



**GOUVERNEMENT**

*Liberté  
Égalité  
Fraternité*



## **INSPIRE-T HealthAge Extension**

Sophie GUYONNET

IHU HealthAge, Gérontopole CHU  
Toulouse, UMR 1295 Axe Mainten



## INSPIRE-T HealthAge >>> specific aims

- **To build a unique Geroscience human bioresources platform** gathering biological, clinical and digital data from 1000 individuals of several chronological ages (from 20 y with no upper limit of ages) and functional capacity levels (from robust to prefrail and frail) over a 10-year follow-up
- To establish **natural trajectories of IC and their link to multi-organ function and biology of aging**, and the interaction with lifestyle behaviors
- To contribute to the **validation of new aging biomarkers related to IC** and therapeutic targets
- **To promote innovative science** (and perform discovery science) by maximizing access to the data to academic and industry researchers

# INSPIRE-T HealthAge >>> update of recruitment and follow-up

- **First 1000 participants are recruited between October 2019 and December 2021** (recruitment from the community in Toulouse area)
- **Exclusion** of people having
  - Severe disease compromising life expectancy at 5 years (or at 2 years for frail older subjects and those aged 80 years or older)
  - Or legally incapable (administrative or judicial decision or under guardianship)
- **Participants are stratified into 10-year age groups**, with oversampling of people older than 70 years
- **Recruitment remains open** to compensate drop-out and keep a minimum pool of 1000 participants, and include population that would have low representability

# INSPIRE-T HealthAge >>> update of recruitment and follow-up

## Recruitment by 10-y age groups, n=1116

**N= 1116 (August 16<sup>th</sup>)**

women: n= 692 (62.0%)

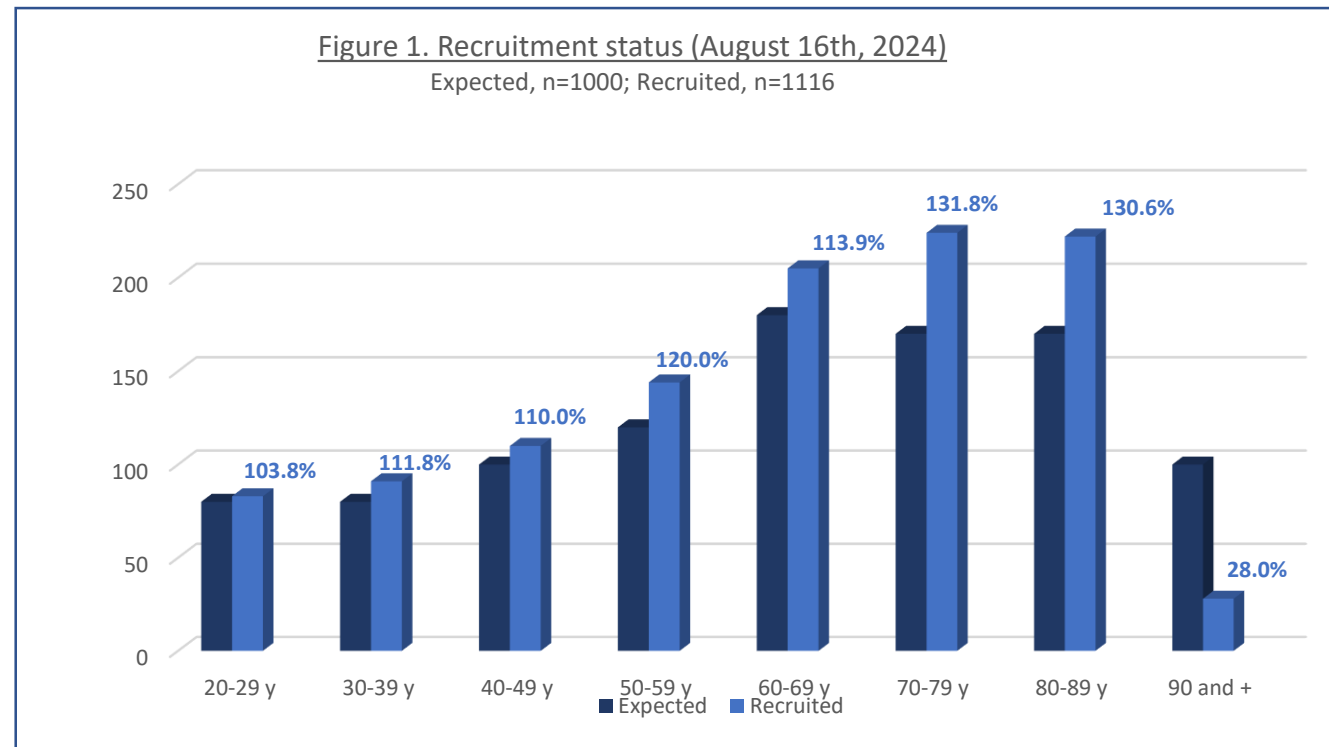
≥ 70 y : n= 483 (43.3%)

