



**BOLOGNA/UNIBO: The arcades
of the oldest university
in the world (founded in 1088)**

Claudio Franceschi

**Alma Mater Studiorum
University of Bologna, Italy
Lobachevsky State University
Nizhny Novgorod, Russia**

Il ruolo della Intelligenza Artificiale nella ricerca clinica e di base

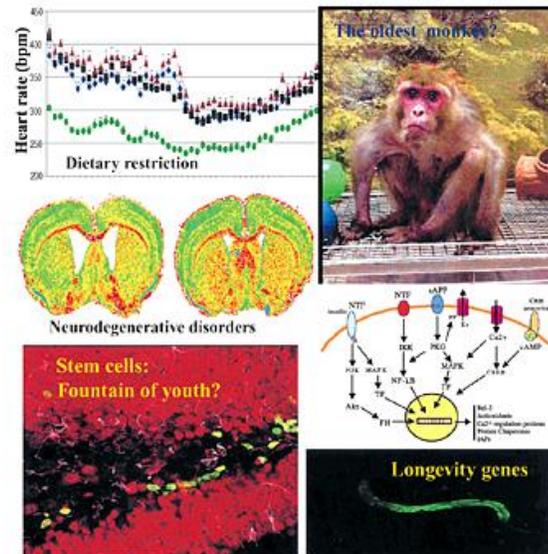
**XVIII Convegno
I CENTRI PER I DISTURBI COGNITIVI
E LE DEMENZE E LA GESTIONE
INTEGRATA DELLA DEMENZA
27 – 28 novembre 2025
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AGEING RESEARCH REVIEWS



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Artificial Intelligence

The theory and development of computer systems able to perform tasks normally requiring human intelligence

Machine Learning

Gives computers "the ability to learn without being explicitly programmed"

Deep Learning

Machine learning algorithms with brain-like logical structure of algorithms called artificial neural networks

LEVITY

**AI applied to aging and longevity:
a terrific opportunity
that cannot be
missed**

Inflamm-aging

An Evolutionary Perspective on Immunosenescence

CLAUDIO FRANCESCHI,^{a,b,e} MASSIMILIANO BONAFÈ,^a SILVANA VALENSIN,^a
FABIOLA OLIVIERI,^b MARIA DE LUCA,^d ENZO OTTAVIANI,^c AND
GIOVANNA DE BENEDICTIS^d

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^d*Department of Cell Biology, University of Calabria, Calabria, Italy*

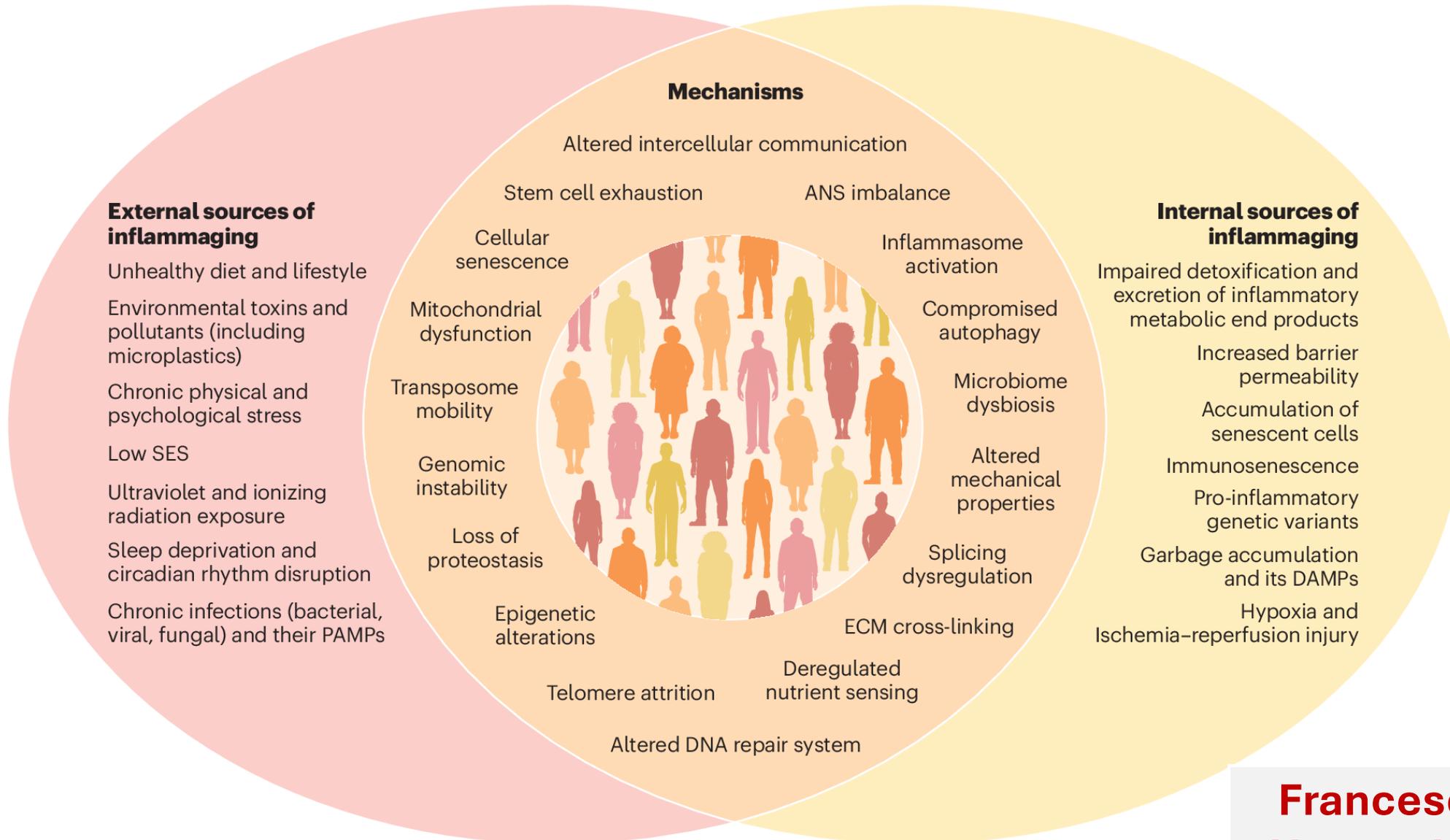
“chronic”, “low grade”, “sterile”

Inflammaging is based on studies on immunosenescence and **the evolution of immune response** and stress from invertebrates to mammals

Ann. N.Y. Acad. Sci., 908, 244-254, 2000

6301 citations (26/11/2025)

INFLAMMAGING: SOURCES & MECHANISMS



**Franceschi et al.,
Nature Aging 2025**

Aging/Inflammaging as an adaptive process

Inflammaging and anti-inflammaging: A systemic perspective on aging and longevity emerged from studies in humans

Claudio Franceschi^{a,b,c,e,*}, Miriam Capri^a, Daniela Monti^d, Sergio Giunta^e, Fabiola Olivieri^e,
Federica Sevini^b, Maria Panagiota Panourgia^b, Laura Invidia^a, Laura Celani^b,
Maria Scurti^b, Elisa Cevenini^b, Gastone C. Castellani^{b,f}, Stefano Salvoli^{a,b,c}

^aDepartment of Experimental Pathology, University of Bologna, via S. Giacomo 12, 40126 Bologna, Italy

^bCentro Interdipartimentale "L. Galvani", University of Bologna, via S. Giacomo 12, 40126 Bologna, Italy

^cER-GenTech laboratory, via Saragat 1, 44100 Ferrara, Italy

^dDepartment of Experimental Pathology and Oncology, University of Florence, Viale Morgagni 50, 50134 Florence, Italy

^eI.N.R.C.A., Department of Gerontological Sciences, via Birarelli 8, 60121 Ancona, Italy

^fDIMORFIPA, University of Bologna, Via Tolara di Sopra 50, 40064 Ozzano dell'Emilia, Italy

AVAILABLE ONLINE 20 NOVEMBER 2006

Mechanisms of Ageing and Development 128 (2007) 92–105

Centenarians are inflamed, but the data suggest that the increase of **pro-inflammatory** molecules is accompanied by a concomitant **adaptive** increase of **anti-inflammatory** molecules

2545 citations (26/11/2025)

GEROSCIENCE: inflammaging and age-related diseases

Advances in Geroscience: Impact on Healthspan and Chronic Disease Perspective

Chronic Inflammation (Inflammaging) and Its Potential Contribution to Age-Associated Diseases

Claudio Franceschi^{1,2} and Judith Campisi^{3,4}

¹DIMES, Department of Experimental, Diagnostic and Specialty Medicine and CIG, Interdepartmental Center “Luigi Galvani”,
University of Bologna, Italy.

²IRCCS Institute of Neurological Sciences, and CNR-ISOF, Bologna, Italy.

³Buck Institute for Research on Aging, Novato, California.

⁴Life Sciences Division, Lawrence Berkeley National Laboratory, California.

J Gerontol A Biol Sci Med Sci (2014) June;69(S1):S4–S9

4538 citations 26/11/2025)

INFLAMMAGING

fits the Antagonistic Pleiotropy Theory **of aging:**

Inflammaging: a new immune–
metabolic viewpoint for
age-related diseases

**A theoretical
unitarian vision
of inflammaging**

Claudio Franceschi^{1,8}, Paolo Garagnani^{2,3,4,5,8}, Paolo Parini³, Cristina Giuliani^{6,7}
and Aurelia Santoro^{2,7}*

NATURE REVIEWS | **ENDOCRINOLOGY** 2018 July 25

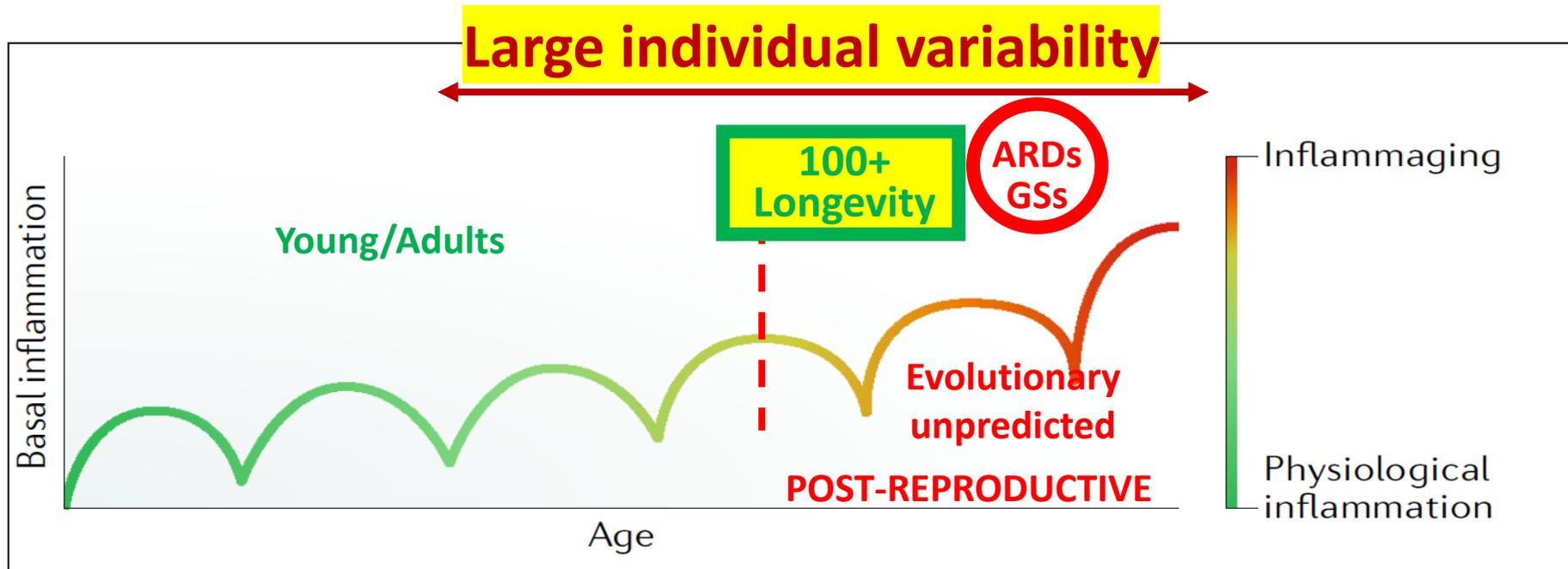
Inflammaging is beneficial at young age but can become **deleterious
at old age** a period of life **largely non predicted by evolution**

3122 citations (26/11/2025)

Inflammaging fits the Antagonistic Pleiotropy theory of aging

Inflammation is the most important, **BENEFICIAL, ADAPTIVE, EVOLUTIONARY-CONSERVED** response to «damage stimuli», and is crucial for repair/survival

When overstimulated, particularly in the post-reproductive period of life, inflammation **can** become **CHRONIC** and **DETRIMENTAL**



Franceschi et al.,
Nat Rev
Endocrinol,
2018

A unitarian perspective of Age-Related Diseases

Chronic inflammation in the etiology of disease across the life span

David Furman ^{1,2,3,4*}, Judith Campisi^{1,5}, Eric Verdin ¹, Pedro Carrera-Bastos⁶, Sasha Targ^{4,7}, Claudio Franceschi^{8,9}, Luigi Ferrucci¹⁰, Derek W. Gilroy¹¹, Alessio Fasano ¹², Gary W. Miller¹³, Andrew H. Miller¹⁴, Alberto Mantovani ^{15,16,17}, Cornelia M. Weyand ¹⁸, Nir Barzilai¹⁹, Jorg J. Goronzy ²⁰, Thomas A. Rando^{20,21,22}, Rita B. Effros²³, Alejandro Lucia^{24,25}, Nicole Kleinstreuer ^{26,27} and George M. Slavich ²⁸

Although intermittent increases in inflammation are critical for survival during physical injury and infection, recent research has revealed that certain social, environmental and lifestyle factors can promote systemic chronic inflammation (SCI) that can, in turn, lead to several diseases that collectively represent the leading causes of disability and mortality worldwide, such as cardiovascular disease, cancer, diabetes mellitus, chronic kidney disease, non-alcoholic fatty liver disease and autoimmune and neurodegenerative disorders. In the present Perspective we describe the multi-level mechanisms underlying SCI and several risk factors that promote this health-damaging phenotype, including infections, physical inactivity, poor diet, environmental and industrial toxicants and psychological stress. Furthermore, we suggest potential strategies for advancing the early diagnosis, prevention and treatment of SCI.

