Biomarkers of Longevity

Current State, Challenges and Opportunities Landscape Overview 2019

Increasing Role of Data Science and Artificial Intelligence in Biomarker Discovery and Monitoring

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Executive Summary

Executive Summary

"Biomarkers of Longevity: Current state, Challenges and Opportunities Landscape Overview 2019" **is an open-access special analytical case study by Aging Analytics Agency that uses comprehensive analytical frameworks to rank and benchmark existing panels of biomarkers of aging, health and Longevity according to their ratios of accuracy vs. actionability, identifying the panels of biomarkers that can have the greatest impact on increasing both individual and national Healthy Longevity in the next few years; providing advice to the industry for the conception, development and maturation of their action plans, and to policy makers in order to combat the problem of Ageing Population and realize that opportunity of National Healthy Longevity.**

The use of biomarkers is an indispensable component of industry analytics and assessment. It is the foundation upon which measurement of Healthy Longevity and the effectiveness of P4 Medicine, Regenerative Medicine and Longevity therapeutics are built. In this sense, the present report is designed as an in-depth review of the state of the art in biomarkers of biological age R&D to advise accurately the market, industry and public sectors. It was produced to offer a panoramic review of the global landscape of aging and Longevity biomarkers, containing selected lists, rankings and enhanced profiles with more than 70 Single Biomarkers directly correlated with the trajectories of age-related diseases and geriatric syndromes and exceeding 100 diverse Biomarker Panels for analytical science-driven comparisons that allow an optimal integration of multiple biomarkers for practical uses, such as drugs discovery and development for Longevity, Longevity therapies development, enhanced and sophisticated aging health monitoring in precision clinics, or development of digital environments aimed at assessing the aging trajectory to mention some particular utilities.

The purpose of the approach offered here is to facilitate the achievement of highly actionable monitoring systems for healthcare in general, and for healthcare during aging in particular; the beneficiary sectors are multiple, including clinical practice itself, but also translational research initiatives, frontier development frames that exploit the current conditioning of the mature field of Longevity, investment intentions in a market with the highest complexification rate in human history, and administrative initiatives for policy programs pointed to health promotion and precise prevention of age-related diseases, whose design and consolidation according to the subsequent criteria will guarantee a renaissance never seen before in economic and social dynamics.

In addition to their purely descriptive and analytical approaches, the report is designed to make key strategic recommendations, advice and guidance regarding biomarker implementations, technologies and techniques, within the reach of companies, other entities, and nations, in order to assist them in optimizing their action plans and strategies, providing specialized guidelines for business and investment core decisions.

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Based on the results of this analysis, the special case study presents its formulation of an ideal Minimum Viable Panel (MVP) of Longevity biomarkers: a panel of biomarkers which though not as precise as possible are precise enough and easily implementable. The report also presents a "most comprehensive" list of biomarkers of aging, devotes analysis to recent novel biomarkers of aging just entering R&D processes today, and highlights the core conclusion that uses of Digital Biomarkers and AI in biomarker discovery, development and assessments will come to be a necessary and indispensable component of Longevity Industry as the volume of data on both biomarkers and the complex networks of how they interact together continues to grow.

The report also delivers extensive profiles of single biomarkers and whole panels: their advantages and strengths, disadvantages and weaknesses, and future perspectives, challenges and opportunities with a focus on technologies currently used for assessment; concrete analysis of routine, advanced and novel biomarkers of aging, emerging tools and platforms, and insights about the impact of these biomarkers on health systems and clinical practice. The central purpose of those characterizations is to submit practical conclusions and recommendations regarding the Most Comprehensive and Most Viable (or Minimum Required) single biomarkers and panels of aging for their immediate implementation, either in biomedical research, therapeutic development and clinical trials, P4 Medicine and overall clinical practice, emphasizing the intersection between this wide new market, digital environments designed for real-time integration of aging and Longevity health metrics, and the new possibilities offered by AI platforms. The ultimate intention of Aging Analytics Agency is to solidly establish the relative and absolute usefulness of these presentations for precise and actionable measurement of biological age and enhanced assessments of health status, age-related diseases, geriatric syndromes, and Longevity.

As the scope of P4 Medicine broadens actively and healthily, the number of biomarkers, measurement technologies and platforms will increase rapidly to the thousands in the coming years; this will provide the opportunity to improve medical stratification to its maximum degree reaching Personalized, Participatory, Precision and Preventive Medicine for both, non-healthy populations and the healthy and young; also, to achieve the conditions for exhaustive and precise studies with samples of only one individual and allowing to prescind from conventional model organisms for biomedical research, due to the enormous flow of biological digital data that will be extracted continuously, individual to individual. These vast amounts of biomarkers data in the form of zeros and ones will make impractical the implementation of P4 Medicine by current, manual means; the construction and evaluation of massive networks of interconnected biomarkers will be carried out by highly specialized digital systems in pattern recognition, trained with aggregate information from hundreds of thousands of individuals minute by minute. Prototypes of these systems already exist, and are beginning to be implemented today.

Executive Summary

Aggregation of biomarkers of Longevity, rather than biomarkers of disease only, and from healthy populations - among the young and the even younger, rather than bedside data from the hospital populations, will be part of everyday life due to the novel Digital Health platforms capable of extracting truly massive amounts of clinical relevance data from a single patient through electronic layers.

These transformations already underway in biomarkers assessment modality will allow to move from the conventional therapeutic approach toward large-scale precision preventive medicine, the necessary vehicle to build both individual and national Healthy Longevity; and this will also be the foundation for the achievement of a unified theory of the root causes of aging and Longevity. The one plus the other, these two emerging together, will provide -are providing- a framework to intervene the process of aging, in a rather accelerated way than gradual. Tech companies rather than healthcare companies will play the leading role in this process; the threshold is already blurring. The use of AI will give sense to the thumping amount of digital biomarkers data, and it will allow the development of undoubtedly multiple optimal biomarker panels for the monitoring of aging and its correction, as well as countless other health biomarkers (digital and non-digital) for AI-driven analysis of each person's deep health status, allowing to orchestrate extremely personalized therapeutic interventions in response to minimal and currently imperceptible fluctuations in all those biomarkers. As the number of data points increases, AI-driven analysis will be strictly necessary in the Longevity industry and the health industry as a whole.

At this point, it is impossible to determine whether biotechnologies for Longevity have been successful if we cannot tell how advanced the aging process is in any given individual; but at the same time the latter will not be feasible until successfully achieving highly actionable Panels that allow to evaluate the aging process in broad healthy and less healthy differentiated ranges of the population spectrum. Is in this sense that Biomarkers are an essential factor in Aging Analytics Agency's strategic agenda, which includes recommendations for the establishment of AI centres in the United Kingdom, the indispensable medium to nail down the implementation of P4 Medicine and also to guarantee competitiveness in this new global health market, in the same way that highly specialized advice for the success of longevity-related government initiatives worldwide. It is important to develop and promote the widespread use of a comprehensive enough Panel of Biomarkers but, primarily, immediately actionable. We have documented many of the aging Biomarkers here and identified from among them those which, by the metrics described - and never reported in pre existing literature-, belong to this category we have named Minimum Required: the Most Viable Products for immediate implementation.

It is our hope that regardless of whether it is adopted wholesale, this entire work may serve as a starting point for discussion on how best to utilize the deep knowledge we already have to maximum effect on health of aging populations and aging economies, as soon as possible.

Methodology

The significance of biomarkers in the Longevity Industry is central since they are the primary metric in Geroscience, Regenerative Medicine, multiple AgeTech implementations and especially in P4 Medicine. Biomarkers also provide the prime source of data for the AI for Longevity industry, Drug Discovery and Development, Clinical Trials and for Translational Research. For these reasons, standardized metrics are needed to evaluate the biomarkers and the Panels that occupy us.

Within the scope of the report, the following methodology will be implemented, outlining the quantitative evaluation approach:

Accuracy Assessment

- It is a measure of the precision of the Single Biomarker or the Panel to predict overall biological age

- Its magnitude depends on the *number* of biomarkers evaluated by the Panel, the *nature* of those biomarkers, the *scientific background* of its direct association with age-related conditions and processes, and *qualitative characterizations* that assigns or removes scores

Availability Assessment

- It measures only the material capacity of extensive implementation for the reference character; i.e., for the single Biomarker or the Panel

- That material implementation capacity is understood as an expression of *market availability* of assays, tests, technologies or platforms, its *invasiveness*, *monetary value*, and the proposed classification framework for *qualitative characterizations* used also in Accuracy Assessments

Actionability Assessment

- Actionability is an expression or combination of both the accuracy and availability of a Biomarker or a Panel

- Actionability Assessment allows to evaluate not only the current material capacity of implementation of a biomarker or a Panel but also its viability for biological age prediction in such an immediate and effective frame of implementation, thus empowering Single Biomarker and Panel comparisons with a purely pragmatic sense

Such precision assessment will maximize the capacities of decision-makers to increase the efficiency of public health programs and policies, as well as decision-making processes in the core of healthcare industries.

Report Value Proposition

1. **What are the current most comprehensive biomarkers and panels to follow the aging trajectory and its related conditions and the most viable or minimum required ones, and how they can be implemented in the most ideal and useful manner?**

2. **What leading personalised and preventive market-ready health assessments can aging biomarkers and panels dispense to the existing pipeline of healthcare entities to maximize their competitive advantage?**

3. **What novel updates and advances in biomarker-related research and development will impact the health industry in the next years? Which of those should be watched closely for integration into clinics and biomedical or healthcare companies' existing pipelines as soon as their conditioning is achieved?**

We feel that our efforts over the course of the past five years have established a solid foundation of knowledge and expertise upon which we intend to summarize the entire landscape of aging and Longevity biomarker utilities in the health industry: the production of this new report entitled ***Biomarkers of Longevity Landscape Overview 2019: Current State, Challenges and Opportunities.***

This report seeks to answer these three specific questions, with an upcoming +300 pages version that will be produced over the next 3-6 months, and a new edition of its content during each financial quarter, incrementally increasing its breadth and depth as we go along, and with each edition providing a deeper, more comprehensive and more precise understanding of the landscape. It will deliver:

- Concrete deep analysis of which biomarkers and biomarker panels are available today; its strengths and weaknesses, their accuracy, availability and current actionability, and the opportunities and challenges related to its uses for real-time and precision monitoring of health status, and ultimately the reversal of biological age;

- Tangible estimations of which biological age biomarkers and implementations are consolidated, or their current conditioning stage for precision assessment of health status and endpoints of clinical trials and therapies;

- Highlights regarding the role of digital biomarkers and AI platforms and how they will become necessary and indispensable components of ageing and Longevity biomarker discovery, research, development and users daily use;

The parties who will have early access to this report will gain deep expertise on how they can optimize their clinics' strategic, technological and scientific prospects in order to deliver the most sophisticated and comprehensive precision health products and services for their clients.

Biomarkers of Longevity
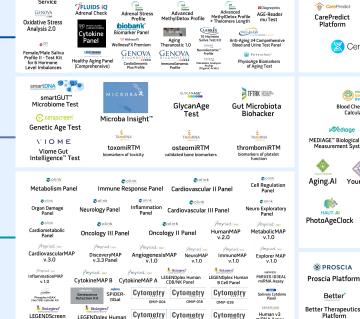
1st edition. Selection and Current Status, 2019

Biomarker Panels

Digital Panel Platforms

Single Biomarkers

Approved for Clinical Use

InsideTracker Inner Age | InsideTracker Ultimate Plan | RGCC aCGH RGCC | RGCC Immune-Frame | GENOVA DIAGNOSTICS Comprehensive Adrenal Stress Profile | B-Cell Memory and Naive Panel | Natural Killer Cell and Natural Killer T-Cell Panel

Health + Ancestry Service | Carnitine Panel | Cytokine Panel, TH1 | Hepatic Function Panel | Regulatory T-Cell Panel | Cytokine Panel

Oxidative Stress Analysis 2.0 | FLUIDS iQ Adrenal Check | Adrenal Stress Profile | Advanced MethylDetox Profile | Advanced MethylDetox Profile + Telomere Length | AGE-Reader mu Test

Cytokine Panel | biobank Biomarker Panel | Aging Theranostic 1.0 | 10 Hormone Saliva Test Kit | Anti-Aging #4 Comprehensive Blood and Urine Test Panel

Female/Male Saliva Profile II - Test Kit for 6 Hormone Level Imbalances | Healthy Aging Panel (Comprehensive) | CardioGenomic Plus Profile | ImmunoGenomic Profile | NeuroGenomic Profile | Metabolic Analysis Profile (Organic Acids) | PhysioAge Biomarkers of Aging Test

Digital Panel Platforms:
Babylon Health Platform | Ada Symptom Checker app | CarePredict Platform | Health Reviser Platform | Google's DeepMind Health AI Platform | Centers for Age Control AgeMeter

Single Biomarkers:
CD4+ T-Cell Recent Thymic Emigrants | CD57+ NK Cells, Peripheral Blood by Flow Cytometry | CD21 (Dendritic Cell) by Immunohistochemistry

Healthcare-Ready (waiting for clinical approval)

smartGUT Microbiome Test | MICROBA Microba Insight | GlycanAge Test | TFTAK Gut Microbiota Biohacker

cerascreen Genetic Age Test | toxomiRTM biomarkers of toxicity | osteomiRTM validated bone biomarkers | thrombomiRTM biomarkers of platelet function

VIOME Viome Gut Intelligence Test

Digital Panel Platforms:
Blood Chemistry Calculator | AI-Powered Radiology Assistant | MEDIAGE Biological Age Measurement System | KenSci Platform | Enlitic Platform | Aging.AI | Young.AI | PathAI Platform | Buoy Health Platform | HAUT.AI PhotoAgeClock | Haut.AI Skin Health | Digital Nutrition Platform

Single Biomarkers:
Telomere Length Test | DNAge Epigenetic Aging Clock | EpiHealth | DNAge Test | EpiLiver | TeloYears + Advanced Ancestry Tests | Epigenetic Age Analysis Version 2.0 | EpiAging | Targeted Seq. for DNA Methylation Analysis | EpiSocialpsych | EpiBreast | Telomere Length and Biological Age Testing

Research Use Only

Metabolism Panel | Immune Response Panel | Cardiovascular II Panel | Cell Regulation Panel

Organ Damage Panel | Neurology Panel | Inflammation Panel | Cardiovascular III Panel | Neuro Exploratory Panel

Cardiometabolic Panel | Oncology III Panel | Oncology II Panel | HumanMAP v.2.0 | MetabolicMAP v.1.0

CardiovascularMAP v.3.0 | DiscoveryMAP v.3.3 Panel | AngiogenesisMAP v.1.0 | NeuroMAP v.1.0 | ImmunoMAP v.1.0 | Explorer MAP v.1.0

InflammationMAP v.1.0 | CytokineMAP B | CytokineMAP A | LEGENDplex Human CD8/NK Panel | LEGENDplex Human B Cell Panel | MiRXES ID3EAL miRNA Assay | Salivary Cytokine Panel

Phospho-H2AX (Ser139) cellular kit | Senescence Detection Kit | SPIDER-βGal | Cytometry OMIP-004 | Cytometry OMIP-018 | Cytometry OMIP-039

LEGENDScreen Human PE Kit | LEGENDplex Human Th Cytokine Panel | Cytometry OMIP-027 | Cytometry OMIP-007 | Cytometry OMIP-029 | Human v3 miRNA Assay

Digital Panel Platforms:
PROSCIA Proscia Platform | freenome Freenome Platform | BenevolentAI Platform | Better Therapeutics Platform | Tempus Platform | ICabonX Platform

AGING ANALYTICS AGENCY

Biomarkers of Longevity

Distribution by **Operational Category**

AGING ANALYTICS AGENCY

Research Kit or Other Laboratory Practice Supplies

ImmunoMAP v.1.0	AngiogenesisMAP v.1.0	CytokineMAP A
MetabolicMAP v.1.0	DiscoveryMAP v.3.3 Panel	CytokineMAP B
NeuroMAP v.1.0	InflammationMAP v.1.0	CardiovascularMAP v.3.0
Explorer MAP v.1.0	HumanMAP v.2.0	LEGENDplex Human B Cell Panel
LEGENDplex Human Th Cytokine Panel	LEGENDplex Human CD8/NK Panel	LEGENDScreen Human PE Kit
Cell Regulation Panel	Cardiovascular II Panel	
Organ Damage Panel	Cardiovascular III Panel	
Immune Response Panel	Metabolism Panel	
Neurology Panel	Neuro Exploratory Panel	Cardiometabolic Panel
Oncology II Panel	Oncology III Panel	
Inflammation Panel	Phospho-H2AX (Ser139) cellular kit	Human v3 miRNA Assay
MiRXES ID3EAL miRNA Assay	Senescence Detection Kit	SPiDER-ßGal