≥ 80 y: n=258 (23.1 %)

robust: n=696 (62.2 %)

prefrail: n=347 (31.1 %)

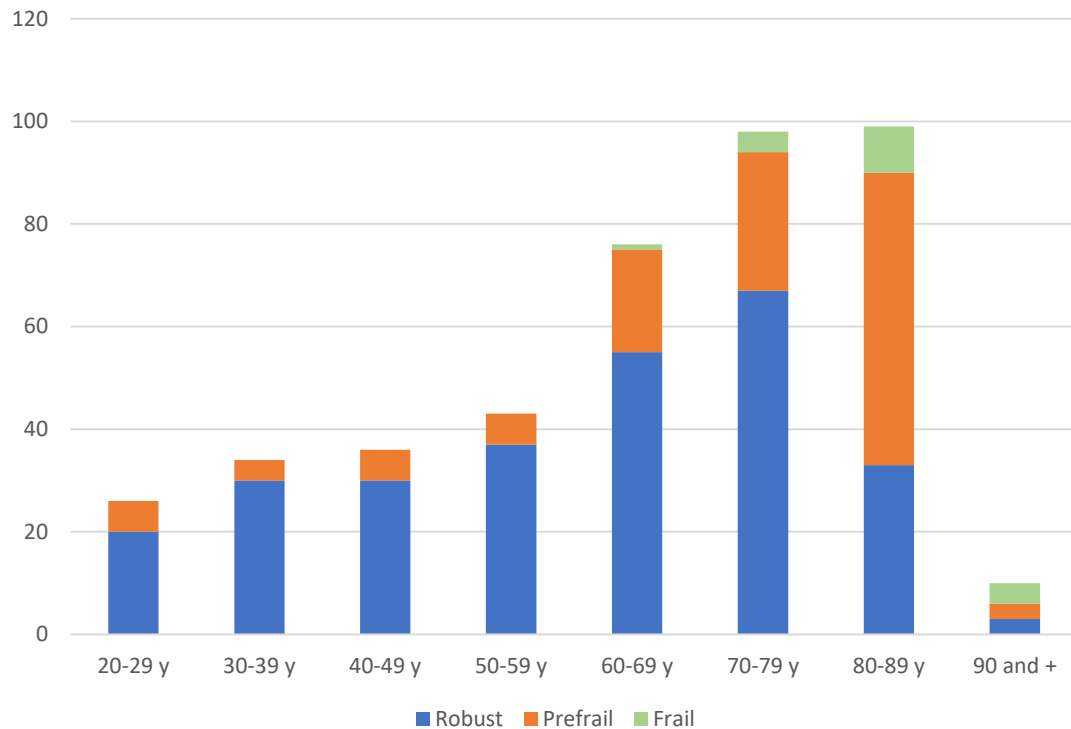
frail: n=64 (5.7 %)



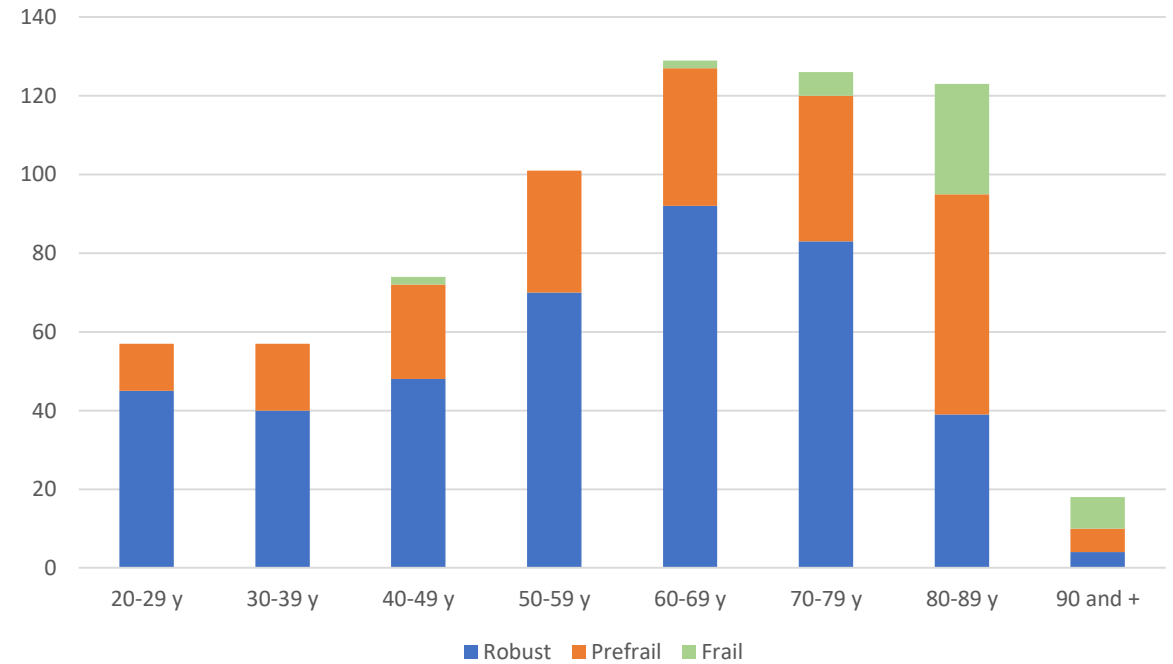
# INSPIRE-T HealthAge >>> update of recruitment and follow-up