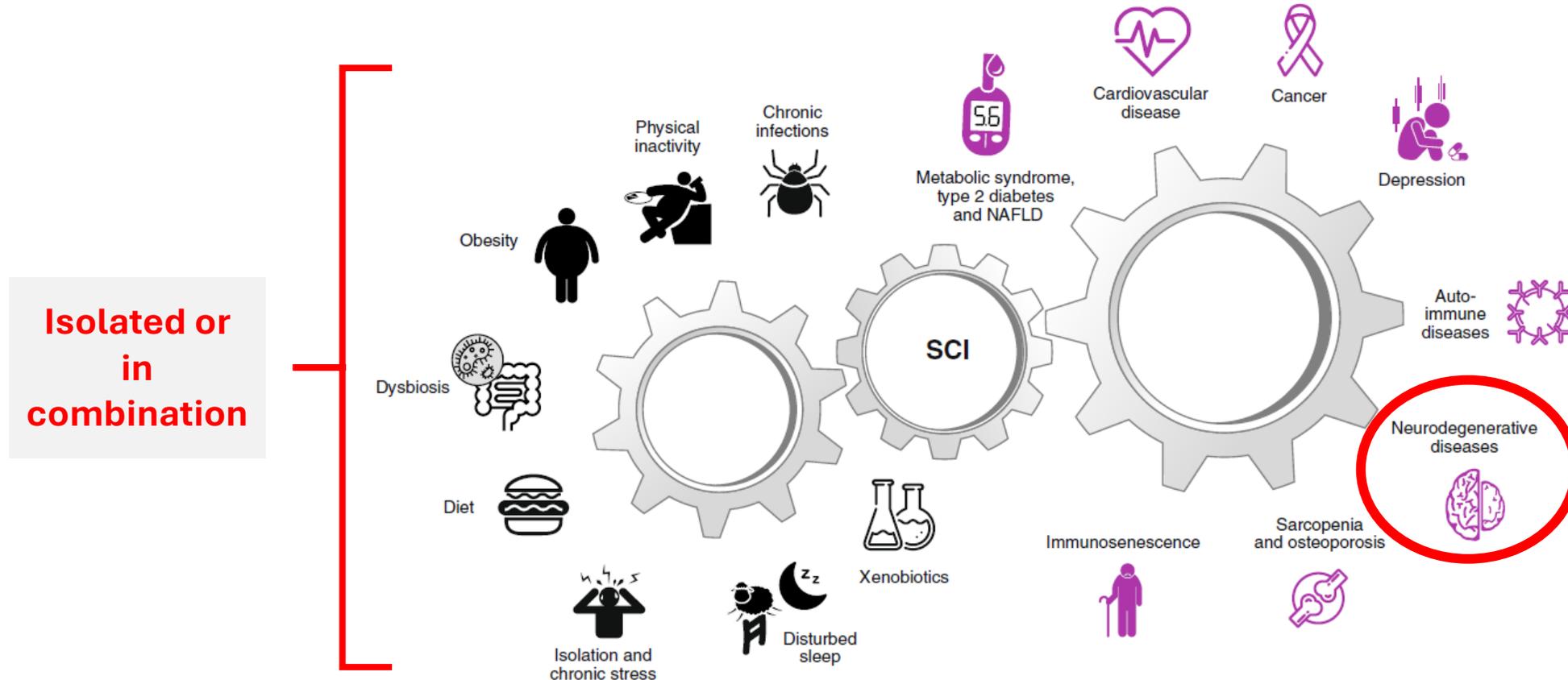
NATURE MEDICINE | VOL 25 | DECEMBER 2019 | 1822-1832 |

Systemic Chronic Inflammation = SCI

5056 citations (26/11/2025)

SCI/Inflammaging: a unitarian perspective of ARDs

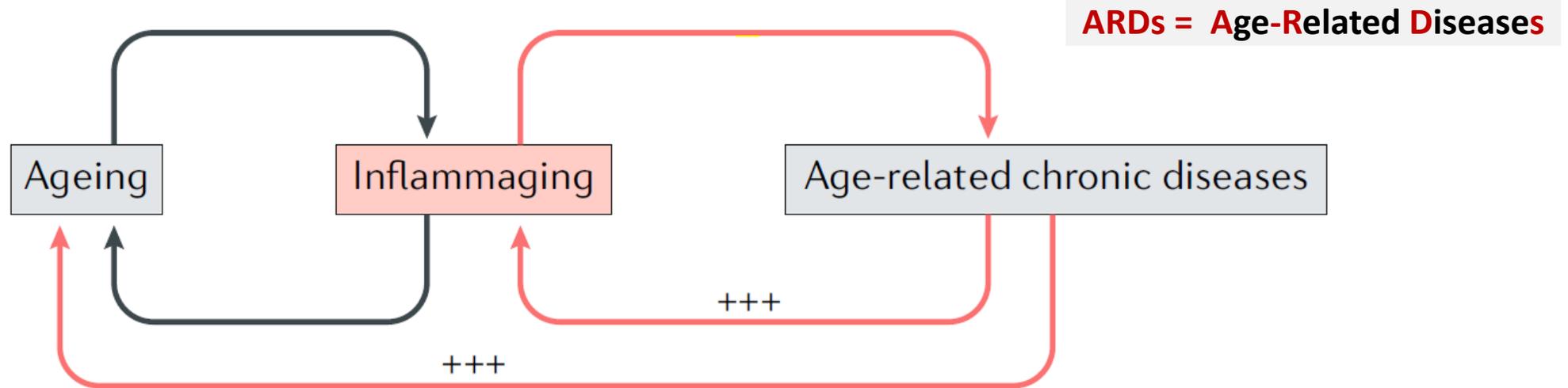
A variety of causes triggers a variety of outcomes (ARDs) through inflammaging



Systemic Chronic Inflammation = SCI

Furman et al., Nature Medicine 2019¹⁹

Inflammaging can be both a cause and a consequence of ARDs



In turn, ARDs accelerate inflammaging and aging

Inflammaging is

evolutionary/historically and geographically-specific

Ageing Research Reviews 113 (2026) 102880

Ageing Research Reviews 113 (2026) 102880



ELSEVIER

Contents lists available at [ScienceDirect](#)

Ageing Research Reviews

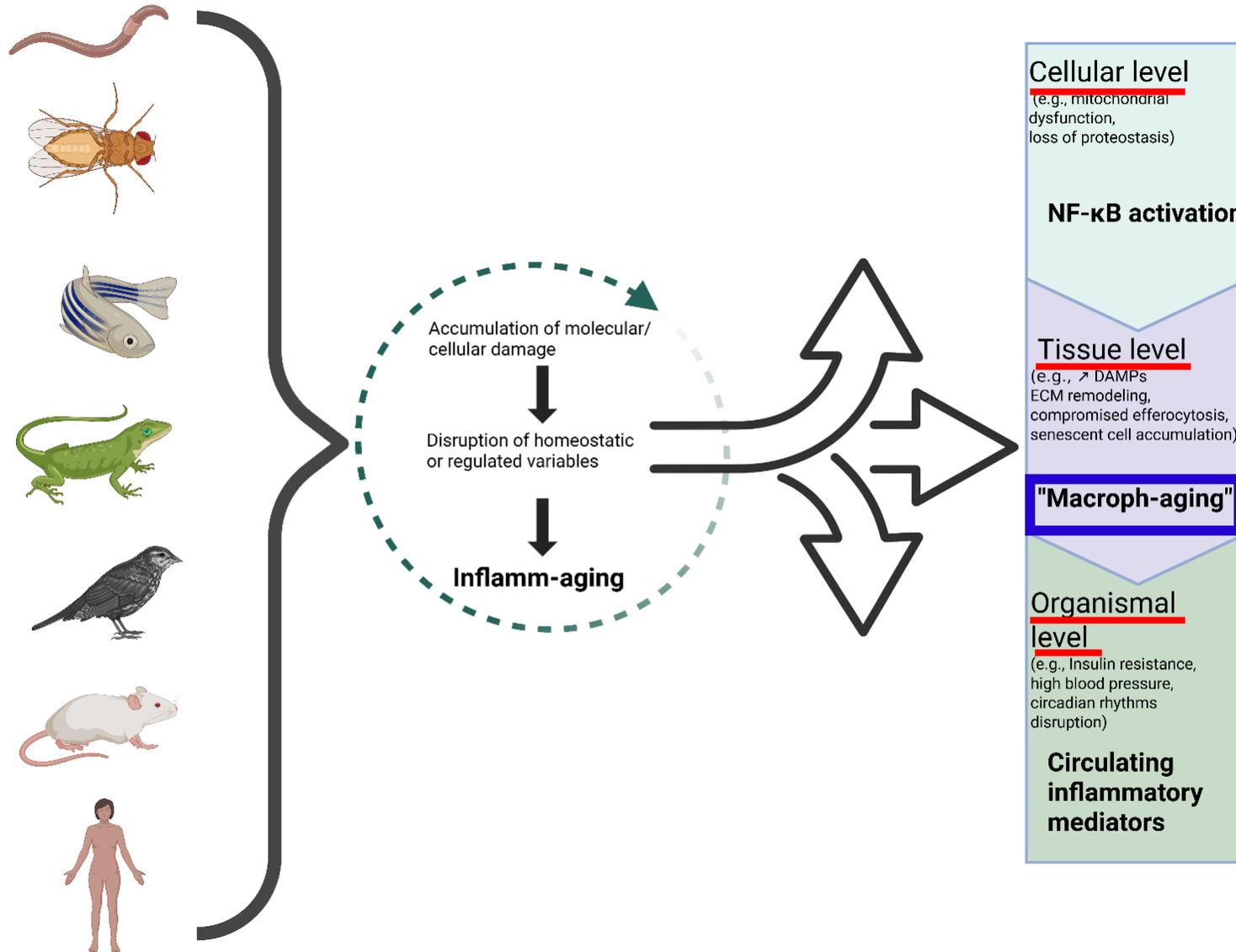
journal homepage: www.elsevier.com/locate/arr

Review article

Inflamm-aging as a diverse and context-dependent process: From species and population differences to individual trajectories

Maximilien Franck^{a,*}, Camille Daunizeau^b, Jacob E. Aronoff^c, Kamaryn Tanner^d, Benjamin C. Trumble^c, Claudio Franceschi^e, Johannes Hertel^{f,g}, Tamás Fülöp^a, Maël Lemoine^h, Michael Gurvenⁱ, Alan A. Cohen^{d,*}

Inflammaging as **A NEAR-UNIVERSAL YET DIVERSE** aspect of aging **ACROSS SPECIES**



The actual form and consequences of inflamm-aging vary across species, environmental/social and biological contexts..

Ageing Research Reviews

Available online 29 August 2025

INFLAMMAGING AND INDIVIDUAL IMMUNOSENESCENCE

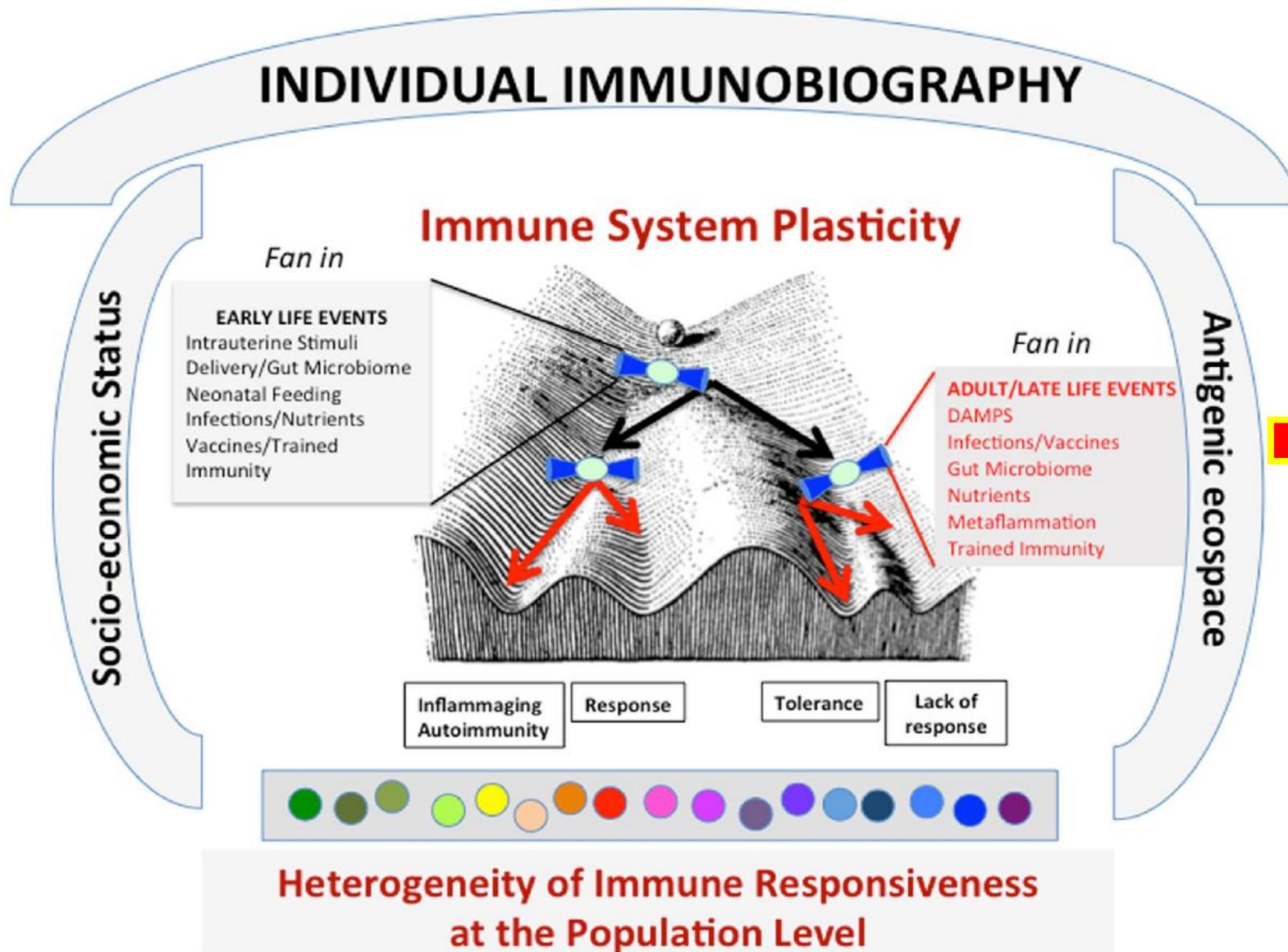
Front Immunol. 2017 Aug 15;8:982.2017

The emerging **INDIVIDUALITY** of the Immune System

Immunobiography and the Heterogeneity of Immune Responses in the Elderly: A Focus on Inflammaging and Trained Immunity

Claudio Franceschi^{1†}, Stefano Salvioli^{2,3*†}, Paolo Garagnani^{2,3}, Magda de Eguileor⁴,
Daniela Monti^{5‡} and Miriam Capri^{2,3‡}

¹Institute of Neurological Sciences of Bologna IRCCS, Bologna, Italy, ²Department of Experimental, Diagnostic and Specialty Medicine (DIMES), University of Bologna, Bologna, Italy, ³Interdepartmental Centre 'L. Galvani' (CIG), University of Bologna, Bologna, Italy, ⁴Department of Biotechnology and Life Science, University of Insubria, Varese, Italy, ⁵Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy



The fundamental
HETEROGENEITY
 of the
IMMUNE AGING
PHENOTYPE,
 becoming with age
 progressively
 more and more
INDIVIDUALIZED

Franceschi et al.,
 Front Immunol 2017

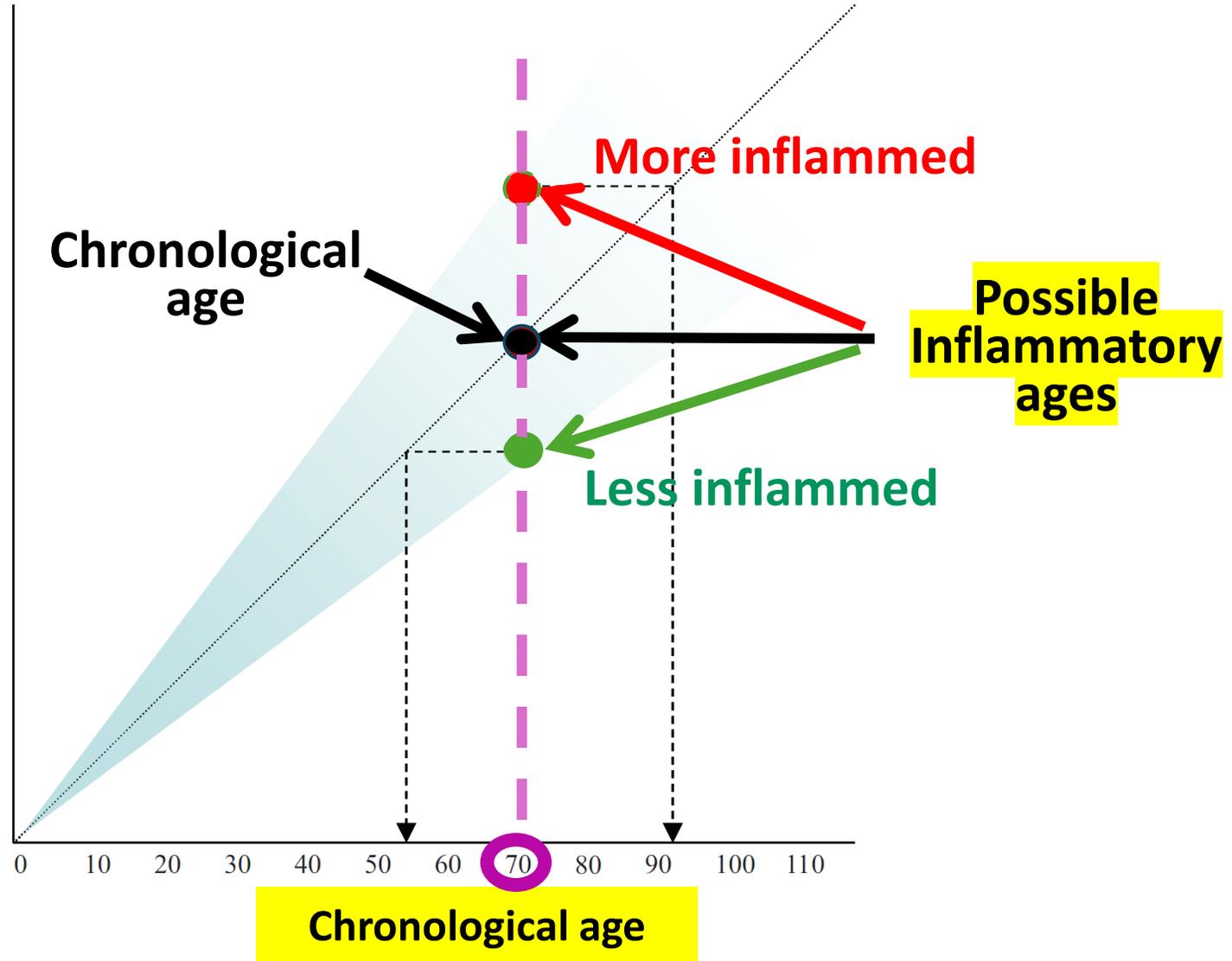
**Data questa fondamentale
variabilita' ed eterogeneita'
e' particolarmente importante
andare oltre l'eta' cronologica
e quantificare l'eta infiammatoria
se possibile a livello individuale**

