Longevity Biomarkers Landscape Overview

Q4 2021

October 2021

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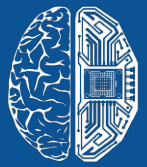
Aging Analytics Agency



Deep Knowledge Group

www.longevity.international

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The growing geriatric population and **increasing prevalence of chronic diseases** are the key factors projected to boost the **diagnostic market growth** over the forecast period. Our report is focused on the diagnostic of aging that include **direct evaluation of biological age** and **prediction** and **prognosis age-related disorders**. The paper provides a thorough list of single biomarkers and biomarker panels of biological age, together with extensive and enhanced profiles. It explores their advantages, disadvantages, future perspectives, challenges and opportunities, with a focus on technologies currently used for assessment.

Biomarkers are an essential factor in the **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 essential to develop and promote the widespread use of panels of biomarkers that are validated and actionable.

Here we also have highlighted the increasingly necessary role of **AI technology** that will play in coordinating the practical implementation of Longevity biomarkers due to the sheer volume of life and health data involved. We believe that the application of AI for Longevity will **bring the greatest real-world benefits** to the industrialization of Longevity to scale, and that will serve as the **main driver of progress** in the widespread extension of healthy Longevity for all segments of society in the coming years.

Approach of the Report

Database

300	495	235
Companies	Investors	R&D Centers

The database was formed based on:

- the **identification of companies and R&D centers** that develop or implement Biomarkers of Aging and age-related diseases;
- the **determination of investors** that contributed money to these companies.

Applied Research and Analytics Methods

Descriptive Analysis	Mixed Data Research	Data Triangulation
Comparative Analysis	Qualitative Data Collection	Data Filtering

Data Sources

Media Overview (Articles and Press Releases)	Industry-Specialised Databases	Publicly Available Sources (Websites)	Industry Reports and Reviews

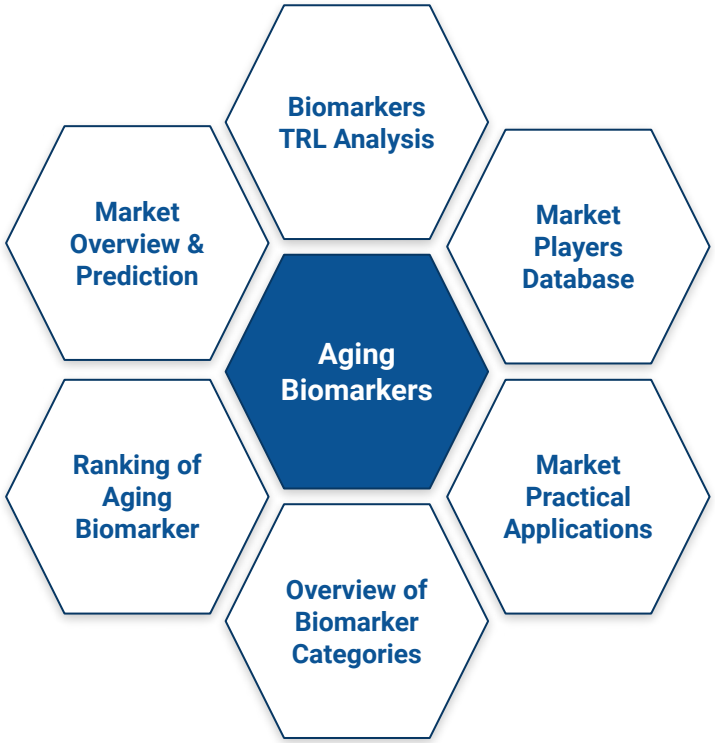
Relying on various research methods and analytics techniques, the analytical provides a comprehensive overview of the Longevity Biomarkers Landscape. This approach has certain limitations, especially when using publicly available data sources and conducting secondary research. Aging Analytics Agency is not responsible for the quality of the secondary data presented herein; however, we do our best to eliminate the said risks using different analytics techniques and cross-checking data. Please note that we did not deliberately exclude certain companies from our analysis, nor was it due to the data-filtering method used or difficulties encountered. The main reason for their non-inclusion was incomplete or missing information in the available sources.

Executive Summary

Aging is a physiological accumulation of functional losses during life, underlined by changes in the molecular mechanisms of the body functioning. The chronological age of the organism does not always indicate well the functional state of the organism. People of the same age can have different levels of health and abilities, as well as different rates of aging. **Biomarkers of Aging** are the key tools for assessing the wide range of physiological processes that underlying aging and the appearance of age-related diseases.

This analytical case study includes an unexampled database that provides a closer look at the companies, clinics, investors, R&D centers leading by the specific mechanisms of aging involved. Key players of this industry are reviewed and analyzed precisely. Market meta-analysis offers a unique view of market patterns and future prospects. The categorization and evaluation of businesses provide information into the distribution of future pressures. Each category of Aging Biomarker is examined separately. Furthermore, in-depth research analyzes provide an overview of product trends and treatment strategy dynamics.

Main Features of the Analytical Case Study



Executive Summary

This report is an overview version of research study on the **longevity biomarkers** aiming to provide :

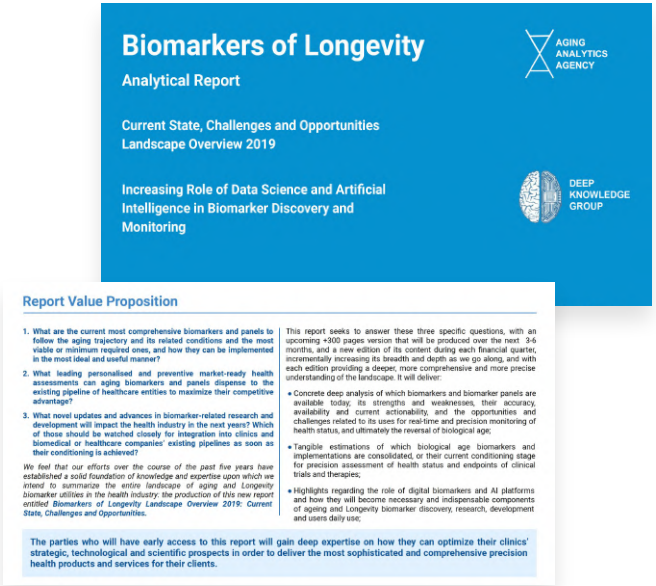
- Concrete deep analysis of which **biomarkers and biomarker panels** are available today; their strengths and weaknesses, accuracy, availability and current actionability, their strength, and weaknesses, and peculiarities of each type of longevity biomarkers related to its uses for real-time and precision monitoring of health status, and 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, the use in insurance risk assessments;
- Highlights regarding the role of **digital biomarkers, digital avatars and AI platforms** and how they will become necessary and indispensable components of aging and Longevity biomarker discovery, research, development and users daily use; overview of mobile apps containing actionable biomarkers or aging clocks.

1. **Existing biomarkers/biomarker panels,** their availability and current actionability.
2. **Application of biomarkers** to longevity, aging, aging clocks and age-related diseases.
3. **Biomarkers' accuracy**, their **strengths**, **weaknesses**, **threats**, and **opportunities**.
4. The increasing role of **digital biomarkers,** especially **digital avatars.**
5. The **importance of AI** in the biomarkers' discovery, validation and implementation.
6. The **implementation of longevity biomarkers in finances** and insurance risk assessments.

Introduction

In 2019, Aging Analytics Agency produced **Biomarkers of Longevity Landscape Overview 2019**, an open-access special analytical case study that uses comprehensive analytical frameworks to rank and benchmark existing panels of biomarkers of aging 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, for use by a wide variety of strategic decision makers including companies, investors, governments and insurance companies.

The report was 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 plans and strategies, providing **specialized guidance for business and investment core decisions**, including a comprehensive list of single biomarkers of aging and panels (their advantages and disadvantages), a concrete analysis of recent novel biomarkers of aging, **an overview of AI platforms** as a necessary and indispensable components of longevity biomarker discovery.



Source: Biomarkers of Longevity Landscape Overview 2019

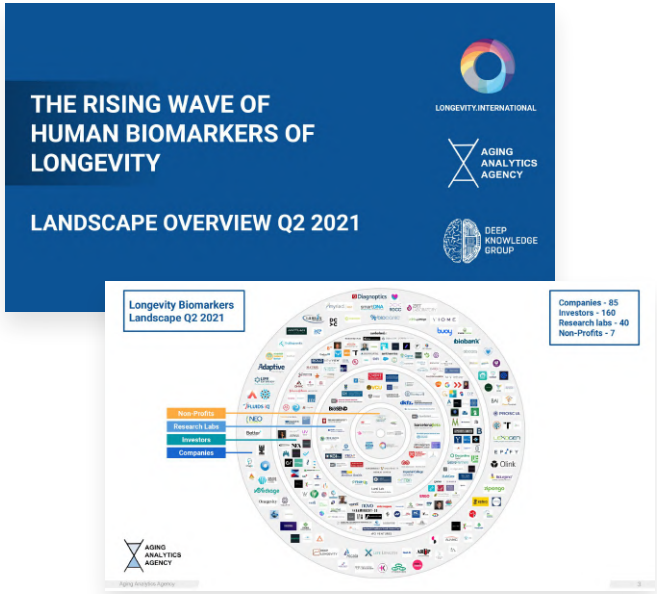
Introduction

The next edition of the **Longevity Biomarker Ecosystem Q2 2021** report was published in May 2021, providing an enhanced overview of 85 companies, 160 investors, and 100 biomarker panels.

Deep Knowledge Group considers longevity biomarkers as a strategic core engine for its longevity activities and as a major catalyst for the development of the whole longevity industry. They represent the major key to transforming aging science theory into practical Human Longevity applications over the next several years. Moreover, biomarker panels can be used as tangible, validated tools to evaluate, benchmark, and compare longevity companies, conducting data-driven evidence-based due diligence.

Therefore, the question of access to the top expertise in longevity biomarkers is of a strategic importance for Deep Knowledge Group.

Further, longevity biomarker panels can be applied for financial products structuring, namely InsurTech and more complex financial products later on (such as for example HALE/QALE derivatives, biological age financial options and futures, and so on).



Introduction

Longevity Biomarkers Landscape Q4 is a special analytical case study by Aging Analytics Agency which is an updated version of The Rising Wave of Human Biomarkers of Longevity: Landscape Overview 2021 and provides a comprehensive overview of the Longevity Biomarkers Landscape, which is rapidly developing.

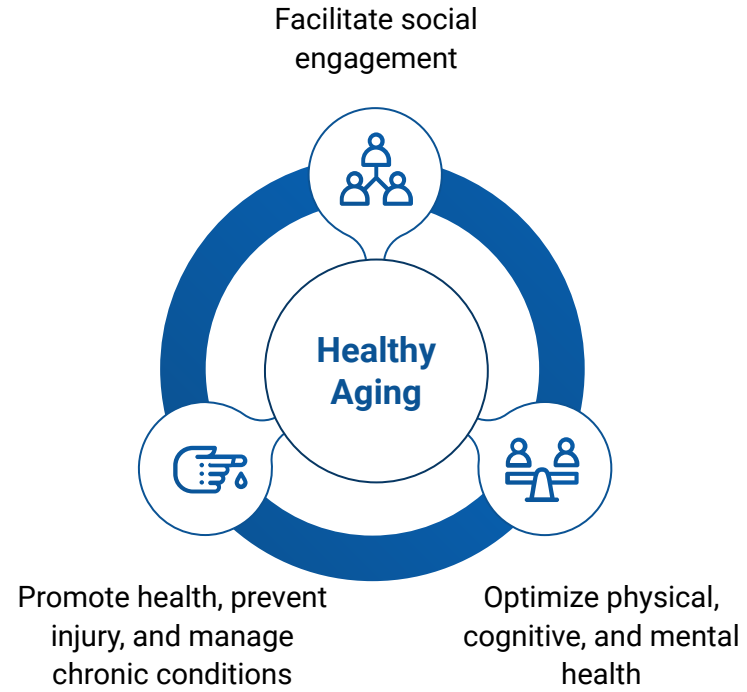
The report includes a **more detailed description of biomarker varieties**, **updated biomarkers classification**, **a timeline of their development**, and **updated private and public sector biomarker adoption guidelines** to help them find the tools they need to optimize their strategies and action plans, as well as specialized guidance for business, investment, and policymaking. Demonstrates professional potential to provide a **fundamental understanding of the significant challenges and opportunities** being faced in this area, or how they can be used to maximize benefit and to avoid potential pitfalls by individuals, institutions, and even entire governments.

Concept of Aging

Aging is a global phenomenon that began some 3.5 billion years ago with the genesis of life. The accumulation of the many changes caused by aging in cells and tissues alter it's function and can finally lead to death. Genetic abnormalities, the environmental factors, illnesses — all of those contribute to aging changes. **9 hallmarks of aging** (listed on the next slide) that were defined to characterize aging process on the cellular level.

Under optimal living conditions, the degree of accumulation of aging changes limits average life expectancy at birth to about 85 years and maximum life span to around 122 years. Due to incremental improvements in living circumstances, such as diet, housing, and medical care, these limitations have been slowly increased over the previous 2000 years. As such, life expectancy in ancient Rome was about 30 years, while reaching to almost 80 years today in the developed countries.

In today's society, healthy aging and well-being are widespread public and governmental objectives. The recognition that much of the cost of health and social care in economically developed countries is consolidated in the last decade or two, as well as the major demographic shift towards higher proportions of older adults in the population in many countries around the world, have sharpened the research focus on aging.



Source: Harman D. Aging: overview

The Hallmarks of Aging

Genomic Instability

Aging can be the consequence of increased DNA damage accumulation. This is due to physical, chemical, and biological agents, as well as DNA replication errors, spontaneous hydrolytic reactions, and reactive oxygen species (ROS).

Telomere Attrition

Telomeres are the chromosomal regions located on the ends of chromosomes. They tend to become increasingly shorter after each DNA replication. When this sequence ends, the cell dies. Telomerase deficiency in humans is associated with age-related diseases.

Epigenetic Alteration

Epigenetic changes involve alterations in DNA methylation, post-translational modification of histones, and chromatin remodeling. It can lead to abnormal function of cell.

Loss of Proteostasis

Proteostasis involves mechanisms for the stabilization of correctly folded proteins, as well as mechanisms for the degradation of abnormal proteins. These processes tend to change during aging.

Deregulated Nutrient Sensing

Nutrient sensing includes trophic and bioenergetic pathways, such as insulin and IGF-1, signaling pathways, and other systems (mTOR, AMPK, and sirtuins).

Mitochondrial Dysfunction

There is a noticeable reduction in ATP generation and increased electron leakage in the respiratory chain caused by aging. It is associated with mitochondrial damage.

Cellular Senescence

Cellular senescence can be defined as a stable arrest of the cell cycle. The accumulation of senescent cells in aged tissues can lead to age-related disease progression.

Stem Cell Exhaustion

Stem cells are cells from which all other cells with specialized functions are generated. There is a substantial decrease in the number of stem cells during life. Recent studies suggest that stem cell rejuvenation may reverse the aging phenotype.

Altered Intercellular Communication

Neurohormonal signaling tends to be deregulated in aging as inflammatory reactions increase, while immunosurveillance against pathogens and premalignant cells declines.

Source: López-Otín, Carlos et al. “The hallmarks of aging.”Cell

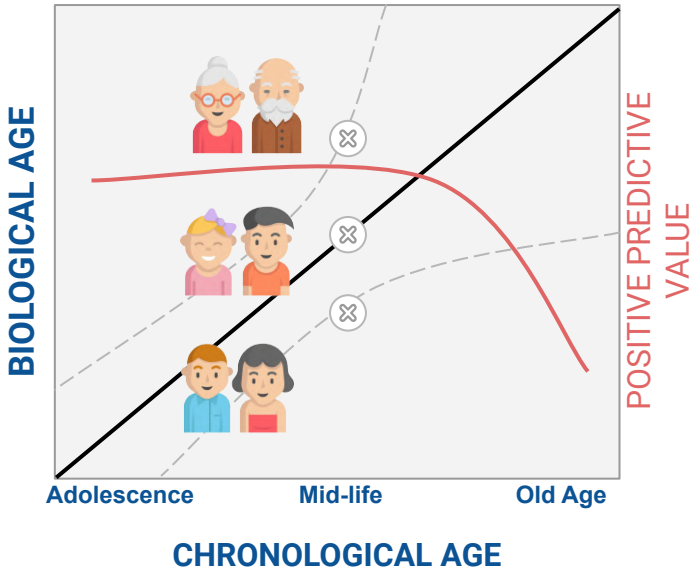
Types of Age

Chronological age is calculated purely based on the passage of time. It is the number of years that a person has lived. As people age, their chances of acquiring a disease or the condition is rising. The health problems that are leading cause of functional decline in advanced chronological age.

Biological age refers to the changes in the body that occur as people get older. Because some individuals are affected by these changes sooner than others, some people are physiologically old at 65, while others are not for another decade or more. However, rather than variations in biological aging, the most notable variances in perceived age among persons of identical chronological age are produced by lifestyle, habit, and subtle impacts of disease.

The scheme on the right describe biological age predictor that is a biomarker associated with chronological age (black line) and assist in risk assessments for age-related diseases. Based on their biological ages (x's axis in figure), individuals of the same chronological age may have varying risks for age-related illnesses. The positive predictive value (red line) of a biological age predictor usually declines from mid-life.

Scheme of Biological Age Prediction



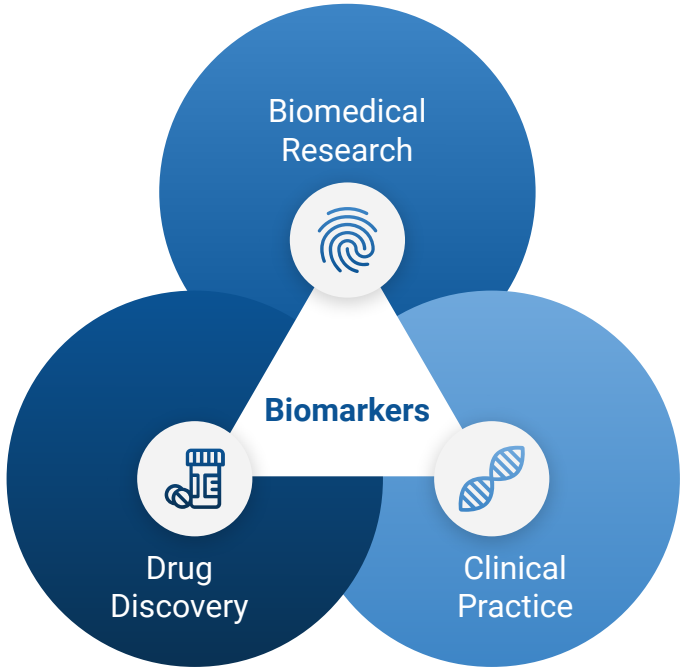
Source: Jylhävä et al. Biological Age Predictor

Concept of 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.

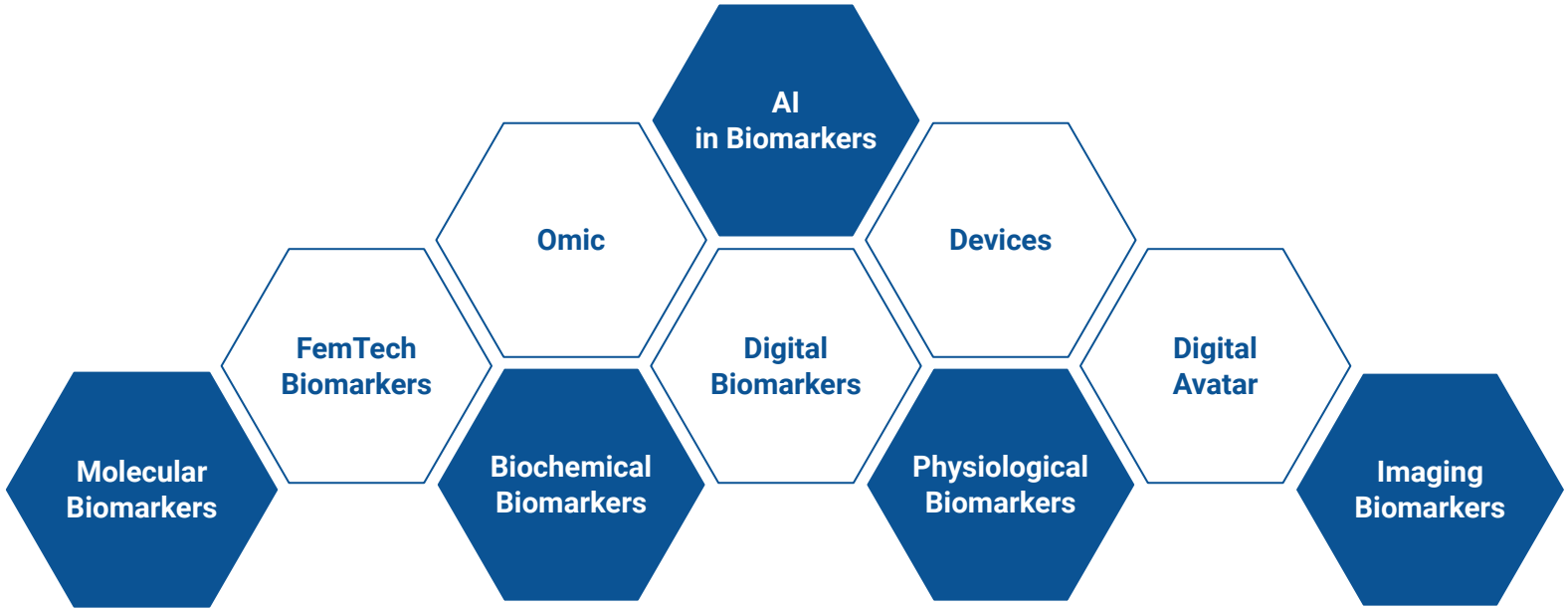
In **biomedical research** and **clinical practice**, biomarkers include measurements that suggest the etiology of, susceptibility to, activity of, or progress of a disease. The use of biomarkers in basic and clinical research as well as in clinical practice has become so commonplace that their presence 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 become 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.



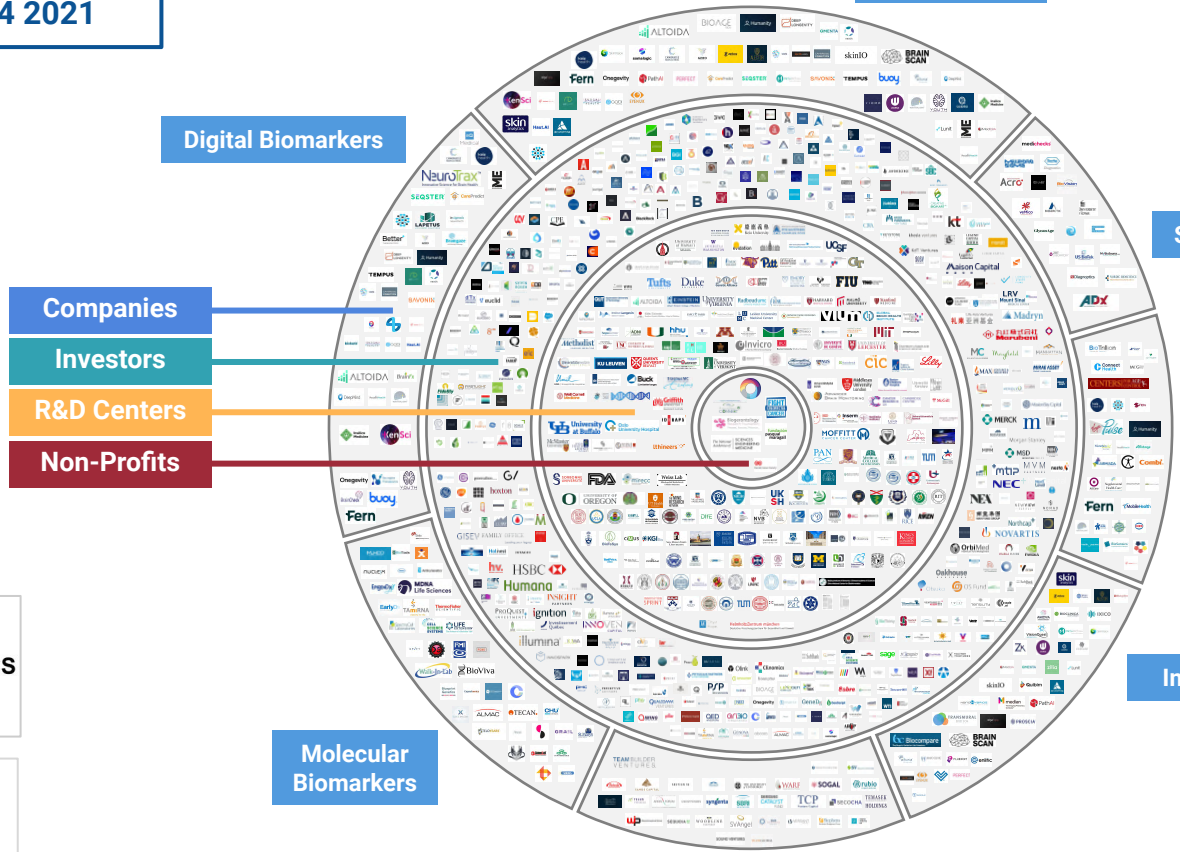
Longevity Biomarkers Framework

Ahead of database creation, we picked the **most significant types of biomarkers of aging**. The categorization of companies is based on the source of biomarkers, their focus level, practical outlook, and methodology. The framework not only brings a **comprehensive view of the market,** but also **sustains relevance in advance to the development** of technologies and research approaches.



Longevity Biomarkers Landscape Q4 2021

Companies - 300
Investors - 495
R&D Centers - 235
Non-Profits - 7



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Classification of Biomarkers of Aging

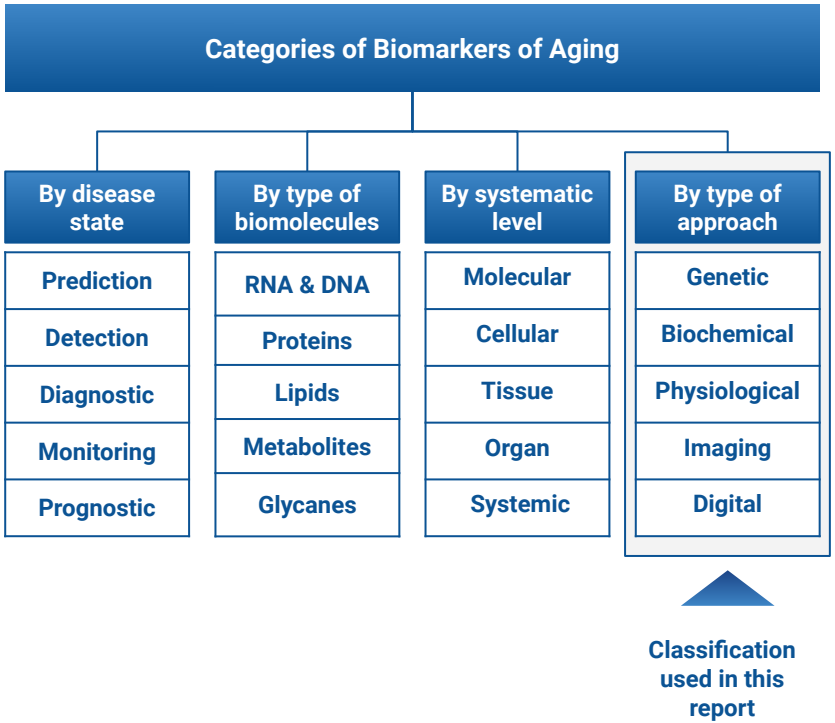
In older adults, chronological age may not be the best predictor of **residual lifespan** and **mortality**, because with age the heterogeneity in health is increasing. **Biomarkers for biological age** and **residual lifespan** are being developed to predict disease and mortality better at an individual level than chronological age.

Classification of Biomarkers of Aging can be based on different parameters, including their characteristics, such as age-related disease state, type of biomolecule, systematic level of diagnostics or type of diagnostic approach.

In our report we have used classification **by diagnostic approach** which includes:

- **Genetic and Biochemical** biomarkers that describe changes on molecular level (mutations or polymorphisms and quantitative gene expression analysis, peptides, proteins, lipids metabolites, and other small molecules in biosamples),
- **Physiological** biomarkers show functional changes of organs,
- **Imaging** biomarkers (computed tomography, positron emission tomography, magnetic resonance imaging) show morphological changes in tissues and organs.
- **Digital** biomarkers are defined as objective, quantifiable physiological and behavioral data that are collected and measured by means of digital devices such as portables, wearables, implantables, or digestibles.

Age-Related Biomarkers Classification



Source: Britannica-aging, Proteomics and System Biology

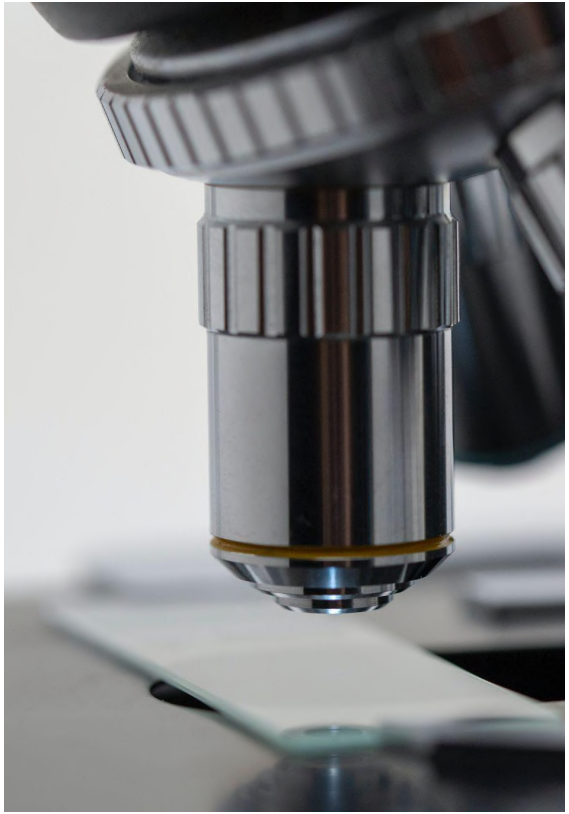
Classification of Biomarkers of Aging

The classification presented in this report is a result of **preliminary studies of large research data present in scientific databases for the domain of Aging and Longevity-associated Biomarkers.**

Due to the large amounts of existing research data on a subject of our studies, diverse options for biomarkers classifications, etc., we are emphasizing that the particular classifications used in our report are not a final and universal one, and it will undergo reconsideration in our next analytics issue.

Firstly, we are aimed to diversify our classifications types. Secondly, the classification we are aiming for shall be more holistic and may include an dynamic, interactive online databases - due to the nature of some biomarkers, some of them being simultaneously correlated with different diseases types (diseases-based classifications - such as cardiovascular, neurodegenerative diseases types) or found simultaneously in different origin sites (allocation-based classifications - such as blood markers types or urine-based biomarkers). For such biomarkers, we are aiming to create an interactive classification, while allowing to highlight the belonging of those cross-biomarkers to the different categories within one classification.

Some biomarkers present in scientific research and used in this report despite being reported, did not passed enough validations yet or being reported recently or a long time ago on in vitro or on vivo models, lacking a clinical data and thus in-patient confirmations. This makes a necessity of a reconsideration of an existing classification used in this report while making a deeper analysis of Aging and Longevity-associated Biomarkers.



Development of Biomarkers of Aging

For the last two decade years, the **increasing prevalence of chronic diseases**, advancements in the **techniques** used for the development of biomarker-based diagnostics, and the **growing geriatric population** are factors likely to **boost the biomarkers market** significantly throughout the forecast period.

A new wave of scientific and commercial interest to Biomarkers of Aging **brings original solutions** for evaluation of biological age. The main mechanisms identified as potential biomarkers of aging are DNA methylation, loss of histones, and histone modification. The uses for biomarkers of aging are ubiquitous and identifying a physical parameter of biological aging would allow humans to **determine our true age**, **mortality**, and **morbidity**. The change in the physical biomarker should be proportional to the change in the age of the species. Thus, after establishing a biomarker of aging, humans would be able to dive into research on **extending life spans** and finding timelines for the **arise of potential genetic diseases**.

Challenges to Develop of Informative Biomarkers for Longevity and Aging

- the **biological variation** between individuals that makes generalizations difficult;
- the **overlapping of aging and disease** processes;
- uncertainty **regarding benign** versus **pathogenic age-related changes**;
- the point at which a process **begins to do damage** to the organism, and, if so, when does it occur;
- when to distinguish **critical damage** from **non-critical**;
- difficult to obtain **funding** for this research.

Butler RN. et al. Biomarkers of aging: from primitive organisms to humans. J. Gerontol

Evaluation of Biomarkers of Aging

Systemic Approach for Aging Rate Assessment

Biomarkers of Aging (AFAR* Criteria)

- Predict the rate of aging;
- Monitor a basic process that underlies the aging process, not the effects of disease;
- Must be able to be tested repeatedly without harming the person;
- Work in humans and in laboratory animals

Biomarkers of Age-related diseases

- Minimally invasive
- Routinely used for Clinical Diagnostics
- Comprehensive
- Reliable

Despite the growing interest to **Aging evaluation** there is still **no gold standard** of reliable biomarkers to predict and monitor Aging rate. Aging is a time-dependent multisystemic functional decline and it is evaluated at different levels: molecular, systemic, physiological.

Several attempts to establish markers of aging have been made over the last 50 years, but the complexity of the aging phenotype poses both **conceptual and practical challenges**.

Despite previous efforts, there is presently **no commonly accepted definition ofBiomarkers of Aging** or either criterias for their selection, resulting in an **absence of reliable, verified methods** for measuring healthy aging.

Biomarkers of healthy aging might be used as surrogate endpoints or outcome measures in trials of treatments aimed at extending life expectancy, and accurate, easily-measured indices of healthy aging could be used in public health-related population surveys.

However, there is **no standard reference for measuring healthy aging**, which makes conducting and assessing aging research across studies problematic.

**AFAR - American Federation for Aging Research*

Source: Lara, Jose et al. “A proposed panel of biomarkers of healthy aging.” BMC medicine

Practical Application of Age-Related Biomarkers

01 Clinical Trials

- New pathways identification
- Age-adjusted clinical trial enrollment

02 Reproductive Longevity

- Reproductive longevity tracking
- Family-planning timelines

03 Preventive medicine

- Feature transfer from aging to disease
- Age-related disease screening and staging
- Immunosenescence analysis

04 Treatment & Diagnostics

- Age-personalized immuno-oncology treatment
- Mortality prediction
- Age-personalized vaccines

05 Healthy Living

- Wellness
- Sport
- Nutrition
- Life insurance

Report Methodology

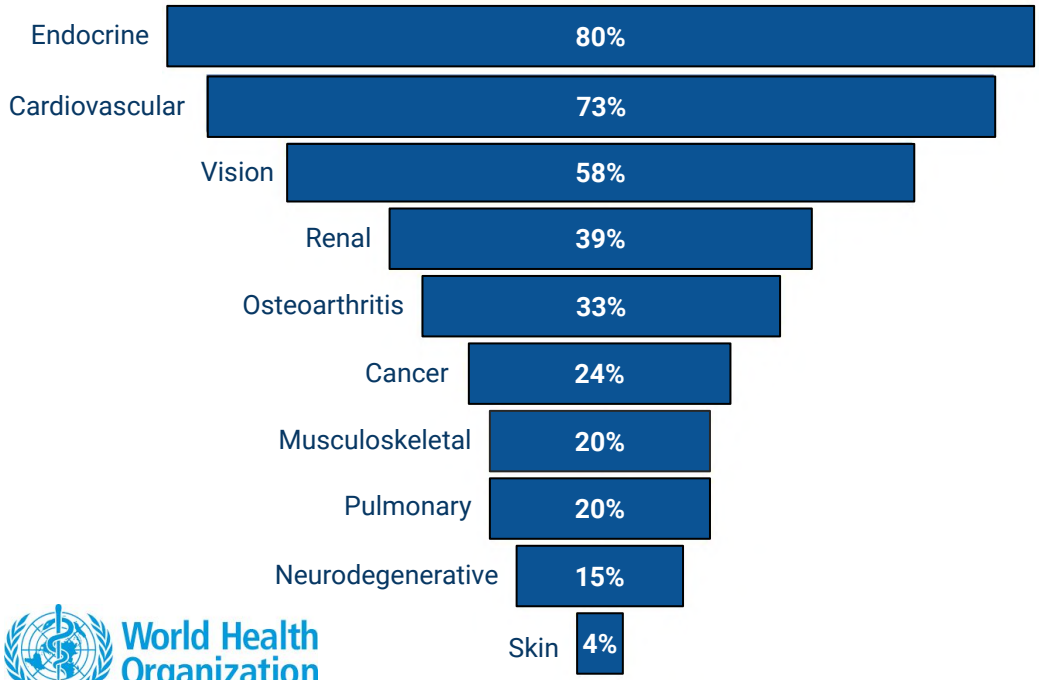
Q4 2021

Reports Comparative Analysis

	2021 Q2	2021 Q4
Companies Number Analyzed	80	300
Single Biomarkers Number Analyzed	150	220 single biomarkers + 130 genetic loci + 200 microRNAs
Biomarker Panels Number Analyzed	100	100
Marketed Longevity Products Number Analyzed	>100	>250

Biomarkers Selection by Prevalence of Age-Related Disorders

Prevalence of Disorders in Patient Group in Age >60, %



The world's **population is aging rapidly**. Between 2015 and 2050, the proportion of the world's older adults is estimated to almost double, from about 12% to 22%. In absolute terms, this is an **expected increase** from 900 million **to 2 billion people** over the age of 60. older adults face special health challenges which need to be recognized.
Multiple studies shown dramatical statistics in older cohort of patients. Approximately 80% of people develop endocrine disorders (33% of them have diabetes), 73% - cardiovascular disease (24% have coronary heart disease), 58% have problem with eyes and vision (18% seniors have amblyopia).

According to this prevalence of age-related disorders, we have selected biomarkers for our analysis.

Biomarkers Classification

Classification by Diagnostic Approach

Molecular	Biochemical	Physiological	Imaging	Digital
• Genetic • Epigenetic • Non-Epigenomic	• Senescence • Metabolic • Inflammatory • Mitochondrial • Cell architecture	• Functional • Morphological • Behavioral • Cognitive / mental • Stress etc.	• Radiological • MRI *(Magnetic resonance imaging)* • PET *(Positron emission tomography)* • Optical	• Smart devices • Neurocognitive biomarkers

Artificial Intelligence and Biomarkers

Omic Biomarkers | **Digital Avatar** | **FemTech Biomarkers**

For this report, we used biomarker **Classification by Diagnostic Approach** because this classification covers the **largest spectre of biomarkers** and **modern approaches for diagnostics**. As a separate **sub-categories** we have selected **Omic biomarker, Digital Avatar, FemTech Biomarker** based on combination of traditional diagnostic approaches and **AI / Machine Learning**. However, this classification is not final and can be changed in the next versions of the report.

Approaches Used for Market Analysis

Companies selection - among thousands of companies related to the Pharma, Biotechnology, Genetics and Life Science industries, only companies that conduct research and clinical trials in field of Biomarkers were selected.

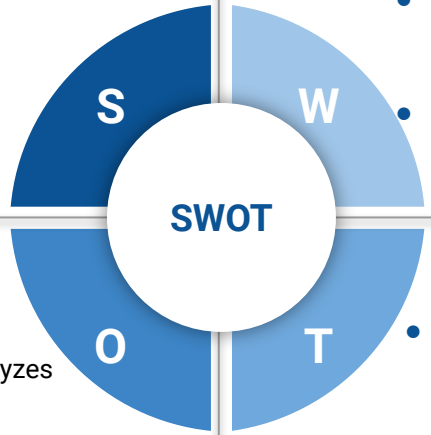
Subcategorization - all Biomarkers companies were divided into 7 recognized categories by main line of research in order to highlight similarities, determine peculiarities and get insights about trends and perspectives of specific category.

Market analysis - the attractiveness and the dynamics of a Biomarkers market players within a Longevity industry, submarkets of Biomarkers were studied. Geographic distribution, subcategorization, investment and revenue analysis were provided to define active hubs of the Biomarkers industry and promising investment trends.

SWOT matrix - complex analytic approach used to identify strengths, weaknesses, opportunities, and threats related to different Biomarkers categories in order to dispose development of study field and business perspectives.

Biomarkers of Aging: SWOT Analysis

- The complex analysis of many biomarkers of aging will result in accurate biological age.
- The biomarkers of aging also analyze diseases predisposition, which helps individuals to understand necessary preventive events.
- Some biomarkers of aging are inexpensive and functional simultaneously (for example, immunological and blood-based).



- There is no single biomarker (or a single set of biomarkers) that enables the reliable and accurate measurement of aging progression in humans.
- The accurate result can be received by a complex approach that includes many types of biomarkers, which can be expensive and public inaccessible.
- The analyzes of some biomarkers of aging (for example, omics biomarkers) are computationally expensive.

- The development of cutting-edge AI and ML technologies will simplify the biomarkers data analyzes and improve the accuracy.
- The spread of novel biotechnologies as NGS and high-throughput proteomics methods will reduce the cost of the tests.
- The spread of wearable devices will give a new costless biomarkers of aging source.

- The environmental and lifestyle factors can influence the biomarker quantity and quality, which may affect the accuracy of the test.
- There is no single approach how to analyze biomarkers of aging data.
- The biomarker data is not inclusive and equitable (lacking in the data from all ages, sexes, races, etc.), which may cause inaccurate results for certain population groups.

Source: Wiley Analytic Science

Concept of TRL

In the report we applied several evaluation metrics — qualitative and quantitative — to assess accuracy, availability, actionability and ethical aspects of single biomarkers or panels of biomarkers. Those included Accuracy Index, Availability Index, Actionability Index, Publication Index — all explained further.

For different types of aging clocks, in the suggested categorization framework, we estimated combined Technology Readiness Level (TRL) using a standard industry classification metric developed by NASA and measuring any technological solution from 1 to 10 — former being a stage of technological research, and 10 being a commercially available solution. We have identified TRL for select single biomarkers in each aging clock category and than applied an average for a category as a whole.

For each type of aging clocks we also conducted Strength, Weaknesses, Opportunities, and Threats (SWOT) analysis based on our qualitative expert assessment criterias.

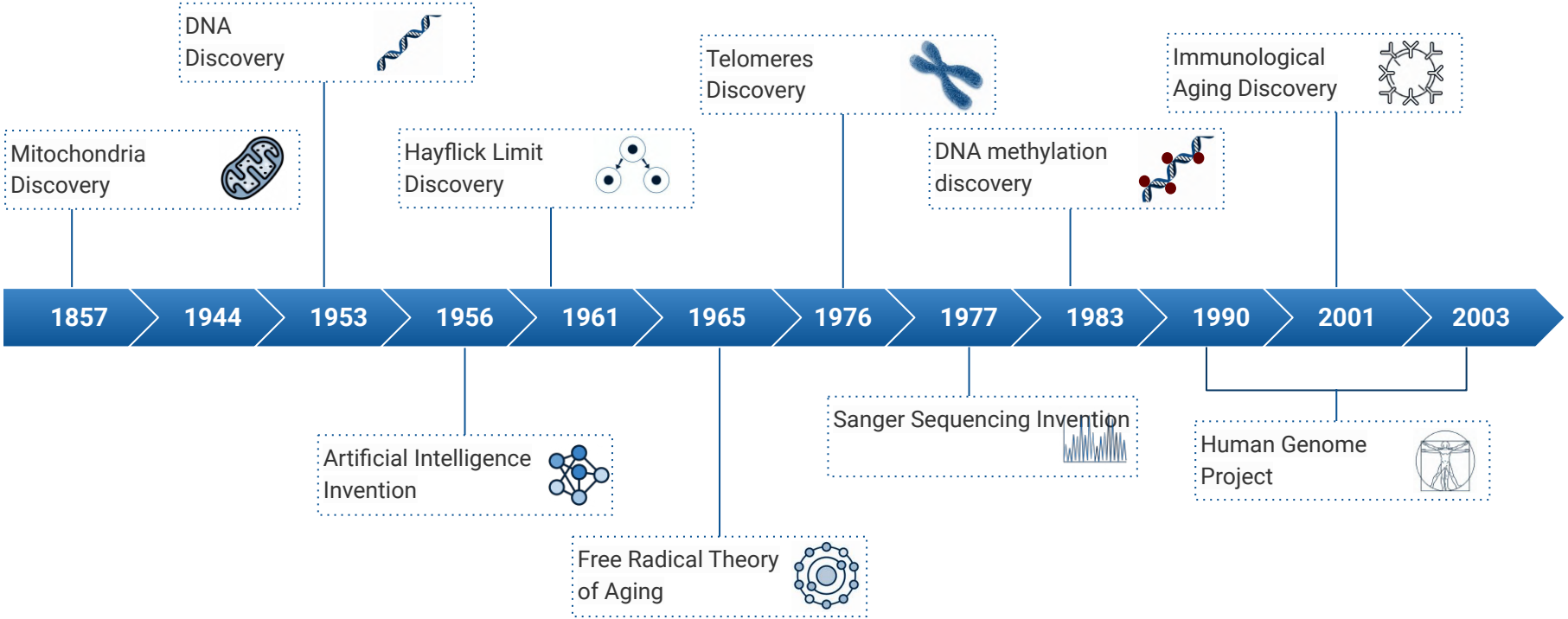
Finally, for the purpose of understanding ethical and legal risks involved in the application of advanced longevity biomarkers in certain consumer-oriented non-medical industries, like the insurance industry, we have made a qualitative risk assessment study and applied Ethical Risk Assessment Index — from 1 to 5 — 1 representing low risk and 5 representing the highest risk.

Technology Readiness Level (TRL) gradation principle:

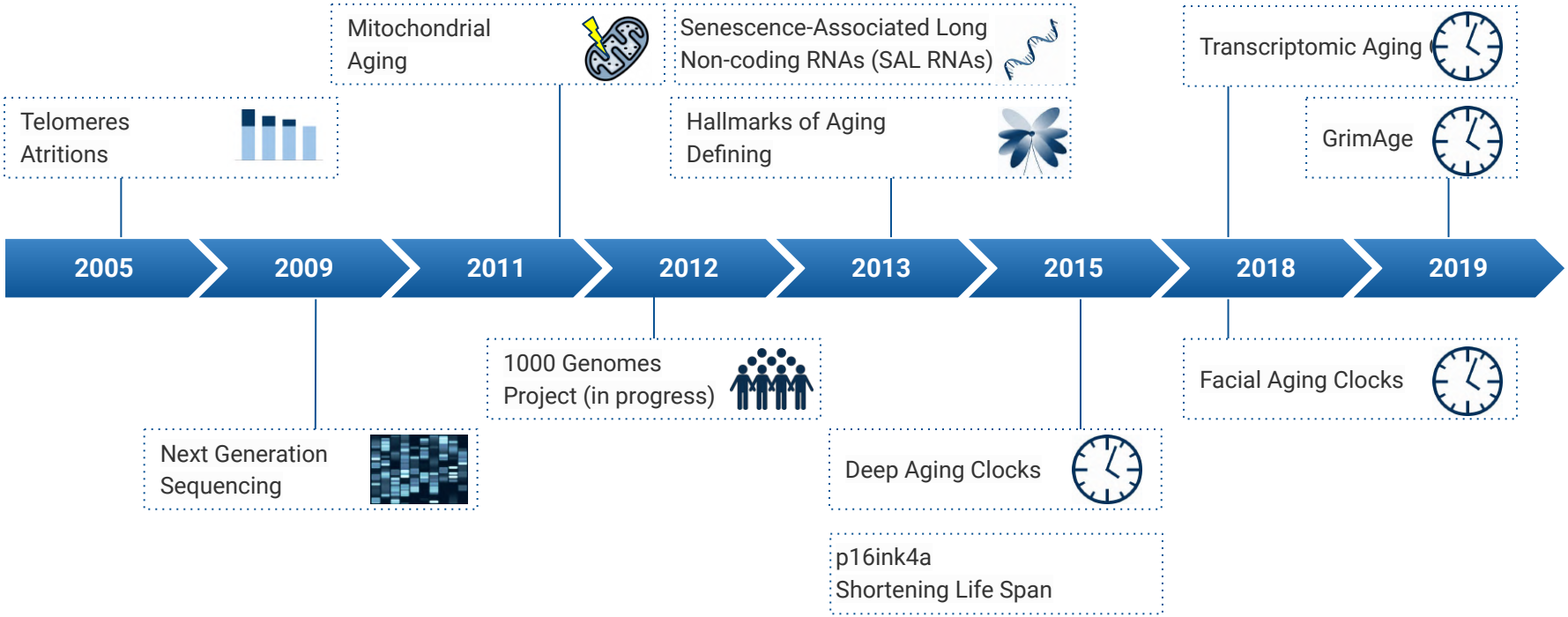
TRL 10	Proven Operations
TRL 9	System Operational
TRL 8	Subsystem Build and Test
TRL 7	Detailed Design and Prototype Validation
TRL 6	Preliminary Design and Prototype Demonstration
TRL 5	Conceptual Design and Prototype Demonstration
TRL 4	Technology Demonstration
TRL 3	Proof-of-Concept
TRL 2	Technology Concept
TRL 1	Technology Research

Source: Straub. In search of technology readiness level (TRL) 10. 2015.

Timeline of Longevity Biomarkers Research



Timeline of Longevity Biomarkers Research

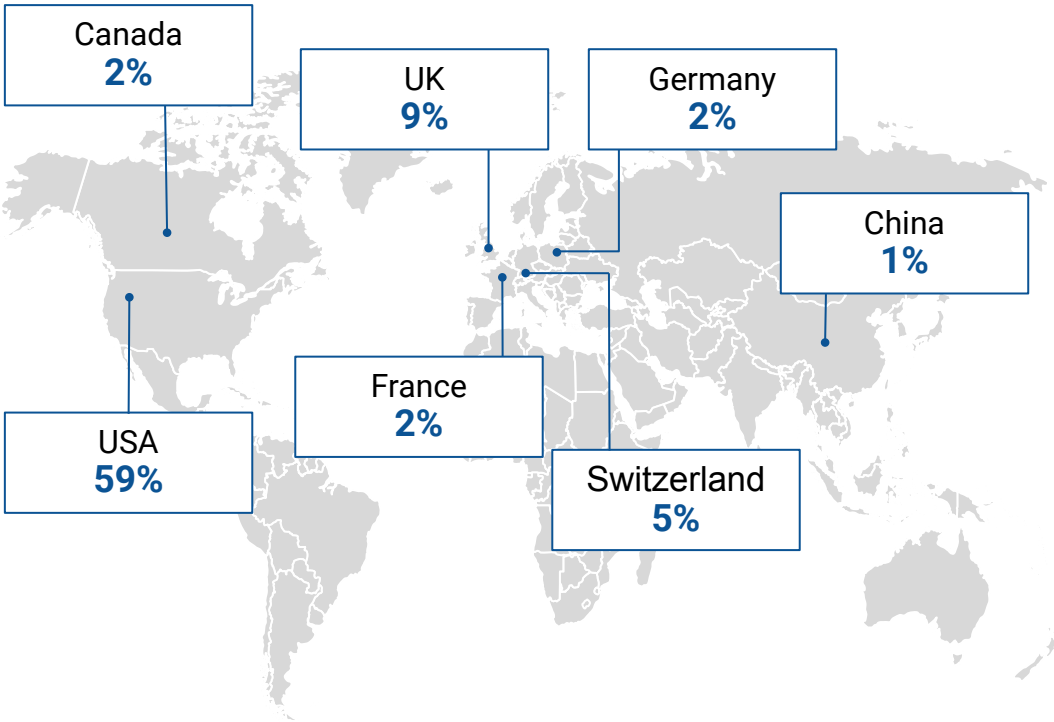


Market Overview

Q4 2021

Biomarkers Market at a Glance

Distribution of Companies by Top Countries



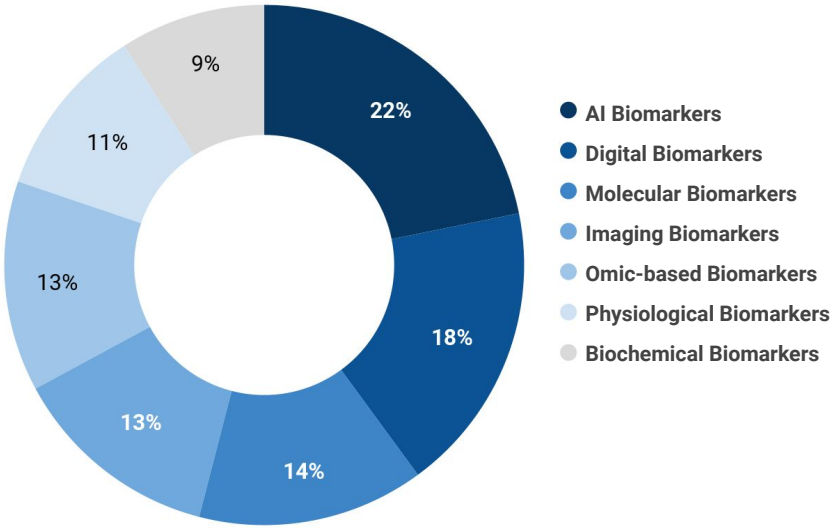
Source: Aging Analytics Agency analysis

Overall companies involved in the Biomarkers development are distributed among **more than 25 countries** of the world. Nevertheless, **top 7 countries concentrate more than 80%** of all companies. The left graph illustrates how companies are distributed among these countries.

The USA is clear leader of the industry by the number of companies - **59%** of companies are allocates there. With great gap follows European region. **Europe** hosts over **17%** of all companies. The top European countries by number of companies are the **UK (9%)**, **Switzerland (5%)**, **France (2%)** and **Germany (2%)**. Switzerland are presented Big Pharma companies (such as **Roche**) as well as biomarkers specialized companies (eg. **Scailyte, Centaura**).

Biomarkers Market at a Glance

Distribution of Companies by Sectors

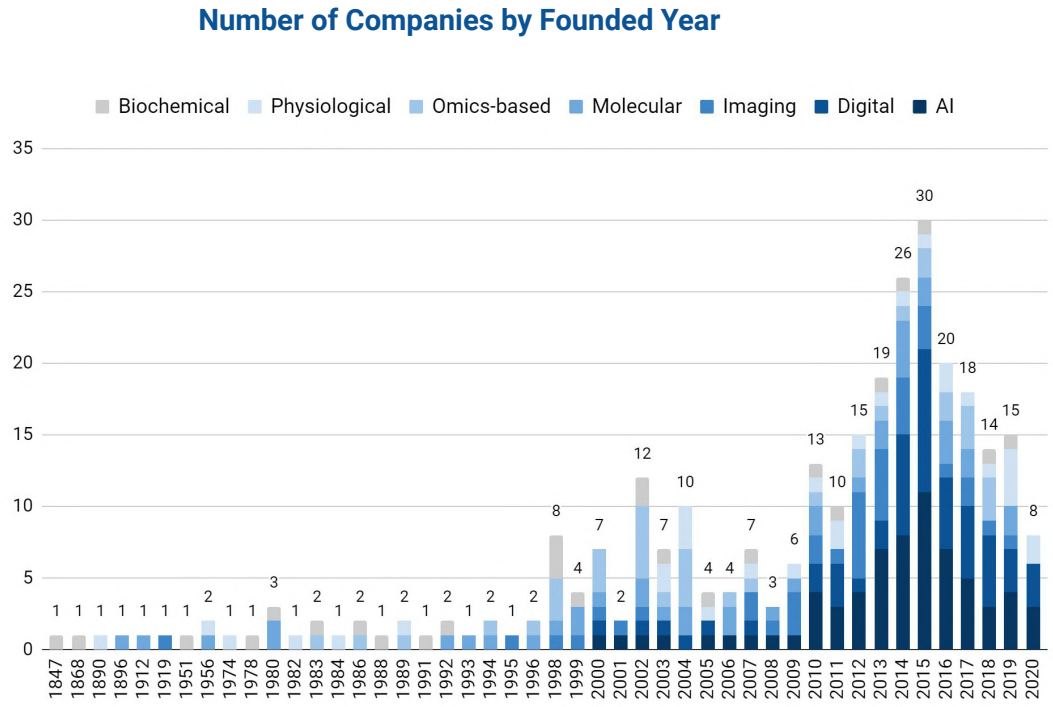


Source: Aging Analytics Agency analysis

The clear trend is towards edge intelligence to sense precisely and **analyze relevant biomarkers explicitly**. In the future, all these applications will rely on systems supported by AI and innovative algorithms. Thus, distribution by fields of studies is presented on the left graph.

Companies are distributed equally among the specific types of Biomarkers. **AI Biomarkers Companies** constitute **22%** of all companies, other **18% - Digital Biomarkers** companies. A little less companies are engaged in the **Molecular Biomarkers** developing - **14%. Imaging Biomarkers** companies and **Omics-based Biomarkers** companies constitute **by 13%** of total amount of companies each. Despite **Biochemical Biomarkers** (i.e. biomarkers of functioning of cellular pathways) offer a broad spectrum of diagnostic capabilities, in this field the least companies are engaged - only **13%** of total amount.