## Age and Frailty Status of INSPIRE-T at baseline by gender, n=1116

Men, n=424

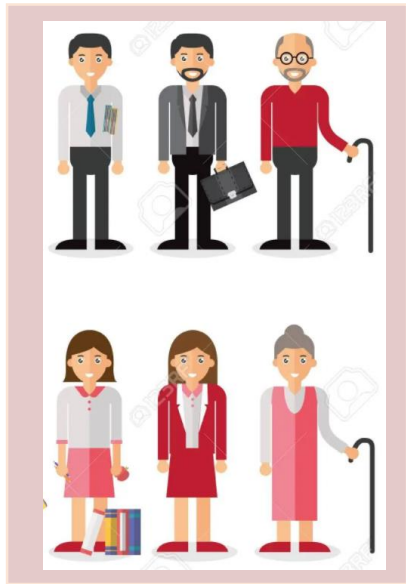


Women, n=692



# INSPIRE-T HealthAge >>> update of recruitment and follow-up

## INSPIRE-T



**1116 volunteers, monocentric,  
20 – 100 and +,10 y follow-up**  
(first volunteer recruited on October 2019)



**Annual visits**  
**CRC (Research facility)**  
**Home (mobile hospital team)**

### **Clinical Data**

Functions (WHO ICOPE Program), current health state (vaccination, incident diseases, medication), lifestyle, socioeconomic factors, body composition (DEXA)

### **Biospecimens (biobanking)**

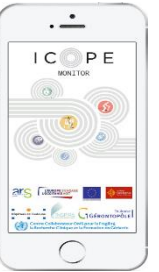
Blood (PBMC), urine, saliva, dental plaque  
Superficial skin, skin biopsies, stool, hair

### **Additional investigations (sub-samples)**

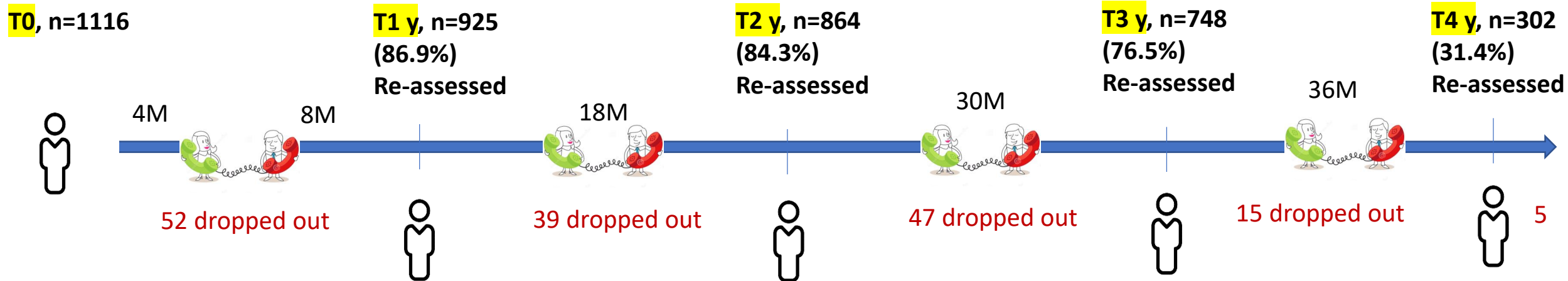
Whole body\*/brain MRI (n=120, baseline);  
Oxygen consumption test (VO2 max), Muscle strength test (n=340, baseline)