INFLAMMATORY CLOCK

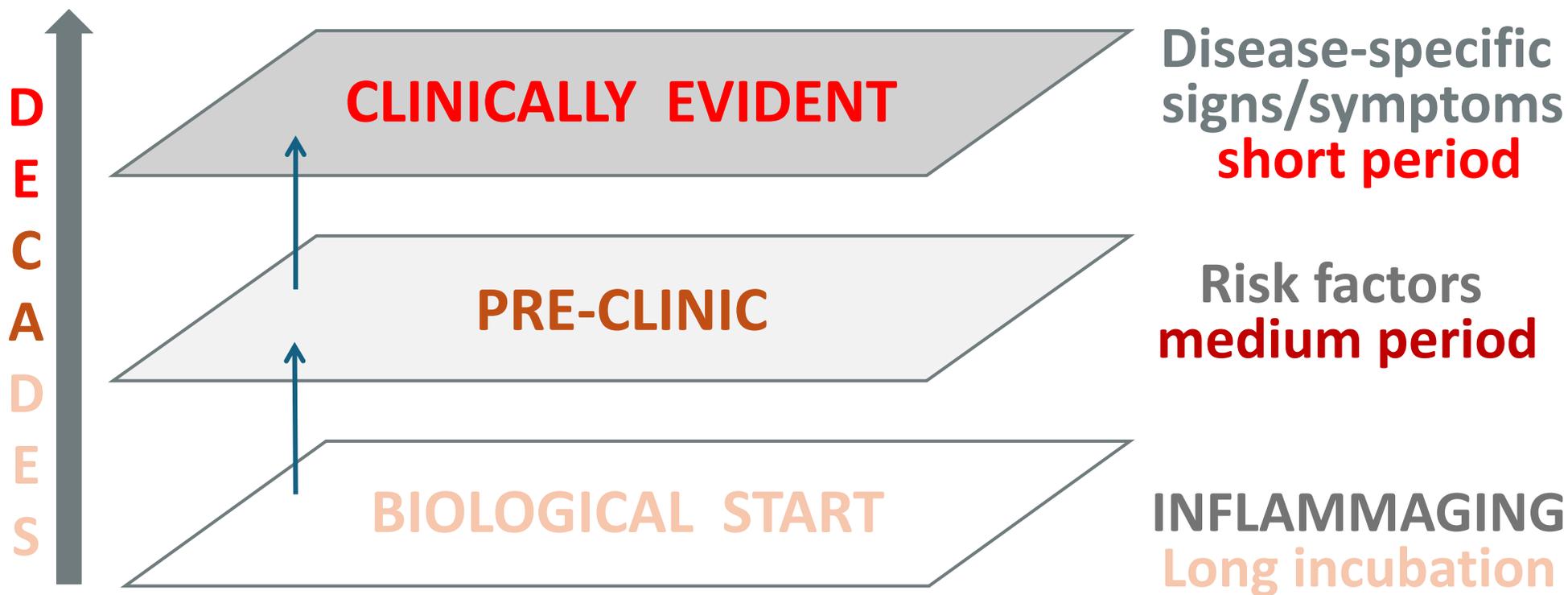
Inflammatory age vs Chronological age

We developed **two Inflammatory Clocks** to quantify the **inflammatory age** in comparison to **chronological age**

Inflammatory marker



Inflammaging and age-associated diseases



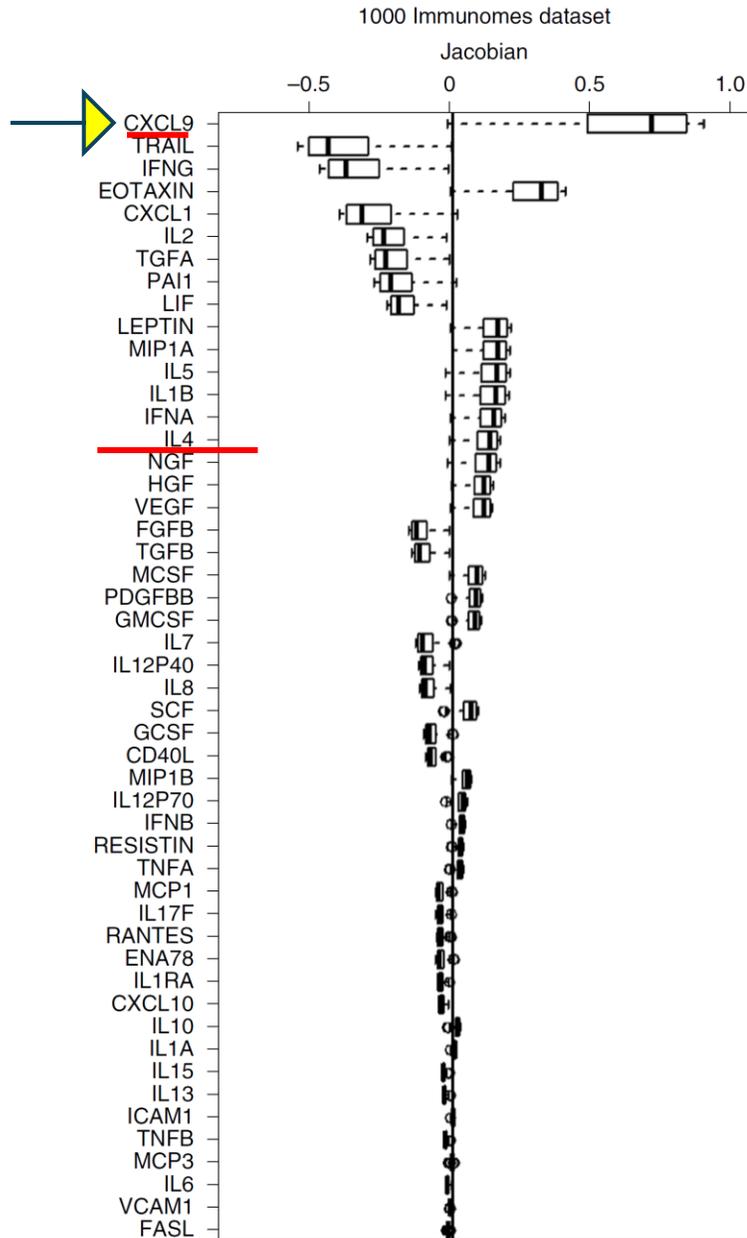


An inflammatory aging clock (iAge) based on deep learning tracks multimorbidity, immunosenescence, frailty and cardiovascular aging

Nazish Sayed^{1,2,3,24} , Yingxiang Huang^{4,24}, Khiem Nguyen⁴, Zuzana Krejciova-Rajaniemi⁵, Anissa P. Grawe⁴, Tianxiang Gao⁶, Robert Tibshirani⁷, Trevor Hastie , Ayelet Alpert⁸, Lu Cui , Tatiana Kuznetsova¹⁰, Yael Rosenberg-Hasson¹¹, Rita Ostan¹², Daniela Monti , Benoit Lehallier , Shai S. Shen-Orr , Holden T. Maecker¹¹, Cornelia L. Dekker , Tony Wyss-Coray , Claudio Franceschi¹⁸, Vladimir Jojic^{5,19}, François Haddad², José G. Montoya²⁰, Joseph C. Wu^{2,21}, Mark M. Davis^{1,16,22} and David Furman  

Nat Aging. 2021 Jul;1:598-615.

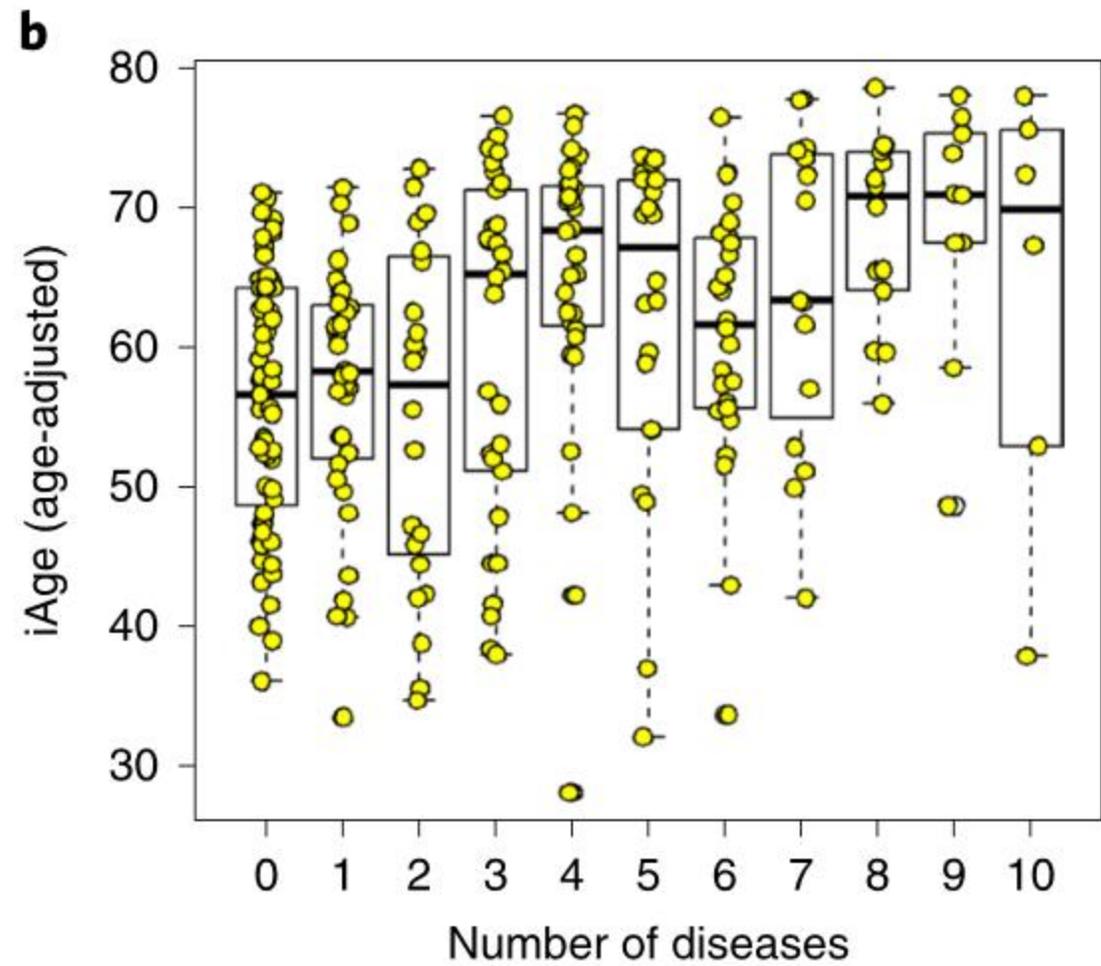
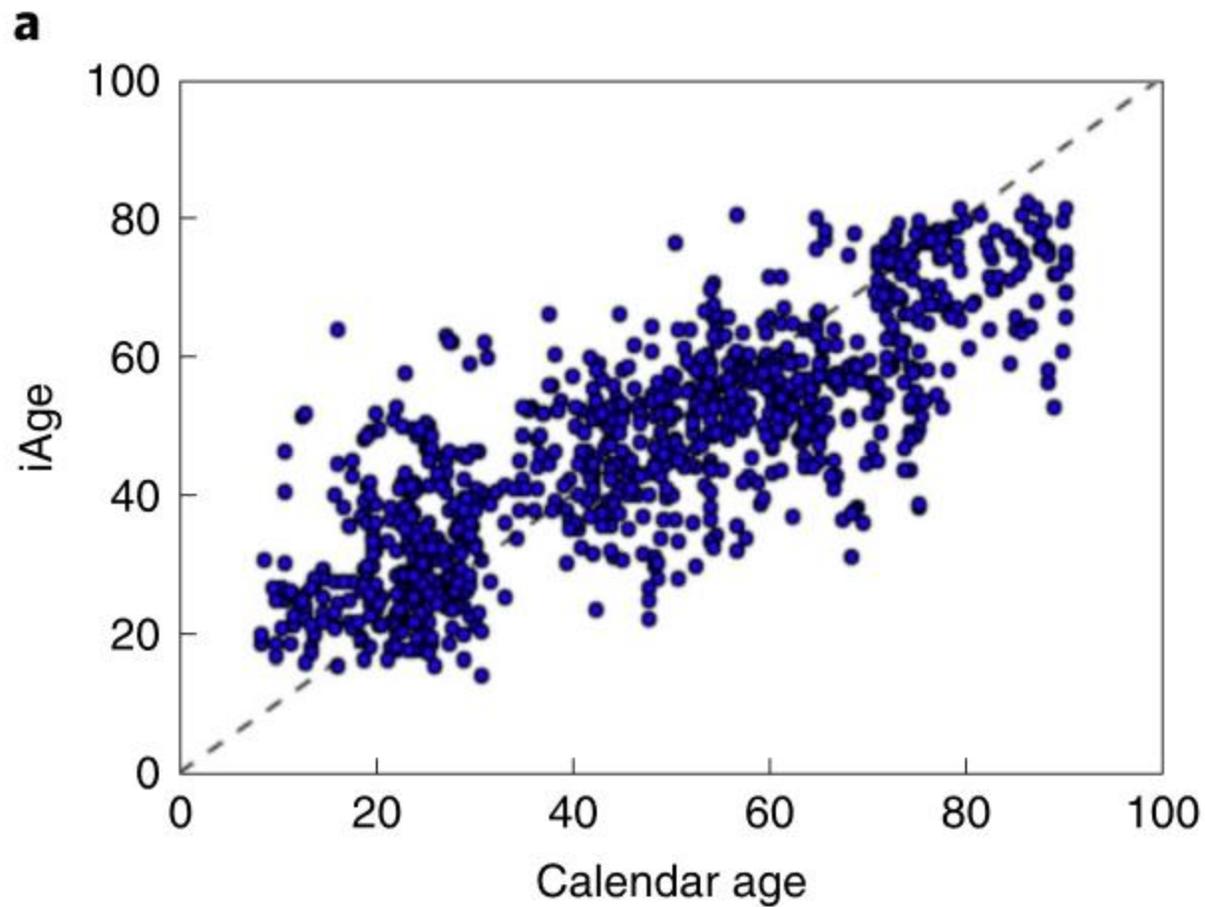
492 citations (26/11/2025)



The top 15 variables contributing to the chronological age-independent inflammatory index (iAGE) are:

- positive** contributors: **CXCL9**, **EOTAXIN**, **Mip-1 α** , **LEPTIN**, **IL-1 β** , **IL-5**, **IFN- α** and **IL-4**;
- negative** contributors **TRAIL**, **IFN- γ** , **CXCL1**, **IL-2**, **TGF- α** , **PAI-1** and **LIF**.