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Medical Test

Aging Theranostic 1.0	WellnessFX Premium
Anti-Aging #4 Comprehensive Blood and Urine Test Panel	InsideTracker Inner Age
Healthy Aging Panel (Comprehensive)	Female/Male Saliva Profile II - Test Kit for 6 Hormone Level Imbalances
	InsideTracker Ultimate Plan
10 Hormone Saliva Test Kit	FLUIDS iQ Adrenal Check	Oxidative Stress Analysis 2.0	NeuroGenomix™ Profile
Comprehensive Adrenal Stress Profile	Metabolic Analysis Profile (Organic Acids)	ImmunoGenomic® Profile
CardioGenomicPlus™ Profile	Adrenal Stress Profile	Advanced MethylDetox Profile + Thelomere Length
Advanced MethylDetox Profile	Immune-Frame	aCGH RGCC
PhysioAge Biomarkers of Aging Test	Health + Ancestry Service
Cytokine Panel	Natural Killer Cell and Natural Killer T-Cell Panel	CD57+ NK Cells, Peripheral Blood by Flow Cytometry
CD21 (Dendritic Cell) by Immunohistochemistry	B-Cell Memory and Naive Panel
Cytokine Panel, TH1	Regulatory T-Cell Panel	Hepatic Function Panel
CD4+ T-Cell Recent Thymic Emigrants	Carnitine Panel	Cytokine Panel

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Informational Purpose Test or Platform

Salivary Cytokine Panel	DNAge™ Epigenetic Aging Clock
Epigenetic Age Analysis Version 2.0	DNAge® Test
Targeted Seq. for DNA Methylation Analysis	Genetic Age Test
EpiLiver	EpiBreast	EpiHealth
EpiAging	EpiSocialpsych	GlycanAge Test
Viome Gut Intelligence™ Test	Microba Insight™	Gut Microbiota Biohacker
smartGUT™ Microbiome Test	Telomere Length and Biological Age Testing
TeloYears + Advanced Ancestry Tests	toxomiRTM biomarkers of toxicity
thrombomiRTM biomarkers of platelet function	Telomere Length Test	osteomiRTM validated bone biomarkers

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Epidemiological or Theoretical Panel Only

biobank uk
Biomarker Panel

Cytometry PART A	Journal of Quantitative Cell Science	ISAC
OMIP-004: In-Depth Characterization of Human T Regulatory Cells.		
Cytometry PART B	Journal of Quantitative Cell Science	ISAC
OMIP-007: Phenotypic Analysis of Human Natural Killer Cells.		
Cytometry PART B	Journal of Quantitative Cell Science	ISAC
OMIP-027: Functional Analysis of Human Natural Killer Cells.		
Cytometry PART B	Journal of Quantitative Cell Science	ISAC
OMIP-018: Chemokine Receptor Expression on Human T Helper Cells.		
Cytometry PART B	Journal of Quantitative Cell Science	ISAC
OMIP-039: Detection and analysis of human adaptive NKG2C+ natural killer cells.		
Cytometry PART B	Journal of Quantitative Cell Science	ISAC
OMIP-029: Human NK-Cell Phenotypization.		

Biomarkers Real-Time Assessment Technology

Centers for Age Control AgeMeter	Health Reviser Platform
MEDIAGE™ Biological Age Measurement System	AGE-Reader mu Test

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AI Platform

PhotoAgeClock	Haut.AI Skin Health	Aging.AI	Young.AI
CarePredict Platform	Enlitic Platform	Freenome Platform
AI-Powered Radiology Assistant	PathAI Platform	Buoy Health Platform
Tempus Platform	BenevolentAI Platform	KenSci Platform
Digital Nutrition Platform		Proscia Platform
Ada Symptom Checker app		Google's DeepMind Health AI Platform
Blood Chemistry Calculator		
Better Therapeutics Platform	Babylon Health Platform	ICabonX Platform

Biomarkers of Longevity

Age-Related Disease

Alzheimer's disease

Parkinson's disease

Cancer

1 Chronic Obstructive Pulmonary disease

2 Maculophaty

3 Periodontitis

Cardiovascular diseases and Diabetes

Rheumatoid arthritis

Sarcopenia

4 Osteopenia and Osteoporosis

Osteoarthritis

5

Aging

Mitochondrial dysfunction
Inflammation
Oxidative stress
Autophagy dysregulation
Cellular senescence
Stem cell exhaustion
Loss of proteostasis
Decreased proteasome activity
Protein aggregation
Dysregulated nutrients sensing
Cell disruption
Cell death
NLRP3 activation
Telomere shortening
Lipofuscinogenesis
PI3 kinase-mTOR signal activation
Gut microbiota alterations

Oxidized proteins
Lipid peroxidation
IL-1β, IL-6, IL-12, IL-18, TNF-α, TGFβ, IFN-γ
8-hydroxyguanosine
8-hydroxy-2'-deoxyguanosine
20S core reduced activity
Senescent cells
Activation of pro-inflammatory cytokines
Increased intestinal permeability

p21CIP1/WAF1
p16INK4A
β-galactosidase activity
SASP
IL-1β, IL-6, IL-18
Chemokines (CXCL8 and CCL2)
Metalloproteinases
Stress markers such as Parkin, and Phosphatase and tensin homolog-induced protein kinase 1

Inflammasome activation
Abs vs self-epitopes
Heat shock proteins

Pro-inflammatory cytokines
Porphyromonas gingivalis express peptidylarginine deiminase generating citrullinated epitopes

IL-6
TNF-α
CRP
Inflammatory markers

IL-8
HGMB1
HGMB2

IL-1
IL-6
TNF-α
CRP

Senescent cells
Activation of pro-inflammatory cytokines
Inflammatory cells (astrocytes)
Increased intestinal permeability
Serotonin system alteration

IL-6
Senescent cells

NT-proBNP, hsTnT, IL-6, IL-15
Apolipoprotein B, Apolipoprotein C-III
Soluble receptor for AGE
Advanced glycation end-products (AGEs)
Osteopontin, Osteoprotegerin
Matrix metalloproteinase 3
Angiopoietin 2, Chromogranin A
LDL, sdLDL
HbA1C, Blood glucose
Growth/differentiation factor 15
Hepatocyte growth factor receptor
Glutathione S transferase α
α-2-Macroglobulin
Trefoil factor 3

IL-1β, IL-6
HGMB1, TNF-α
Matrix metalloproteinases
Abs vs modified self-epitopes

Biomarkers

Mechanisms shared with Aging Process

AGING ANALYTICS AGENCY

Introduction

Introduction

Aging Analytics Agency is currently developing a comprehensive, open-access report, Biomarkers of Longevity: Current state, Challenges and Opportunities Landscape Overview 2019, a special analytical case study that uses comprehensive analytical frameworks to rank and benchmark existing panels of biomarkers of aging, health and Longevity according to their ratios of accuracy vs. actionability, identifying the panels of biomarkers that can have the greatest impact on increasing both individual and national Healthy Longevity in the next few years.

The use of biomarkers is an indispensable component of industry analytics and assessment. It is the foundation upon which measurement of Healthy Longevity and the effectiveness of Longevity therapeutics is built. The report is designed as an in-depth review of the state of the art in biomarkers development to advise accurately the market, industry and public sectors when addressing the challenges related to our following conclusions and forecasts about the immediate future of the Biomarker and Longevity industries as a whole:

As the scope of P4 Medicine broadens, the number of biomarkers and measurement technologies and platforms will increase rapidly to the thousands in the coming years. This makes the implementation of P4 medicine impractical by current, manual means.

Aggregation of biomarkers of longevity and aging, rather than biomarkers of disease, and from healthy populations - among the young and the even younger, rather than bedside data from the hospital populations, will be part of everyday life due to the novel Digital Biomarkers capable of extracting truly massive amounts of clinical relevance data from a single patient through electronics.

That described shift will allow to move from the conventional therapeutic approach toward precision preventive medicine, and will also be the foundation for a unified theory of the root causes of aging and longevity; both providing a framework to intervene the process. Tech companies rather than healthcare companies will play the leading role in this process.

The use of AI will give sense to this thumping amount of data, and it will allow the development of surely multiple optimal panels of aging biomarkers as well as other health biomarkers (digital and non-digital) for analysis of each person's outcomes, and for orchestrating extremely personalized therapeutic interventions in response to fluctuations in those biomarkers. As the number of data points increases, it becomes not only optimal, but strictly necessary to use AI and big data analysis in not only the longevity industry, but in the health industry as a whole.
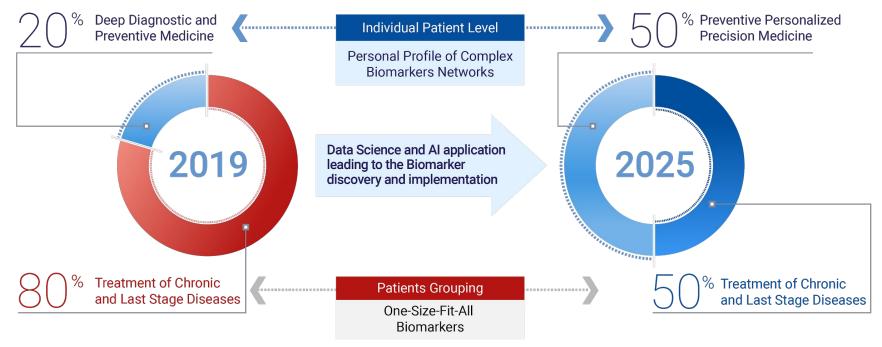
Introduction

The report is designed to make key strategic recommendations regarding technologies and biomarkers implementations within the reach of companies, entities and nations in order to assist them in optimizing their developmental action plans and strategies, providing specialized guidance for business and investment core decisions. It will deliver:

- **A "most comprehensive" list of single biomarkers of aging and Panels, their advantages and strengths, disadvantages and weaknesses, and future perspectives, challenges and opportunities with a focus on technologies currently used for assessment;**

- **Concrete analysis of recent novel biomarkers of aging just entering R&D processes today, emerging tools, and novel assay platforms awaiting approval or standardization for clinical implementation, one step away of being market-ready within the next several years;**

- **Highlights respecting why AI platforms will come to be a necessary and indispensable component of Longevity biomarker discovery, research and development;**

- **Overview of different categories of panels, whether for Research Use Only or Approved for Clinical Use;**

- **Conclusions and practical recommendations regarding the Most Comprehensive Panels and the Most Viable (Minimum Required) Panels for immediate implementation, either in biomedical research, therapy development, P4 medicine and clinical practice, emphasizing the relative and absolute usefulness of these Panels for precision measurement of biological age and enhanced assessments of health status, age-related diseases, geriatric syndromes, and Longevity.**

The parties with early access to this report will gain deep expertise on how they can optimize their development and implementation strategies, and how to analyze the technological and scientific backgrounds and prospects of the Longevity industry in order to deliver sophisticated action plans aimed for remaining at the forefront in the broad and changing field of healthcare.
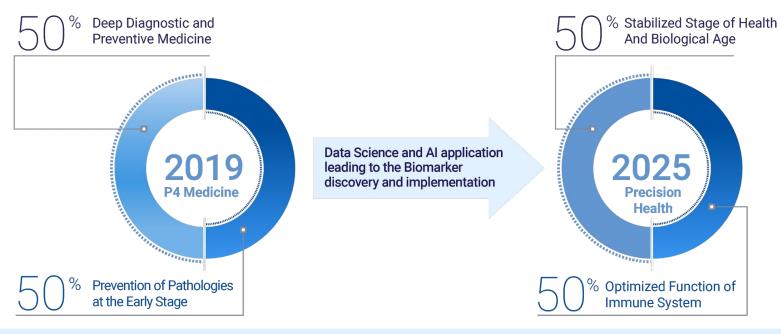
Biomarkers for Paradigm Shift from Treatment to Prevention

20% Deep Diagnostic and Preventive Medicine

Individual Patient Level

Personal Profile of Complex Biomarkers Networks

50% Preventive Personalized Precision Medicine

2019

Data Science and AI application leading to the Biomarker discovery and implementation

2025

80% Treatment of Chronic and Last Stage Diseases

Patients Grouping

One-Size-Fit-All Biomarkers

50% Treatment of Chronic and Last Stage Diseases

Jamie Metzl for Longevity. Technology: "First, we're increasingly understanding the biomarkers of aging. And that is giving us a language of measurement. We can assess with more precision whether certain interventions are working or not working. With the new tools of AI and machine learning we're really seeing is a super convergence of different technologies that are all pushing forward, including the science of human Longevity."

Biomarkers for Paradigm Shift from P4 Medicine to Precision Health

50% Deep Diagnostic and Preventive Medicine

2019
P4 Medicine

50% Prevention of Pathologies at the Early Stage

Data Science and AI application leading to the Biomarker discovery and implementation

50% Stabilized Stage of Health And Biological Age

2025
Precision Health

50% Optimized Function of Immune System
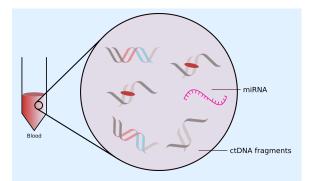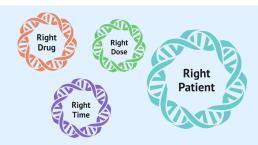
Since 2013, Deep Learning systems have surpassed human performance in multiple applications, such as face and image recognition. Predictors of chronological age, and biological age - or functional age-, are rapidly gaining popularity and with this a deep outburst of research and development is awakened, both in the scientific and industrial spheres. A new market is brewing. AI has shown that it is possible to overcome the best human ophthalmologists or radiologists, the best conventional predictors of complex pathologies such as Parkinson's and Alzheimer's have been surpassed. And in this framework, AI-driven biomedical research and development efforts are now already facing aging.

Introduction to Biomarkers

A **Biomarker** or a **biological marker** is a characteristic that is objectively measured and evaluated as an indicator of some biological state, condition or process. Biomarkers are used in many scientific fields and commercial activities, and subjected to several and dissimilar classifications that follow different criteria. Regarding health related activities:
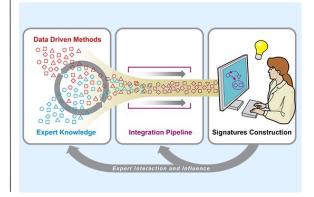
In **biomedical research** and **clinical practice**, biomarkers include measurements that suggest the etiology of, susceptibility to, activity of, or progress of a disease. The use of biomarkers in basic and clinical research as well as in clinical practice has become so commonplace that their presence as primary endpoints in clinical trials is now accepted almost without question.

In **drug discovery and development**, biomarkers can be used to predict or identify safety problems related to a drug candidate, for patient selection for clinical study enrollment, stratification of patients during study, identification of toxic responses before they becomes clinically evident, in addition to reveal an expected or unexpected pharmacological activity such as reversal, deceleration or acceleration of biological age, the particular case that appeals us.

Increased knowledge around the human genome and other omics, and correlations with disease risks and progression are expected to shift the current biomarker focus. Drug companies have been increasing their investment into exploratory biomarkers that focus on areas such as infectious diseases, central nervous system (CNS) disease conditions and cardiovascular diseases to broaden their overall biomarker research and development strategies. For example, CNS disease conditions such as schizophrenia, Parkinson's and Alzheimer's are finding initial success in biomarker identification for targeted therapies.

Introduction to Biomarkers. Conventional Classification Frameworks

For practical purposes, single biomarkers and biomarker panels used in the setting of biomedical research, drug discovery and development, and clinical practice are often classified following any of the criteria outlined below:

- **Clinical Outlook.** In relation to clinical specialties, to organ systems and related vital functions, and to subordinated diseases of each one. We find biomarkers for oncology profiling, cardiology and hematology profiling, neurology profiling, endocrinology, infectious diseases, immunology, and so forth. Due to the low degree of specificity, here we usually find large biomarker panels and not single biomarkers.

- **Disease and Conditions Outlook.** Within each clinical specialty or often overlapping a number of them, the set of biomarkers that make up the profile of a pathology or set of related pathologies. These categories are usually subsets of each one in the previous criterion, also using panels much more often than single biomarkers.

- **Functional and Structural Outlook.** Based on its association with specific functional and structural variables, either physical, anatomical, histological or physiological. For example, biomarkers for locomotor function, or for strength, balance, bone density, body impedance or waist circumference, in this case all closely interconnected parameters. This approach is usually subordinate to the previous two. Due to its higher degree of specificity, it usually allows the use of single biomarkers or small panels, although large panels are more descriptive.

- **Source Outlook.** By the source of the biological material or data, and its processing methodology. The clinical evaluation usually addresses a small amount of biomarkers related to one or a few conditions, or to the general state of health. A broad examination of the biomarker network provided by each test could allow the extraction of a large amount of data about health status.

- **Focus Level Outlook.** Based on the focus level, or the associated diagnostic or therapeutic depth, biomarkers can be divided by the domain to which they belong on the organismic scale.There are six categories or levels, Biochemistry, Genomic, Proteins and Cell Signalling, Cellular, Tissue and Organ markers, each one correlated with a particular set of evaluations, potential interventions, and an order of physical magnitude. Thus, Organ biomarkers are related to Regenerative medicine, and Biochemical ones include lipid-, glyc- and metabolomics among others.