**Functions monitoring**  
**(Appl. ICOPE Monitor)**  
**every 6-month**



# INSPIRE-T HealthAge >>> follow-up visits



**958 ALWAYS INVOLVED**  
(134 dropped-out + 24 death since 2019)

**RETENTION STRATEGIES +++**

# INSPIRE-T HealthAge >>> accomplishments (1) - Biomarkers

## Exploring hallmarks of aging (whole population, baseline)

HALLMARKS	Elements	Elements	Elements	Elements
Epigenetics	DNA Methylation	microRNA	Histone modification	Transposable
Stem Cells	Proliferation	Plasticity		
Inflammation	Adaptive immune	Senescence	Resident macrophages	Cell-signaling
Metabolism	Mitochondria	Nutrient Sensing	Circadian	
Quality control	DNA repair	Telomeres	Proteostasis	Autophagy
Plasticity	Stress response	Resilience		



C. Lopez-Otin et al. Cell 153, June 6, 2013

**Metabolic footprint**  
Isabelle Ader, Restore,  
Toulouse

**Epigenetic clock (Horvath,  
Hannum, Levine, GrimAge)**  
JM Lemaitre, IRMB, Montpellier

**Inflammatory aging clock**  
David Furman, Buck  
Institute, US

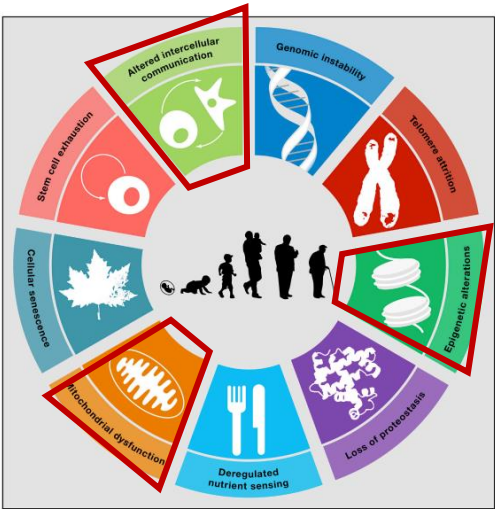
**Mitochondrial dysfunction (Scenith)**  
L Martinez, I. El Costa, I2MC & INFINITY,  
Toulouse



# INSPIRE-T HealthAge >>> accomplishments (1) - Biomarkers

## Exploring hallmarks of aging (whole population, baseline)

HALLMARKS	Elements	Elements	Elements	Elements
Epigenetics	DNA Methylation	microRNA	Histone modification	Transposable
Stem Cells	Proliferation	Plasticity		
Inflammation	Adaptive immune	Senescence	Resident macrophages	Cell-signaling
Metabolism	Mitochondria	Nutrient Sensing	Circadian	
Quality control	DNA repair	Telomeres	Proteostasis	Autophagy
Plasticity	Stress response	Resilience		