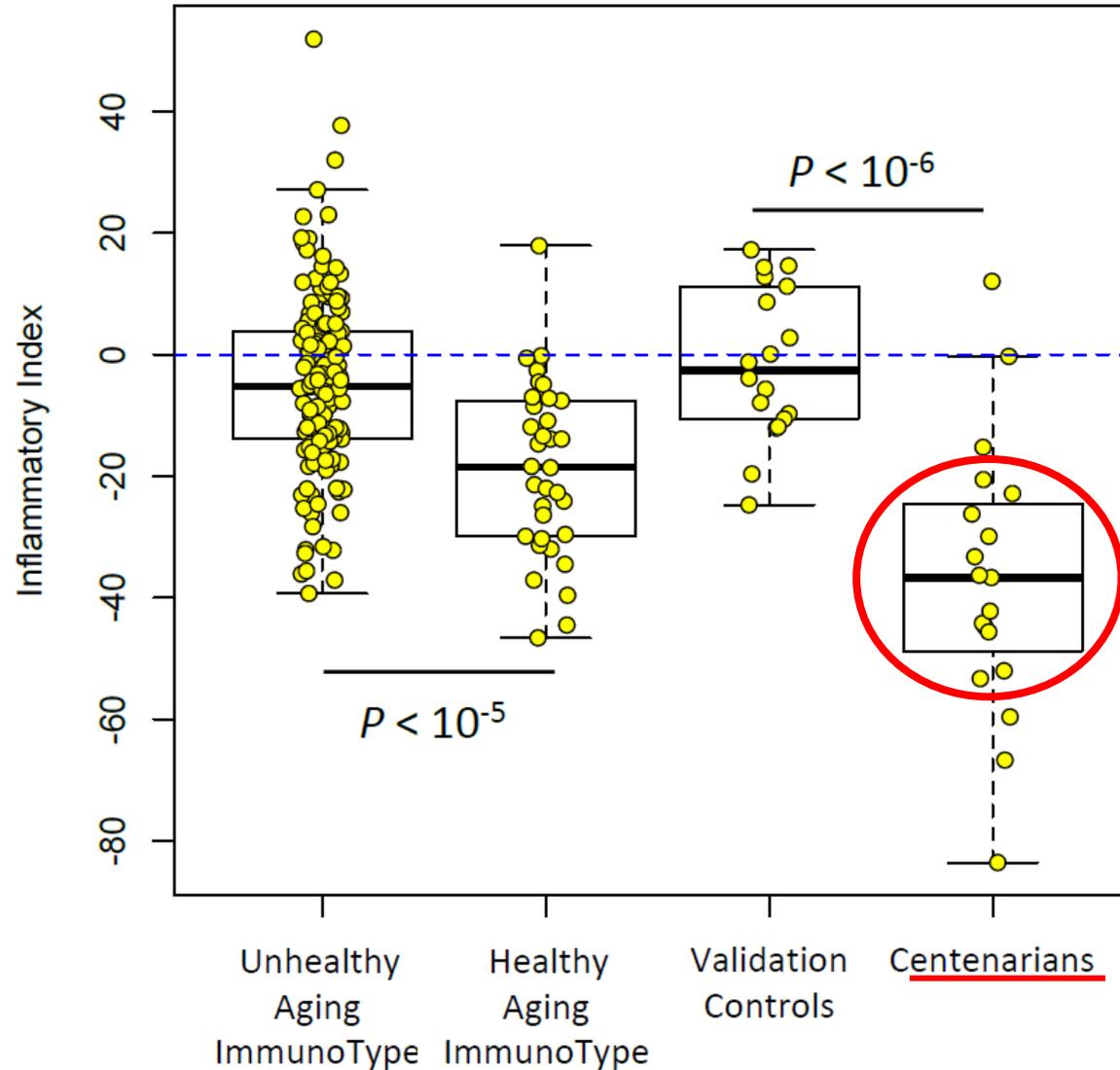
NATURE AGING | VOL 1 | JULY 2021 | 598-615 |



Furman et al., Nature Aging 2021

Inflammatory Index

(inflammatory age *minus* chronological age)



From an inflammaging point of view centenarians are much younger than their chronological age

Furman et al., 2021

Small immunological clocks identified by deep learning and gradient boosting

Alena Kalyakulina^{1,2,3*†}, Igor Yusipov^{1,2,3†}, Elena Kondakova^{3,4},
Maria Giulia Bacalini⁵, Claudio Franceschi^{2,3}, Maria Vedunova³
and Mikhail Ivanchenko^{2,3}

**The second
personalized
Inflammaging clock**

TYPE Original Research

PUBLISHED 25 August 2023

DOI 10.3389/fimmu.2023.1177611

- The study involved:
- 1. a group of **300 healthy volunteers (227 women and 113 men, 21-101 years old)** recruited in the Nizhny Novgorod region.
- **43 ESRD (End-Stage chronic Renal Disease) patients** in hemodialysis.

The 10 most important **immunological** features that were selected for the construction of the small immunological clocks

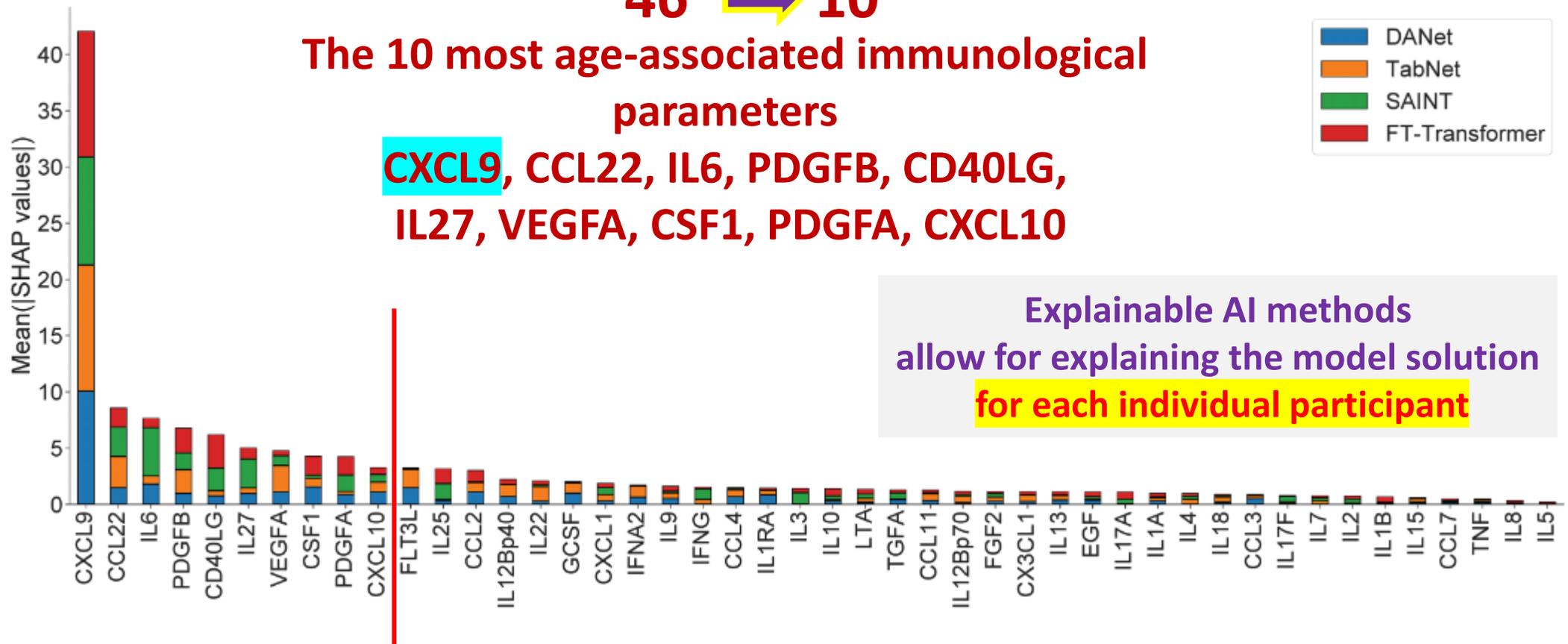
Ranking of the features according to their averaged absolute SHAP values in the best models:
 DANet (blue), TabNet (orange), SAINT (green), FT-Transformer (red).

The 10 selected biomarkers with the highest importance values are taken for building small models.

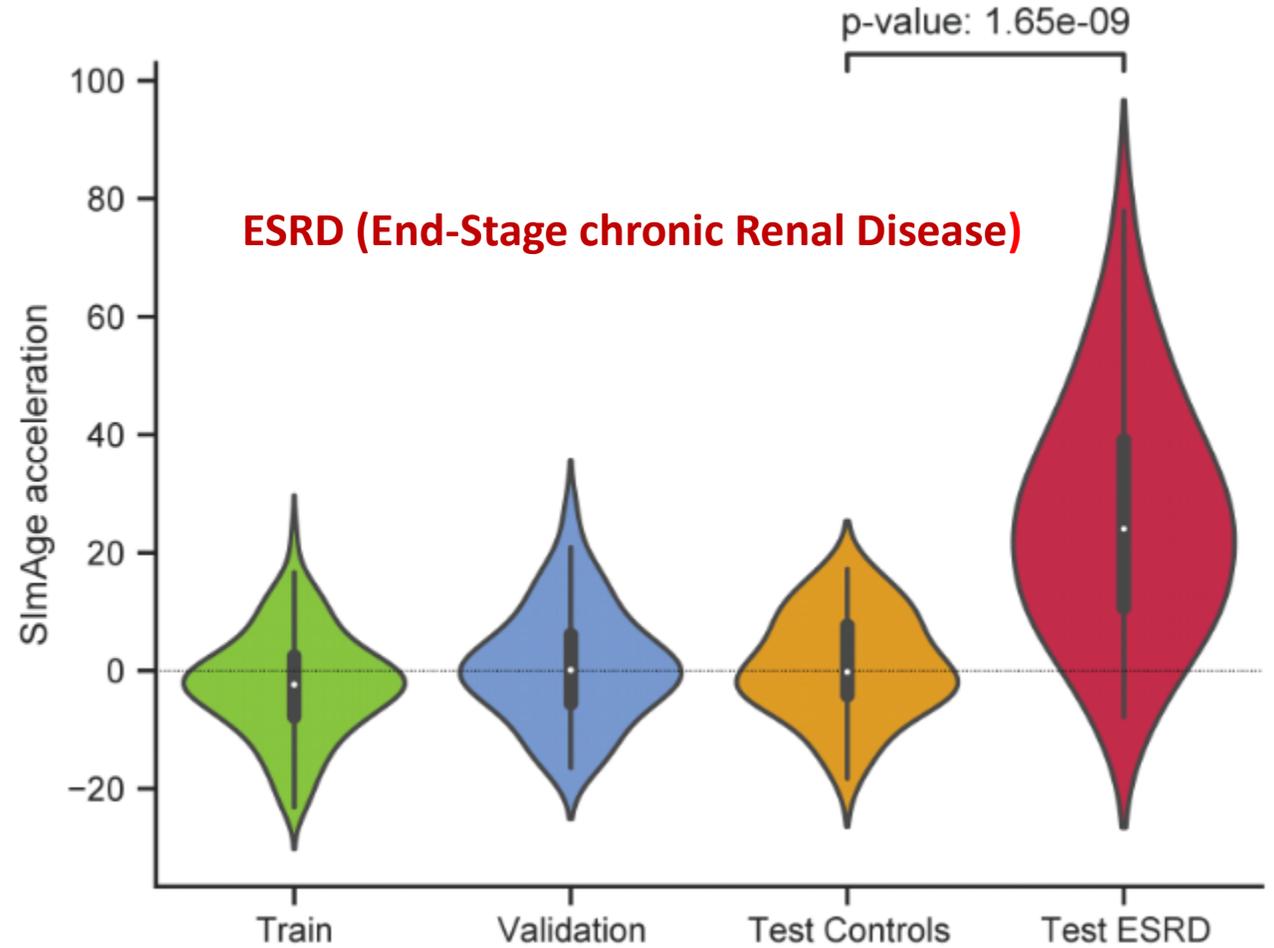
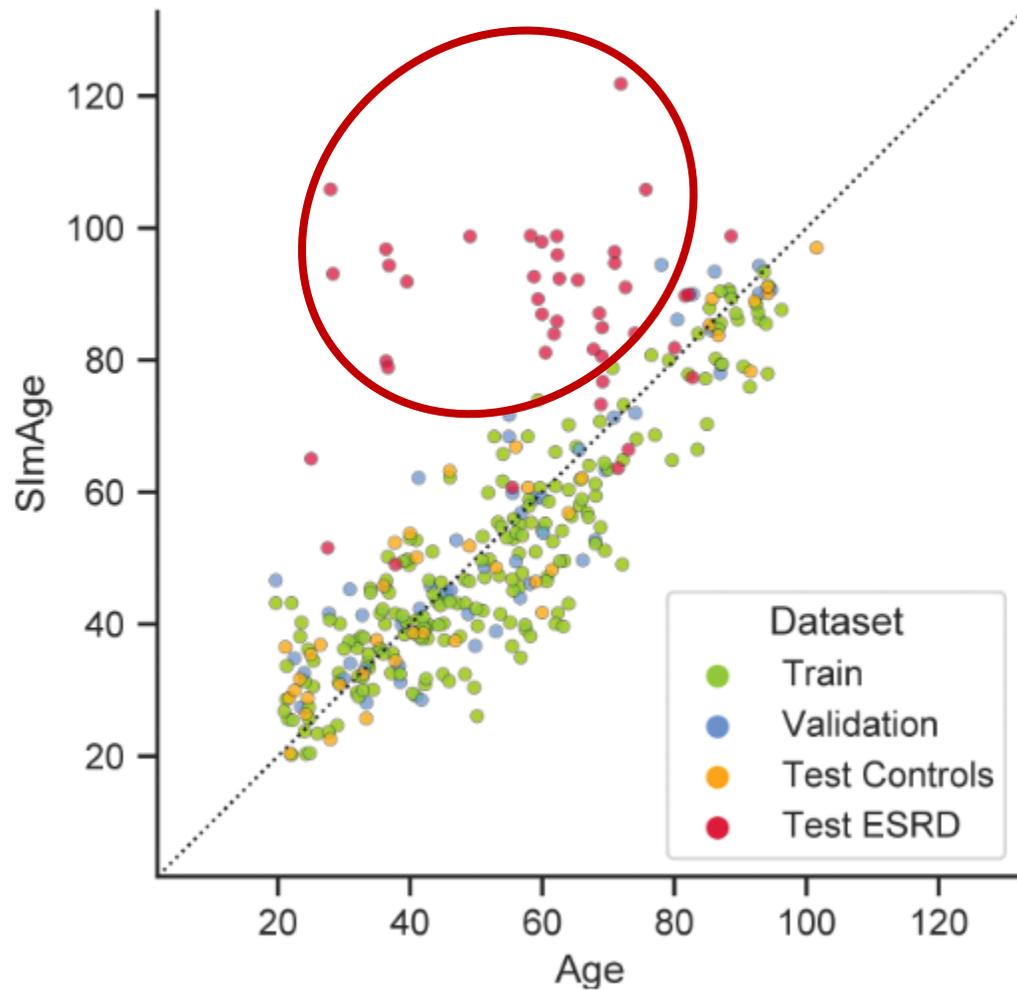
46 → **10**

The 10 most age-associated immunological parameters

CXCL9, CCL22, IL6, PDGFB, CD40LG, IL27, VEGFA, CSF1, PDGFA, CXCL10



Results for the best model predicting age on a small number of immunological biomarkers (SlmAge).