Biomarkers Market at a Glance

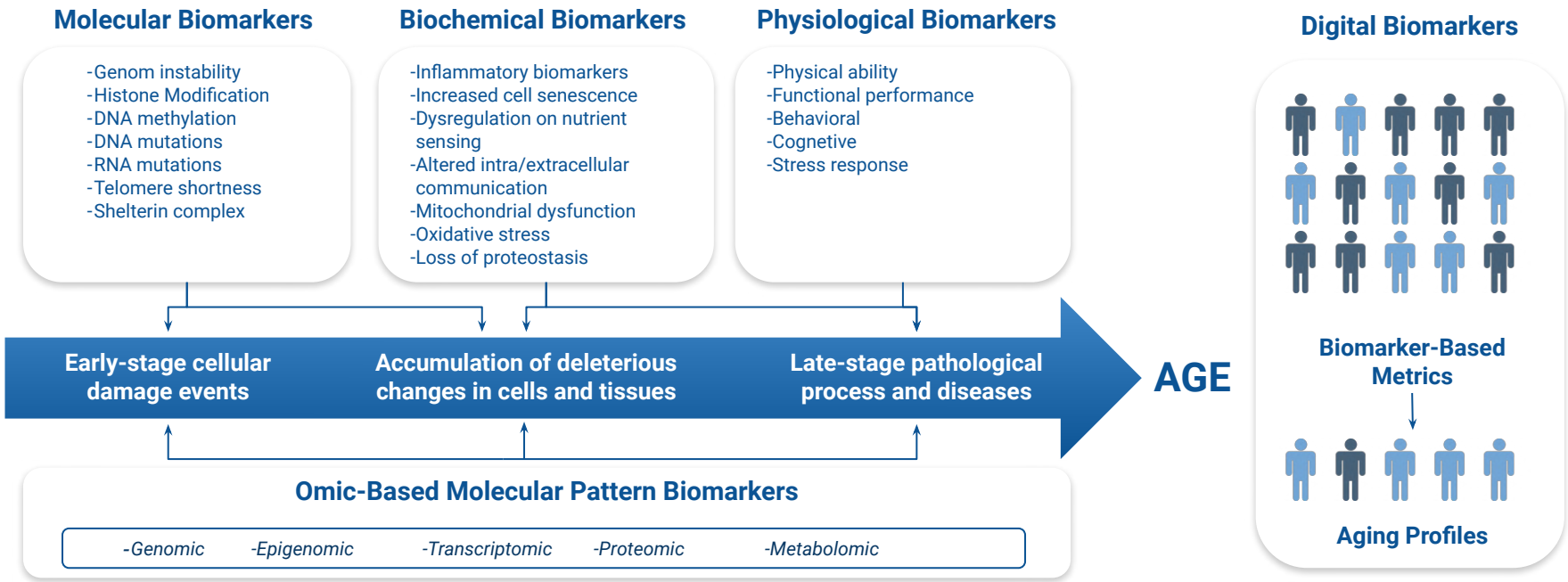


Companies that nowadays would be classified as **Biochemical, Physiological or Molecular** have began developing already **in the 19-20th century.** In contrast, **AI and Digital companies** have boosted since **the beginning of the 21st century** and pushed the growth of the whole Biomarker industry. The **development of innovative data analysis tools (ML, DL, Reinforcement learning (RL))** provides new opportunities for every innovative industry and Biomarkers are not an exception. Particularly, disruptive growth of **Digital-based Biomarkers companies** is observed **since 2013,** the publication of the first multitissue methylation aging clock by Steven Horvath. Despite the researcher using traditional ML approaches, the results suggest that gradual changes during aging can be tracked using various data types with reasonable accuracy. That trend of combining AI with biomedical research will keep progressing forward as it is believed to strongly increase efficiency. Biomarkers development show wave like pattern and present state indicates that a new market expansion is coming.

Source: Aging Analytics Agency analysis

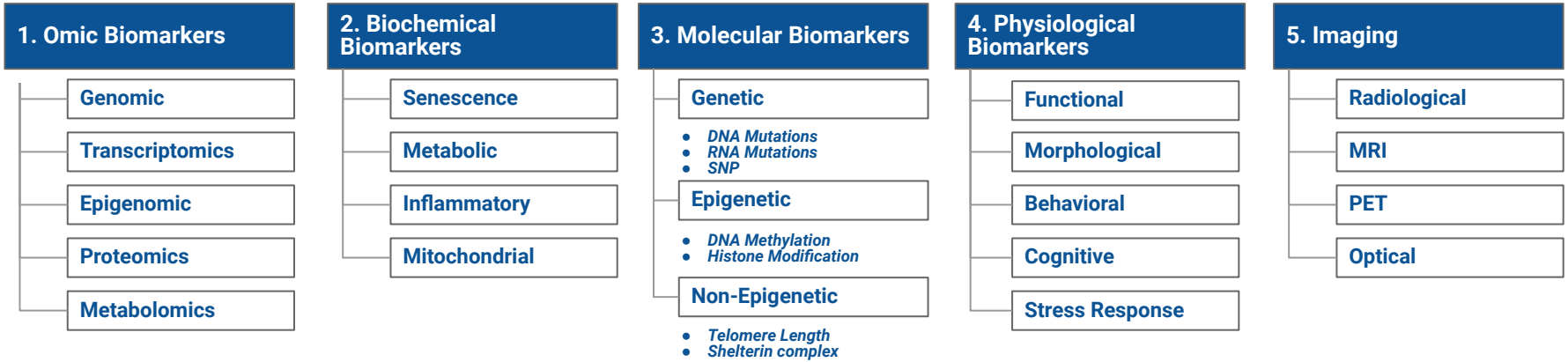
Longevity Biomarkers: General Overview

Category Characterization



The rapidly decreasing costs of high-throughput sequencing and other massively parallel technologies, such as mass spectrometry, are enabling their use in clinical research and clinical practice. Exome and genome sequencing are already being used to aid diagnosis, particularly of rare diseases, to inform cancer treatment and progression and, in early efforts, to create predictive models of disease in healthy individuals. Now this methods are widely applied for aging evaluation and prediction of age-related disease.

Biomarkers of Aging Summary



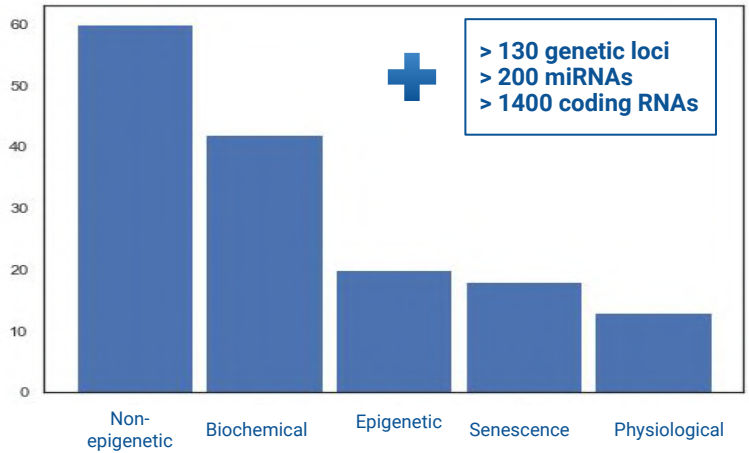
Aging affects physiological functions and can be defined as the accumulation of damage in molecules, cells and tissues over a lifetime. This process often **decreases an organism's capacity to maintain homeostasis** in stress conditions, and entails a greater **risk for many diseases** (cancer, cardiovascular and neurodegenerative disorders) and **premature mortality**. Identification of factors that regulate aging is limited by the complexity of the process and by the considerable heterogeneity among individuals and even among tissues within a body. **At the cellular level**, the most prominent event in an aging tissue is cell senescence, a consequence of exposure to intrinsic and extrinsic aging factors:

- accumulation of DNA damage
- epigenetic changes in DNA structure
- wrong gene expression
- altered cell metabolism and functionality

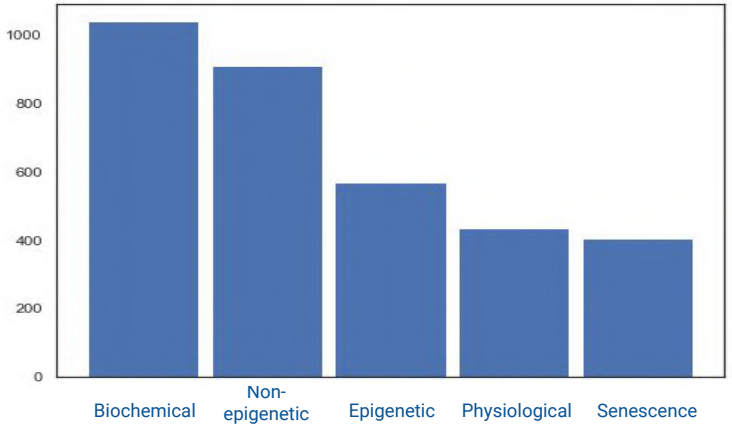
In this report we review the **best known biomarkers** for diagnosis of aging and make **analysis of global market** and companies that work in this area.

Biomarkers of Aging Summary

The Total Number of Biomarkers in Each Category



Total Mentions of Each Biomarker Category in Reviews

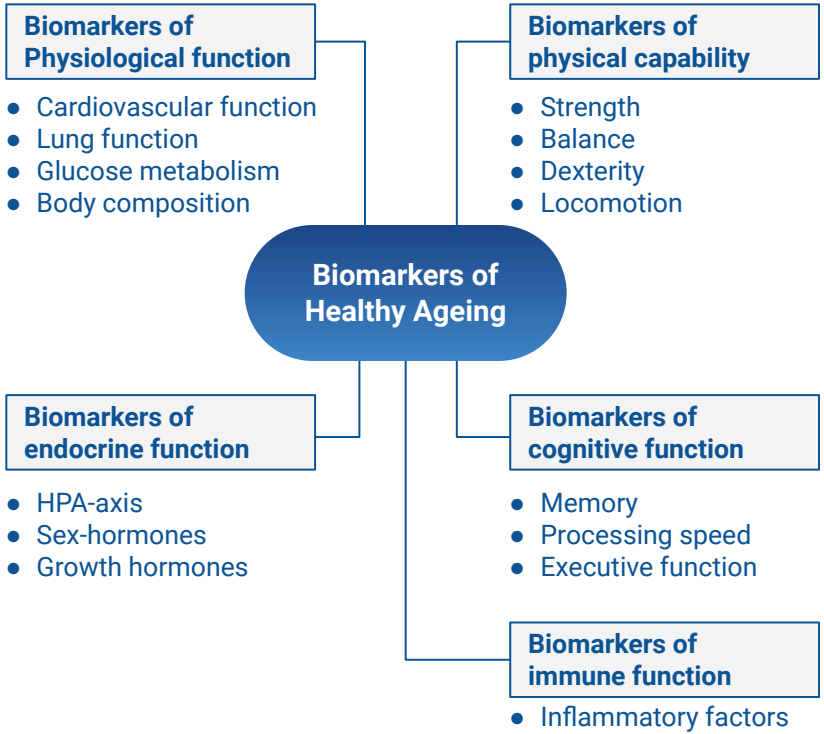


To date, the publications provide data on **more than 150 potential biomarkers of aging**. Biomarkers can be classified in a variety of ways based on their function, cell location, detection method, and other factors. Based on the availability of marker identification as well as their cellular and molecular roles, we have presented a mixed classification. According to the number of biomarkers and their citations, the main groups ofBiomarkers of Aging are **routine laboratory** (e.g. insulin, IL6, hsCRP, NT-proBNP), **non-epigenetic** (e.g. Telomere length, Shelterin complex, glycans) and **epigenetic** (e.g. DNA methylation, histone modifications).

In addition, more than **130 genetic loci** as well as over **1500 coding and non-coding RNAs** with a strong link with chronological age and the aging process have already been identified.

Biomarker Panels: Several are Better than One

Proposed Panel of Biomarkers of Aging



Given the heterogeneity and variability in any disease, a single biomarker may not be able to sufficiently reflect the pathological phenomenon itself or its underlying complexity. **Almost all single biomarkers have considerable fallibility.** This reason, coupled with the disruptive burst of biotechnology, the massive capture and aggregation of data and deep biomedical knowledge facilitated by frontier tech in the field of research and development, has kindled interest in and accelerate progress toward **Biomarker Panels** design.

A **Biomarker Panel is a group of biomarkers that reflect different interconnected processes or parameters** of a disease or health status, creating complex networks of biomedical outputs. In the particular context ofBiomarkers of Aging, a biomarker panel is some integrated composition of those biological indicators predicting functional capacity at a certain time in the future in more optimal ways than single biomarkers and chronological age itself.

Source: A proposed panel of biomarkers of healthy aging

Molecular Biomarkers

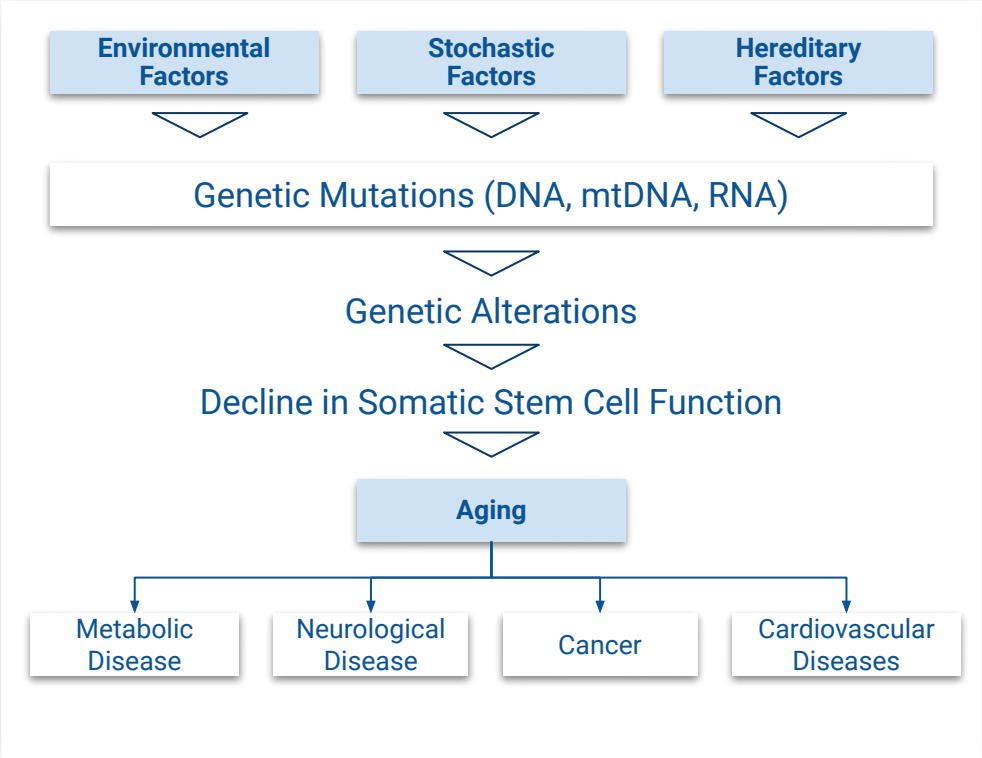
Category Characterization

The **environmental conditions** (stress, pesticides), **individual genotype** (genomic and mitochondrial DNA) and **stochastic factors** can induce **genetic and epigenetic alterations** that cause a decline in somatic stem cell function that can be the origin of metabolic, degenerative diseases, cancer and aging in the individuals.

In our report we have **analysed companies** which **offer Molecular Biomarkers for aging and age-related disease** that are clinically approved and have significant scientific evidence.

We include in our analysis **genes associated with age-related disease** as Endocrine disorders (Diabetes, hypothyroidism), Cardiovascular disorders (stroke, heart failure etc),Vision disorders (glaucoma, cataract), neurodegenerative (Alzheimer's, Parkinson, Sclerosis) etc. as well as **genes and mutations responsible for progeroid syndromes** (age-related monogenic hereditary disorders) and **populations of centenarians** whose lifespan is approximately twice the mean predicted for the population at the time of their birth will help to establish the function of a specific genotype in an individual's lifespan.

Genetic Factors' Influence in Aging and Lifespan



Molecular Biomarkers Framework

By Research Field

Genetic

- Genetic Mutations (DNA, mtDNA, RNA)
- SNP Genotyping

Epigenetic

- DNA Methylation
- Telomere Length

Non-Epigenetic

- Shelterin Complex
- Telomere Length

Molecular Biomarker market has been segmented by the approach in Genetic and Epigenetic diagnostic of **aging and age-related disease**. Also this market has been segmented by their **end-user of product**:

- accredited clinical laboratories,
- at-home tests,
- biotech companies (developing new biomarkers),
- service.

The growth amongst these segments will help you analyse meagre growth segments in the industries, and provide the users with **valuable market overview** and **market insights** to help them in **making strategic decisions** for identification of core market applications.
The most informative and **reliable genes** and their **mutations** associated with Aging has been proposed.

Key Companies: Molecular Biomarkers

Genetic

Genetic Mutations

DNA

ALMAC, GRAIL, RGCC, MAYO CLINIC LABORATORIES, Blueprint Genetics, Radboudumc, CHU de Poitiers Télémédecine, CBI Toulouse Centre de Biologie Intégrative, Assistance Publique Hôpitaux de Paris, HUG Hôpitaux Universitaires Genève, IMOMA, CHUV, St.Mary's, Universität Zürich

mtDNA

BAYLOR GENETICS, Ambry Genetics A Konica Minolta Company, athena diagnostics, MDNA Life Sciences, NHS East London NHS Foundation Trust, VCGS Leaders in Genetic Health, CENTOGENE THE RARE DISEASE COMPANY

RNA

ALMAC, TAmiRNA stability for life., HUG Hôpitaux Universitaires Genève, MAYO CLINIC LABORATORIES

SNP Genotyping

CD Genomics The Genomics Services Company, Assistance Publique Hôpitaux de Paris, CHUV, CBI Toulouse Centre de Biologie Intégrative, Radboudumc, MAYO CLINIC LABORATORIES, XVIVO BIOSCIENCES, RGCC, SALIMETRICS

Epigenetic

DNA Methylation

genknowme Personalized prevention solutions, MUHDO YOUR HEALTH MATTERS, St.Mary's General Hospital, ACTIVE MOTIF, adela, MDxHealth, RGCC, VitaLife MD Add Vitality to Your Life, Inherent Biosciences, AGELESSLX, TECAN, BioViva, TWIST BIOSCIENCE, ELYSIUM, LIFE EXTENSION, GRAIL, ZYMO RESEARCH, Capsulomics, Chronomics, NUCLEIX, MODERN WELLNESS DIAGNOSTIC SERVICES, CC DIAGNOSTICS, EarlyDx, MAYO CLINIC LABORATORIES, EPIGENDX, myDNAge, FOXO, Extended Longevity, US EPI, EPIFY, FMI Friedrich Miescher Institute for Biomedical Research

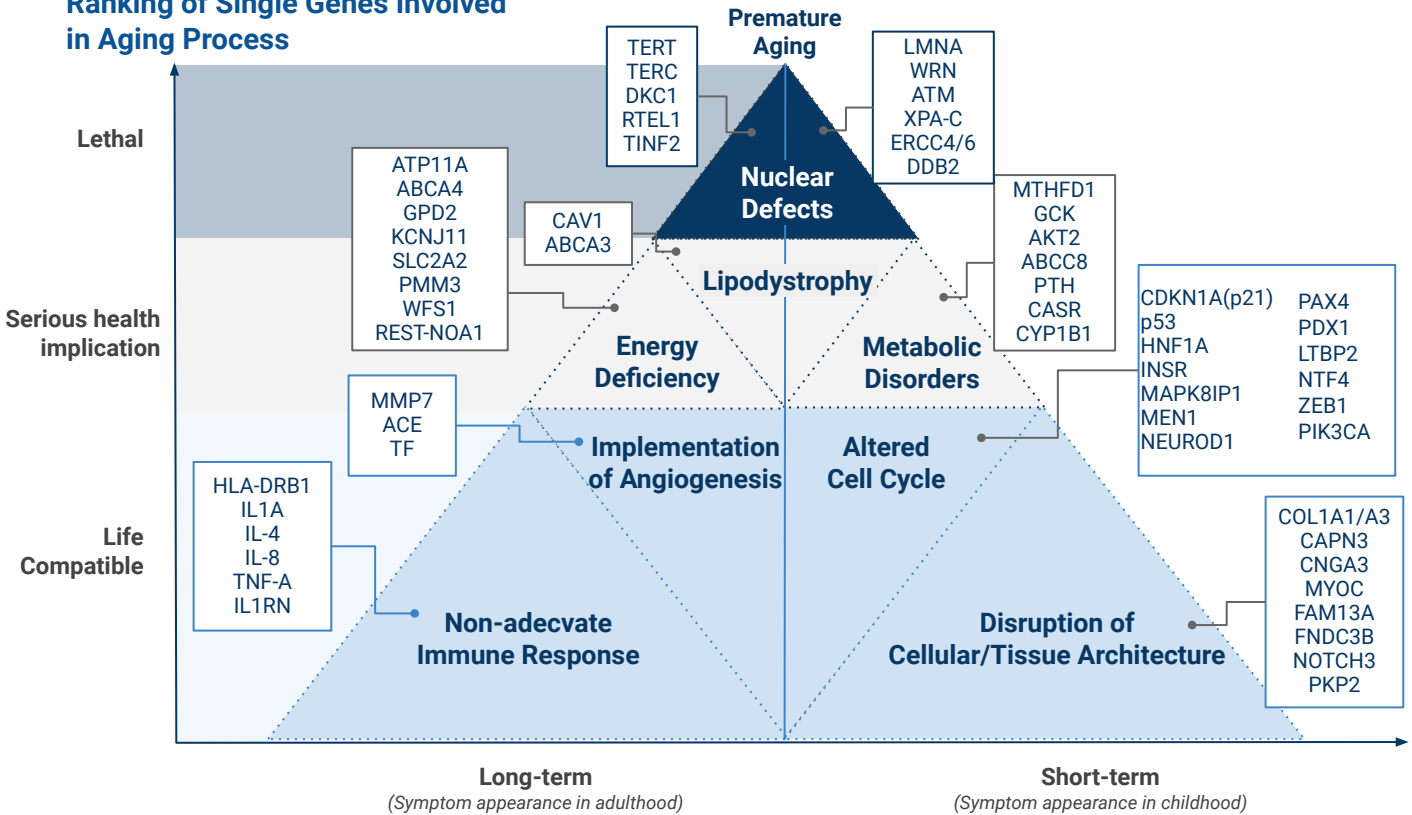
Non-Epigenetic

Telomere Length

BioTools, Cell Science Systems, TELOYEARS Know how well you're aging., ThermoFisher SCIENTIFIC, Dako, ScienCell Research Laboratories, Roche, TELOMERE DIAGNOSTICS, Extended Longevity, kpbs, LIFE LENGTH, SpectraCell Laboratories Science + Health + Solutions, SelfDecode, Istituto Giannina Gaslini

Aging Genetics and Aging

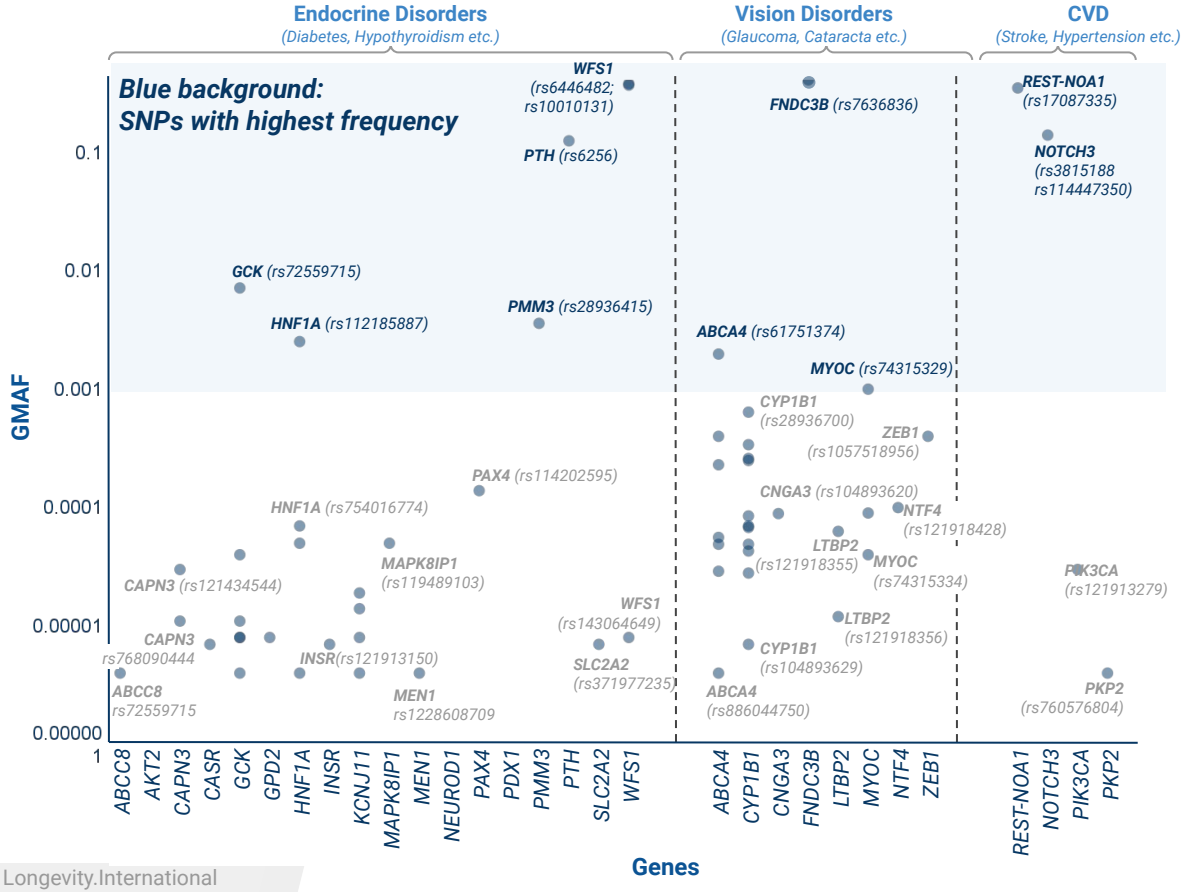
Ranking of Single Genes Involved in Aging Process



We have **analysed the published genetic studies** for two different populations: **1. centenarians** whose lifespan is approximately twice the mean predicted for the population at the time of their birth; **2. patients with extremely accelerated aging** as progeria, Werner syndrome etc. These data has helped us to **select the certain genetic factors** which act as modulators of the aging process. Presented **genes are associated with lifespan, resistance to diseases** that lead to early death.

In families whose members show **exceptional longevity,** in addition to other **environmental factors**, **family habits** (lifestyle, nutrition) are thought to influence survival, although data are limited on the contribution of these factors to greater resistance to disease.

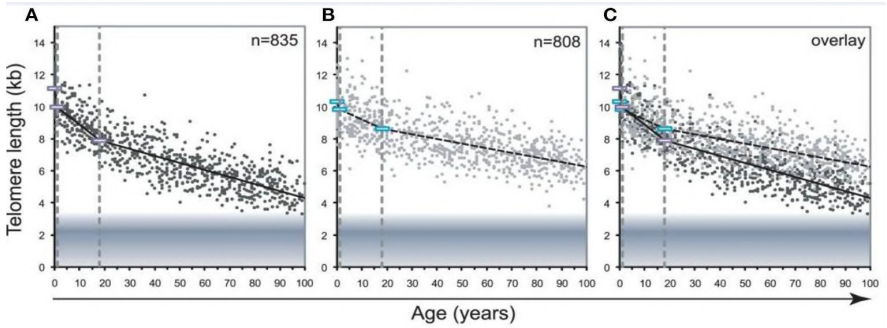
Frequency for Clinical Approved SNPs Associated with Age-Related Diseases



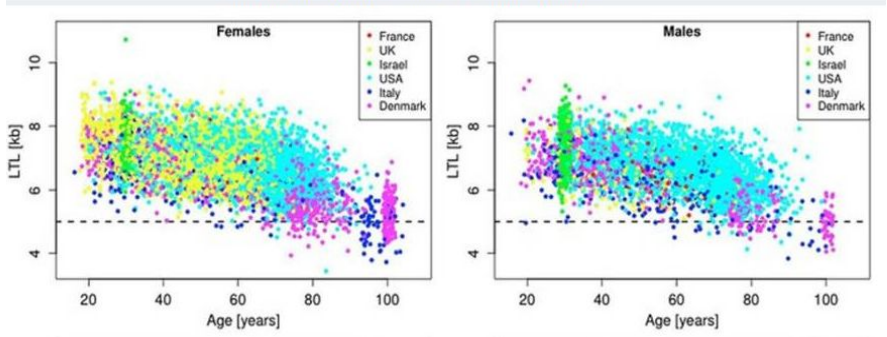
The **single gene mutation** are used for diagnostic the risk of age-related disease such as **Diabetes, Glaucoma, Stroke** etc. Most of disease associated genes are rare with **GMAF** (Global Minor Alele Frequency) less than 0.001. Another polymorphisms are more popular and make **significant impact** in disease development in elder patients (>60 years). Analysis of **ClinVar Database** and literature lets us select more **important genes** which can **implicate health in young people** and **accelerate their aging**: **GCK** (glucokinase), **HNF1A** (hepatocyte nuclear factor-1 alpha; HNF-1α), **PMM3** (phosphohexomutase), **PTH** (parathyroid hormone), **ABCA4** (ATP-binding cassette), **FNDC3B** (fibronectin type III domain containing 3B), **MYOC** (myocilin), **REST-NOA1** (nitric oxide-associated protein 1), and **NOTCH3** (notch receptor 3). This is only a sample of genes selected for the most frequent disorder in old people.

Telomere Length as a Marker of Biological Age: Issues and Limitations

Decline in TL with Age Differs Between Lymphocytes and Granulocytes



Decline in TL with Age Differs Between Countries



Telomere Length can only provide a rough estimate of aging rate, according to studies, and is scarcely a clinically meaningful marker for aging and longevity.

Several unresolved issues are currently impeding the adoption of telomeres as a routine marker in clinical practice. The significant **inter-individual variability of telomeres** is a critical issue. Also, telomeres might **differ between various tissue types**. Moreover, depending on the sampling site, telomeres can **vary even within the same organ**.

It's also unclear whether results from circulating leukocytes can be extrapolated to other tissues. In addition, the rate of age-related telomere attrition **differs significantly between different types of leukocytes**.

However, **telomeres could be a very informative biomarker when used along with other markers**. For example, in a combined cohort study, telomeres and DNAm clock explained 2.8 and 28.5% of the variance in age, respectively, and 29.5% when they were combined.

Source: Telomere Length as a Marker of Biological Age: State-of-the-Art, Open Issues, and Future Perspectives

Clinical Trials And R&D Notable Cases

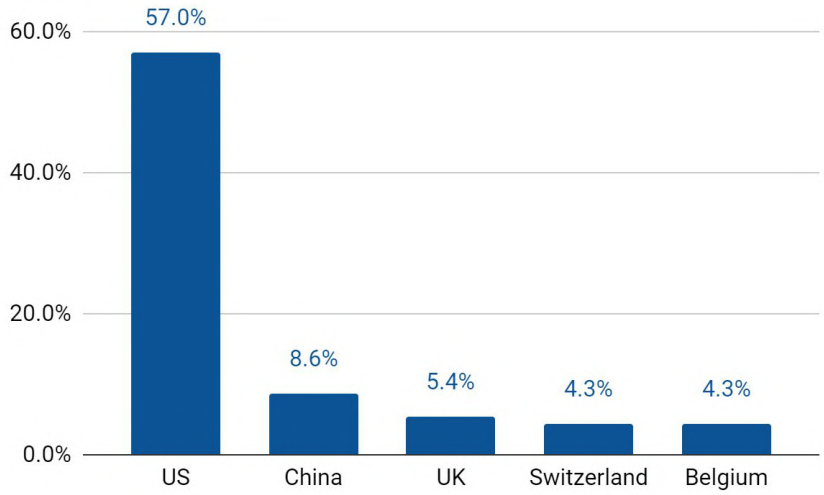
XVIVOS is focused on developing novel algorithms and user-friendly interfaces for analyzing in vitro (or ex vivo) Big Data from high-throughput assays which are applicable to personalized medicine. In the process of achieving this, XVIVOS works with researchers and pharmaceutical companies to improve the analysis platform. The goal of XVIVOS is to integrate these data with pharmacogenomics, in order to discover the best drug for each patient. Further, XVIVOS also facilitates relationships between patients and researchers to assist with novel drug discovery when no current therapies exist.

Salimetrics' assay kits and CLIA-certified testing services are used to measure salivary analytes related to stress, behavior and development, inflammation, sleep, reproduction, health and immune function. Salimetrics continues to be a key partner in bringing best-in-class solutions to salivary bioscience research. By using Salimetrics, researchers can find and implement solutions where the full potential of salivary measures have yet to be realized.

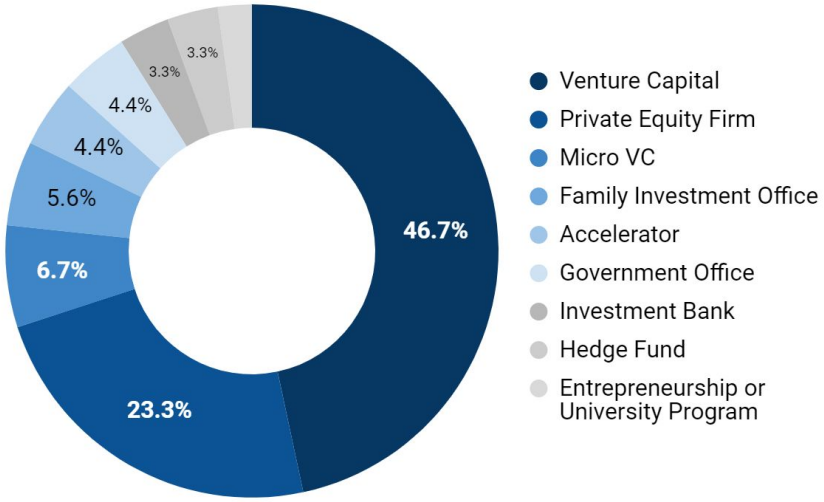
Swiss DNAlysis offers genetic tests developed by our experts in various fields. Laboratory analysis and storage exclusively performed in Switzerland accredited by Swiss Federal Office of Public Health following Swiss patient data protection rules, eligible for coverage by health insurance. Next-generation sequencing technology, confirmation of positive tests with Sanger sequencing, double-checking of negative results with MLPA, evaluation of mutation significance with several databases.

Market Overview: Global Market and Investors

Countries with the Largest Number of Investors, %



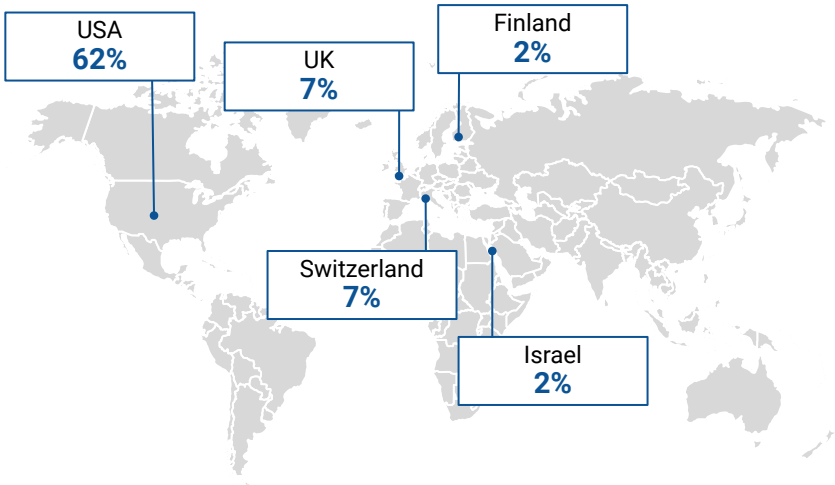
Main Type of the Investors, %



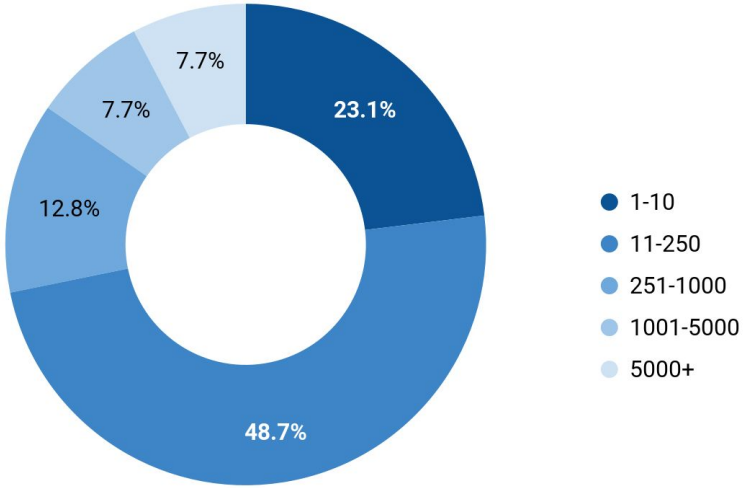
The main part of the investors in Molecular Biomarkers are from the **United States** and accounts for **57%** of the total investors. Investors from **China constitute close to 9% o**f total number of investors. The rest of countries from top 5 by number of investors are European countries: **the UK (5.4%), Switzerland, and Belgium (by 4.3% each)**.
Venture Capital and Micro VC constitute more than a half of all investors **(53.4%)**. **Private Equity Firms** are around **23.3%** of all.

Market Overview: Geography of Companies

Distribution of Companies by Country, %



Distribution of Companies by Number of Employees, %



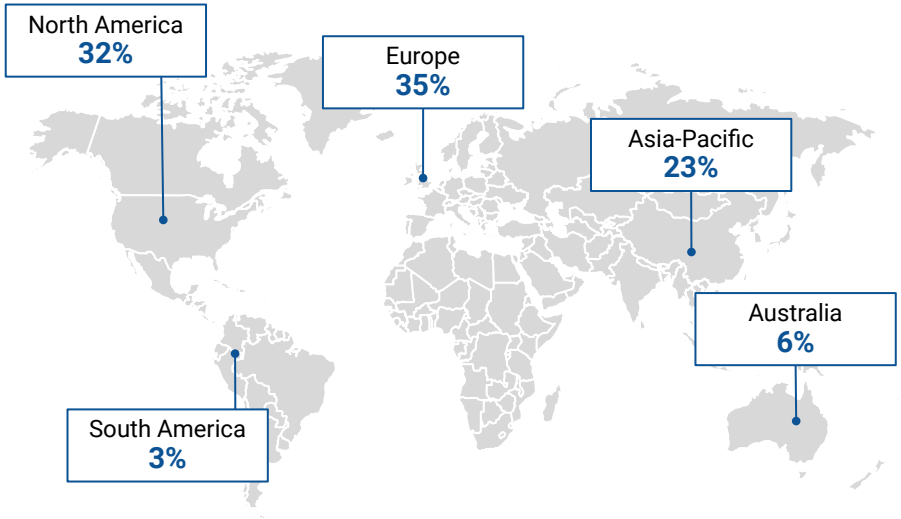
There is thigh geographic concentration of companies involved in the Molecular Biomarkers area - **90% of companies are allocated in the top 5 countries. Close to 62% of all companies** that conduct activities are **from the USA**. **Other 26%** are from **Europe**: in particular by 7% is in the UK and Switzerland each and 2% is in Finland.

Around a quarter of all firms (23%) are **micro-sized** with 1-10 employees, the other **49%** of companies have **no more than 250 employees**. However, there is **close to 8%** of large companies with **more than 5000 employees.**

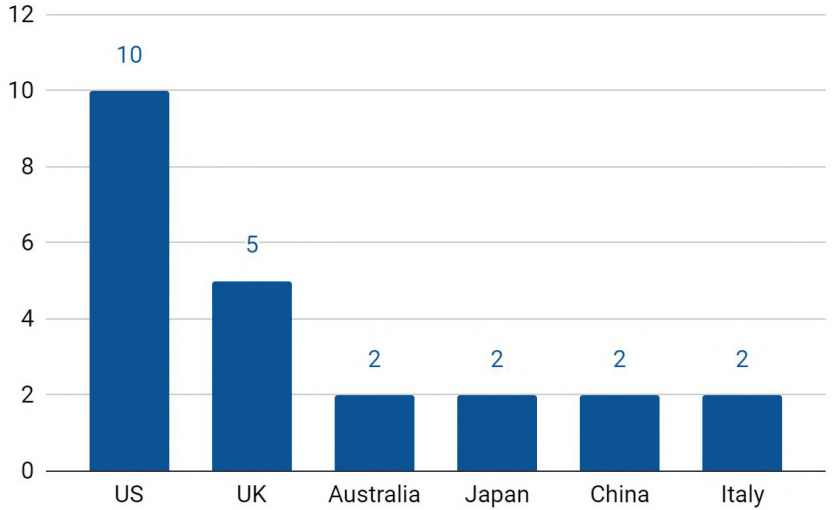
Source: Aging Analytics Agency analysis

Market Overview: R&D Centres

Distribution of R&D Centres by Region, %



Top Countries by Number of R&D Centres

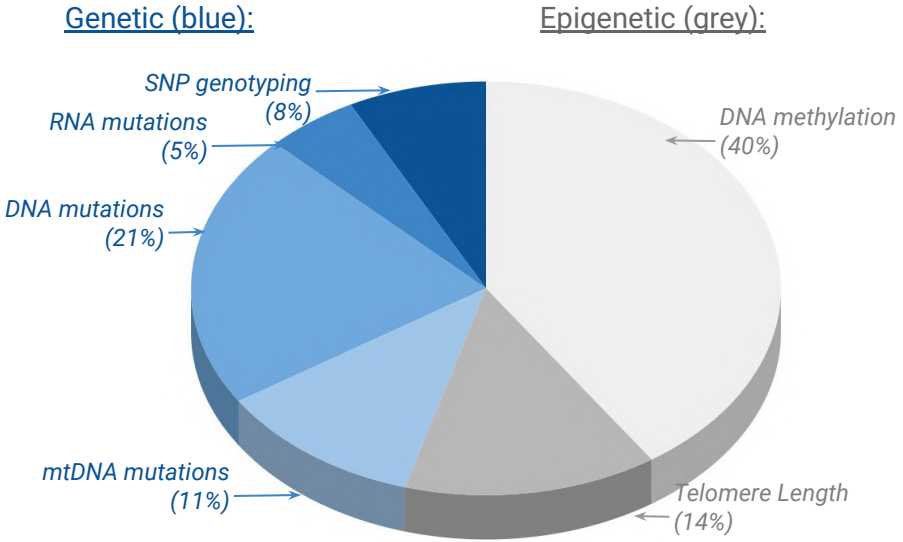


R&D Centres that conduct research on Molecular Biomarkers are distributed all over the world. However, two-thirds are concentrated in North America and Europe, with the other **23% in Asia-Pacific**. **Around 6%** of R&D Centres are **in Australia**, **while 3% (2)** are in **South America.** There are 10 R&D centres in the US and half as much in the UK, which makes these countries centres of R&D activities in the Molecular Biomarkers area.

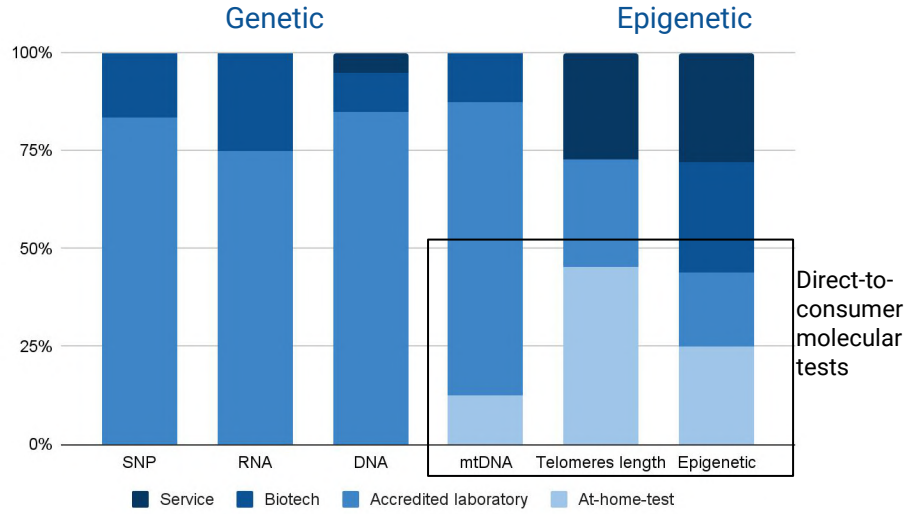
Source: Aging Analytics Agency analysis

Market Overview: Distribution of Companies by Approach

Distribution of Companies by Molecular Testing Approach



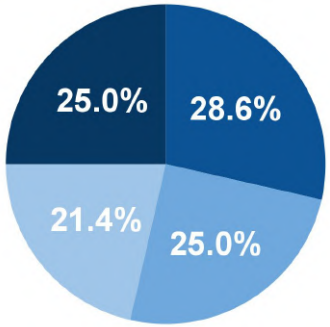
Approach vs Type of Company



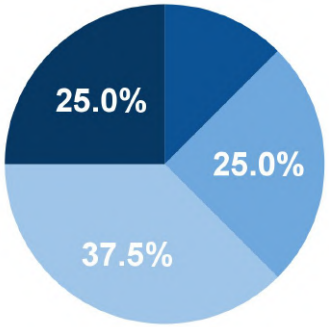
Growing trends of **healthy lifestyle** and rising **health care awareness programs** have created the **demand for predictive and wellness molecular testing**. Genetic testing helps to predict future risk of disease and offers information and data about the genetic makeup of a child. In the market more than **50% share Epigenetic tests** for prediction **biological age** via measuring level of **methylated DNA** and **Telomere Length**. The **Direct To Consumer segment** is expected to **hold largest market share** over the forecast period due to growing awareness related to at-home genetic tests.

Market Overview: Distribution of Approaches in the Top Countries

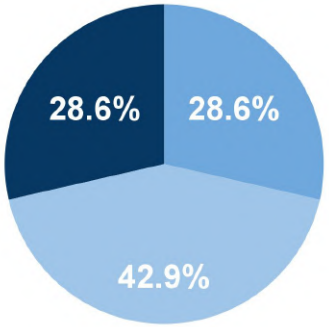
- Clinical test
- At-home test
- Biotech
- Service



North America



Switzerland



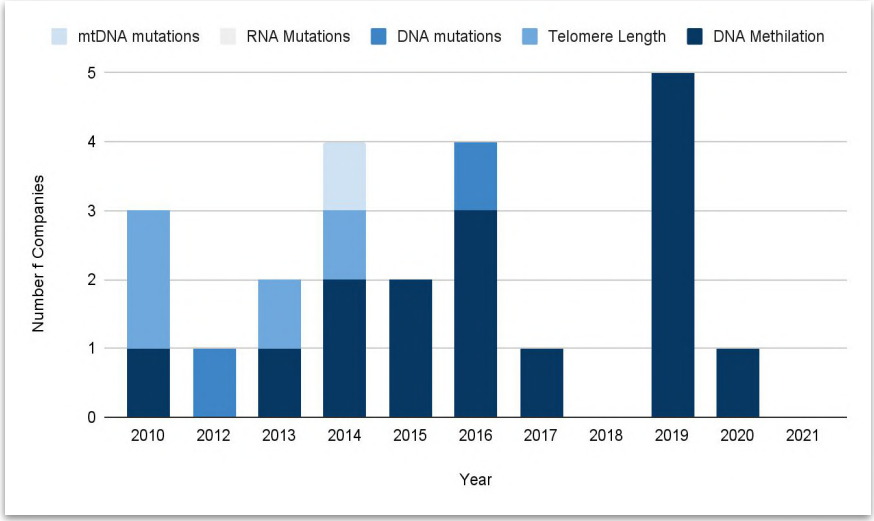
Europe (!)

Note: (!) In EU, the execution of health-related genetic at-home-tests, especially for predictive or diagnostic purposes, is restricted.

The global Aging Genetic Diagnostic market size is approximately **$ 2.0 billion**. It is expected to expand at a **CAGR of 10.00%** from this period. The COVID-19 pandemic slowed up growth for this industry. The most companies (>65%) are located in **USA**, ~17% in Europe and 7% in Switzerland. This region characterized **rise in commercial interest** and **government support** for genomics and sequencing technologies, **high demand for personalized medicine**, and the presence of a substantial number of translational and academic research organizations. The increasing focus by governments of various countries, to regulate and create awareness regarding genetic tests, has successfully resulted in the faster adoption of these tests across the world. The increasing R&D funding, along with the strong market presence by major players in the market, has created a strong entry barrier for new entrants.

Market Trends of Molecular Biomarker for Aging Diagnostics

New Companies: Molecular Biomarkers

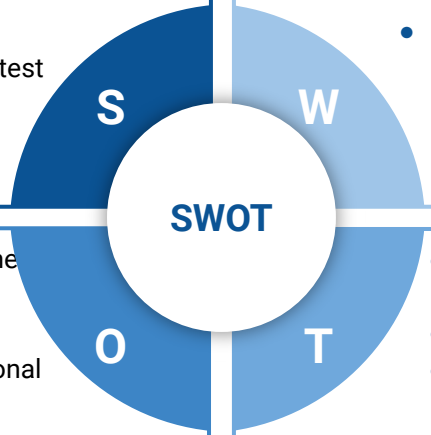


Key Market Trends

- Development new biomarkers
- Growth the number Epigenetic testing
- Early diagnostics of age-related disorders
- Growth of direct-to-customer market
- Digitalization

How it is shown on graph for the last decade all new companies produce **Epigenetic tests**. This type of tests replaced other genetic tests even at-home-tests of Telomere Length which are saled directly to the customers. More than **50%** analyzed companies don't present detailed information about their founds, localization of head quarter and year of foundation. These companies often **don't have own product/test kit** and **do analysis in outsourcing laboratories**. High cost on genomic research equipment and complexity in predictive genetic testing are major factors that may restrain the market to a certain extent going ahead. Moreover, lack of trained professionals and inadequate funding are expected to create further challenges for market growth.

Molecular Biomarkers: SWOT Analysis



- Hereditary predisposition to disease can be diagnosed before manifestation of the disease.
- Molecular testing helps to predict future risk of disease and offers information and data about the genetic makeup of a child.
- Non-invasive technology for sample collection.
- Growth of number of companies that offer at-home test for self-diagnostic.

- High cost of testing for customers.
- High cost on genomic research equipment and complexity in predictive genetic testing are major factors that may restrain the market to a certain extent going ahead.
- Lack of trained professionals.

- The rise in commercial interest and governme support for genomics and sequencing technologies
- The high demand for personalized medicine
- The presence of a substantial number of translational and academic research organizations.

- The most companies offered not-reliable biomarkers confirmed on a small group of patients.
- Currently no FDA approved at-home Molecular Test.
- Some European countries restrict using and sail at-home genetic tests directly to customers.
- The increasing R&D funding, along with the strong market presence by major players in the market, has created a strong entry barrier for new entrants.

Key Takeaways: Molecular Biomarkers

Genetic testing helps to **predict future risk of disease** and offers information and data about the genetic makeup of a child. In the market more than **50% share Epigenetic tests** for prediction biological age via measuring level of **Methylated DNA** and **Telomere Length**.

The **Direct To Consumer segment** is expected to hold largest market share over the forecast period due to growing awareness related to at-home genetic tests. The most companies are located in **USA (>65%)** , **Europe (17%)** and **Switzerland (7%)**.

This **market develops slower** in comparison with other biomarker markets. The **increasing focus by governments** of various countries, to regulate and create awareness regarding genetic tests, has successfully resulted in the **faster adoption of these tests** across the world but presence major players in the market has created a **strong entry barrier for new entrants**.

Genetic and Epigenetic testing are in priority and many companies **offer at-home test** for **healthy living** and **wellness diagnostics**. Customer directed companies often **don't have own product/test kit** and do analysis in **outsourcing laboratories**.

High cost on genomic research equipment and **complexity** in predictive genetic testing are major factors that may **restrain the market** to a certain extent going ahead. Moreover, **lack of trained professionals** and **inadequate funding** are expected to create further **challenges for market growth**.

Many **diagnostic panels** include **clinically approved polymorphisms** as well as **investigational molecular biomarkers** without appropriate study on clinical populations. It makes a risk for customers to get **non-reliable information** with **incorrect interpretation** of diagnostic results.

Biochemical Biomarkers

Biochemical Biomarkers for Systemic Aging Evaluation

No Consensus Set of Biomarkers of Biological Aging

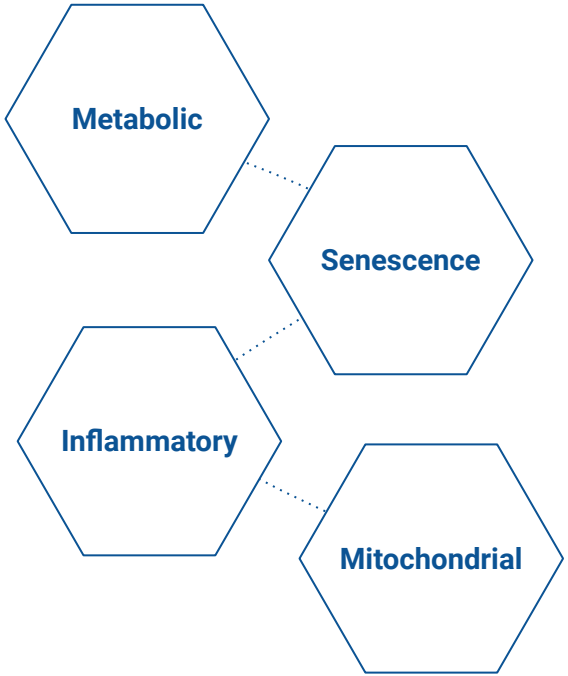
Biological Aging	Biomarkers
Genomic Instability	Plasma of DNA, SNP variations, mtDNA copy number, post-irradiation DNA damage/repair, g-H2AX, PARPII
Telomere Attrition	Blood leukocyte telomere length. Telomerse RNA
Epigenetic	Epigenetic clocks, DNA methylation patterns, Line - I DNA methylation, H4K I6 acetylation
Proteostasis	Proteostasis: Autography (p62, mRNA, LC3I +
Nutrient Sensing	Insulin-like GF1, insulin signaling, metabolomics
Mitochondrial	Mitochondrial Respiration, mitochondrion number, DNA copy number, protein level
Cellular Senescence	p16, SA-BettaGal, p53, p21, g-M2A, cytokines, chemokines, MMPs, TIMPs
Stem Cell Exhaustion	Clonal composition, lineage, self-renewal capacity, proliferative response level, senescence
Cell Communication & Inflammation	Circulating Factors e.g. IL-6, TNF, TGF, eotaxin, microglobulins, VEGF

Despite the growing interest to **Aging evaluation** there is still no gold standard of reliable biomarkers to predict and monitor aging rate. Aging is a time-dependent multisystemic functional decline, and it is evaluated at different levels: molecular, Biochemical, physiological.

Biochemical markers help to assess **the current state of the whole organism** via analysis of key parameters of cell and organ systems. Some Biochemical Markers (p16, SIRT, NAD level) correspond to the strict Criteria for **Biomarkers of Aging** proposed by AFAR. Some Biochemical Markers (glucose level, lipid panel, hormone panel etc) are routinely used for Diagnostic purposes and help to detect the **Age-related diseases** as consequences of Aging. Due to the fact that biological processes of Aging are the most important risk factors for chronic disorders and disabilities, only systemic analysis of both **Biomarkers of Aging** and **Biomarkers of Aging-related diseases** may help to get essential information of nutritional changes, lifestyle correction and possible necessary treatment to support **Long Healthy Life**.

Biochemical Biomarkers Framework

By Research Field

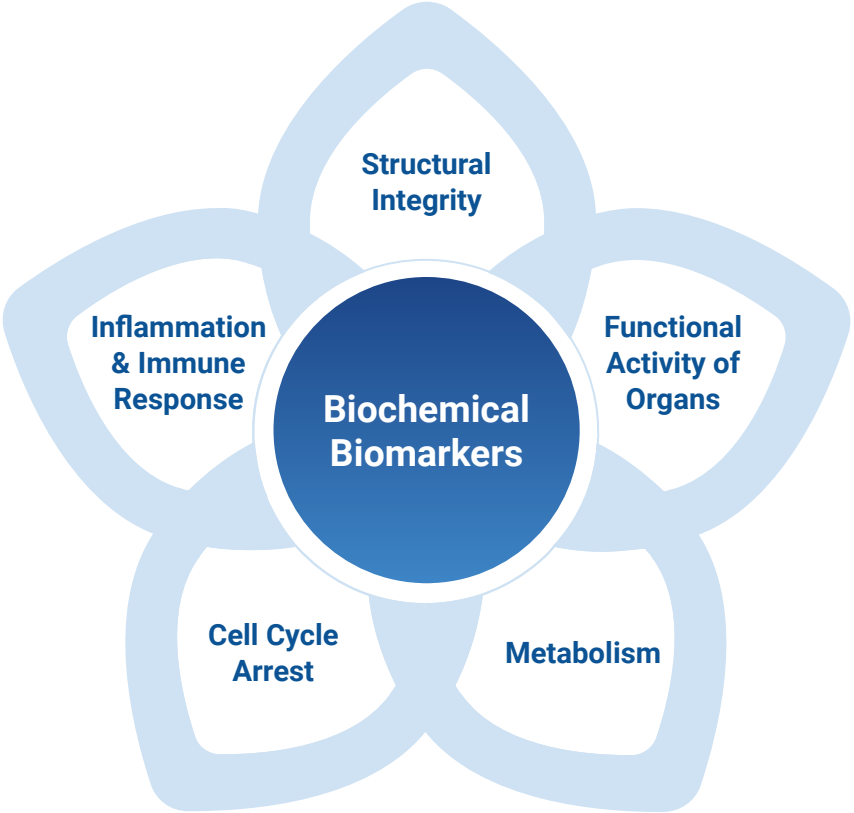


Selected companies offered **Biochemical Biomarkers** diagnostic has been splitted on four sub-categories by the **biological pathway** involved into **aging and age-related disease**. Also this market has been segmented by their **end-user of product**:

- accredited clinical laboratories,
- at-home tests,
- biotech companies (developing new biomarkers),
- service.

Also **invasivity of biomarker** as well as **sample types** (blood, urine, salvia etc.) are described as a main characteristics demanded for this category.
We have **evaluated companies** by the gradation of their clinical products **according to sensitivity of biomarkers to age-related disease** and **fold-change in older patients after 60 years**. The most reliable companies have been selected by this characteristics.
Besides, this analysis brings a **comprehensive view of the market structure** and **development.**

Biochemical Biomarkers Characterization



Biochemical Biomarkers are divided to subgroups in accordance with corresponding processes which may be evaluated.

The most abundant is a subgroup of **Metabolic** markers which help to assess both **structural integrity** and **functional activity of systems of organs**, and variety of **metabolic processes** in organism. Metabolic markers involve both well-known routine laboratory tests widely used for clinical diagnostics and innovative tests recently developed to provide possibility of early detection of Aging changes in organism, as well as evaluating risk of Age-related disorders.

Markers reflecting such crucial for Aging preventing processes as **Cell cycle**, **Basal systemic hormonal regulation** are of great interest in terms of Aging evaluation. Such markers form a subgroup of **Senescence** markers.

Human aging is characterized by a chronic, sterile, low-grade inflammation which is called **Inflammaging** and may be assessed by **Inflammation** markers. This subgroup involves both routine markers of **General Inflammaging** (C-reactive protein, proinflammatory interleukins) and markers of **Age associated Autoimmune Inflammaging** and **Leak Gut induced Inflammaging**.

Mitochondrial markers reflect **state of Mitochondria**, important organelles which serve as powerhouses of the cell and participate in central metabolic pathways. **Mitochondrial** markers are mainly used for **Diagnostics of Mitochondrial disorders** at present moment, but are also perspective for **Aging** evaluation. Some companies start to offer Mitochondrial marker tests to assess **aging rate**.