C. Lopez-Otin et al. Cell 153, June 6, 2013

### Metabolic footprint

Isabelle A  
To

### Epigenetic clock (Horvath, Hannum, Levine, GrimAge)

emaitre, IRMB, Montpellier

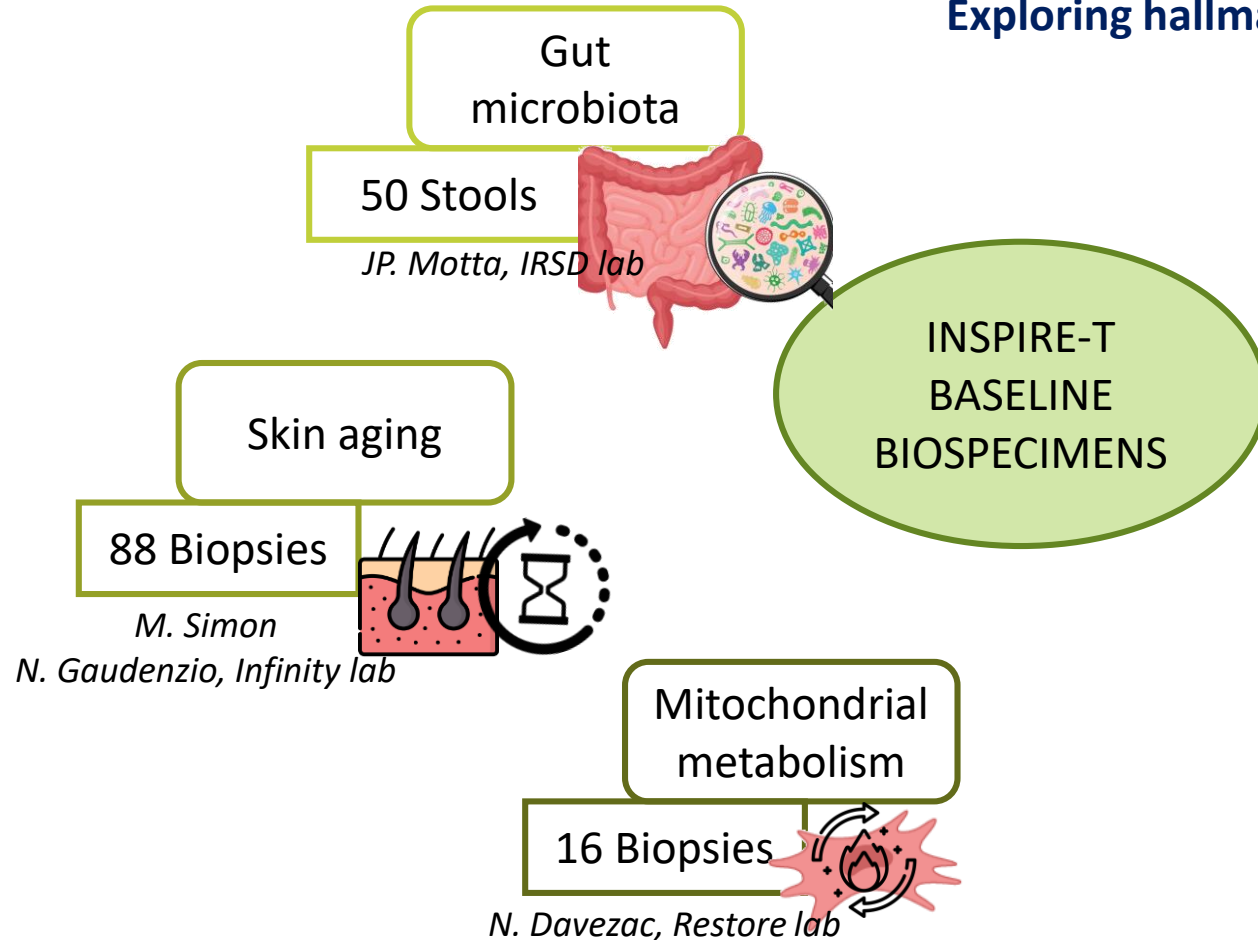
**NEXT : CELLULAR SENESENCE**  
(Nathan Lebrasseur, Paul F Glenn  
Center for the Biology of Aging  
Research, Mayo Clinic) – 28  
candidate SASP biomarkers

**Inflammatory aging clock**  
David Furman, Buck  
Institute, US

scenith)  
INFINITY,

# INSPIRE-T HealthAge >>> accomplishments (1) - Biomarkers

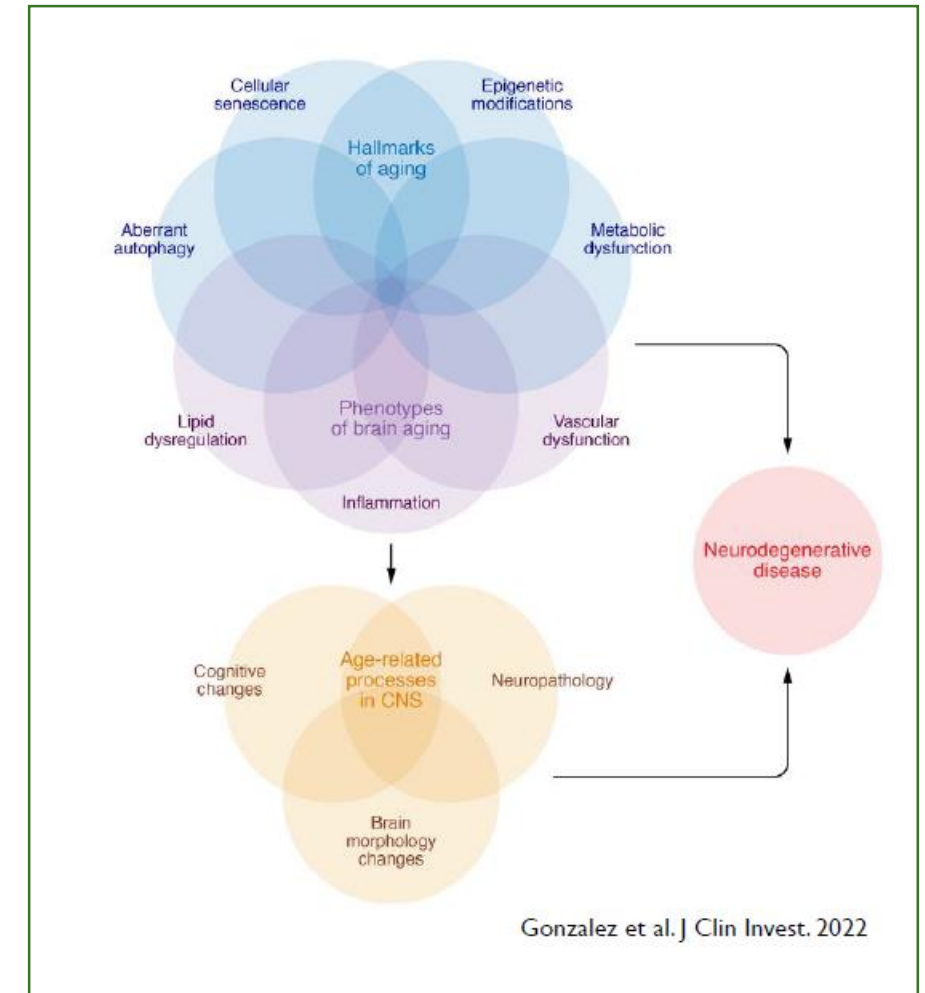
Exploring hallmarks of aging (subsamples, baseline)