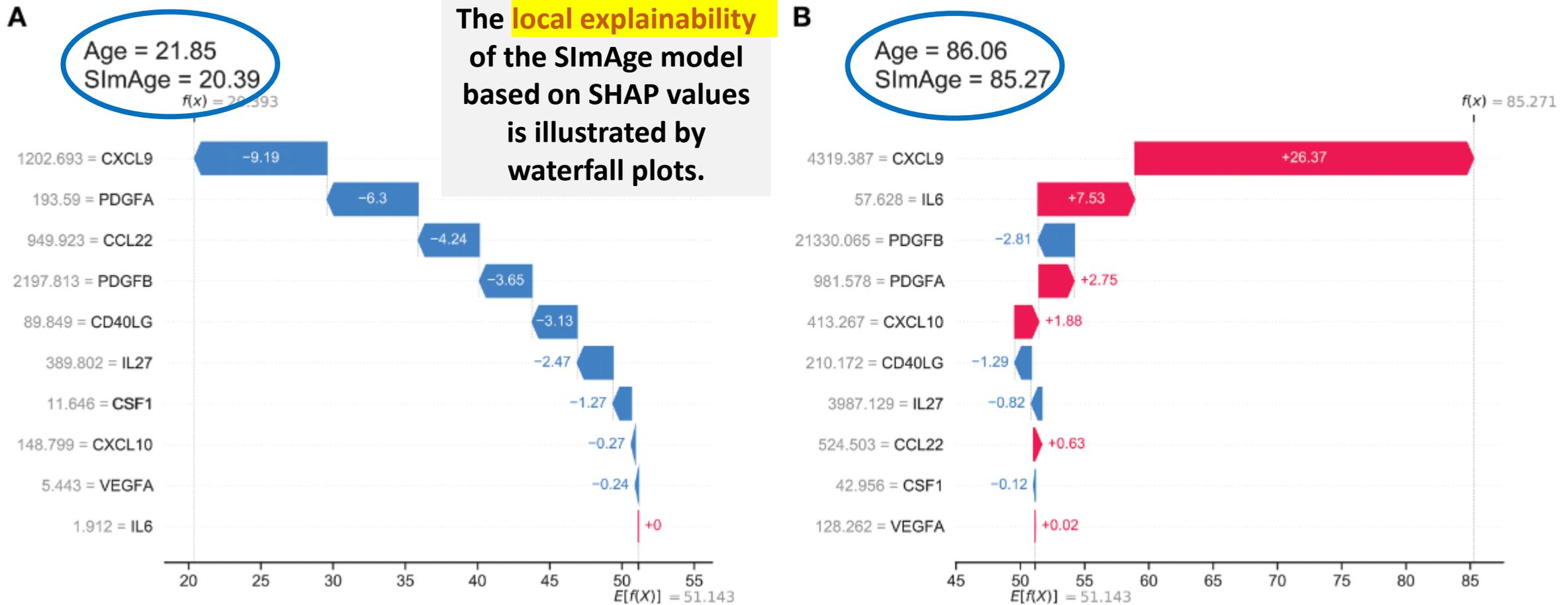


eXplainable Artificial Intelligence

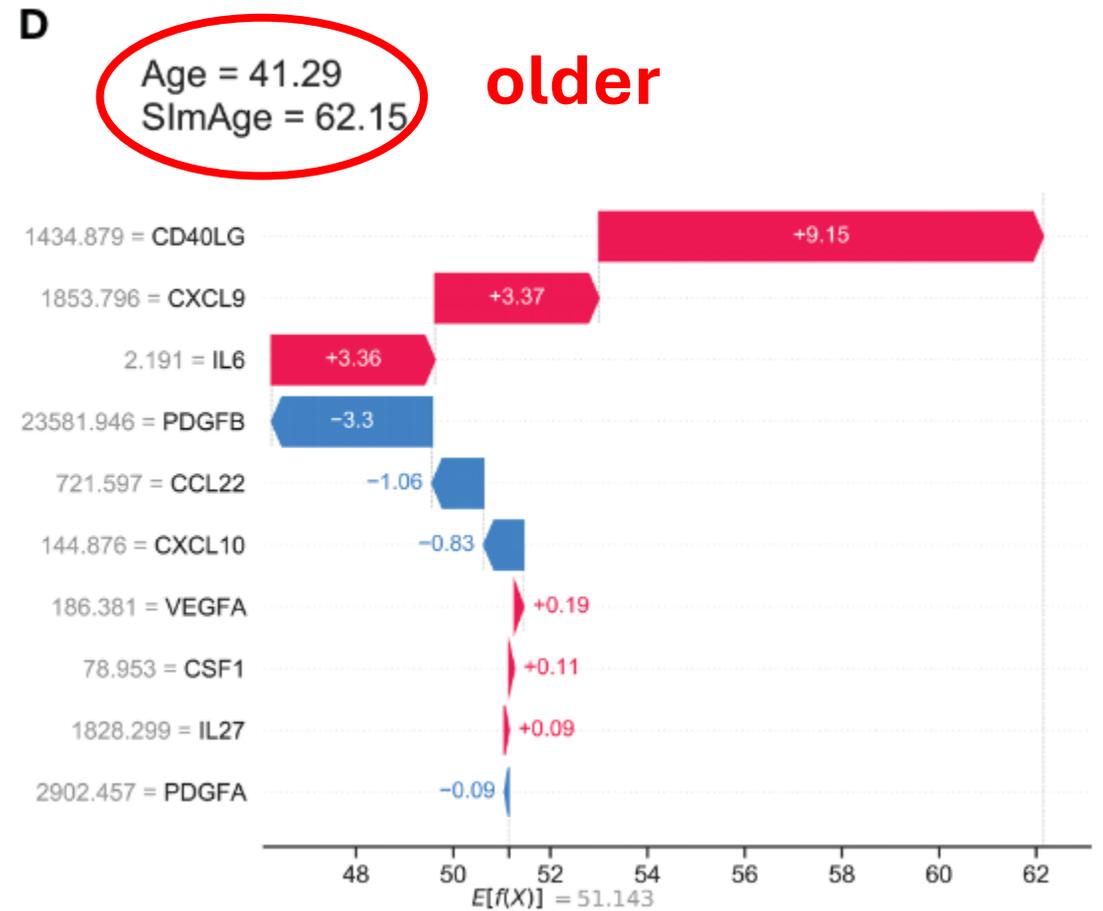
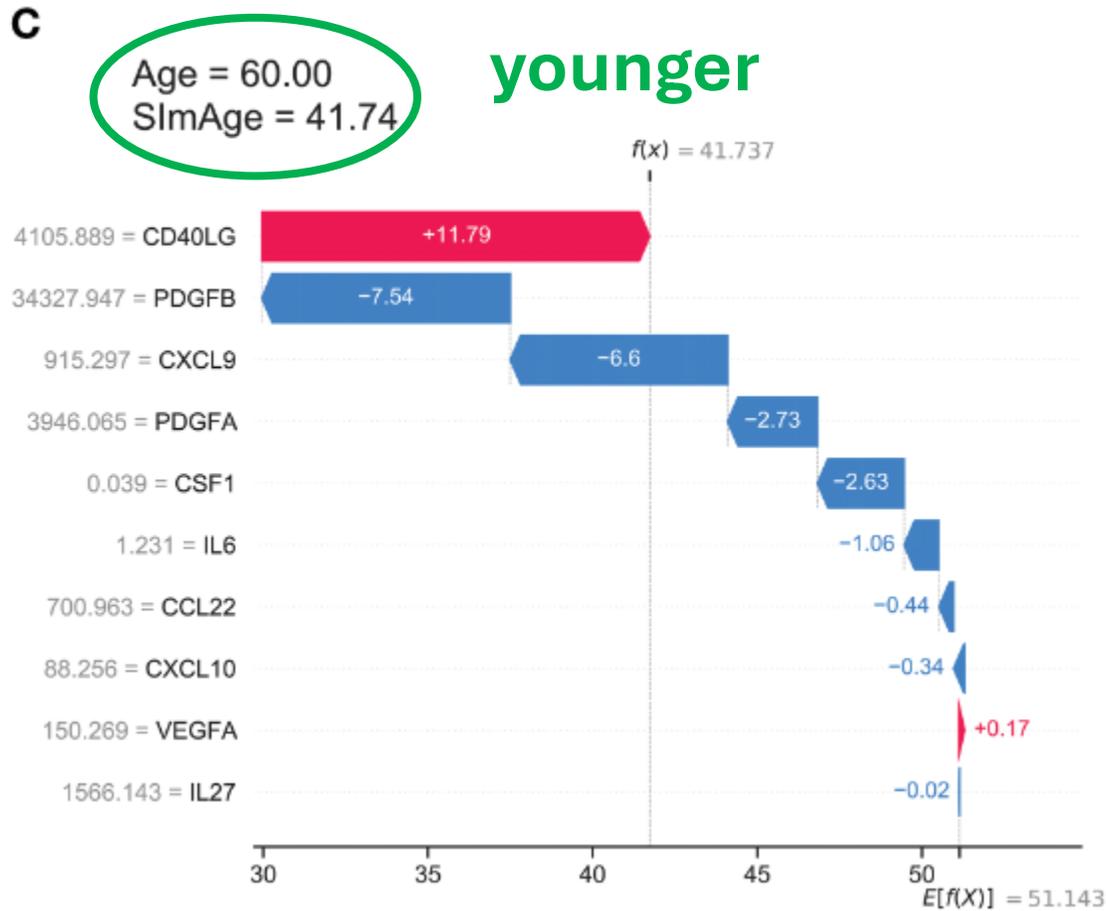
- **SHAP VALUES** (SHapley Additive exPlanations) **measure how much each feature** (such as each inflammatory marker) **contributes to the model's prediction** and have the greatest influence on the trait.
- **LOCAL EXPLAINABILITY:** SHAP-values indicate **the contribution of each characteristics** (*in this case each inflammatory marker*) **to the cognitive age of each specific person.**
- Local explainability is illustrated by **waterfall plots**, where features pushing the prediction **higher** are shown in **red**, while those pushing the prediction **lower** are in **blue**.

The local explainability of the SImAge model based on SHAP values is illustrated by waterfall plots.

The bottom part of each WATERFALL PLOT starts with the expected value of the model output $E[f(X)]$. Each row shows by how much in the positive (red) or negative (blue) direction each feature shifts the prediction relative to the expected value to the final model prediction for that sample $f(X)$.



The **local explainability** of the SImAge model based on SHAP values is illustrated by waterfall plots.





Contents lists available at [ScienceDirect](#)

Ageing Research Reviews

journal homepage: www.elsevier.com/locate/arr

Review article

eXplainable Artificial Intelligence (XAI) in aging clock models

Alena Kalyakulina^{a,b,c,*}, Igor Yusipov^{a,b,c}, Alexey Moskalev^a, Claudio Franceschi^a,
Mikhail Ivanchenko^{a,c}

^a Institute of Biogerontology, Lobachevsky State University, Nizhny Novgorod 603022, Russia

^b Research Center for Trusted Artificial Intelligence, The Ivannikov Institute for System Programming of the Russian Academy of Sciences, Moscow 109004, Russia

^c Department of Applied Mathematics, Institute of Information Technologies, Mathematics and Mechanics, Lobachevsky State University, Nizhny Novgorod 603022, Russia

Kalyakulina et al., Ageing Research Reviews, 2024

...we now can go beyond...



A Meta-Analysis of Brain DNA Methylation Across Sex, Age, and Alzheimer's Disease Points for Accelerated Epigenetic Aging in Neurodegeneration

Camilla Pellegrini¹, Chiara Pirazzini¹, Claudia Sala², Luisa Sambati^{1,3}, Igor Yusipov⁴, Alena Kalyakulina⁴, Francesco Ravaoli⁵, Katarzyna M. Kwiatkowska⁵, Danielle F. Durso⁶, Mikhail Ivanchenko⁴, Daniela Monti⁷, Raffaele Lodi^{1,3}, Claudio Franceschi⁴, Pietro Cortelli^{1,3}, Paolo Garagnani^{5,8,9,10} and Maria Giulia Bacalini^{1}*

Front Aging Neurosci. 2021 Mar 11;13:639428

In this study we considered **publicly available DNAm datasets of four brain regions (temporal, frontal, entorhinal cortex, and cerebellum)** from healthy adult subjects and **AD patients**, and performed a meta-analysis to identify sex-, age-, and AD-associated epigenetic profiles.

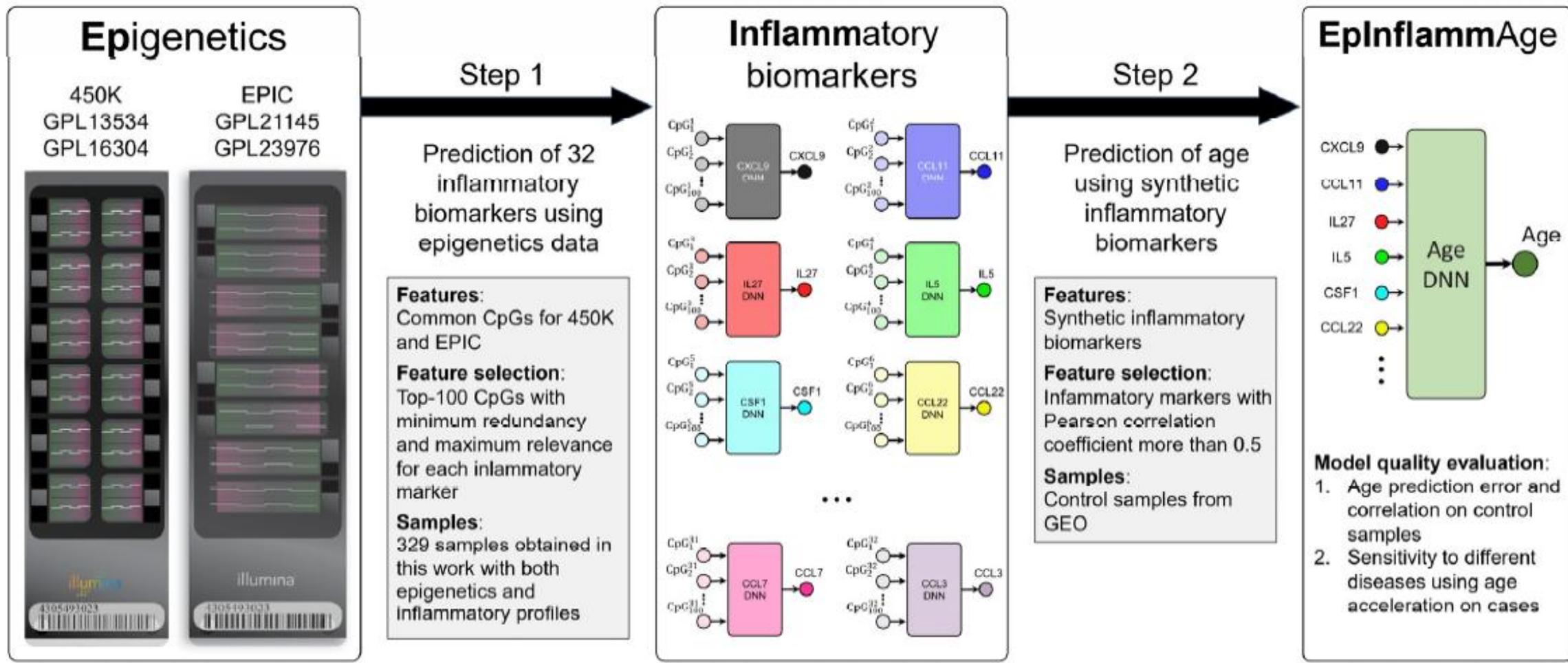
EpInflammAge: Epigenetic-Inflammatory Clock for Disease-Associated Biological Aging Based on Deep Learning

Alena Kalyakulina ^{1,2,*}, Igor Yusipov ^{1,2} , Arseniy Trukhanov ³ , Claudio Franceschi ² , Alexey Moskalev ² 
and Mikhail Ivanchenko ^{1,2}

Int J Mol Sci. 2025 Jun 29;26(13):6284.