- **Omic Outlook.** In relation to the *-omic* field to which they belong, what will determine the types of technologies and evaluation methods.

- **Application Outlook.** More typical of the market analysis, according to the activities in which biomarkers are applied, or 'what are they used for'.

- **Type Outlook.** Indispensable. Classification according to characteristics of its operational definition, or 'how are they used for'.

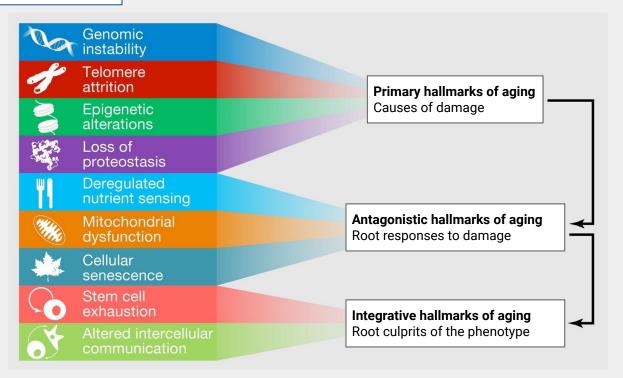# Biomarker Conventional Classification Frameworks

Clinical Outlook
- Biological Age measurement | Ophthalmology
- Alcohol/drug treatment | Gastroenterology
- Oncology | Orthopaedics
- Cardiology | Hematology
- Neurology | Rheumatology
- Endocrinology | Sleep disorders
- Maternal-Fetal medicine | Urogynecology
- Infectious diseases | Dentistry
- Dermatology | Otolaryngology
- Allergology | Immunology

Diseases and Conditions Outlook
- Osteoporosis | Arthritis
- COPD | Sarcopenia
- Aging-associated Metabolic Syndrome | Osteopenia
- Type II Diabetes | Obesity
- Cancer | Alzheimer's Disease
- Amyotrophic Lateral Sclerosis | Parkinson's Disease
- Hypertension | Cerebrovascular Disease
- Atherosclerosis | Mild Cognitive Impairment
- Cardiovascular Disease | Dementia
- Coronary Artery Disease | Multiple Sclerosis
- Deep Vein Thrombosis | Coordination impairment
- Blindness | Age-related Macular Degeneration

Functional and Structural Outlook
- Locomotor function; Dexterity
- Bone density; Bone mass hip
- Muscle mass; Body impedance; Abdominal fat
- Blood pressure; Lipid profile; Glycated Hb
- Lung capacities; Transpulmonary pressure
- Processing speed; Working memory; Visual memory
- Endocrine profile; HPA axis
- Chronic inflammatory status

Source Outlook
- Digital biomarkers + AI
- Human Biomonitoring
- Imaging
- Laboratory procedures (Blood, Saliva, Biopsy)
- Pedigree and Family History
- Routine and Comprehensive Physicals

Focus Level Outlook
- Biochemistry level
- Genomic level
- Proteins and Cell Signalling level
- Cellular level
- Tissue level
- Organs level

Omic Outlook
- Genomics | Transcriptomics
- Epigenomics | Foodomics
- Metabolomics | Nutritional genomics
- Proteomics | Pharmaco-genomics
- Lipidomics | Pharmaco-microbiomics
- Glycomics | Toxico-genomics

Application Outlook
- Drug Discovery and Development
- Drug Formulation
- Preclinical Trials
- Clinical Trials
- Diagnostic Development
- Diagnostic
- Disease Risk Assessment
- Screening
- P4 Medicine
- Regenerative Medicine
- Research

Type Outlook
- Efficacy - *Pharmacodynamic*
- Efficacy - *Predictive*
- Efficacy - *Prognostic*
- Efficacy - *Surrogate and Diagnostic*
- Validation
- Safety

Age Mechanism Outlook
- Genomic Instability
- Telomere Attrition
- Epigenetic Alterations
- Loss of Proteostasis
- Deregulated Nutrient Sensing
- Mitochondrial Dysfunction
- Cellular Senescence
- Stem Cell Exhaustion
- Altered Intercellular Communication

Special mention apart, biomarkers in pharmaceutical industry research and development are predominantly described based on a **Type Outlook** classification, the most widely used criterion; that is, as validation, safety and efficacy biomarkers, and likewise also as surrogate and diagnostic, prognostic, predictive, and pharmacodynamic biomarkers, all categories that are not mutually exclusive since specific clinical setting can determine how the biomarker is used and interpreted. In the particular sphere of aging, age-related diseases and geriatric syndromes, biomarkers are usually classified according to an **Aging Mechanism Outlook:** by the root causes and the mechanisms or phenomena triggered by these causes; for instance, *loss of proteostasis* triggers *inflammaging* mechanisms, although this is not the single cause of age-related low grade inflammation.

Aging Mechanism Outlook. The proposed nine hallmarks of aging are grouped into three categories. Those hallmarks considered to be the primary causes of cellular damage. Those considered to be part of compensatory or antagonistic responses to the damage. These responses initially mitigate the damage, but eventually, if chronic or exacerbated, they become deleterious themselves. Integrative hallmarks that are the end result of the previous two groups of hallmarks and are ultimately responsible for the functional decline associated with aging.

Sources Image: López-Otín C., et al. The hallmarks of aging. 2013.

What are Biomarkers of Aging?

Aging is a major risk factor for most chronic diseases and functional impairments. Within a homogeneous age sample there is considerable variation in the extent of disease and functional impairment risk, revealing a need for valid biomarkers to aid in characterizing complex aging processes. The identification of biomarkers is further complicated by the diversity of biological living situations, lifestyle activities and medical treatments.

Thus, there has been no identification of a single biomarker or gold standard tool that can successfully monitor healthy aging, or perhaps not until the recent development of Horvath's Epigenetic Clock and Glycomic Biomarkers.

How do we know when a biomarker is a **Biomarker of Aging**? It depends on how it is sourced. The current approach to biomarkers is to take them from people at various stages of a disease's known progress, which in practice means sourcing them from hospital patients. Isolating biomarkers of aging, however, means collecting data which marks the difference between healthy people only, e.g. between the young and even younger, with no traces of any officially recognised diseases.

> **A special focus of Aging Analytics Agency, is the use and recommendation of AI for the development of an optimal Panel of Biomarkers of Aging – a specific niche where the implementation is lagging behind the science. This is one of the most important diagnostic services that could be offered, and yet it does not receive the attention it deserves compared to the amount of tangible benefits it can deliver.**

The diagnostic technologies of the future should be anchored to Panels of Aging Biomarkers digitally obtained. This will enable the current state of health of each patient to be continually and precisely monitored, allowing the effectiveness of interventions and micro-adjustments to interventions to be continuously assessed in detail, enabling an unprecedented degree of precision and prevention in biomedicine, and an unprecedented degree of prescience in biomedical research. **This, in a nutshell is the nature of the aforementioned digital transformation of the Longevity Industry.**

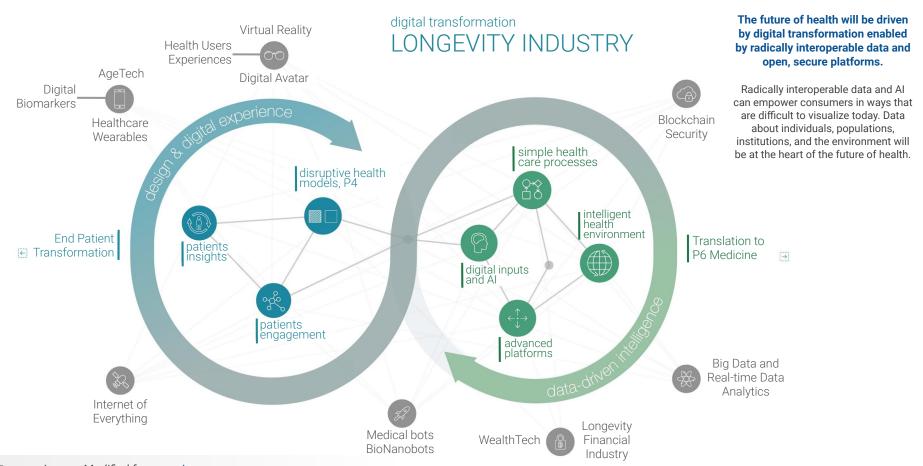| Ten winning business archetypes after health's digital transformation |
|---|
| **Data + platforms** |
| Data convener |
| Science and insights engine |
| Data/platform infrastructure builder |
| **Well-being + care delivery** |
| Health products developer |
| Consumer-centric health "virtual home + community" |
| Specialty care operator |
| Localized health hub |
| **Care enablement** |
| Connectors and intermediaries |
| Individualized financer |
| Regulator |
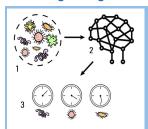
Digital Transformation of the Health and Longevity Industry

digital transformation
LONGEVITY INDUSTRY

The future of health will be driven by digital transformation enabled by radically interoperable data and open, secure platforms.

Radically interoperable data and AI can empower consumers in ways that are difficult to visualize today. Data about individuals, populations, institutions, and the environment will be at the heart of the future of health.

Virtual Reality

Health Users Experiences

Digital Avatar

AgeTech

Digital Biomarkers

Healthcare Wearables

design & digital experience

End Patient Transformation

disruptive health models, P4

patients insights

patients engagement

Internet of Everything

Medical bots BioNanobots

simple health care processes

intelligent health environment

digital inputs and AI

advanced platforms

data-driven intelligence

Blockchain Security

Translation to P6 Medicine

Big Data and Real-time Data Analytics

WealthTech

Longevity Financial Industry

Sources **Image:** *Modified from* everis.

What are Biomarkers of Aging?

Biomarkers of Aging are biomarkers that could predict functional capacity at some later age better than will chronological age. Stated another way, biomarkers of aging would give the true Biological Age, which may be different from the Chronological Age.

1. Gut microbiota profile
2. Neural network; Feature selection
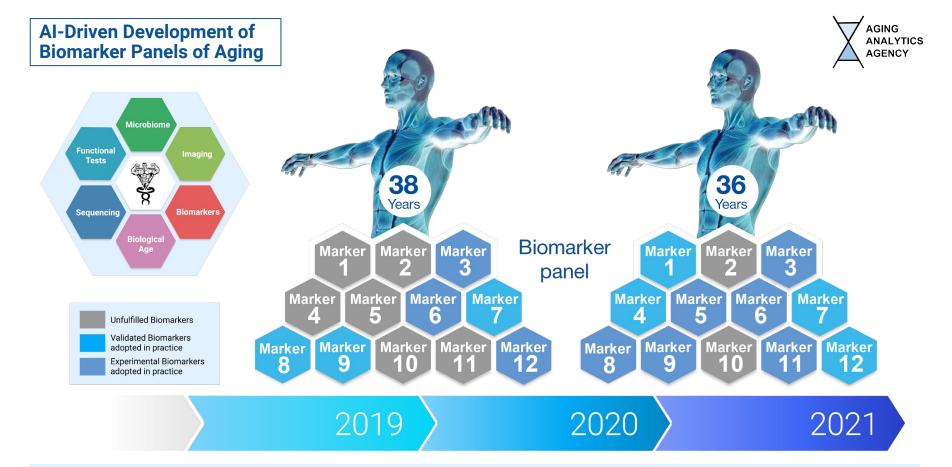3. Effects microbiota elicit on age prediction

Within this frame, **Biological Age** is intended as a synthetic index constituted by a single marker or the combination of few biological markers which, alone or integrated with functional markers, not only correlates with chronological age but is/are capable of identifying individuals "younger" or "older" than their chronological age in the same demographic cohorts; i.e., with a different health status, globally or in relation to a particular vital function or organ system, allowing this index to accurately predict future health status and functional capacity.

Validated Biomarkers of Aging would allow for testing interventions to extend lifespan, because changes in the biomarkers would be observable throughout the lifespan of the organism. Although maximum lifespan would be a means of validating biomarkers of aging, it would not be a practical means for long-lived species such as humans because longitudinal studies would take far too much time.

Ideally, biomarkers of aging should:

- Assay the biological process of aging itself and not only the predisposition to disease, since the vast majority of the aging process occurs without pathological manifestation;

- Cause a minimal amount of trauma to assay in the organism, thus enabling continuous measurement and analysis that do not cause morphofunctional damage, which ultimately results in aging;

- Be measurable with high reproducibility during extremely short intervals compared to the lifespan of the organism.

With such biomarkers, it should be possible to obtain Trajectories of Aging, where the "accelerated" ones would predict unhealthy aging and diseases, while the "decelerated" ones would be associated with healthy aging and longevity. The possibility to draw Trajectories of Aging is a fascinating, far-reaching perspective, especially in consideration of the long incubation preclinical period that characterizes most of the major age-related chronic diseases, being also considered the critical time window for effective treatments. Biomarkers of Biological Age could greatly contribute to identify the subjects characterized by higher risk to develop overt clinical diseases who would have a major benefit from tailored preventive treatments.

AI-Driven Development of Biomarker Panels of Aging

Microbiome

Functional Tests

Imaging

Sequencing

Biomarkers

Biological Age

38 Years

36 Years

Biomarker panel

Unfulfilled Biomarkers

Validated Biomarkers adopted in practice

Experimental Biomarkers adopted in practice

Marker 1 | Marker 2 | Marker 3

Marker 4 | Marker 5 | Marker 6 | Marker 7

Marker 8 | Marker 9 | Marker 10 | Marker 11 | Marker 12

Marker 1 | Marker 2 | Marker 3

Marker 4 | Marker 5 | Marker 6 | Marker 7

Marker 8 | Marker 9 | Marker 10 | Marker 11 | Marker 12

2019   **2020**   **2021**

Artificial Intelligence will use Digital Biomarkers to reality-check the proposed longevity therapies and filter out inappropriate or impractical biomarkers from those effective.

Precision Prevention, Diagnosis, Treatment and Prognosis

As the Precision Health industry is grown and developed to scale, we will see an increasing emphasis on the creation and validation of a wide diversity of Biomarkers of Aging come into use, which will enable the extension of healthspan and the maintenance of optimal health for the majority of citizens' lifespans via continuous, AI-empowered monitoring of fluctuations in personalized Biomarkers of Aging.

P4 Medicine will be the central platform giving effective usefulness to Aging Biomarkers for healthcare. It is not possible to think about extension of life expectancy and healthspan without P4 Medicine.

A patient may see that their biological age is 36 in 2021 — younger than a couple of years before, and younger than their chronological age of 37.

34 Years

38 Years

36 Years

2019 2020 2021

Gathering Aging Biomarkers means collecting data which marks the difference between healthy people only, e.g. between the young and even younger, with no traces of any officially recognised diseases. The continuous monitoring of small changes in such biomarkers, and the continuous and commensurate micro-adjustment of treatments in response, allows for some de facto reversal of biological age.

Report Methodology

Report Methodology in Details

To calculate the final score of a Single Biomarker or a Biomarker Panel, 3 types of Indexes are applied:

Accuracy Index - value expressed within the range [0.0-1.0].
It is a measure of the precision to predict overall biological age, based on the accuracy of each single biomarker scanned by the Panel. Thus, it is defined with formulas for both, single biomarkers and groups of biomarkers, and the output of the latter as an expression of the values projected by the first ones. The magnitudes depend not only on the number of biomarkers evaluated by the Panel, but on the nature of those biomarkers, the experimental background of its association with age-related conditions and processes, and a proposed classification framework that assigns or removes scores for qualitative characterizations; in this sense, the fundamental parameter used by the index is scientific support mined by sampling journal publications from specialized literature which successfully correlate each biomarker with temporary progression of aging. As expected, this framework equals the comprehensiveness of a biomarker or a panel with its precision or accuracy degree.

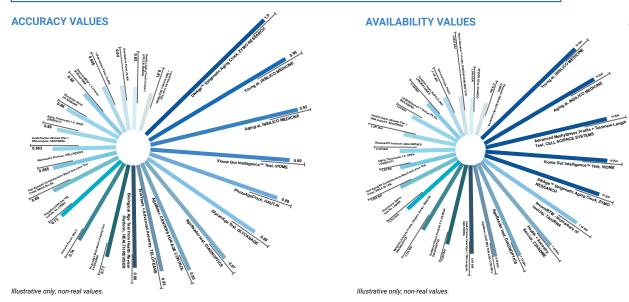**Availability Index** - value expressed within the BAI range [0.0-10.0 BAI].
Value that is calculated by omitting the significance degree of the biomarker as an indicator of age-related health status, assuming the implicit condition of correlation between the biomarker and temporary progression of aging. It measures only the material capacity of extensive implementation for the reference character, understood as an expression of the availability of assays or tests, its invasiveness, monetary value, the proposed classification framework for qualitative characterizations used also in Accuracy Assessments, and so on.