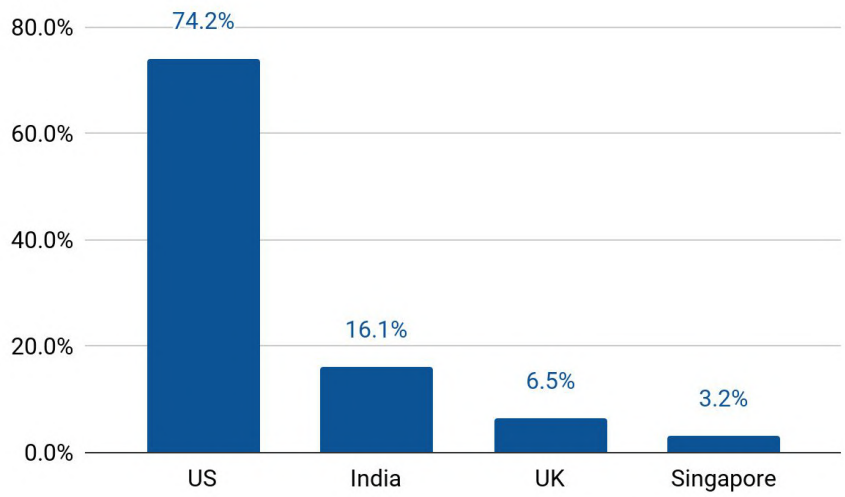
Scope of Companies with Biochemical Biomarkers Approaches

	Metabolic	Senescence	Inflammation	Mitochondrial
Aging	JINFINITI PRECISION MEDICINE, Walk-In-Lab, LIFE EXTENSION, FLUIDS iQ, BioViva	BioVision, ThermoFisher Scientific, JINFINITI, labcorp, MyBioSource.com, SALIMETRICS, ZRT Laboratory, Creative Biomart, Sapere Bio	JINFINITI, FLUIDS iQ, GlycanAge, veMico	JINFINITI, FLUIDS iQ
Age-Related Diseases	ADx, Bioarctic, Lilly, Nordic Bioscience, C2N, Portea, Aprinoia, Alcala Labs, myriad RBM, Grass Roots Labs, 122 Labs, Mayo Clinic Laboratories, US BioTek, SALIMETRICS, Washington University in St. Louis, Acro, Alpha Diagnostics, San Diego State University, LIFE EXTENSION, Roche, Millipore Sigma, medichecks, 10WA, Sigma-Aldrich, ZRT Laboratory, SpectraCell Laboratories, University of San Diego, cerascreen, sysmex, Prodrome	Prodrome, FLUIDS iQ, Sapere Bio, Quest Diagnostics, Diagnoptics	Prodrome, SALIMETRICS, Landmark Medical Centre, Walk-In-Lab, Roche, LIFE EXTENSION, US BioTek, Acro, San Diego State University	US BioTek, abcam, ARUP Laboratories, NHS, Religen, Cleveland Clinic Laboratories, Agilent, BioVision, Sigma-Aldrich, Children's Hospital of Philadelphia, Prodrome, San Diego State University, ThermoFisher Scientific

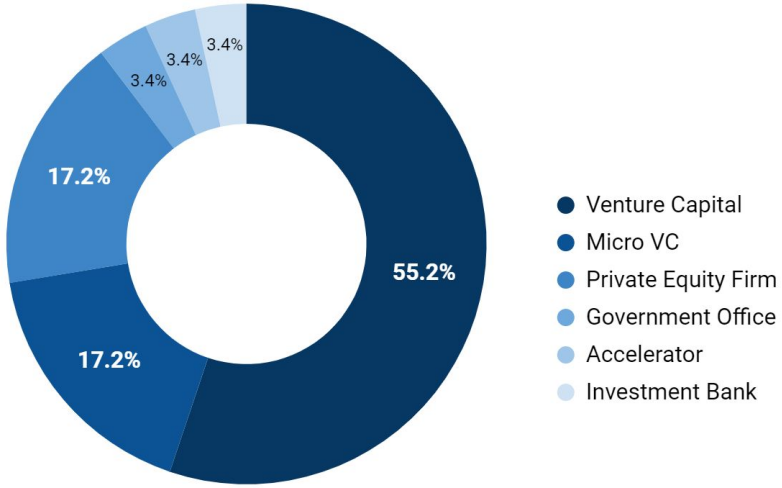
Biomarkers of **Metabolic state** are the most popular in the market as tool of assessment the **risks**, **detection** and **monitoring** of **Age-related diseases**. This fact may be explained by tests availability, low costs, reliability, good correlations between changes in organism state and biomarkers levels. Some companies provide **Senescence, Metabolic, Inflammation**, and **Mitochondrial** markers to evaluate **Aging**.

Market Overview: Global Market and Investors

Countries with the Largest Number of Investors, %



Main Type of the Investors, %

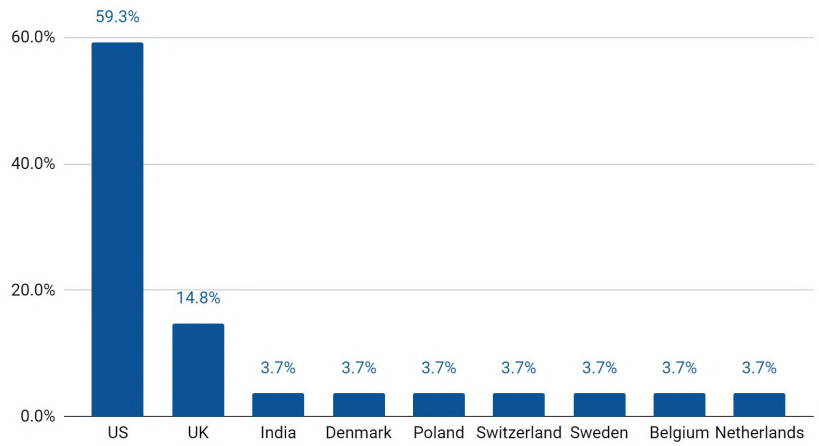


The main part of the investors in the Biochemical Biomarkers are from **the US (74%). Other 16% are form India.** Together countries host more than 90% of all investors.

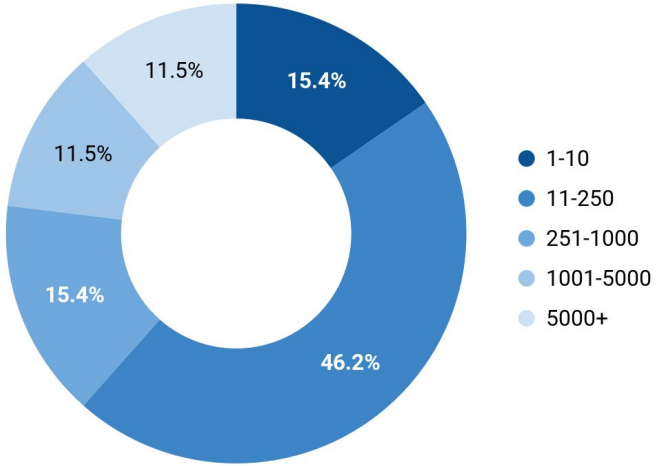
Venture capital and Micro VC constitute 72.4% of all investors. Other 17.2% are Private equity firms. Government Offices, Accelerators, and Investments Banks are by 3.4% each.

Market Overview: Geography of Companies

Distribution of Companies by Country, %



Distribution of Companies by Number of Employes, %



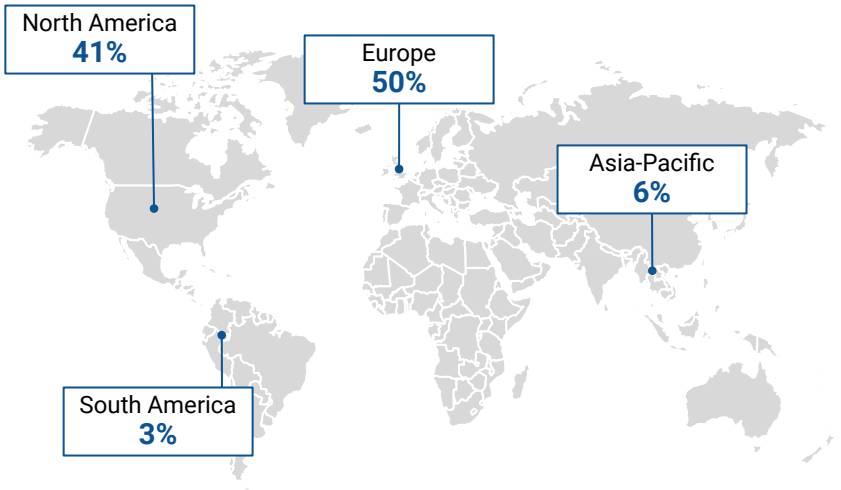
Biochemical Biomarkers Market business activity is mainly concentrated in the developed countries (with exception of India, which is a developing country). More than **59%** of companies developing Systemic Biomarkers are located **in the US**, other **37%** are **in Europe.** Around 15% of total companies are situated in the UK.

More than **60%** of companies are **either micro-companies or small** with employees up to 10 or up to 250. The rest of the companies are almost equally distributed among medium-sized (up to 1000), large-sized companies (up to 5000) and enterprises with more than 5000 employees.

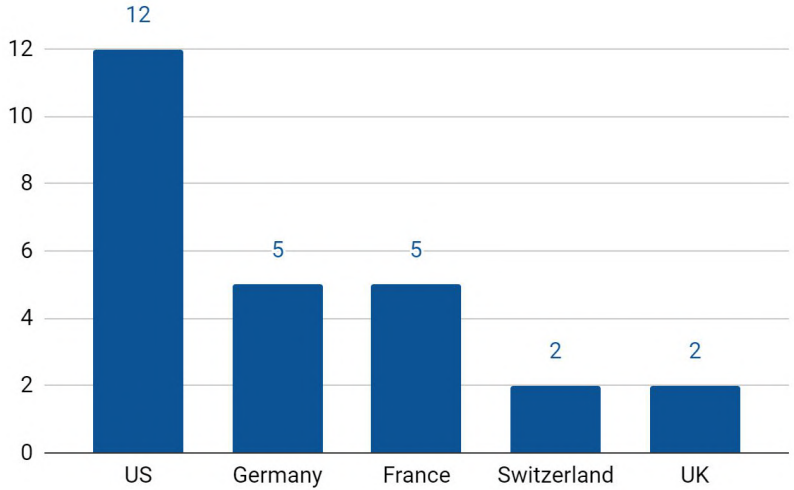
Source: Aging Analytics Agency analysis

Market Overview: Geography of R&D Centres

Distribution of R&D Centres by Regions, %



Top 5 Countries by Number of R&D Centres

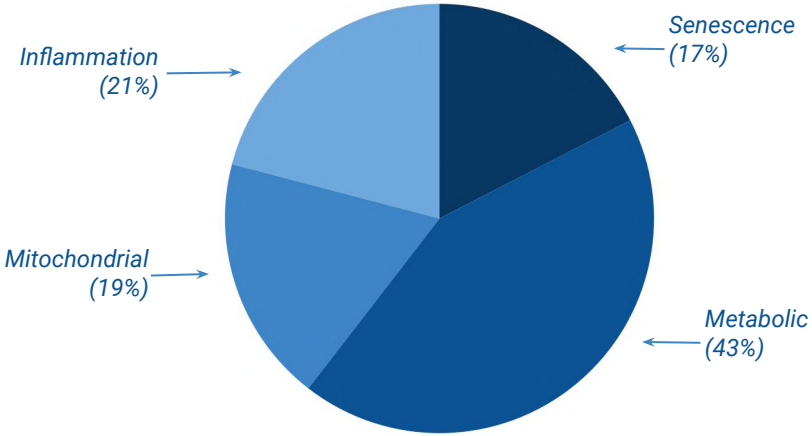


There are **half of the R&D centres** that conduct studies in Biochemical Biomarkers **situated in Europe**. **Germany and France** host **by 5** R&D centres, and **Switzerland with the UK other 4 centres.** The American R&D centres are around 41% of the total number and represent whole Northern American region. The rest of 9% of R&D centres are located in Asia-Pacific and South American regions.

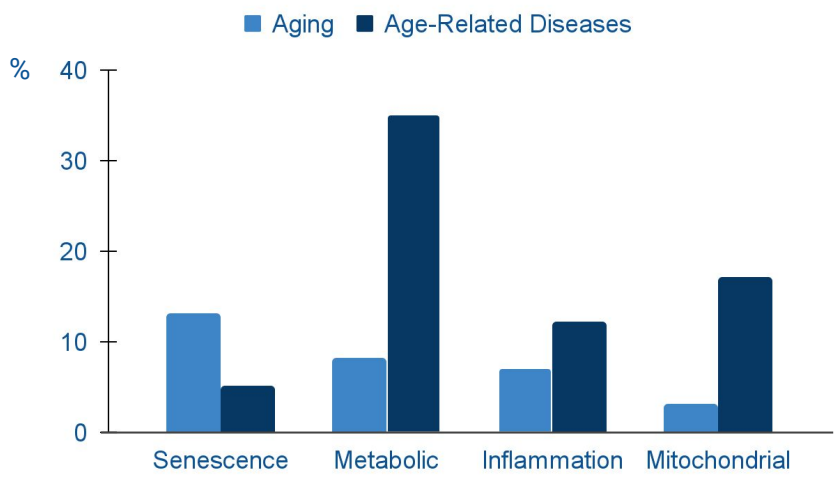
Source: Aging Analytics Agency analysis

Market Overview: Distribution of Companies by Approach

Distribution of Companies by Biomarker Type

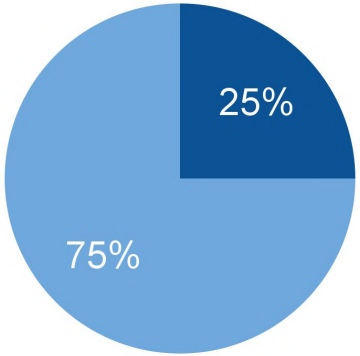


Distribution of Companies by Test Application

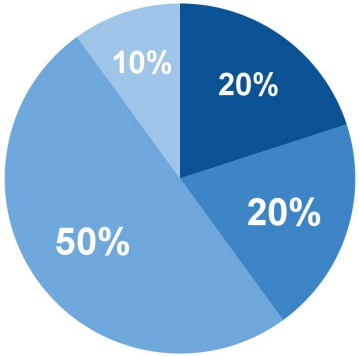


The most popular approach (**43%** of companies) for evaluation of **Age-related diseases** is **Metabolic** markers assessment. Such tests are routine and informative. Only several markers from this group are used for evaluation of **Aging**. **Inflammation** markers (**21%** of all companies) are used both for assessment of **General health state/Age-related disorders**, and for detection of **Inflammaging**. The **Senescence** markers testing is provided by **17%** of companies. **Mitochondrial** dysfunction markers (**19%** of companies) are used mainly as diagnostic tool to reveal **Age-related diseases**.

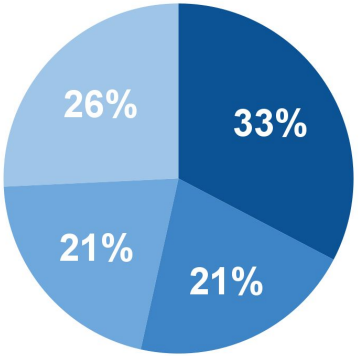
Market Overview: Distribution of Approaches in the Top Countries



Asia



Europe



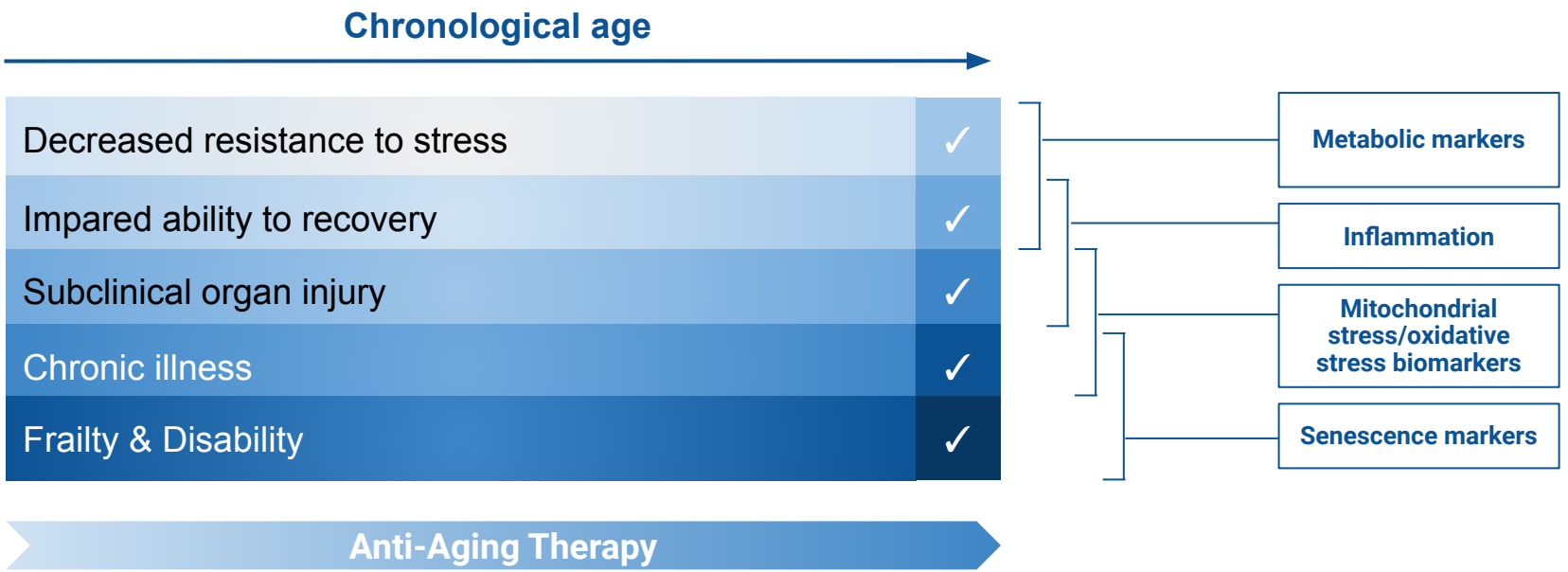
North America

Clinical test · At-home test · Biotech · Service

The **vast majority of Companies** that provide Systemic Biomarkers testing is located in the **United States** and accounts for **70%** of the whole range of analyzed companies. Accredited laboratories with **Clinical tests** prevail and account for **33%** of the amount of analyzed companies in the **United States.** The **European region** follows with **20%** of companies, and the majority of companies are located in **UK**. **Biotech companies** developing innovative tests for further clinical use prevail both in the **European region** and in the **Asian region**.

Source: Aging Analytics Agency analysis

Biochemical Biomarkers vs. Aging Stages



Different groups of **Biochemical biomarkers** allow monitoring of **Aging** at different stages, as well as assessing the risks of **Age-related diseases** developing, and suitable **therapies** selecting. The earliest are **metabolic markers**, followed by markers of **inflammation**, **mitochondrial dysfunction,** and, finally, **senescence**. This sequence corresponds to the **Aging stages** chronology.

Gradation of Companies by End-User & Biomarker Type

The most of analyzed companies provides Metabolic biomarkers testing in form of **Clinical test** (performed in laboratory under healthcare worker assignment), or **At-home test** (at-home sample collection with subsequent shipping to the laboratory for analysis). At-home tests are expected to be more and more popular in future due to such advantages: possibility to evaluate health state with accurate & reliable lab results, easy to order test, easy to collect sample for biomarker assessment, results are delivered fast, there is ever no need for leaving the home. **Biotech** companies are developing new biomarkers to improve current evaluation of **Aging** as well as **Age-related disorders**, especially **Neurological diseases** and **Dementia**.

Sample Type Categorization

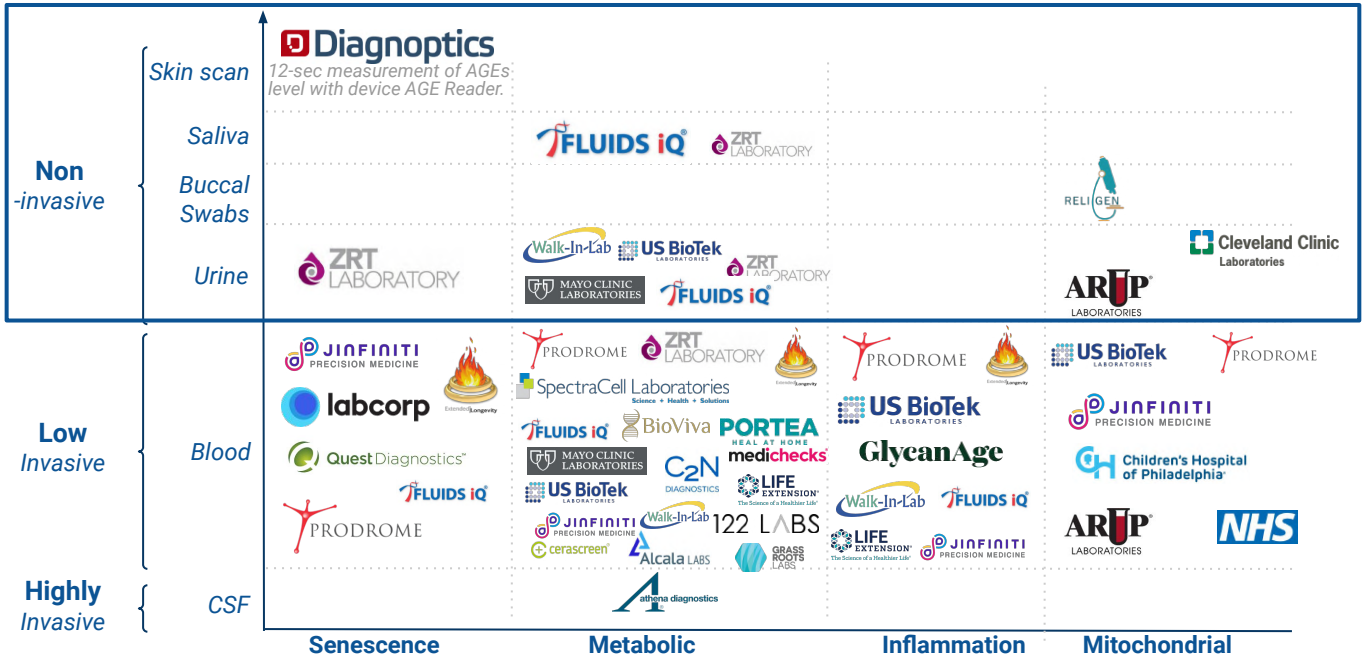
Sample type for Biochemical marker assessment	Availability	Informativity (amount of different biomarkers present in sample)	Applicability for general state assessment	Collection procedure	Need for qualified personnel for collection	Possibility of at-home collection
Blood	**+++**	**+++**	**+++**	**Slightly invasive**	**+/-**	**+**
Urine	**+++**	**++**	**+++**	**Non-invasive**	**-**	**+**
Saliva	**+++**	**++**	**+**	**Non-invasive**	**-**	**+**
CSF*	**+**	**++**	**-**	**Invasive**	**+**	**-**

* CSF- cerebrospinal fluid

Blood Sample is the most well-known type of fluid for clinical analysis and remains the most attractive sample type for Biochemical biomarkers assessment in **Aging/Longevity** area. **Blood Sample** provides **informative snapshot of organism state**, great possibilities to measure a **variety of different markers,** can be **easily collected** both in laboratory, and at home (blood spot, finger prick tests). Less number of biomarkers may be detected in **Urine** and **Saliva**, but these fluids are also attractive due to **simple** and **non-invasive collection** procedure. **CSF** becomes reliable sample type for **early detection of Neurological Age-related disorders**.

Invasivity of the Marketed Aging Diagnostic Test

Invasivity Gradation of Biochemical Biomarkers Marketed Tests



Sample collection doesn't need a medical professional assistance

AGE - advanced glycation end products
CSF - cerebrospinal fluid

The vast majority of tests currently available in the market are **Blood based tests**, routinely used for analysis in accredited laboratories. Kits for **minimally invasive at-home blood sample collection** are provided by several companies (**Walk-in-Lab, ZRT Laboratories, FLUIDS iQ, GlycanAge, BioViva USA, Medichecks**). **Dried urine method** proposed by **ZRT's** and **Fluids iQ** offers a discreet, convenient at-home testing, eliminates the burden of regular jug urine collection. **ZRT's** and **Fluids iQ** also provides several biomarkers testing in **Saliva**.

Invasivity of the Innovative Diagnostics Tests

Invasivity Gradation of Innovative Diagnostic Tests

*CSF - cerebrospinal fluid

Despite the non-invasive sample collection of **Urine** and **Saliva**, biomarkers detection in such sample types is not intensively developed. Only **Salimetrics** is currently running the programs of Metabolic and Inflammation markers assessment in **Saliva**.

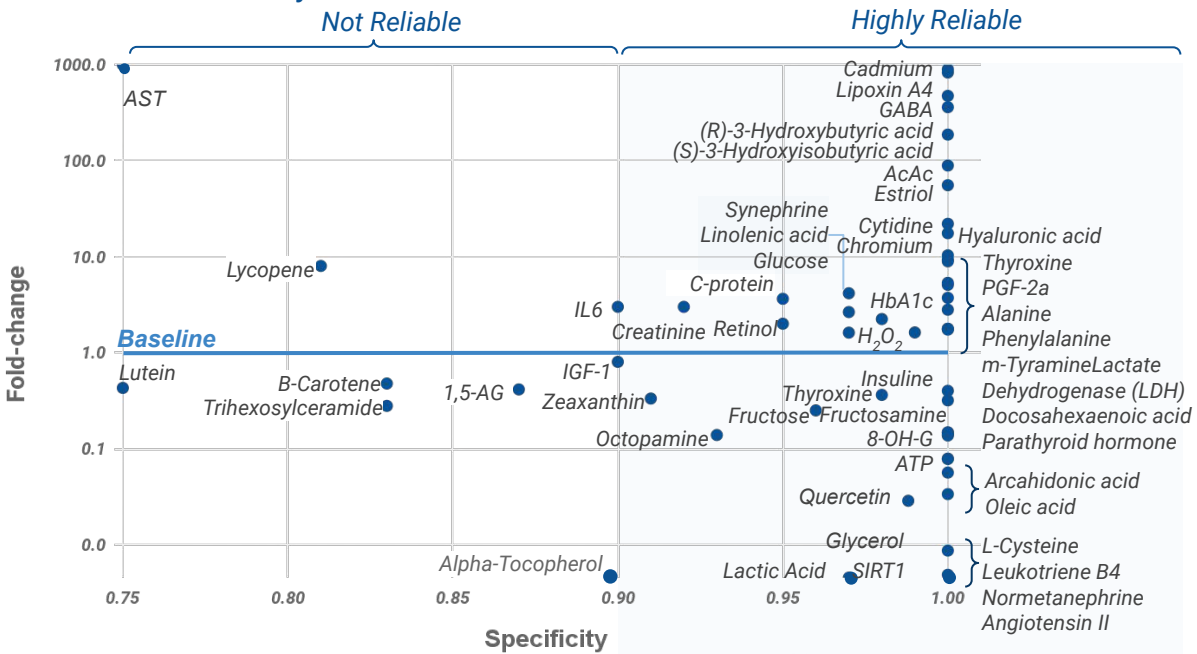
Most of new markers developed as perspective for evaluation of Aging and Age-related diseases are **Blood based**. New blood biomarkers which could enable **early diagnosis of Alzheimer's disease** (**Eli Lilly, Sysmex/Eisai**) attract great attention.

ADx NeuroSciences, BioArctic are developing **CSF tests** for **Parkinson's disease** and **Alzheimer's disease**.

There are no biomarkers today that can evaluate risk of development and mirror of **Age-related Neurological diseases** progression. And listed above trials may change for better the current situation.

Reliability of Clinical Biomarkers for Diagnostic Aging and Age-Related Diseases

Clinical Biomarkers Reliability



'Healthy living' tests

Clinical tests

Validation of a biomarker is a necessary component to delivery of high-quality diagnostic data necessary for effective use of biomarkers. Typically, validation takes into account the **sensitivity** of biomarker and **fold-change its level/activity** in patients vs healthy individuals. Many hurdles exist within aging and longevity research and development that pertain to biomarker validation and qualification.

On the chart are shown **clinically approved biomarkers** for **age-related disease** that are used in "anti-aging" diagnostic panels. The most commercial tests for healthy living use non-specific biomarkers. **Only handful of companies (Jinfinity, veMico, Prodrome, Cerascreen)** that offer **tests** that measure **highly reliable aging markers**.

Informativity of the Senescence Biomarkers

Biological Pathways	Biomarker	Biological Role	Changes of Biomarker Level in Aging	Indication	Biotech Companies	At-home tests	Clinical tests
Cell cycle	**p16**	Inhibitor of CDK 4/6; **induces senescence**	↑ **Increased**	**Heart disease Oncology**	Sapere Bio		
Hypothalamic-pituitary-adrenal axis	**DHEAS***	Sex steroids precursor	↓ **Decreased**	**Senescence**	LIFE EXTENSION	FLUIDS iQ	
Pineal clock	**Melatonin**	Regulator of circadian rhythms, antioxidant, immunomodulator	↓ **Decreased**	**Depression, Insomnia**		ZRT LABORATORY	
Autophagosomal-lysosomal network	**β-gal***	Lysosomal degradation of glycoproteins and glycollipids	↑ **Increased**	**MPS***		JINFINITI PRECISION MEDICINE	labcorp, Quest Diagnostics
DNA repair & prevention of Replicative senescence	**NADase**	NAD degrading enzyme	↑ **Increased**	**Senescence**		JINFINITI PRECISION MEDICINE	
	NAD *(in plasma)*	NAD is a **coenzyme** for **NAD-dependent Sirtuin-1**	↓ **Decreased**	**Senescence**			
	SIRT1*	**Prevents Aging** and **related diseases** via the deacetylation of histones; activates **autophagy**	↓ **Decreased**	**Senescence**		JINFINITI PRECISION MEDICINE	
DNA methylation	**DNMTs */ choline system**	Choline is a methyl donor *for* histone methylation	↑ **Increased**	**Neuro, Stroke, Heart disease**			PRODROME
Aging phenotype / Multisystem functional decline	**AGEs***	**Harmfull**, may be formed via spontaneous glucose binding to the biomolecules with their normal functions loss	↑ **Increased**	**Heart disease Diabetes mellitus**			Diagnoptics

** AGEs - Advanced Glycation Endproducts; DNMTs - DNA Methyltransferase; DHEAS - dehydroepiandrosterone sulfate; MPS - mucopolysaccharidoses; SIRT1 - Sirtuin-1; β-gal - beta-galactosidase.*

Informativity of the Metabolic Biomarkers

System / Organ	Biomarker	Biological Role	Changes in Aging	Indication	Biotech Companies	At-home tests	Clinical tests
Nutrient status	**Vitamin panel** **Mineral panel**	**Coenzymes**; **Vitamin D** - **regulator** of whole metabolism, **Folate** - DNA **methylation**, Cell **division**	⇩ **Decreased**	**Wellness** **Multiple**		cerascreen, medichecks, JINFINITI PRECISION MEDICINE, Walk-In-Lab	Alcala LABS, LIFE EXTENSION, SpectraCell Laboratories, US BioTek LABORATORIES
Endocrine system	**Thyroid Panel** **Sex hormones** **Growth hormone** **Cortisol**	**FSH, TSH*, T3, T4** - **Metabolism** regulators **Estradiol, Testosterone** - **Multisystem** control **Tissue & Organs Renewal** **Stress** hormone, **increases blood glucose**	⇩ **Decreased** ⇩ **Decreased** ⇩ **Decreased** ⇧ **Increased**	**Wellness** **Multiple**	LANDMARK MEDICAL CENTER, veMico Extending Healthy Living	cerascreen, medichecks, Walk-In-Lab, ZRT LABORATORY, FLUIDS iQ	LIFE EXTENSION, GRASS ROOTS LABS, Alcala LABS, US BioTek LABORATORIES
Glucose metabolism	**Insulin** **Glucose** **HbA1C***	Regulator of **glucose utilisation**, cell **growth** High glucose **accelerates Aging** Retrospective Marker of High glucose	⇩ **Decreased** ⇧ **Increased** ⇧ **Increased**	**Cardiovascular** **Metabolic** **Dementia**	Roche, LANDMARK MEDICAL CENTER, SAN DIEGO STATE UNIVERSITY, University of San Diego	122 LABS, cerascreen, ZRT LABORATORY, JINFINITI PRECISION MEDICINE, Walk-In-Lab	LIFE EXTENSION, Alcala LABS, PORTEA HEAL AT HOME, MAYO CLINIC LABORATORIES
Cardiovascular system	**Lipid panel**	**Cholesterol, LDL, TAGs*** increase, and **HDL*** decreases **Atherosclerosis risk**	⇧ **Increased** ⇩ **Decreased**	**Cardiovascular** **Metabolic** **Dementia**	Roche, LANDMARK MEDICAL CENTER, SAN DIEGO STATE UNIVERSITY	cerascreen, ZRT LABORATORY, Walk-In-Lab, JINFINITI PRECISION MEDICINE, medichecks	Alcala LABS, LIFE EXTENSION, SpectraCell Laboratories, PRODROME
Liver	**Liver panel**	**Albumin** - Marker of chronic **liver dysfunction**; **ALT*** - liver cells **destruction** markers; **ALP*** - **cholestasis** marker	⇩ **Decreased** ⇩ **Decreased** ⇧ **Increased**	**Wellness** **Liver**		medichecks, Walk-In-Lab, JINFINITI PRECISION MEDICINE	GRASS ROOTS LABS, PORTEA HEAL AT HOME
Renal system	**Kidneys panel**	**eGFR*** (based on **cystatin C, creatine) -** marker of **renal filtration ability**	⇩ **Decreased**	**Wellness** **Kidneys**		medichecks, Walk-In-Lab	ARUP LABORATORIES, GRASS ROOTS LABS, PRODROME, PORTEA HEAL AT HOME
Nervous tissue	**Ng, NPTX2,** **Aβ. tau, P-tau,** **GFAP** **α-Syn***	**NPTX2, Ng** support **synapse integrity** **Aβ 42** - major component of **Amyloid plaques** **Tau, P-tau*** - major components of **NTF*** **GFAP** - risk of **AD** **α-Syn** is linked to the presence of **Lewy bodies**; key protein involved in **PD pathology**	⇩ **Decreased** ⇧ **Increased**	**AD** **Dementias** **PD**	ADx, IOWA, BIOARCTIC, Washington University in St. Louis School of Medicine, Lilly, sysmex, NORDIC BIOSCIENCE Biomarkers & Development		C2N DIAGNOSTICS, athena diagnostics

** FSH - follicule stimulating hormone; TSH - thyroid stimulating hormone; HbA1C - Glycated hemoglobin; LDL - low densuty lipoprotein; HDL - high density lipoprotein; TAGs - triacylglycerols; eGFR - estimated glomerular filtration rate; Aβ - beta-amyloid; P-tau - phosphorylated Tau protein; GFAP - Glial fibrillary acidic protein; Ng - Neurogranin; NPTX2 - Neuronal Pentraxin 2; NTF - neurofibrillary tangles; α-Syn - Alpha-synuclein; AD- Alzheimer's disease; PD - Parkinson's disease*

Informativity of the Inflammation Biomarkers

Process	Biomarker	Biological Role	Changes in Aging	Indication	Biotech Companies	At-home tests	Clinical tests
General inflammaging	**C-Reactive Protein**	Activates **Innate immune system**	↑ **Increased**	**Aging, CD**			
	IL1-β	Key **proinflammatory cytokine**	↑ **Increased**	**Aging**			
	IL-6	**Promotes Inflammation**	↑ **Increased**	**Aging, CD**			
	IL-8	Attracts neutrophils in **inflammatory** regions	↓↑ **Basal decreased Induced increased**	**Aging,**			
	IL-18	Potent **proinflammatory cytokine**	↑ **Increased**	**Aging, CD**			
	TNFα	**Proinflammatory cytokine**	↑ **Increased**	**Aging**			
	IgG glycans	**Promote Inflammation** contributing to **Aging**	↑ **Increased**	**Aging**			
Autoimmune inflammaging	**Rheumatoid Factor**	Autoantibody contributing to **RA pathology**	↑ **Increased**	**RA**			
	ANA	Strongly age-dependant autoantibodies	↑ **Increased**	**ATI disorders**			
Leak Gut induced Inflammaging	**Anti-DGP antibodies**	**DGP** activates immune system to **destroy gut epithelium**	**Unclear**	**Celiac disease**			
	Zonulin	Modulates the **permeability of Gut**	↑ **Increased**	**Welness Food sensitivities**			
	Histamine / DAO ratio	**Histamine** - mediator of **inflammation**, **DAO** inactivates histamin	↑ **Increased**	**Gut inflammation**			
	GTAs	Digestion	**Unclear**	**Aging Inflammation**			

CD - Cardiovascular diseases; IL - interleukin; TNFα - Tumor necrosis factor alpha; RA - rheumatoid arthritis; ANA - antinuclear antibodies; ATI - autoimmune; anti-DGP antibodies – antibodies specific for deamidated gliadin peptide; DAO - Diamine oxidase; GTAs - Gastrointestinal tract acids

Informativity of the Mitochondrial Biomarkers

Biological Pathways	Biomarker	Biological Role	Changes in Aging	Indication	Biotech Companies	At-home tests	Clinical tests
Mitochondrial energy metabolism	**PDH* activity**	**PDH** converts **Pyruvate** to acetyl-CoA for subsequent oxidation in mitochondria	⇩ **Decreased**	**MD, Metabolic, Cancer, AD**			Mayo Clinic Laboratories
	Organic acids	**Lactate, Pyruvate** - glycolysis end-products, and **Beta-Hydroxybutyric Acid -** markers of MD	⇧ **Increased**	**MD, Metabolic, Cancer, AD**			Mayo Clinic Laboratories, ARUP Laboratories, US BioTek Laboratories, Prodrome
	NADH levels	**NADH** is a marker of ETC* dysfunction	⇧ **Increased**	**MD, Metabolic, Cancer, AD**			Children's Hospital of Philadelphia
	Complex I, II, III and IV of ETC	Transport of electrons and formation of proton gradient for OXPHOS*	⇩ **Decreased**	**MD**			RELIGEN
	Carnitine	Transport of FFA* to mitochondria for oxidation	⇩ **Decreased**	**MD, frailty**			ARUP Laboratories
Mitochondrial synthetic function	**Creatine**	Partly produced in mitochondria; reflects mitochondrial dysfunction	⇧ **Increased**	**MD**			ARUP Laboratories
Mitochondrial translation	**FGF21***	Marker of mitochondrial transfer-RNA mutations and mtDNA deletions	⇧ **Increased**	**Mitochondrial myopathies**			NHS
	GDF15*	Marker of mitochondrial translation defects or mtDNA deletions	⇧ **Increased**	**Mitochondrial myopathies**			Mayo Clinic Laboratories
Oxidative stress	**ROS***	**Harmful**, formed as side product by ETC	⇧ **Increased**	**Aging, AD, PD**		JINFINITI PRECISION MEDICINE	
	F2-Isoprostanes	Oxidative stress marker	⇧ **Increased**	**Aging, OS, Diabetes, CD, AD**	LIFE EXTENSION		
	Oxidative damage markers	**8-OHdG** - oxidative DNA damage marker **oxidized LDL-C, MDA*** - oxidative damage	⇧ **Increased**	**Aging**	San Diego State University	FLUIDS iQ, JINFINITI PRECISION MEDICINE	
	Antioxidant capacity	Blood **glutathione**, **total antioxidant capacity** - markers of ability to neutralize ROS	⇩ **Decreased**	**MD**		JINFINITI PRECISION MEDICINE	Children's Hospital of Philadelphia

** PDH - pyruvate dehydrogenase ; MD - mitochondrial diseases; ETC - electron transport chain; OXPHOS - oxidative phosphorylation ; FFA - free fatty acids; FGF21 - fibroblast growth factor 21; GDF15 - growth differentiation factor 15; ROS - reactive oxygen species; 8-OHdG - 8-hydroxydeoxyguanosine; LDL - low density lipoprotein; MDA - malondialdehyde; AD - Alzheimer's disease; PD - Parkinson's disease; CD - cardiovascular disease; OS - oxidative stress*

Practical Applications of Biochemical Biomarkers

Tests for **Biochemical markers assessment** involve large group of routine laboratory tests optimized and validated through years of laboratory use to ensure the most comprehensive and accurate results for **Diagnostics**, **Monitoring** and **Prognostics** of variety of Diseases (Cardiovascular, Metabolic, Autoimmune, Infectious, Oncological, Mitochondrial etc).

Diagnostics, Monitoring & Prognostics

US BioTek Laboratories · Mayo Clinic Laboratories · Grass Roots Labs · Alcala Labs · ARUP Laboratories · labcorp

Some companies **(FLUIDS iQ, Walk-in-Lab)** provide **multi-analytes panel** as so called **Health Tests** (**Wellness Tests**) to **monitor current state of health**, detect possible illness at early stage, to make any necessary lifestyle changes to **maintain good health**.

Health Tests

FLUIDS iQ · Walk-In-Lab

Medichecks, Life Extension propose tests for measuring key blood markers and tracking them to fine-tune regimens of **Nutrition**, **Training**, and **Recovery** and reach the best **Sport and Fitness Performance**.

Sport and Fitness Performance

medichecks · Life Extension — The Science of a Healthier Life

Several companies **(GlycanAge, FLUIDS iQ, Jinfinity)** provide **Healthy Aging Tests** which help to evaluate if **Aging Rate** is a normal, to estimate the risk of **Age-related diseases** and to get information to make important decisions about diet and lifestyle to ensure **Long Healthy Life**.

Healthy Aging

GlycanAge · Life Extension — The Science of a Healthier Life · Jinfinity Precision Medicine · Prodrome · FLUIDS iQ

Other possible **Applications of Biochemical markers** tests involve evaluation of an individual's **toxic burden (US BioTek Laboratories), nutrient status** (**SpectraCell**), state of **skin, hair and nails** (**Life Extension**) for a **Targeted Nutritional** and **Detoxification Programs**.

Other

US BioTek Laboratories · Life Extension — The Science of a Healthier Life · SpectraCell Laboratories — Science + Health + Solutions

AT-home tests

Jinfiniti Precision Medicine has developed lab tests to measure biomarkers of aging in patient's blood. It offers tests that measure NAD, senescence, inflammation, oxidative stress, or other hallmarks of aging, so patient can make better decisions directed at improving his healthspan. The **AgingSOS™** test contains 13 biomarkers that can be used to maximize patient's healthy longevity including circulating and intracellular NAD, SA-β-galactosidase, reactive oxygen metabolites, total antioxidant capacity, vitamin D, high sensitivity C-reactive protein and others.

Walk-in-Lab offers **Anti-Aging Tests**, including **Arthritis** (C-reactive protein, rheumatoid factor, antinuclear antibodies etc.), **Osteoporosis** (vitamin D, Calcium, phosphorus etc.), **Hair Loss (Alopecia), Discount Panel** and **Anti-Aging Hormones Blood Tests** (testosterone, estradiol, prolactin, cortisol atc.) used to determine the main groups of biomarkers of aging reflecting and affecting the rate at which the body ages.

GlycanAge is the biological age test that measures patient's response to lifestyle change.
GlycanAge determines patient's biological age by looking at the state of the immune system and inflammation. It analyses the glycans attached to IgG. The type of glycans attached to IgG are able to change the function of IgG from pro-inflammatory to anti-inflammatory and vice versa. The balance between them determines patient's general health status and biological age.

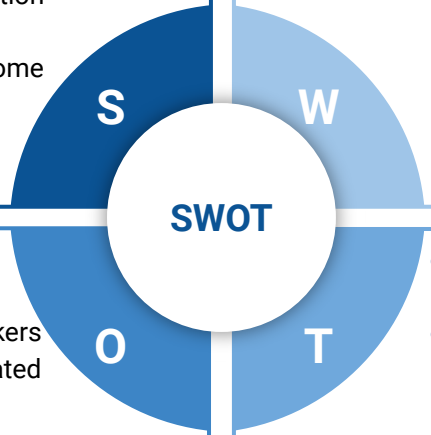
Clinical tests

Life Extension offers **Healthy Aging Panel Test** of blood and urine for biomarkers of aging including thyroid hormones, vitamins (vitamin B12, folate, vitamin D, 25-hydroxy), cardiovascular risk markers (Apolipoprotein B, homocysteine, C-reactive protein), insulin resistance markers (Hemoglobin A1C, glucose, insulin, ferritin) and general health markers (complete metabolic panel with lipids, complete blood count and urinalysis)

Prodrome developed **ProdromeScan Blood Test** that measures hundreds of biomarkers and key biochemical systems critical for optimal health and longevity. The test panel involves markers of mitochondrial function, inflammation (gastrointestinal tract acids), C-reactive protein, metabolic markers and marker of DNA methylation (longevity).

SpectraCell designed the Micronutrient Test (MNT) which **measures 31 specific micronutrients** — vitamins, minerals, amino acids, antioxidants and metabolites—and how they affect cellular function in a person. The MNT uncovers deficiency so that it can be effectively treated, thus facilitating real prevention. Not only will correcting intracellular deficiencies slow aging and degenerative disease progression, but it can also prevent as well as repair cellular dysfunction, and by extension disease.

Biochemical Biomarkers: SWOT Analysis



- Easy to use for diagnostic of age-related disorders.
- Low cost of test kit and service.
- Variability of diagnostic markers.
- Enough trained professionals.
- The most technologies for sample collection are non-invasive (urine, saliva, blood).
- Growth of number of companies that offer at-home test for self-diagnostic.

- High competition in the market.
- No clinically approved direct biomarkers for aging.
- No biomarkers that can evaluate risk of development and mirror of age-related diseases' progression.

- Combination of biomarkers can improve prediction.
- CDEs and quality control examples are available.
- The development of the new blood-based markers as perspective for evaluation of aging and age-related diseases.

- The procedure of sample collection sometimes is invasive (for example CSF) and has risk for health.
- The most commercial tests for “healthy living” use non-specific biomarkers.

Key Takeaways: Biochemical Biomarkers

Despite on developing new approaches to diagnostics **Biochemical biomarkers** are **the most reliable, cheap** and **available** tool of assessment the risks, **detection and monitoring of Age-related diseases**. Companies offer Senescence, Metabolic, Inflammatory, and Mitochondrial markers to evaluate Aging.

The noticeable popularity of **at-home tests** on the market can be explained by possibility to **evaluate health state** with **accurate & reliable** results, **easy to order** test, easy to collect sample for biomarker assessment, **results are delivered fast**, there is ever no need for leaving the home.

Metabolic biomarkers share **47% of the market**. They can be applied for diagnostics as Age-related disorders. Among new developed biomarkers dominate kits for **Neurodegenerative Disorders** like Alzhimer's, Dementia etc.

USA is a leader for production and development of biomarker kits and providing of diagnostic service for Aging. Around **70% of companies** are located there.

According to the practical application Biochemical Biomarkers are used for **Diagnostics, Monitoring, Prognosis of Age-related Disorders, Healthy Life tests, Sport and Fitness** as well as **Healthy Aging Control**.

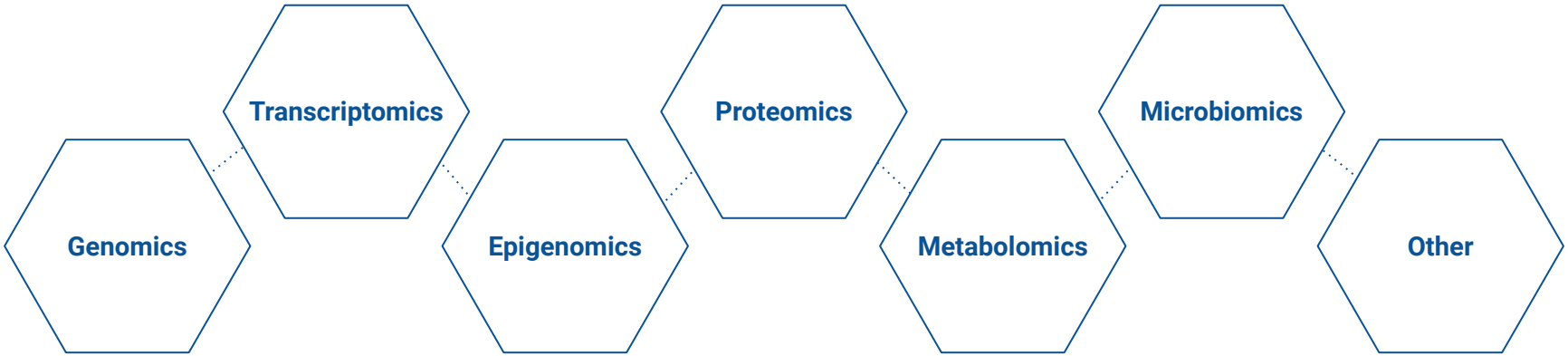
The leaders on the market are **Jinfinity, Fluids iQ, Medichecks, Walk-in-Lab, GlycanAge, veMico, Cerascreen**, as well as **Prodrome, SpectraCell, Life Extension**. These companies offer **at-home tests** and **clinical tests,** respectively, that measure highly reliable and clinically approved aging markers.

Omics Biomarkers

Omic Biomarkers Framework

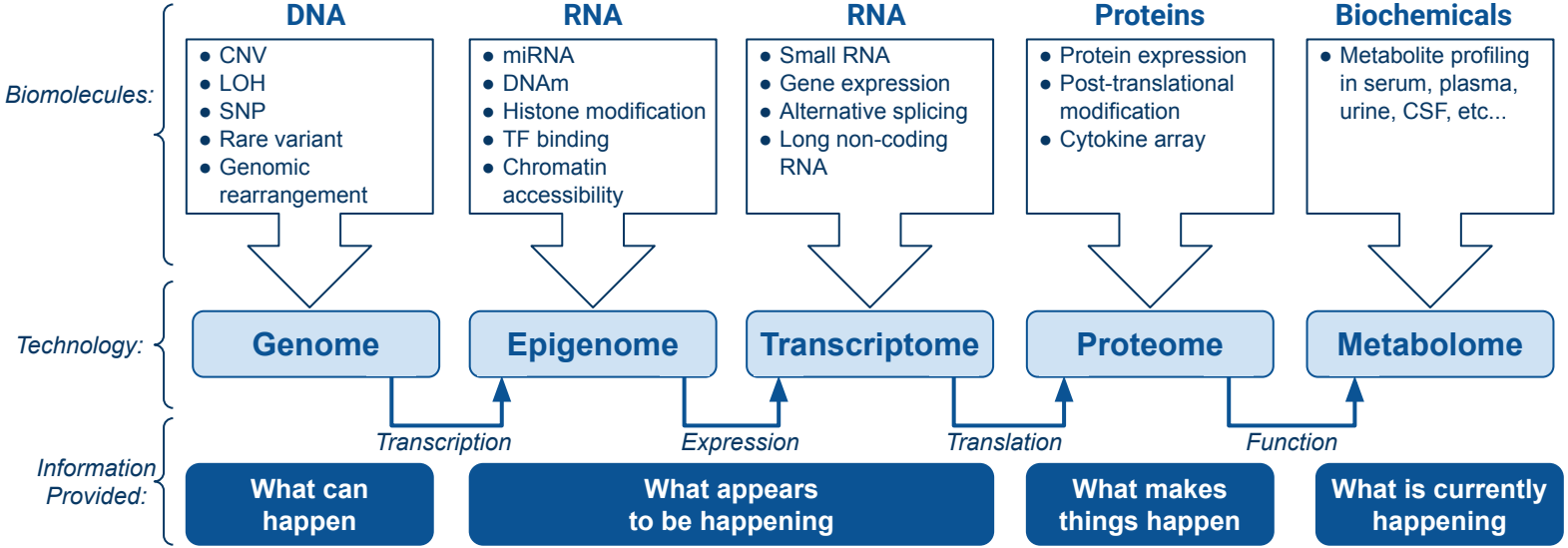
Ahead of database creation, we picked the **most significant fields of omic diagnostics for aging and age-related disease**. The categorisation of companies is based on the main technologies applied for prediction of aging progression and **supported by the latest scientific evidence.** Also companies were distinguished by their area in the market - accredited clinical laboratories, at-home tests, biotech companies (developing new biomarkers), service. Thus, the framework not only brings a **comprehensive view of the market** but also **sustains relevance in advance to the development** of technologies and research approaches.

By Research Field



Omic Approaches in Clinical Diagnostic of Aging and Age-Related Disorders

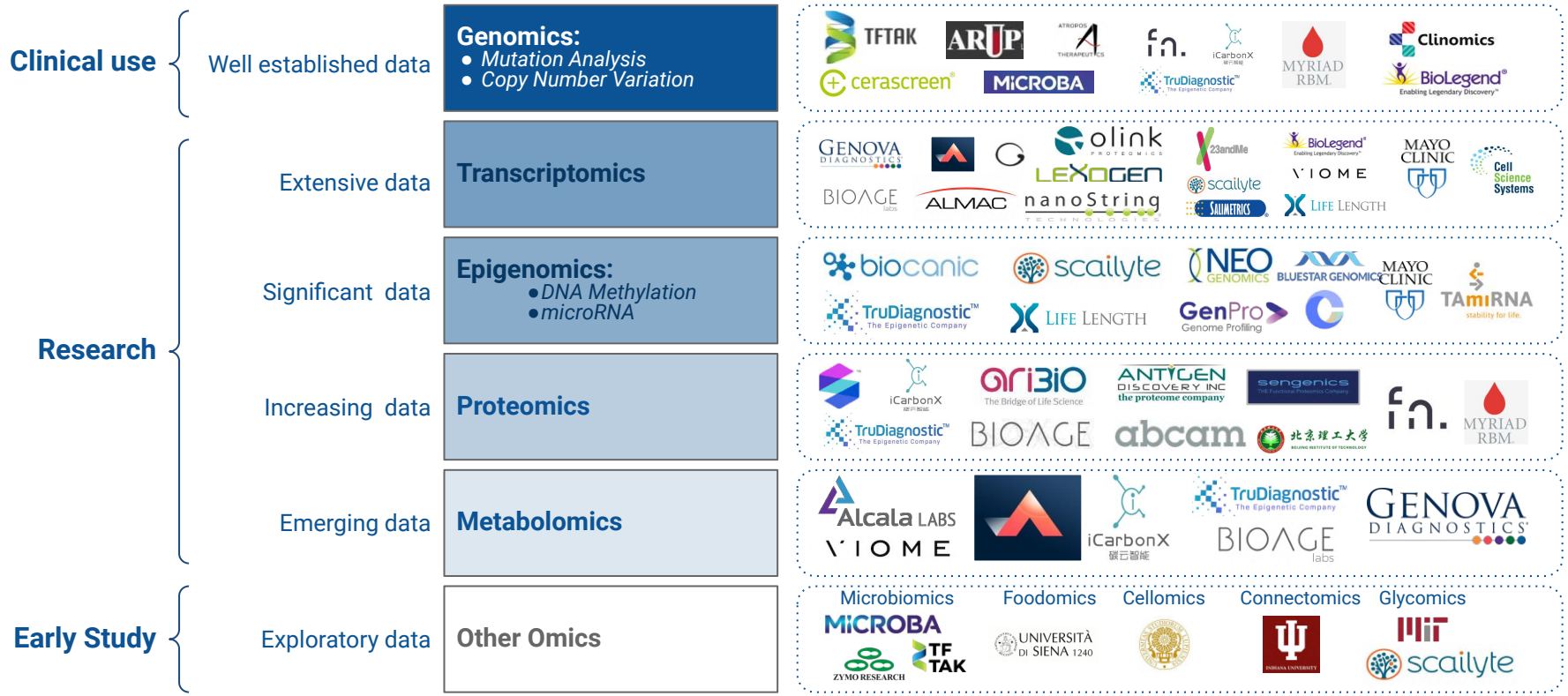
Relationship between single and multi omics data analysis



For **evaluation of aging and age related diseases** traditional diagnostic classifies patients into groups according to their clinical characteristics (ie, phenotypes). However, these classifications do not provide insight into the functional or pathobiological mechanisms of the disease within the individual (ie, endotype). **Omics is the comprehensive assessment** of the molecules that **constitute a cell, tissue, or organism**. Integration of multi-omics data, such as genomics, proteomics, and metabolomics, along with clinical data **allows for better understanding of age-related disease pathogenesis** and will be **important for prognosis of aging** and **predicting, diagnosing, and treating disorders**.

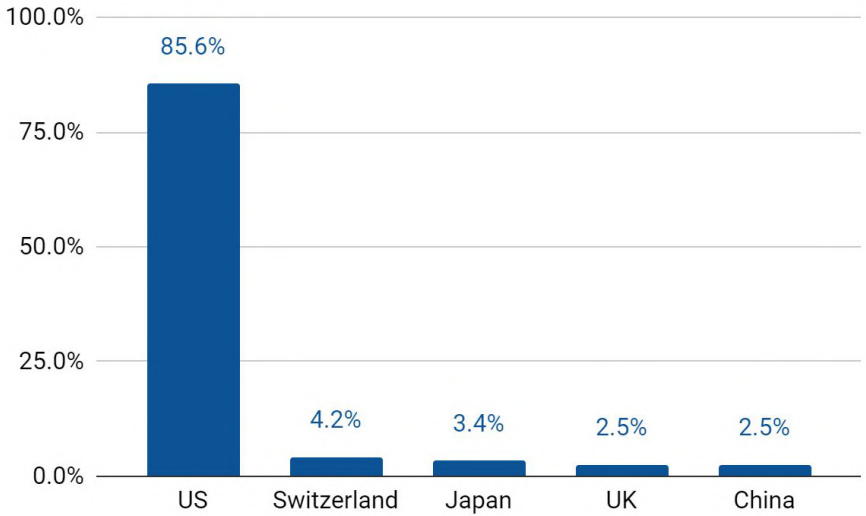
Modified from Z. Momenni et al. // Journal of Biomedical Informatics Volume 107, July 2020, 103466

Gradation of Individual Omics Technologies for Studying of Aging

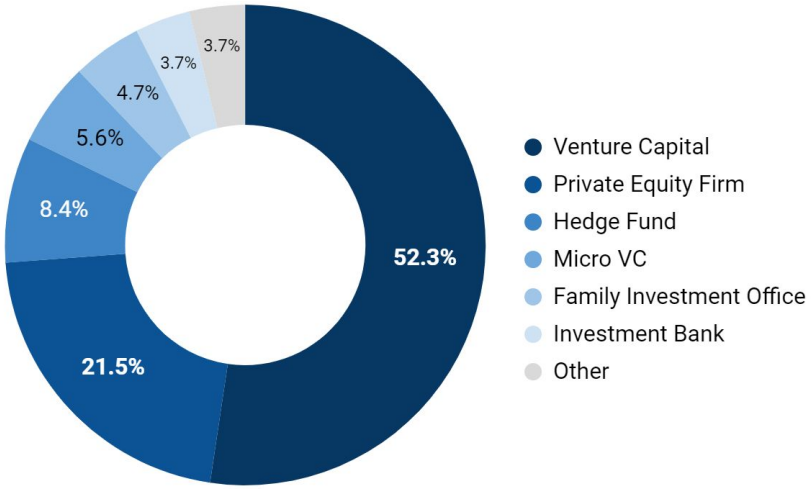


Market Overview: Global Market and Investors

Countries with the Largest Number of Investors, %



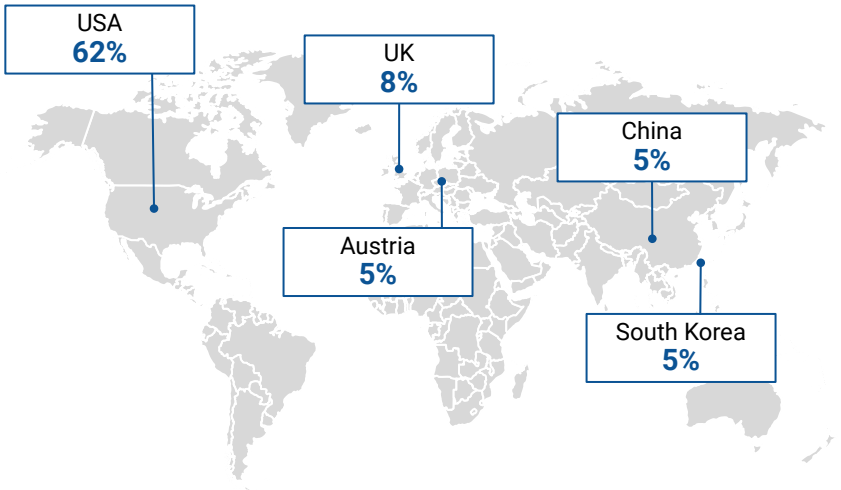
Main Type of the Investors, %



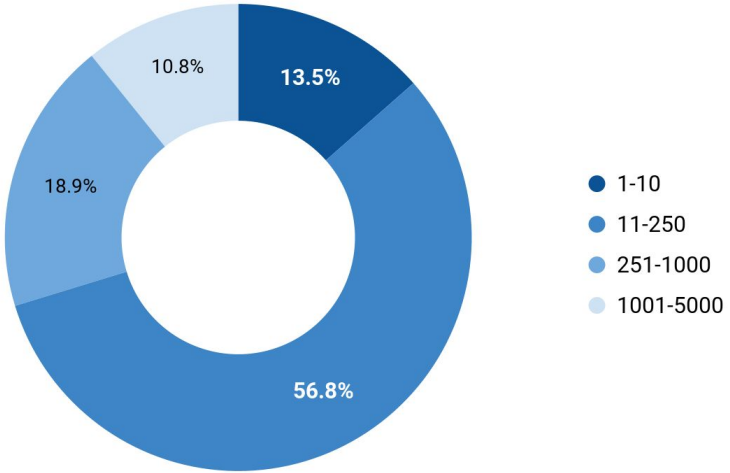
Investors in OMICS-based market are highly concentrated - more than 97% of all investors are from the top 5 countries.
More than 85% of the investors in the OMICS-based Biomarkers are **from the US**. **Other top countries** by number of investors constitute another **12.6% of investors.**
Venture Capital (52.3%) and Private Equity Firms (21.5%) are the most common type of investors in the OMICS-based Biomarkers. Another 26% of investors are other types of investors, including Hedge Funds, Family Investment Office and Investment Banks.