- **EpInflammAge** is an **explainable deep learning tool** that **integrates epigenetic and inflammatory markers** to create a highly accurate, disease-sensitive biological age predictor.
- This novel approach **bridges two key hallmarks of aging: epigenetic age and inflammatory age.**

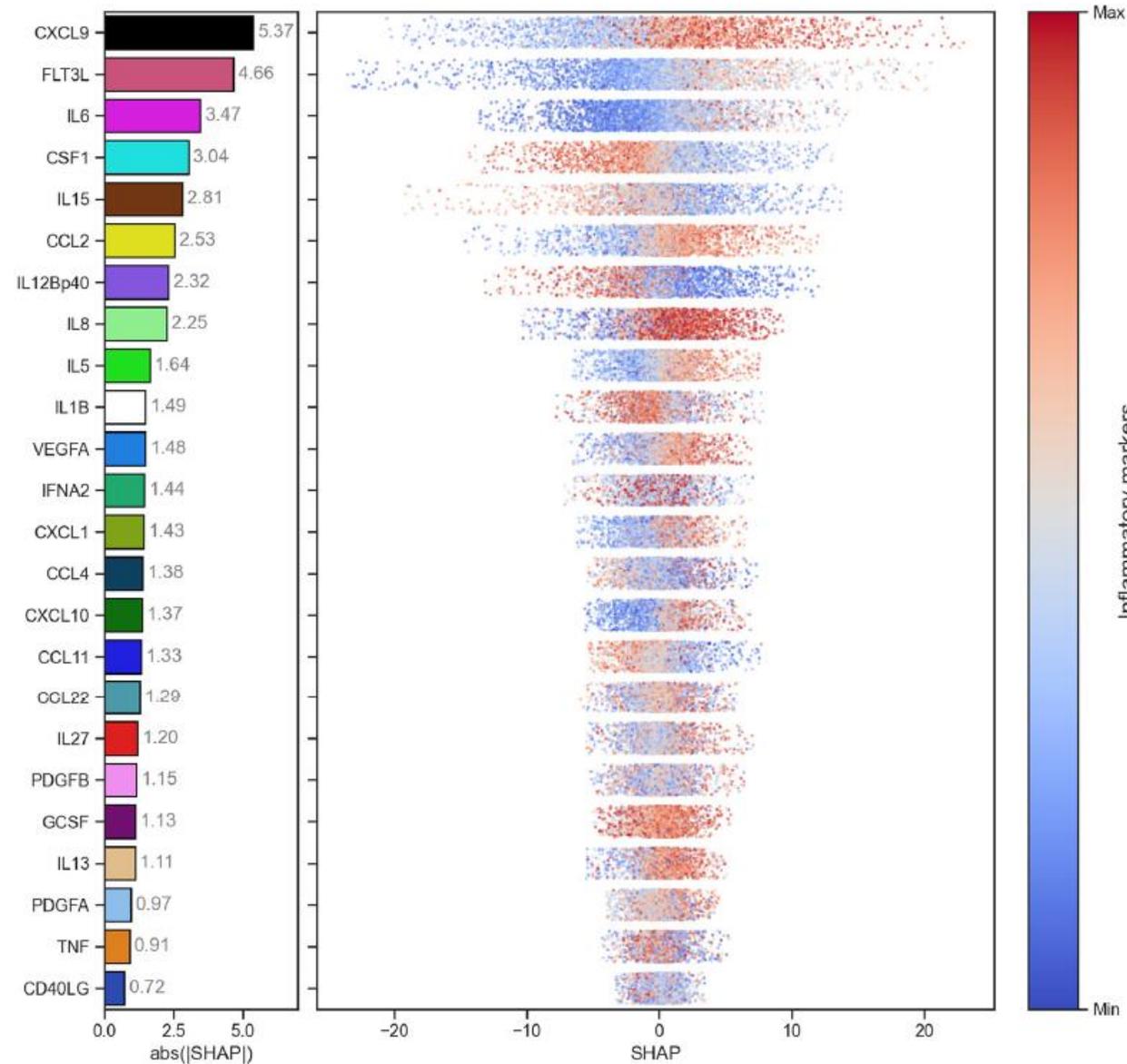
- **DEEP NEURAL NETWORKS** and **EPIGENETIC AND INFLAMMATORY DATA FROM THE SAME PARTICIPANTS**, were used to predict the blood levels of 24 cytokines.
- Open-source epigenetic data (**25 thousand samples**) was used for generating **synthetic inflammatory biomarkers** and training an age estimation model with a **Pearson correlation coefficient of 0.85** in healthy controls and a **MAE of 7 years**.



- **Explainable AI revealed the contribution of each feature to the age prediction.** The sensitivity to multiple diseases due to combining inflammatory and epigenetic profiles is promising for both research and clinical applications.
- **EpInflammAge is released as an easy-to-use web tool** that generates the age estimates and levels of inflammatory parameters for methylation data, with the detailed report on the contribution of input variables to the model output for each sample.

XAI and the EpiInflammAge model

Bar plot illustrate the absolute SHAP values for all the 24 inflammatory parameters



Cognitive aging clock based on Explainable artificial
intelligence

npj Aging 2025, in press

Mikhail I. Krivonosov^{1,2}, Tatiana A. Khabarova², Elena V. Kondakova^{1,2}, Tatiana A. Shvets^{3,2}, Vera N. Gorbunova⁴, Claudio Franceschi¹, Sofia A. Polevaia^{2,3}, and Mikhail V. Ivanchenko^{1,2}

¹Institute of Biogerontology, Lobachevsky State University, Nizhny Novgorod, 603022 Russia

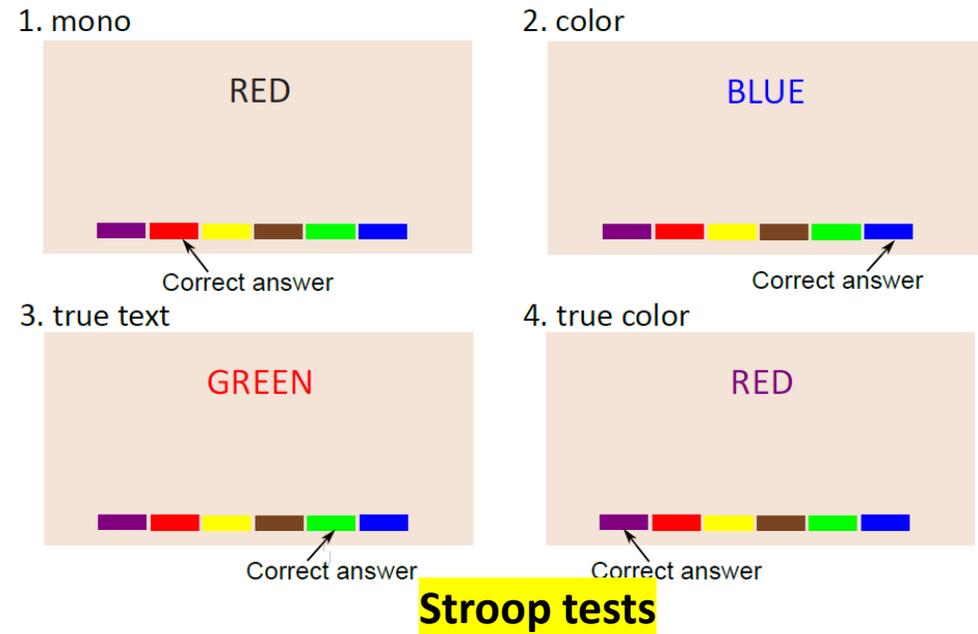
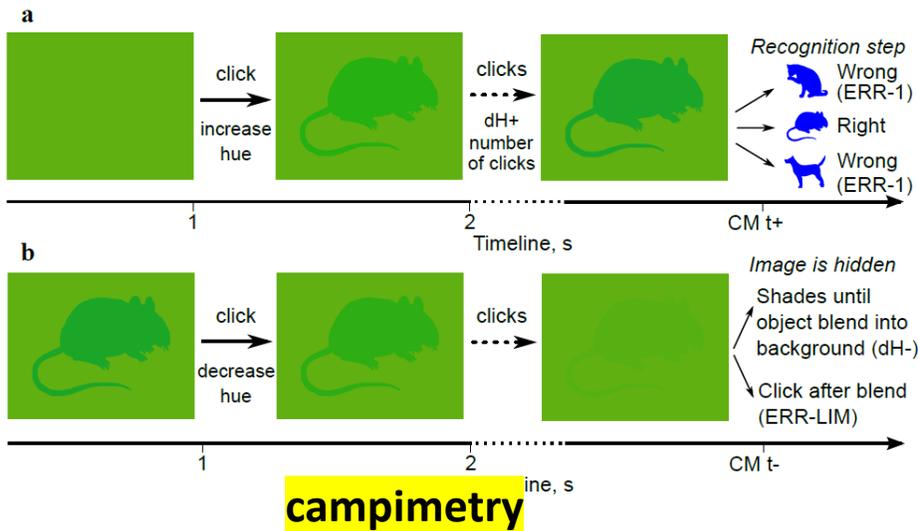
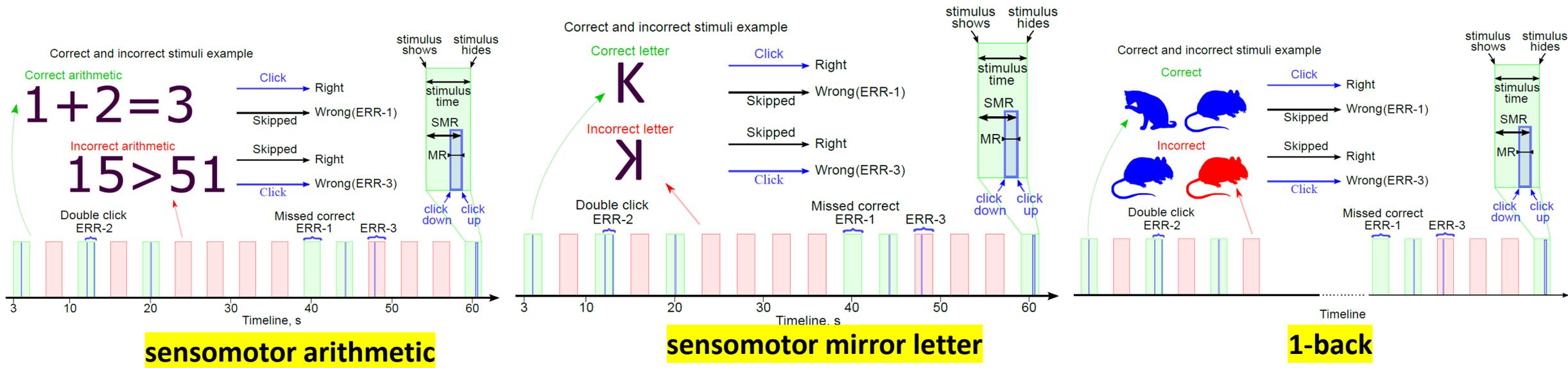
²Research Center in Artificial Intelligence, Lobachevsky State University, Nizhny Novgorod, 603022 Russia

³Department of Psychophysiology, Lobachevsky State University, Nizhny Novgorod, 603022 Russia

⁴Privolzhsky Research Medical University, Nizhny Novgorod, 603005 Russia

August 21, 2025

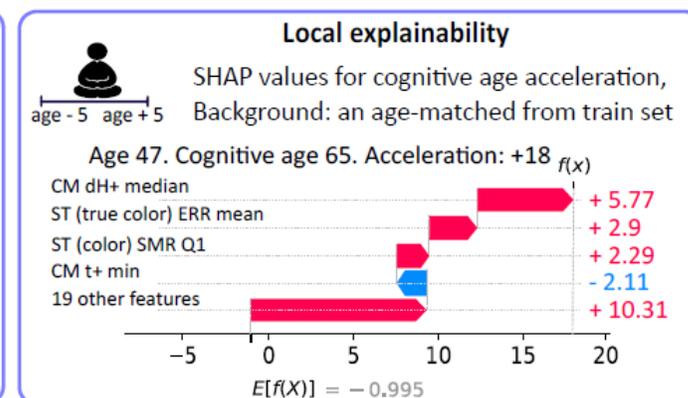
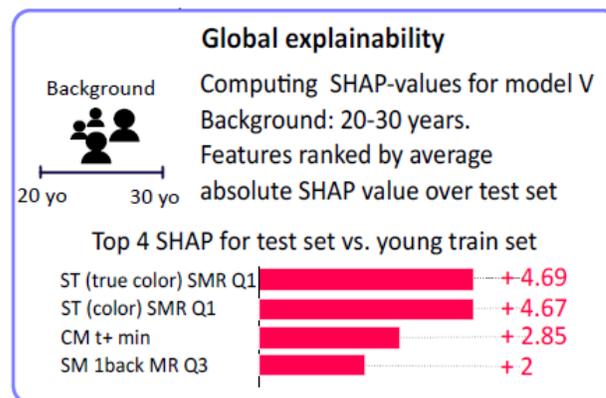
The study involved **1814 participants** of both sexes, aged **20–85 years** (729 males and 1085 females).



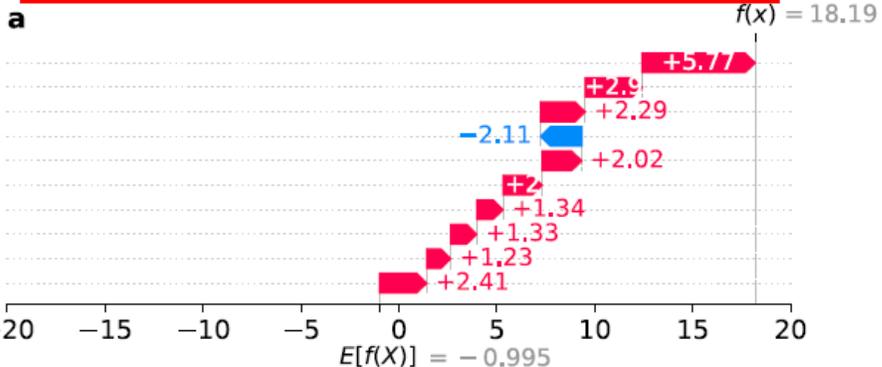
capturing **sensory and verbal perception**, **working memory** and **decision making** in the context of cognitive conflict.

The following **machine-learning models** were examined:

1. Support Vector Machine
2. Random Forest,
3. Linear regression
4. k-Nearest Neighbors
5. multilayer perceptron (MLP)
6. gradient boosting models AdaBoost
7. Gradient Boosting
8. Bayesian regression model BayesianRidge
9. gradient boosting model LightGBM (Light Gradient-Boosting Machine) from the LightGBM package.



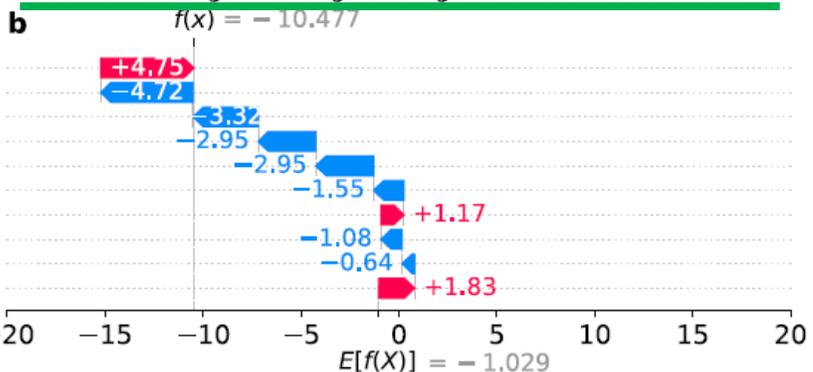
Sex: Female. Age: 47. Cognitive age: 65. Acceleration: +18.19



6 hue steps
55.2 %
1064 ms
2.8 s
8.9 hue steps
1377 ms
176 ms
133 ms
6.5 hue steps

CM dH+ median
ST (true color) ERR mean
ST (color) SMR Q1
CM t+ min
CM dH- mean
ST (true color) SMR Q1
SM arithmetic MR Q1
ST (true color) MR min
CM dH+ diff Q3
14 other features

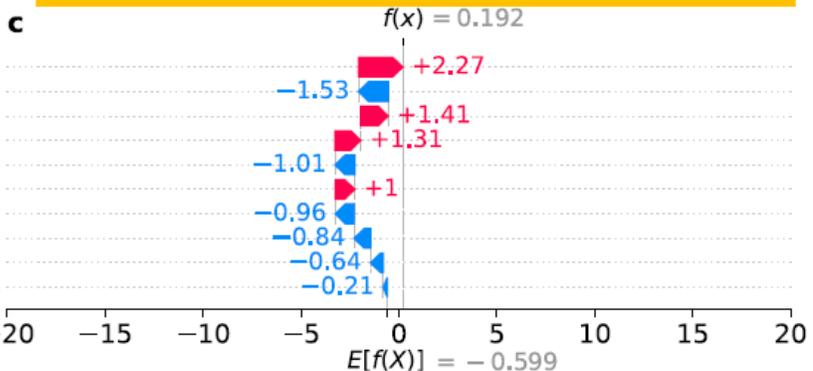
Sex: Female. Age: 47. Cognitive age: 37. Acceleration: -10.48