Actionability Index - value expressed within the range [0.0-1.0].
Actionability is estimated as an expression of both the accuracy and availability of a biomarker or a Panel. The Availability Index value is transferred to the range [0.0-1.0]. Then, an operation is performed combining the previous measurements and converting them into a new metric that takes into account both factors; this is done by decreasing the absolute contribution of Accuracy Index, since it must be taken into account along with availability for assessment of actionability but does not contribute equivalently, being of lesser relative relevance in the terms described in the preceding pages. This comprehensive value allows to evaluate not only the current material capacity of implementation of a biomarker or a Panel but also its viability for biological age prediction in such an immediate and effective frame of implementation, thus empowering single biomarker and Panel comparisons with a purely pragmatic sense. It is a weighted expression of a biomarker or a Panel's individual and effective availability combined with a mathematical modification of its Accuracy Index that only admits near-real values for extremely high accuracy outputs of correlation with biological age, minimizing the contribution of said term for medium-high, medium and low magnitude outputs.

Indexes Values for Single Aging Biomarkers and Aging Panels

ACCURACY VALUES

Illustrative only; non-real values.

AVAILABILITY VALUES

Illustrative only; non-real values.

ACTIONABILITY VALUES

	Accuracy	Availab.	Actionab.
InsideTracker Inner Age + DNA analysis, SEGTERRA	0.61	5.541	0.4631
Healthy Aging Panel (Compr), LIFE EXTENSION	0.63	2.708	0.3338
Metabolism Panel, OLINK	0.64	1.33	0.2713
Inflammation Panel, OLINK	0.645	1.33	0.2745
DiscoveryMAP v. 3.3 Panel, MYRIAD RBM	0.65	1.116	0.267
Biomarker Panel, UK BIOBANK	0.66	0	0
Aging Theranostic 1.0 OPEN LONGEVITY	0.66	3.45	0.3903
InsideTracker Ultimate Plan + DNA analysis, SEGTERRA	0.663	3.291	0.3843
WellnessFX Premium, WELLNESSFX	0.665	3.375	0.3998
Anti-Aging #4 Comprehensive Blood and Urine Test Panel, WALK-IN LAB	0.69	8.7	0.673
Phospho-H2AX (Ser139) Cellular kit, CISBIO	0.72	2.79	0.3987
Immune-Frame, RGCC	0.74	3.125	0.43
PhysioAge Biomarkers of Aging Test, PHYSIOAGE	0.77	2.416	0.4172
Biological Age Test, HEALTH REVISER	0.8	4.4	0.54
TeloYears + Advanced Ancestry, TELOYEARS	0.83	1.833	0.4361
AGE-Reader mu Test, DIAGNOPTICS	0.87	7.1666	0.7387
Aging.ai, INSILICO MEDICINE	0.93	10	0.9324
DNAge™, ZYMO RESEARCH	1.0	10	1.0

Illustrative only; non-real values.

Aging Analytics Agency uses detailed mathematical procedures to assign a value (or numerical factor) to each of the three variables taken into account in the evaluation of single biomarkers and whole biomarker panels. Many qualitative considerations are made when assigning scores to these three variables. In first place, the **CONDITIONING STAGE CATEGORY** of the single biomarker or the panel; that is, if they are approved or not for clinical use. Second, its **OPERATIONAL CATEGORY**; if they are offered in the market as *laboratory research kits*, as *medical tests*; if the company gives *access to the prices*; if it is a *theoretical panel* or one *employed in epidemiological surveys*, in which case it is not materially offered to the market by the entity; if it is a *real-time evaluation technology for a set of biomarkers*, which could decrease availability due to the increase in cost but actually increases it because it allow large-scale assessment of vast amounts of patients, and so on. Thus, the numerical evaluation is to some extent subordinated to a multiplicity of qualitative factors considered by our highly specialized professionals in the field of biotechnology and pharmaceutical intelligence.

Indexes Values for Single Aging Biomarkers and Aging Panels

NAME	COMPANY or ENTITY	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY	Accuracy Index (*)	Availability Index	Actionability Factor	Actionability Index (**)
Biomarker Panel	**UK BIOBANK**	Approved for Clinical Use	**Epidem. or Theoretical Panel Only** (BAI=0; ACTIONAB.=0)	0.66	0 BAI	N/A	**0**
DiscoveryMAP v. 3.3 Panel	**MYRIAD RBM**	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)	0.65	1.166 BAI	$(0.65)^2 + 0.1166 = 0.5391$	**0.2695**
Metabolism Panel	**OLINK**	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)	0.64	1.33 BAI	$(0.64)^2 + 0.133 = 0.5426$	**0.2713**
Inflammation Panel	**OLINK**	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)	0.645	1.33 BAI	$(0.645)^2 + 0.133 = 0.549$	**0.2745**
Healthy Aging Panel (Comprehensive)	**LIFE EXTENSION**	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)	0.63	2.708 BAI	$(0.63)^2 + 0.2708 = 0.6677$	**0.3338**
InsideTracker Ultimate Plan + DNA analysis	**SEGTERRA**	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)	0.663	3.291 BAI	$(0.663)^2 + 0.3291 = 0.7686$	**0.3843**
WellnessFX Premium	**WELLNESSFX**	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)	0.665	3.375 BAI	$(0.665)^2 + 0.3375 = 0.7797$	**0.3898**
Aging Theranostic 1.0	**OPEN LONGEVITY**	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)	0.66	3.45 BAI	$(0.66)^2 + 0.345 = 0.7806$	**0.3903**
Phospho-H2AX (Ser139) Cellular kit	**CISBIO**	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)	0.72	2.79 BAI	$(0.72)^2 + 0.279 = 0.7974$	**0.3987**
PhysioAge Biomarkers of Aging Test	**PHYSIOAGE**	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)	0.77	2.416 BAI	$(0.77)^2 + 0.2416 = 0.8345$	**0.4172**

Indexes Values for Single Aging Biomarkers and Aging Panels

NAME	COMPANY or ENTITY	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY	Accuracy Index (*)	Availability Index	Actionability Factor	Actionability Index (**)
Immune-Frame	**RGCC**	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)	0.74	3.125 BAI	$(0.74)^2 + 0.3125 = 0.8601$	**0.43**
TeloYears + Advanced Ancestry	**TELOYEARS**	Healthcare-Ready	**Informational Purpose Test**	0.83	1.833 BAI	$(0.83)^2 + 0.1833 = 0.8722$	**0.4361**
InsideTracker Inner Age + DNA analysis	**SEGTERRA**	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)	0.61	5.541 BAI	$(0.61)^2 + 0.5541 = 0.9262$	**0.4631**
Health Reviser Platform	**HEALTH REVISER**	Approved for Clinical Use	**Biomarkers Real-Time Assessment Technology** (+5 Availability Weight Points)	0.8	4.4 BAI	$(0.8)^2 + 0.44 = 1.08$	**0.54**
Anti-Aging #4 Comprehensive Blood and Urine Test Panel	**WALK-IN LAB**	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)	0.69	8.7 BAI	$(0.69)^2 + 0.87 = 1.3461$	**0.673**
AgeReader test	**DIAGNOPTICS**	Approved for Clinical Use	**Biomarkers Real-Time Assessment Technology** (+5 Availability Weight Points)	0.87	7.1666 BAI	$(0.87)^2 + 0.71666 = 1.4735$	**0.7367**
Aging.AI	**INSILICO MEDICINE**	Healthcare-Ready	**AI Platform** (+5 Availability Weight Points)	0.93	10 BAI	$(0.93)^2 + 1 = 1.8649$	**0.9324**
DNAge™ Epigenetic Aging Clock	**ZYMO RESEARCH**	Healthcare-Ready	**Informational Purpose Test**	1.0	10 BAI	$(1.0)^2 + 1 = 2$	**1.0**

(a) Their respective values presented in this chart are illustrative only; they were not calculated based on their actual availability or accuracy. For real values, access the full Report.
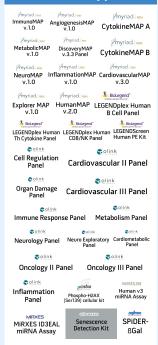
(*) Accuracy results depend on the number of replicates for each biomarker per study and between studies, therefore it is expected that biomarkers with a lot of empirical support but few background studies (eg, gold standard ones; Horvath's Clock, Gut Microbiome Age Clocks, Advanced Glycation End-products Clocks) may have lower values than markers less correlated with aging but a large amount of experimental background (more replicas), like HbA1C, estrogens, testosterone and so on. The results, then, are always weighed against the total empirical support for each biomarker, which depends on the quality of the publications rather than merely the quantity, this being evaluated by our life sciences team at Aging Analytics Agency, highly trained in the analysis of Big Data from scientific publications.

(**) The numerical evaluation of Actionability is to some extent subordinated to a multiplicity of qualitative factors considered by our highly specialized professionals in the field of biotechnology and pharmaceutical intelligence. These qualitative considerations can be summarized in the following categorical delimitations:

- *Research Use Only Panels or Single Biomarkers: Availability Index is reduced in 2 Points, because it negatively conditions the implementation of the panel; there is little to no implementation of the Panel in healthcare assessment, even less in Longevity assessment.*

- *Research Kits or Other Laboratory Practice Supplies (OLPS) multiplies Accuracy Index by a RKOLPS coefficient (= 0.5) that causes the total value to fall, unless the supply is specifically designed for the evaluation of biological age or aging itself: these kits and OLPSs are not usually designed for this purpose, and evaluation of accuracy becomes highly subjective.*

- *A Medical Test Panel or Single Biomarker increases availability in 2 Points, but never exceeding the maximum 24 Points: facilitates large-scale implementation.*

- *A Real-Time Assessment Technology for a Biomarker or a Panel, increases availability in 5 Points, but never exceeding the maximum 24 Points: facilitates ultra large-scale implementation and analysis.*

- *AI Platforms for biomarkers inputs, increases availability in 5 Points, but never exceeding the maximum 24 Points: facilitates ultra large-scale implementation and analysis.*

- *Epidemiological or Theoretical Panel Only are those not in the market; they are references to scientific articles, or to academic developments or public developments not necessarily published in journals. The availability is 0 BAI, and in the same way actionability falls to zero (0); they are not part of the practical recommendations of this report.*

- *When the company or entity does not share prices, it is immediately assumed x> maximum tolerable in the calculation of Availability Index, thus causing the magnitude of the Availability Index to fall.*

Biomarkers of Longevity

Distribution by **Operational Category**

Research Kit or Other Laboratory Practice Supplies

- ImmunoMAP v.1.0 (Myriad RBM)
- AngiogenesisMAP v.1.0 (Myriad RBM)
- CytokineMAP A (Myriad RBM)
- MetabolicMAP v.1.0 (Myriad RBM)
- DiscoveryMAP v.3.3 Panel (Myriad RBM)
- CytokineMAP B (Myriad RBM)
- NeuroMAP v.1.0 (Myriad RBM)
- InflammationMAP v.1.0 (Myriad RBM)
- CardiovascularMAP v.3.0 (Myriad RBM)
- Explorer MAP v.1.0 (Myriad RBM)
- HumanMAP v.2.0 (Myriad RBM)
- LEGENDplex Human B Cell Panel (BioLegend)
- LEGENDplex Human Th Cytokine Panel (BioLegend)
- LEGENDplex Human CD8/NK Panel (BioLegend)
- LEGENDScreen Human PE Kit (BioLegend)
- Cell Regulation Panel (Olink)
- Cardiovascular II Panel
- Organ Damage Panel (Olink)
- Cardiovascular III Panel
- Immune Response Panel (Olink)
- Metabolism Panel
- Neurology Panel (Olink)
- Neuro Exploratory Panel (Olink)
- Cardiometabolic Panel (Olink)
- Oncology II Panel (Olink)
- Oncology III Panel (Olink)
- Inflammation Panel (Olink)
- Phospho-H2AX (Ser139) cellular kit (cosbio)
- Human v3 miRNA Assay (nanoString)
- MiRXES ID3EAL miRNA Assay
- Senescence Detection Kit (abcam)
- SPiDER-ßGal (Dojindo)

Medical Test

- Aging Theranostic 1.0 (Open Longevity)
- WellnessFX Premium (WellnessFX)
- Anti-Aging #4 Comprehensive Blood and Urine Test Panel (Walk-In-Lab)
- InsideTracker Inner Age (InsideTracker)
- Healthy Aging Panel (Comprehensive) (LifeExtension)
- InsideTracker Ultimate Plan (InsideTracker)
- Female/Male Saliva Profile II - Test Kit for 6 Hormone Level Imbalances
- 10 Hormone Saliva Test Kit (LABRIX)
- FLUIDS iQ Adrenal Check (FLUIDS iQ)
- Oxidative Stress Analysis 2.0 (Genova)
- NeuroGenomic Profile (Genova)
- Comprehensive Adrenal Stress Profile (Genova)
- Metabolic Analysis Profile (Organic Acids) (Cell Science Systems)
- ImmunoGenomic Profile (Genova)
- CardioGenomicPlus Profile (Genova)
- Adrenal Stress Profile
- Advanced MethylDetox Profile + Thelomere Length (Cell Science Systems)
- Advanced MethylDetox Profile (Genova)
- Immune-Frame (RGCC)
- aCGH RGCC (RGCC)
- PhysioAge Biomarkers of Aging Test (PHYSIOAGE)
- Health + Ancestry Service (23andMe)
- Cytokine Panel (MAYO CLINIC LABORATORIES)
- Natural Killer Cell and Natural Killer T-Cell Panel (ARUP)
- CD57+ NK Cells, Peripheral Blood by Flow Cytometry (ARUP)
- CD21 (Dendritic Cell) by Immunohistochemistry (ARUP)
- B-Cell Memory and Naive Panel (ARUP)
- Cytokine Panel, TH1 (ARUP)
- Regulatory T-Cell Panel (ARUP)
- Hepatic Function Panel (ARUP)
- CD4+ T-Cell Recent Thymic Emigrants (ARUP)
- Carnitine Panel (ARUP)
- Cytokine Panel (ARUP)

Informational Purpose Test or Platform

- Salivary Cytokine Panel (SALIMETRICS)
- DNAge™ Epigenetic Aging Clock (ZYMO RESEARCH)
- Epigenetic Age Analysis Version 2.0 (Osiris Green)
- DNAge® Test (BioViva)
- Targeted Seq. for DNA Methylation Analysis (HKG-epi THERAPEUTICS Ltd)
- Genetic Age Test (cerascreen)
- EpiLiver (HKG-epi THERAPEUTICS Ltd)
- EpiBreast (HKG-epi THERAPEUTICS Ltd)
- EpiHealth (CHRONOMICS)
- EpiAging (HKG-epi THERAPEUTICS Ltd)
- EpiSocialpsych (HKG-epi THERAPEUTICS Ltd)
- GlycanAge Test (GLYCANAGE)
- Viome Gut Intelligence™ Test (VIOME)
- Microba Insight™ (MICROBA)
- Gut Microbiota Biohacker (TFTAK)
- smartGUT™ Microbiome Test (smartDNA)
- Telomere Length and Biological Age Testing (LIFE LENGTH)
- TeloYears + Advanced Ancestry Tests (TELOYEARS)
- toxomiRTM biomarkers of toxicity (TAmRNA)
- thrombomiRTM biomarkers of platelet function (TAmRNA)
- Telomere Length Test (Cell Science Systems)
- osteomiRTM validated bone biomarkers (TAmRNA)

Epidemiological or Theoretical Panel Only

biobank uk Biomarker Panel

- OMIP-004: In-Depth Characterization of Human T Regulatory Cells. (Cytometry Part A / Journal of Quantitative Cell Science / ISAC)
- OMIP-007: Phenotypic Analysis of Human Natural Killer Cells. (Cytometry Part A / Journal of Quantitative Cell Science / ISAC)
- OMIP-027: Functional Analysis of Human Natural Killer Cells. (Cytometry Part A / Journal of Quantitative Cell Science / ISAC)
- OMIP-018: Chemokine Receptor Expression on Human T Helper Cells (Cytometry Part A / Journal of Quantitative Cell Science / ISAC)
- OMIP-039: Detection and analysis of human adaptive NKG2C+ natural killer cells. (Cytometry Part A / Journal of Quantitative Cell Science / ISAC)
- OMIP-029: Human NK-Cell Phenotypization. (Cytometry Part A / Journal of Quantitative Cell Science / ISAC)

Biomarkers Real-Time Assessment Technology

- Centers for Age Control AgeMeter
- Health Reviser Platform
- MEDIAGE™ Biological Age Measurement System (Mediage)
- AGE-Reader mu Test (Diagnoptics)

AI Platform

- PhotoAgeClock (HAUT.AI)
- Haut.AI Skin Health (HAUT.AI)
- Aging.AI
- Young.AI
- CarePredict Platform (CarePredict)
- Enlitic Platform (enlitic)
- Freenome Platform (freenome)
- AI-Powered Radiology Assistant (zebra)
- PathAI Platform (PathAI)
- Buoy Health Platform (buoy)
- Tempus Platform
- BenevolentAI Platform (BenevolentAI)
- KenSci Platform (KenSci)
- Digital Nutrition Platform (zipongo)
- Proscia Platform (PROSCIA)
- Ada Symptom Checker app (ada)
- Google's DeepMind Health AI Platform (Google DeepMind)
- Blood Chemistry Calculator (nourish balance thrive)
- Better Therapeutics Platform (Better)
- Babylon Health Platform (babylon)
- ICabonX Platform (iCarbonX)

Biomarkers of Longevity

Distribution by **Amplitude Level**

AGING ANALYTICS AGENCY

Panels

Single Biomarker

Digital Panel Platform

Baseline Amplitude Level

Maximum Amplitude Level
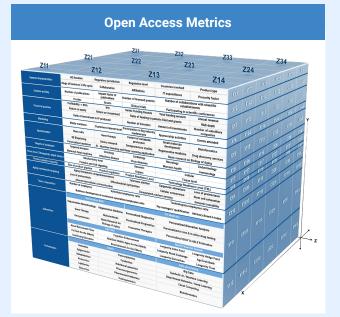
Distribution by **Conditioning Stage**

- The Conditioning Stage Classification Framework allows to differentiate degrees of availability vs. accuracy in strata or layers according to the current state of Panels uses.