Market Overview: Geography of Companies

Distribution of Companies by Country, %



Distribution of Companies by Number of Employees, %



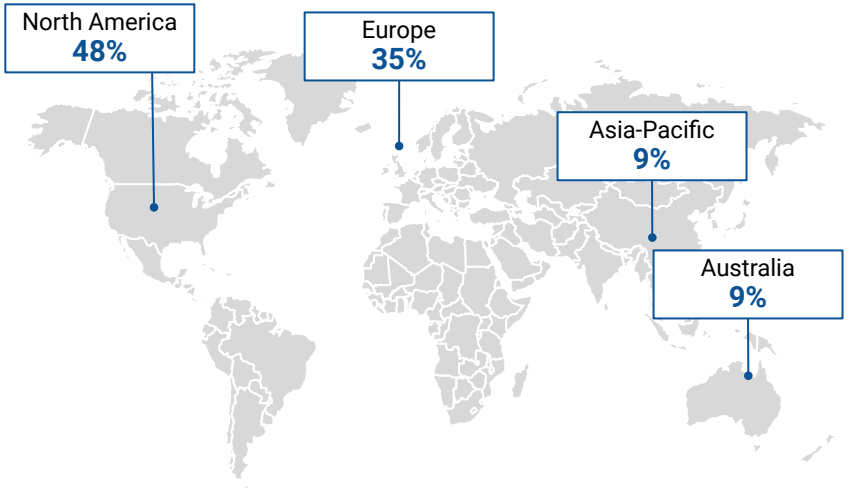
More than **60%** of the companies are located **in the USA**, the following are in Europe and in the Asia-Pacific region. The greatest part (around 8%) of European companies are situated in the UK.

More than **70%** of firms are either have **up to 10 or up to 250 employees**. However, the rest companies are a big corporations with employees up to 5000.

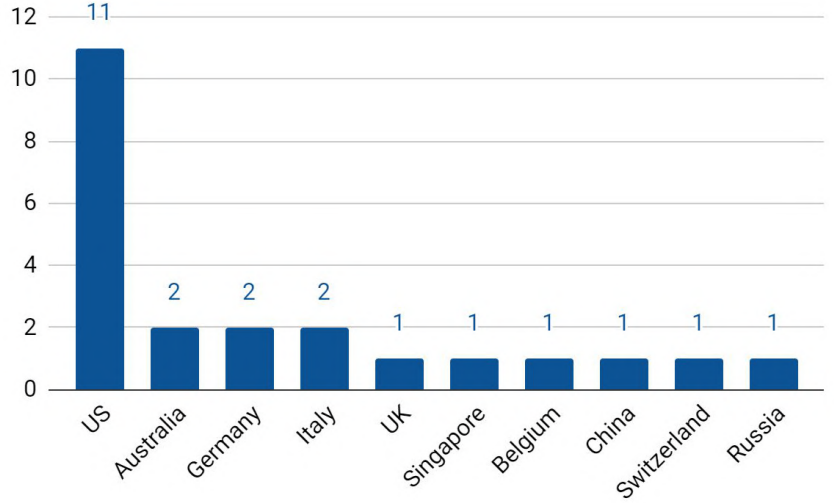
Source: Aging Analytics Agency analysis

Market Overview: R&D Centres

Distribution of R&D Centres by Regions, %



Top Countries by Number of R&D Centres,%

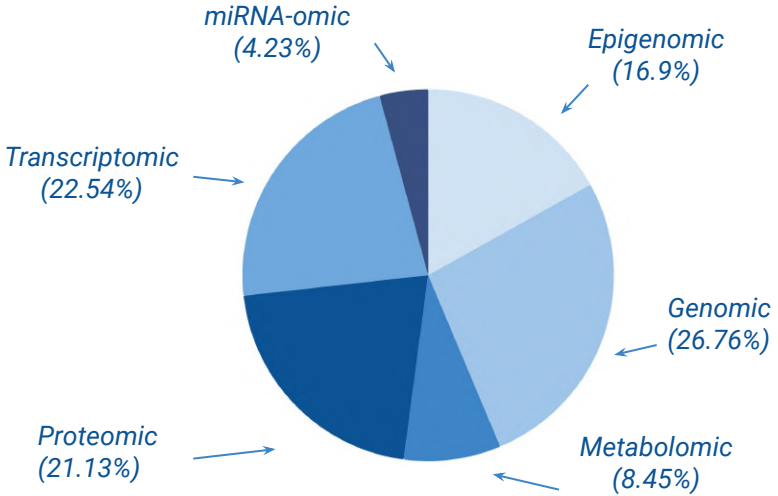


The top region by R&D activity in the OMICS-based Biomarkers is North America, **the US** in particular, with **11 R&D Centres.** The second top region is Europe. Its R&D Centres take 35% of all and distributed all over the continent. **Asia-Pacific and Australia** each have **2 R&D Centres (by 9% of total).**

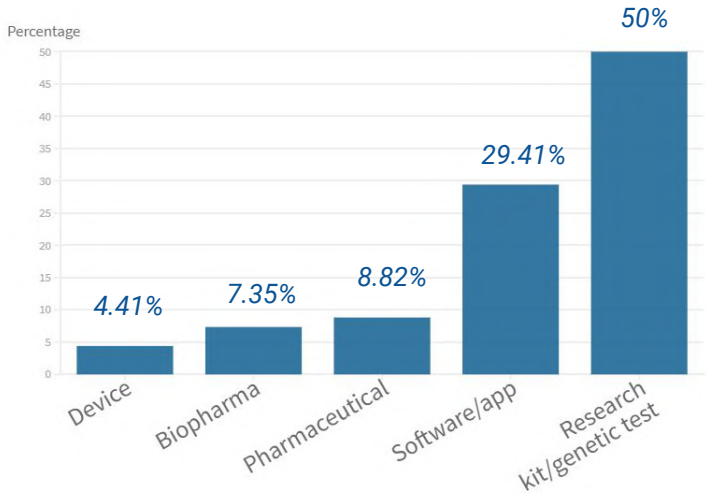
Source: Aging Analytics Agency analysis

Market Overview: Distribution of Companies by Approach

Distribution of Companies by biomarker type

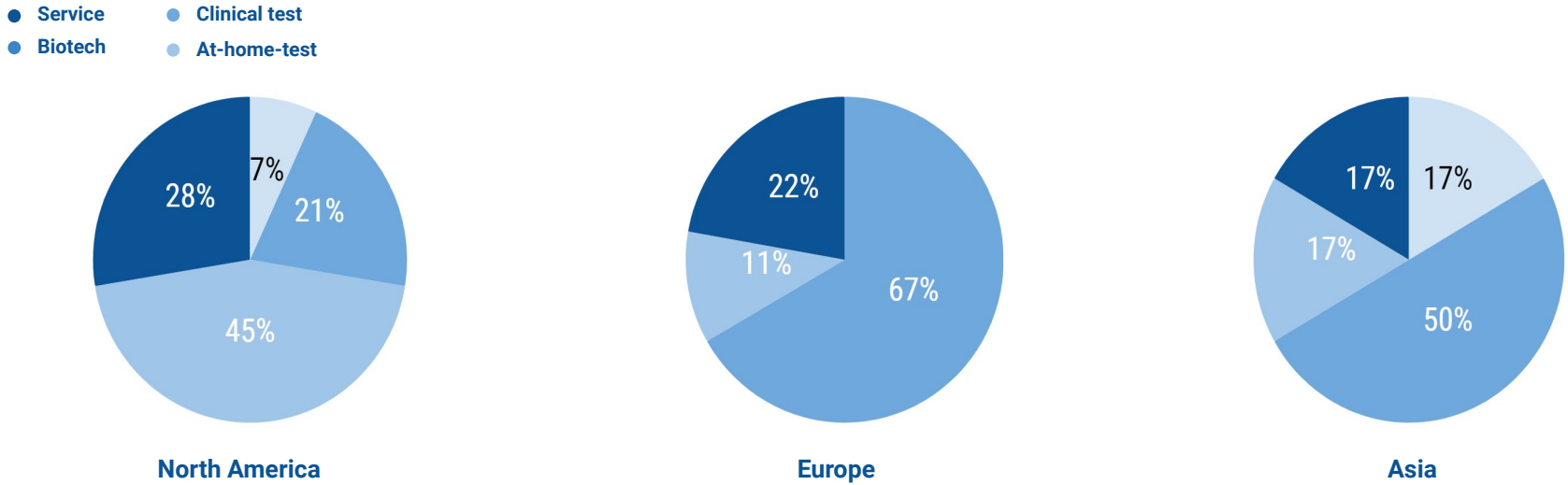


Distribution of companies by product type



The most popular biomarker type among companies is **genomic biomarker - 26.76%** of all companies use it for analysis. Following are transcriptomic and proteomic biomarkers: they are used by **22.54% and 21.13%** of companies. Then there are **epigenomic and metabolomic biomarkers**, which are utilized by **16.9% and 8.45%** of companies respectively. Finally, the least share is occupied by miRNA, which is analyzed by **4.23%.** The most of the companies are involved in research kit/genetic test development. However, there is a promising number of companies building a software and applications.

Market Overview: Distribution of Approaches in the Top Countries



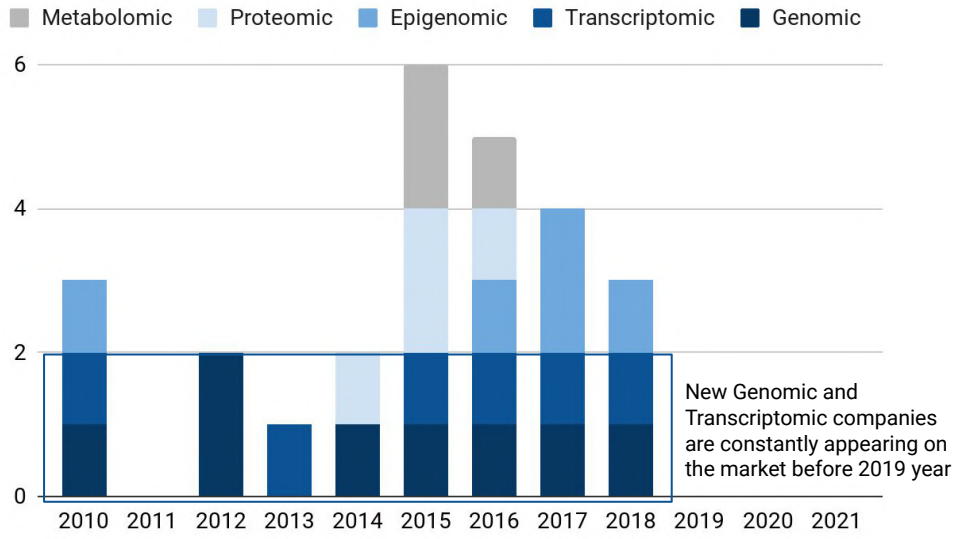
The global spatial Omic's market size is expected to reach **$ 500 million** by **2030**. It is expected to expand at a **CAGR of 10.00%** from this period. The COVID-19 pandemic slowed down many industries worldwide. However, this market did not face the extensive negative impact of the pandemic. **Startups** and **well-established players** continued their **product development** and launched novel solutions. The **USA is a leader** in this area and **share ~60.4%** of all companies on the market. This region characterized **rise in commercial interest** and **government support** for genomics and sequencing technologies, **high demand for personalized medicine**, and the presence of a substantial number of translational and academic research organizations.

Key Market Trends

Key Market Trends

- Clinical application
- From Omic to Multi-Omic assay
- Early prediction of age-related disorders
- Proteomic biomarkers quantification
- Growth of direct-to-customer market
- Digitalization

New Companies: Omic Biomarkers



First omic companies appears in the market after 2000. For the last decade the number of these companies grow slowly, **only 18 new companies** appeared on the market. More the all **no any development** of the new companies after 2019. The **Genomic** and **Transcriptomic** biomarker are the top categories in this development. Currently, **genomic tests are relatively niche market** with a number of services **available over the internet**. However, the commercialisation of personal genome sequencing is set to grow and, in future, it **could become a routine part of clinical practice**.

Clinical Trials And R&D Notable Cases

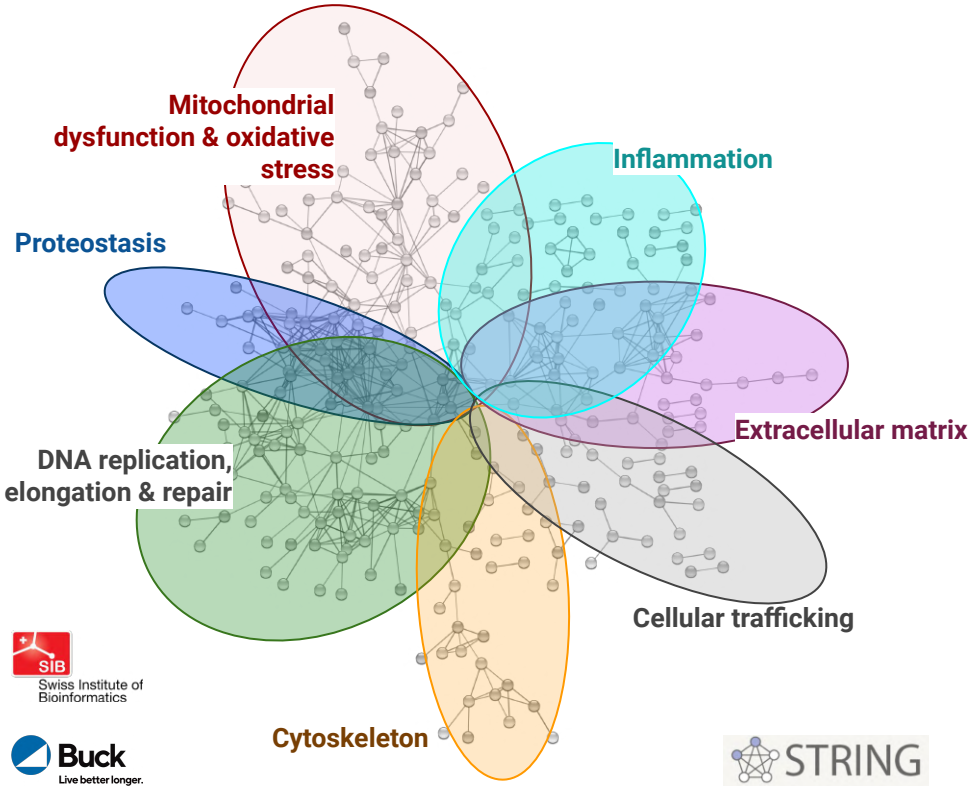
TruDiagnostic is a CLIA-certified and HIPAA-compliant lab which uses a multi-omic approach with the primary focus in DNA Methylation. TruDiagnostic began with TruAge – a test that measures Biological Age by looking at Methylation. Now this laboratory also provide a full suite of aging related metrics. This includes telomere length measurements, intrinsic and extrinsic age calculations, immune cell subset deconvolution, current pace of aging, and more.

Clinomics is a leading company for early diagnosis of cancer/diseases based on genome and pursues to overcome aging and diseases through liquid biopsy and Multi-Omics technology. Clinomics specializes in offering a genome-based, early cancer diagnostic service through the technology of Multi-Omics analysis and simultaneous detection of CTC and cfDNA in the blood with our internationally renowned biomedical information processing abilities.

BioAge is biotech companies developing mapping human aging from the ground up. BioAge utilizes broad anti-aging pathways to target specific age-related diseases. BioAge has a unique proprietary biobank of longitudinal data and AI platform for identifying longevity targets. The company is building deep molecular profiles of these samples, incorporating proteomics, metabolomics, and transcriptomics to identify the best drug targets for healthy aging.

Key Pathways Involved in Aging*

Pathway Analysis on the Clusters of Co-expressed Genes



Understanding the aging biology mechanisms is fundamental to the pursuit of age-related diseases. In this way, aging is characterized by a gradual decline in physiological functions, involving the increased number in senescent cells into the body. Analysis of **biomarker expression in human cells** shows the several **pathways that lead to senescence**, including **mitochondrial dysfunction and oxidative stress**, **persistent inflammation**, as well as **deregulated proteostasis**.

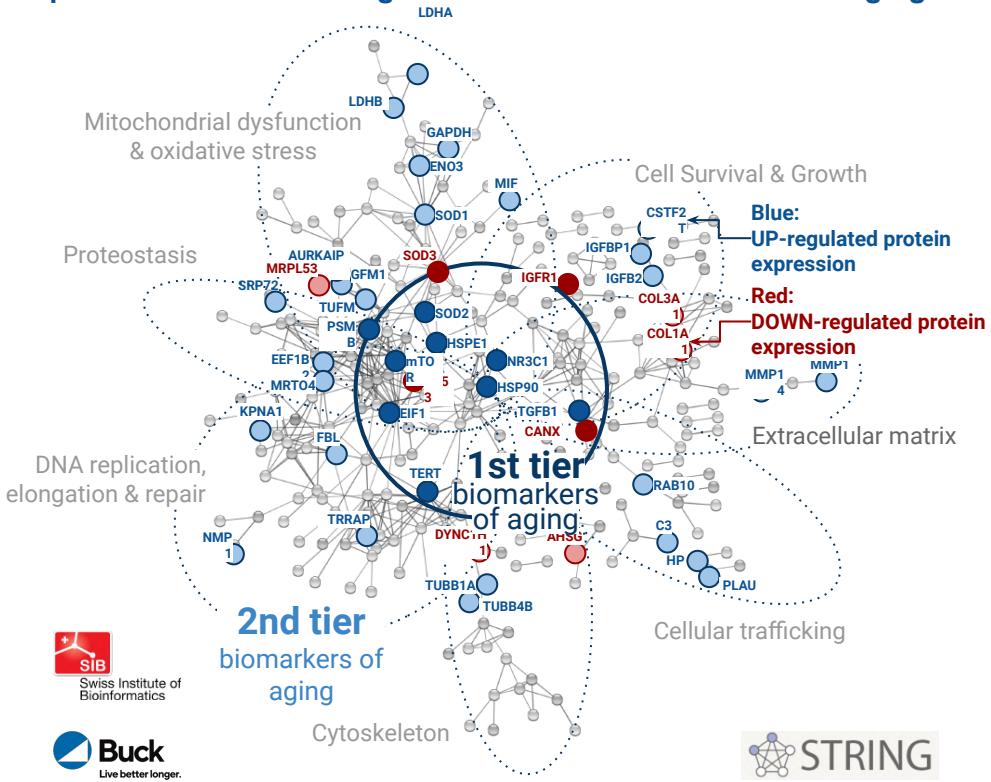
In addition, senescence can be induced by cellular replication, which resulted from **telomere shortening.** Taken together, it is possible to draw a common pathway unifying aging to age-related diseases, and the central point of this process, senescence, can be the target for new therapies, which may result in the healthspan matching the lifespan.

Note: *Analysis of protein-protein interaction based on the biomarkers reported in literature and* **STRING** *database. The interactions include direct (physical) and indirect (functional) associations; they stem from computational prediction. Interaction score: > 0.07.*

Note: *based on single-cell genomic analysis of human lung fibroblasts.

Single Biomarkers Involved in Aging*

Specific UP- or DOWN-regulated Proteins Associated with Aging



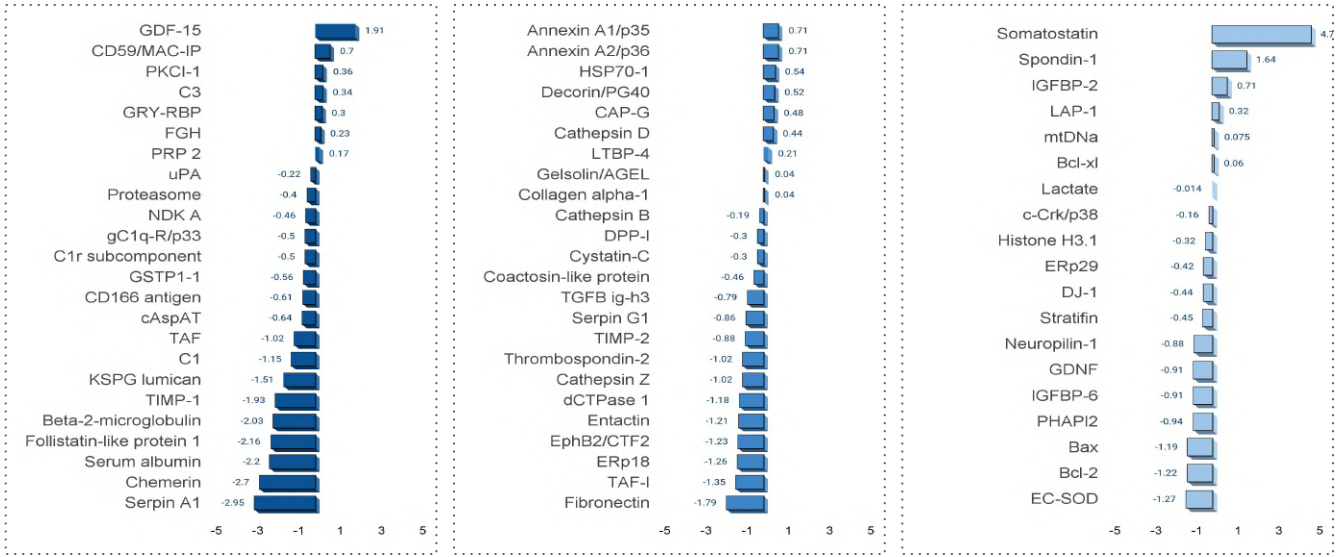
The **senescence-associated secretory phenotype (SASP)** has recently emerged as a **driver of and promising therapeutic target for multiple age-related conditions**, ranging from neurodegeneration to cancer. The complexity of the SASP, typically assessed by a few dozen secreted proteins, **has been greatly underestimated**, and a small set of factors cannot explain the diverse phenotypes it produces in vivo.
Proteome analysis show potential biomarkers of aging in human lung fibroblasts. Some of them are **UP-regulated** (SOD2, HSP90, mTOR, TGFB1 etc.) another are **DOWN-regulated** (TP53, IGFR1, CANX, COL1A1 etc.). On the chart the proteins with significantly altered (q-value <0.05 and **>2-fold change**) secretion by senescent compared with quiescent cells following genotoxic, oncogenic, or ATV treatment stress are shown.

Note: *Analysis of protein-protein interaction based on the biomarkers reported in literature and **STRING** database. The interactions include direct (physical) and indirect (functional) associations; they stem from computational prediction. Interaction score: > 0.07.*

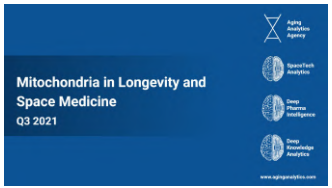
Note: *single-cell genomic analysis of human lung fibroblasts.

Plasma Proteomic Assay in Older Adults

Changes of Biomarkers Level in Plasma in Older Patient (>60 years) vs Young, Log2(Old/Young)



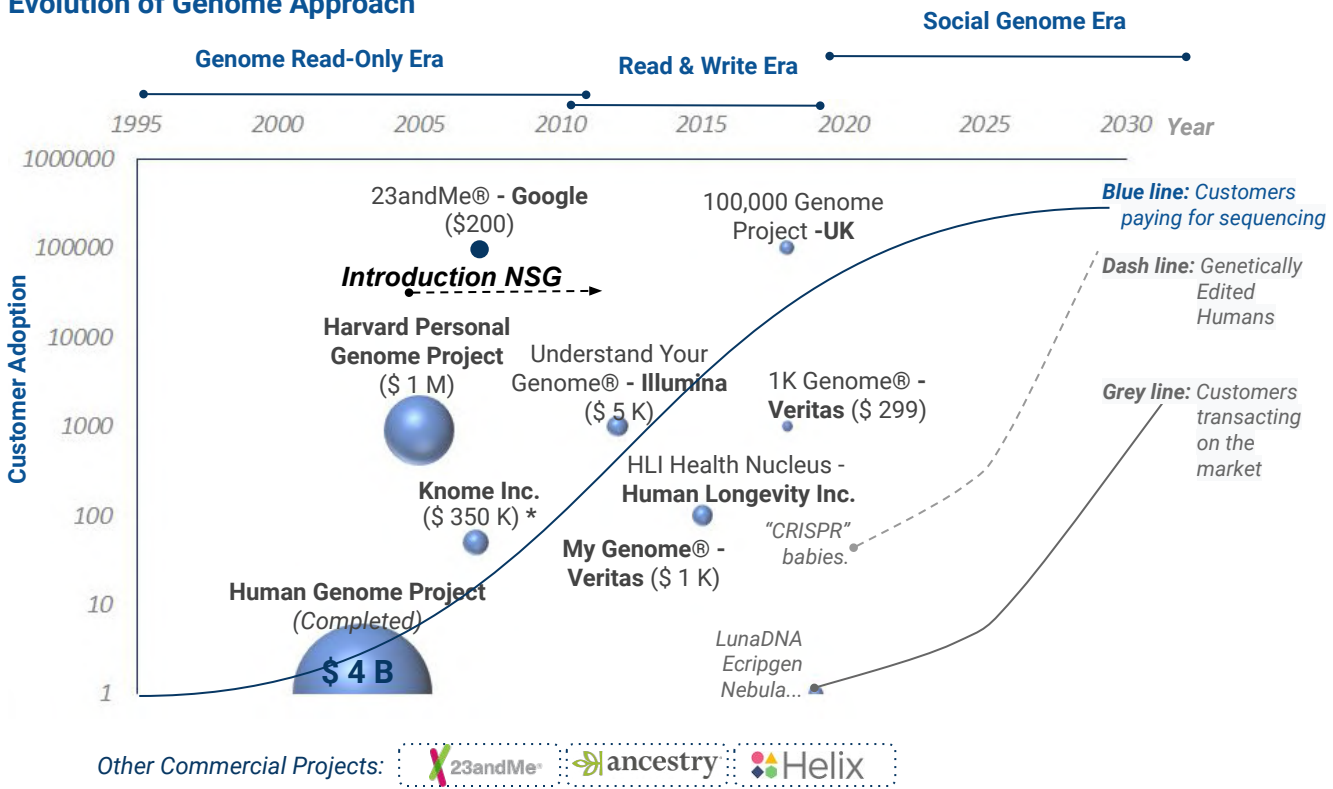
Buck
Live better longer.



While unbiased transcriptome and in vitro proteome analyses are valuable, they do not directly assess the presence of secreted proteins in human body. Thus, proteomic studies are needed to accurately and quantitatively identify SASP factors as they are present in the secretomes of senescent cells. BLSA's (Baltimore Longitudinal Study of Aging) analyses identify several **candidate biomarkers of cellular senescence** that overlap with aging markers in human plasma, including **GDF15**, **Somatostatin**, **SOD**, **Fibronectin**, and **SERPINs**, which **significantly correlated with age in plasma from a human cohort**, and facilitate the identification of potential senescence biomarkers to assess the burden, originating stimulus, and tissue of origin of senescent cells in vivo.

Humanity Has Reached to the Era of the Social Genome

Evolution of Genome Approach



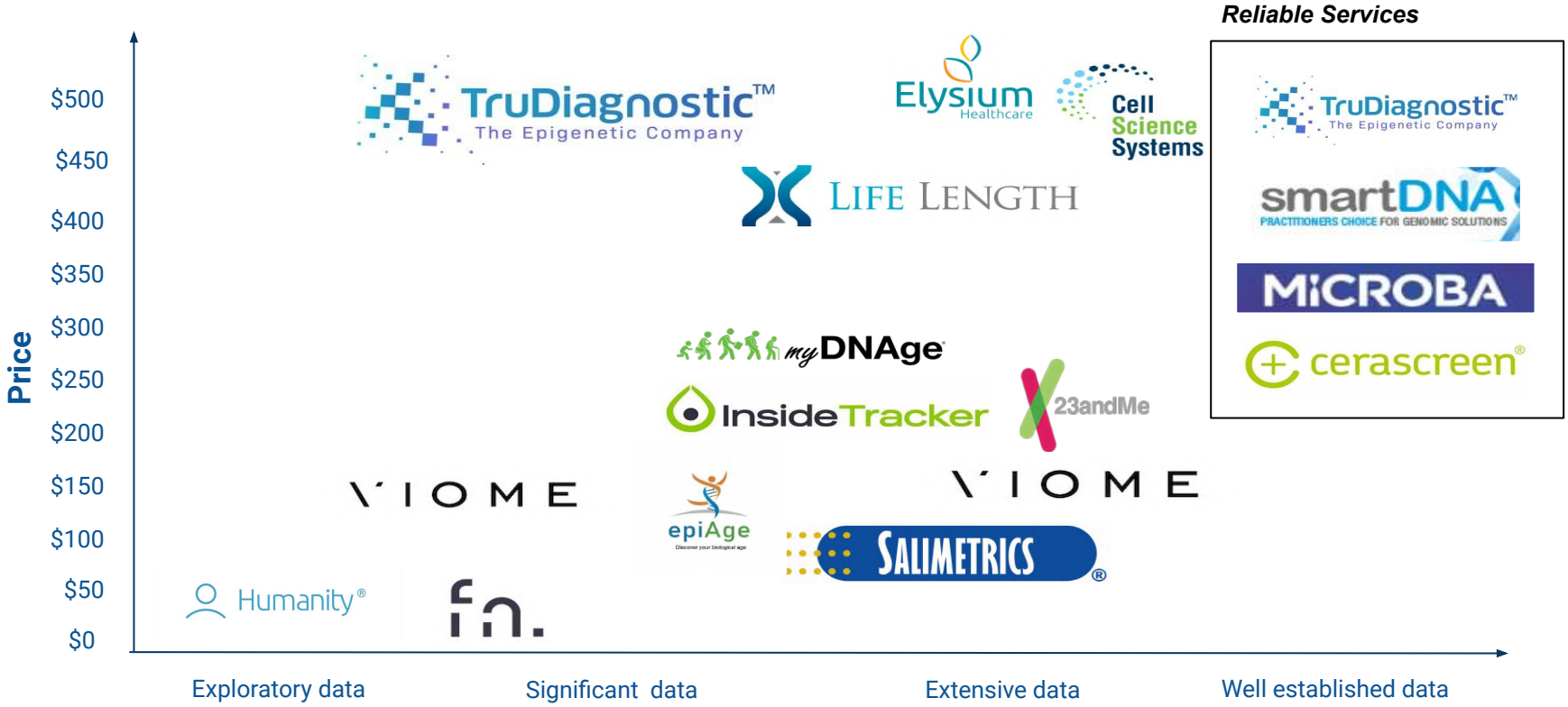
Other Commercial Projects: 23andMe, ancestry, Helix

Potentially New Products on the Market:

- **Health and life insurance** products that take into account genetic risks.
- **Reproductive services** that include gene editing and enhancements.
- Escalation of DNA data marketplaces like **Nebula Genomics** and **Luna DNA**.
- Integration of your genomic data with other **"omics sciences"** such as microbiomics, transcriptomics, proteomics, and metabolomics.
- **Healthcare services** that incorporate genetic information into clinical algorithms.

** Acquired by Tute Genomics, Inc. in 2015 (which later becomes a subsidiary of PierianDX, Inc. in 2016)*

Prices vs. Gradation of Individual Omics Technologies



Blood-Based Biomarker Panel AgingSOS™ by Jinfiniti Precision Medicine

The Suite of Biomarkers in AgingSOS™ Panel

Biomarkers	Basic	Best	Elite
Circulating NAD (plasma NAD)	•	•	•
SA-β-galactosidase (β-gal)	•	•	•
Reactive oxygen metabolites (ROM)	•	•	•
Total antioxidant capacity (TAC)	•	•	•
Vitamin D	•	•	•
High sensitivity C-reactive protein (hs-CRP)	•	•	•
Glycated serum protein(GSP)	•	•	•
Low density lipoprotein (LOL)	•	•	•
Albumin	•	•	•
Alanine aminotransferase ALT)	•	•	•
Alkaline phosphatase (ALP)	•	•	•
High density lipoprotein (HDL)	•	•	•
Intracellular NAD		•	•
Creatinine			•
Vitamin C			•
Cortisol			•
NAD degrading enzyme (NADase)			•
SIRT1			•
IL-6			•
IL-8			•
IL1-β			•
TNFα			•
Calcium			•
Яштс			•
8-oxo-dG (oxidative DNA damage)			•
Lactate dehydrogenase (LDH)			•
Molecular age			•

AgingSOS™ is a biomarker panel that evaluates molecular and cellular activities that change with age and predispose aging people to develop age-related diseases like cancer, diabetes, and atherosclerosis, etc.

Indicators of **chronic inflammation**, **cellular senescence**, **oxidative stress, antioxidant capacity, protein glycation, tissue stress and damage, and micronutrients** are among the **over 25 biomarkers** in the AgingSOS™ test that are crucial for aging and age-related disorders.

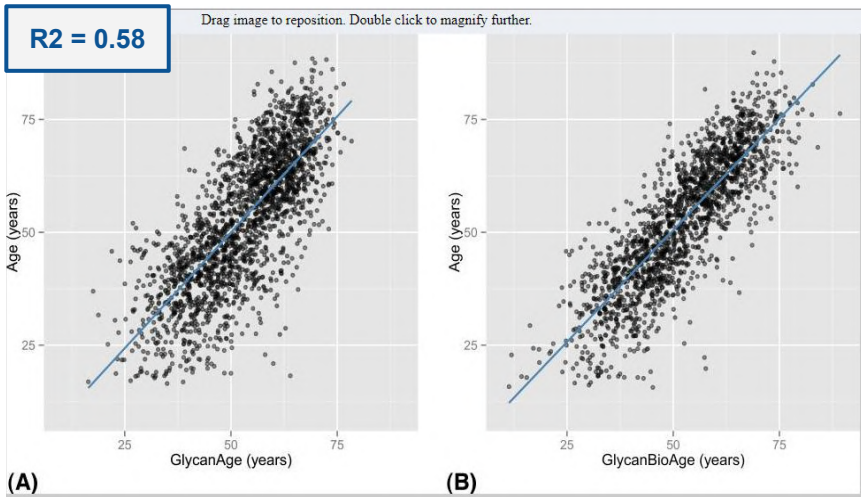
Finally, AgingSOS™ gives information on overall wellness, as evaluated by the unique **W-Index™**, the risk of developing age-related diseases, and viable solutions to increase wellness and minimize illness risk through lifestyle modifications and nutritional supplementation.

Calculation of W-Index™ is based on Jinfiniti's proprietary formula derived from artificial intelligence analysis with an extensive database on healthy and diseased people.

Source: Jinfinity Precision Medicine

GlycanAge: Biomarker Panel Based on the IgG Glycation

Prediction of Chronological Age from IgG Glycans



Several **IgG glycans** (including FA2B, FA2G2, and FA2BG2) change dramatically with age, according to the study, and the combination of these three glycans **can explain up to 58 percent of the variance in chronological age**, far more than other biological age indicators like telomere lengths.

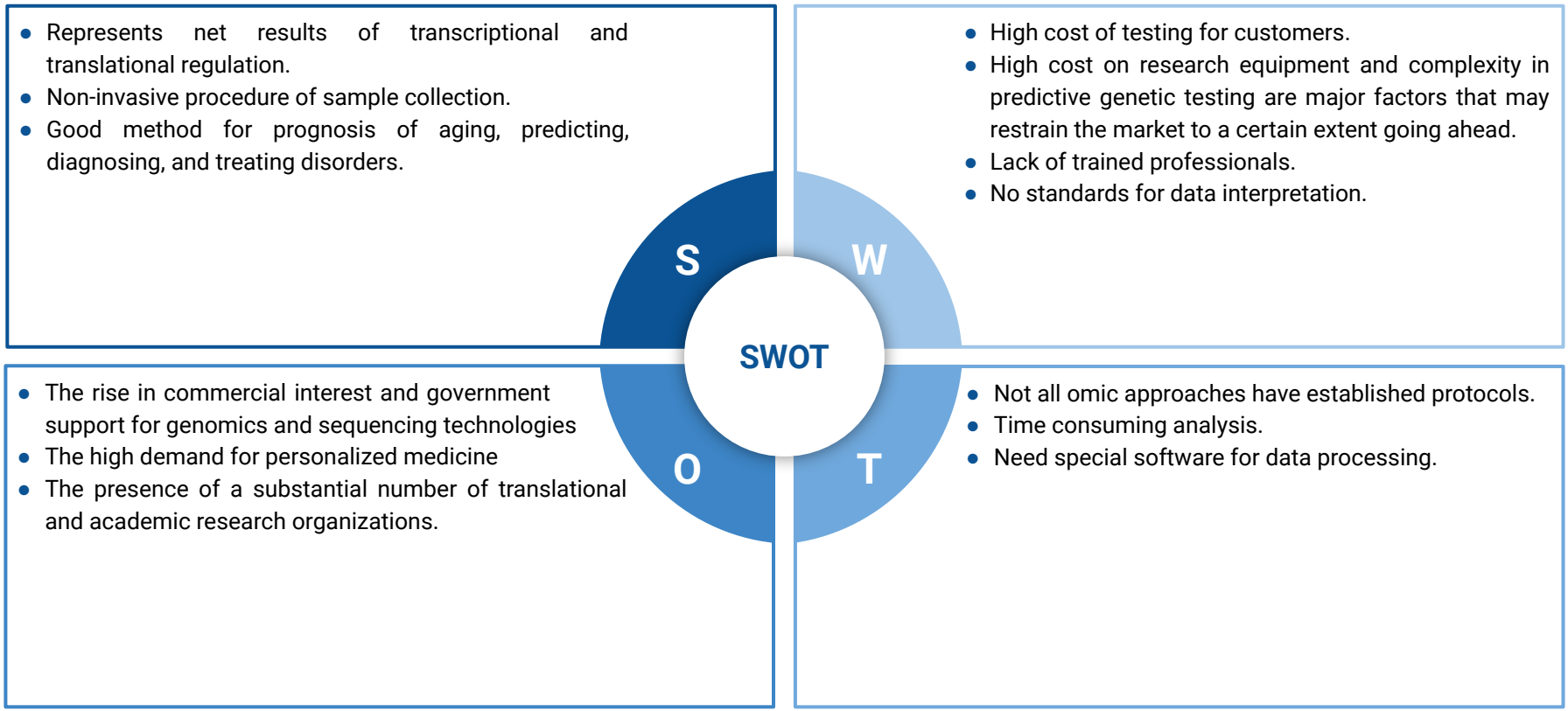
GlycanAge is a sophisticated test that looks at the status of the immune system and inflammation to determine the biological age. **The various glycans linked to IgG are examined in this assay**. IgG's activity can be changed from pro-inflammatory to anti-inflammatory depending on the type of glycans attached to it. The balance between them determines one's overall health and, as a result, one's biological age.

A person is not required to attend a laboratory in order to take a test. Only a GlycanAge set should be purchased. The finger is then pricked on its own and a drop of blood is transferred to special strips included in the kit. Following that, the materials are mailed.

Finally, a person receives the results of his analysis in the mail, together with a description of the biological and chronological age. Following that, the company arranges for a session with an expert who will advise on how to minimize or slow biological aging.

Source: Glycans Are a Novel Biomarker of Chronological and Biological Ages

Omic Biomarkers: SWOT Analysis



- Represents net results of transcriptional and translational regulation.
- Non-invasive procedure of sample collection.
- Good method for prognosis of aging, predicting, diagnosing, and treating disorders.

- High cost of testing for customers.
- High cost on research equipment and complexity in predictive genetic testing are major factors that may restrain the market to a certain extent going ahead.
- Lack of trained professionals.
- No standards for data interpretation.

- The rise in commercial interest and government support for genomics and sequencing technologies
- The high demand for personalized medicine
- The presence of a substantial number of translational and academic research organizations.

- Not all omic approaches have established protocols.
- Time consuming analysis.
- Need special software for data processing.

Key Takeaways: Omic Biomarkers

- Only **Genomic biomarkers** reach to clinical application and are successfully used for diagnostics as age-associated disorders as prognosis of aging in patients.
- More than **60%** of commercially available omic tests are **transcriptomic, metabolomic and proteomic** for personal using without medical assistance.
- The most of the companies are involved in **research kit/genetic test development**. However, there is a promising number of companies building a **software and applications**. Approximately **60%** of companies are located in **North America**.
- The modern market is characterized rise in **commercial interest** and **government support** for genomics and **sequencing technologies**, high demand for **personalized medicine**, and the presence of a substantial number of **translational and academic research organizations**. From the other hand, genomic tests are relatively **niche market** with a number of services available over the internet.
- According to the **Genomic assay** the **main biological pathways** that can have clinical and commercial interest are **Mitochondrial Dysfunction & Oxidative Stress**, **Proteostasis Loss**, **DNA Replication, Elongation & Repair** & **Transcription and Inflammation**
- Biomarkers confirmed via **Proteomic assay** of human plasma are **GDF15, Somatostatin, SOD, Fibronectin,** and **SERPINs**. They are significantly correlated with age and can be promising markers of age-related changes.

FemTech Biomarkers

Femtech Biomarkers Overview

1. FemTech can be related to software, products and services, and diagnostics that use technology to support women's health.
2. In the FemTech market, Reproductive Health is the largest focus but FemTech is not entirely limited to this category.
3. Other popular and widespread areas in FemTech include Pregnancy & Nursing, General Healthcare, Diagnostics, and Periods.
4. Metrics are tackled via platforms (apps, telehealth, etc.), deep tech (AI, ML and big data), and devices (wearables, sensors, remote patient monitoring.)
5. The FemTech industry can be be understood as a continuum process – pre-care → during care → post-care.

Why FemTech is Becoming More Important Now?

The contribution of a woman's health potential throughout pregnancy is enormous. Moreover, the health of the reproductive system, overall health, and controlled pregnancy all play a significant role in the birth of a healthy kid. Specialized medical attention should be given to maximize pregnancy success for both the baby and the mother.

Women are standing up for their rights in all aspects of life, like workplace, health, and equality now more than ever. With the rise of more women dedicating themselves to career, women are deciding to have children later in life and thus require more medical intervention.

More women start thinking about themselves as an individual with own necessities and want to take care of their health in every sphere, including general healthcare, sexual healthcare, emotional wellbeing, pregnancy, period, etc.

Considering these facts, there is a demand for improvement and efficiency of women's healthcare to meet these demands.

Source: FemTech Industry 2021/Q2 Landscape Overview

Femtech Biomarkers

The term **biomarker** (biological marker) refers to a broad range of measures that capture what is happening in a cell or organism at a given moment. Biomarkers are objective medical signs (as opposed to symptoms reported by the patient) used to measure the presence or progress of disease or treatment effects. The **female biomarkers** are specific to a woman's body and oriented on events that may happen only in a woman's organism. In this report, the female biomarkers are divided into five subcategories: **biomarkers of female cancers, fertility biomarkers, pregnancy biomarkers, biomarkers of female reproductive health, biomarkers of general women's health**. All these categories connect with each other, and most companies belong to few categories.

Biomarkers of female cancers refer to biomarkers that diagnose or predict women cancers (breast, ovarian, endometrial cancers, etc.).

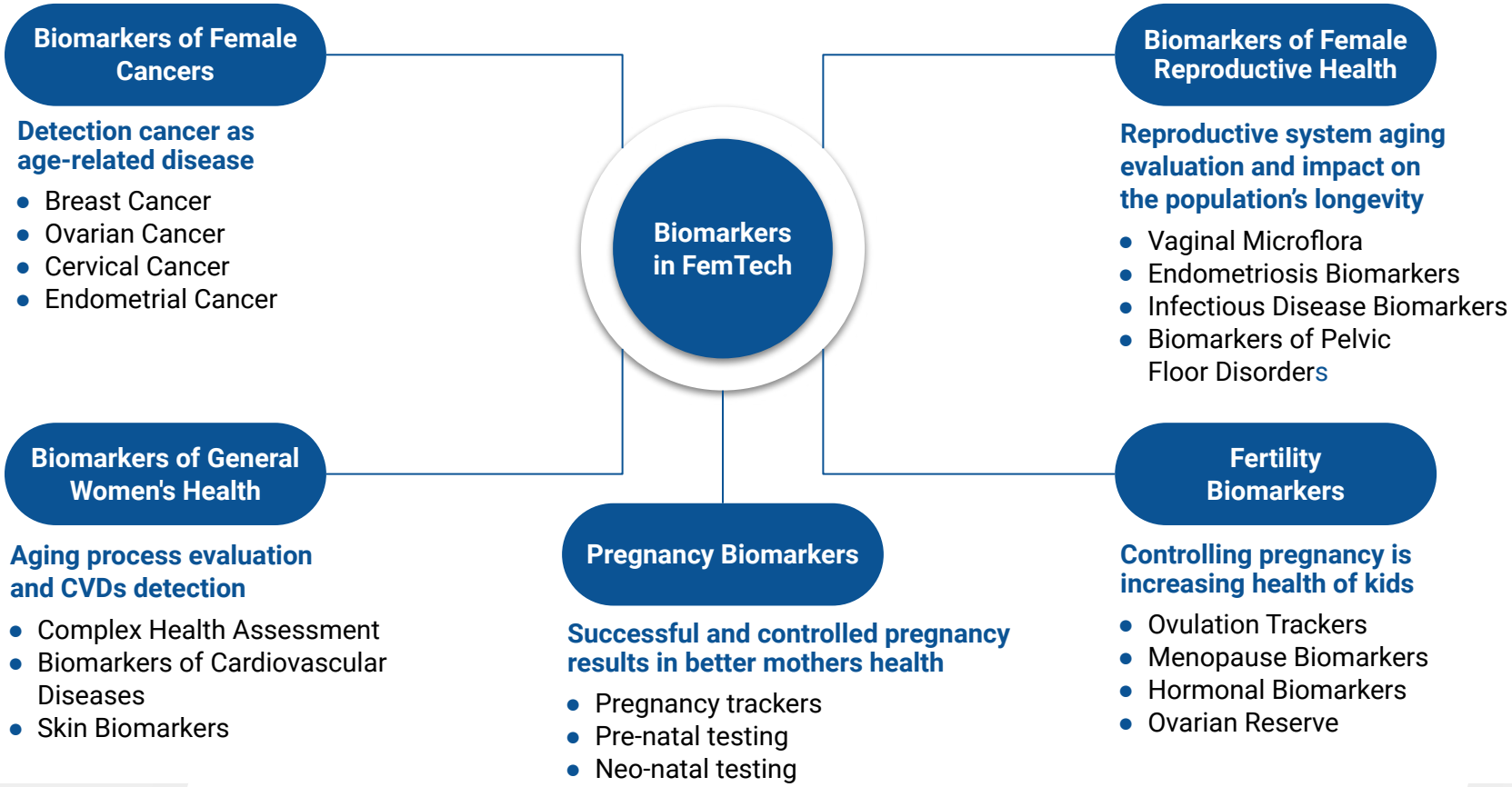
Fertility biomarkers refer to biomarkers that assess women capability of getting pregnant and giving birth.

Pregnancy biomarkers refer to companies that develop or implement biomarkers to monitor various events during pregnancy.

Biomarkers of female reproductive health category refers to biomarkers that diagnose or predict various conditions in women reproductive system that can affect life quality.

Biomarkers of general women's health refer to biomarkers of any women body system except reproductive. It can be cardiovascular, gastrointestinal, skin etc.

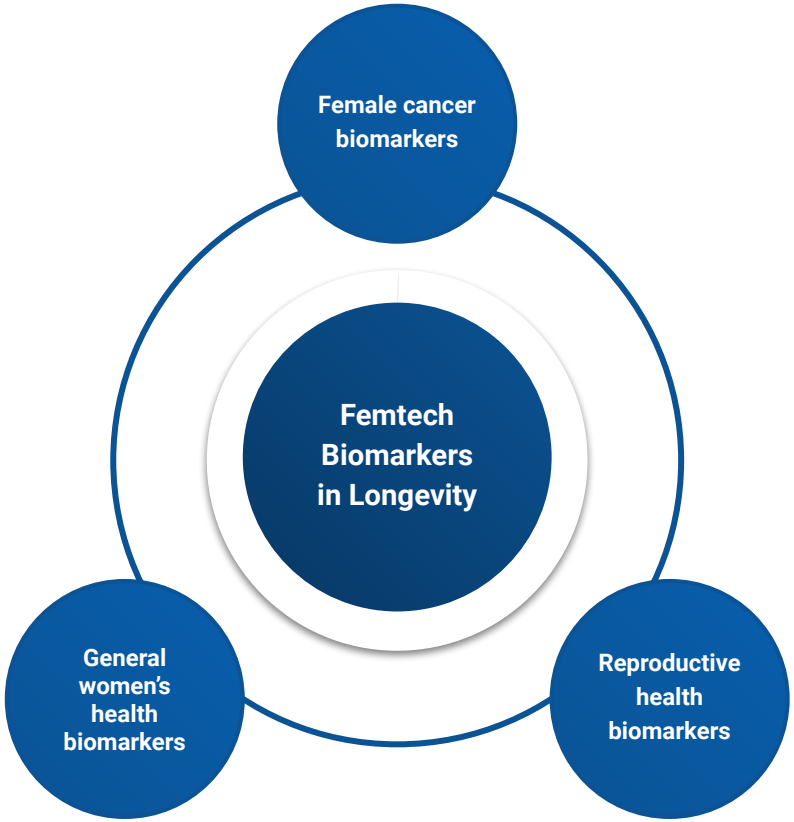
Femtech Biomarkers



Femtech Biomarkers in Longevity

The aging process leads to the loss of functions in several physiological systems, which are often accompanied by the development of age-related diseases. Biomarkers of aging are tools used to provide a quantitative foundation upon which to estimate the overall health status and the therapeutic efficacy of clinical, health-span-extending interventions.

Femtech biomarkers indeed provide specific information about functional activity and the overall health status of female organisms. Thus, detecting and analyzing Femtech biomarkers enables a personalized approach in the aging-related field. Nowadays, many biomarkers of aging define not only one but a restricted set of physiological functionalities whose disruptions are known to trigger the onset of specific aging-related disorders. Furthermore, the following Femtech Biomarkers can be linked with longevity: biomarkers of female cancer as one of the leading causes of mortality (breast, ovarian, cervical, endometrial cancer), reproductive health biomarkers as the indicator of population aging, and finally, biomarkers of general women's health.



Source: aging Research Reviews

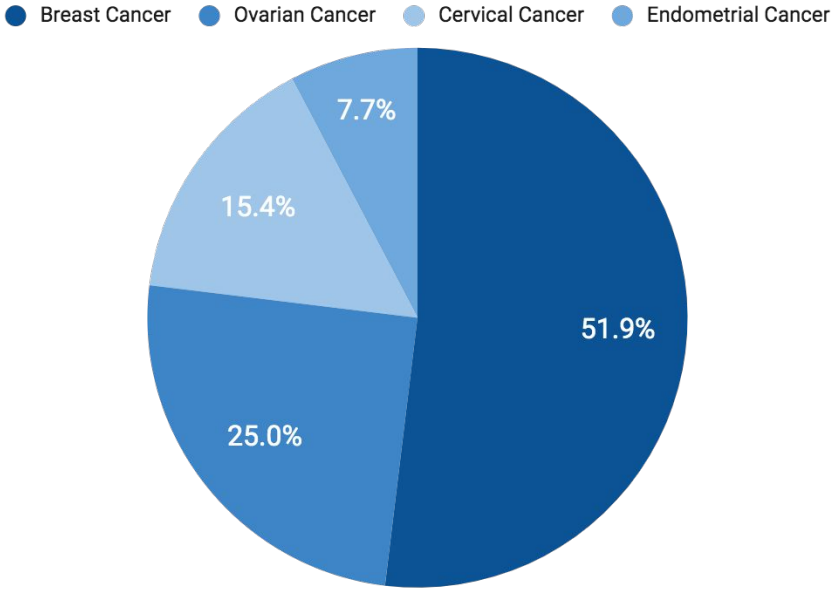
Biomarkers of Female Cancers

Cancer is a significant threat to women's health and wellbeing. Statistics says that **about 1 out of 8 women facing this disease over the life span (13%).** Only in the United States, the estimated number of new breast cancer cases in 2021 was 281,550, while the percentage of death was 7.2. **Due to in time diagnostics and the proper treatment, 90% of women have a positive outcome, but this number can be extended.** Among the most frequent types of cancer remains breast cancer, ovarian cancer, cervical cancer and endometrial cancer.

We have divided all women cancer biomarkers respectively to the cancer type. The most common cancer is **breast cancer** (statistics stated above), so the most extensive fracture of cancer biomarker research was devoted to this topic. Breast cancer can be both hereditary and non-hereditary. Therefore, the diagnostics include genetic, biochemical, ultrasound and MRI imaging, biopsy and cyto biomarkers.

This urgent need promoted the development of numerous companies that provide up to date diagnostics via **genetic and biochemical testing, portable testing devices like ultrasound devices for mammography or cervical fluid trackers, and overall body assessment and imaging tools.**

Distribution by Subcategories, %



Source: National Cancer Institute

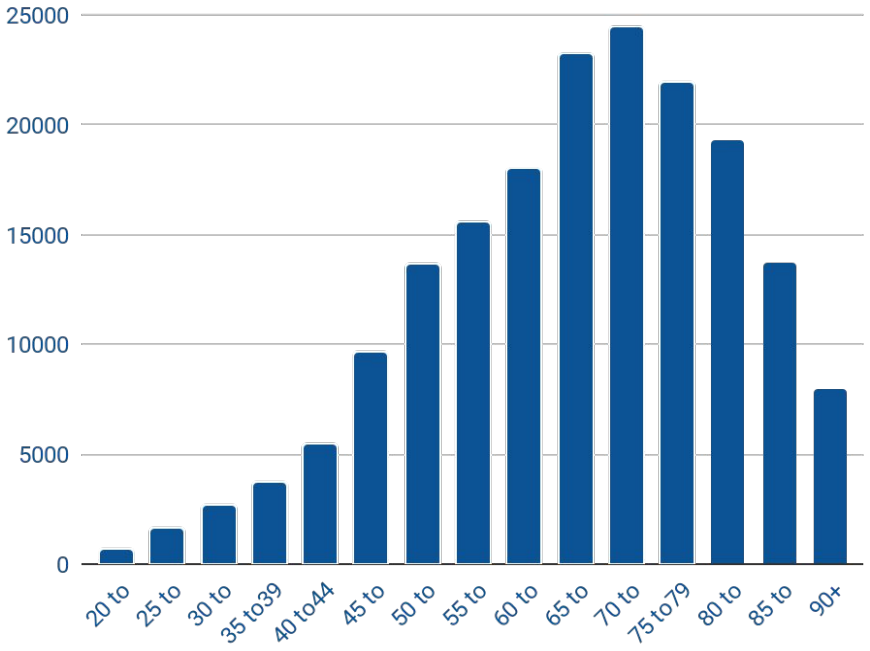
Biomarkers of Female Cancers in Longevity

Cancer is a great threat to female longevity. Usually, the presence of cancer positively correlates with aging due to metabolic, genetic, and physiological dysregulation. Female cancer is not an exception. Statistics say that the number of cancer cases gradually increases and reaches its peak at 70-74 years. However, after this, it declines. The reason for that is simple, not that many people survive to the age of 75-100.

If we talk about female cancers, the highest risk of developing **breast cancer** is women aged 25-49 (about 43%). In older adults, it declines to 21%. Survival rates of women diagnosed with breast cancer are 76%, reflecting the efficiency of new treatment technologies.

Assessment of female cancer biomarkers can not only predict suitable treatment but also **prevent the onset of cancer and promote longevity.** Biomarkers show the key pathways of cancer development, so prevention might include changes in lifestyle, nutrition, quitting bad habits, regular health assessments to monitor not only whole-body functioning but separate systems as well (reproductive).

Age and a Number of Cancer Cases in Female Population per 100,000 People, UK



Source: Cancer Research UK

Biomarkers of Female Cancers Notable Cases

IsonoHealth provides the world's first portable and automated 3D-breast ultrasound scanner called ATUSA. It combines a patented 3D ultrasound scanner and AI technology to **make whole breast scans and localize breast lesions** with consistent accuracy matching the best operators using traditional ultrasound equipment.

Ovation Diagnostics is a cancer diagnostics company focused on improving the detection of ovarian cancer. **Using a novel biomarker present in urine samples of ovarian cancer patients, they are establishing a laboratory assay and a rapid lateral flow test which will offer women an efficient, non-invasive and accessible technique of detecting ovarian cancer.** The novel test will show higher specificity and sensitivity for ovarian cancer in comparison to existing methods of detection.