# INSPIRE-T HealthAge >>> accomplishments (1) - Biomarkers

## Linking Aging Biology with Brain Health (whole population, baseline)

- Assessment of Phospho-Tau 217, Nfl, GFAP (Lumipulse, Fujeribio) in the whole population at baseline
- Collaboration with Oskar Hansson (Sweden)



# INSPIRE-T HealthAge >>> accomplishments (1) - Biomarkers

ALL PARTICIPANTS	
Total Cholesterol, HDL, LDL	Baseline
IF1	Baseline
Apo Isoforms (Apo A1, A2, A4 ApoD, apoH, ApoJ, ApoL1, ApoM, ApoA ApoB100, ApoE phenotypes)	Baseline

SUBSAMPLES	
Immune profile by Scenith (Single Cell ENergetic metabolism by profiling Translation inHibition) Technology T Cells subsets (CD8, CD4 Th, CD4 Treg, CD25, CD57) Translation level, Mitochondrial dependence, FAAO capacity, PD1, HLADR, Mitochondrial IF-1	Baseline



# INSPIRE-T HealthAge >>> accomplishments (2) - Publications

*The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences*, 2024, **79**(7), glae112  
<https://doi.org/10.1093/gerona/glae112>  
Advance access publication 27 April 2024

Research Article



## Predictive Capacity of the Integrated Care for Older People Screening Tool for Intrinsic Capacity Impairments: Results From the INSPIRE-T Cohort

Kelly Virecoulon Giudici, PhD,<sup>1,\*</sup>  Philippe de Souto Barreto, PhD,<sup>1,2</sup> Sophie Guyonnet, PhD,<sup>1,2</sup> John R. Beard, MD, PhD,<sup>3</sup>  Catherine Takeda, MD,<sup>1</sup> Christelle Cantet, MSc,<sup>1,2</sup> Sandrine Andrieu, MD, PhD,<sup>1,4</sup> and Bruno Vellas, MD, PhD,<sup>1,2</sup> for the IHU HealthAge INSPIRE Platform Group

ORIGINAL ARTICLE

*Journal of Cachexia, Sarcopenia and Muscle* 2024; **15**: 1134–1145  
Published online 18 April 2024 in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/jcsm.13457

## Cross-sectional interactive associations of physical activity and sedentary behaviour with physical capacity across adulthood

Jérémy Raffin<sup>1,2\*</sup> , Yves Rolland<sup>1,2,3</sup>, Mylène Aubertin-Leheudre<sup>4,5</sup>, Jaqueline Aragoni da Silva<sup>1,2</sup>, Sophie Guyonnet<sup>1,2,3</sup>, Fabien Pillard<sup>6,7</sup>, Bruno Vellas<sup>1,2,3</sup>, Philippe de Souto Barreto<sup>1,2,3</sup> & for the INSPIRE group

*J Nutr Health Aging*. 2023;  
Published online

Original Research

## Body Composition, Physical Function, and Dietary Patterns in People from 20 to Over 80 Years Old

L. Lengelé<sup>1</sup>, N.A. Grande de França<sup>1</sup>, Y. Rolland<sup>1,2</sup>, S. Guyonnet<sup>1,2</sup>, P. de Souto Barreto<sup>1,2</sup>

1. Gérontopôle de Toulouse, Institute on Aging, Toulouse University Hospital (CHU Toulouse), Toulouse, France; 2. Maintain Aging Research team, CERPOP, Université de Toulouse, Inserm, Université Paul, Sabatier, Toulouse, France.