- **Research Use Only** Panels and tests, as immunophenotyping of T cells, B cells and so on, could be highly decisive for aging and Longevity assessments, nevertheless there is virtually no availability for healthcare evaluations. Sometimes they are used, but only in very particular health conditions and frequently at the cost of making mistakes: the methodology is usually not well standardized, the results are sometimes confusing, the association with aging conditions and Longevity is not so linear or clear. At the same time, RUO Panels are often very expensive ones; ELISA kits, chromatographic assays or those involving NMR, and other laboratory kits not usually used in clinical practice. Here, poor availability and poor accuracy overlap; this is the stratum that worse availability vs. accuracy ratio per Biomarker would have. Aging Analytics Agency does not intend to exclude these presentations from the practical purposes of its studies; here we consider Panels such as those offered by Olink, BIOLEGEND, Myriad, all companies and products deeply involved in P4 Medicine as they facilitate the study and assessment of the proteome specifically, and other-omic levels in general.

- Routine and **Approved for Clinical Use** tests for our selected Single Biomarkers have usually a high correlation degree with age-related diseases and aging conditions; they often show good availability and excellent actionability. We could focus mainly on these, but what will provide an increase in their precision and utility for Longevity assessments is to combine them with the so-called "Healthcare-Ready" Panels.

- **Healthcare-Ready** tests (or "Used for Informational Purposes" tests) are those RUO sensu lato; although they are not Approved for Clinical Use - as they lack clinical validity at some degree-, they are offered by companies and clinics to give complementary information on the state of health or Longevity. Thus, they may or may not provide useful information, which should be analyzed in conjunction with data provided by validated, ACU tests. This category has good general availability, despite constituting Non-Approved for Clinical Use presentations; so they are considered quantitatively equivalent to ACU in availability calculations, but without being ACU at a qualitative level. Healthcare-Ready Panels are almost ready for the healthcare market, although they are not implemented in these terms: they have an informative purpose only. Nevertheless, its continuous use in such configuration and in conjunction with already validated Panels will allow a better interpretation of the outputs or endpoints, enhanced standardization of the results, wide access to the products, and therefore its very prompt clinical validation. The increasing access of individuals to this presentation stratum is an incredible new phenomenon in regard to the health care market; it should be used to introduce health endpoints in Digital Panel Platforms already conditioning for assessments of biological age, aging itself and Longevity; that is, in a way that other RUO Panels are not yet ready to achieve.

Distribution by **Amplitude Level**

- An analytical and comparative approach of aging biomarkers makes it necessary for certain single ones to be considered as equivalent to whole Panels, since they are strongly and self-sufficiently correlated with chronological age. This is the case regarding some classic examples such as telomere length assays (*Telomere Length Test* from Cell Science Systems; *Telomere Length and Biological Age Testing* from Life Length) or CpGs dinucleotides Methylation tests (*DNAge™ Epigenetic Aging Clock* from Zymo Research; *Epigenetic Age Analysis Version 2.0* from Osiris Green), among others. The single biomarkers selected in this report are almost always significantly correlated with chronological age - they are indicators of biological age on their own-, although not usually with particular pathologies and conditions associated with the progression of aging; thus, its clinical interpretation or validity is usually limited. The dramatic reduction in costs for most of these advanced assessments allows those biomarkers to be currently used for informational purposes complementary to clinical validity tests, having good availability. In the other hand, a few single biomarkers selected as Panels do not present such correlation with chronological age; they would only describe it to some extent, or not, depending on their calculated accuracy index.

- In the same way, in a market study it can be seen that some of these Single Biomarkers are not integrated in Panels which also justifies this criterion. These forms of presentation are at an equivalent amplitude level regarding to their correlation with chronological age; in practice, one of these Single Biomarkers can be equivalent, in terms of Accuracy for biological age assessment, to an entire Panel.

- A **Digital Panel** is a platform in which data sets from Digital Biomarkers and non-Digital Biomarkers (eg, blood, physical, physiological or other tests outputs) are introduced and integrated by an algorithm and analyzed to establish a biological age secondary output, allowing a real-time health status assessment. Note that they include Digital Biomarkers, but are not restricted to them; they also include AI platforms, but not limited to these.

- **Real-time monitoring combining Single Biomarkers and entire Panels from different sources provides a much higher level of amplitude** (or **comprehensiveness**) than the other two presentations; for this case study, highly consolidated Platforms only have been considered, this is, in terms of their documented precision and reliability. Thus, all of them have comparatively a maximum degree of amplitude, or maximum Accuracy (1.0), with availability being the conditioning factor of actionability.

Open Access and Proprietary Metrics

Open Access Metrics

Proprietary Metrics

The methodology and metrics featured in this teaser for this contracted analytical case study are public and could have been used in a number of other open-access Aging Analytics Agency reports, whereas a large portion of the analytical frameworks used for the report's benchmarking are proprietary, available to potential partners via NDA. These include both absolute values (quantitative or qualitative) and dynamic parameters to analyze metrics as they change over time. The following are examples of parameters used in assessment of P4 Medicine clinics, so many of them may concern this report while others may not.

Selected Biomarkers List

1. Gait (Walking) Speed
2. Timed Get Up and Go
3. Chair Rising
4. Grip Strength
5. Standing Balance
6. Purdue Pegboard Test
7. Spirometry: Forced Expiratory Volume in 1 Second (FEV1)
8. Bone Density, Bone Mass Hip: Dual X Ray Absorptiometry for Bone Health
9. Broadband Ultrasound Attenuation (BUA) at Heel for Bone Health
10. Computed Tomography for Bone Health
11. Dual X Ray Absorptiometry for Estimated Leg Muscle Mass
12. Bioelectrical Impedance Analysis for Muscle Mass
13. Computed Tomography for Muscle Mass
14. Magnetic Resonance Imaging for Muscle Mass
15. Body Potassium for Muscle Mass
16. Abdominal Fat; Waist Circumference
17. Body Mass; Body Mass Index; Body Weight
18. Blood Pressure; Sphygmomanometry
19. Standard Lipid Profile: Total Cholesterol; LDL-C; HDL-C; Triglycerides
20. Glycated haemoglobin (HbA1C)
21. Fasting Plasma Glucose
22. Verbal Fluency
23. Digit-Symbol Coding
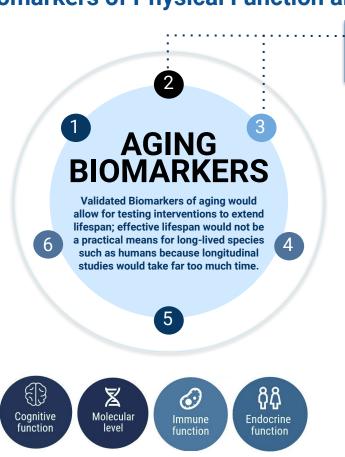24. Digit Span Backward
25. Boston Naming Test
26. Stroop Task
27. Block Design Test
28. Raven's Progressive Matrices
29. Rey Auditory Verbal Learning Test
30. Benton Visual Retention Test
31. Adiponectin
32. DHEAS:Cortisol Ratio
33. DHEAS
34. Growth Hormone; IGF-1
35. Leptin
36. Ghrelin
37. Melatonin
38. Estrogens
39. Somatostatin
40. Testosterone
41. Thyroid Hormones
42. B Cells
43. CMV Seropositive
44. C-Reactive Protein
45. Dendritic Cells
46. Natural Killer Cells
47. Neutrophils
48. Lymphocyte/Granulocyte ratio
49. Immune Risk Profile
50. Telomere Length in Leukocytes
51. T Cell Phenotype
52. CpGs Dinucleotides
53. miR-34a
54. miR-1, miR-133a, miR-499 and miR-208a
55. miR-137, miR-181c, miR-9, and miR-29a/b
56. IFN-γ
57. High-Sensitivity C-Reactive Protein (hs-CRP)
58. Lipoxins
59. TNF-α
60. IL-1
61. IL-6
62. IL-10
63. IL-12
64. p16INK4a
65. β-galactosidase
66. Small Dense Low-Density Lipoprotein (sdLDL)
67. High Density Lipoprotein (HDL)
68. AGEs
69. NT-proBNP
70. γ-H2A.X
71. Protein Carbamylation
72. Mitochondrial DNA Copy Number
73. Cell-Free DNA
74. Telomere Length Aging Clock
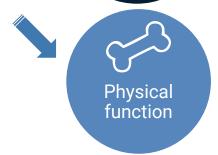75. Biomarkers of Oxidative Stress
76. Gut Microbiome Transcriptome

AGEING BIOMARKERS
- Physiological function
- Physical function
- Cognitive function
- Immune function
- Endocrine function
- Molecular level

Biomarker Domains Classification Framework.
Biomarkers of Physical Function and Physiology.

Biomarkers of Physical Function and Physiology

Complex changes affecting the structure and function of cells, tissues and organ systems are a hallmark of aging and can be detected by the third or fourth decade of life. These may translate, eventually, into functional loss, chronic disease and finally death.

AGING BIOMARKERS

Validated Biomarkers of aging would allow for testing interventions to extend lifespan; effective lifespan would not be a practical means for long-lived species such as humans because longitudinal studies would take far too much time.

1
2
3
4
5
6

Cognitive function

Molecular level

Immune function

Endocrine function

Physiological function

Physical function

Body Composition.
Muscle mass: Bioelectrical Impedance Analysis; Computed Tomography; Dual-energy X-ray Absorptiometry; Magnetic Resonance Imaging; Body Potassium.
BMI.
Body Weight.
Waist Circumference and abdominal fat.

Bone Health.
Broadband Ultrasound Attenuation.
Computed Tomography.
Dual-energy X-ray Absorptiometry.
All have been used extensively to measure bone health.

Cardiovascular Function.
*Standard Lipid Profile.
Blood Pressure.
*(Ideally: Advanced Lipoprotein Testing like VAP test).

Lung Function.
FEV1.

Glucose Metabolism.
HbA1C.
Fasting Glucose.
*(Ideally: Skin Autofluorescence Tests like AGE-Reader mu ones).
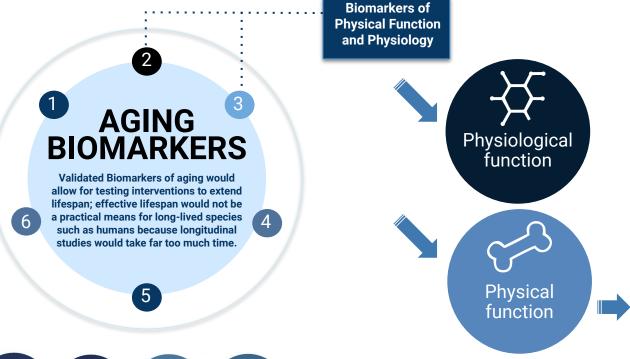
Biomarker Domains Classification Framework.
Biomarkers of Physical Function and Physiology.

Biomarkers of Physical Function and Physiology

AGING BIOMARKERS

Validated Biomarkers of aging would allow for testing interventions to extend lifespan; effective lifespan would not be a practical means for long-lived species such as humans because longitudinal studies would take far too much time.

1 2 3 4 5 6

Cognitive function

Molecular level

Immune function

Endocrine function

Physiological function

There is strong evidence supporting the validity and reliability of these measures, and their use in healthy aging studies have key advantages.

Physical function

Strength.
Grip Strength.
Balance.
Standing Balance.
Dexterity.
Purdue Pegboard Test.
Locomotor Function.
Chair Rising.
Gait Speed.
Timed Get Up and Go.

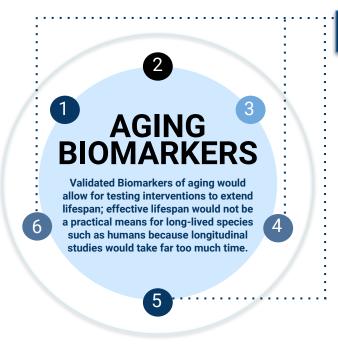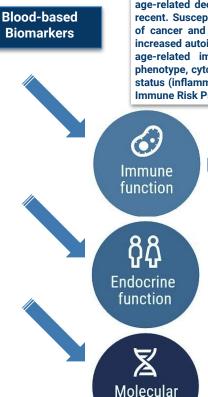# Biomarker Domains Classification Framework.
Blood-based Biomarkers.

AGING BIOMARKERS

Validated Biomarkers of aging would allow for testing interventions to extend lifespan; effective lifespan would not be a practical means for long-lived species such as humans because longitudinal studies would take far too much time.

1 2 3 4 5 6

Cognitive function

Physiological function

Physical function

Blood-based Biomarkers

Whilst the field of immunology is well developed, the study of age-related decline in immunity, termed immunosenescence, is more recent. Susceptibility to both bacterial and viral pathogens, incidence of cancer and loss of tolerance to one's own tissues evidenced by increased autoimmunity are clearly related to aging. Studies assessing age-related immune and inflammatory function, including T-cell phenotype, cytomegalovirus serostatus and pro-inflammatory cytokine status (inflammaging), have been the basis for the development of the Immune Risk Profile (IRP).

Immune function

Endocrine function

Molecular level

IRP.
Defined by an inverted CD4/CD8 ratio and associated with increased numbers of CD8 + CD28 cells.
Lymphocyte/Granulocyte ratio.
Neutrophils.
B Cells.
NK Cells.
T Cells phenotype.
Dendritic Cells.
CMV serostatus.
CRP.
Telomere Length in Leukocytes.

Biomarker Domains Classification Framework.
Blood-based Biomarkers.

Blood-based Biomarkers

AGING BIOMARKERS

1 2 3 4 5 6

Validated Biomarkers of aging would allow for testing interventions to extend lifespan; effective lifespan would not be a practical means for long-lived species such as humans because longitudinal studies would take far too much time.

Cognitive function

Physiological function

Physical function

Immune function

Endocrine function
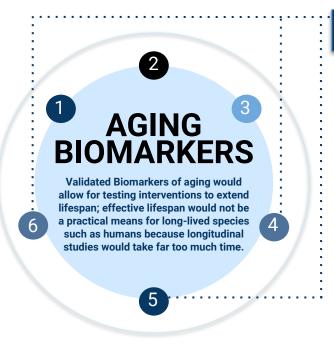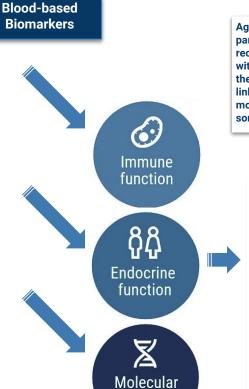
Molecular level

Age-related changes in the endocrine system, particularly among the sex hormones, are well recognized and studies have established causal links with health outcomes. For most of these Biomarkers, there is strong consensual evidence that changes are linked with risk of physical frailty and premature mortality, despite the non-linear relationship between some Biomarkers and aging.

Adiponectin.
Ghrelin.
Leptin.
DHEAS.
DHEAS:Cortisol ratio.
Growth Hormone, IGF-1.
Estrogens.
Testosterone.
Somatostatin.
Melatonin.
Thyroid Hormones.

Biomarker Domains Classification Framework.
Blood-based Biomarkers.

Blood-based Biomarkers

Common theories of aging, where age linearly correlates with ROS, DNA damage, mitochondrial dysfunction and shortening of the telomeres, are well established in humans. New approaches contemplate the role of epigenetics, cellular senescence, inflammaging, genomic instability, translational regulation and proteome changes. Taken together, very old humans demonstrate a different picture of aging regarding the accumulation of DNA damage, antioxidant defense capacity, genome instability and telomere shortening by evidenced better DNA repair capacity and higher telomerase activity.

AGING BIOMARKERS

Validated Biomarkers of aging would allow for testing interventions to extend lifespan; effective lifespan would not be a practical means for long-lived species such as humans because longitudinal studies would take far too much time.