MobileODT is an AI-based health-tech company that establishes medical device technologies for cervical cancer screening. It supports the World Health Organization strategic mission to eliminate cervical cancer by 2050. **"Eva System" is an innovative product that provides next-level cervical examination, complete digital solution for magnified cervical visualization, documentation and teleconsultation.**

Pregnancy Biomarkers

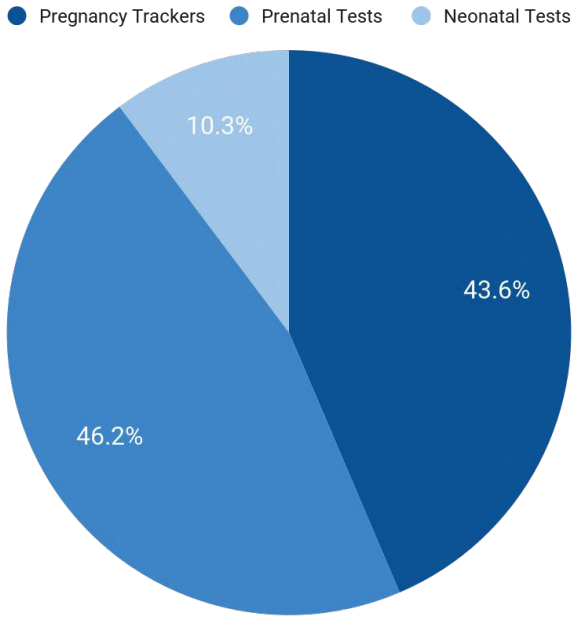
The **pregnancy category** refers to companies that develop or implement biomarkers to monitor various events during pregnancy. This category was roughly subdivided into three subcategories: **pregnancy trackers**, **prenatal testing**, and **neonatal testings**.

The **pregnancy trackers** are biomarkers that observe how pregnancy go, determine the risk of preterm birth and preeclampsia, and assess the correctness of fetal development. Additionally, there are few tests with biomarkers for pregnancy detection. This subcategory contains many devices such as portable ultrasound or electrocardiograms to at-home fetal condition detection.

The **prenatal testing** subcategories refers to fetal testing mainly for specific genetic abnormalities. These tests include screening for single-gene disorders that can cause such conditions as cystic fibrosis, sickle cell disease, spinal muscular atrophy, and chromosomal abnormalities such as Down syndrome. Additionally, many companies in this subcategory perform paternity tests.

The **neonatal subcategory** is the smallest subcategory which refers to newborn screenings. Often, these tests detect biomarkers of rare genetic, hormone-related, and metabolic conditions that can cause serious health problems.

Distribution by Subcategories, %



Pregnancy Biomarkers: Notable Cases

Sera Prognostics was founded to develop diagnostic tests for the early prediction of a woman's individualized risk of premature birth, preeclampsia, and other pregnancy complications. Sera's tests are designed to give women and their physicians the power and time to make a difference in maternal and newborn health with individualized treatment and care plans. Their PreTRM test detects protein levels in the blood that are highly predictive of premature birth.

SERA PROGNOSTICS®

Ravgen specializes in non-invasive prenatal genetic testing and paternity testing. Ravgen is focused on developing non-invasive prenatal diagnostic tests based on fetal DNA present in maternal blood. They diagnose single-gene disorders, such as cystic fibrosis, sickle cell anaemia and spinal muscular atrophy, chromosomal abnormality - Down Syndrome, and establish paternity. The main feature of these tests is that they can be implemented in the early stages of pregnancy.

RAVGEN

Metabolomic Diagnostics is a deep-tech company specialized in the development of novel biomarkers for complex diseases. The company aims to develop biomarkers that can determine in early pregnancy the risk of developing complications in women's later pregnancy. And the establishment of personalized care in time may help her to avoid such complications. The company focuses on preeclampsia, gestational diabetes, preterm birth, and in-uterine growth restriction.

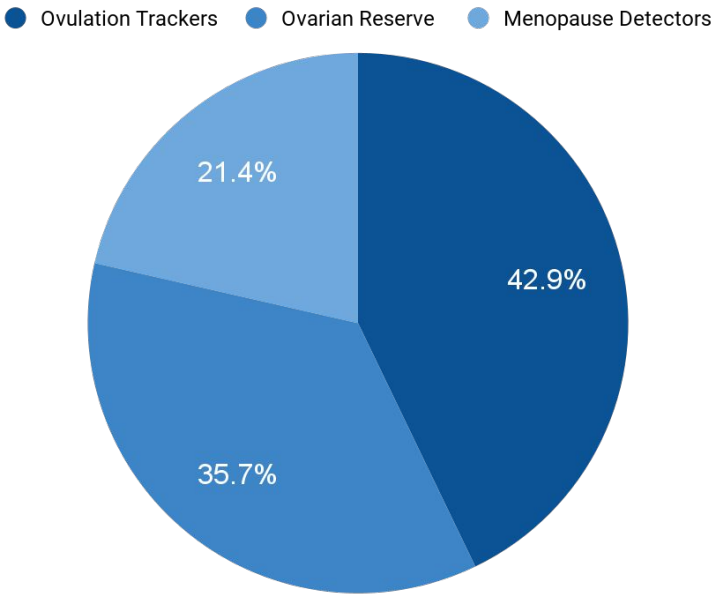
METABOLOMIC DIAGNOSTICS

Fertility Biomarkers

The fertility rate is a standard metric for assessing women capability of getting pregnant and giving birth. Nowadays, the mean number of children per woman is only around 2, while during the previous century it was from 4 to 7. The reason for that can be the modern way of life as well as various environmental factors. As women age, the rate of giving birth decreases due to ovocytes depletion and reproductive system aging. **If at 25 years chance of natural pregnancy is 25%, by the age of 40, it is only 5%. Infertility affects 10% of women between the ages of 15 and 44 in the U.S.**

Assessment of fertility(infertility) can be done by checking up a wide range of fertility biomarkers. It includes **ovulation trackers, ovarian reserve analysis, menopause detectors, and biochemical tests for hormones and microelements.** Ovulation tracker helps women define what is happening with their body during this cycle period and find out the best days to conceive. Hormonal balance assessment usually includes tests for Estradiol, Progesterone, Luteinizing Hormone, Follicle-Stimulating Hormone, etc., and inform not only about fertility or infertility but also the general health of women. Ovarian reserve check-up is a good way to analyze the potential chances of getting pregnant. We decided to add menopause detectors to this biomarkers group because it is the logical end of the fertility period.

Distribution by Subcategories, %



Source: Centers for Disease Control and Prevention

Pregnancy and Fertility Biomarkers in Longevity

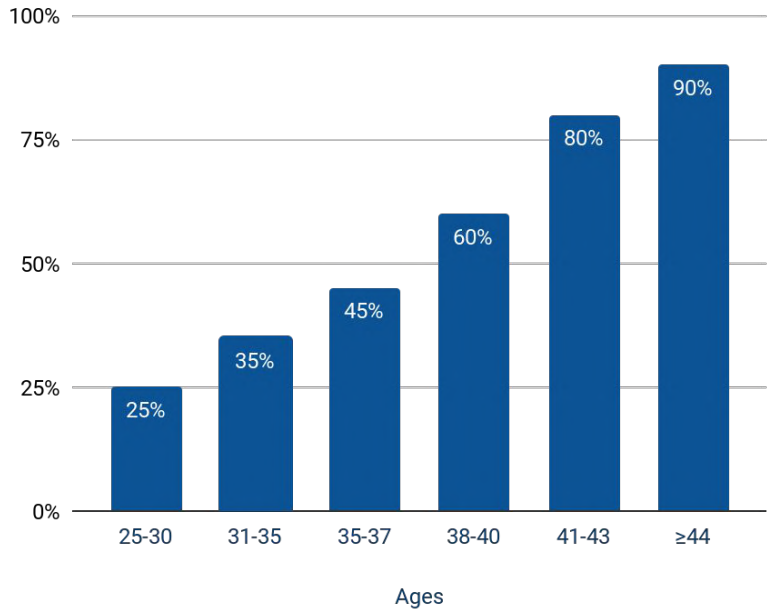
Pregnancy and fertility biomarkers measure reproductive capabilities and the general health of women at any age. On the other hand, **infertility** is a harbinger of various health risks in women, such as early mortality. Infertility status presented in a woman's reproductive years is an early biomarker of risk stratification later in life, which includes not only absence of pregnancy but also adverse health events that underlying reasons of infertility.

In general, infertility increases with age due to the accumulation of **genetic mistakes** in oocytes. It can be caused by different environmental factors such as radiation, chemicals, smoke, free radicals, and toxins. But these mistakes can be a reason for female infertility as well.

Another reason for infertility can be ovarian reserve depletion. The biomarker that clinicians use to estimate the number of oocytes is the **Anti-Müllerian hormone**. The overall levels of AMH decline accelerated after 40 years of age, so it is considered to be a biomarker of reproductive aging.

Overall, even though the percentage of infertility cases increases with age, there are various ways to cure it, **eliminating its causes**.

Percentage of Genetically Abnormal Embryos in Different Age Groups, %



Source: Fertility and Sterility, 2014

Fertility Biomarkers: Notable Cases

MiraCare markets the first FDA and CE registered comprehensive women's health monitoring platform with 99% of accuracy in clinical trials. It provides a palm-sized device for personalized ovulation tracking, fetal health monitoring, measuring ovarian reserve and detecting menopause at home, with expandability into chronic disease monitoring. The data automatically syncs to the Mira app. Using AI technology, it learns personal health patterns. Telemedicine connects users with doctors.

NOWDiagnostics develops and manufactures diagnostic tests that utilize a single drop of blood, serum or plasma and deliver results within minutes. One of the products is **the ADEXUSDx® hCG Test** - an immunoassay used for the qualitative detection of human chorionic gonadotropin in blood, plasma, or serum. Indeed, human chorionic gonadotropin detection helps health care professionals in the diagnosis of early pregnancy.

EverlyWell is a digital health company that establishes consumer testing, virtual care, at-home collection tests, and digital results. It provides a number of women's health tests, including ovarian reserve test, perimenopause test, postmenopause test and women's fertility test. All of these tests utilize finger prick sample collection to quickly and accurately measure the levels of specific hormones in the blood.

Biomarkers of Female Reproductive Health

The **health of reproductive system biomarkers** category refers to biomarkers that diagnose or predict various conditions in women reproductive system. This category was subdivided into three subcategories: infectious disease, vaginal microflora, endometriosis biomarkers, and pelvic floor disorders biomarkers.

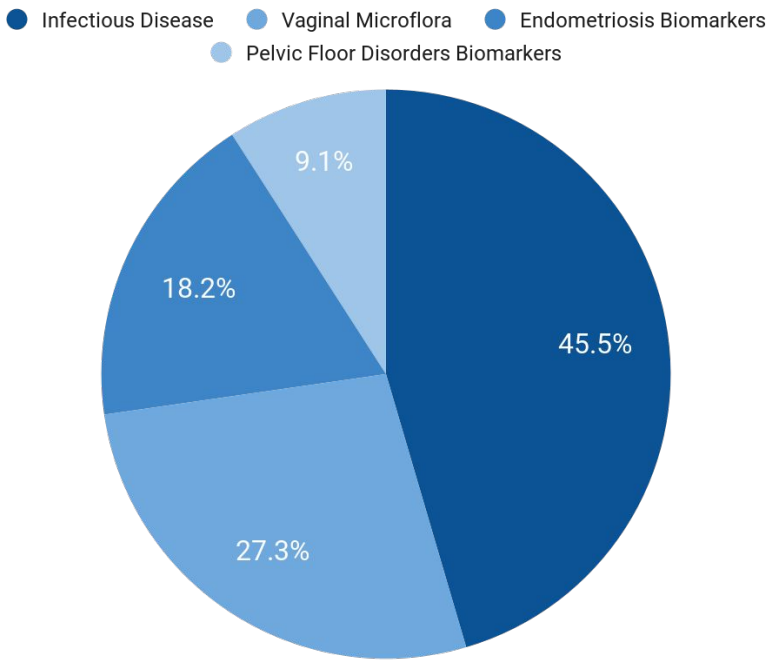
The **infectious disease** subcategory covers different tests that screen for women contagious diseases. Most of the companies focus on human papillomaviruses (HPVs). It is not surprisingly - about 80% of sexually active people are infected with HPV at some point in their lives. Moreover, two HPV types (16 and 18) cause 70% of cervical cancers and pre-cancerous cervical lesions. Other infectious diseases are STDs (HIV, HSV-2, chlamydia, gonorrhoea, etc.).

Many companies develop **vaginal microflora biomarkers**. The disorders in the vaginal microflora may cause such conditions as vaginosis and vaginitis.

The **endometriosis biomarkers** are also the subcategory with rapid development. The importance of early diagnostic of this condition lies in the fact that endometriosis often causes infertility.

The last subcategory is **pelvic floor disorders biomarkers**.

Distribution by Subcategories, %



Source: WHO

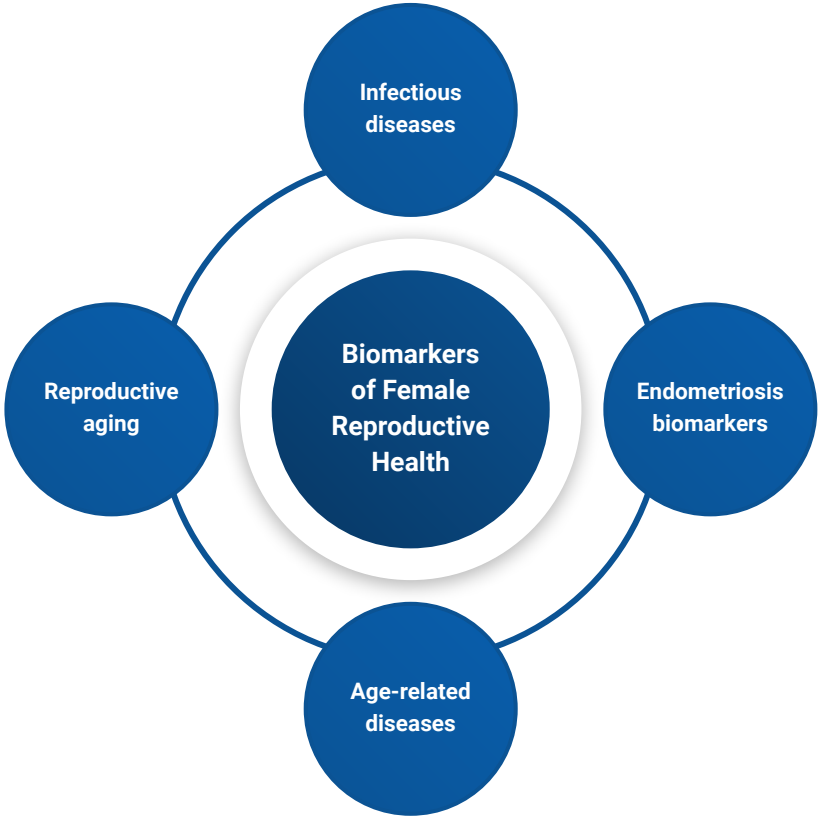
Biomarkers of Female Reproductive Health in Longevity

Female reproductive health plays an essential role in women's longevity. Firstly, one should consider the impact of women's reproductive health on the population's longevity. Thus, reproductive diseases decrease the probability of pregnancy.

Another important reproductive health biomarkers are **infectious disease.** Some of them are known to causing specific types of cancer. Indeed, cancer is one of the major causes of human mortality. As mentioned earlier, two types of human papillomaviruses(16 and 18) cause 70% of cervical cancers and pre-cancerous cervical lesions.

Endometriosis biomarkers can indicate the probability of endometrial as well as ovarian cancer development.

Female reproductive aging is usually associated with various **age-related diseases**, such as type 2 diabetes mellitus and a decline in fertility 5–10 years before menopause. Biomarkers of reproductive aging give insight into pathological processes underlying such changes in female organisms and provide information on possible ways to treat them. All in all, **Biomarkers of Female Reproductive Health** are a good key for early diagnostics of many illnesses and age-related diseases, which is **key to the proper treatment and healthy longevity.**



Biomarkers of Female Reproductive Health: Notable Cases

DotLab is a women's healthcare technology company developing a breakthrough, a non-invasive blood test that aids in diagnosing active endometriosis. The test analyzes microRNA biomarkers associated with endometriosis with the help of Machine Learning. The test was developed based on over a decade of peer-reviewed scientific research and development, demonstrating the association of microRNAs to endometriosis and infertility.

LetsGetChecked is an at-home health testing platform that connects customers to regulated laboratory testing to manage better and control one's individual health. They have a broad panel of various at-home tests: HPV, herpes, hepatitis B&C, Chlamydia, Gonorrhea, Trichomoniasis, HIV, Syphilis, Gardnerella, Mycoplasma are among them.

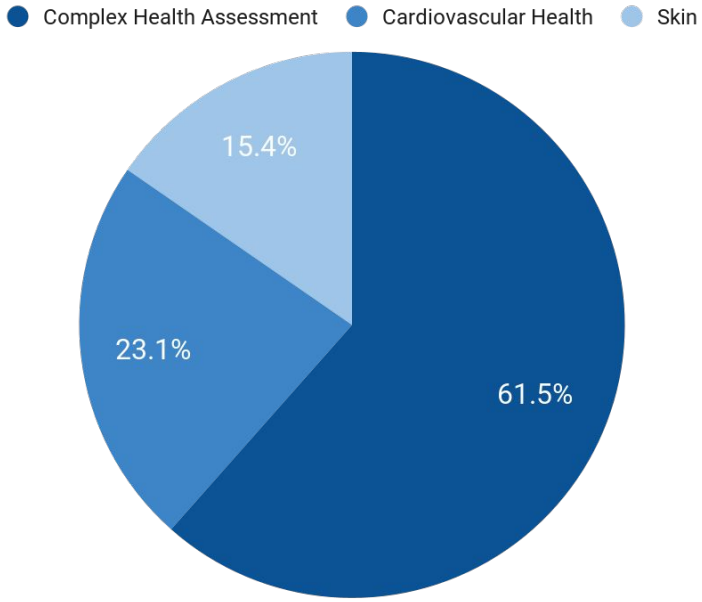
Gyntools was founded to provide a comprehensive remote diagnosis solution for vaginitis. Today, there is not a single comprehensive diagnostic tool that can diagnose all six primary conditions of vaginitis. The Gyntools system (Gyni) remotely analyses correctly (95%) all six primary vaginitis conditions, infectious and non-infectious, within five minutes with the help of Deep Learning. Gyni cost-effectively enables laboratory-quality results and requires only web communication and five minutes of waiting.

Biomarkers of General Women's Health

Women health includes not only the health of the reproductive system, fertility and cancer diagnosis but also **complex assessment of body state.** The body systems can not function independently—changes in one system influence on work of other anyway. Therefore, it is usually hard to define which part of the body the problem or disease occurs, so there is a need for a regular complex health assessment to monitor all available general health biomarkers.

Special attention is needed to **monitor cardiovascular health biomarkers and skin health as well.** Cardiovascular diseases are the number one killer for females. Statistics says that **every fifth woman dies of heart disease**. The main risk factors are obesity, an unhealthy diet, physical inactivity and drinking too much alcohol. Almost every woman face at least one of these factors regularly. So there is a need for regular assessment of cardiovascular health biomarkers. Some of the companies focus on the development of transportable heart trackers to make the affordable home assessment. Another focus is **skin health biomarkers**. Skin is a mirror of processes occurring in our body. The common skin disorders include acne, psoriasis, eczema and various food allergies. Right diagnostics and monitoring of skin health biomarkers can prevent not only the development of such disorders but also notice metabolic changes in other organ systems.

Distribution by Subcategories, %

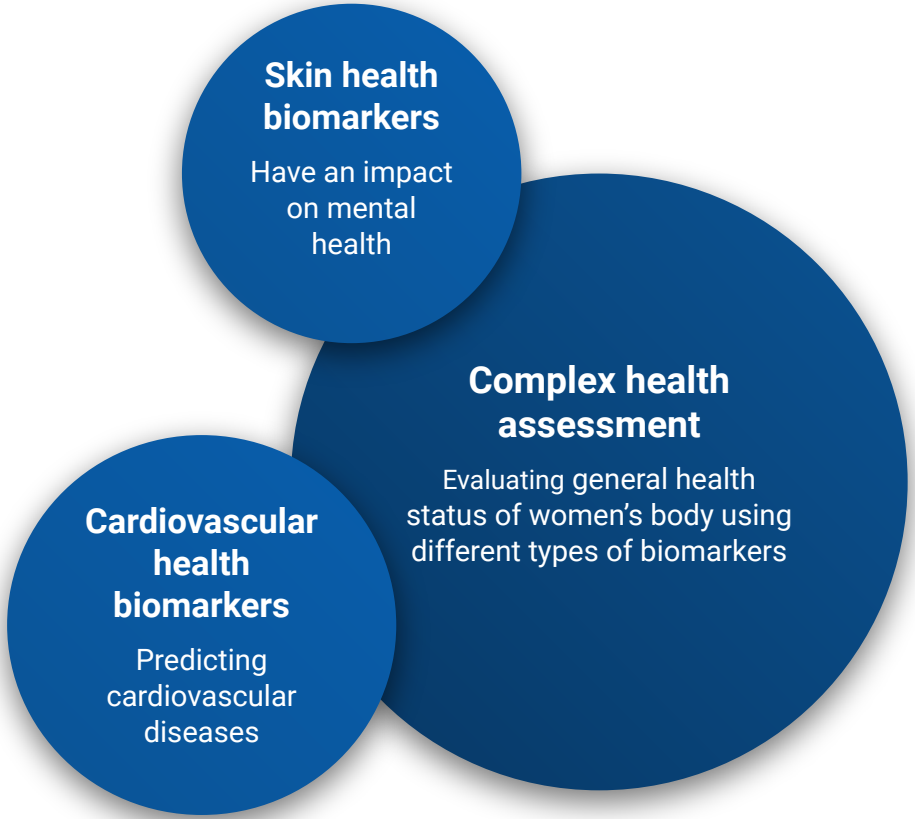


Source: Centers for Disease Control and Prevention

Biomarkers of General Women's Health in Longevity

Biomarkers of General Women's Health have shown a sufficiently strong association with aging. They include **cardiovascular health biomarkers** and **skin health biomarkers** as well. **Complex health assessment** also belongs to the Biomarkers of General Women's Health, indicating the general health status of women's organism.

For instance, cardiovascular diseases are known as one of the leading causes of mortality. As mentioned above, every fifth woman dies of heart disease. Skin health biomarkers play a significant role not only in metabolic health evaluation but also in mental health. Unfavourable mental health status can cause stress, which is indeed known as one of the aging factors. Aging can be defined as a complicated, multifactorial, time-dependent process. Thus, **compex health assessment** certainly helps consider all of mentioned above factors in different relationships and their impact on life expectancy.



Biomarkers of General Women's Health: Notable Cases

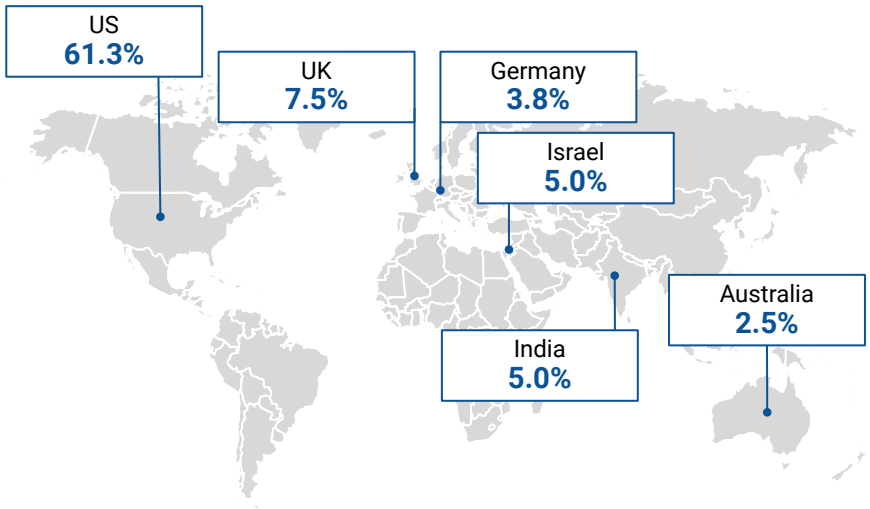
Gina Life is a femtech company developing a platform of biomarkers strategy supported by AI technology and data science. A unique and proprietary biomarkers panel is used for early detection in women's health space. A personalised test can be generated for every woman providing early detection of women related diseases.

Bloomer Tech uses biometric sensors in everyday women's clothing to read metrics such as electrocardiograms, pulse rates, respiratory rates, heart rhythm, etc. Data are analysed using machine learning and are accessible to users, doctors and medical professionals for real-time personalised healthcare.

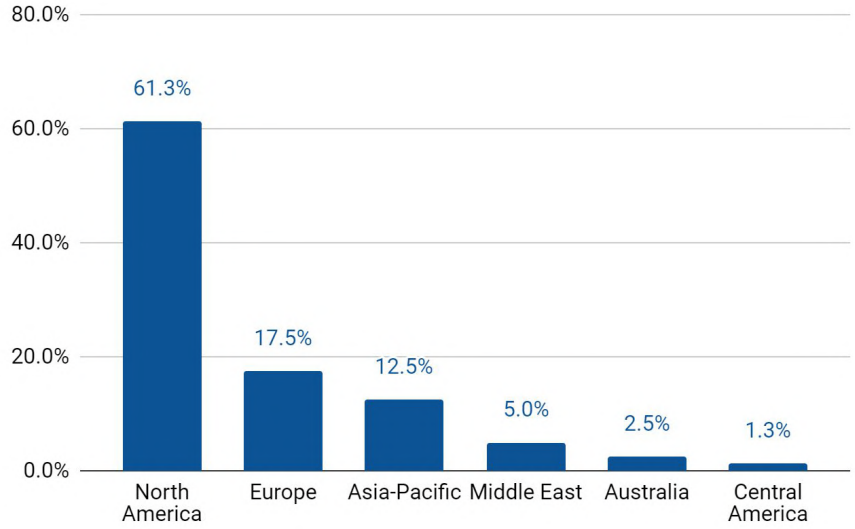
Lonvivo offers custom skincare recommendations based on genotypic, clinical, and demographic characteristics. Using AI technology, they recognise and analyse the signs of skin problems and propose the most effective personalised solutions.Collecting personal preferences, they can understand better customers needs and provide more tailored experience.

Market at a Glance: FemTech Companies

Distribution of Companies by Country, %



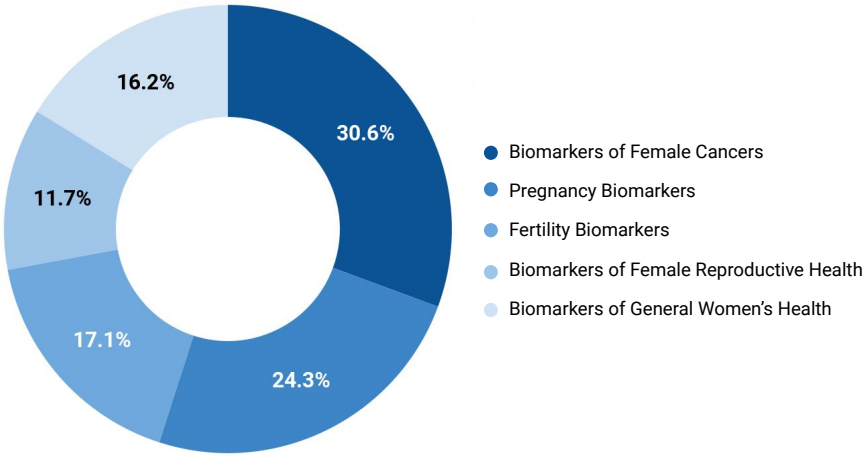
Regions with the Largest Number of Companies



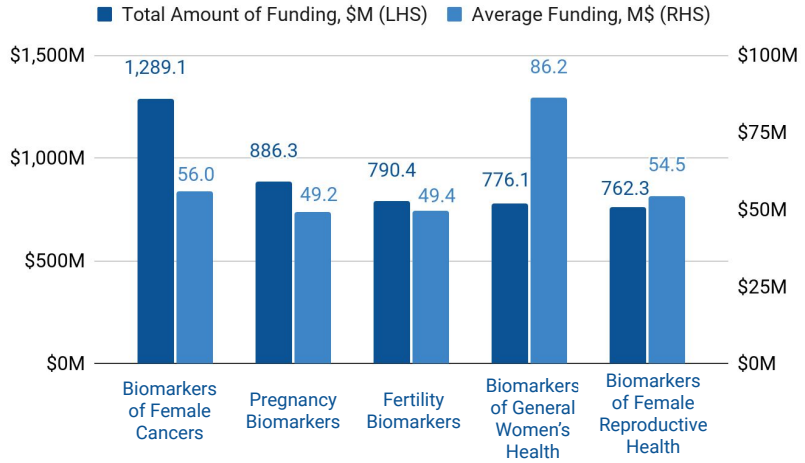
Most of the companies involved in the developing biomarkers of female health are allocated in the North America region **(in the US particularly 61.3%)**. Top second region is **Europe** where located **17.5% of companies.** Most of European companies are situated in the UK and Germany - business and research centres of the region. Almost 13% of companies are from Asia-Pacific region. **Around 5% of all companies are located in India.**

Market at a Glance: FemTech Companies

Distribution of Companies by Category, %



Funding Amount by Category, $M

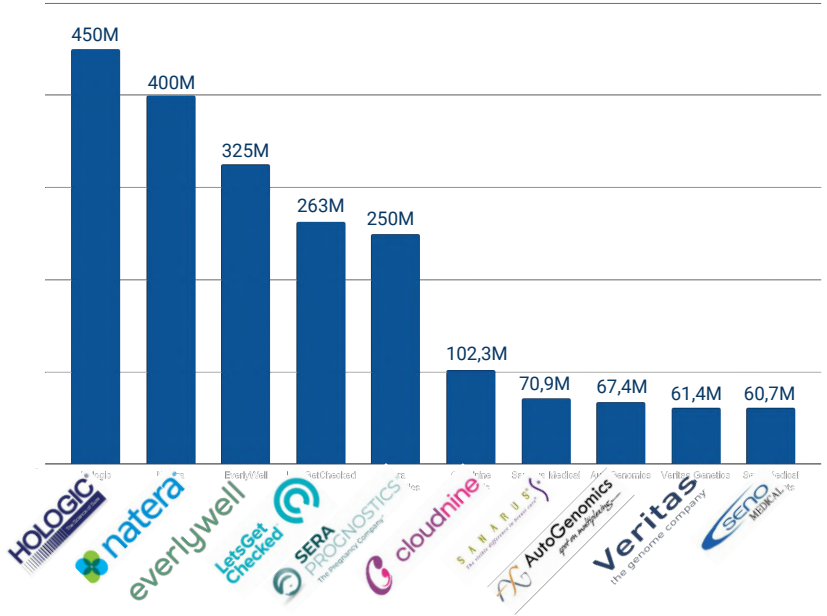


The **one third** of companies are involved in the field of Women Cancers Biomarkers - close to 31% of total number of companies. Companies involved in the development **Biomarkers of Female Cancers receive around $1.3B investments**, however, this field is only the second by average amount of investments.

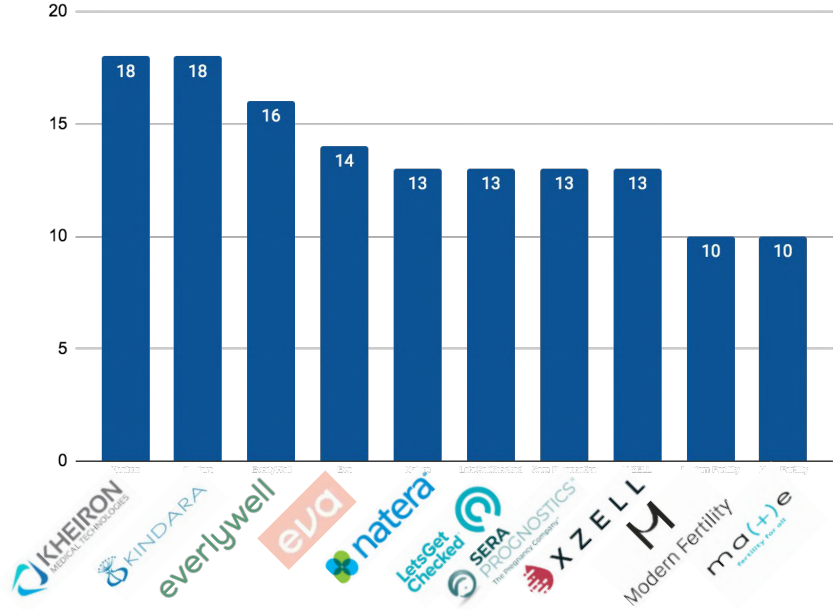
Around 24% of all companies are operates in the Pregnancy Biomarkers field. This area receives around $886M of investments. **Around 17% and 16%** of companies are doing **Fertility Biomarkers and Biomarkers of Female Reproductive Health respectively.** Being the last area by total amount of funding, Health of Reproductive System Biomarkers is the third by average amount.

Market at a Glance: FemTech Companies

Top Companies by Funding, $M



Top Companies by Investors Number

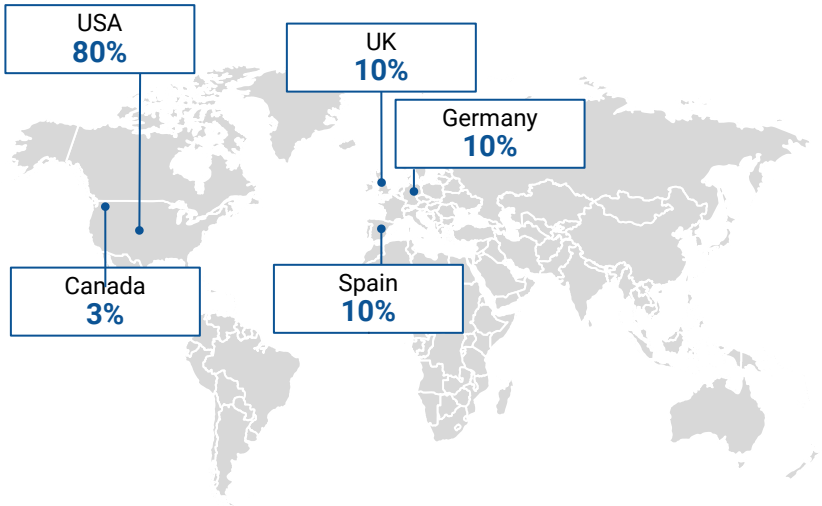


The company with the most significant funding is **HOLOGIC**, and its financing constitutes ~**450M$**. The second place is taken by **Natera** (**400M$**). Notably, both companies belong to the female cancers biomarkers category.

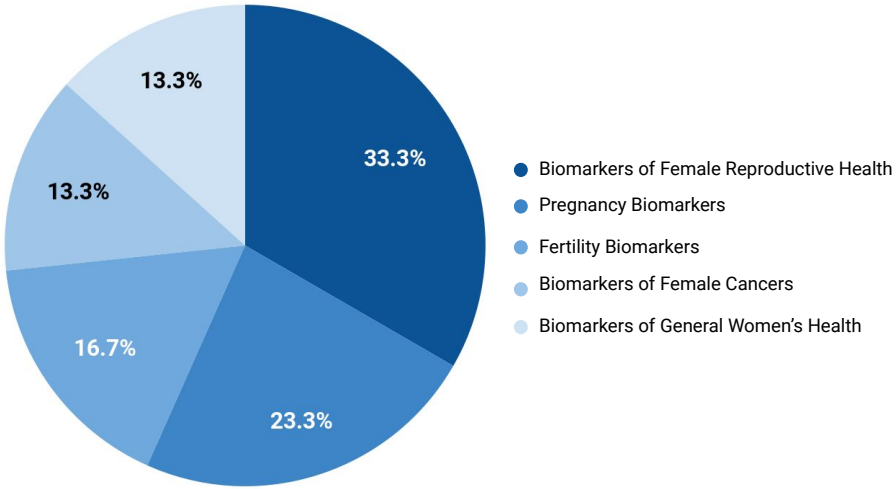
The companies with the most significant number of investors are **Kheiron** and **Kindara** (**18 investors**).

Market at a Glance: R&D Centres

Distribution of R&D Centres by Country, %



Distribution of R&D Centres by Category, %



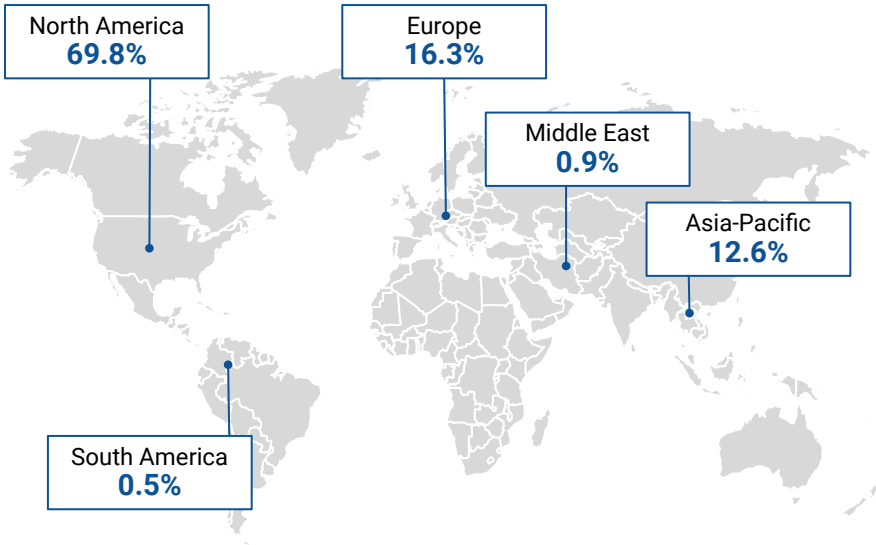
The **vast majority of R&D Centres** that conducts research of female biomarkers are located in the **United States (30%).** The United States is distantly followed by **Canada, Germany, Spain,** and **the UK** which make up by **10%** of all R&D Centers.

The major domain in which female biomarkers research are being conducted is Health of reproductive system biomarkers **- one third of R&D centres** conduct research in this field. It follows by **Pregnancy biomarkers and Fertility biomarkers**, which are studied by **23.3% and 16.7%** of R&D centres respectively. **Overall close to 73% of R&D centres explore biomarkers related to the reproductive health of women.**

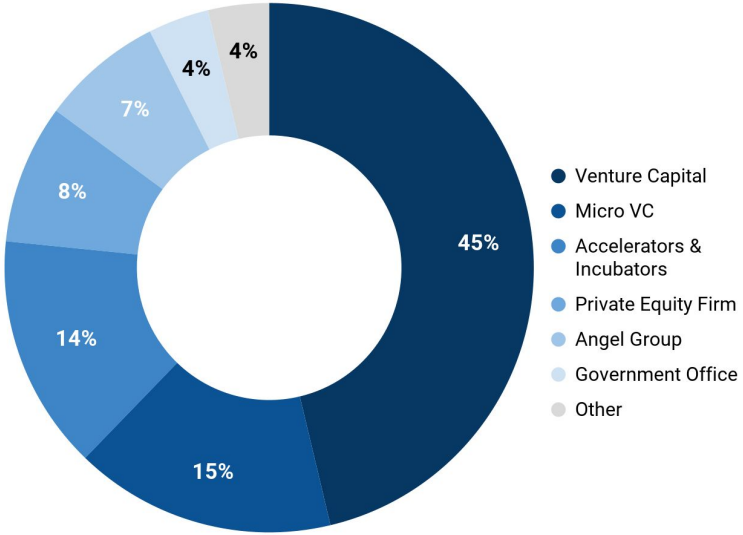
Source: Aging Analytics Agency analysis

Market at a Glance: Investors

Distribution of Investors by Regions, %



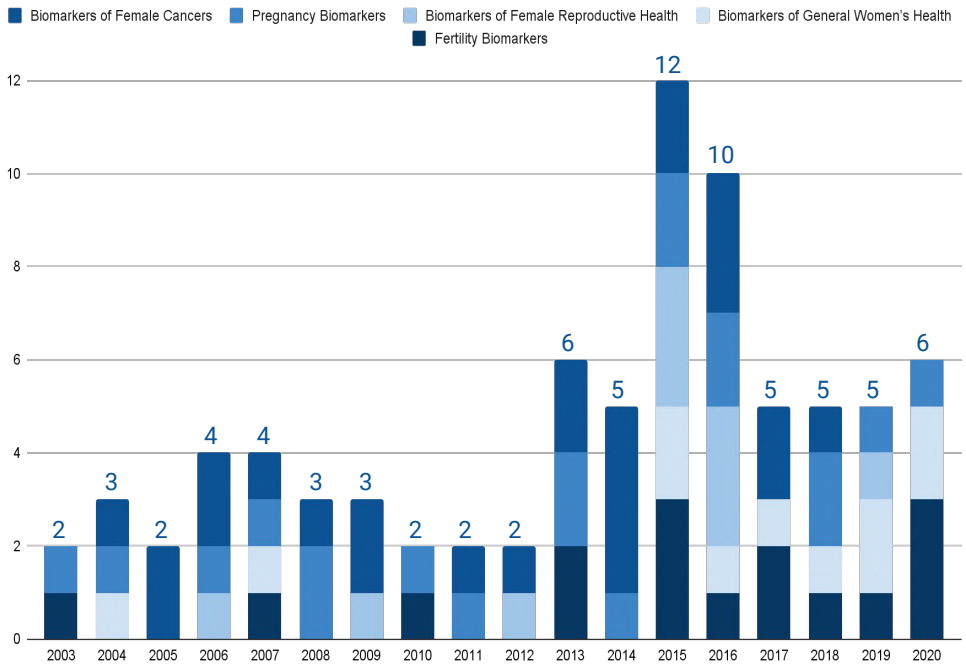
Main Type of Investors, %



The US is firmly in the lead in terms of the number of FemTech Biomarkers Investors **(69.3%). The UK** ranks the second (**9.3%**) and alone covers more than a half investors from **Europe region (16.3% of total)**. There are **12.6% of Asian investors** that mainly located in India (4.7%), China (3.3%) and Japan (2.8%).
More than **45%** of investors are **Venture capital** firms. Other 29% are small risky investors - **Micro VC (15%) and Accelerators (14%).**

Market Trends

New Companies: FemTech Biomarkers



The graph illustrates **the growth in the number of companies on the market** since 2003**.**

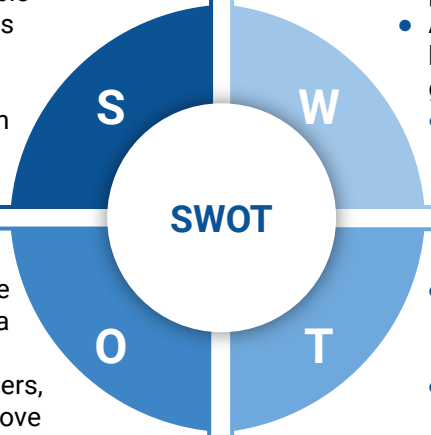
There has been a **rapid development** of companies that research/develop/implement FemTech biomarkers **since 2013**. The biomarker of **female cancers** is a top category in this development. Due to the FDA approval of new efficient breast cancer therapy, the investments in this area increased.

Due to the improvement of general awareness of women general and reproductive health biomarkers **after 2015 year** evolved, many new companies focused on **fertility, reproductive and general health, and cancer.**

The upward trend is also noticeable for the area of **fertility/infertility biomarkers**. The reason for that might be an increase in the number of women trying to conceive at the age of 30-40.

Source: Medical Oncology

FemTech Biomarkers: SWOT Analysis



- The comprehensive analysis of FemTech biomarkers will provide precise health status information of women.
- FemTech biomarkers can also be used to assess the early stages of a female disease as well as a individual's predisposition to it, which can assist people understand what preventive measures and treatments are required.
- Some FemTech biomarkers can be tested in both the home and the clinic, so women can monitor her heath state in comfortable surrounding.

- In case FemTech Biomarkers usually are concerned on female health they can not identify disease states at other organ systems, and it can be difficult to pinpoint the true issue without usage of other biomarkers panels.
- A complicated approach using several FemTech biomarkers, which can be costly and inaccessible to the general public, can yield an accurate result.
- Because the list of FemTech biomarkers is short, more research is required.

- The advancement of cutting-edge AI and machine learning technologies will make biomarker data analysis easier and more accurate.
- New biotechnologies such as portable analyzers, wearable devices, and digital technologies will improve quality of check-ups while lowering prices.
- The creation of new tests and treatments based on the study of the molecular mechanisms using FemTech biomarkers is a critical step toward eliminating of numerous female related diseases.

- The quantity and quality of biomarkers can be influenced by menstruation cycles which can impair the test's accuracy.
- There is a lot of disputed material in existing data archives, thus more investigation is needed.
- The biomarker data is incomplete, which could lead to erroneous conclusions for some demographic groups.

Key Takeaways: FemTech Biomarkers

FemTech is a constantly growing field of information technology that **combines solutions** and **startups** focused on women's health. This area includes **devices and applications related to a woman's reproductive and general health, menstrual cycle, fertility, pregnancy and women diseases. Women are playing a key role in sustaining a healthy population, thus their health is crucial for population longevity.**

Biomarkers of women's health development also focus on **fertility and pregnancy issues**. **Developments in those areas encourage and enable** better and more controlled pregnancy, resulting in an **increase in the number of healthier and desired kids**. Such positive population dynamics will increase the **overall longevity of future generations**.

Biomarkers in FemTech refer to 4 main areas of women life: **general health, reproductive health, fertility, pregnancy and women cancers**. The most considerable numbers of companies are focusing on developing cancer biomarkers because at least 13% of the female population face this disease during their lifespan (every eight women). Technology advances are made in the field of **home diagnostics**.

The most significant numbers of companies, investors and R&D centers are located in North America. The main focus of funding are biomarkers of **general women health and cancer**. And there is no surprise because they cover two main areas of women health and diseases and impact the wellbeing and longevity of women.

Regular assessment of FemTech biomarkers can not only increase the quality of female life but also **promote longevity**. These biomarkers reflect not only overall women's health but help to notice the onset of **reproductive age and age-related diseases**, which is key to eliminating causes that underlying physiological and molecular changes occurring in women's bodies during aging. The right treatment can reduce the speed of aging and promote a longer life span.

Physiological Biomarkers

Physiological Biomarkers Overview

Physiological biomarkers refer to measurements of physical capability and physiological function. It is a person's ability to perform the physical tasks of everyday living, are useful markers of current and future health. These anthropometric measurements and noninvasive tests are one of the clearest ways to assess age-related changes. The main advantages of physiological biomarkers are their simplicity and public accessibility.

The most common physiological biomarkers are **handgrip strength and gait speed**. These biomarkers assist in the evaluation of generalized weakness and frailty in middle-aged and older adults. Another example is physiological function biomarkers such as **pulmonary function tests, blood pressure, and pulse-wave velocity**, which might show specific organs' functional decline.

The physical capability and physiological function biomarkers are mostly implemented in clinics for the **overall health assessment of middle-aged and older adults**. However, such biomarkers are detectable only in the late stage of aging, so they are not helpful for early diagnostics.

Additionally, physical capability test are used in **population-based studies**. These objective measures complement self-reports, improve validity and reproducibility.

Physiological Biomarkers Examples

- **Handgrip strength**
- **Gait speed**
- **Chair rise time**
- **Standing balance**
- **Pulmonary function tests**
- **Pulse-wave velocity**

Source: Wiley Analytic Science

Devices for Physiological Biomarkers Assessment

Measurement of physiological biomarkers can be done biochemically or by using different devices. For instance, **Ultrasound diagnostics** of various organs and body parts, **Sphygmomanometer** for blood pressure measurements, **Glucometer** for blood sugar monitoring, **Spirometer** for measurement of lung capacity. Most of these devices are portable, so they can be used for **home diagnostics**.

The market of devices for physiological health measurements is growing so devices like **smartphones, smart watches** and **smart weights** can monitor BMI, heart rate, sleep quality and quantity, ECG monitors, and blood pressure. Recently, developers added a new feature - an oxygen level sensor. It became really popular due to COVID-19. The disease is causing hypoxia, so people diagnosed with this disease need to regularly monitor their oxygen level in order to avoid complications of the disease.

However, we can`t be sure about the accuracy of such devices, so there is a need for **regular clinical check-ups**. For example, to perform **Electroencephalography and Electrocardiography**.

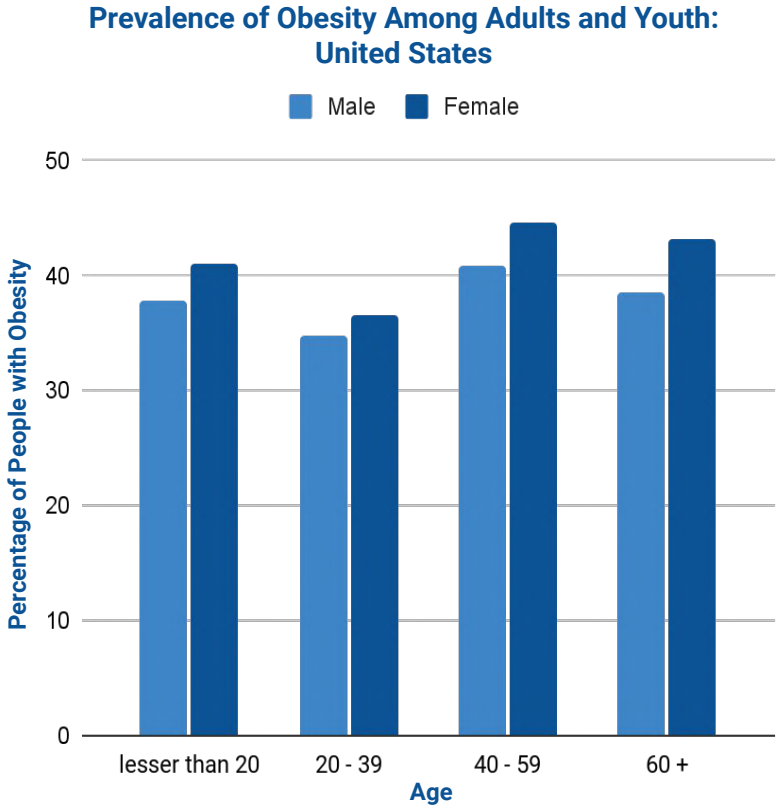
Obesity May Accelerate the Aging Process

BMI is a good physiological biomarker not only for overall physiological health assessment but also for the identification of the onset of **age-related diseases**. There are four categories: meaning below 18.5 defines underweight, 18.5–24.9 stands for a healthy weight, 25–29.9 defines overweight, and 30 and above reflects obesity. According to statistics, **in the USA percentage of obese people is 31.9%**.

Normal BMI **promotes longevity** in case there is a lower risk for different diseases onset. High meanings increase the rates of incidence of **heart disease, type 2 diabetes, sleep apnea, and colorectal cancer, which are some of the main age-related diseases**.

Insufficient weight is also dangerous because it increases the risk of **malnutrition, osteoporosis, anemia, and a range of problems that can result from various nutrient deficiencies.** It can also be a symptom of a **hormonal, digestive, or other problems**, which doesn't promote longevity.

The interesting fact is that obesity promotes **telomere shortening** due to oxidative stress. Also, obesity negatively correlates with **mitochondrial function** which stands for normal energy metabolism in cells.



Source: Obesity May Accelerate the Aging Process, Centers for Disease Control and Prevention

Biomarkers of Physical Function Domain Overview

Measures of physical capability

- Grip strength
- Walking speed
- Chair rise time
- Standing balance

Poor performance

Risks and threats

- Higher mortality rates
- Cardiovascular disease
- Dementia
- Institutionalisation and difficulties performing activities of daily living (ADLs)

Disadvantages

- Increasing proportion of people unable to perform these tests at older ages
- Considerable variability in the protocols of assessment
- Facilitate identification of those people performing best who cannot be distinguished by self-reported measures

Types of measures of physical capability

- Locomotor function
- Strength
- Balance
- Dexterity

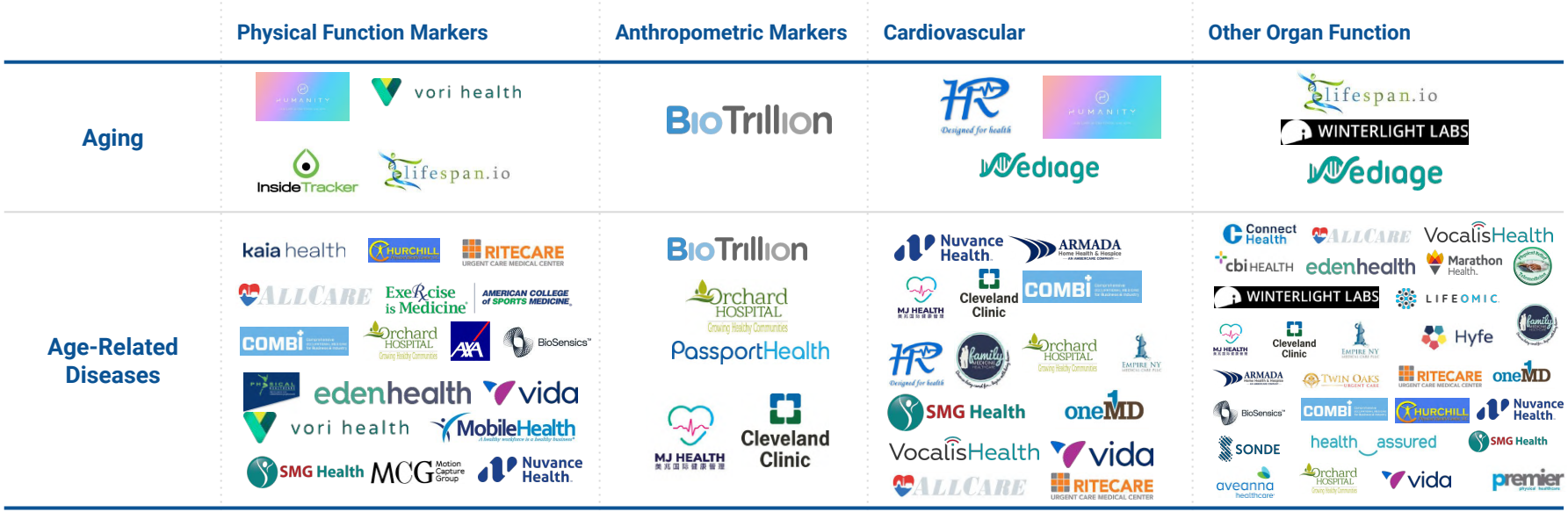
\+

Self-reports

2 Key Advantages

- Validity and reproducibility improvement
- Capturing changes over time
- Reducing the influence of cognitive function, culture, language and education
- Enable the study of variation in functioning across the full spectrum

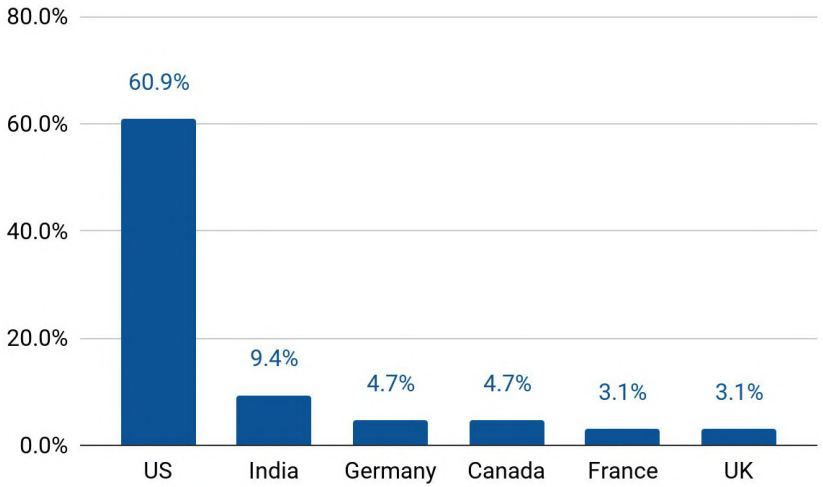
Scope of Companies with Physiological Biomarker Approaches



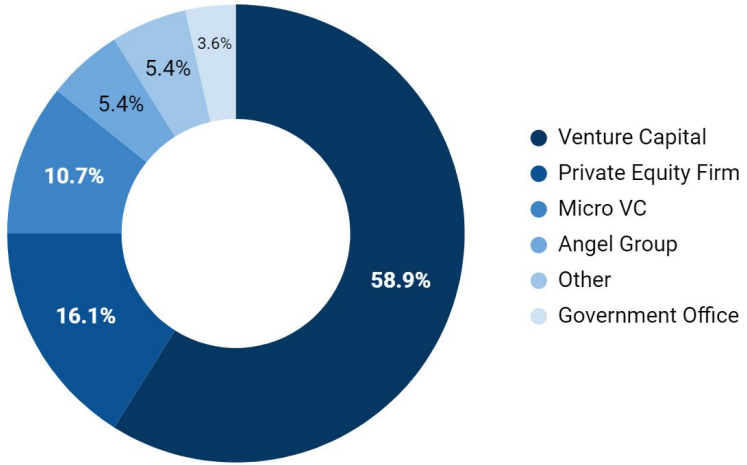
Physiological biomarkers are popular in the market as useful tests in **Sports physical examination**, **Occupational health management**, **Healthcare services**. The great benefits of physiological markers are their **reliability**, **informativity**, and **non-invasive procedure of measurement**. Some companies provide solutions for assessment and tracking physiological biomarkers to evaluate **Aging rate**. Markers of **Physical function** of body (balance, lift ability, walking speed) as well as **Cardiovascular** system markers (blood pressure, heart rate, EKG) are routinely used and prevail in the market. At the same time innovative markers (facial features, vocal markers) are perspective to be used both as clinical assays and at-home tests for purposes of **Longevity medicine.**

Market Overview: Global Market and Investors

Countries with the Largest Number of Investors, %



Main Type of the Investors, %

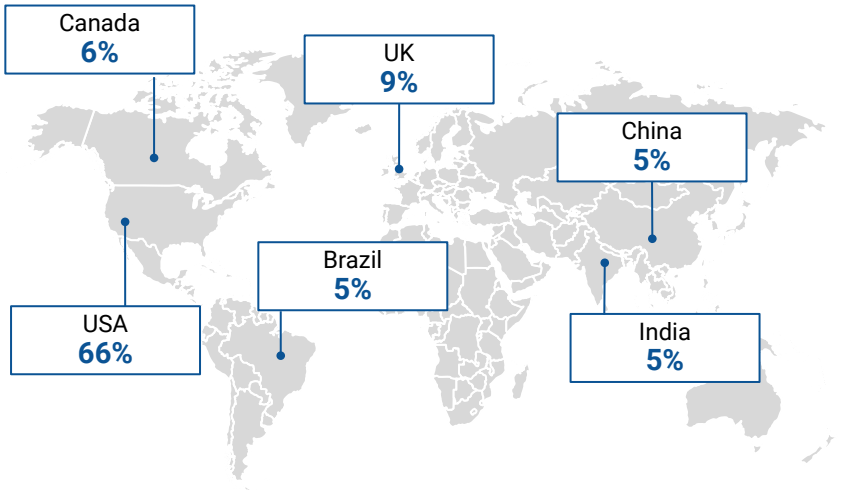


Around 61% of all investors are form the US. Together with Canada, American region hosts close to 66% of all investors in the Physiological Biomarkers industry. **Other 9% are form India.** The rest of the top countries by number of investors are European countries.