Corresponding Author: Laetitia Lengelé, Gérontopôle de Toulouse, Institute on Aging, Toulouse University Hospital (CHU Toulouse), Toulouse, France, [lengelelaetitia@gmail.com](mailto:lengelelaetitia@gmail.com)

GeroScience  
<https://doi.org/10.1007/s11357-024-01245-6>

ORIGINAL ARTICLE



## Body composition and aging: cross-sectional results from the INSPIRE study in people 20 to 93 years old

Marguerite Briand  · Jeremy Raffin · Emmanuel Gonzalez-Bautista · Patrick Ritz · Gabor Abellan Van Kan · Fabien Pillard · Marie Faruch-Bilfeld · Sophie Guyonnet · Cédric Dray · Bruno Vellas · Philippe de Souto Barreto · Yves Rolland

# INSPIRE-T HealthAge >>> accomplishments (2) - Publications

nature aging

Letter

<https://doi.org/10.1038/s43587-023-00522-x>

## Reference centiles for intrinsic capacity throughout adulthood and their association with clinical outcomes: a cross-sectional analysis from the INSPIRE-T cohort

Received: 10 May 2023

Accepted: 9 October 2023

Wan-Hsuan Lu<sup>1,2,3</sup>✉, Yves Rolland<sup>1,2,3</sup>, Sophie Guyonnet<sup>1,2,3</sup>,  
Philippe de Souto Barreto<sup>1,2,3</sup> & Bruno Vellas<sup>1,2,3</sup>

bioRxiv preprint doi: <https://doi.org/10.1101/2024.08.09.607252>; this version posted August 12, 2024. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

## A Novel Blood-Based Epigenetic Clock for Intrinsic Capacity Predicts Mortality and is Associated with Clinical, Immunological and Lifestyle Factors

Matías Fuentealba<sup>1</sup>, Laure Rouch<sup>2,4</sup>, Sophie Guyonnet<sup>2,4</sup>, Jean-Marc Lemaitre<sup>3</sup>, Philippe de Souto Barreto<sup>2,4</sup>, Bruno Vellas<sup>2,4</sup>, Sandrine Andrieu<sup>2,4,5</sup>, David Furman<sup>1,2,6</sup>

**Back-up slides:**  
Summary of the INSPIRE-T design for support

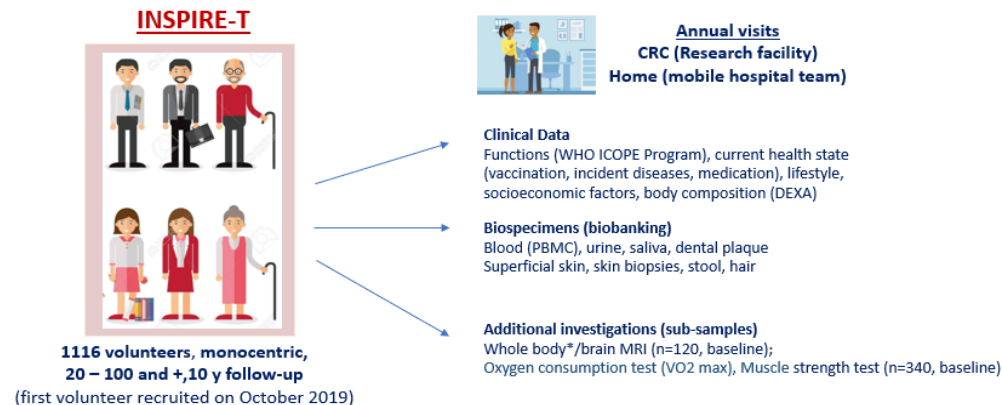
# Inspire-T >>> Study Population

- **Recruitment from the community in Toulouse area (France)**
- **Inclusion criteria**
  - Aged 20 years-old or over; both sexes; affiliated to a social security scheme
- **Exclusion** of people having
  - Severe disease compromising life expectancy at 5 years (or at 2 years for frail older subjects and those aged 80 years or older)
  - Or legally incapable (administrative or judicial decision or under guardianship)
- **Stratification over 10-year age groups**
- **Oversampling older people to be able to investigate major clinical events**