1 2 3 4 5 6

Cognitive function

Physiological function

Physical function

Immune function

Endocrine function

Molecular level

DNA Methylation.
CpGs dinucleotides.
Translational Regulation.
miR-34a.
miR-1, miR-133a, miR-499 and miR-208a.
miR-137, miR-181c, miR-9 and miR-29a/b.
Inflammaging.
IL-1β, IL-6, IL-10, IL-12.
TNF-α.
IFN-γ.
hs-CRP.
Lipoxins.
Cellular Senescence.
β-galactosidase.
p16INK4a.

Biomarker Domains Classification Framework.
Blood-based Biomarkers.
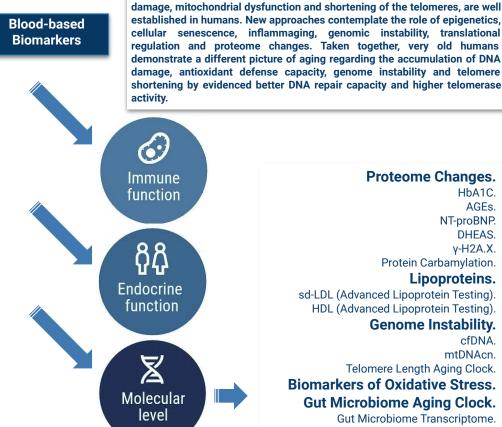
AGING BIOMARKERS

1 2 3 4 5 6

Validated Biomarkers of aging would allow for testing interventions to extend lifespan; effective lifespan would not be a practical means for long-lived species such as humans because longitudinal studies would take far too much time.

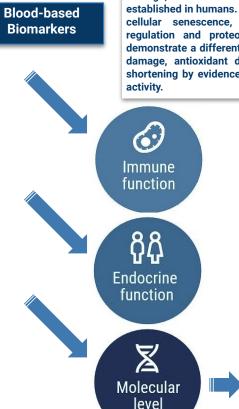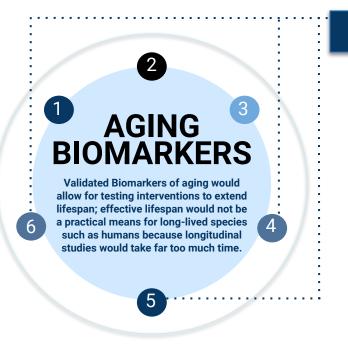Cognitive function

Physiological function

Physical function

Blood-based Biomarkers

Common theories of aging, where age linearly correlates with ROS, DNA damage, mitochondrial dysfunction and shortening of the telomeres, are well established in humans. New approaches contemplate the role of epigenetics, cellular senescence, inflammaging, genomic instability, translational regulation and proteome changes. Taken together, very old humans demonstrate a different picture of aging regarding the accumulation of DNA damage, antioxidant defense capacity, genome instability and telomere shortening by evidenced better DNA repair capacity and higher telomerase activity.

Immune function

Endocrine function

Molecular level

Proteome Changes.
HbA1C.
AGEs.
NT-proBNP.
DHEAS.
γ-H2A.X.
Protein Carbamylation.
Lipoproteins.
sd-LDL (Advanced Lipoprotein Testing).
HDL (Advanced Lipoprotein Testing).
Genome Instability.
cfDNA.
mtDNAcn.
Telomere Length Aging Clock.
Biomarkers of Oxidative Stress.
Gut Microbiome Aging Clock.
Gut Microbiome Transcriptome.

Biomarker Domains Classification Framework.
Cognitive Biomarkers.

Cognitive Biomarkers

AGING BIOMARKERS

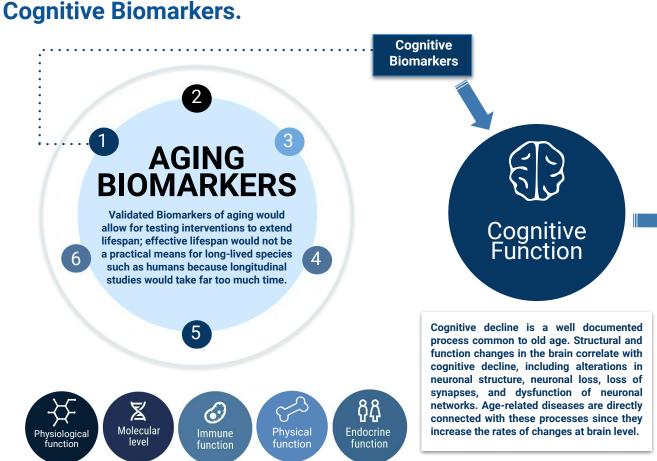Validated Biomarkers of aging would allow for testing interventions to extend lifespan; effective lifespan would not be a practical means for long-lived species such as humans because longitudinal studies would take far too much time.

1 2 3 4 5 6

Physiological function

Molecular level

Immune function

Physical function

Endocrine function

Cognitive Function

Cognitive decline is a well documented process common to old age. Structural and function changes in the brain correlate with cognitive decline, including alterations in neuronal structure, neuronal loss, loss of synapses, and dysfunction of neuronal networks. Age-related diseases are directly connected with these processes since they increase the rates of changes at brain level.

Executive Function.
Verbal Fluency.
Processing Speed.
Digit-Symbol Coding.
Working Memory.
Digit Span Backward.
Crystallized Ability.
Boston Naming Test.
Attention.
Stroop Task.
Non-Verbal Reasoning.
Raven's Progressive Matrices.
Visual Memory and Visuospatial Ability.
Benton Visual Retention Test and Block Design Test.
Verbal Memory & Learning
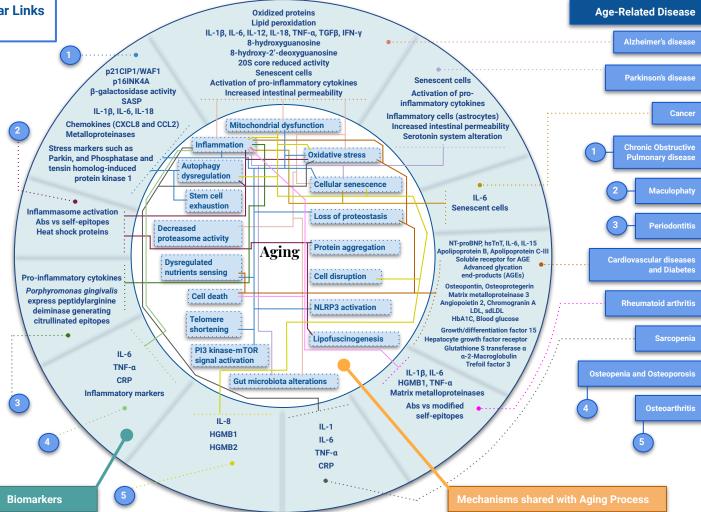Rey Auditory Verbal Learning Test.

Age-Related Diseases and Molecular Links with Root Causes of Aging.

The longstanding question if old age is itself a disease has been addressed since ancient times, starting from the Roman playwright Terentius, who claimed *senectus ipsa est morbus*, "*old age itself is a disease*", and Cicero who some decades later argued in De Senectute *pugnandum, tamquam contra morbum sic contra senectutem*, "*we have to fight against aging, as we do against a disease*". These quotations elegantly summarize a long-held view of aging and old age addressed by several scholars.

Notwithstanding, with the birth of modern medicine in the nineteenth century, this discussion suddenly ended up in considering aging and diseases as separate phenomena.

Age-Related Diseases, *Geriatric Syndromes* and *Aging itself* are not separate entities, both should be considered as parts of a continuum and, to support this hypothesis, we at Aging Analytics Agency highlight the meeting points between these phenomena and the need to focus on their basic and shared molecular and cellular mechanisms.

To establish the links between these basic mechanisms shared by *Aging*, *Age-Related Diseases* and *Geriatric Syndromes*, international experts identified nine pillars or root-causes which actually include adaptation to stress, loss of proteostasis, stem cell exhaustion, metabolism derangement, macromolecular damage, inflammation, epigenetic modifications and senescence, among others. Many chronic diseases and pathological conditions, some of which are considered here, are at least in part determined by (some of) these root-causes or shared mechanisms.

Age-Related Disease

Alzheimer's disease

Parkinson's disease

Cancer

1 Chronic Obstructive Pulmonary disease

2 Maculophaty

3 Periodontitis

Cardiovascular diseases and Diabetes

Rheumatoid arthritis

Sarcopenia

Osteopenia and Osteoporosis

4 Osteoarthritis

5

Oxidized proteins
Lipid peroxidation
IL-1β, IL-6, IL-12, IL-18, TNF-α, TGFβ, IFN-γ
8-hydroxyguanosine
8-hydroxy-2'-deoxyguanosine
20S core reduced activity
Senescent cells
Activation of pro-inflammatory cytokines
Increased intestinal permeability

Senescent cells
Activation of pro-inflammatory cytokines
Inflammatory cells (astrocytes)
Increased intestinal permeability
Serotonin system alteration

p21CIP1/WAF1
p16INK4A
β-galactosidase activity
SASP
IL-1β, IL-6, IL-18
Chemokines (CXCL8 and CCL2)
Metalloproteinases
Stress markers such as Parkin, and Phosphatase and tensin homolog-induced protein kinase 1

Inflammasome activation
Abs vs self-epitopes
Heat shock proteins

Pro-inflammatory cytokines
Porphyromonas gingivalis express peptidylarginine deiminase generating citrullinated epitopes

IL-6
TNF-α
CRP
Inflammatory markers

IL-6
Senescent cells

NT-proBNP, hsTnT, IL-6, IL-15
Apolipoprotein B, Apolipoprotein C-III
Soluble receptor for AGE
Advanced glycation end-products (AGEs)
Osteopontin, Osteoprotegerin
Matrix metalloproteinase 3
Angiopoietin 2, Chromogranin A
LDL, sdLDL
HbA1C, Blood glucose
Growth/differentiation factor 15
Hepatocyte growth factor receptor
Glutathione S transferase α
α-2-Macroglobulin
Trefoil factor 3

IL-1β, IL-6
HGMB1, TNF-α
Matrix metalloproteinases
Abs vs modified self-epitopes

Aging (central circle)

Mitochondrial dysfunction
Inflammation
Oxidative stress
Autophagy dysregulation
Cellular senescence
Stem cell exhaustion
Loss of proteostasis
Decreased proteasome activity
Protein aggregation
Dysregulated nutrients sensing
Cell disruption
Cell death
NLRP3 activation
Telomere shortening
Lipofuscinogenesis
PI3 kinase-mTOR signal activation
Gut microbiota alterations

IL-8
HGMB1
HGMB2

IL-1
IL-6
TNF-α
CRP

Biomarkers

Mechanisms shared with Aging Process

AGING ANALYTICS AGENCY

Selected Biomarker Panels List

1. WellnessFX Premium, WELLNESSFX
2. Anti-Aging #4 Comprehensive Blood and Urine Test Panel, WALK-IN LAB
3. Aging Theranostic 1.0, OPEN LONGEVITY
4. InsideTracker Ultimate Plan, SEGTERRA
5. InsideTracker Inner Age, SEGTERRA
6. Biomarker Panel, UK BIOBANK
7. Healthy Aging Panel (Comprehensive), LIFE EXTENSION
8. Female/Male Saliva Profile II - Test Kit For 6 Hormone Level Imbalances, ZRT LABORATORY
9. 10 Hormone Saliva Test Kit, LABRIX
10. Adrenal Stress Profile, CELL SCIENCE SYSTEMS
11. Adrenal Check, FLUIDS iQ®
12. Comprehensive Adrenal Stress Profile, GENOVA DIAGNOSTICS
13. Oxidative Stress Analysis 2.0, GENOVA DIAGNOSTICS
14. Metabolic Analysis Profile (Organic Acids), GENOVA DIAGNOSTICS
15. Immune-Frame, RGCC
16. Cytokine Panel, MAYO CLINIC LABORATORIES
17. Salivary Cytokine Panel, SALIMETRICS
18. Advanced MethylDetox Profile, CELL SCIENCE SYSTEMS
19. Advanced MethylDetox Profile plus Telomere Length Test, CELL SCIENCE SYSTEMS
20. Genetic Age Test, CERASCREEN
21. AGE-Reader mu Test, DIAGNOPTICS
22. GlycanAge Test, GLYCANAGE
23. Viome Gut Intelligence™ Test, VIOME
24. SmartGUT™ Microbiome Test, SMARTDNA
25. Microba Insight™, MICROBA
26. Gut Microbiota Biohacker, TFTAK CENTER OF FOOD AND FERMENTATION TECHNOLOGIES
27. Health plus Ancestry Service, 23ANDME
28. Array Comparative Genomic Hybridisation (aCGH) RGCC, RGCC
29. ImmunoGenomic® Profile, GENOVA DIAGNOSTICS
30. NeuroGenomic™ Profile, GENOVA DIAGNOSTICS
31. CardioGenomicPlus™ Profile, GENOVA DIAGNOSTICS
32. PhysioAge Biomarkers of Aging Test, PHYSIOAGE
33. DiscoveryMAP v. 3.3 Panel, MYRIAD RBM
34. Explorer MAP™ v. 1.0, MYRIAD RBM
35. HumanMAP® v. 2.0, MYRIAD RBM
36. CardiovascularMAP® v. 3.0, MYRIAD RBM
37. InflammationMAP® v. 1.0, MYRIAD RBM
38. ImmunoMAP® v. 1.0, MYRIAD RBM
39. NeuroMAP™ v. 1.0, MYRIAD RBM
40. MetabolicMAP® v. 1.0, MYRIAD RBM
41. CytokineMAP A, MYRIAD RBM
42. CytokineMAP B, MYRIAD RBM
43. AngiogenesisMAP® v. 1.0, MYRIAD RBM
44. LEGENDScreen™ Human PE Kit, BIOLEGEND
45. LEGENDplex™ Human B Cell Panel (13-plex), BIOLEGEND
46. LEGENDplex™ Human CD8/NK Panel (13-plex), BIOLEGEND
47. LEGENDplex™ Human Th Cytokine Panel (13-plex), BIOLEGEND
48. Regulatory T-Cell Panel, ARUP LABORATORIES
49. Cytokine Panel, ARUP LABORATORIES
50. Cytokine Panel, TH1, ARUP LABORATORIES
51. Carnitine Panel, ARUP LABORATORIES
52. Hepatic Function Panel, ARUP LABORATORIES
53. B-Cell Memory and Naive Panel, ARUP LABORATORIES
54. Natural Killer Cell and Natural Killer T-Cell Panel, ARUP LABORATORIES
55. OMIP-004: In-Depth Characterization of Human T Regulatory Cells
56. OMIP-007: Phenotypic Analysis of Human Natural Killer Cells
57. OMIP-018: Chemokine Receptor Expression on Human T Helper Cells
58. OMIP-027: Functional Analysis of Human Natural Killer Cells
59. OMIP-029: Human NK-Cell Phenotypization
60. OMIP-039: Detection and analysis of human adaptive NKG2C+ natural killer cells

Selected Biomarker Panels List

61. Cardiometabolic Panel, OLINK
62. Cell Regulation Panel, OLINK
63. Cardiovascular II Panel, OLINK
64. Cardiovascular III Panel, OLINK
65. Immune Response Panel, OLINK
66. Inflammation Panel, OLINK
67. Metabolism Panel, OLINK
68. Neurology Panel, OLINK
69. Neuro Exploratory Panel, OLINK
70. Oncology II Panel, OLINK
71. Oncology III Panel, OLINK
72. Organ Damage Panel, OLINK
73. Human v3 miRNA Assay, NANOSTRING
74. MiRXES ID3EAL miRNA Assay, MiRXES
75. OsteomiRTM - Validated Bone Biomarkers, TAmiRNA
76. ThrombomiRTM - Biomarkers of Platelet Function, TAmiRNA
77. ToxomiRTM - Biomarkers of Toxicity, TAmiRNA
78. DNAge™ Epigenetic Aging Clock, ZYMO RESEARCH
79. Epigenetic Age Analysis Version 2.0, OSIRIS GREEN
80. DNAge® Test, BIOVIVA
81. EpiHealth, CHRONOMICS
82. EpiAging, HKG EPITHERAPEUTICS
83. EpiSocialpsych, HKG EPITHERAPEUTICS
84. Targeted Sequencing For DNA Methylation Analysis, HKG EPITHERAPEUTICS
85. EpiLiver, HKG EPITHERAPEUTICS
86. EpiBreast, HKG EPITHERAPEUTICS
87. TeloYears plus Advanced Ancestry Tests, TELOYEARS
88. Telomere Length and Biological Age Testing, LIFE LENGTH
89. Telomere Length Test, CELL SCIENCE SYSTEMS
90. CD4+ T-Cell Recent Thymic Emigrants (RTEs), ARUP LABORATORIES
91. CD21 (Dendritic Cell) by Immunohistochemistry, ARUP LABORATORIES

92. CD57+ NK Cells, Peripheral Blood by Flow Cytometry, ARUP LABORATORIES
93. Phospho-H2AX (Ser139) Cellular Kit, CISBIO
94. Senescence Detection Kit, ABCAM
95. SPiDER-ßGal, DOJINDO MOLECULAR TECHNOLOGIES
96. Young.AI, INSILICO MEDICINE
97. Aging.AI, INSILICO MEDICINE
98. PhotoAgeClock, HAUT.AI
99. Haut.AI Skin Health, HAUT.AI
100. AgeMeter, CENTERS FOR AGE CONTROL
101. Health Reviser Platform, HEALTH REVISER
102. MEDIAGE™ Biological Age Measurement System, MEDIAGE
103. CarePredict Platform, CAREPREDICT
104. Enlitic Platform, ENLITIC
105. Freenome Platform, FREENOME
106. AI-Powered Radiology Assistant, ZEBRA MEDICAL VISION
107. PathAI Platform, PATHAI
108. Buoy Health Platform, BUOY HEALTH
109. BenevolentAI, BENEVOLENT
110. Tempus Platform, TEMPUS
111. KenSci Platform, KENSCI
112. Proscia Platform, PROSCIA
113. Google's DeepMind Health AI Platform, DEEPMIND TECHNOLOGIES
114. ICarbonX Platform, ICARBONX
115. Blood Chemistry Calculator, NOURISH BALANCE THRIVE
116. Ada - Symptom Checker App, ADA HEALTH GMBH
117. Babylon Health Platform, BABYLON HEALTH
118. Digital Nutrition Platform, ZIPONGO
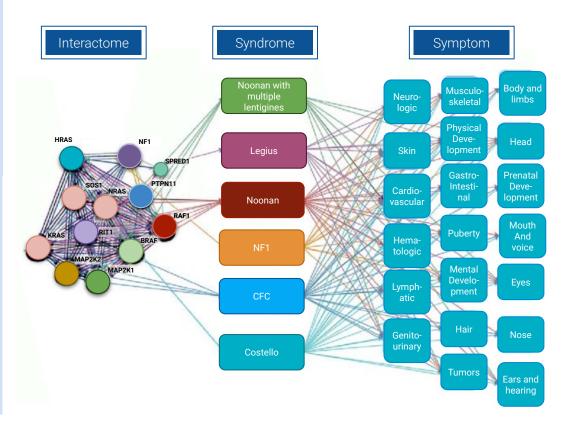119. Better Therapeutics Platform, BETTER THERAPEUTICS

Complex Biomarker Network.

