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IHU HealthAge
GEROSCIENCE & PREVENTION

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How to use the INSPIRE-T HealthAge lifespan as a Geroscience trial cohort following the ADNI model ?
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The Alzheimer's Disease Neuroimaging Initiative (ADNI) Project >> History

- The overall goal of the ADNI is **to optimize and validate biomarkers for clinical trials** while **sharing all data and biofluid samples** with the global scientific community
- ADNI has standardized and validated amyloid beta and tau PET imaging, MRI, and CSF biomarkers for AD
- It has **provided critical data for the design of the clinical trials for anti-amyloid therapeutics by pharmaceutical companies**, including aducanumab (Biogen), lecanemab (Eisai), donanemab and solanzeumab (Lilly), verubecstat (Merck), crenezumab (Genentech) and ganterenumab (Roche)
- Over 5600 scientific papers have been published using ADNI data reflecting ADNI's **promotion of data-sharing and open science**
- Two main limitations: lack of diversity and generalizability (ADNI4) and complexity of ADNI data

The ADNI Project >> Keys of success

- ADNI has a **very clear statement of its overall goal and specific aims**
- ADNI is a **public private partnership**
- **All data are shared** without any embargo and following an “easy” process (data-sharing site, data dictionaries, data use agreement)
- The governance of ADNI includes **specific cores with leaders**

THE INSPIRE-T HUMAN COHORT >> Clinical Assessments and questionnaires

	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 >> Clinical Assessments and questionnaires

	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,...)		✓	✓	✓	

THE INSPIRE-T HUMAN COHORT >> Availability of biofluid data

ALL PARTICIPANTS

Plasma and serum from blood	Baseline – All visits
Whole blood	Baseline – All visits
Red Blood Cell	Baseline – All visits
PBMCs	Baseline – All visits
Urine	Baseline – All visits
Saliva	Baseline – All visits
Dental plaque (biofilm)	Baseline – All visits

SUBSAMPLES

Feces	Baseline – Every 2 years
Hair Bulbs	Baseline – Every 2 years
Cells (Fibroblasts)	Baseline
Skin Biopsy	Baseline
Cutaneous surfaces samples (swabbing, delamination; exposed/non exposed area)	Baseline

THE INSPIRE-T HUMAN COHORT >> Additional investigations

SUBSAMPLES

Whole body/Brain MRI	Baseline
VO2 max (+blood samples before/after the test)	Baseline
Muscle Strength test	Baseline

Could INSPIRE-T become an ADNI-like project for Geroscience ?

Major Issues

- Lack of specific statistically testable hypotheses
- Lack of a plan to replicate some previous finding which looks good
- Lack of a plan for identification, validation and discovery of biomarkers
- Lack of a governance including specific core and leaders

Could INSPIRE-T become an ADNI-like project for Geroscience ?

Strategies for the future

- Identify our overall goal and specific aims
- Develop a series of testable hypothesis
 - Identify the most important papers published dealing with the various theories of causes of aging and the existing biomarkers of aging in humans (but also in animals)
- Identify a series of findings which could be replicated in the Inspire-T cohort
- Build the Inspire-T governance with specific core and internal/external leaders (Biomarker Core for the management of the biofluids, Genetic Core, Omics Core) – These cores need to collaborate with a biostatistics and bioinformatics core that can be also created
- Reinforce/create strong links with pharmaceutical companies today involved in the design of the clinical trials for geroprotectors

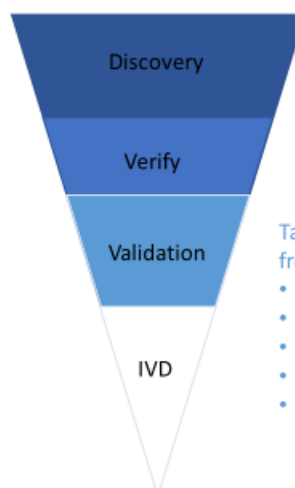
Relevant biomarkers in the field of Geroscience

2 pillars :

Discovery with targeted proteomics
(O'link/Somalogics)

Validation of new biomarkers
(mouse vs human)

*Cross Validation / Collaboration /
other cohorts?
(Moqri&al. 2024)*



Targeted and robust analysis of known biomarkers from previous studies (Inspire T / Aging cohorts) :

- TNFR1 – GDF15 (MAPT Cohort)
- SASP (IL-6, CRP...)
- Metabolic dysfunction
- Telomer?
- Tissue specific biomarkers

R&D => robust IVD Analysis in Geroscience (clinical) / Collaboration private company