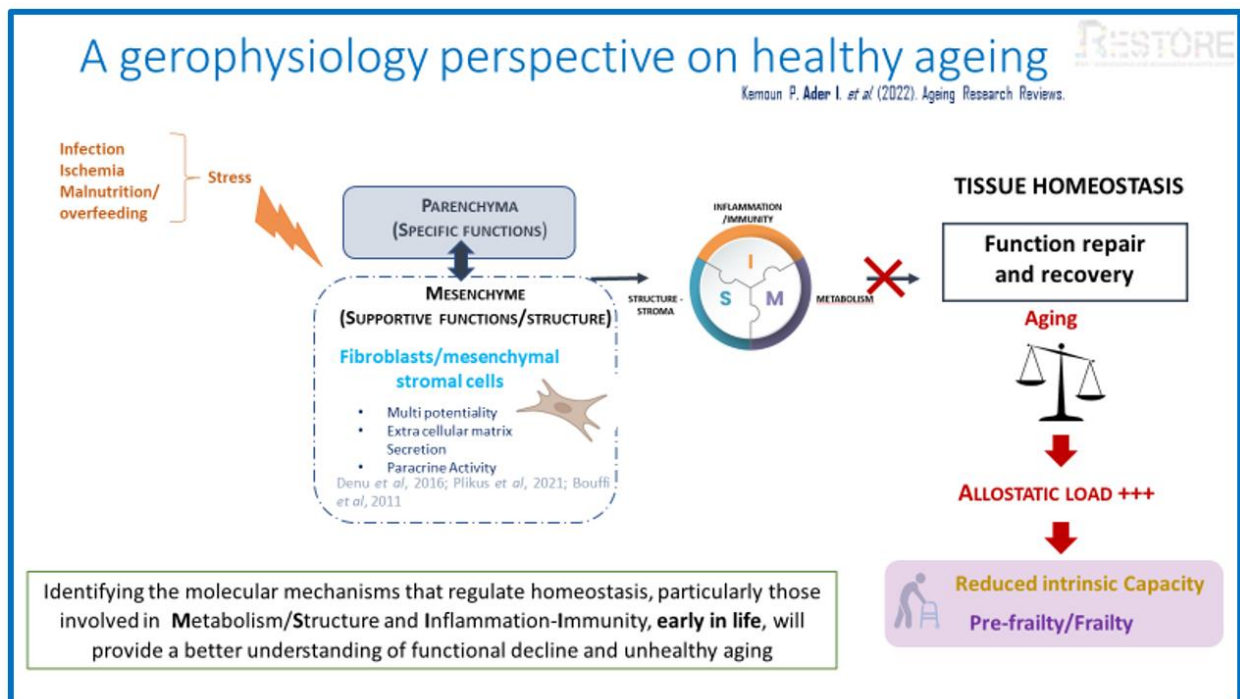
#### MULTISCALE APPROACH ON INSPIRE-T COHORT TO IDENTIFY HEALTH MARKERS

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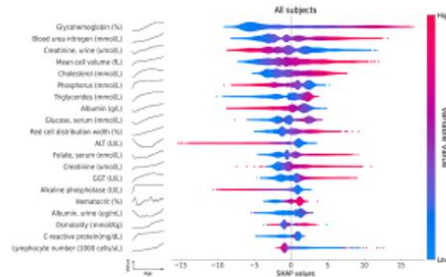




## Hypothesis: Energy metabolism predicts and regulates age-related functional decline ?

### Energy metabolism predicts physiological age

- ✓ Prediction of physiological age, chronic disease and mortality by machine learning (PPA) (NHANES cohort, 60,000 individuals, 20 years of follow-up)



- ✓ 26 routinely dosable metabolic variables predict physiological age, chronic disease and mortality

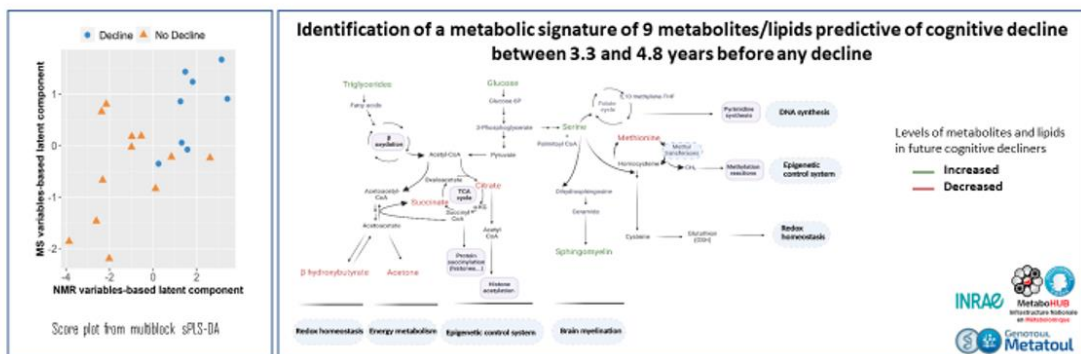
- I Ader, L. Penicaud, P. Kemoun, D. Bernard, E. Doumard, P. Monsarrat, L. Castella. A method for determining a physiological age of a subject. PATENT: Ep N°22305353  
 - Bernard D\*, Doumard E\*, Ader I et al/ Explainable machine learning framework to predict personalized physiological aging. Aging Cell. 2023



## A metabolic signature may predict cognitive decline

Multimodal metabolomics of blood samples from amyloid-positive individuals, **before any signs of cognitive decline**, to predict those who progressed to cognitive decline from those who remained intact (MMSE follow up over a period 3 to 5 years)

- Multi-metabolomics (NMR and Mass Spectrometry): 2 independent data sets, 392 metabolites.
- Integration of data from the 2 data sets.



- Tremblay-Franco M, Canlet C, Carrière A, Nakhle J ... Ader I. Integrative multi-modal metabolomics to early predict cognitive decline among Amyloid positive community-dwelling older adults. *J Gerontol A Biol Sci Med Sci.* 2024  
 - Ader I, Vellas B, Castella L, Tremblay-Franco M, Canlet C. PATENT: EP 23 306 392.4. Methods for predicting cognitive decline.



# Healthy aging biomarkers: the INSPIRE's contribution

Ader I et al, J Frailty Aging, 2021



- ✓ More than 1000 volunteers 20-103 years old
- ✓ Follow-up: 10 years
- ✓ Clinical data (eCRF): 1551 variables
- ✓ 5 functions to monitor health status



Kemoun P, Ader I et al, Ageing Research Reviews, 2022

## Our Project

**1-Systemic scale (plasma)** : To determine a map of energetic metabolism associated with functional decline and intrinsic capacity



**2-Cell scale (dermal fibroblasts from skin biopsies)**: Identifying health markers, molecular targets and understanding mechanisms associated with age and intrinsic capacity



RESTORE