It has previously been reported that gene/protein and phenotype networks could be assembled into an integrated network. The different units of all the *omic* levels are interconnected, weaving a complex network of biomarkers highly correlated with a disease, condition or biological trait or state: the Interactome. Thus, a pathology can be identified and corrected in multiple levels. More network data, greater predictive power and controllability of the biological state.

Clinical symptoms can be correlated with mutated proteins. According to T. Kunej et al., alignments between interactome and phenome levels can reveal new links between diseases, symptoms, -*omes* and knows genes, as well as connections between previously unrelated diseases, as in the illustration: a network model for 6 syndromes belonging to the RASopathy class of disorders; Noonan syndrome with multiple lentigines, Legius, Noonan, NF1, cardiofaciocutaneous and Costello syndromes, and the string associations between different levels of biomarkers for this set of disorders. This biomarkers network approach is rarely used in genomics, despite its potential for novel discoveries and medical interventions.

Selected Biomarker Panels

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
WellnessFX Premium	WELLNESSFX	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Anti-Aging #4 Comprehensive Blood and Urine Test Panel	WALK-IN LAB	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Aging Theranostic 1.0	OPEN LONGEVITY	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
InsideTracker Ultimate Plan	SEGTERRA	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
InsideTracker Inner Age	SEGTERRA	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Biomarker Panel	UK BIOBANK	PANEL	Approved for Clinical Use	**Epidem. or Theoretical Panel Only** (BAI=0; ACTIONAB.=0)
Healthy Aging Panel (Comprehensive)	LIFE EXTENSION	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Female/Male Saliva Profile II - Test Kit For 6 Hormone Level Imbalances	ZRT LABORATORY	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
10 Hormone Saliva Test Kit	LABRIX	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Adrenal Stress Profile	CELL SCIENCE SYSTEMS	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)

Selected Biomarker Panels

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
Adrenal Check	FLUIDS iQ®	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Comprehensive Adrenal Stress Profile	GENOVA DIAGNOSTICS	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Oxidative Stress Analysis 2.0	GENOVA DIAGNOSTICS	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Metabolic Analysis Profile (Organic Acids)	GENOVA DIAGNOSTICS	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Immune-Frame	RGCC	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Cytokine Panel	MAYO CLINIC LABORATORIES	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Salivary Cytokine Panel	SALIMETRICS	PANEL	Research Use Only (-2 Availab. Weight Points)	**Informational Purpose Test or Platform**
Advanced MethylDetox Profile	CELL SCIENCE SYSTEMS	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Advanced MethylDetox Profile plus Telomere Length Test	CELL SCIENCE SYSTEMS	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Genetic Age Test	CERASCREEN	PANEL	Healthcare-Ready	**Informational Purpose Test or Platform**

Selected Biomarker Panels

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
AGE-Reader mu Test	**DIAGNOPTICS**	PANEL	Approved for Clinical Use	**Biomarkers Real-Time Assessment Technology** (+5 Availability Weight Points)
GlycanAge Test	**GLYCANAGE**	PANEL	Healthcare-Ready	**Informational Purpose Test or Platform**
Viome Gut Intelligence™ Test	**VIOME**	PANEL	Healthcare-Ready	**Informational Purpose Test or Platform**
SmartGUT™ Microbiome Test	**SMARTDNA**	PANEL	Healthcare-Ready	**Informational Purpose Test or Platform**
Microba Insight™	**MICROBA**	PANEL	Healthcare-Ready	**Informational Purpose Test or Platform**
Gut Microbiota Biohacker	**TFTAK CENTER OF FOOD AND FERMENTATION TECHNOLOGIES**	PANEL	Healthcare-Ready	**Informational Purpose Test or Platform**
Health plus Ancestry Service	**23ANDME**	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
Array Comparative Genomic Hybridisation (aCGH) RGCC	**RGCC**	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
ImmunoGenomic® Profile	**GENOVA DIAGNOSTICS**	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
NeuroGenomic™ Profile	**GENOVA DIAGNOSTICS**	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)

Selected Biomarker Panels

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
CardioGenomicPlus™ Profile	GENOVA DIAGNOSTICS	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
PhysioAge Biomarkers of Aging Test	PHYSIOAGE	PANEL	Approved for Clinical Use	**Medical Test** (+2 Availability Weight Points)
DiscoveryMAP v. 3.3 Panel	MYRIAD RBM	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Explorer MAP™ v. 1.0	MYRIAD RBM	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
HumanMAP® v. 2.0	MYRIAD RBM	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
CardiovascularMAP® v. 3.0	MYRIAD RBM	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
InflammationMAP® v. 1.0	MYRIAD RBM	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
ImmunoMAP® v. 1.0	MYRIAD RBM	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
NeuroMAP™ v. 1.0	MYRIAD RBM	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
MetabolicMAP® v. 1.0	MYRIAD RBM	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)

Selected Biomarker Panels

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
CytokineMAP A	MYRIAD RBM	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
CytokineMAP B	MYRIAD RBM	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
AngiogenesisMAP® v. 1.0	MYRIAD RBM	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
LEGENDScreen™ Human PE Kit	BIOLEGEND	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
LEGENDplex™ Human B Cell Panel (13-plex)	BIOLEGEND	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
LEGENDplex™ Human CD8/NK Panel (13-plex)	BIOLEGEND	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
LEGENDplex™ Human Th Cytokine Panel (13-plex)	BIOLEGEND	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Regulatory T-Cell Panel	ARUP LABORATORIES	PANEL	Healthcare-Ready	**Medical Test** (+2 Availability Weight Points)
Cytokine Panel	ARUP LABORATORIES	PANEL	Healthcare-Ready	**Medical Test** (+2 Availability Weight Points)
Cytokine Panel, TH1	ARUP LABORATORIES	PANEL	Healthcare-Ready	**Medical Test** (+2 Availability Weight Points)

Selected Biomarker Panels

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
Carnitine Panel	**ARUP LABORATORIES**	PANEL	Healthcare-Ready	**Medical Test** (+2 Availability Weight Points)
Hepatic Function Panel	**ARUP LABORATORIES**	PANEL	Healthcare-Ready	**Medical Test** (+2 Availability Weight Points)
B-Cell Memory and Naive Panel	**ARUP LABORATORIES**	PANEL	Healthcare-Ready	**Medical Test** (+2 Availability Weight Points)
Natural Killer Cell and Natural Killer T-Cell Panel	**ARUP LABORATORIES**	PANEL	Healthcare-Ready	**Medical Test** (+2 Availability Weight Points)
OMIP-004: In-Depth Characterization of Human T Regulatory Cells	**N/A**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Epidem. or Theoretical Panel Only** (BAI=0; ACTIONAB.=0)
OMIP-007: Phenotypic Analysis of Human Natural Killer Cells	**N/A**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Epidem. or Theoretical Panel Only** (BAI=0; ACTIONAB.=0)
OMIP-018: Chemokine Receptor Expression on Human T Helper Cells	**N/A**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Epidem. or Theoretical Panel Only** (BAI=0; ACTIONAB.=0)
OMIP-027: Functional Analysis of Human Natural Killer Cells	**N/A**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Epidem. or Theoretical Panel Only** (BAI=0; ACTIONAB.=0)
OMIP-029: Human NK-Cell Phenotypization	**N/A**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Epidem. or Theoretical Panel Only** (BAI=0; ACTIONAB.=0)
OMIP-039: Detection and analysis of human adaptive NKG2C+ natural killer cells	**N/A**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Epidem. or Theoretical Panel Only** (BAI=0; ACTIONAB.=0)

Selected Biomarker Panels

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
Cardiometabolic Panel	**OLINK**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Cell Regulation Panel	**OLINK**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Cardiovascular II Panel	**OLINK**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Cardiovascular III Panel	**OLINK**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Immune Response Panel	**OLINK**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Inflammation Panel	**OLINK**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Metabolism Panel	**OLINK**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Neurology Panel	**OLINK**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Neuro Exploratory Panel	**OLINK**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Oncology II Panel	**OLINK**	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)

Selected Biomarker Panels

AGING
ANALYTICS
AGENCY

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
Oncology III Panel	OLINK	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Organ Damage Panel	OLINK	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Human v3 miRNA Assay	NANOSTRING	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
MiRXES ID3EAL miRNA Assay	MiRXES	PANEL	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
OsteomiRTM - Validated Bone Biomarkers	TAmiRNA	PANEL	Healthcare-Ready	**Informational Purpose Test or Platform**
ThrombomiRTM - Biomarkers of Platelet Function	TAmiRNA	PANEL	Healthcare-Ready	**Informational Purpose Test or Platform**
ToxomiRTM - Biomarkers of Toxicity	TAmiRNA	PANEL	Healthcare-Ready	**Informational Purpose Test or Platform**
DNAge™ Epigenetic Aging Clock	ZYMO RESEARCH	SINGLE BIOMARKER	Healthcare-Ready	**Informational Purpose Test or Platform**
Epigenetic Age Analysis Version 2.0	OSIRIS GREEN	SINGLE BIOMARKER	Healthcare-Ready	**Informational Purpose Test or Platform**
DNAge® test	BIOVIVA	SINGLE BIOMARKER	Healthcare-Ready	**Informational Purpose Test or Platform**

Selected Biomarker Panels

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
EpiHealth	CHRONOMICS	SINGLE BIOMARKER	Healthcare-Ready	Informational Purpose Test or Platform
EpiAging	HKG EPITHERAPEUTICS	SINGLE BIOMARKER	Healthcare-Ready	Informational Purpose Test or Platform
EpiSocialpsych	HKG EPITHERAPEUTICS	SINGLE BIOMARKER	Healthcare-Ready	Informational Purpose Test or Platform
Targeted Sequencing For DNA Methylation Analysis	HKG EPITHERAPEUTICS	SINGLE BIOMARKER	Healthcare-Ready	Informational Purpose Test or Platform
EpiLiver	HKG EPITHERAPEUTICS	SINGLE BIOMARKER	Healthcare-Ready	Informational Purpose Test or Platform
EpiBreast	HKG EPITHERAPEUTICS	SINGLE BIOMARKER	Healthcare-Ready	Informational Purpose Test or Platform
TeloYears plus Advanced Ancestry Tests	TELOYEARS	SINGLE BIOMARKER	Healthcare-Ready	Informational Purpose Test or Platform
Telomere Length and Biological Age Testing	LIFE LENGTH	SINGLE BIOMARKER	Healthcare-Ready	Informational Purpose Test or Platform
Telomere Length Test	CELL SCIENCE SYSTEMS	SINGLE BIOMARKER	Healthcare-Ready	Informational Purpose Test or Platform
CD4+ T-Cell Recent Thymic Emigrants (RTEs)	ARUP LABORATORIES	SINGLE BIOMARKER	Healthcare-Ready	Medical Test (+2 Availability Weight Points)

Selected Biomarker Panels

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
CD21 (Dendritic Cell) by Immunohistochemistry	**ARUP LABORATORIES**	SINGLE BIOMARKER	Healthcare-Ready	**Medical Test** (+2 Availability Weight Points)
CD57+ NK Cells, Peripheral Blood by Flow Cytometry	**ARUP LABORATORIES**	SINGLE BIOMARKER	Healthcare-Ready	**Medical Test** (+2 Availability Weight Points)
Phospho-H2AX (Ser139) Cellular Kit	**CISBIO**	SINGLE BIOMARKER	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Senescence Detection Kit	**ABCAM**	SINGLE BIOMARKER	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
SPiDER-ßGal	**DOJINDO MOLECULAR TECHNOLOGIES**	SINGLE BIOMARKER	Research Use Only (-2 Availab. Weight Points)	**Research Kit or OLPS** (Accuracy Index x *RKOLPS coefficient*)
Young.AI	**INSILICO MEDICINE**	DIGITAL PANEL PLATFORM	Healthcare-Ready	**AI Platform** (+5 Availability Weight Points)
Aging.AI	**INSILICO MEDICINE**	DIGITAL PANEL PLATFORM	Healthcare-Ready	**AI Platform** (+5 Availability Weight Points)
PhotoAgeClock	**HAUT.AI**	DIGITAL PANEL PLATFORM	Healthcare-Ready	**AI Platform** (+5 Availability Weight Points)
Haut.AI Skin Health	**HAUT.AI**	DIGITAL PANEL PLATFORM	Healthcare-Ready	**AI Platform** (+5 Availability Weight Points)
AgeMeter	**CENTERS FOR AGE CONTROL**	DIGITAL PANEL PLATFORM	Approved for Clinical Use	**Biomarkers Real-Time Assessment Technology** (+5 Availability Weight Points)

Selected Biomarker Panels

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
Health Reviser Platform	HEALTH REVISER	DIGITAL PANEL PLATFORM	Approved for Clinical Use	**Biomarkers Real-Time Assessment Technology** (+5 Availability Weight Points)
MEDIAGE™ Biological Age Measurement System	MEDIAGE	DIGITAL PANEL PLATFORM	Approved for Clinical Use	**Biomarkers Real-Time Assessment Technology** (+5 Availability Weight Points)
CarePredict Platform	CAREPREDICT	DIGITAL PANEL PLATFORM	Approved for Clinical Use	**AI Platform** (+5 Availability Weight Points)
Enlitic Platform	ENLITIC	DIGITAL PANEL PLATFORM	Healthcare-Ready	**AI Platform** (+5 Availability Weight Points)
Freenome Platform	FREENOME	DIGITAL PANEL PLATFORM	Research Use Only (-2 Availab. Weight Points)	**AI Platform** (+5 Availability Weight Points)
AI-Powered Radiology Assistant	ZEBRA MEDICAL VISION	DIGITAL PANEL PLATFORM	Healthcare-Ready	**AI Platform** (+5 Availability Weight Points)
PathAI Platform	PATHAI	DIGITAL PANEL PLATFORM	Healthcare-Ready	**AI Platform** (+5 Availability Weight Points)
Buoy Health Platform	BUOY HEALTH	DIGITAL PANEL PLATFORM	Healthcare-Ready	**AI Platform** (+5 Availability Weight Points)
BenevolentAI	BENEVOLENT	DIGITAL PANEL PLATFORM	Research Use Only (-2 Availab. Weight Points)	**AI Platform** (+5 Availability Weight Points)
Tempus Platform	TEMPUS	DIGITAL PANEL PLATFORM	Research Use Only (-2 Availab. Weight Points)	**AI Platform** (+5 Availability Weight Points)