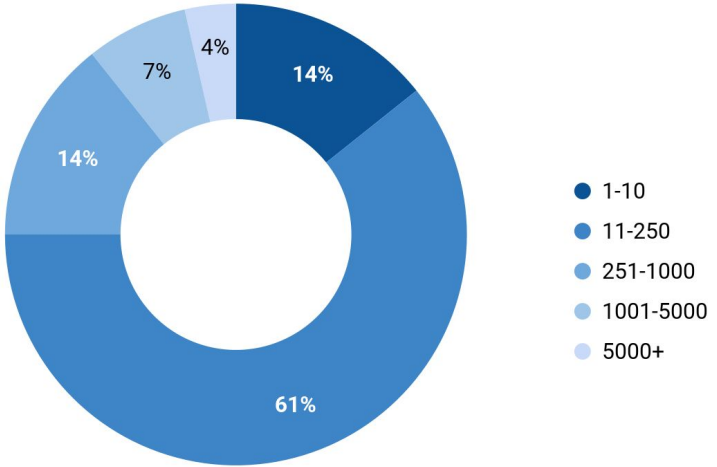
Close to 59% of all investors are **Venture Capital**, other 11% are Micro VC. **Private equity firms constitute 16.1% of all investors.**

Market Overview: Geography of Companies

Distribution of Companies by Country, %



Distribution of Companies by Number of Employees, %



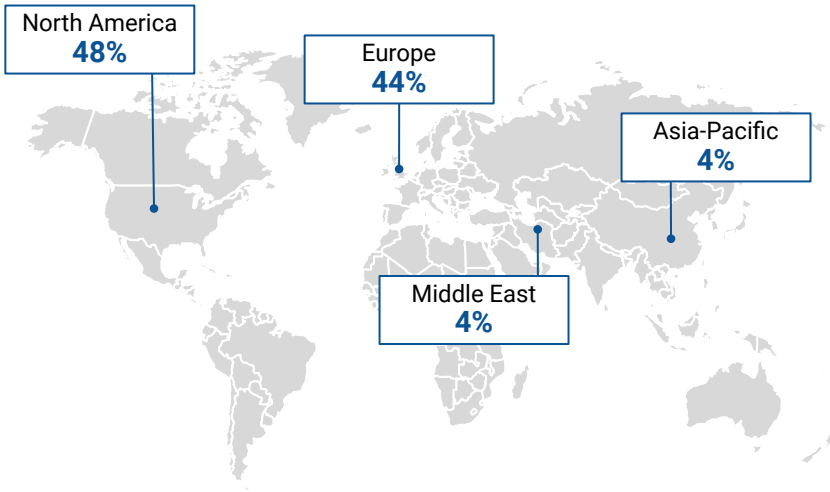
Most of the companies **(88%)** that conduct their activities in the field of Physiological Biomarkers are concentrated **in the 5 countries** all over the world. There are **66%** of companies allocated **in the US.** The other **6%** of companies are situated **in Canada** and **5%** are situated in **Brazil**. In total, more than three quarters (27 companies) are located in the Western hemisphere.

The market is dominated by **small companies - 75%** of companies have up to 250 employees. However, there are 11% of big players - companies with more than 1000 employees.

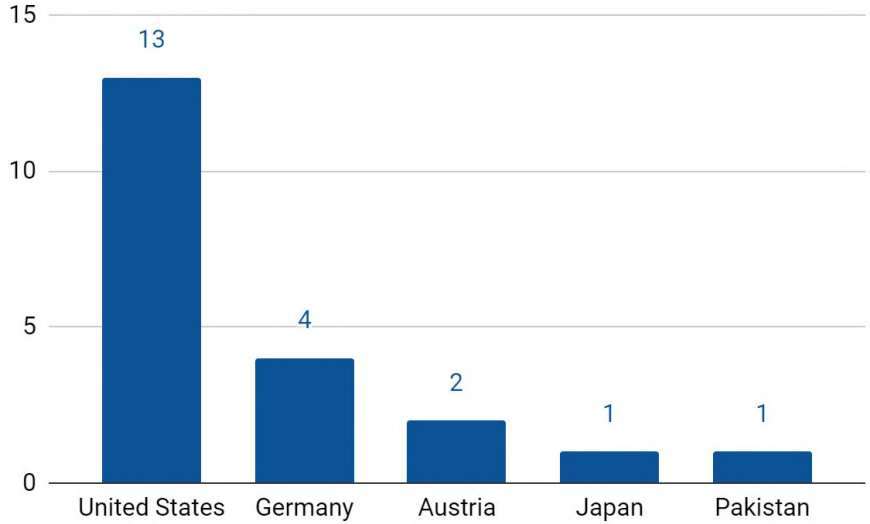
Source: Aging Analytics Agency analysis

Market Overview: R&D Centres

Distribution of R&D Centres by Regions, %



Top Countries by Number of R&D Centres

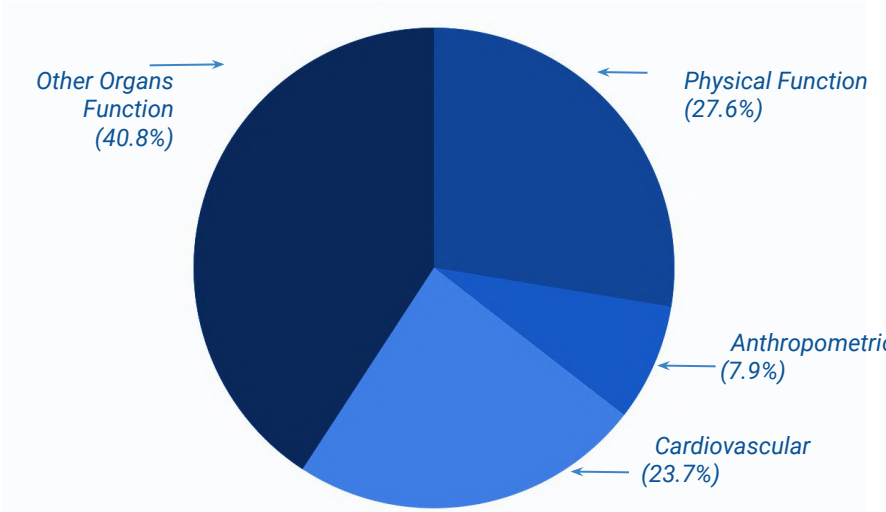


R&D activity in the area of Physiological Biomarkers is **divided almost equally between North America and European regions** - around 48% of all R&D centres are in the US and the other 44% are in Europe, concentrating mostly in Germany and Austria. However, there are **also few R&D centres** involved in the field **in Asia** (Japan in particular) and in the Middle East.

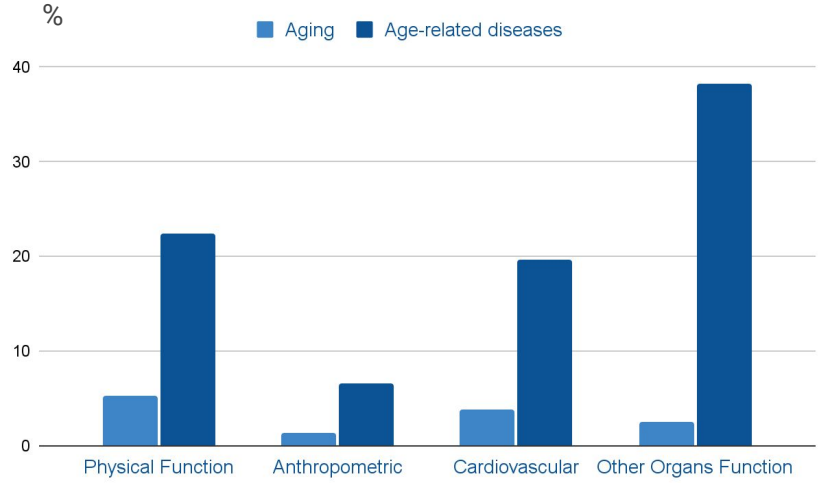
Source: Aging Analytics Agency analysis

Market Overview

Distribution of Companies by Marker Type



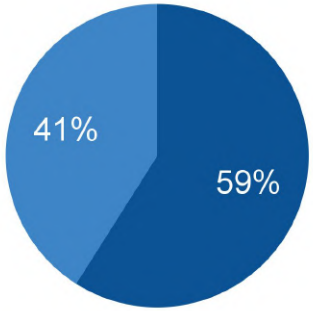
Distribution of Companies by Test Application



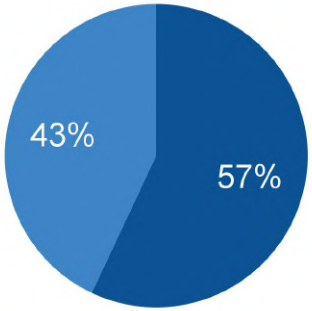
The most popular approaches are assessment of **Physical function** (**27.6%** of companies) as well as **Cardiovascular** Biomarkers (**23.7%** of companies). This fact is linked to long-term history of physical examination for patient's state evaluation in clinical practice. Tests for assessment Biomarkers of **Other Organs Function** (spirometry, audiometry, vision tests, reflexes etc) are also widely used and provided by different companies (**40.8%** of companies). **Anthropometric** markers are less represented in market (**7.9%** of companies). All subcategories of **Physiological** markers are used mainly as tool to detect and monitor **Age-related diseases, for annual Health examination, Pre-employment & Sports physicals check up**.

Market Overview: Distribution of Approaches in the Top Countries

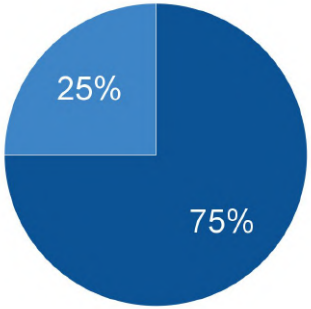
- Clinical test
- At-home test



North America



Europe



Asia

The **vast majority of companies** that provide **Physiological Biomarkers** testing are located in the **United States** (**68%** of the total range of analyzed companies). The **European region** follows, with **13%** of companies located in **UK**, and **5%** of companies located in **Germany**. Then the **Asian region** follows with **6%** of companies, and **5%** of companies are located in **Australia**. **Clinical testing** of physiological markers still prevails in market. At the same time, the part of companies offering **At-home test** systems comprises **41%** in **United States**, **43%** in **Europe**, and **25%** in **Asia region** and **Australia**. **At-home tests linked to digital platforms** are expected to be more popular in future as fast, stress-free, non-invasive and informative tools for **Health** and **Aging Rate** monitoring.

Practical Applications of Physiological Biomarkers in Longevity

Handgrip strength and gait speed indicate the generalized weakness and frailty caused by the progressive loss in skeletal muscle mass and strength, known as sarcopenia.

Poor performance in tests of grip strength, walking speed, chair rise time and standing balance, and so on, are associated with **higher mortality rates**.

The skin strength, elasticity and diminution of subdermal fat can define the person's **biological age** with high accuracy by 3D facial imaging.

The risk of osteoporosis can be assessed by altered body composition and bone health measurements with dual-energy X-ray absorptiometry (DEXA).

Lower levels of physical capability are associated with **higher risk of cardiovascular disease (CVD), dementia, institutionalisation and difficulties performing activities of daily living (ADLs).**

Physiological Biomarkers Applications

- **Sarcopenia diagnostics**
- **Risk of osteoporosis evaluation**
- **Risk of CVD evaluation**
- **Risk of dementia evaluation**
- **Biological age estimation**

Source: Wiley Analytic Science, International Journal of Cardiology

Physiological Biomarkers in Practical Use for Aging Rate Evaluation (1/2)

Marker type	Biomarker	What is assessed	Digital platform	Application	At-home tests
Physical Function	**Walking speed** **Fitness activity**	Marker of **Frailty**	*Humanity App* *InsideTracker App* *Mediage Mobile Health* *Vori Health*	**Aging rate evaluation** **Wellness**	
	Muscle movement time	Marker of **Age-associated impairments** in motor control systems	*AgeMeter® App*	**Aging rate evaluation**	
	Alternate button tapping	Marker of **Muscle coordination**	*AgeMeter® App*	**Aging rate evaluation**	
Anthropometric Markers	**Digital eyes & face biomarkers**	Real-time motor, cognitive, and emotional abilities of **Brain**	*BioEngine4D*	**Aging rate evaluation** **Neurology**	
	BMI	Indicator of the **Energy metabolism balance**	*InsideTracker App* *Mediage Mobile Health*	**Aging rate evaluation**	
	Height & weight	**Abdominal obesity**	*Mediage Mobile Health*	**Aging rate evaluation** **General Check up**	
	Waist circumference	**Abdominal obesity**	*Mediage Mobile Health*	**Aging rate evaluation**	

Physiological Biomarkers in Practical Use for Aging Rate Evaluation (2/2)

Organ	Biomarker	What is assessed	Digital platform	Application	At-home tests
Cardiovascular system	**Heart rate**	Indicator of **Heart functioning**	*Humanity App* *InsideTracker App*	**Aging rate evaluation**	
	Blood pressure	Index of **Cardiovascular activity**	*Mediage Mobile Health*	**Aging rate evaluation**	
	Pulse rate	Marker of **increased arterial stiffness** / **stress** / **autonomous nervous system** function	*Health Reviser*	**Aging rate evaluation**	
Ear	**Highest audible pitch**	**Ability to hear sounds**	*AgeMeter® App*	**Aging rate evaluation**	
Eyes	**Visual reaction time**	**Ability to respond quickly to visual stimuli**	*AgeMeter® App*	**Aging rate evaluation**	
	Visual perception	**Ability to perceive light stimuli**	*AgeMeter® App*	**Aging rate evaluation**	
Lungs	**Forced vital capacity**	**Lung function** test	*AgeMeter® App*	**Aging rate evaluation**	
	forced expiratory volume	**Lung function** test	*AgeMeter® App*	**Aging rate evaluation**	
Brain	**Decision reaction time**	**Brain activity**	*AgeMeter® App*	**Aging rate evaluation**	
	Memory	**Ability** to to **reconstruct the experience** and **make relevant judgments**	*AgeMeter® App*	**Aging rate evaluation**	

Physiological Biomarkers: Notable Cases

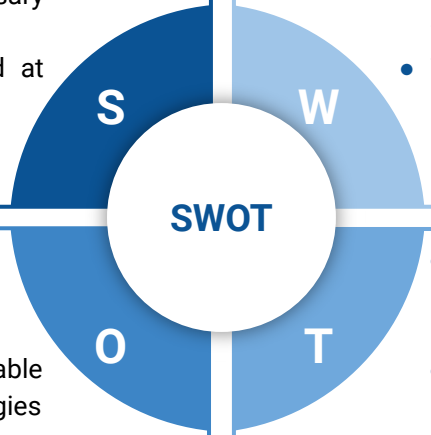
Babylon is a company that makes healthcare affordable and accessible all over the world. They deliver it through the devices people already own, e.g. smartphones. Babylon is combining AI and technology with human expertise, and their areas of expertise are **24/7 access to doctors, Dedicated Care Advisor, Personalized Care Plans, Seamless referrals to specialists, Digital health tools, Chronic disease management**.

Mediage is a company that provides digital healthcare services targeted at promoting the healthy life of people. It is connecting digital healthcare data globally based on innovative health information analytics. They provide **genetics check-ups, analysis on major disease, cancer, and mortality risks based on the biological age health index, nutrition recommendations, mobile check-ups and counseling, and big health data platform.**

Sonde is detecting changes in your health from changes in your voice. With a short voice sample Sonde, symptom detection technology can tell if you are at **risk for leading health conditions, including asthma, COPD, COVID-19, depression, and anxiety.** Organizations use Sonde's respiratory vocal biomarker platform to enable non-invasive and accessible biomarkers in their programs.

Source: aginganalytics.com

Physiological Biomarkers: SWOT Analysis



- The complex analysis of many physiological biomarkers will give information onto accurate health states.
- The physiological biomarkers also analyze both early-stage and predisposition to certain diseases, which helps individuals to understand necessary preventive measures and treatment.
- Some physiological biomarkers can be measured at home surroundings as well as at clinics.

- The physiological biomarkers can define a few pathogenic states at the same time, so it can be hard to define the real problem.
- The accurate result can be received by a complex approach that includes many physiological biomarkers, which can be expensive and public inaccessible.
- Their research is needed because the list of physiological biomarkers is incomplete

- The development of cutting-edge AI and ML technologies will simplify the biomarkers data analyzes and improve the accuracy.
- The spread of novel biotechnologies as portable analyzers, wearable devices, and digital technologies will increase quality and decrease costs.
- The study of the molecular mechanism underlying physiological biomarkers is a key way for understanding and eliminating numerous diseases via the development of new screening procedures and treatment.

- The environmental and lifestyle factors can influence the biomarker quantity and quality, which may affect the accuracy of the test.
- Existing data repositories have a lot of controversial information, so more investments in research are needed
- The biomarker data is not full (lacking in the data from all ages, sexes, races, etc.), which may cause inaccurate results for certain population groups.

Key Takeaways: Physiological Biomarkers

Physiological biomarkers refer to measurements of physical capability and physiological function. They are generally accepted by publicity and non-invasive and reflect **overall physical and physiological state of body**. Also, they can show early onset of various diseases and prevent their progression.

The new trend of the market is development of **home assessment and monitoring devices** that are portable and can be used in home diagnostics. These enables people to go to diagnostics centers lesser and provides assessment of physiological state changes over longer period of time. There are many mobile apps with online doctors consultations and AI based recommendations that **increase efficacy of treatment**.

The regular physiological biomarkers check-ups also **promotes longevity**. These biomarkers can reflect **the onset of various age-related diseases and pathological pathways involved**, so, the clinicians can adjust specific therapy to eliminate the basic causes of such changes and promote healthy longevity.

The market is dominated by **small companies - 75%** of companies have up to 250 employees. However, there are 11% of big players - companies with more than 1000 employees, what indicates that this industry is just building up and most of tech progress is right now in hands of startups.

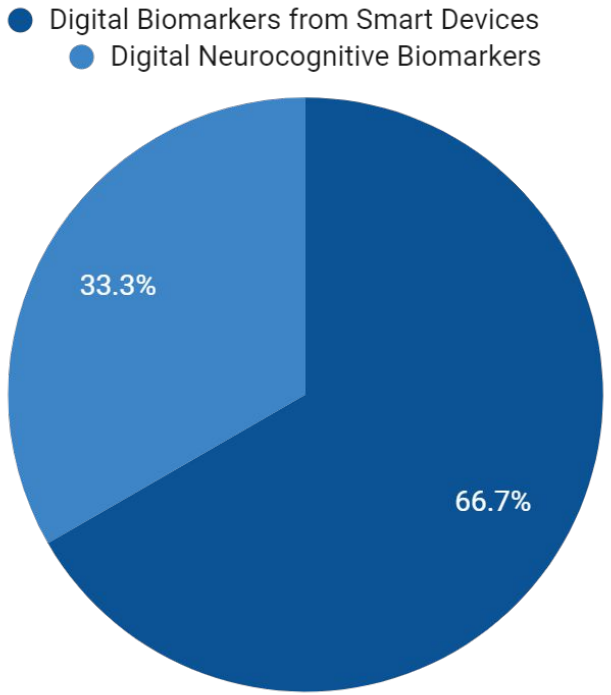
Digital Biomarkers

Digital Biomarkers Overview

Digital biomarkers can be roughly divided into two subcategories: **digital biomarkers from smart devices and digital neurocognitive biomarkers**. The main advantage of digital biomarkers is that they are cheap, publicly accessible, and do not require the assistance of medical professionals. The digital biomarkers are defined as objective, quantifiable physiological and behavioural data. These products have created new opportunities, enabling remote monitoring for biomedical research, decentralized clinical trial designs, and routine patient care. Additionally, digital biomarkers can predict some diseases, and they are commonly used in aging clocks.

The digital biomarkers market is rapidly growing since its usage in therapeutic areas is increasing. The development of digital biomarkers would be most beneficial for pharmaceutical companies since it can inform pharmaceutical scientists about the influence of the drug on the patient's health. Factors influencing the growth of the market are: the platform developed for assessing the data must be free from data biases, the clinical assessment of data platform and digital biomarkers is essential, additionally sharing the data across clinicians, laboratories, hospitals are a way for better results, and finally decreasing the cost.

Distribution of Companies by Category, %



Source: Wiley Analytic Science

Digital Biomarkers Trends

AI Technologies

Currently, AI technologies are used for deep analysis of aging-biomarkers, mortality risk score, aging-clocks development. Researchers are working on the metabolic profile of all-cause mortality risk.

Smart Devices

Challenge in smart device manufacturing and data analysis relate to measurement accuracy, non-invasiveness and comprehensive research approaches. Digital biomarkers obtained from smart devices are also proceed using AI/ML technologies

Personalized Medicine

AI and ML approaches in analyzing biomarkers data allow to predict individual health status as well as aging pattern. Specific database development will help to implement individual approaches in personalized medicine.

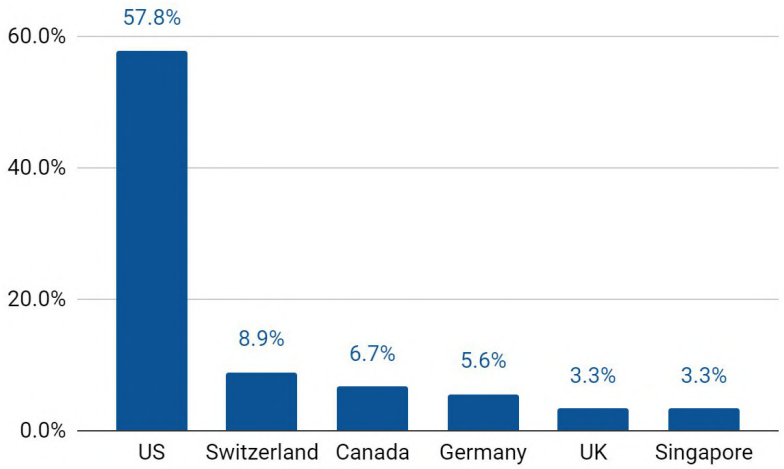
Due to the huge amount of data, obtained from different types of biomarkers, the leading trend is related to deep and precise analysis. Most of the companies in digital biomarkers' field collect data from smart devices and/or online and proceed them using modern AI technologies.

Sources: Aging Research Reviews, Nature

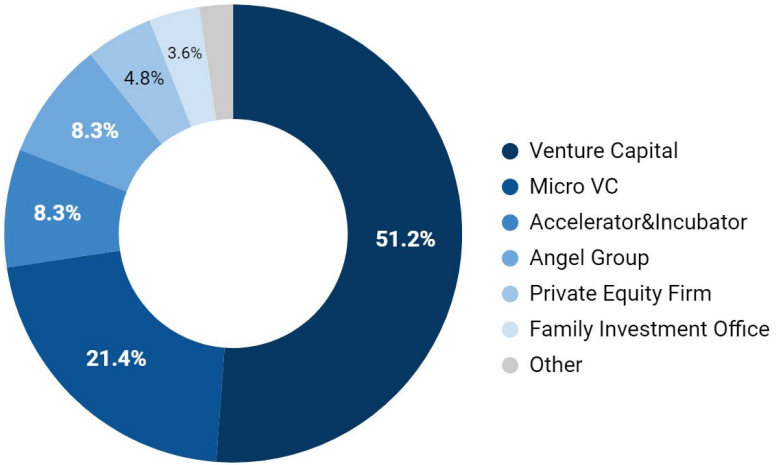
Key Companies: Digital Biomarkers

Market Overview: Global Market and Investors

Countries with the Largest Number of Investors, %



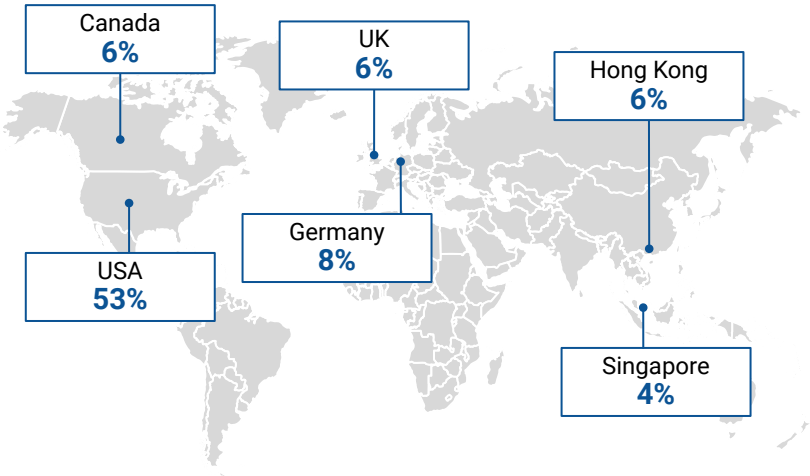
Main Type of the Investors, %



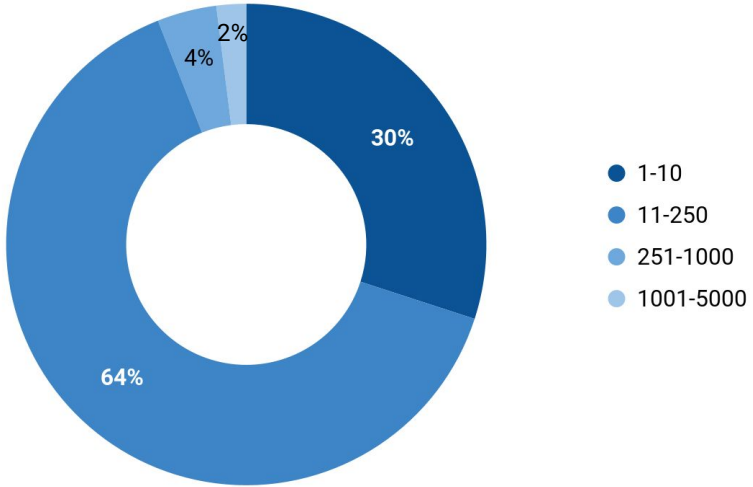
More than a half (57.8%) of investors, who finance Digital Biomarkers companies, **are from the US**. **The second country** by the number of investors with great gap is **Switzerland.**
The most common types of investors are **Venture Capital (51.2%) and Micro Venture Capital (21.4%)** companies. Both are funding innovative companies to invest to seed early-stage emerging companies. **Accelerators and Incubators together with Angel Group** are also quite common (by 8.3%). Their aim is not only to finance, but also **to provide with insights and to guide.**

Market Overview: Geography of Companies

Distribution of Companies by Country, %



Distribution of Companies by Number of Employees, %



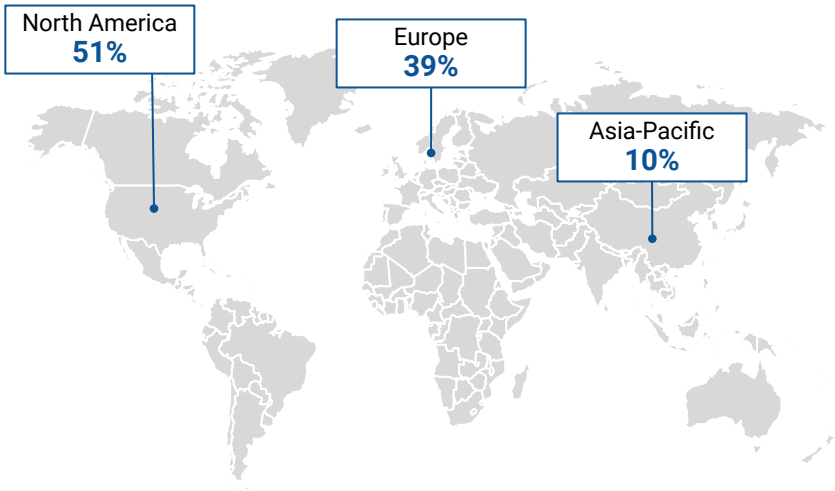
Around 83% of all companies are allocated **in the top 5 countries**. A little **more than a half of the companies (53%)** is concentrated in **the USA**. Other 14% are in the European countries - Germany and the UK for instance. The other 10% is Asia-Pacific companies situated in Hong Kong and Singapore.

More than 90% of all companies **are either micro or small companies** with 1-250 employees. Production in this sector is knowledge intense, and require experience, understanding, and information, rather than a great labour force.

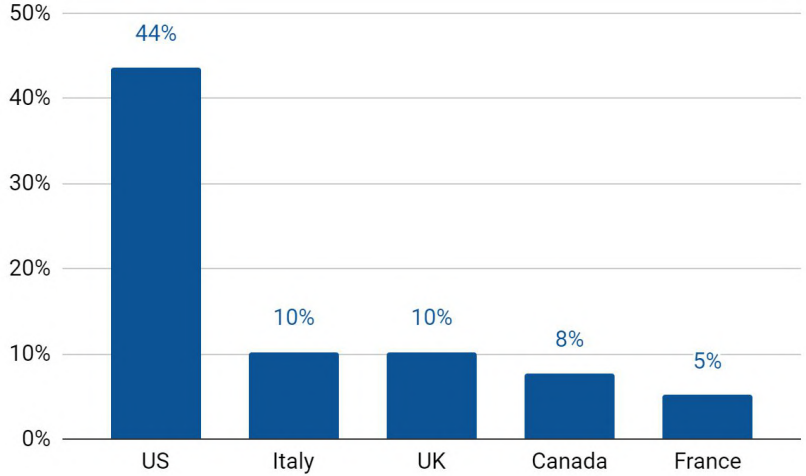
Source: Aging Analytics Agency analysis

Market Overview: R&D Centres

Distribution of R&D Centres by Region, %



Top 5 Countries by Number of R&D Centres, %



Close to half (51%) of the R&D Centres are allocated **in Northern America.** Other 39% are scattered across all Europe, including **Italy, UK, and France with 10%, 10% and 5%** of a total number of R&D Centres respectively. The rest of the R&D Centres - nearly 10% - are in the Asia-Pacific region. Nearly 77% of all R&D Centres are concentrated in the top 5 countries.

Source: Aging Analytics Agency analysis

Practical Applications of Digital Biomarkers in Longevity

Cardiovascular health disorders, such as heart stroke, coronary artery disease, heart attack are associated with high mortality rate.Some of them can be even “silent” - the damage is done, but the person is not aware of it. Monitoring and evaluating **cardiovascular health biomarkers**, obtained from smart devices, helps to predict and control cardiovascular disorders

Neurocognitive digital biomarkers are used to identify and predict such neurocognitive disorders as Alzheimer's disease, amyotrophic lateral sclerosis (ALS), brain tumours, epilepsy, Parkinson's, autism spectrum disorders, dyslexia, etc. Many of them are associated with aging. Furthermore, analyzing neurocognitive biomarkers can significantly improve life quality among the eldery.

Aging-clocks are established with the help of ML technologies. Huge massive of data obtained from digital biomarkers are used to develop aging models and predict life expectancy

Digital Biomarkers Applications

- **Several types of cancer prediction**
- **Control of drug release**
- **Give information about cardiovascular health**
- **Predict aging-related neurocognitive disorders**
- **Implementation in aging-clocks**

Source: Wiley Analytic Science

Digital Biomarkers from Smart Devices

Digital biomarkers from smart devices are parameters collected and processed by such devices as portables, wearables, implantables or digestibles.

Most commonly, these biomarkers are accounting such physiological conditioning as the temperature of human skin (by digital thermometer), blood pressure (by digital sphygmomanometer), body motion (by gyroscope, accelerometer, and magnetometer), heart rhythms (by wearable electrocardiograph), heart rate (by photoplethysmography device), and blood oxygen levels (by noninvasive pulse oximeter). These measurements complement and can even **replace traditional physiological tests**. Additionally, some devices can measure biochemical parameters in body fluids. These biochemical parameters are pH, blood oxygen saturation, protein concentration, amino acids, lipids, electrolytes and metabolites, hormones, and pathogenic bacteria. Moreover, such devices can control the not only concentration of biomarkers but also automatically controlled drug release.

Digital Biomarkers from Smart Devices Examples

- **Human Skin Temperature**
- **Blood Pressure**
- **Body Motion**
- **Heart Rhythms**
- **Blood Oxygen Saturation**
- **Drug Concentration**

Source: Wiley Analytic Science

Digital Biomarkers from Smart Devices: Notable Cases

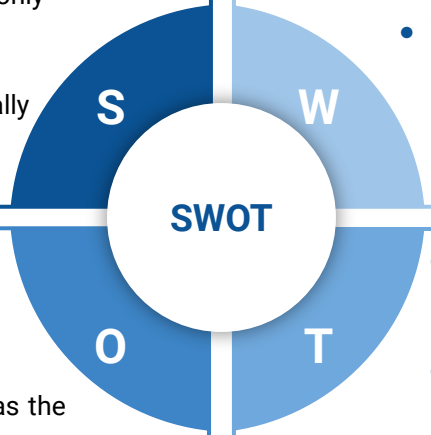
Deep Longevity is a biotechnology company which transforms longevity R&D through AI-discovered biomarkers of aging. Using innovative deep learning algorithms and generative approaches, they develop novel tools for aging research that can be applied in many industries to make people live better, longer, and healthier lives. They also provide tracking of aging process with the Young.AI app which predicts biological age using digital biomarkers.

Youth Laboratories is a data analytics company, which specialize in processing digital images and videos of human skin to develop diseases biomarkers and to evaluate the physical well-being of a human and lifestyle. Their aim to slow down or even reverse age-associated changes starting from the human skin.

Insilico Medicine provides a fully-integrated drug discovery software suite which uses a number of digital biomarkers to discover and prioritize novel targets, find new molecules for drug-development and design clinical trials. Insilico Medicine develops internal drug discovery programs in cancer, dermatological diseases, fibrosis, Parkinson's Disease, Alzheimer's Disease, ALS, diabetes, sarcopenia, and aging.

Source: Wiley Analytic Science, Nature

Smart Devices Biomarkers: SWOT Analysis



- Measurements are complement and could even replace traditional physiological tests, which is simple and useful for customers
- There are a number of aging-related biomarkers. Thus, the analysis of smart devices biomarkers can not only predict overall health status, but also longevity.
- Some devices can define circulating biochemical parameters, measure concentrations and automatically control drug release .

- There is no single biomarker (or a single set of biomarkers) that enables the reliable and accurate measurement of aging progression in humans.
- There are always limits of detection and limits of quantitation in biomarkers measuring.
- The analyzes of some biomarkers requires complex computational methods which can be definitely expensive.

- The obtained biomarkers data can be analyzed with the cutting-edge AI and ML technologies which will improve aging analytics and provide personalized medicine.
- A wide range of wearable smart-devices can serve as the source of longevity biomarkers
- Innovative devices manufacturing can provide high quality health/longevity monitoring for all segments of customers
- The score/causal longevity models development using AI/ML technologies

- The environmental and lifestyle factors can influence the biomarker quantity and quality, which may affect the accuracy of the test.
- There is no single approach how to analyze biomarkers data.
- The biomarker data is not inclusive and equitable (lacking in the data from all ages, sexes, races, etc.), which may cause inaccurate results for certain population groups.

Digital Neurocognitive Biomarkers

Digital neurocognitive biomarkers are special tests that are established for neurocognitive disorders identifying and predicting. Neurocognitive disorders include Alzheimer's disease, amyotrophic lateral sclerosis (ALS), brain tumours, epilepsy, Parkinson's, autism spectrum disorders, dyslexia, etc. Many of these disorders are typical for older adults and appear with age. These diseases significantly influence the life quality of patients and their closest people because of the need for constant care. The prediction of the appearance of these diseases and even early detection can significantly improve the patients' outcomes and quality of life because of preventive events. That is the reason for digital neurocognitive biomarkers importance.

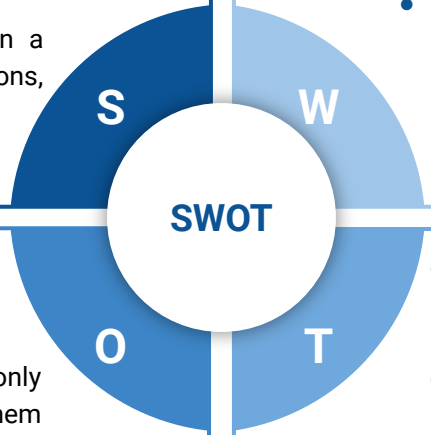
The specific neurocognitive biomarkers assess cognitive parameters, including memory (working and episodic), attention, learning ability, problem-solving, information processing speed, executive function etc., and such neural parameters as speech fluency and consistency, voice parameters, movements clarity, eye tracking, hands micromovements and micro-errors, gait micro-errors, posture changes, eye pupil dilation, dual-task micro-errors, etc.

Digital Neurocognitive Biomarkers Examples

- **Memory (Working and Episodic)**
- **Attention**
- **Information Processing Speed**
- **Voice and Speech Parameters**
- **Hands Micro-movements**
- **Eye Tracking**

Source: Wiley Analytic Science

Digital Neurocognitive Biomarkers: SWOT Analysis



- Several studies indicate the link between neurocognitive biomarkers and aging.
- Digital neurocognitive biomarkers analysis can provide precision and individual approach in diagnostic/treatment of neurocognitive disorders
- Some mental tests would have a similar value in a variety of different health-related implementations, including measurements of functional age in panels.

- There are always limits of detection and limits of quantitation in biomarkers measuring.
- Some of technologies must be further approved by FDA, etc.
- There is not single neurocognitive biomarker for precise prediction of several complex diseases

- The development of unique statistical model which will present the link between neurocognitive biomarkers and aging.
- Development of innovative devices which will not only detect neurocognitive biomarkers but also analyze them and treat several neurocognitive diseases
- Manufacturing of low-cost, modular touch screen device for integrating multiple cognitive and biometric assessment technologies.

- The environmental and lifestyle factors can influence the biomarker quantity and quality, which may affect the accuracy of the test.
- There is no single approach how to analyze biomarkers data.
- Some mental/writing tests have their accuracy limit

Digital Neurocognitive Biomarkers: Notable Cases

EVOCAL Health is innovative digital diagnostics company which predict health-status using the Power of Vocal Biomarkers and AI technology. EVOCAL health is establishing a sophisticated Healthcare Intelligence Algorithm based on AI and Machine Learning, that utilizes vocal biomarkers such as voice-, breathing-, and coughing noises to detect diseases.

Altoida is a company engaged in the brain health with precision neurology. They are establishing a precision neurology platform to enable more accessible, accurate, effective diagnostics and monitoring brain health using just customer's smartphone or tablet. Furthermore, Altoida received FDA Breakthrough Device Designation in July 2021.

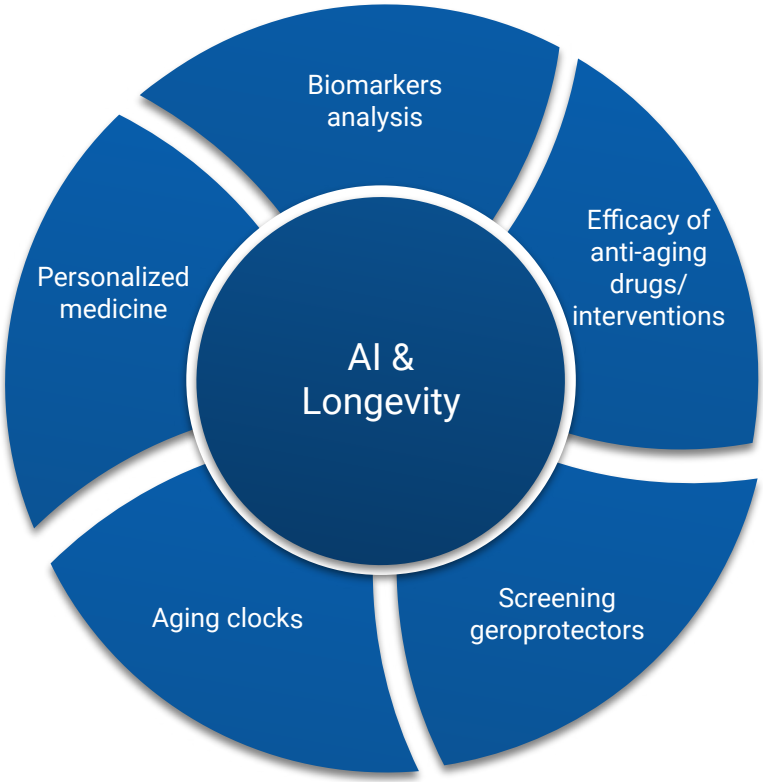
Braingaze suggest mind tracking solutions that solve major challenges around cognitive disorders like ADHD and Mild Cognitive Impairment. Their solutions are: BGaze ACE which is an AI software for ADHD diagnostic, BGaze clinic - a system that use advanced eye-tracking hardware to detect involuntary biomarker micro-eye movement patterns, and BGaze Therapy - a game designed for child to improve attention skills. The product was created especially for children with ADHD, ASD, and Dyslexia.

Digital Biomarkers and AI Overview

Digital biomarkers are widely analyzed with the help of **AI technologies**. AI technology provides biomarkers of aging discovery and aging research. We divide digital biomarkers into two categories: digital biomarkers collected from smart devices and neurocognitive biomarkers. Thus, biomarkers from both categories can be analyzed using different approaches of AI technology.

Machine learning age predictors collect and analyze a number of data on organismal and population level, and also on cellular/tissue level. One should however distinguish between the chronological and biological age. **DL-based aging clocks** evaluate biological age from biological data and perform linear or non-linear regressions for getting the chronological age of the individual. The training protocol of aging clocks is used to minimize the difference, called aging acceleration, between the physiological age — identified by the model — and the actual chronological age of the individual.

Biomarkers, can be analyzed by the AI are: imaging biomarkers, blood tests, neurocognitive biomarkers, physiological biomarkers, "omics" biomarkers, epigenetic biomarkers, multimodal biomarkers (such as oxidative stress biomarkers, blood pressure, platelets count, etc.)



Source: Aging Research Reviews

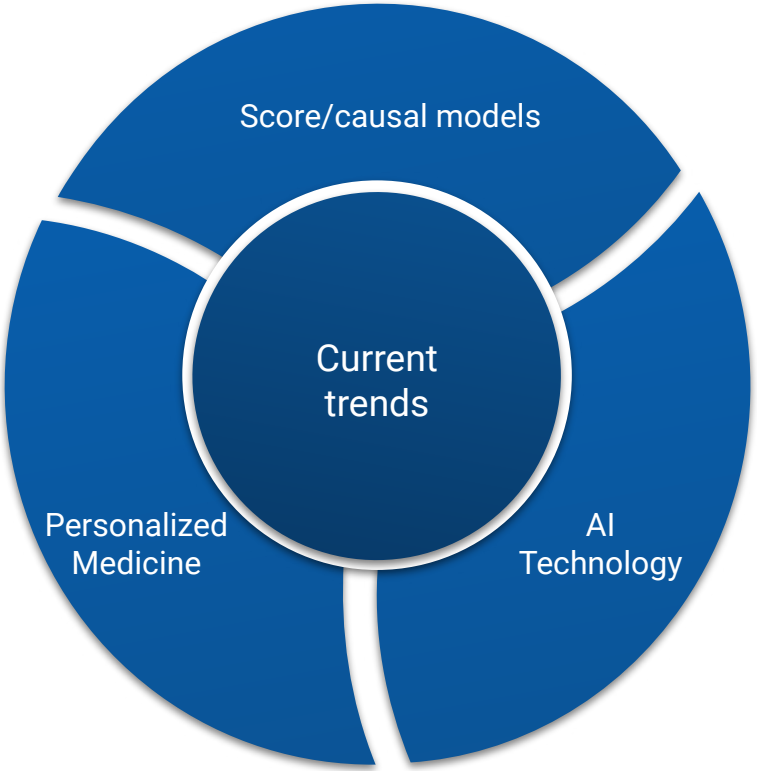
Research Approach in Digital Longevity Biomarkers

Current **research approaches in identifying longevity biomarkers** can be classified in following:

- AI technology
- Personalized medicine
- Score/Causal models

Innovative experimental techniques have allowed the generation and processing of a **large amount of aging-related data**, including genomic, transcriptomic, microRNA, proteomic, antigen, methylation, imaging, metagenomic, mitochondrial and physiological.

Recently, researchers found a **metabolic profile of all-cause mortality risk**, which included 14 circulating biomarkers and constructed a risk score to predict mortality not only among the young population but also in the elderly. The risk score improved risk prediction beyond conventional risk factors. In perspective, such risk score could potentially be developed into an algorithm to be utilized in clinical practice to guide treatment strategies, predict longevity, etc.



Source: aging Research Reviews, Nature

Databases for Deep Learning in Aging Research

As soon as digital biomarkers use a lot of AI, there is a need for **unique databases** for AI training and validation. These databases mainly consist of **genes, pathways associated with aging, and geroprotectors** which are chemical compounds that promote longevity. The most popular databases for Deep Learning in aging research are below.

Human aging Genomic Resources - collection of databases and tools designed to help to study the genetics of human aging. It consists of **Cell Age** - a manually curated database of genes associated with cell aging, and **GenAge**, which specializes on genes, associated with aging. GenAge include data about genes related to longevity and/or aging in model organisms and aging-related human genes.

HAGR
Human Ageing
Genomic Resources

Geroprotectors - a curated database of geroprotectors. It include data about more than 200 chemical compounds that can promote longevity, and furthermore some of them are approved for human use. It also contains more than 250 life-extension experiments in 11 wild-type model organisms.

GEROPROTECTORS

AgingChart - online crowd sourced pathway annotation database, which provides data about 114 pathways, networks, and concept maps on all topics related to aging, from gene-centered pathways to those describing aging processes, age-related diseases, longevity factors, and anti-aging strategies.

Key Takeaways: Digital Biomarkers

Nowadays, data, obtained from **digital biomarkers,** helps to solve a number of **health and aging-related problems**. Thus, collecting and comprehensive analyzing of several biomarkers can **predict aging-related diseases, neurocognitive disorders, establish general health status, and improve access to personalized medicine**.

Digital biomarkers represent **objective and quantifiable physiological and behavioral data**. One can divide digital biomarkers into two categories: **digital biomarkers collected from smart devices and neurocognitive biomarkers**. Common digital biomarkers are physiological parameters such as blood pressure, blood oxygen saturation, biochemical blood parameters, and specific neurocognitive biomarkers.

Digital biomarkers refer to 2 areas of human's health: **general health and neurocognitive health**. The most considerable numbers of companies are focusing on **AI technologies** and **Machine Learning**. Advances are made in developing risk score which can predict mortality in elderly and among young people as well.

The digital biomarkers market is mainly focused on **AI approaches** in analysis of obtained data, **longevity prediction** with the help of universal causal models, aging-related databases, personalized medicine and non-invasive methods of biomarkers data extraction.

Around 83% of all companies are allocated **in the top 5 countries**. A little **more than a half of the companies (53%)** is concentrated in **the USA**. Other 14% are in the European countries - Germany and the UK for instance. But this trend could possibly change soon, in case of significantly **lower cost of digital biomarkers' development.**

Imaging Biomarkers

Executive Summary

Key definition 1: ***Medical Imaging*** *- refer to the imaging techniques that assist with identification of disease/condition based on imaging biomarkers patterns, or to determine pharmacological response to treatment by changes in characteristically imaging biomarkers.*

Key definition 2: ***Imaging biomarkers*** *- biological characteristic or features that is measured from biological image. Imaging biomarker serve as an indicator of the health status, disease or condition progression.*

Imaging application can be applied to probe various pathological conditions- it is a versatile approach. Moreover, imaging may help to find details that might be not available for measuring by others approaches. It may include determination of: tumor size shrinkage / increase, reduction / expending of the metastatic sites, improvement / assess of the brain activity during functional tests, choosing an appropriate patient group while applying MRI or CT to distinguishing ischemic stroke from cerebral hemorrhage. All of those data would be unavailable without imaging approaches.

Main Features of the Analytical Case Study

- **Database of Selected Companies, R&Ds and Investors focused on Medical Imaging platforms, softs, devices, etc.**
- **Overview of Main Sectors of Medical Imaging companies**
- **Role of AI in Medical Imaging**
- **Review of Notable Medical Imaging Companies**
- **Medical Imaging Market trends overview**

Medical Imaging Sector Overview

1. Medical Imaging platforms, software or devices that can be related to digital health systems used to process images of various body parts for diagnostic, treatment - monitoring or research purposes.

2. In the Medical Imaging market, AI-based medical imaging represent fast-growing sector. AI-processing allows for automated, accurate and faster way of clinical data analysis.

3. AI-based medical imaging do not represent a ready-to-use product until it`s algorithms trained on vast clinical case data to be able to recognise patterns of disease or to predict disease risk.

4. The access to large, high-quality datasets of clinical case data represent a bottleneck for Medical Imaging. Yet, a plenty of such images sets already exist - in particularly for Radiology sector.

Why Medical Imaging sector is Becoming More Important Now?

According to recent reports, the global medical imaging market size was valued at USD 15.9 billion in 2020 and is expected to grow further.

The **trends driving** the development of **Medical Imaging sector** are arising of **an aging population** and the increasing **need for early-stage diagnostic** among elderly and youths.The high-yield niche in preventive and personalized diagnostics will be occupied by AI medical imaging due to the nature of its algorithms - neuronal networks, deep-learning able to identify patterns that clinicians may not be thought to look for or even to detect an initial disease trays more accurately than clinicians.

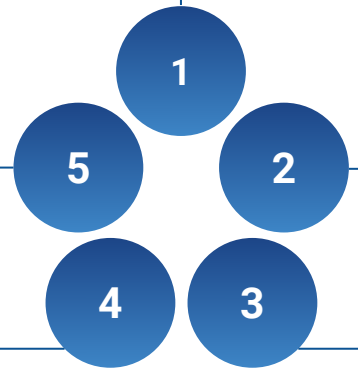
The main limit for the wide application of such AI technologies - clinical data that is used for their training - then vaster it is - then more precise AI prognostic and diagnostic.

Considering these facts, there is a demand for autonomous, quality accurate and predictive imaging-processing tools. To facilitate the creation of such, there is a need in access to clinical case imaging data.

Imaging Sectors Categorization

The system below describes the most common application areas of the digital Imaging software, devices and platforms that used in in the clinical and R&D. As such, we distinguished 5 sectors and categorized companies accordingly. It worth to highlight that over 80% of our selected companies is applying Artificial Intelligence, Deep Learning, and Neural Networks algorithms for the processing of the imaging data in order to develop autonomous, precise diagnostic tool that will help clinicians, researchers, clinical trails organizations for more accurate and faster diagnostics.

Neuroimaging - large profilization of Medical Imaging software, devices and platforms - that focused on MRI, fMRA, CT, angiography scans, ect. scans analysis for finding a signs and characteristic patterns of pathological conditions or to trace a treatment progress in the brain



Tools for clinical trials and R&D - Forster processing of big data of imaging samples that producing through clinical trials.

Ophthalmic Imaging - (microvasculature and optic nerve)to identify ocular-related diseases as diabetic retinopathy, age-related macular degeneration, glaucoma ect.)

Immunohistochemistry diagnostics sector is aiming to assist pathologists in accurate diagnoses and speed up the sample processing

Radiological imaging - the category include various software, platforms for radiological imaging for various body parts. The imaging produced is based on X-rays, positron emission tomography, and other

Imaging Sectors

Neuroimaging

- Functional imaging (diagnose metabolic, psychiatric diseases)
- Structural Imaging (diagnose disease that affecting brain morphology - Parkinson's / Alzheimer's diseases)

Ophthalmic Imaging

- Eye-related disease assess
- Estimate risk of systemic conditions like cardiovascular diseases, hypertension, stroke.
- Identify signs of neurological disorders as Alzheimer's disease or MCI

Radiological imaging

- Cardiovascular radiology,
- Chest radiology
- Gastrointestinal radiology,
- Genitourinary radiology
- Head and Musculoskeletal radiology
- Neuroradiology

Immunohistochemistry diagnostics

- Vital molecular diagnostic and treatment assessment tool

Tools for clinical trials and R&D

- Insights into Mechanisms of Drug Action
- Improves the efficiency of drug screening
- Reducing the cost of the later clinical trials and quicker trails completion

Key Companies: Imaging Biomarkers

Neuroimaging

APRINOIA Therapeutics

AVALON Ai

BRAIN SCAN

QMENTA

Combinostics

imagilys

Radiological imaging

bioxydyn

DAWAKO

IQBMI

Lunit

TRANSMURAL BIOTECH

zebra MEDICAL.VISION

CORVISTA®

quibim

HEALTHMYNE

ENLITIC

16BIT

Ophthalmic Imaging

VisionQuest BIOMEDICAL

zilia

EYENUK™

Immunohistochemistry diagnostics

aiforia® AI for image analysis

PathAI

PROSCIA®

NanoHYBRIDS ADVANCED IMAGING SOLUTIONS

FLUIDIGM

ZIONEXA CDx Imaging for Oncology

AKOYA BIOSCIENCES®

VISIOPHARM®

Tools for clinical trials and R&D

IMAGING ENDPOINTS CONNECTING IMAGING TO THE CURE

MedQIA

BIOCLINICA AN ERT COMPANY

ALTIS LABS

median The Imaging Phenomics Company®

IXICO

Neuroimaging

Neuroimaging is used to diagnose neurological and psychiatric diseases or assess the pharmacology of neurotargeting drug. Neuroimaging image a structure, function of the nervous system. The types of neuroimaging techniques used are divided on 2 main categories: **Structural Imaging** and **Functional Imaging.** Structural imaging applied to diagnose or to evaluate therapy progression for the disease that affect brain morphology - such as Alzheimer's disease. While functional imaging may diagnose and evaluate the treatment for mental conditions (depression, schizophrenia, ect.) - that affecting neuronal activity or metabolic disease (that involve blood flow abnormalities). Neuroimaging examination allows to promote **brain maintenance** - early disease detection helps to preserve/delay regression of cognitive functions. As a result it may helps to **expand healthier cohort of aging population.**

There is a growing trend in **multimodal neuroimaging** - simultaneous data collection about the same specimen with two or more imaging techniques (modalities). Different modalities may assess the state of pathology on different levels allowing for comprehensive diagnostics and advanced treatment.

Functional Imaging

It allows to measure activity in certain brain areas that known for specific mental functions. In clinics, it used to diagnose metabolic, psychiatric diseases via detecting neuronal activity, blood flow abnormalities, ect.

Structural Imaging

Used both in clinic and research. Based on identifying of structural (physical) abnormalities to diagnose a disease (neurological disorder, tumor) or an injury.

Methods includes:

1. Positron emission tomography
2. Electroencephalography
3. Functional magnetic resonance imaging
4. Functional ultrasound imaging
5. Functional near-infrared spectroscopy
6. Magnetoencephalography

1. Computed Tomography Scan
2. Magnetic resonance imaging

Neuroimaging: Notable Cases

Avalon AI offers cloud-based analysis for structural, diffusion and functional MRI brain scans. **The AI technology for automated derivation of brain biomarkers** and comparison with a normative population is used. In addition, the company announced the **development of the world's most accurate brain degeneration predictor** based on structural and functional MRI brain data.

Imagilys combines the development of a software suite for processing scans of the central nervous system, the use of the most advanced neuroimaging techniques, as well as the identification of a wide range of neuroimaging biomarkers. Using structural, functional MRI and PET, **determination of conventional and novel neuroimaging biomarkers for Alzheimer's disease, multiple sclerosis, stroke, and disorders of consciousness** is carried out.

BrainScan is a company that developed the **BrainScan.ai system**, created on the basis of training the AI-algorithm with more than 246 108 brain CT scans. The system has been shown to be highly effective in auto-detecting up to 14 different brain lesions. It enables radiology workflow to be improved, under-reporting to be reduced, and patients to be prioritized.

Ophthalmic Imaging

Ophthalmic imaging is a specialized form of medical imaging focused on the diagnostic and treatment of disorders of the eye. Considerable advantage is that eye's microvasculature and optic nerve structure is able to be studied non-invasively. Thus, it gives accessible biomarkers that are related not only to ocular diseases. Due to microvasculature accessibility, ophthalmic images may estimate risk of systemic conditions like cardiovascular diseases, hypertension, stroke. Optic nerve morphology may contain signs of neurological disorders as Alzheimer's disease or Mild cognitive impairment.

At present, there is a growing interest in developing imaging biomarkers, some of them are already supported by a good body of evidence. Imaging technologies now allows **assessing the tear film stability and volume, meibomian gland morphology and function, and ocular surface microanatomy** - those data may allow for dry eye disease diagnosis. One of the highly-informative biomarkers detectable with imaging techniques is an **ocular oxygenation level** and it`s certain range can be an indicator of such diseases as glaucoma, diabetic retinopathy, age-related macular degeneration. If left untreated, those conditions led to blindness irrivertably within years - their early diagnostic able to save a vision. Including cataracts, those four eye diseases considered as a **major age-related eye diseases (AREDs)** that are affecting senior people.

Age-related Eye Diseases - Top Cases

1. **Age-related macular degeneration** - damage to the macular eye's part that controls sharp, straight-ahead vision - is the leading cause of loss of vision in people over 65.
2. **Glaucoma** - condition which result in the optic nerve (a.k.a retina) damage in continuous high intraocular pressure.
3. **Diabetic retinopathy** - complication of diabetes resulted in the retina damage. Led to blindness if untreated.
4. **Cataracts** - the clouding of the lens of your eye, which is normally clear, causing symptoms such as blurry vision.

Ophthalmic Imaging: Notable Cases

VisionQuest Biomedical brings image-based AI technology for diagnosing retinopathy and everyday eye care. The company provides **Eye Star and Aspire AI-powered software design to detect diabetic eye disease and malarial retinopathy** using a low-cost, easy to use, and user-friendly system. Such identification of eye imaging biomarkers makes it possible to increase the efficiency of diagnosis and treatment of eye diseases, while maintaining the quality of life and its duration.

Zilia is a health technology firm that identifies and quantifies **imaging biomarkers in the eye** utilizing modern approaches such as visualization, continuous and real-time measurements of oxygenation in the human eye, and Artificial Intelligence. It allows for earlier diagnosis of a variety of ocular, neurological, and systemic disorders, as well as lower healthcare expenses and improve patient quality of life.