8 hue steps
975 ms
975 ms
0.4 hue steps
2.1 s
2.5 s
1304 ms
0.5 extra click
3.1 s

CM dH+ median
ST (true color) SMR Q1
ST (color) SMR Q1
CM dH- mean
CM t+ min
CM t+ Q1
ST (true text) SMR Q3
CM ERR LIM mean
CM t- Q1
14 other features

Sex: Male. Age: 48. Cognitive age: 49. Acceleration: +0.20



3.4 s
3 hue steps
1408 ms
2.1 hue steps
102 ms
7.9 s
1.2 ms
1760 ms
1.2 hue steps

CM t+ min
CM dH+ median
ST (true color) SMR Q1
CM dH- mean
SM arithmetic MR min
CM t- Q1
CM t- diff std
ST (true text) SMR Q3
CM dH+ diff Q3
14 other features

MULTIPLE ORGAN CLOCKS

Nervous system

- Brain MRI
- EEG
- Retina

XAI: Saliency Maps, Attention Maps, LIME, SmoothGrad, CAM, SHAP, Grad-CAM, PFI, G-Back

Respiratory system

- Chest X-ray

XAI: Saliency Maps, Grad-CAM

Cardiovascular system

- Biochemistry
- Immunology profile
- Whole blood DNAm
- CircRNA of whole blood
- Photoplethysmography pulsation waveform
- Heart MRI
- Carotid ultrasound
- ECG

XAI: PFI, SHAP, DeepPINK, Saliency Maps, Attention Maps, VIM, CAM, Grad-CAM

Skeletal and muscular systems

- Bone X-ray
- Orthopantomograms
- Skeletal muscles' gene expression

XAI: Attention Maps, DeepLIFT, Grad-CAM, CAM, SHAP

Integumentary System

- Skin microbiome
- Epidermal transcriptome

XAI: SHAP

Endocrine and digestive systems

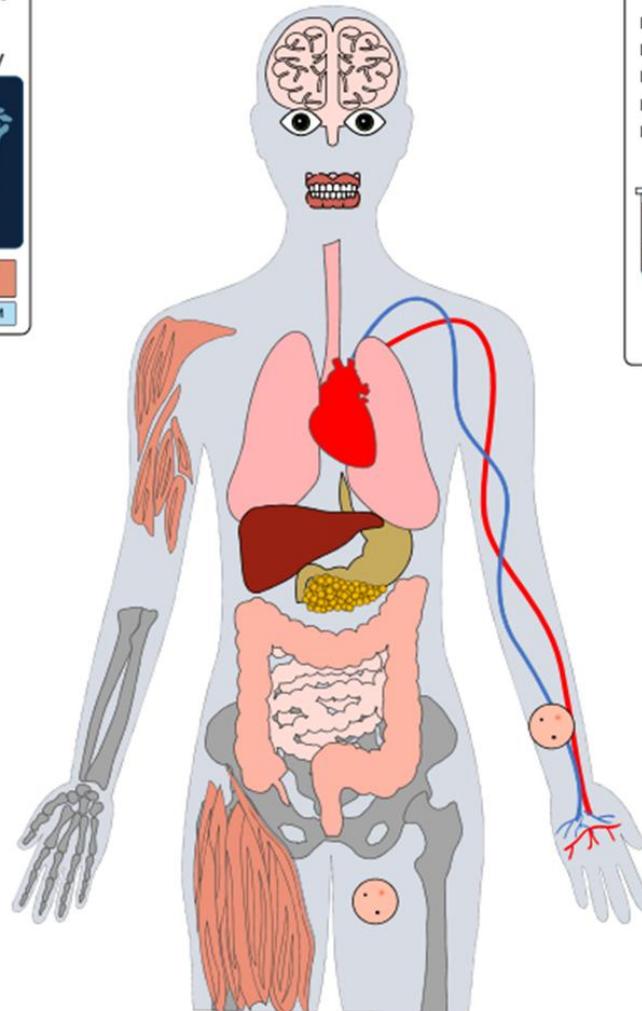
- Liver and pancreas MRI
- Gut microbiome

XAI: Attention Maps, ALE, PFI

Aggregated information

- Whole-body MRI
- Face images
- Pan-tissue clocks
- Electronic records

XAI: DeepPINK, Grad-CAM, Saliency Maps, Attention Maps, PFI, POP, SHAP



Kalyakulina et al., ARR 2024

MULTI-OMICS & MULTIPLE CLOCKS TO STUDY AGING IN YOUNG PEOPLE

Cell Reports

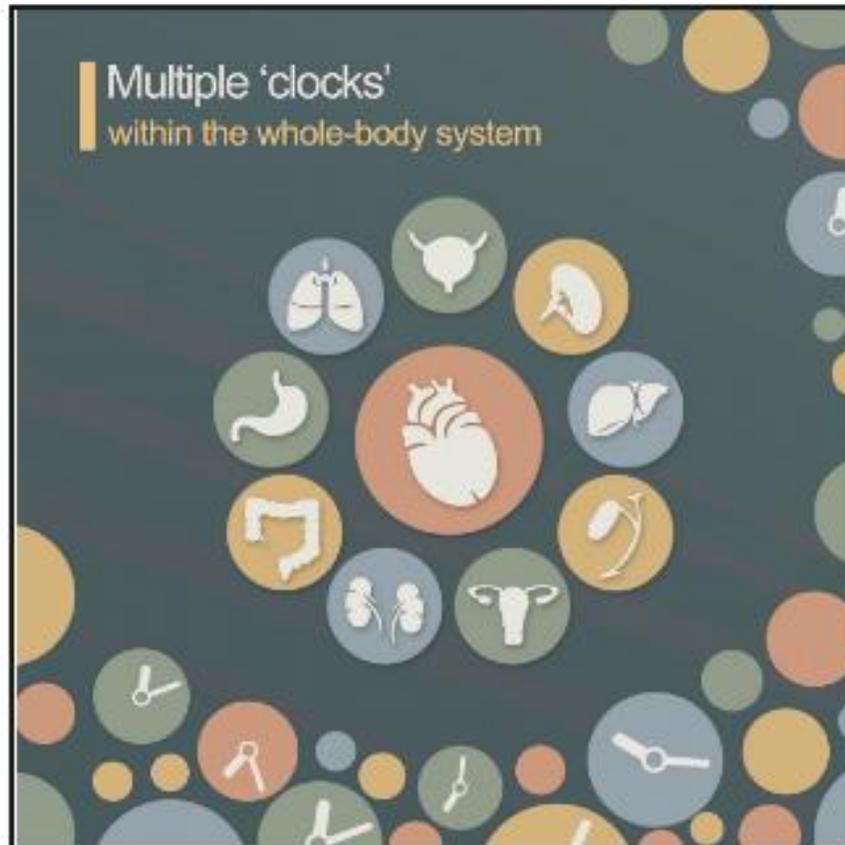
Cell Rep. 2022 Mar 8;38(10):110459

Distinct biological ages of organs and systems identified from a multi-omics study

Graphical abstract

402 features were measured

including **74 metabolomic features**, 34 clinical biochemistry features, 36 immune repertoire features, **15 body composition features**, 8 physical fitness features, 10 electroencephalography (EGG) features, **16 facial skin features**, and **210 gut microbiome features**



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In brief

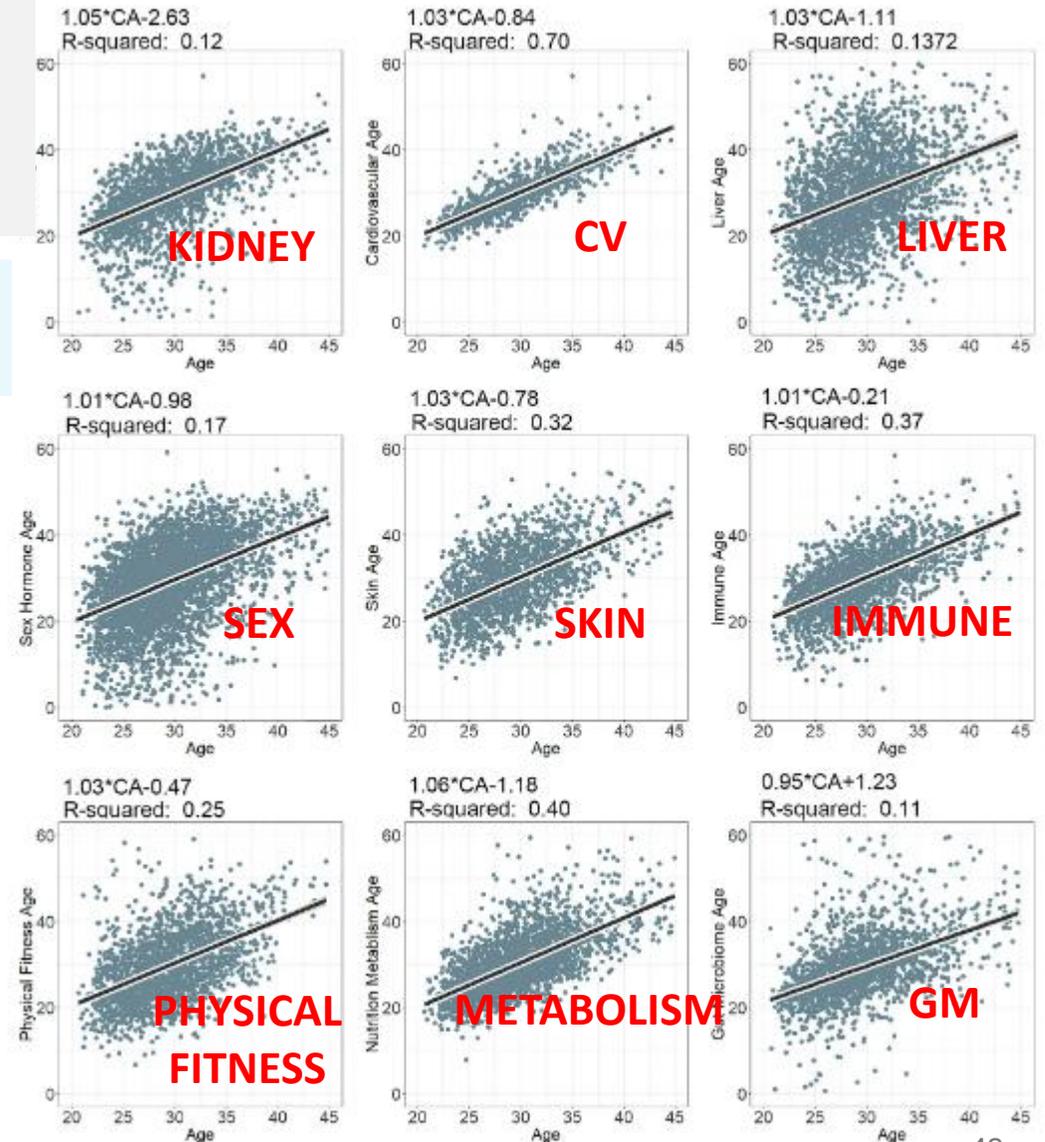
Nie et al. estimate biological ages of organs and systems using 402 multi-omics features from 4,066 individuals and demonstrate several applications. They find that organs and systems are aging at different rates, and biological ages could be utilized for population stratification, mortality prediction, and phenotypes of genetic association studies.

4,066 individuals aged between 20 and 45 years of age

Individual variability of the aging rates of organs and systems

The body as a mosaic of clocks

- One possible explanation is the presence of **multiple cellular clocks**, being organs and system composed of a mixture of different cell types.
- In addition, this phenomenon can be **different in each person**.



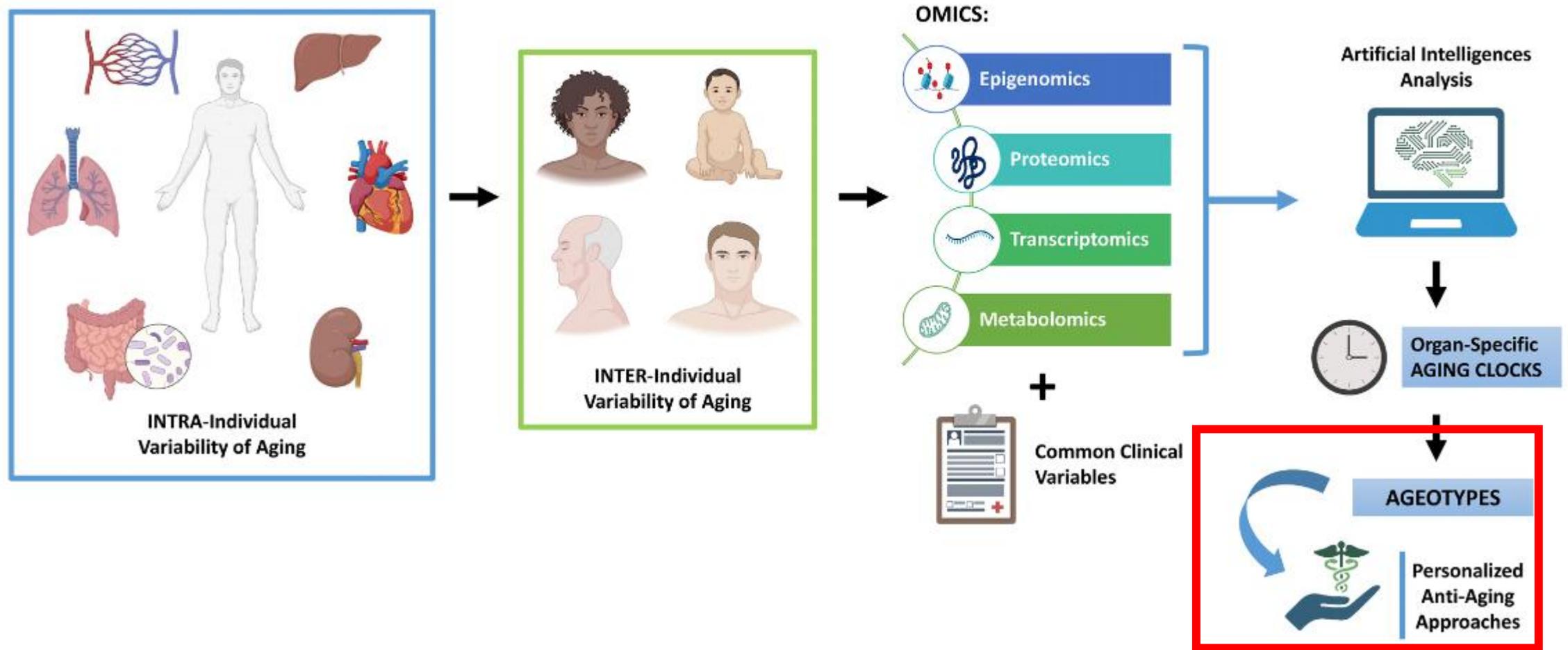
Highlights

- Constructing biological ages of organs/systems using multi-omics features
- Organs and systems are aging at different rates
- Specific biological age could predict disease of corresponding organs
- Biological ages of organs and systems have diverse genetic architectures

Nie et al., CR 2022

Organ-specific biological clocks: Ageotyping for personalized anti-aging medicine.

Prattichizzo F, Frigé C, Pellegrini V, Scisciola L, Santoro A, Monti D, Rippo MR, **Ivanchenko M**, Olivieri F, **Franceschi C**. *Ageing Res Rev.* 2024 Mar 4;96:102253.



Toward precision interventions and metrics of inflammaging

Nat Aging. 2025 Aug;5(8):1441-1454

Received: 20 January 2025

Accepted: 3 July 2025

Published online: 14 August 2025

Claudio Franceschi ^{1,2}, Fabiola Olivieri ^{3,4}✉, Alexey Moskalev⁵,
Mikhail Ivanchenko ^{1,2} & Aurelia Santoro ⁶✉

Here, we discuss **the heterogeneity of inflammaging**, proposing that it emerges as a consequence of **each individual's lifelong exposures to inflammatory stimuli**, shaped by a unique combination of genetics, lifestyle, socioeconomic conditions and environmental factors such as infections and pollution.