Selected Biomarker Panels

NAME	COMPANY or ENTITY	AMPLITUDE LEVEL	CONDITIONING STAGE CATEGORY	OPERATIONAL CATEGORY
KenSci Platform	KENSCI	DIGITAL PANEL PLATFORM	Healthcare-Ready	**Biomarkers Real-Time Assessment Technology** (+5 Availability Weight Points)
Proscia Platform	PROSCIA	DIGITAL PANEL PLATFORM	Research Use Only (-2 Availab. Weight Points)	**Biomarkers Real-Time Assessment Technology** (+5 Availability Weight Points)
Google's DeepMind Health AI Platform	DEEPMIND TECHNOLOGIES	DIGITAL PANEL PLATFORM	Approved for Clinical Use	**AI Platform** (+5 Availability Weight Points)
ICarbonX Platform	ICARBONX	DIGITAL PANEL PLATFORM	Research Use Only (-2 Availab. Weight Points)	**AI Platform** (+5 Availability Weight Points)
Blood Chemistry Calculator	NOURISH BALANCE THRIVE	DIGITAL PANEL PLATFORM	Healthcare-Ready	**AI Platform** (+5 Availability Weight Points)
Ada - Symptom Checker App	ADA HEALTH GMBH	DIGITAL PANEL PLATFORM	Approved for Clinical Use	**AI Platform** (+5 Availability Weight Points)
Babylon Health Platform	BABYLON HEALTH	DIGITAL PANEL PLATFORM	Approved for Clinical Use	**AI Platform** (+5 Availability Weight Points)
Digital Nutrition Platform	ZIPONGO	DIGITAL PANEL PLATFORM	Healthcare-Ready	**AI Platform** (+5 Availability Weight Points)
Better Therapeutics Platform	BETTER THERAPEUTICS	DIGITAL PANEL PLATFORM	Research Use Only (-2 Availab. Weight Points)	**AI Platform** (+5 Availability Weight Points)

Most Viable Panels

ACCURACY VALUES OF MOST VIABLE PANELS

.6657 .7214 .7771 .8328 .8885 .9442 1.0

AVAILABILITY VALUES OF MOST VIABLE PANELS

3.82 4.85 5.88 6.91 7.94 8.97 10

Accuracy chart values:

- DNAge™ Epigenetic Aging Clock, ZYMO RESEARCH — 1.0
- Young.ai, INSILICO MEDICINE — 0.96
- Aging.ai, INSILICO MEDICINE — 0.93
- Viome Gut Intelligence™ Test, VIOME — 0.90
- PhotoAgeClock, HAUT.AI — 0.89
- GlycanAge Test, GLYCANAGE — 0.88
- AgeReader test, DIAGNOPTICS — 0.87
- Biological Age Test from Health Reviser Platform, HEALTH REVISER — 0.85
- PhysioAge Biomarkers of Aging Test, PHYSIOAGE — 0.83
- TeloYears + Advanced Ancestry, TELOYEARS — 0.80
- AgeMeter, CENTERS FOR AGE CONTROL — 0.77
- Immune-Frame, RGCC — 0.74
- Phospho-H2AX (Ser139) Cellular kit, CISBIO — 0.72
- Anti-Aging #4 Comprehensive Blood and Urine Test Panel, WALK-IN LAB — 0.69
- WellnessFX Premium, WELLNESSFX — 0.665
- InsideTracker Ultimate Plan + DNA analysis, SEGTERRA — 0.663
- Aging Theranostic 1.0, OPEN LONGEVITY — 0.66
- Biomarker Panel, UK BIOBANK — 0.66
- Discovery/MAP v 3.3 Panel, MYRIAD RBM — 0.65
- Inflammation Panel, OLINK — 0.645
- Metabolism Panel, OLINK — 0.64
- Healthy Aging Panel, LIFE EXTENSION — 0.63
- InsideTracker Inner Age (Compr.) + DNA analysis, SEGTERRA — 0.61

Availability chart values:

- Young.ai, INSILICO MEDICINE — 10 BAI
- Aging.ai, INSILICO MEDICINE — 10 BAI
- Advanced MethylDetox Profile + Telomere Length Test, CELL SCIENCE SYSTEMS — 10 BAI
- Viome Gut Intelligence™ Test, VIOME — 10 BAI
- DNAge™ Epigenetic Aging Clock, ZYMO RESEARCH — 10 BAI
- toxomiRTM - biomarkers of toxicity, TAmiRNA — 7.54 BAI
- Health + Ancestry Service, 23ANDME — 7.26 BAI
- AgeReader test, DIAGNOPTICS — 7.16 BAI
- AgeMeter, CENTERS FOR AGE CONTROL — 6.20 BAI
- InsideTracker Inner Age + DNA analysis, SEGTERRA — 5.54 BAI
- Oxidative stress Analysis 2.0, GENOVA DIAGNOSTICS — 4.925 BAI
- Metabolic Analysis Profile (Organic Acids), GENOVA DIAGNOSTICS — 4.125 BAI
- 10 Hormone Saliva Test Kit, LABRIX — 3.812 BAI
- Anti-Aging #4 Comprehensive Blood and Urine Test Panel, WALK-IN LAB — 3.625 BAI
- Aging Theranostic 1.0, OPEN LONGEVITY — 3.45 BAI
- WellnessFX Premium, WELLNESSFX — 3.375 BAI
- InsideTracker Ultimate Plan + DNA analysis, SEGTERRA — 3.291 BAI
- LEGENDScreen™ Human PE Kit, BIOLEGEND — 3.25 BAI
- Cytokine Panel, MAYO CLINIC LABORATORIES — 3.166 BAI
- Immune-Frame, RGCC — 3.125 BAI
- NeuroGenomic™ Profile, GENOVA DIAGNOSTICS — 3.0833 BAI
- NeuroGenomic™ BAI — 3.0416
- SPIDER-4Gal, DOJINDO — 2.79 BAI
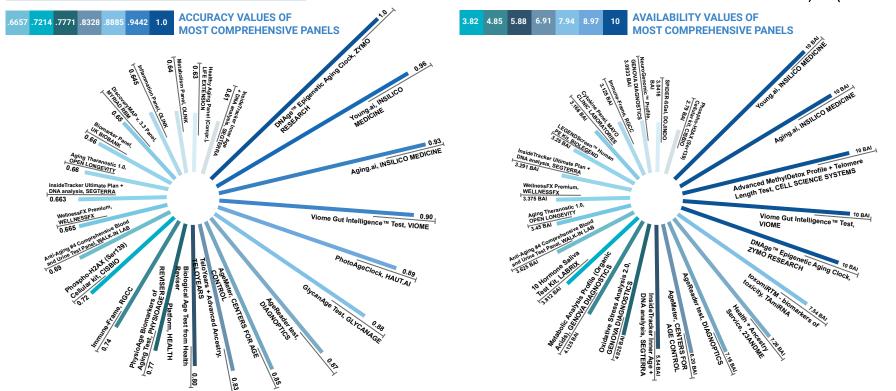- Phospho-H2AX (Ser139) Cellular kit, CISBIO — 2.79 BAI

It is Aging Analytics Agency's hope that our comparative analytics framework and methodology will serve as a useful long-term analytical tool for aging single biomarkers and panels assessment to identify the most advanced, available and actionable resources to create, manage, optimize and improve action plans for the health and Longevity industry, market and public sectors.

Most Comprehensive Panels

ACCURACY VALUES OF MOST COMPREHENSIVE PANELS

Scale: .6657 | .7214 | .7771 | .8328 | .8885 | .9442 | 1.0

- DNAge™ Epigenetic Aging Clock, ZYMO RESEARCH — 1.0
- Young.ai, INSILICO MEDICINE — 0.96
- Aging.ai, INSILICO MEDICINE — 0.93
- Viome Gut Intelligence™ Test, VIOME — 0.90
- PhotoAgeClock, HAUT.AI — 0.89
- GlycanAge Test, GLYCANAGE — 0.88
- AgeReader test, DIAGNOPTICS — 0.87
- Biological Age Test from Health Reviser REVISER3AGE Platform, HEALTH — 0.85
- AgeMeter, CENTERS FOR AGE CONTROL — 0.83
- TeloYears + Advanced Ancestry, TELOYEARS — 0.80
- PhysioAge Biomarkers of Aging Test, PHYSIOAGE — 0.77
- Immune-Frame, RGCC — 0.74
- Phospho-H2AX (Ser139) Cellular kit, CISBIO — 0.72
- Anti-Aging #4 Comprehensive Blood and Urine Test Panel, WALK-IN LAB — 0.69
- WellnessFX Premium, WELLNESSFX — 0.665
- InsideTracker Ultimate Plan + DNA analysis, SEGTERRA — 0.663
- Aging Theranostic 1.0, OPEN LONGEVITY — 0.66
- Biomarker Panel, UK BIOBANK — 0.66
- Discovery/MAP v 3.3 Panel, MYRIAD RBM — 0.65
- Inflammation Panel, OLINK — 0.645
- Metabolism Panel, OLINK — 0.64
- Healthy Aging Panel, LIFE EXTENSION — 0.63
- InsideTracker Inner Age (Compr.) + DNA analysis, SEGTERRA — 0.61

AVAILABILITY VALUES OF MOST COMPREHENSIVE PANELS

Scale: 3.82 | 4.85 | 5.88 | 6.91 | 7.94 | 8.97 | 10

- Young.ai, INSILICO MEDICINE — 10 BAI
- Aging.ai, INSILICO MEDICINE — 10 BAI
- Advanced MethylDetox Profile + Telomere Length Test, CELL SCIENCE SYSTEMS — 10 BAI
- Viome Gut Intelligence™ Test, VIOME — 10 BAI
- DNAge™ Epigenetic Aging Clock, ZYMO RESEARCH — 10 BAI
- toxomiRTM - biomarkers of toxicity, TAmiRNA — 7.54 BAI
- Health + Ancestry Service, 23ANDME — 7.26 BAI
- AgeReader test, DIAGNOPTICS — 7.16 BAI
- AgeMeter, CENTERS FOR AGE CONTROL — 6.20 BAI
- InsideTracker Inner Age + DNA analysis, SEGTERRA — 5.54 BAI
- Oxidative stress Analysis 2.0, GENOVA DIAGNOSTICS — 4.925 BAI
- Metabolic Analysis Profile (Organic Acids), GENOVA DIAGNOSTICS — 4.125 BAI
- 10 Hormone Saliva Test Kit, LABRIX — 3.812 BAI
- Anti-Aging #4 Comprehensive Blood and Urine Test Panel, WALK-IN LAB — 3.625 BAI
- Aging Theranostic 1.0, OPEN LONGEVITY — 3.45 BAI
- WellnessFX Premium, WELLNESSFX — 3.375 BAI
- InsideTracker Ultimate Plan + DNA analysis, SEGTERRA — 3.291 BAI
- LEGENDScreen™ Human PE Kit, BIOLEGEND — 3.25 BAI
- Cytokine Panel, MAYO CLINIC LABORATORIES — 3.166 BAI
- Immune-Frame, RGCC — 3.125 BAI
- NeuroGenomic™ Profile, GENOVA DIAGNOSTICS — 3.0833 BAI
- SPIDER-4Gal, DOJINDO — 3.0416 BAI
- Phospho-H2AX (Ser139) Cellular kit, CISBIO — 2.79 BAI

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Conclusions

The use of biomarkers is an indispensable component of industry analytics and assessment. It is the foundation upon which measurement of Healthy Longevity and the effectiveness of P4 (Precision, Preventive, Personalized, Participatory) Medicine and Longevity therapeutics is built. This special analytical case study is designed as an in-depth review of the state of the art in biomarkers of biological age to advise private and public sector participants effectively.

It was produced to offer a panoramic review of the global landscape of aging and Longevity biomarkers, containing selected lists, rankings and enhanced profiles of more than 50 single biomarkers directly correlated with the trajectories of age-related diseases and syndromes, and exceeding 100 diverse biomarker panels for analytical data-driven comparisons that allow for an optimal integration of multiple biomarkers for practical use, achieving highly actionable monitoring systems for healthcare, clinical practice, translational research, frontier developments that exploit the current conditions of the rising Longevity industry, and the execution of public policies aiming to increase National Healthy Longevity that will result in a renaissance never seen before in economic and social dynamics.

In addition to their purely descriptive and analytical approaches, the report is designed to make key strategic recommendations, and to offer guidance regarding biomarker implementations, technologies and techniques within the reach of companies and nations today, in order to equip them with the tools necessary for optimizing their strategy and action plans, providing specialized guidelines for business, investment and policy decision making. The report delivers a most comprehensive list of single biomarkers and biomarker panels of biological age together with extensive and enhanced profiles: their advantages, disadvantages, future perspectives, challenges and opportunities, with a focus on technologies currently used for assessment; concrete analysis of routine, advanced and novel biomarkers of aging, emerging tools and platforms, and insights about the impact of these biomarkers on health systems and clinical practice. A special treatment tracing the role of Digital Biomarkers and AI platforms as necessary and indispensable components of the Longevity biomarker industry is also delivered, highlighting the fact that AI and data science are increasingly necessary to handle the increasing volume of biomarker, life and health data.

Conclusions

The report's central conclusion is that as the scope of P4 Medicine broadens actively and healthily, the number of biomarkers, measurement technologies and platforms will increase rapidly to the thousands in the coming years. This will provide the opportunity to improve medical stratification to its maximum degree, enabling the adoption of Personalized, Participatory, Precision and Preventive Medicine for both the young, the middle aged and the old.

This will also enable the conditions necessary for conducting more exhaustive and precise studies with samples of only one individual, and a shift away from testing therapies using conventional model organisms and toward a more human-centered approach, due to the enormous flow of biological digital data that will be extracted continuously, individual to individual.

These vast amounts of continuous biomarker data will make impractical the implementation of P4 Medicine by current, manual means without the use of AI and advanced data science techniques and technologies.

Aggregation of biomarkers of Longevity, rather than biomarkers of disease only, and from healthy populations (e.g. the young, middle aged and healthy elderly), rather than bedside data from hospital populations, will be part of everyday life due to the novel digital health platforms capable of extracting truly massive amounts of relevant clinical data from single patients.
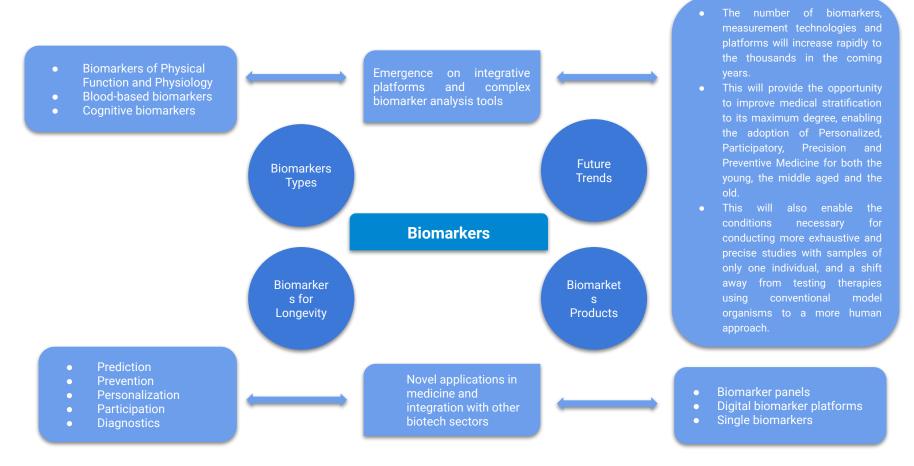
It is impossible to determine whether biotechnologies for Longevity have been successful if we cannot tell how advanced the aging process is in any given individual; but at the same time the latter will not be feasible until successfully achieving highly actionable panels that allow for evaluating the aging process in broad healthy and less healthy differentiated ranges of the population spectrum.

It in this sense that biomarkers are an essential factor in Aging Analytics Agency's strategic agenda, which includes policy proposals to national and international governance bodies on how to effectively increase National Healthy Longevity via practical implementation of P4 medicine technologies. It is important to develop and promote the widespread use of a panel of biomarkers that is precise enough and immediately actionable.

The report documents many aging biomarkers, and identifies from among them those which, by the metrics described (and which have never been reported in pre existing literature), belong to the category we have named Minimum Required: the Most Viable Products for immediate implementation.

It is our hope and commitment that regardless of whether it is adopted wholesale, the results of the report's analysis can guide relevant counterparties on how to optimally utilize existing technologies to maximize the health of aging populations and aging economies, as soon as possible.

Conclusions

Biomarkers of Physical Function and Physiology
- Biomarkers of Physical Function and Physiology
- Blood-based biomarkers
- Cognitive biomarkers

Emergence on integrative platforms and complex biomarker analysis tools

- The number of biomarkers, measurement technologies and platforms will increase rapidly to the thousands in the coming years.
- This will provide the opportunity to improve medical stratification to its maximum degree, enabling the adoption of Personalized, Participatory, Precision and Preventive Medicine for both the young, the middle aged and the old.
- This will also enable the conditions necessary for conducting more exhaustive and precise studies with samples of only one individual, and a shift away from testing therapies using conventional model organisms to a more human approach.

Biomarkers Types

Future Trends

Biomarkers

Biomarkers for Longevity

Biomarkets Products

- Prediction
- Prevention
- Personalization
- Participation
- Diagnostics

Novel applications in medicine and integration with other biotech sectors

- Biomarker panels
- Digital biomarker platforms
- Single biomarkers

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