# Inspire-T >>> Design

## THE INSPIRE-T HUMAN COHORT >> Methodology



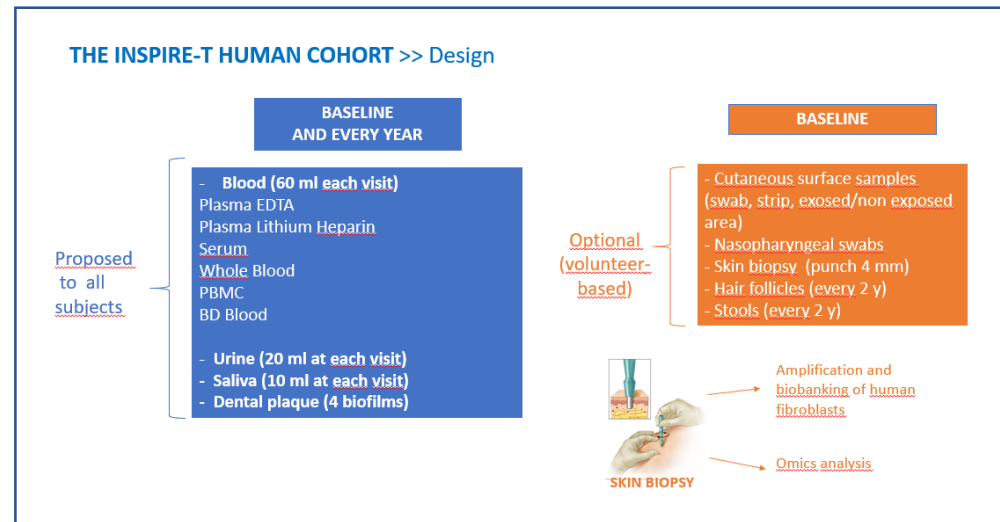
## THE INSPIRE-T HUMAN COHORT >> Data collection for the whole cohort

	Before inclusion	Inclusion	Every 4 month (Year 1) then 6 month	Yearly Visits	Biannual visits
Information note / informed consent	✓				
Socio-demographics		✓			
Physical examinations					
Medical history		✓		✓	
Medication		✓	✓	✓	
Vaccination		✓	✓	✓	
Current and incident diseases		✓	✓	✓	
BMI, waist & hip circumferences		✓		✓	
Heart rate, blood pressure		✓		✓	
Self-reported visceral pain		✓		✓	
Skin elasticity		✓		✓	
Cutaneous itching/pruritus		✓		✓	
Biobanking		✓		✓	
Lifestyle information (physical activity, sedentarity time, smoking, alcohol consumption, solar exposure, sleep)		✓		✓	

## THE INSPIRE-T HUMAN COHORT >> Data collection for the whole cohort

	Before inclusion	Inclusion	Every 4 month (Year 1) then 6 month	Yearly Visits	Biannual visits
Frailty (Fried phenotype)		✓		✓	
Functional status (ADL, IADL)		✓		✓	
Cognitive status (MMSE, cognitive composite score for people < 70 y)		✓		✓	
Physical performance (SPPB, Chaire rise test (30 sec))		✓		✓	
Depressive symptoms (PHQ-9)		✓		✓	
Nutritional status, appetite (MNA, food frequency, SNAQ)		✓		✓	
Oral status (OHAT)		✓		✓	
Participant-reported outcomes for cognition (CFI) and mobility, fatigue and social isolation (PROMIS)		✓		✓	
Objective physical activity and sleep parameters (activPAL accelerometer) – subsample, n=604		✓			✓
Vision assessment (WHO simple eye chart, Amsler grid)		✓		✓	
Audition (Audiometry)				✓	
Body composition (DEXA)		✓			✓
ICOPE Monitor App (Step 1, IC domains)		✓	✓	✓	
Adverse events (new diagnosis, fracture,...)		✓	✓	✓	

# Inspire-T >>> Collection of biospecimens (biobanking)



	T0	Each year	Every 2 years	Nb theoretical aliquot or sample /subjet	Frequency
<b>Whole cohort</b>					
Blood (PBMC) – 60 ml				20 -26 (0,5 ml)	
After overnight fast (min 6h)	X	X		2 (1 ml)	10
Urine – 20 ml	X	X		16-20 (1 ml)	10
Saliva – 10 ml	X	X		4-10 (1 ml)	10
Dental plaque	X	X		4	10
<b>Sub-sample (volunteer-based)</b>					
Nasopharyngeal swabs	X			2	1
Cutaneous surfaces samples (swabbing, delamination) – exposed and non exposed area	X			4	1
Skin biopsy - 4 mm, punch	X			-	1
Cells (Fibroblasts)	X			-	1
Feces	X		X	-	5
Hair bulb	X		X	-	5

**INCLUDING :**

- Plasma EDTA (0,5 ml) – 12 aliquots
- Plasma Hep Lit (0,5 ml) – 4 aliquots
- Plasma BDP100 Blood (0,5 ml) – 6 aliquots
- PBMC (aliquot 1 ml, nb cellules/ml) – 1 to 3 aliquots (10 millions cells/aliquot)
- Whole blood (aliquot 1 ml) – 2 aliquots
- RBC (0,5 ml) – 4 aliquots
- Serum (0,5 ml) – 8 aliquots