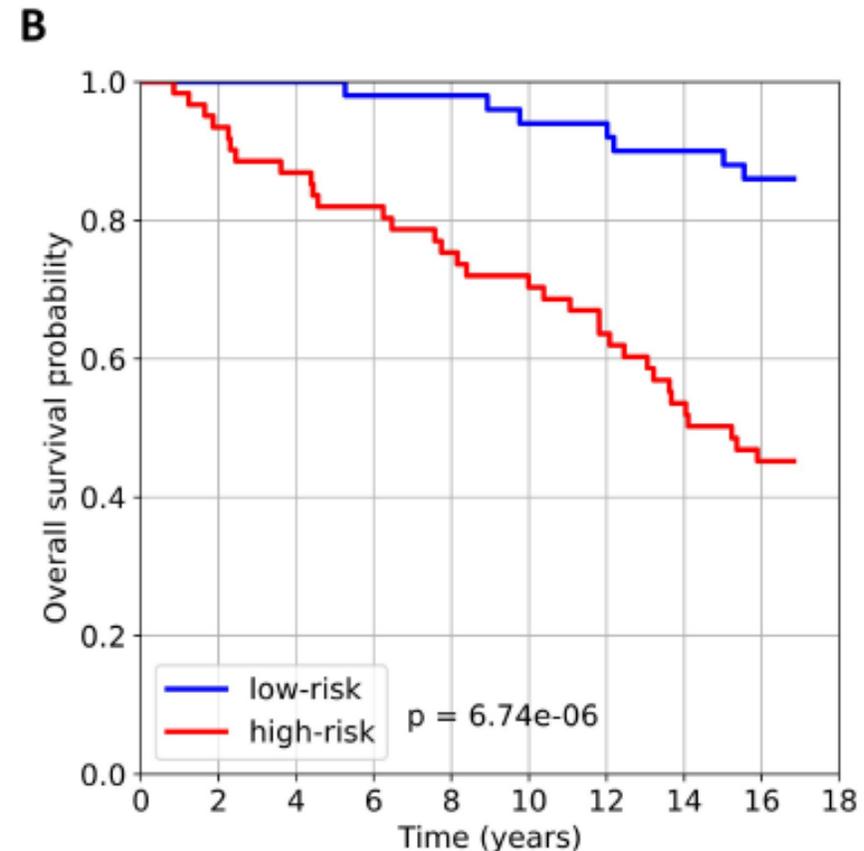
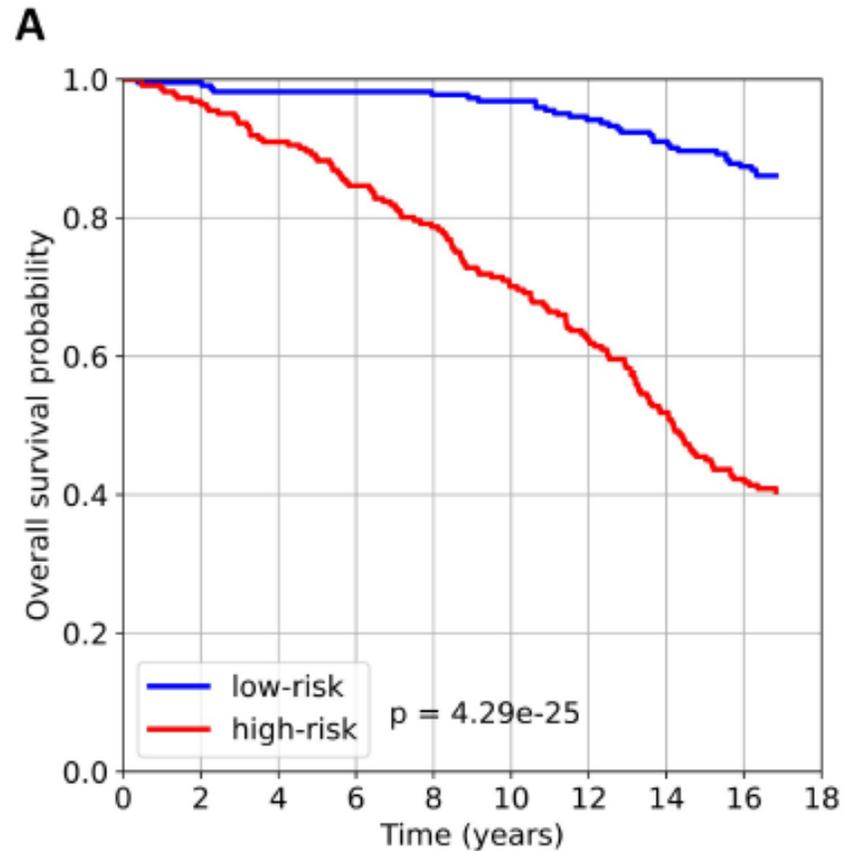
**Explainable artificial intelligence model
predicting the risk of all-cause mortality in patients with T2DM.**

Vershinina O, Sabbatinelli J, Bonfigli AR, Colombaretti D, Giuliani A, Krivonosov M, Trukhanov A, **Franceschi C**, **Ivanchenko M**, **Olivieri F**.

Front Endocrinol (Lausanne). **2025 Oct** 17;16:1689312.

- This study analyzed a cohort of **554 patients (aged 40-87 years) with type 2 diabetes mellitus (T2DM)** over a maximum **follow-up period of 16.8 years**, during which 202 patients (36%) died.
- Key survival-associated features were identified, and **multiple machine learning (ML) models were trained and validated to predict all-cause mortality risk.**
- To improve model interpretability, **Shapley additive explanations (SHAP) was applied** to the best-performing model.

Kaplan–Meier survival curves for the low-risk and high-risk groups in the train (A) and test (B) datasets, respectively.



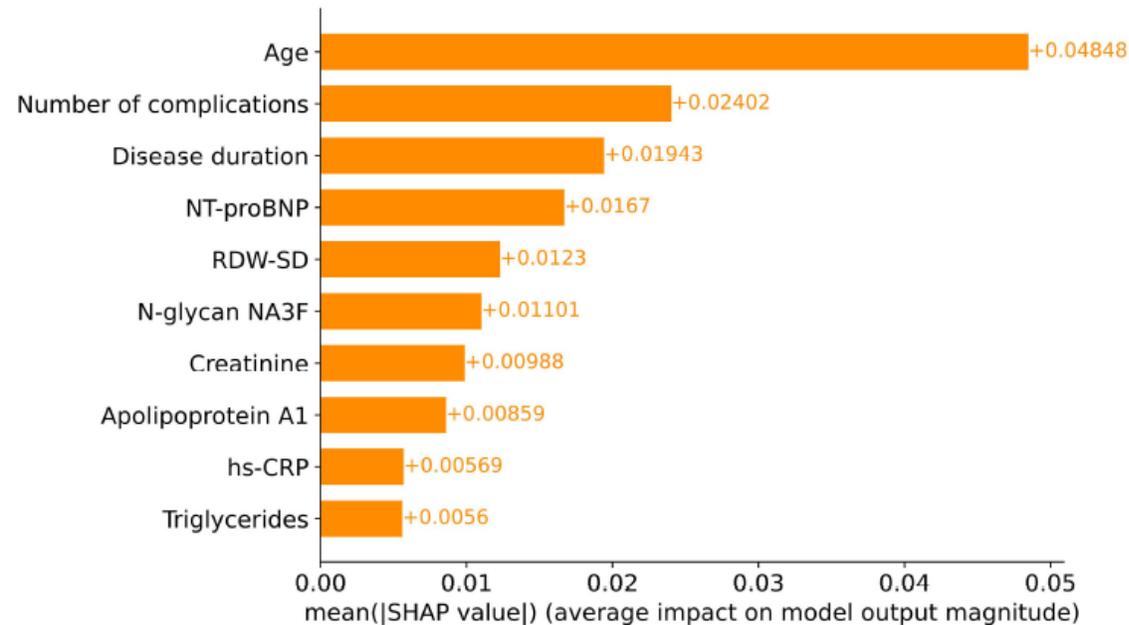
The model is predictive and clinically interpretable using 10 markers (age, number of complications, NT-proBNP, triglycerides, creatinine, hs-CRP, RDW-SD, apolipoprotein A1, disease duration, N-Glycan NA3F).

SHAP VALUES (SHapley Additive exPlanations)

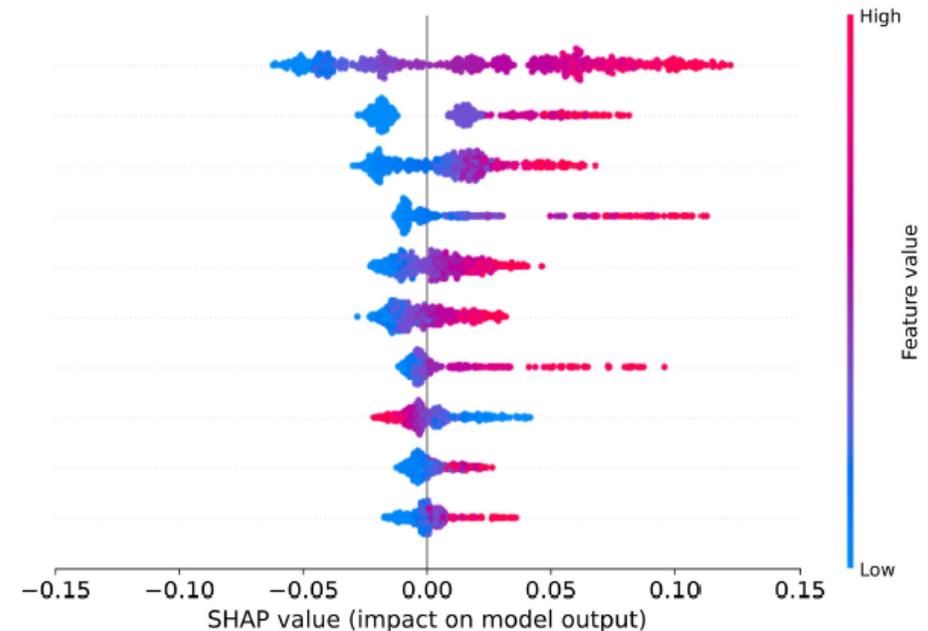
(A) Feature importance ranking across all participants based on mean absolute SHAP values.

(B) SHAP summary plot showing the directional relationship between feature values and model outputs, with color intensity indicating feature values (red: high, blue: low).

A

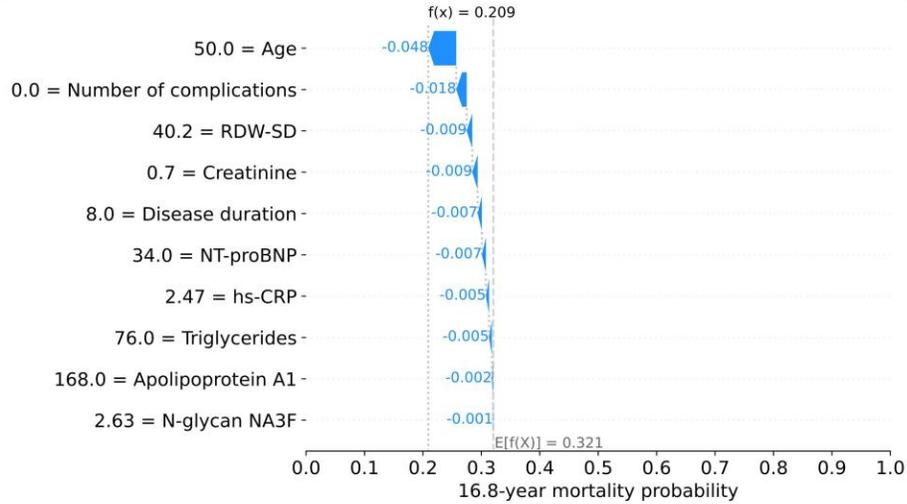


B

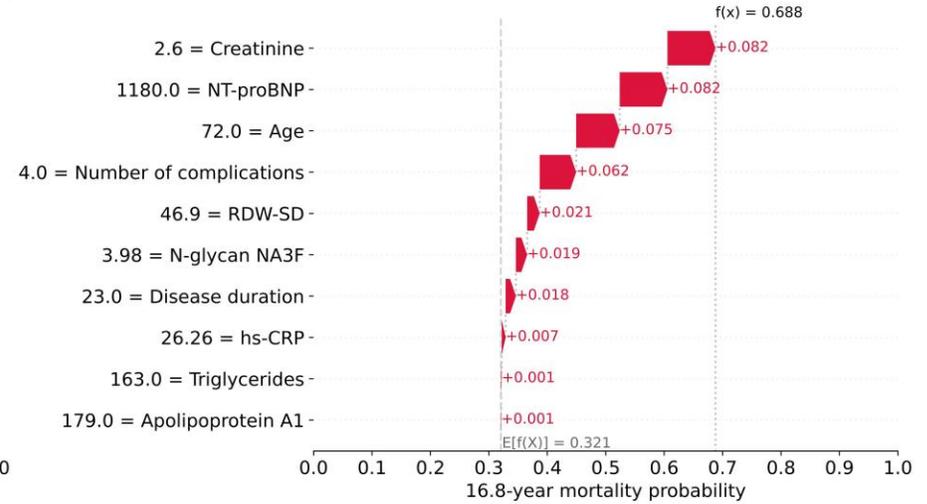


Local explanation of individual predictions using SHAP waterfall plots

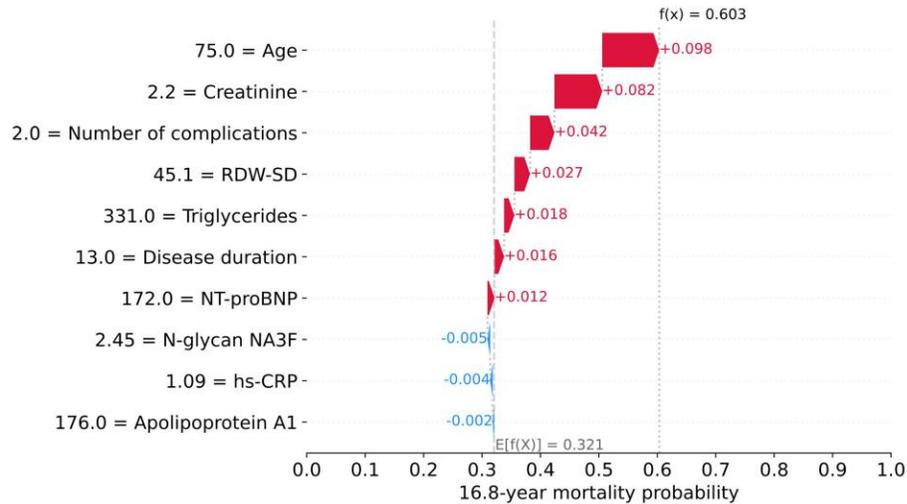
A



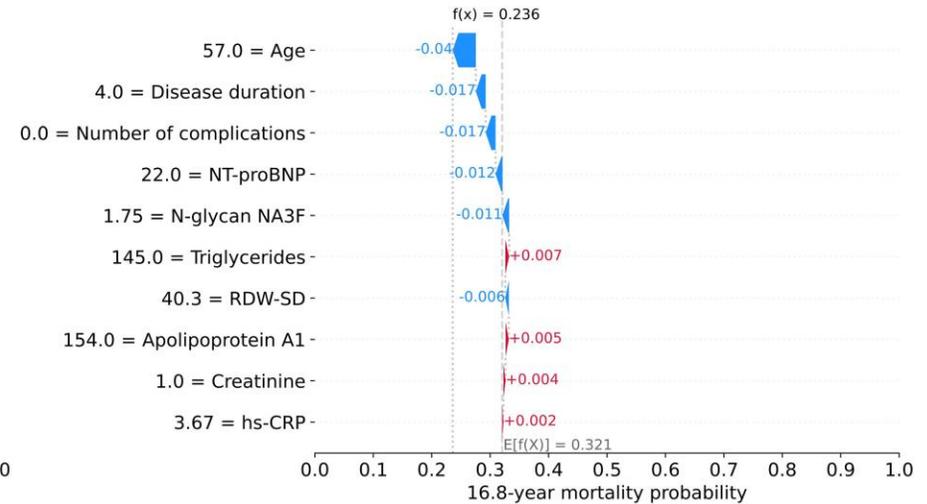
B



C



D





**Thanks
4 your
attention**

**BOLOGNA/UNIBO: the arcades of the oldest university in the
Western world (founded in 1080)**