Eyenuk, Inc. is a healthcare technology company that develops innovative AI-driven diagnostic solutions for imaging biomarker identification. The company provides the **EyeArt® AI Eye Screening System, a well-validated AI technology for autonomous detection of diabetic retinopathy** that has been evaluated on two million photos acquired in real-world clinical settings. It is expected that the similar AI-based diagnostic systems will be effectively applied to reveal other vision-threatening conditions as well as provide predictions of the overall health quality and biological age of a person.

Radiological Imaging

Radiological Imaging - wide branch of the medical imaging techniques used in the diagnosis and treatment of disease. The main principle of those imaging is employing of radiant energy - although a name, it may include methods that both involve radiation (such as X-ray, CT) or does not involve it (MRI, Ultrasound). Radiological images are noninvasive and could be applied broadly to detect various imaging biomarkers. Radiological Imaging biomarker can be a lesion pattern in the lung detected by X-ray, MRI or CT - that may be a sign of neoplasm or tuberculosis (the last one has a characteristic lesion - a caseating granuloma). Furthermore, imaging markers with specific characteristics might be used to determine the degree or stage of these abnormalities.

Diagnostic radiology may also specialize in such subspecialties: gastrointestinal radiology (stomach, intestines and abdomen), genitourinary radiology (reproductive and urinary systems), cardiovascular radiology (heart and circulatory system), chest radiology (heart and lungs), head and neck radiology, musculoskeletal radiology (muscles and skeleton), neuroradiology (brain and nervous system), emergency radiology.

Common techniques used by radiologists

Do not include radiation

1. **Magnetic resonance imaging is non-radiation** allows to create 3D imaging of organs and tissues by radiofrequency waves originated from a powerful magnet. MRI used to detect injuries, tumors, infections, lesions. It is a common method used for brain imaging.

2. **Ultrasound imaging - non-radiation** detection based on ultrasound waves that provide real-time imaging of the probed zone. It is widely used in diagnostics.

Include radiation

1. X-ray - uses a low-dose radiation - mostly for bones and joints - widely applies due to quick results and low cost

2. Computerized tomography (CT) scan - use x-ray and produce highly detailed 3D scan - it may erect muscle and bone disorders, injuries, internal bleeding, tumor metastasis.

3. Mammography - use low dose radiation to detect structural abnormalities in the breast tissues - may diagnose breast cancer at early stages.

4. Nuclear Medicine - apply radioactive tracer injected in bloodstream. Used to image organs and other structures - may diagnose some endocrine and gastrointestinal disorders, cancers.

Radiological Imaging: Notable Cases

HealthMyne is an applied radiomics company that specializes in collecting novel data and predictive biomarkers from medical imaging. The company's AI-based solutions provide access and easily translate ground-breaking radiomic insights into use in cancer research, treatment planning, clinical management, and overall health assessment. The future efforts of the HealthMyne team are aimed at revealing the still-untapped potential of imaging data for more accurate and personalized patient care.

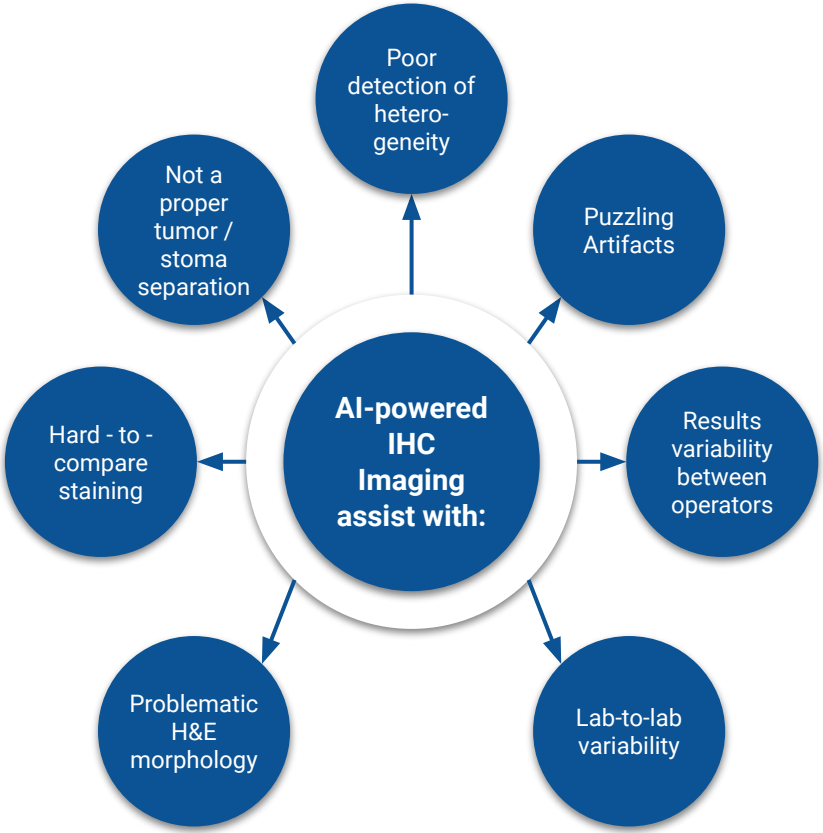
Enlitic creates AI-powered clinical and non-clinical workflow solutions to address high-value clinical and operational challenges in the healthcare infrastructure. **The Enlitic Curie™ platform** standardizes data automatically and provides radiologists with AI-based reading, reporting, and research options. This technology simply fits into any existing healthcare infrastructure to increase productivity, efficiency, and quality.

Bioxydyn provides high-standard, quantitative MRI imaging solutions to the pharmaceutical industry as well as for clinical and academic studies. Bioxydyn's imaging biomarkers are based on state-of-the-art technology and leading scientific studies. The company focuses on advanced functional MRI biomarkers in oncology, pulmonary pathology, liver disease, and neurology conditions.

Immunohistochemistry Imaging

Immunohistochemistry (IHC) is an imaging technique allows visualizing if the biomarkers within cells/tissues. It is a main technique applied by pathologists. IHC is based on the ability of antibodies to bind to the specific antigens and as a result to demonstrate the presence or absence, level of expression, localization as well as distribution of the protein of interests within tissues/cellular samples. Pathologists use a panel of different antibodies that target tissue specific proteins (biomarkers), such as estrogen receptor for gynecological cancers, or cytokeratin 20 for gastrointestinal cancers.

It is widely used in research and in medical purposes. In clinical settings, IHC is used to assist physicians to evaluate tissue specimens with a respect to healthy and disease conditions. Based on the biomarkers' visualization, pathologists can conclude on disease/ condition status. For example, IHC is a vital tool to diagnose malignant and classify tumors - it helps to choose a correct treatment protocol. IHC is also used in drug development to validate the efficacy of a drug, as it allows tracking the disease/condition progression. Currently, IHC imaging sector undergo modifications of AI-implementations and digitalization, enabling more reliable results.



Immunohistochemistry Notable Cases

PathAI prioritizes the improvement of patient outcomes with AI-based technology in order to provide the most accurate diagnosis and efficient treatments. The AI-powered platform detects and analyzes new cellular and tissue patterns in order to uncover pathology-based traits that are used to acquire new insights into drug development and treatment domains. PathAI high-precision solutions increase the number of biomarker-positive patients while preserving or improving treatment response efficacy.

Proscia develops and deploys AI-based digital products in the field of tissue pathology. The company provides **Concentriq® - the digital platform** that allows integration of AI applications from many sources and helps to view results alongside all other pathology data. Proscia also supports **DermAI**, which uses a very accurate algorithm based on over 13.000 photos to automatically classify dermatopathology slides.

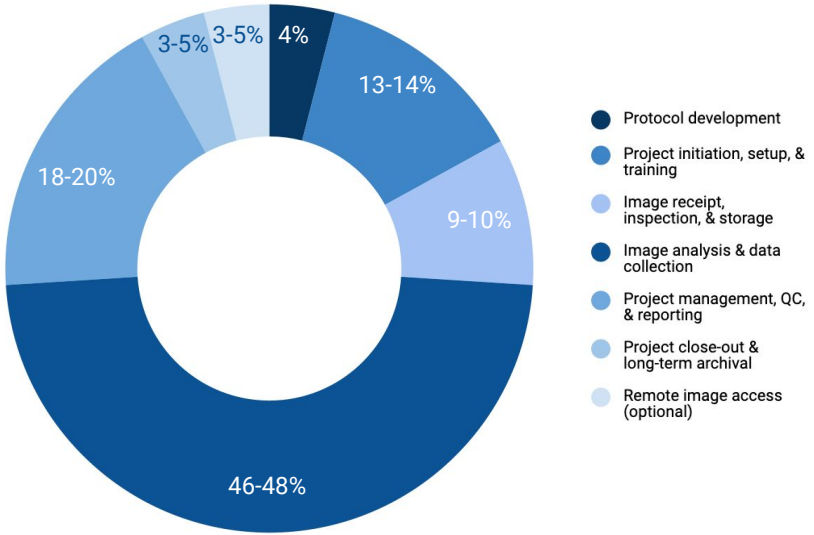
Visiopharm® is a global leader in AI-driven digital precision pathology software, and its image analysis and tissue mining solutions assist researchers and medication developers all over the world. Their **AI image analysis platform** makes it possible to apply, train, and create high-quality deep learning algorithms to achieve breakthrough outcomes in different fields of work. Along with a variety of machine learning techniques, the Visiopharm software also includes **three types of deep learning classifiers**.

Clinical Trials And R&D Imaging

Medical Imaging use in clinical trials (especially in oncological and neurological areas) **is expanding.** Despite the high cost, Imaging provide benefits: it provides evidences for decision-making, insights into Clinical Pharmacology and Mechanisms of Drug Action, improves the efficiency of drug screening, reducing the cost of the later clinical trials, and quicker trails completion. Those benefits are available with conventional Medical Images softs - yet the one based on AI provide additional advantages. Currently, while using imaging in clinical trials, 46-48% of Imaging-Related Clinical Trials costs are spent on Imaging analysis and data collection. AI-powered imaging software able to reduce overall imaging trial cost - it has a highly scalable capacity enabling large-scale screenings; allows for rapid scan processing, as well as well-trained algorithms allows for accurate analysis

The example is the measurement of the shrinkage of the solid tumors - classical endpoint in the response evaluation of the anti-cancer drug treatment. For neurological disorders, beta-amyloid plaques can be detected via tracers and consequent imaging, MRI scans, shows the rate of hippocampal atrophy.

Sample Breakdown of Imaging-Related Clinical Trials Costs



Clinical Trials And R&D Notable Cases

Median brings together imaging specialists and advanced imaging technologies in order to simplify and improve the quality of clinical trials. The **software platform iSee®** extracts biomarkers using multiple imaging criteria as well as carries out expert oversight of images, automating and standardizing lesion identification, selection, and assessment. In addition, Median's **AI-powered diagnostic software, iBiopsy®**, supports doctors with end-to-end technology by providing accuracy, well-timed diagnosis, and avoiding invasive procedures for patients.

median
The Imaging Phenomics Company®

IXICO is a well-known neuroimaging provider, collaborating with pharma and biotech companies to improve the outcomes of CNS clinical trials. Using advanced data-driven technology, the company develops and implements innovative neuroimaging biomarkers and image processing techniques that give accurate, rich structural and functional information. IXICO's AI neuroimaging algorithms for Alzheimer's, Parkinson's, and Huntington's disease detecting are based on over 100,000 MRI and PET brain scans from CNS clinical trials.

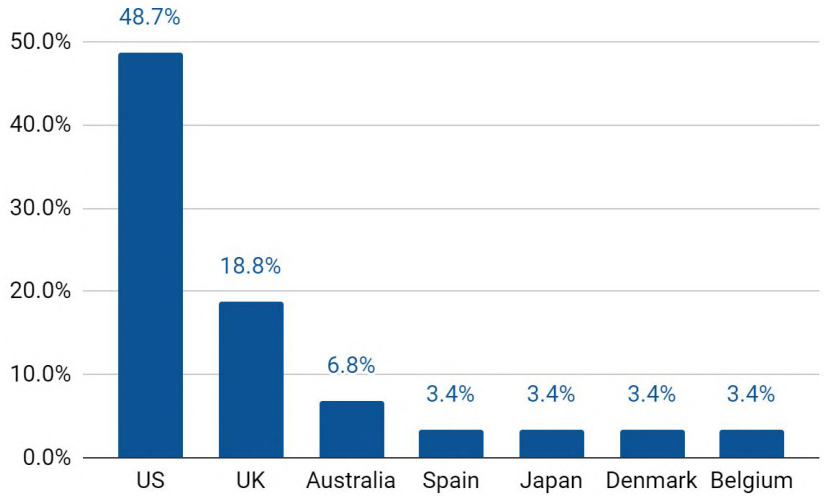
IXICO

MedQIA provides an automated AI-powered technology platform to manage imaging for oncology, lung, innovative, and post-market trials. Their **cloud platform and self-improving AI algorithms** allow them to automate complex procedures, control quality, and maintain transparent metrics for each step in the imaging workflow. This contributes to increased efficiency and lower-cost investigations with a shorter turnaround time.

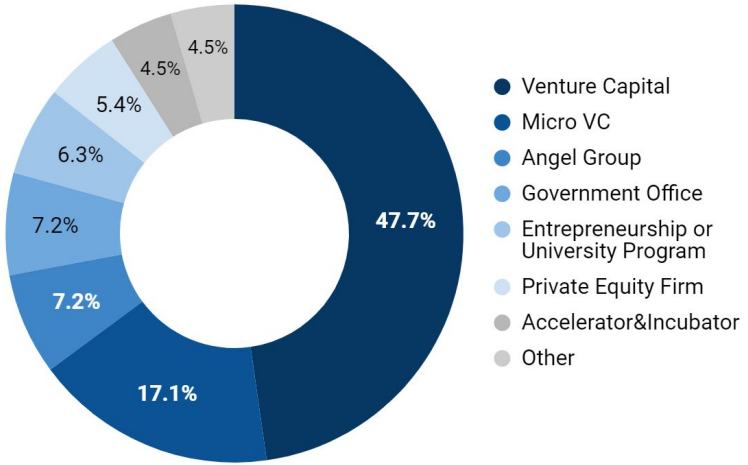
MedQIA

Market Overview: Global Market and Investors

Countries with the Largest Number of Investors, %



Main Type of the Investors, %

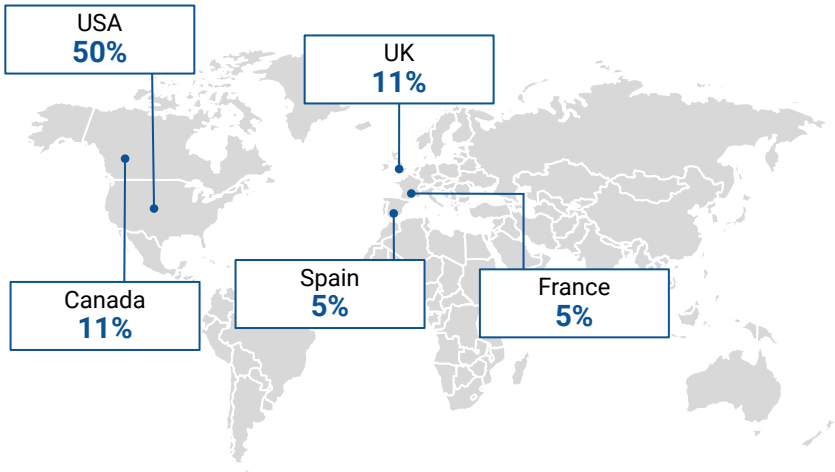


A little less than a half (48.7%) of investors in Imaging Biomarkers are from the US. Investors from **the UK constitute around 18.8%.** Around 29% of all investors are from the top European countries (the UK, Spain, Denmark, and Belgium).

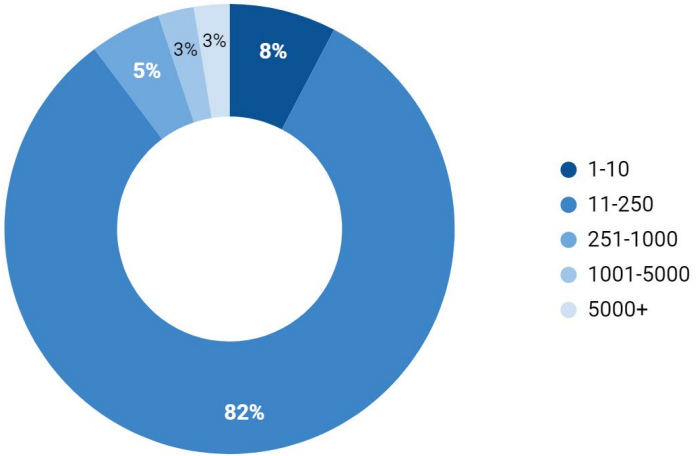
Around 65% of investors are Venture Capital and Micro VC companies. Government Offices and different business encouraging programs account for the other 13.5% of all investors.

Market Overview: Geography of Companies

Distribution of Companies by Country, %



Distribution of Companies by Number of Employees, %



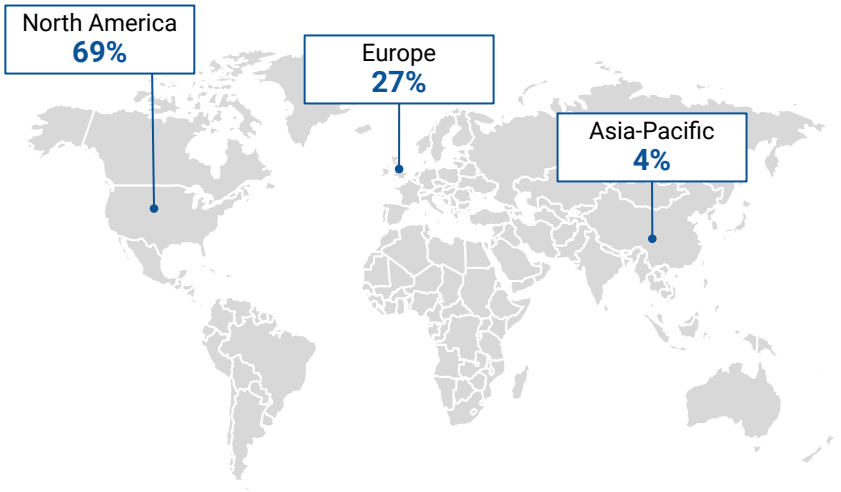
The top 5 countries accumulate more than 90% of all companies that research Imaging Biomarkers. **Half of the companies** is allocated **in the US**. **The other 11% of companies are in Canada**, which makes Northern America the domain of the Imaging Biomarkers sector. The rest of the companies are primarily allocated in Europe. There are **11%** of companies for **the UK,** and **10%** together from **Spain and France - by 5%** in each.

More than 80% of all companies are small companies **with 11-250 employees**. However, there are large and very large companies on the market with more than 5000 employees.

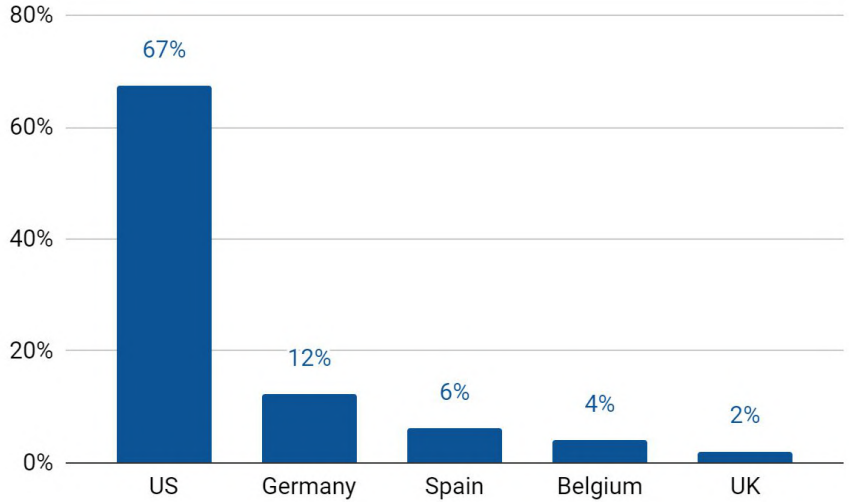
Source: Aging Analytics Agency analysis

Market Overview: R&D Centres

Distribution of R&D Centres by Regions, %



Top Countries by Number of R&D Centres,%



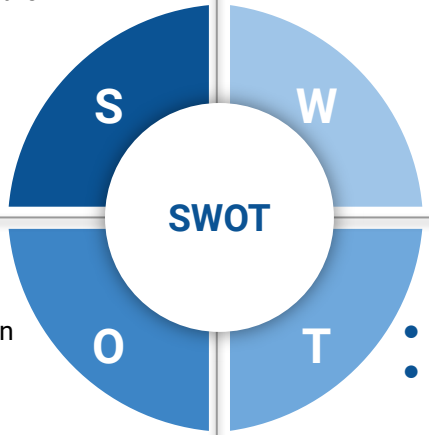
The **vast majority** of R&D centres **(69%)** that conduct research in Imaging Biomarkers area, is situated **in Northern America,** 67% are in the US. **Other 27% are in Europe,** with 12% in Germany, 6% in Spain, 4% in Belgium. In Asia-Pacific region there is also 4% of R&D centres.

Source: Aging Analytics Agency analysis

Imaging Biomarkers: SWOT Analysis

- Easy to obtain images are actionable and can be scaled up for population
- Use is not time-consuming
- Can detect diseases that are not detected well by other types of biomarkers

- Most can be performed only in clinical conditions
- Yet have strong statistical inaccuracies
- List of possible diseases for detection is limited



- Database expansion is already resulting in detection enforcement and increase of quality
- Can be possibly made a home-use solution for smartphone users
- Can be a key biomarker type used for actionable digital solutions

- May result in misdiagnosis
- Use of home-use molecular biomarkers may decrease the popularity of Imaging biomarkers

Source: Wiley Analytic Science

Key Takeaways: Imaging Biomarkers

The diversity of applications, noninvasive nature - which allows **for full-body screening**, and intrinsically quantifiable nature are substantial advantages of Imaging Biomarkers. The most recent trend in this sector is **increasing actionability and availability** for customers.

Imaging Biomarkers can be used **for diagnostics** (the identification of disease signs), **prediction** (predispose of disease risk), **prognostication** (the prediction of prognosis), and **treatment assessment.** Taken together, Imaging Biomarkers carry valuable characteristics for expanding people`s Longevity and **contribute to Healthier Aging** while providing early diagnostics and estimating the disease risks.

Imaging biomarkers are the cornerstone of modern **radiology,** and they're also a crucial tool in clinical trials for assessing **pharmaceutical efficacy and patient safet**y. They play an important role in the evaluation of treatments and drug efficacy, as well as treatment decisions.

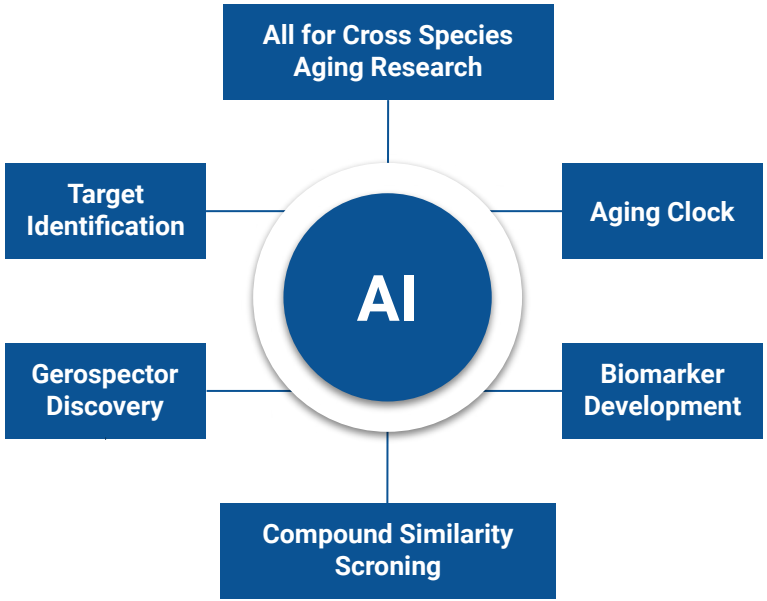
Sophisticated **AI-based software and platforms** are increasingly being implemented in the imaging biomarker sector. These platforms allow for **large-scale screenings;** fast image processing and accurate analysis eliminating variability between different diagnostic laboratories.

AI and Biomarkers

Increasing Necessity Role of AI in Longevity Research

Currently, there is a necessitating paradigm shift toward more excellent prevention, personalization, precision and patient participation, utilizing all available tools and technologies that are market-ready today to optimize healthy longevity. **Artificial Intelligence is considered a significant engine and driver of future Longevity science and industry**.

The unique role of **AI in longevity lies in P4 medicine**. P4 medicine is a medical model that separates people into different groups—with medical decisions, practices, interventions and products being tailored to the individual patient based on their predicted response or risk of disease. The main difference between P4 medicine and the traditional medical approach is that P4 is directed to the individual patients' wellness, while the conventional approach is directed to population wellness. P4 is defined by the fact that its constituent leading-edge technologies have already achieved a state of market-readiness and clinical implementation, consists of those Longevity-relevant technologies and techniques that are in practice today, what remains to be done in terms of actually applying them for the extension of Healthy Longevity is primarily a matter of data mining, analysis and management, driven by **advances in biomedicine, data science and Artificial Intelligence**.

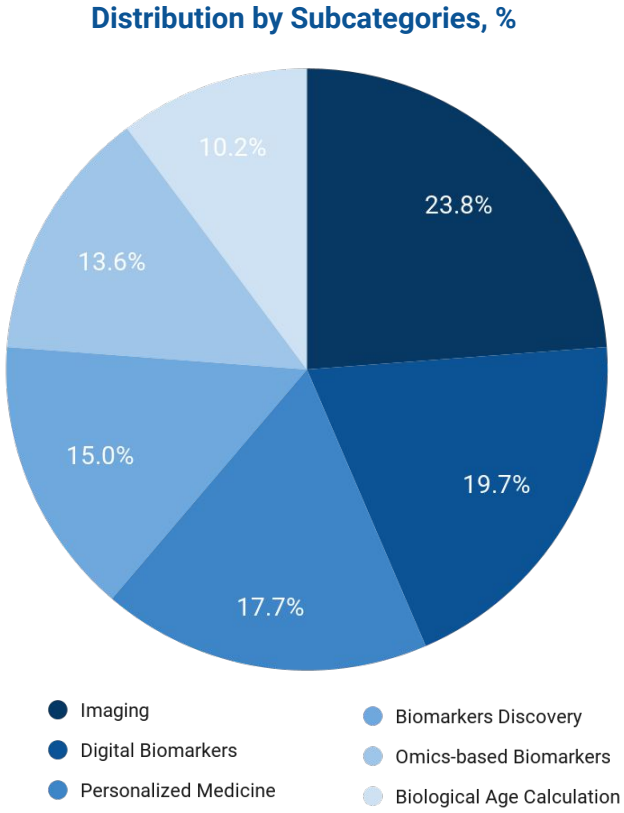


AI in Biomarkers Overview

Artificial intelligence (AI) is a broad discipline of computer science concerned with creating intelligent machines that can accomplish activities that would normally need human intelligence. It is widely embedded in our everyday life and its implementation in clinical researchers and the pharmaceutical industry.

Artificial intelligence-enabled algorithms develop impartial hypotheses for prospective biomarkers or combinations, exploring all feasible scenarios, and **provide better analysis and decisions for precise diagnostics and treatment**.

AI-based biomarkers are divided into subgroups such as imaging, digital biomarkers, personalized medicine biomarkers, omics-based biomarkers, new biomarkers discovery, and biological age calculations via different biomarkers of aging measurement. They are preferably used in imaging, digital biomarkers and in personalized medicine. However, this technology is new and quickly spreads in other fields of study which means that these are **not all possible implementations of AI-based biomarkers**.



AI and Biomarkers

AI for imaging biomarkers is implemented for processing photos, MRI, X-ray, CT, histological sections and other medical and non-medical images. This subcategory is the biggest - **23.8% of all companies use AI for imaging**. The reason for such prevalence of AI for imaging is the high degree of development of algorithms that are used, for example, CNN - **Convolutional Neural Networks**. The AI for imaging diagnostics shows impressive accuracy and sensitivity in the identification of imaging abnormalities and promises to enhance tissue-based detection and characterisation. The level of development of AI for medical images is so high that sometimes it is already used in regular hospitals.

Digital biomarkers are currently in the stage of rapid development. A bunch of new companies developing or realizing digital biomarkers open every month. There are two reasons for this: the first is the rapid development of **intelligent devices and the Internet of Things**; the second is **cheapness and simplicity** in implementing digital biomarkers. However, digital biomarkers produce an extremely high amount of data which is difficult to process with standard statistical methods. In that stage, the AI is implemented - **19.7% of companies using AI for biomarkers use it for digital biomarkers**. AI is used for digital biomarkers data processing to **diagnose particular conditions or aging evaluation**.

Personalized medicine is a medical approach that refers to the drugs and treatments that are designed and applied using precise, individual methods of dosing, drug compositions, and efficient ways of delivery. Biomarkers are measurable indicators of a biological state that are primary metric in precision medicine. Patients evaluate their health with the special tools, approaches and services that **monitor their biomarkers with AI-empowering** to set some adjustments to their behavioural, lifestyle and therapeutic regimens **to improve treatment results and overall health state**. **AI-empowered biomarkers monitoring** can **predict the risk of diseases** long before their actual onset and progression.

AI Contribution into Longevity Biomarkers Development

The **application of AI and data science to Longevity** has the most significant potential to create a real-world impact on human Longevity in a short timeframe and the with the highest cost-effectiveness ratio. However, despite being the component with tremendous promise, **AI is underrepresented and under financed within the Global Longevity Industry**.

AI for longevity is the "smart money" sector of the industry that can achieve tremendous results and accelerate timelines in the progress of tangible, real-world Healthy Human Longevity, even with modest funding levels compared to other sectors. There is a prediction that **AI will play a central role in the Longevity space within several years**. It will include the aggregation, development, and deployment of biomarkers of aging, health, and longevity, preventive medicine diagnostics and prognostics, and precision health technologies.

The apex of AI for Human Biomarkers of Longevity, and its most robust and advanced embodiment, will be the enabling force for creating a so-called **digital avatar of the full human body**, using thousands if not tens of thousands of personalized biomarkers, with at least several hundred precise Biomarkers of Aging and Longevity. These will include not only biological but also psychological and behavioral biomarkers. To find out more about digital avatars, see section "Digital Avatars", page 207.

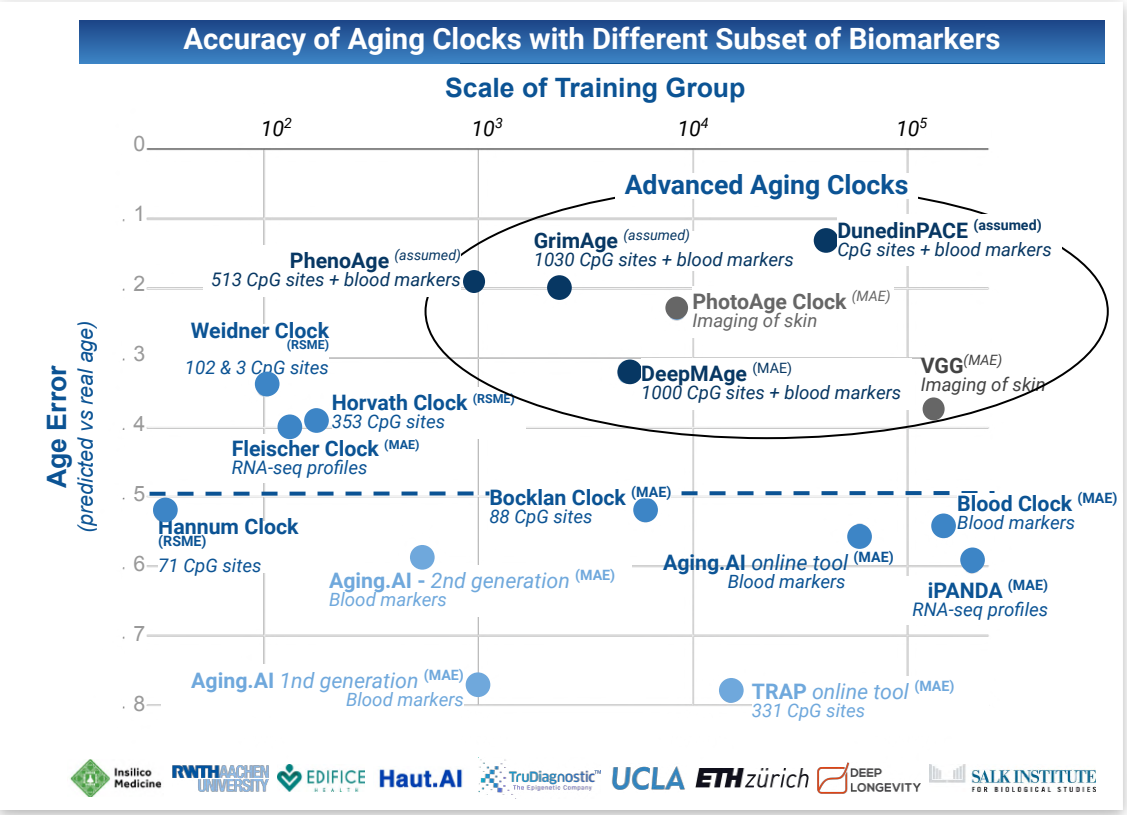
Deep Aging Clocks Description

Types of Deep Aging Clocks			
Methylation aging clocks	**Hematological aging clock**	**Imaging aging clocks**	**Transcriptomic aging clocks**
Actually the first developed aging clocks(2013). Methylation aging clocks predict aging and associate it with DNA methylation	Hematological aging clocks are developed from blood biomarkers data.Blood biomarkers data can be obtained from simple and universal blood tests.	Imaging aging clocks can be developed using only photographic data. Furthermore, many genetic and phenotypic disorders can be diagnosed from a picture.	Transcriptomic aging clocks are based on gene expression data from several tissues. Transcriptomic data enable the identification of the genes most implicated in specific diseases, such as cancer.

Multiple data types can be used to predict aging and explain the link between aging and mortality, disease, general wellbeing, or other biological processes such as methylation, gene expression, microbiome, and imaging data. Processing the huge amount of data using ML/DL technologies provide different types of deep aging clocks which represent specific aging-models.

Source: Trends in Pharmacological Sciences

Comparison of Aging Clock: Accuracy of Different Algorithms



To determine biological age and predict life expectancy, a set of similar or dissimilar biomarkers is most often used. **The DNA methylation (DNAm) clocks** combined with blood markers are currently the most accurate biological clocks. Their developers claimed 2-3 times higer accuracy than conventional DNAm Clocks like Horvath and Hannum.

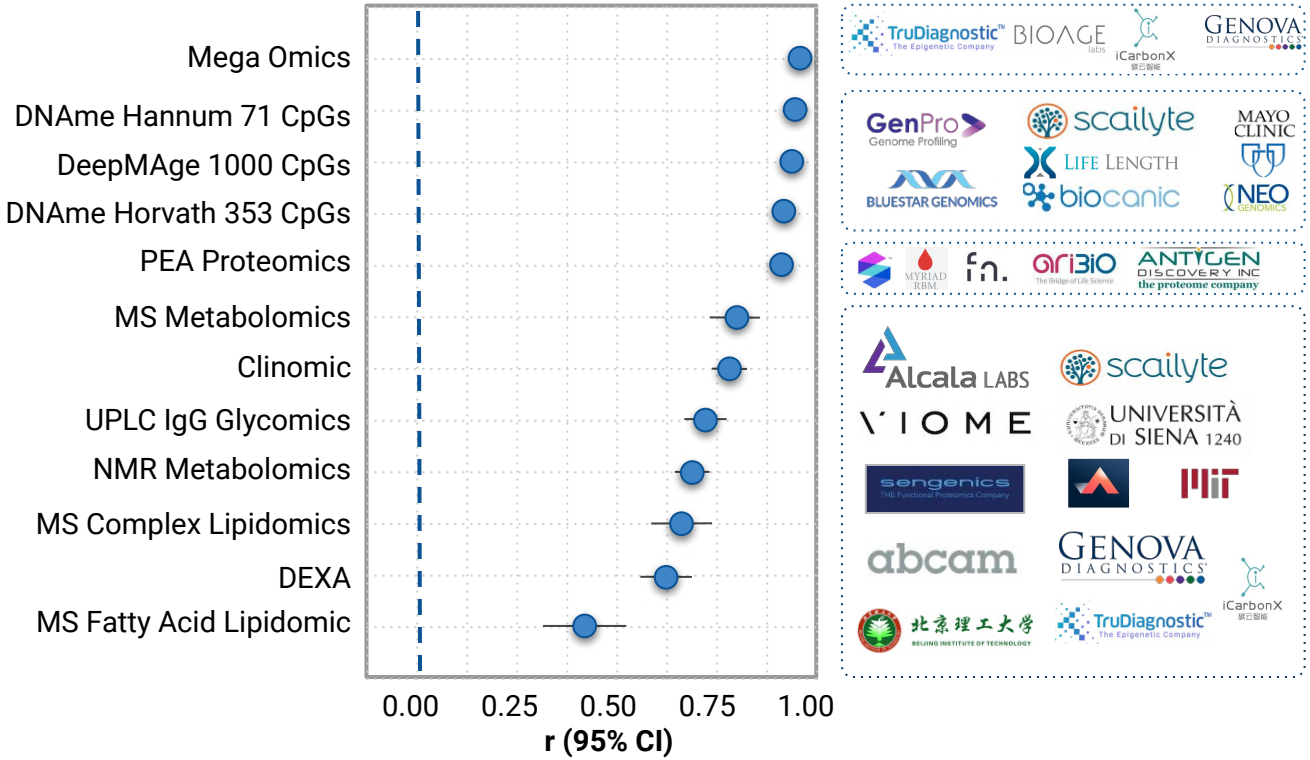
DunedinPACE *(TruDiagnostic)*, **GrimAge** and **PhenoAge** *(University of California LA)* were created using **Elastic net model** extension of linear regression that adds regularization penalties to the loss function during training. Beside, **DeepMAge** *(Deep Longevity)* created using feed-forward neural networks, stands out among this bunch.

Other advanced clocks, like **PhotoAge Clock** *(HautAI)* and **VGG** *(ETH Zurich)* are based on analysis of skin scans. They precisely predict chronological age.

Some clocks based **biochemistry profiles** provide a different perspective on aging, but they have yet to surpass the **MAE 5 year mark**.

Comparison of Omic Companies that Use Aging Clock Algorithms

Correlation of Predicted Age vs. Real Age



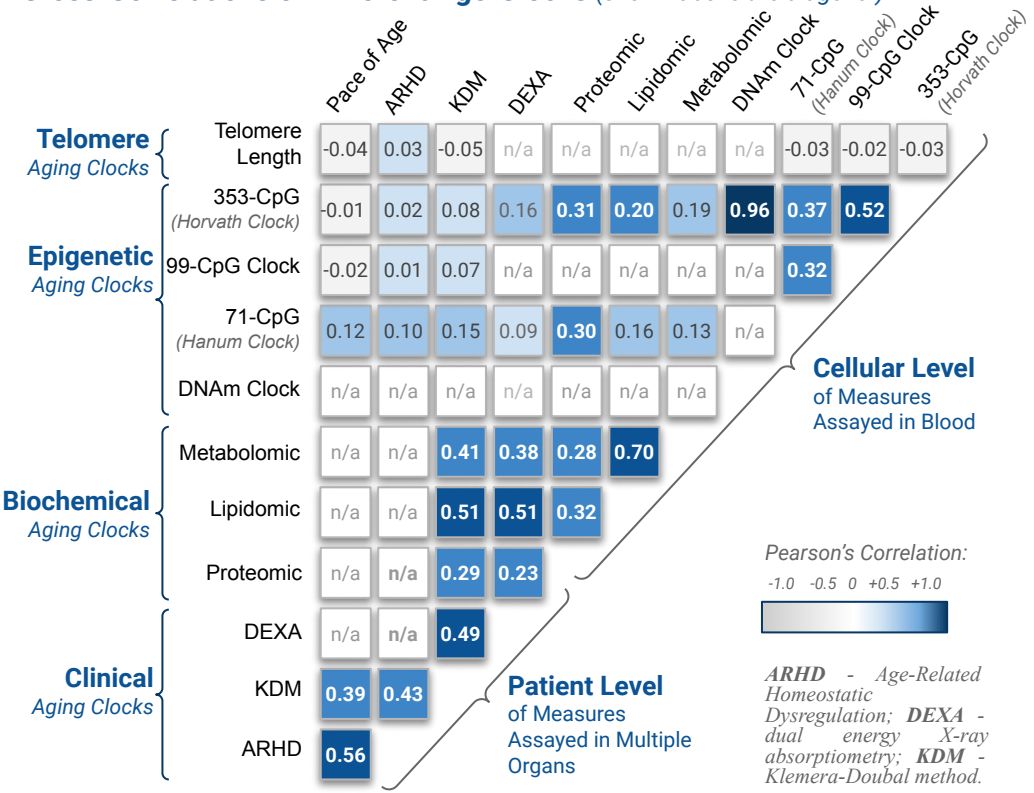
Omic-based Aging Clocks have the potential to be clinically useful. Here, we perform comparable correlation between chronological and biological age for **12 omic clock**s trained on the **chronAge algorithm**. Data are presented on the chart highlighting the potential for accurate aging clock.

According to accuracy level of method, we ranged companies that use presented Aging Clocks. **The most accurate are Mega Omic** that use combined omic data from different type of biomarkers

Source: E. Macdonald-Dunlop // bioRxiv. 2021 Feb (doi: https://doi.org/10.1101/2021.02.01.429117)

Comparison of Biological Age Between Clocks

Cross-Correlations of Different Age-Clocks *(shown above the diagonal)*



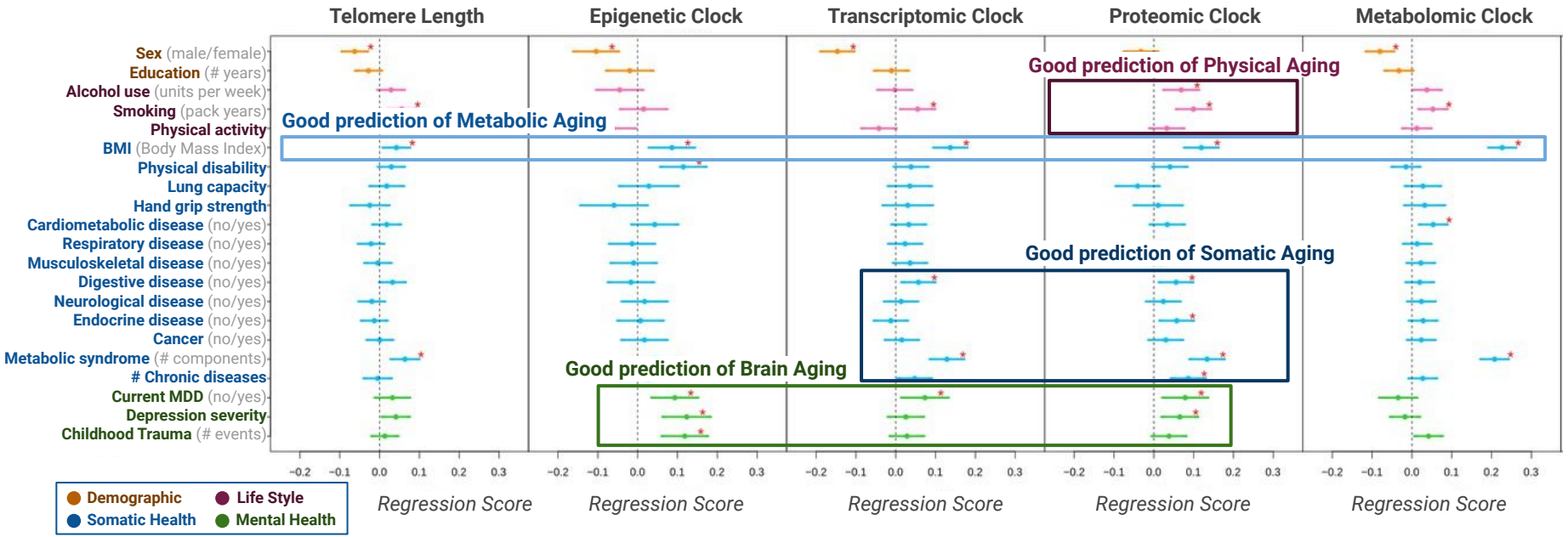
All modern aging clocks are proven to be invaluable tools for biogerontology since they **offer a unique opportunity to quantify the aging process**. This ability is essential for **testing geroprotective interventions** and studying **age-related diseases**. While all biological clocks aim to measure the biological aging process, there is limited evidence for cross-correlations among different clocks. Some studies has shown significant differences in the Telomeres, Clinical Biomarker and DNAm clocks operate, more specifically the **low correlation between their predictions** and their **unequal sensitivity** to certain age-related diseases.

Epigenetic Clocks were correlated with each other in the **r = 0.3–0.5** range *(P < 0.001 for all)*. **Clinical Aging Clocks** algorithm measures were correlated with one another in the **r = 0.4–0.6** range (P < 0.001 for all). However, **Telomere Clocks** was **not significantly correlated** with estimates from epigenetic clocks or clinical-biomarker algorithms (**r = −0.05–0.03**; P > 0.05 for all), and correlations of epigenetic clock measures with clinical-biomarker-algorithm measures were generally low.

Source 1: D.W. Belsky // Am J Epidemiol. 2018 Jun; 187(6): 1220–1230.
Source 2: E. Macdonald-Dunlop // bioRxiv. 2021 Feb (doi: https://doi.org/10.1101/2021.02.01.429117)

Biological Relevance of Omic-based Aging Clocks

Associations between Biological Aging Measured by Omic-based Aging Clock and Health Determinants

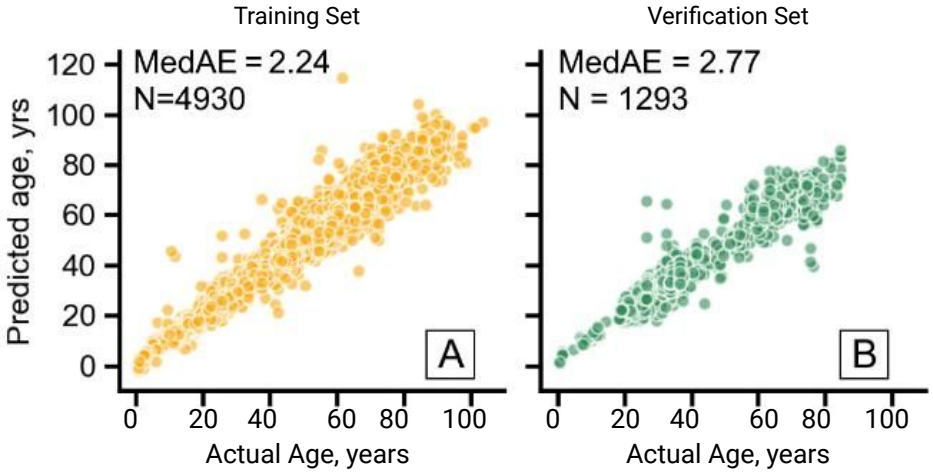


One important concern is the clock's biological relevance, but some developers determine their biological relevance post-factum. R. Jansen et. all (2020) has shown **associations** of most popular **omic-based aging clocks** with several **demographic** (sex, education), **lifestyle** (physical activity, smoking, alcohol use), **somatic health** (BMI, hand grip strength, lung function, physical disability, chronic diseases), and **mental health** (current depression, depression severity, childhood trauma) determinants. Except for proteomic aging, sex was associated with all biological aging indicators: **women were biologically younger than men**. Education was not associated with any biological aging indicator. **Proteomic Clocks are universal** for determination of total Aging level in body.

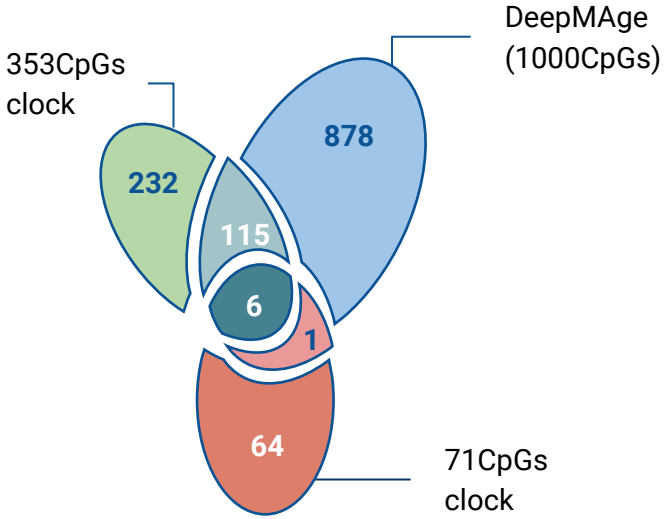
Source: Jansen, Han, et al. eLife 2021;10:e59479. DOI: https://doi.org/10.7554/eLife.59479

Deep Learning for the DNAm Aging Clock: Improving Accuracy

Prediction of Chronological Age by DeepMAge - DNAm Aging Clock Based on Neural Networks



Scatter plot in panel A shows the per-fold predictions obtained during cross-validation, and the other panels show the predictions by the final model. MedAE = Median absolute error measured in years, N = Number of samples in a corresponding cohort



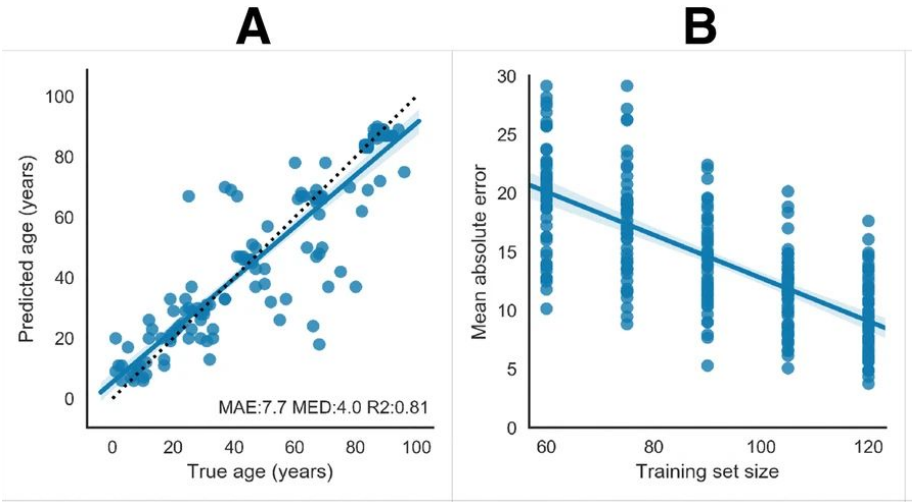
DeepMAge is the **first deep learning DNAm aging clock** that performs better than linear regression models (**medAE = 2.77 years**). **DeepMAge is more accurate** in predicting the age of healthy individuals than **Horvath clock** (MedAE = 3.51 years) and **Hannum clock** (RMSE = 3.9 years).

DeepMAge uses 1,000 CpG sites, 121 of which are shared with the Horvath clock (353 CpG) and 7 with the Hannum clock (71 CpG). The genes where the DeepMAge CpGs are located are enriched with those taking part in cardio- and neurodevelopmental processes.

Source: DeepMAge: A Methylation Aging Clock Developed with Deep Learning

Age Prediction Using the Human Transcriptome

Gene Expression Data from Human Fibroblasts to Predict Age



The dataset of **genome-wide RNA-seq profiles** of human dermal fibroblasts was used to develop a machine learning algorithm that **predicts human age** to a **median error of 4 years** and a **7.7-year mean absolute error**.

Using data on gene expression has long been an appealing direction in biochorology. However, until recently, there were no algorithms that could accurately identify a person's age. Today, there is already reason to believe that transcriptome data will become a reliable predictor of age and longevity in the future.

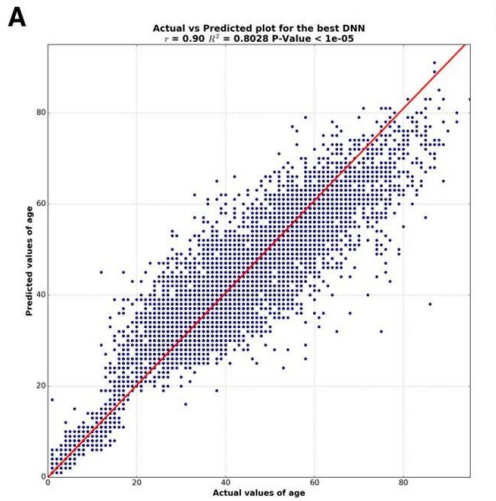
It is reported that the **ensemble of linear discriminant analysis classifiers** predicted ages that differed from true chronological age by a median **absolute error of 4 years** and a **mean absolute error of 7.7 years**. An extensive **RNA-seq dataset of fibroblast cell lines** obtained from 133 healthy individuals and 10 patients with Hutchinson-Gilford progeria syndrome was used to train the ML algorithm.

This predictor is comparable to the 7.8-year mean error produced from transcriptomic data in the blood and is not far off from the performance of **Horvath's DNAm clock** (3.9-year median absolute error) or **Putin's deep learning method based on blood biomarkers** (5.5-year mean absolute error).

Source: Predicting age from the transcriptome of human dermal fibroblasts

Blood-Based Algorithm for Prediction of Human Age

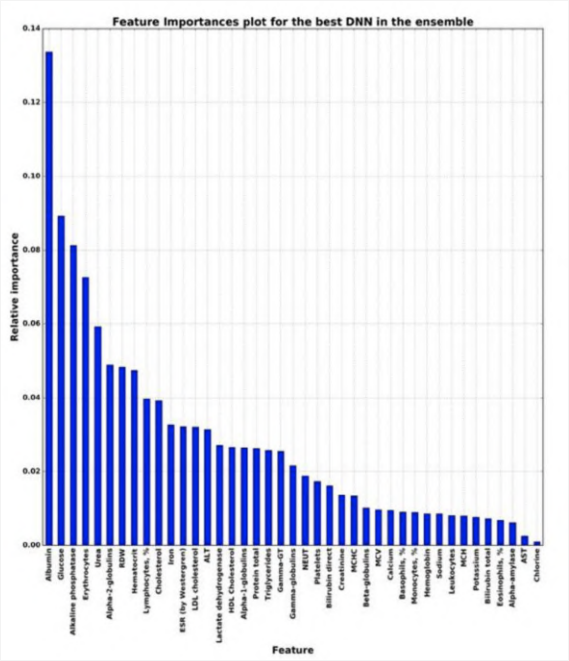
Deep Neural Networks to Predict Chronological Age Using a Blood Test



62,419 anonymized blood biochemistry and cell count tests were used to train the deep neural networks (DNNs) ensemble. Each record consisted of a person's age, sex, and **46 standardized blood markers**. The best performing DNN demonstrated a **mean absolute error of 6.07 years** in predicting chronological age.

The **5 most important markers** for predicting human chronological age according to DNNs processing: **albumin, glucose, alkaline phosphatase, urea and erythrocytes**.

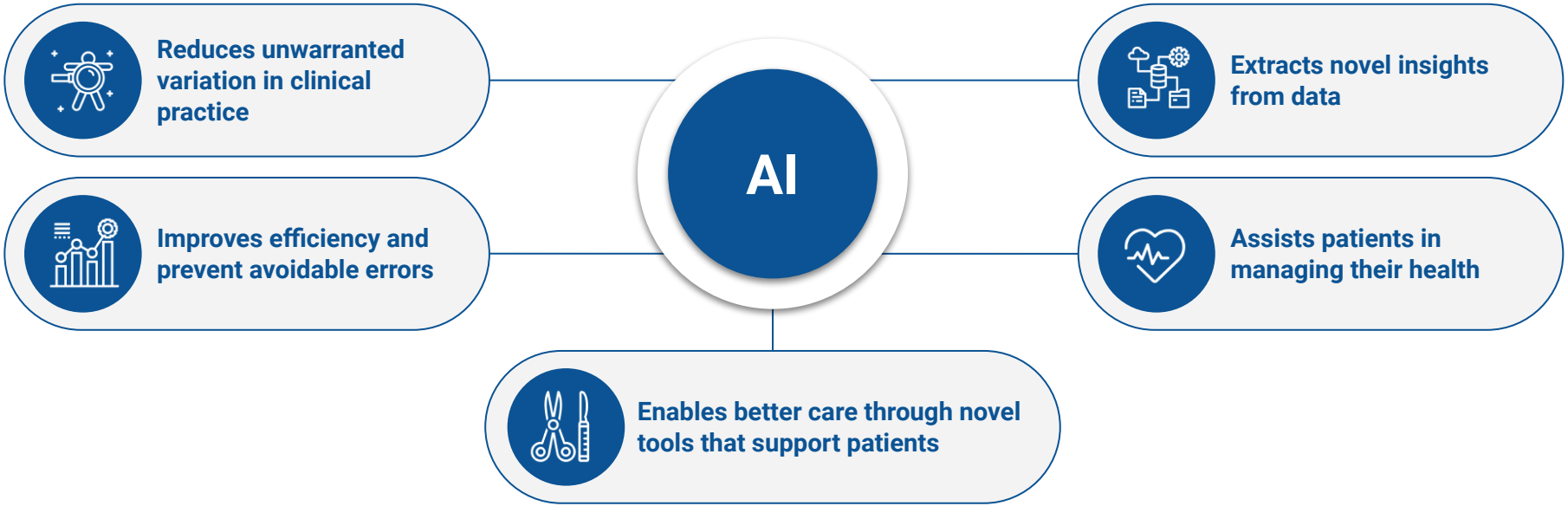
To allow for public testing and evaluate the real-life performance of the predictor, an online platform called **Aging.AI** was developed.



Source: Deep biomarkers of human aging: Application of deep neural networks to biomarker development

Benefits of AI in Healthcare

Artificial Intelligence holds enormous potential for improving the health of millions of people around the world. It can be used to improve the speed and accuracy of diagnosis and screening for diseases; to assist with clinical care; strengthen health research and drug development, and support diverse public health interventions, such as disease surveillance, outbreak response, and health systems management. Besides, these amazing, but already well-known benefits of AI application, there a few potentials of AI for healthcare that are mainly unknown for public. **AI has the potential to solve challenges such as:**



Source: *analyticsindiamag.com*

To find out more about AI in healthcare, see DPI report "AI in Drug Development"

WHO Reported 6 Principles of AI Implementation in Healthcare

1	**Protect human autonomy**	Humans should remain in control of healthcare systems and medical decisions; privacy and confidentiality should be protected, and patients must give valid informed consent through appropriate legal frameworks for data protection.
2	**Promoting human well-being, safety and the public interest**	The designers of AI technologies should satisfy regulatory requirements for safety, accuracy and efficacy for well-defined use cases or indications. Measures of quality control in practice and quality improvement in the use of AI must be available.
3	**Ensuring transparency, explainability and intelligibility**	Sufficient information should be published or documented before the design or deployment of an AI technology. The information must be easily accessible and facilitate meaningful public consultation and debate.

Source: *WHO*

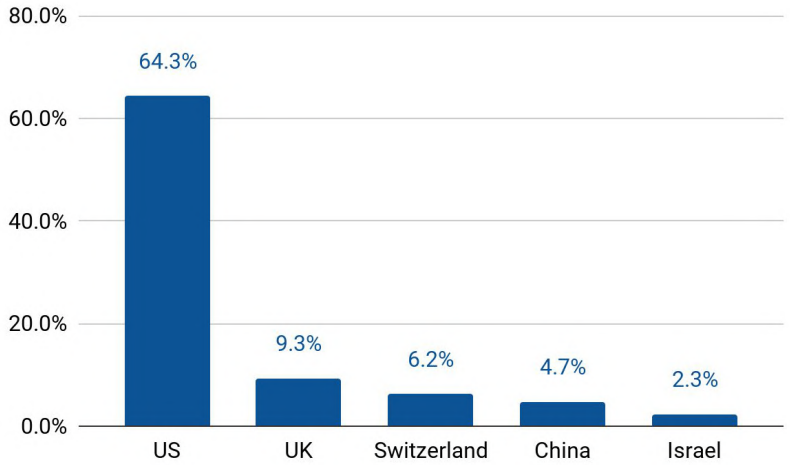
WHO Reported 6 Principles of AI Implementation in Healthcare

4	**Fostering responsibility and accountability**	The stakeholders are responsible to ensure that AI technologies are used under appropriate conditions and by appropriately trained people.
5	**Ensuring inclusiveness and equity**	Inclusiveness requires that AI for health be designed to encourage the widest possible equitable use and access, irrespective of age, sex, gender, income, race, ethnicity, sexual orientation, ability or other characteristics protected under human rights codes.
6	**Promoting AI that is responsive and sustainable**	Designers, developers and users should transparently assess AI applications during actual use to determine whether AI responds adequately to expectations and requirements. AI systems should be designed to minimize their environmental consequences and increase energy efficiency. Governments and companies should address anticipated disruptions in the workplace, including training for health-care workers to adapt to the use of AI systems, and potential job losses due to use of automated systems.

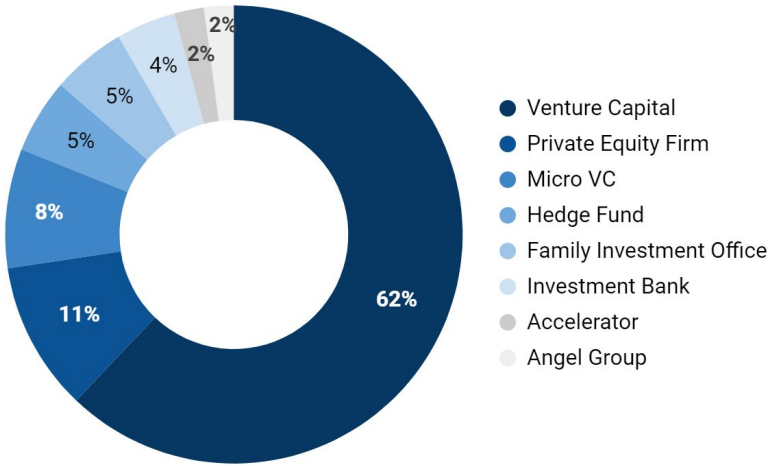
Source: *WHO*

Market Overview: Global Market and Investors

Top 5 Countries with the Largest Number of Investors, %



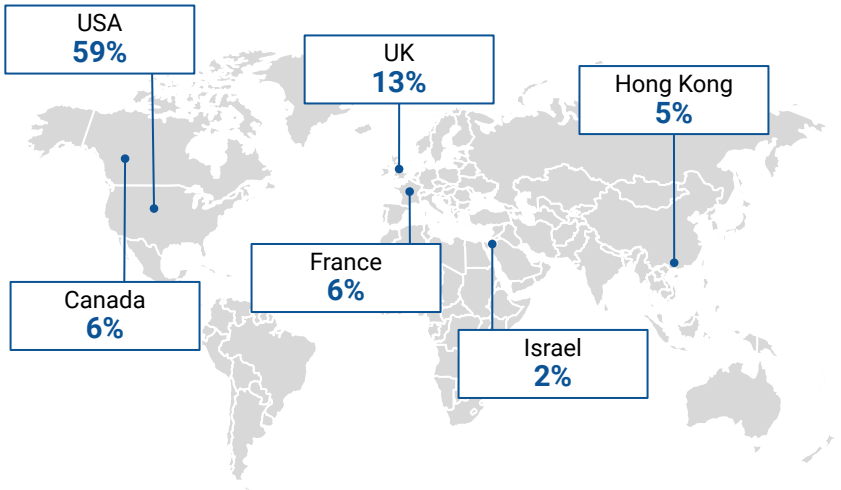
Main Type of the Investors, %



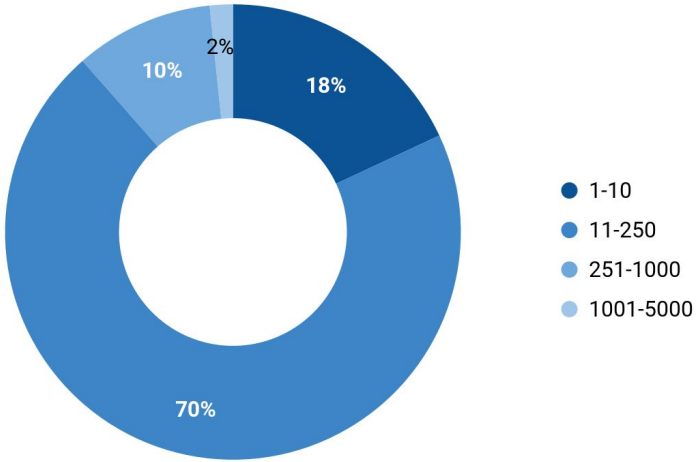
The main part of the investors are allocated **in the US (64%).** The other **9%** of investors are from **the UK.** Besides the US and European countries among top countries by number of investors are **China** with around **5%** of investors and **Israel with 2%.**
The Venture Capital investors are the main type of investors with **more than 62%** of total. By a wide margin Private Equity Firm and Micro VC are the following types of investors in the top.

Market Overview: Geography of Companies

Distribution of Companies by Country, %



Distribution of Companies by Number of Employees, %



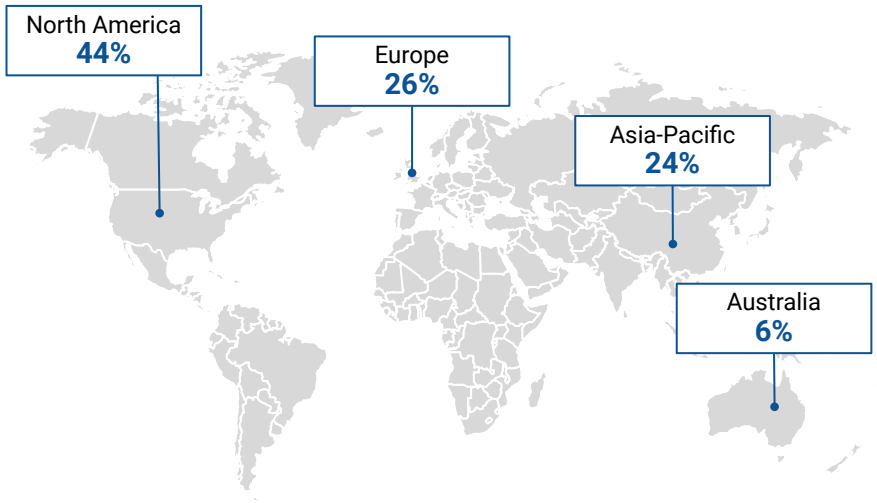
The vast majority of companies that conduct Artificial Intelligence researches is located **in the United States** and accounts for **59%** of the whole range of analyzed companies. In Northern America, The United States is followed by the European region, particularly by **the United Kingdom and France** with the total companies amount equal **to 13% and 6% respectively.**

Around 88% of all firms are either **micro or small-sized,** with a number of employees from 1 to 250. Medium and large firms with more than **250 employees are only 12%.**

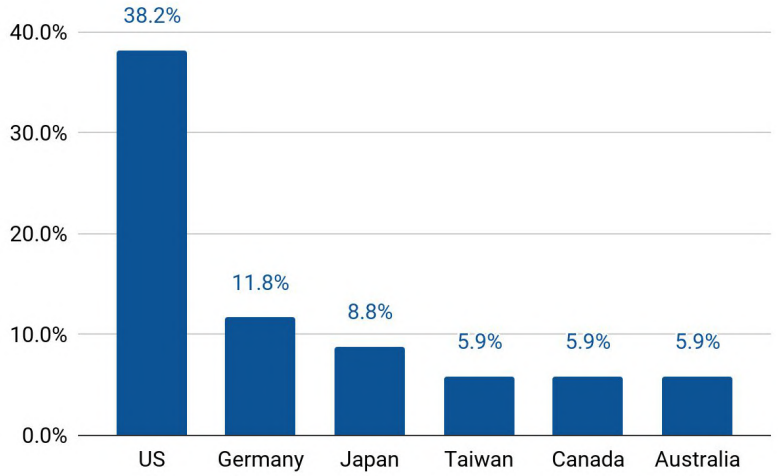
Source: Aging Analytics Agency analysis

Market Overview: R&D Centres

Distribution of R&D Centres by Region, %



Top 5 Countries by Number of R&D Centres, %



Around 44% of all R&D Centres that conduct studies on Artificial Intelligence in the Biomarker sphere are allocated **in Northern America** - 38% in the US and other 6% in Canada. **In Europe and Asia-Pacific** regions are situated by **26% and 24%** respectively.

A little less than a half of R&D Centres of Europe are allocated **in Germany - around 12% or 4 centres.** Japan and Taiwan with 9% and 6% of total R&D Centres respectively concentrate more than half of all Asia-Pacific R&D Centres.

Source: Aging Analytics Agency analysis

AI in Biomarkers: Notable cases

Scailyte is a company that is using AI for **biomarkers discovery**. On a multiomics level, ScaiVision (patented analytical machinery) allows them to evaluate and recognize unusual events from single-cell data. They have the ability to quickly turn around big data cohorts obtained from clinical trials and pinpoint exact biological targets.

Cogenica is a company that uses **omic-based biomarkers** for precision medicine. It has advanced automated Clinical Decision Support tool for genetic analysis, allowing them to quickly understand next-generation sequencing data, increase case throughput, and improve health outcomes, which makes a significant difference in people's lives.

Centaura is a company that involves AI in **age calculators** work. Centaura's mission is to explore the biological foundations of aging-related processes and create tailored medicines to tackle their core causes in order to **prevent and reverse aging**, keeping individuals healthy and effective both mentally and physically.

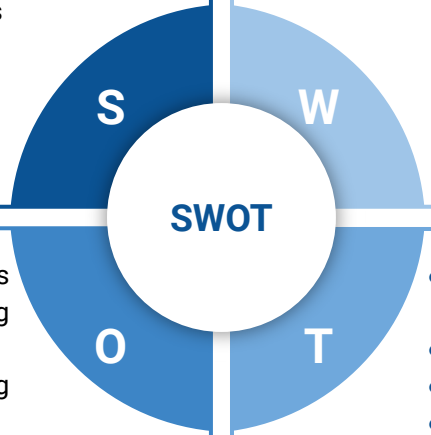
AI in Biomarkers: Notable cases

Proscia is a company that uses AI for **imaging biomarkers assessment**. With its Concentriq® digital pathology platform and pipeline of computational applications, Proscia is pushing labs beyond the limits of traditional tools. These technologies are revolutionizing pathology's economics and practice, putting the power of modern, data-centric medicine to work in the fight against cancer.

Savonics is digital based biomarker platform. Their **digital mobile platform** was designed by a team of leading data neuropsychologists, engineers, and scientists based on hundreds of years of test history. This digital neuropsychologist is used by many researchers, providers, and consumers. They provide solutions and tools to engage better understanding of cognitive health and make progress in the fight against dementia.

Tempus is a company that aims on making **precision medicine** a reality through the power of data and artificial intelligence application. They enable physicians to make real-time, data-driven decisions to deliver personalized patient care, while facilitating the discovery, development, and delivery of optimized therapeutic options for patients through distinct solution sets.

AI Biomarkers: SWOT Analysis



- Collecting vast amounts of data from the daily lives of people not in a hospital and provide continuous monitoring of health state
- Use powerful statistical algorithms for multi-omics data operating.
- Individual patient level approach which provides solutions for both preventive and personalized medicine decisions
- Increasing percentage of deep diagnostic and
- preventive medicine.
- Advanced Biomarker-based Prognostics
- Non-invasive

- Use only the data from mobile apps, or devices, not medical equipment.
- A lack of digital biomarkers popularization.
- Lack of accurate measurement of some physical biomarkers by mobile devices.

- Possibility to create new apps, mobile and wireless devices or human chips for collecting and integrating data and using Big data.
- AI biomarkers can be used to improve drug development and treatment.
- Continuous monitoring powered by Big Data Analytics.
- Advanced Biomarker-based prognostics.
- AI-driven in silico personalized treatment optimization.
- AI-driven personalized in vivo drug optimization.
- Treatment optimization based on patient genetics.

- Possibility to hack collected data or use in criminal cases or in geopolitical migration processes.
- Risks associated with the microchips technologies.
- The problem of tests standardization.
- The problem of the data storage technologies.
- The productivity of machine and computer analysis.
- The problem of integrating data from molecules, cells, organs, the individual, families, communities, and the natural and man-made environment.

Key Takeaways: AI Biomarkers

Artificial intelligence (AI) is a broad discipline of computer science concerned with creating intelligent machines that can accomplish activities that would normally need human intelligence. It is widely embedded in our everyday life and its implementation in clinical researchers and the pharmaceutical industry.

AI-based biomarkers are divided into subgroups such as **imaging**, **digital biomarkers**, **personalized medicine biomarkers**, **omics-based biomarkers**, **new biomarkers discovery**, and **biological age calculations** via different biomarkers of aging measurement.

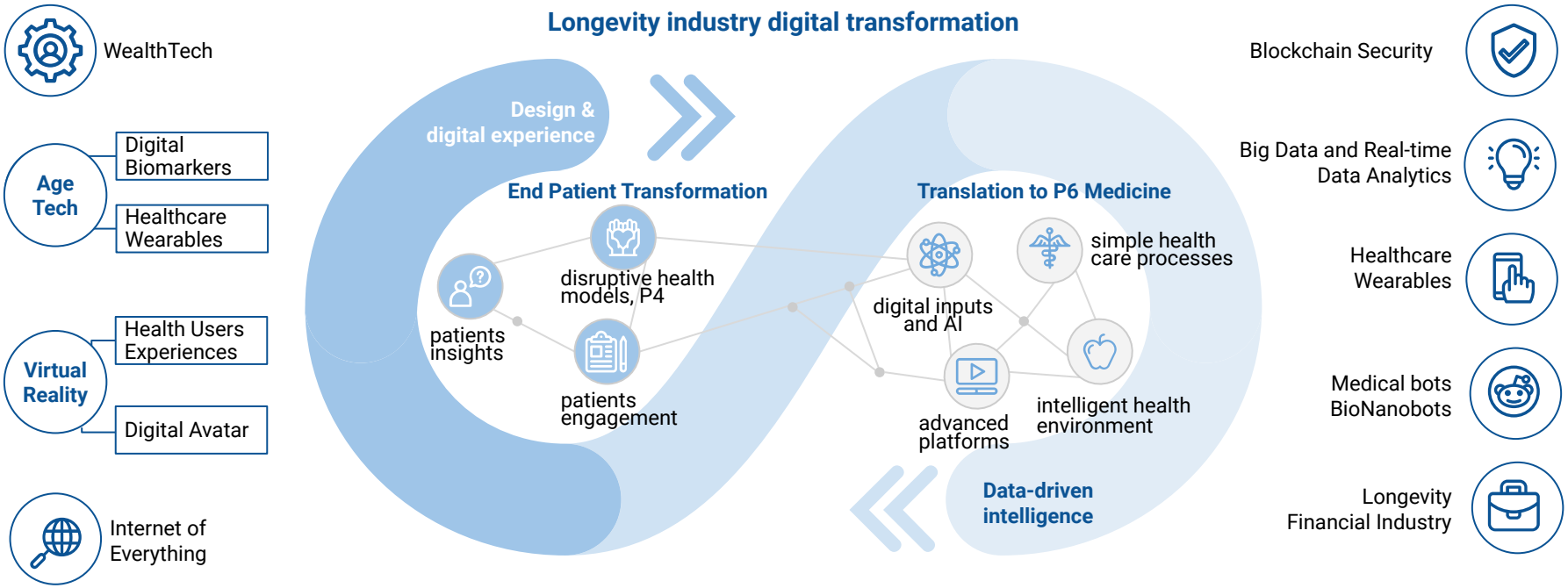
The unique role of **AI in longevity lies in P4 medicine**. P4 already has leading-edge technologies that achieved a state of market readiness and clinical implementation. However, applying them is primarily a matter of data mining, analysis and management, driven by advances in biomedicine, data science and Artificial Intelligence.

The apex of AI for Human Biomarkers of Longevity, and its most robust and advanced embodiment, will be the enabling force for creating a so-called **digital avatar of the full human body**, using thousands if not tens of thousands of personalized biomarkers, with at least several hundred precise Biomarkers of Aging and Longevity. To find out more about digital avatars, see section “Digital Avatars”, page X.

The vast majority of companies that conduct Artificial Intelligence researches is located **in the United States** and accounts for **59%** of the whole range of analyzed companies. In Northern America, The United States is followed by the European region, particularly by **the United Kingdom and France** with the total companies amount equal **to 13% and 6% respectively.**

The Next Frontier: Towards a “Digital Avatar”

Digital Transformation of the Health and 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.

Source: Image: Modified from Everis

Precision Diagnostics

Collect your data today:

- Biological specimen
- Biomarker analysis
- Database of personal biomedical data stored on blockchain

Future benefits:

- Data driven analysis of Biomarkers dynamics over time
- Analyse the changes in your digital avatar
- Personalized interventions

Digital avatar visualizes a combination of Biomarkers and other diagnostic results

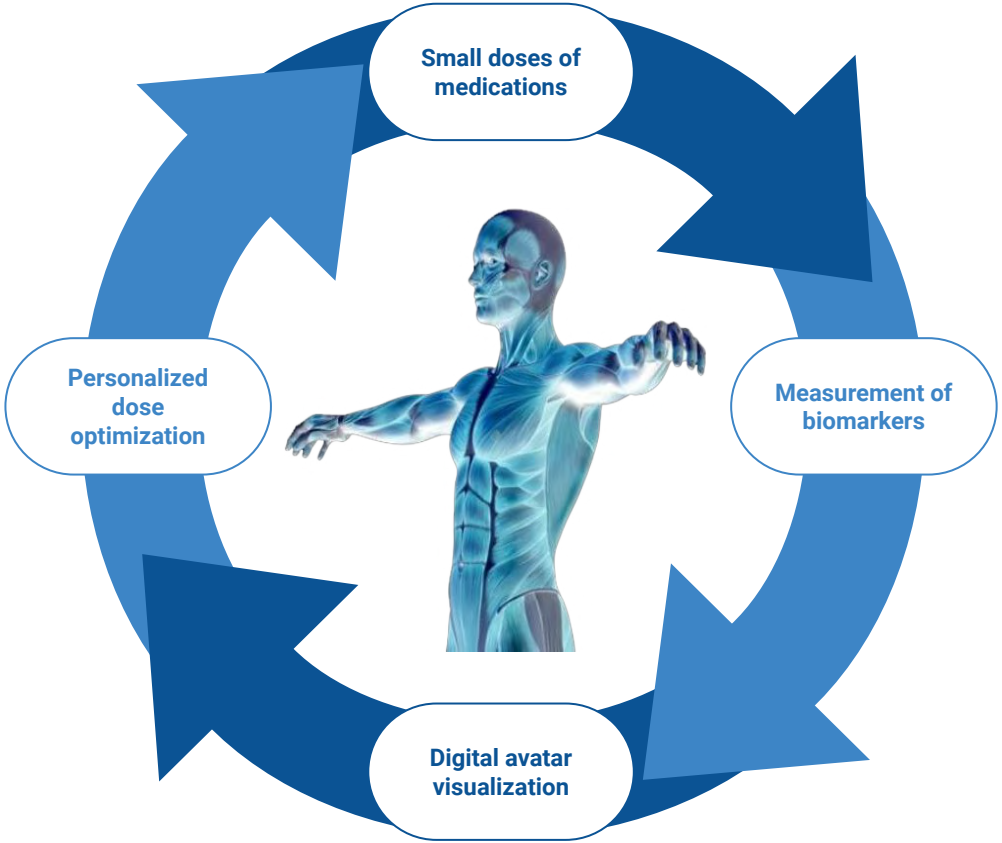
A large part of health **information is digitized**, which allows us to compile enormous amount of data, access global servers, and compare patient information, sort of a dynamic repository of information that is constantly being updated. The massive advance as far as these databases **facilitates doctors in their diagnostic process**, their ability to measure, analyze, compare patients, and produce medical reports that are more accurate and personalized, that will, in turn, lead to the best available therapy or treatment of the time.
The intensive application of AI to all stages of Longevity and Preventive Medicine R&D, and healthcare, has the potential to rapidly accelerate the clinical translation of experimental, validated and non-validated biomarkers, toward diagnostics, prognostics and therapeutics, to empower patients to ultimately become the CEOs of their own health through continuous AI-driven monitoring of minor fluctuations in biomarkers, and the rapid development of the global Longevity Industry to scale.

Source: Digital Health. Fundación Innovación Bankinter;Biomarkers of Human Longevity

Biomarkers and Data Science in the Core of P4 Medicine

Not only new methods of standard industry benchmarking and forecasting need to be developed to **combat the issues of overcomplexity and multidimensionality in the Longevity Industry,** but new methods of testing the basic safety and efficacy of Longevity and Precision Health prevention, diagnostics, prognostics and therapeutics need to be adapted as well, **moving away from the use of model organisms,** towards a more human-centric approach.

Digital biomarkers satisfy all these new industry requirements: they can be continuously tested on all users, notifying adverse micro-effects and ultra-stratifying patients. Total precision of complex tests is granted by magnifying the number of possible measures, the only possible actionable way of creating big enough dataset is development of **digital avatar**.



Data Science for Biomarkers

- Multi-Omics Sequencing
- Multi-modal total body Imaging
- Qualitative functional tests
- Data from wearable devices

The diagnostic technologies of the future are grounded in colossal bodies of data which are incomprehensible by current linear methods, and that will span every stage in the development of a pathology, from the exposome to the epigenome.

- Non-invasive continuous monitoring of biomarkers
- 3D integration of cross-sectional tissue and organ imaging
- Whole-body and organ specific biological age calculation based on biomarkers

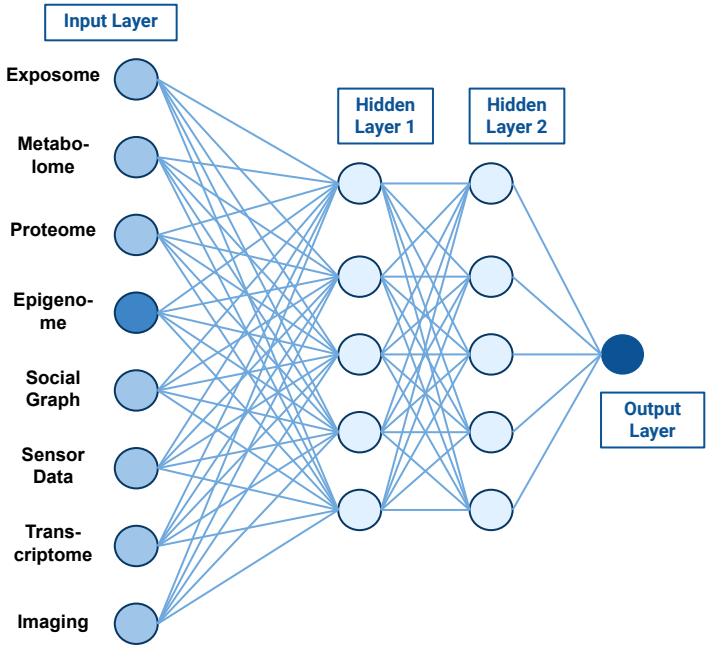
To shorten that translation delay from Research Use Only (RUO) and non-validated biomarkers and panels, to an Approved for Clinical Use (ACU) condition in the field of age-related diseases health care, and for a deep impact on applied health in a world of aging populations, it is an essential challenge, to obtain a set of biomarkers already Approved for Clinical Use with high availability and actionability, and use it in conjunction with others, market- and healthcare-ready although less conventional biomarkers gathered in digital real-time monitoring environments. **That will enable a sufficiently accurate assessment of the overall process of aging, calculation of biological age, and analysis of the progression of particular elderly conditions nested by biomarker networks leading to the creation of a Most Viable Product, or the Minimum Required Panel.**

Biomarker networks, which consist of the alignment between interactome and phenome levels, reveals new disease genes and connections between previously unrelated diseases or traits. Despite a great potential for novel discoveries, this approach is still rarely used in genomics and other *omics*. A biomarker network is a group of functionally related units of indicators, of any biological level, that contribute to the same phenotype - understanding by *phenotype* a molecular, metabolic, immune, physiological or physical trait, and so on-, pathological or not. The *interactome* - the whole set of molecular interactions for a trait, a condition, a disease, a cell or another biological unit-, and the *phenome* - the set of all phenotypes expressed by that unit-, are complexly connected at multiple levels. At the root of these networks is the epigenome. Only AI-driven methods can efficiently address such complexity, those colossal bodies of data that can be currently entered into multiple and different digital platforms.

Data Science and AI Making Complex Biomarkers Available

Unlocking the value of **epigenetic data** for actionable insights will drive aging research, precision medicine, and ultimately population health. Fundamental questions should be addressed by integrative personal **omics** profiling with epigenomics at its center, combining genomic, transcriptomic, proteomic, metabolomic, and autoantibody profiles from an individual to reveal dynamic molecular changes in health and disease. With the evolution of better technologies and digital capacity, enormous amounts of *omics* data will be produced and stored in the digital space and researchers will need AI to be able to keep track of it. AI is already transforming **the world of medicine** and will help healthcare providers make faster and more accurate diagnoses. Based on epigenetic data, deep learning algorithms will predict the **risk of a disease** in time to prevent it and will help scientists understand how interindividual epigenetic variability leads to disease. However, ensuring security and privacy in transmitting and storing personal epigenetic profiles will require building a new and open multi-omics data ecosystem. **Blockchain, an open-source technology** that uses a distributed database for secure transactions, has the potential to address many of the challenges related to security and privacy with personal health information. Blockchain technology enables integrating data from a distributed network of participants in the healthcare value chain on a global scale.

Multilevel artificial neural network to support epigenetics research.



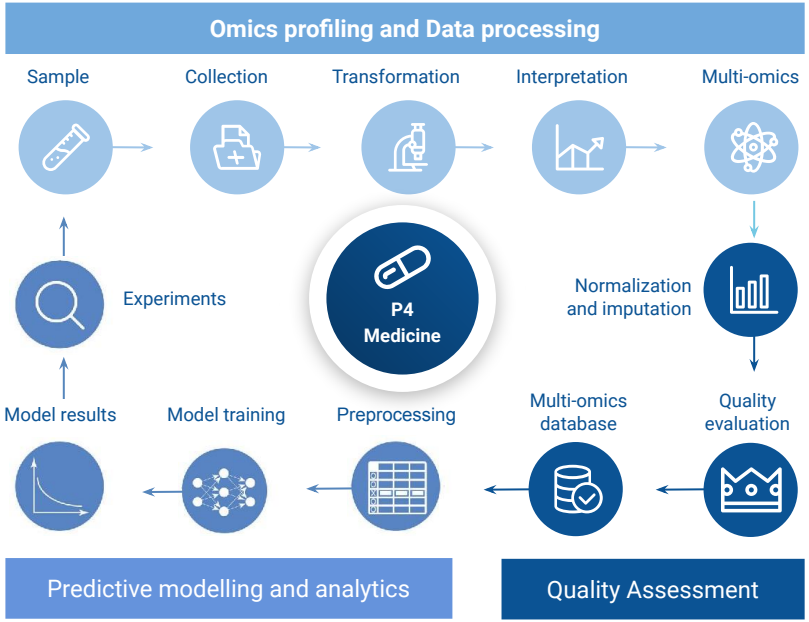
Note: At the input layer, multi-omics and demographic data are fed into the network. Each circular node represents an artificial neuron and each line represents a connection from the output of one neuron to the input of another. Machine learning enables data-driven decision systems to continuously learn from new epigenetic data and adapt itself to deliver "reliable and repeatable" results.

Source: Schumacher. Epigenetics of Aging and Longevity. 2018.

Data Science and AI Making Complex Biomarkers Available

Machine and Deep Learning, systems health and multi-omics technologies revolutionize the way we acquire and process data. At their core, **AI algorithms** dissect the data to learn their structure and associations within, often without the need of specific knowledge on processes and models that generated them. The strength of AI techniques is proportional to the size and quality of the data amassed. At the same time, sequencing and molecular technologies can generate a vast amount of **high quality data** in an inexpensive, reproducible way and hence they allow an unprecedented system-level view of any organism. These datasets, which can come from a variety of sources, equipment and experimental settings, are in their majority not ready to serve as training sets to computational models, Machine and Deep Learning methods, as they have not been created with that function in mind. As such, there is a clear need for methods that process, normalize, integrate and transform the plethora of heterogeneous multi-omics data to cohesive compendia that can be used as a training grounds for further analysis and learning.

Machine and Deep Learning analytics has been applied in biology to deal with the intrinsic complexity in omics data with a long history and its integration in recent years. The high-level overview of the machine- learning analytic pipeline for integrated multiomics data consists of data preprocessing, modeling, and active learning. Once a model is constructed and evaluated, active learning guides what experiments to perform next to minimize uncertainty in the model.



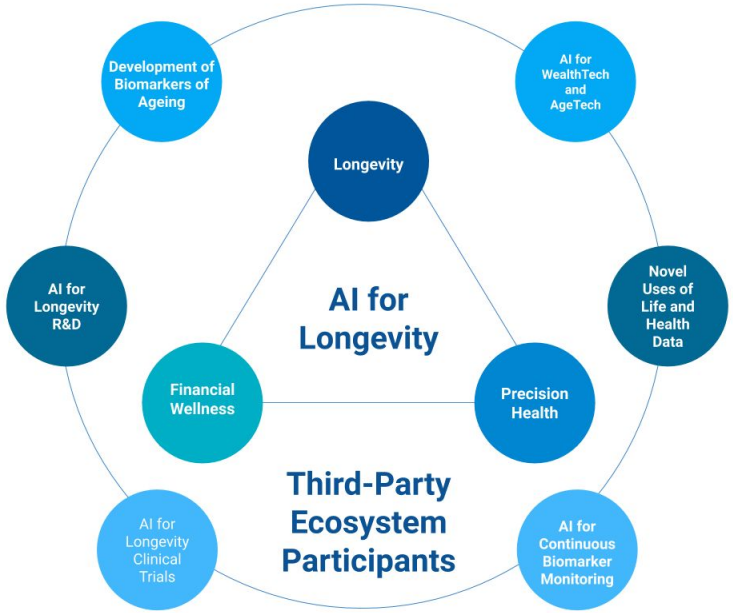
Three major steps involved in AI-driven multi-omics: Data acquisition, multi-omics integration and predictive modeling. An end-to-end pipeline for *multi-omics* data as a source of biomarkers for health care, biological age precise calculation and extension of lifespan.

Source: Kim et al. Data integration and predictive modeling methods for multi-omics datasets. 2017

Data Science and AI Making Complex Biomarkers Available

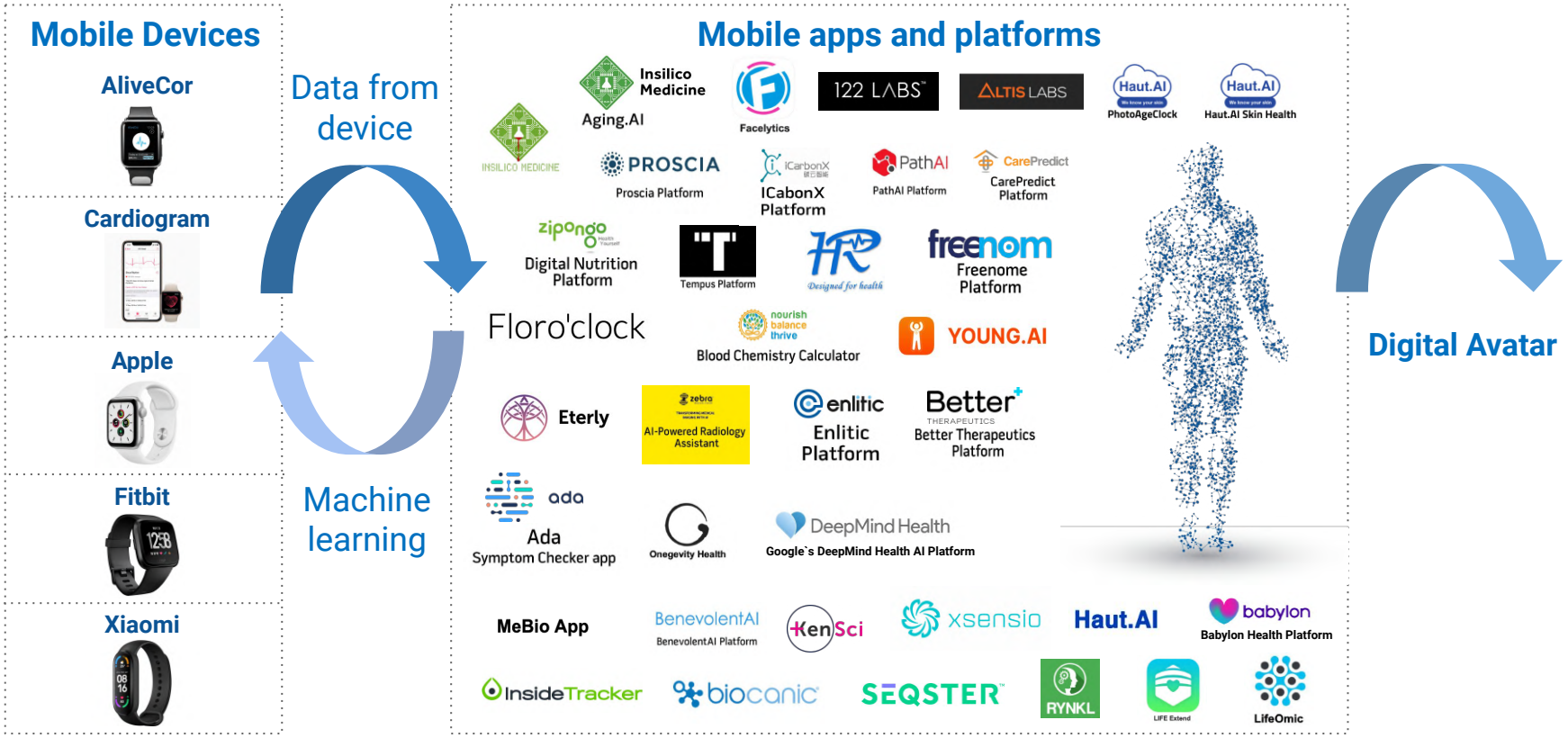
Key points:

- As the complexities of Longevity science and technology increase, and as the volume of data continues to amass, **the role of AI** in both analyzing and understanding becomes completely **necessary for continued progress and industry development**
- While **AI for Longevity** is still an **emerging and underrepresented sector** within the global Longevity Industry, its extreme disruptive potential makes its eventual emergence as a core and integral area of growth and development inevitable
- **AI for Longevity** will become one of the most impactful sectors within the industry in the next several years, and make its potential to accelerate the continued development of the industry apparent in almost every sector, **from Longevity R&D to therapeutic development, P4 Medicine, biomarker discovery,** and even non-biomedical sectors such as the Longevity Financial Industry.



Awareness of the importance of utilising Artificial intelligence within aging and longevity research is rapidly increasing in academia and industry. Modern deep learning techniques used to develop age predictors offer new possibilities for diverse data types. This will enable a holistic view to identify novel biomarkers, but it will also bring novel geroprotectors and will become the core of drug discovery and healthcare in biotechnological, pharmaceutical and health industries, integrating them like never before.

AI and Digital Platforms: Towards a “Digital Avatar”



Progress in Artificial Intelligence Enables Creation of “Digital Avatars”

Digital Avatar is a graphic representation that is associated with a user to serve as their identification. Avatars can be a picture, artistic drawing, or a three-dimensional representation. With the advent of the digital revolution, its use has spread to many fields, including medicine. Currently, the digital avatar is being used in medical education, such as for training models using augmented reality in order to explain anatomy to students with a three-dimensional human body. The digital avatar in health allows planning a path and observe the body of a patient in alternate scenarios.

A virtual profile of all health data can be generated through collection of multiple types of data, some of which are visualized also in 3D through devices or augmented reality. **Biomarkers serve to diagnose issues and evaluate the overall health status and predict the aging rates of each individual.** Gathering more of this type of data, e.g. periodic blood tests, will enable a complex, highly personal picture of each person, whose predictive power will be proportional to the quantities of input classes and the intrinsic capabilities of the AI-driven analysis aimed at recreating biomarker networks.

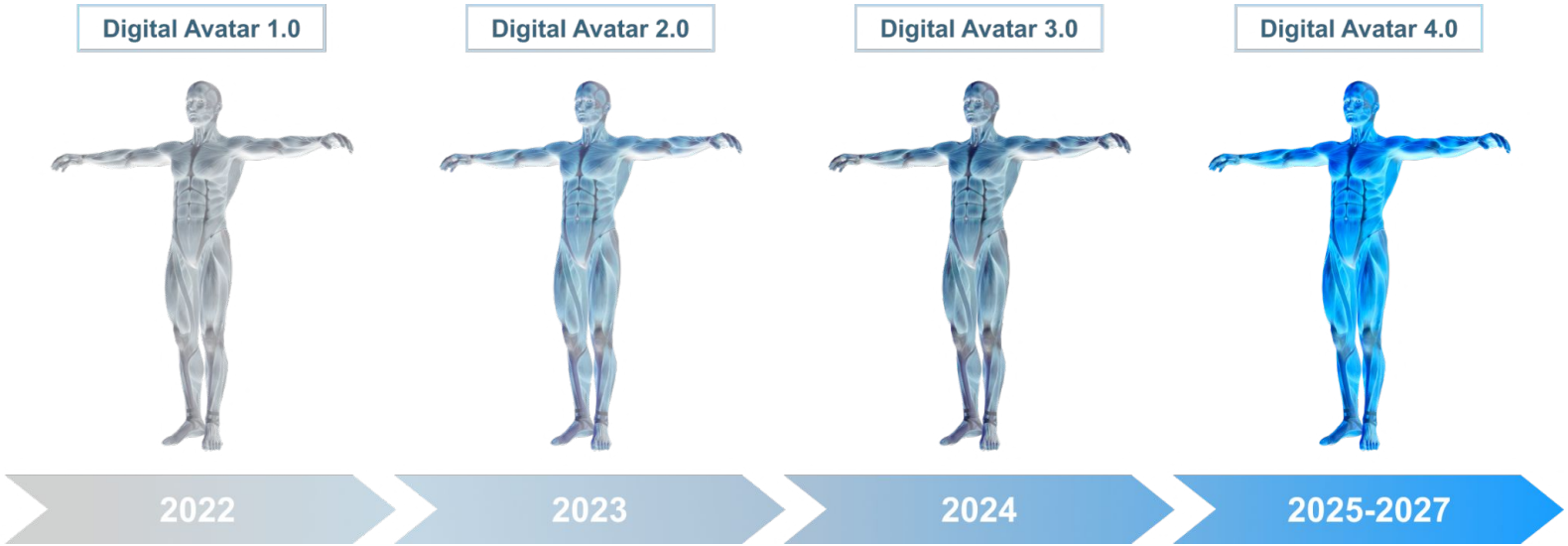
With the technologies of healthcare advancing, **the digital avatar will evolve from a data collection and disease focused tool to a truly longevity focused tool.** Instead of looking at unidimensional, disease-linked biomarkers, it will be able to look at the whole organism in an overarching health point of view, and focus mainly on prevention and extending patient healthspan.

Source: Digital Health. Fundación Innovación Bankinter

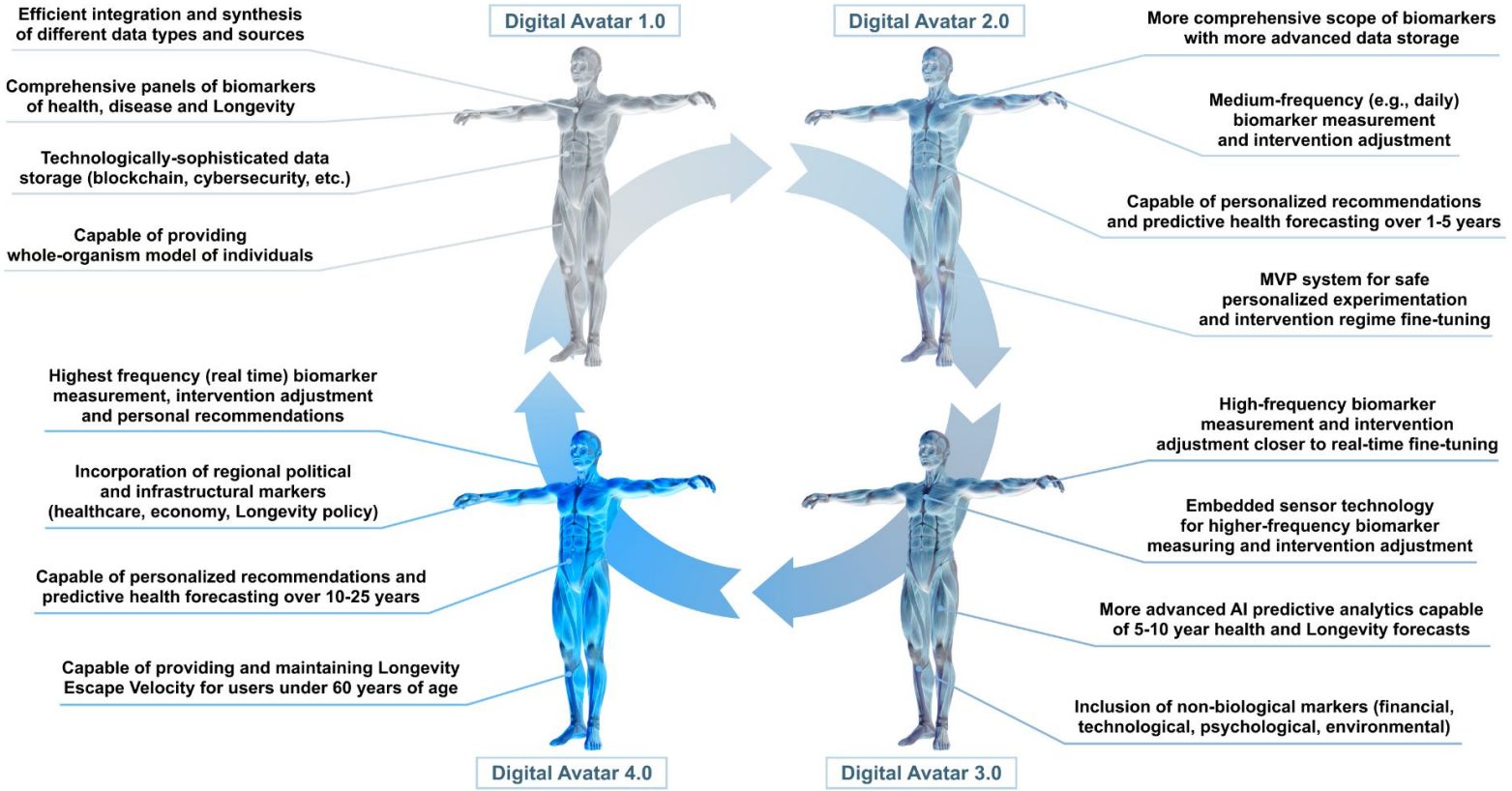
The Evolution of Digital Human Avatar

Envisaged a **five-stage evolution of Digital Human Avatars** from 0.5 (the current state of Avatars available on the market) to 4.0. This classification framework is based on a number of specific factors including:

- their technological sophistication;
- their use of AI for assessment, predictive analytics, and personalized recommendations;
- the frequency with which they measure the biomarkers that they encompass;
- the overall scope of markers impacting health, Longevity, performance, and QALY across the full human lifecycle, from biology to behavior, technology, and environment that they are capable of measuring, integrating and predicatively analyzing.



The Evolution of Digital Human Avatar



Longevity Biomarkers and Financial Industry

Biomarkers for Financial Market

The value of the information derived from the biomarkers cannot be reduced to the scientific only. Many **financial instruments can be optimized using biomarkers-based longevity and/or mortality indices.** Such instruments shows great value for a whole variety of entities, both governmental and privately held, providing optimized hedging solutions.

Besides different types of financial instruments, biomarkers assessment can become a **crucial part of the valuation and due diligence processes for Longevity- and Pharma-related companies.** It is well known that companies participating in drug development are highly exposed to the risks related to the human validation (i.e. clinical trials). It is often hard to predict and assess whether a solution provided by a given company is relevant to the market. In this case, biomarkers-derived information might play a crucial role in the assessment of the company's performance, allowing to evaluate how its services affecting human Longevity.

These two different approaches suggest great improvements in the financial market enabling **optimized risk management** both in terms of Longevity risks hedging, and investment risks reduction.

Who can benefit?

- Independent Financial Advisors
- Private Equity Funds
- Private Banks & Wealth Managers
- Corporations
- Asset Management Companies
- Venture Capital Funds
- Challenger Banks
- Retail Banks
- Pension Funds
- Insurance Companies

Reverse Mortgage

A reverse mortgage is a type of loan that is used by homeowners at least 62 years old who have considerable equity in their homes. By borrowing against their equity (at rates starting at less than 3.5% per year), seniors get access to cash to pay for cost-of-living expenses late in life, often after they've run out of other savings or sources of income. In comparison with traditional asset-backed loans, **reverse mortgage loans provide the elderly with a means of hedging longevity risk by helping to maintain a sustainable level of retirement income**, while retaining tenure in the home.

From the borrower's perspective, the most notable merit of a reverse mortgage is clearly that the borrower is not required to repay the loan until he or she dies or leaves the home. Another favorable feature is the "non recourse" clause. When the loan is terminated, the borrower (or his or her estate) only needs to repay the loan amount or proceeds from the sale of the house price: whichever is the lesser sum.

There are some challenges for the Longevity economy which drive the popularity of reverse mortgages for retirees: **a low-interest financial environment** that provides insufficient returns on pension savings, **generous retirement age** and **early withdrawal rules, a great fluctuation in the labor market, an erosion of traditional family support systems** and **a significant proportion of one-person households**

How Does a Reverse Mortgage Work?

You're 62 or older and have equity invested in your home

You need to access to that equity to pay your daily expenses

A reverse mortgage allows you to borrow against your home's equity with no monthly payment required as long as you stay in your home

The loan is repaid once the house is sold

Crossover Risk for Reverse Mortgage Lender

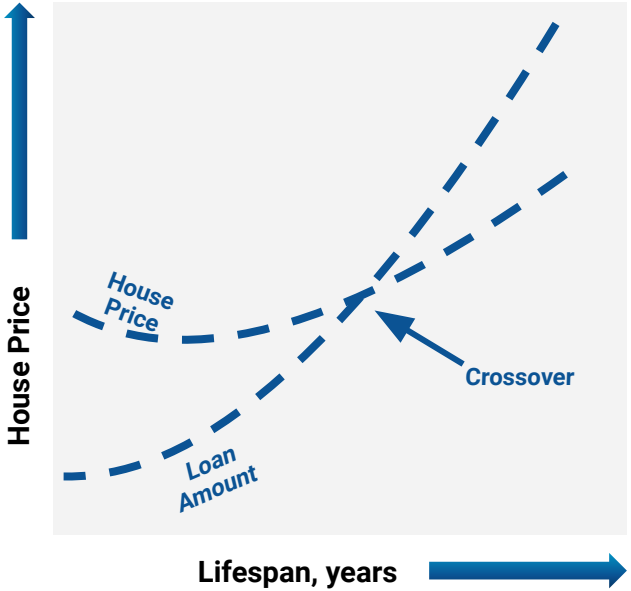
Although **reverse mortgage loans** provide many attractive benefits to retirees, they also **involve many risks** from the lender's perspective. The risk in reverse mortgage loans can be summarized **as the "crossover risk".**

If the loan value exceeds the collateral house value at any point of contact time, the lender is limited to recover only the proceeds of the sale of the house equity when a reverse mortgage loan is terminated. **Any excess is therefore considered a loss to the lender.** Since the interest rate is usually higher than the house price value increasing, the loan value will undoubtedly exceed the house value at some future point.

On the other hand, however, **if the loan is terminated before the crossover,** any excess of the proceeds from the sale will revert to the borrower rather than becoming **the lender's gain.** This feature of reverse mortgages is reminiscent of options contracts.

Due to the dramatic **improvement in the mortality rate** since the 1970's, **longevity risk has become the most crucial risk** in a reverse mortgage product, as a result, banks and other lenders should form reserve capital to cover the longevity risk or it to capital markets via insurance contracts, longevity derivatives etc. In both cases **the effective measure of longevity risk**, such ah biomarkers-based biological age prediction models is a key aspect of the lender policy.

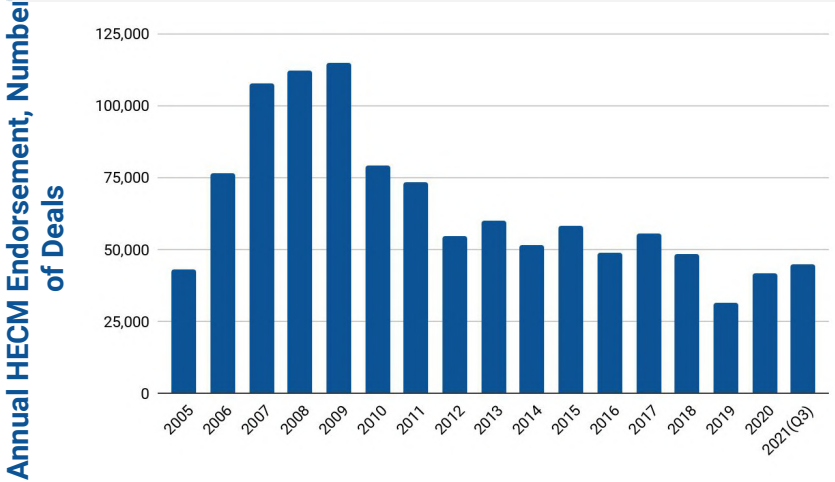
Crossover Risk Scheme

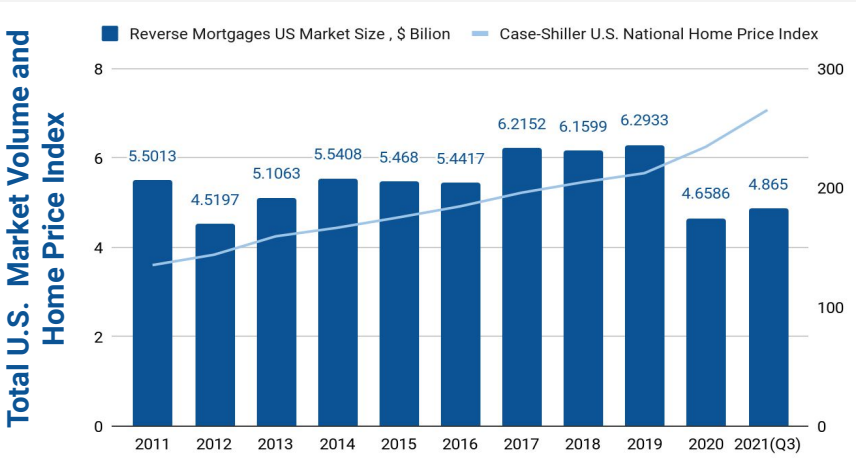


Source: Longevity Derivatives and Financial Instruments

The USA Market of Reverse Mortgages

The **Home Equity Conversion Mortgage**, or HECM, is the federally insured **reverse mortgage product.** It is insured by the Federal Housing Administration (FHA), a branch of the U.S. Department of Housing and Urban Development (HUD). HECMs account for nearly all reverse mortgages made today in the U.S**. On the left graph** there is the number of HECMs made in each year since the program began. Due to the bubble on the American real estate market and the World Financial crisis 2008, the big banks and other financial institutions became indifferent to this financial instrument, as they couldn't find an efficient way to deal with some specific idiosyncratic risks. However, **increasing demand for reverse mortgages** due to drives described early and more efficient risk-management algorithms will undoubtedly increase the volume of loans and their market value soon. Over the past two years, the decline in market size is due to weakened demand due to the pandemic and the completion of transactions (sales of mortgaged real estate), concluded more than ten years ago.





Source: Longevity Derivatives and Financial Instruments

Longevity Risk / Longevity-derived Financial Instruments

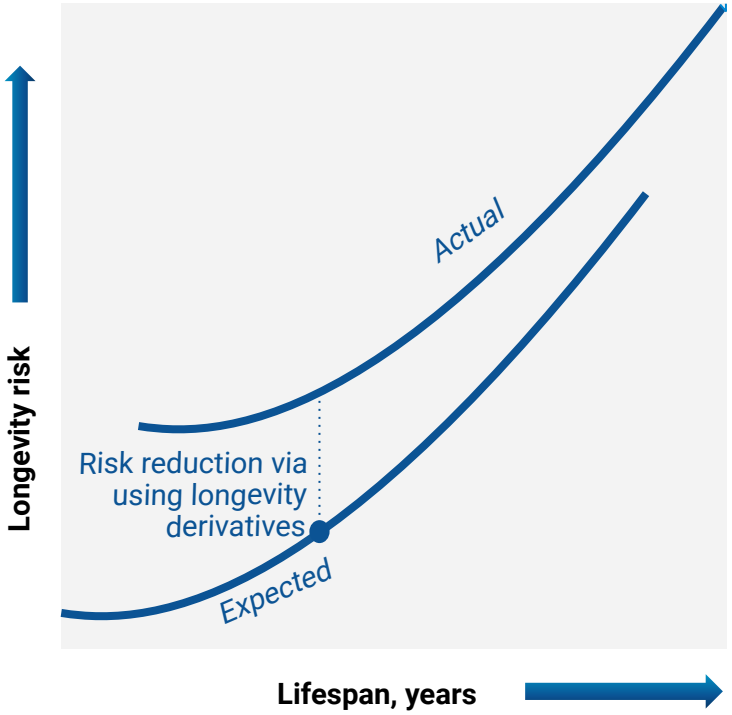
A new global capital market, **the Life Market,** is developing and "longevity pools" are on their way to becoming the first major asset class of the twenty-first century. **Longevity risks arrive due to inaccurate predictions of the level of mortality rate and numbers of retirees.**

Thus, **Longevity-derived financial** instruments are used in order to hedge such risks. In general, these derivatives are designed to **generate income for investors due to increased Longevity,** as well as reduce the negative impact for companies suffering from Longevity risks. Longevity risks have a weak correlation with other financial risks.

Although the **Longevity Derivatives Market has many economic agents,** the main ones are **hedgers** (pension funds and insurance companies, have an incentive to transfer Longevity risk off their books), **speculators,** and **arbitrageurs** (investment banks and hedge funds are interested in acquiring exposure to longevity risk since it has a **low correlation with classic market risk factors,** therefore small beta coefficient attracts investors a lot).

New opportunities are opening up for all these agents because of the increased accuracy of risk assessment and forecasting and selection of the correct risk management tool.

Hedging with Longevity Derivatives

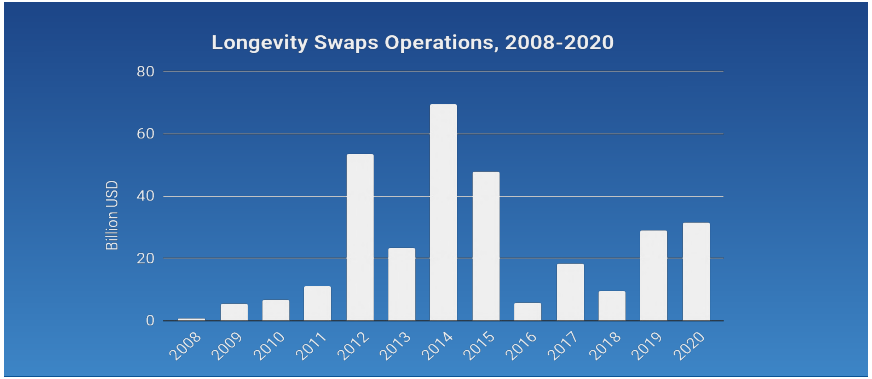


Source: Longevity Derivatives and Financial Instruments

Longevity Risks for Companies and Governments

Longevity risks are of great interest for both governmental and private institutions

The graph below depicts the dynamics of **longevity swaps' operations** in the period of 2008-2020 years. During this period, deals for the amount of $313 billion had been struck. The amount of new operations correlates with life insurance market size. For example, the insurance market size in the US also significantly dropped after the 2015 year and slightly recovers during the 2016-2020 years (IBISWorld, 2020).



Governments tend to have **a two-dimensional interest in Longevity securities.** First, **for hedging** financial institutions sensitive to such risks, second, **for securing** its own exposure, as it is a significant holder of the Longevity risks: via the pay-as-you-go state pension system; via its obligations to provide health care for the elderly and for other similar reasons.

Ensuring an efficient annuity market and efficient capital market for Longevity risk transfers means that government can affect and reduce concentration risk and provide construction of national longevity indices.

Government helps **to share Longevity risk fairly** across generations and provides **a fair risk premium.** When issuing longevity derivatives based on biological age, the government could insure age-related diseases and implement more advanced and actionable metrics for pension programs.

Government = Insuring age-related diseases + Minimising of spended resources + Using accurate and realistic health indicators

Sources: Artemis, Longevity Derivatives and Financial Instruments

Longevity-derived Swaps and Forwards

By definition, **a swap is a financial instrument**, namely — derivative contract through which two parties **exchange the cash flows or liabilities from two different financial instruments.** Swaps said to have two legs, where each cash flow comprises one leg of the swap.

As for Longevity swaps, **Longevity swap is a reinsurance structure** where the client pays a fixed pre-agreed annual premium to the reinsurer plus an annual fee. The premium consists of the expected annuity payment and a margin. The annuity payment time is based on the Longevity of the given pensioner.

Longevity swaps have a number of features making them interesting for all parties involved, namely, they allow dealing with Longevity risks aside from the investment risks, this, in turn, allows trustees to diversify their risks and operate more efficiently. Longevity swaps also **allow excluding the upfront funding practice** and hence to reduce counterparty risks. Probably, one of the most important things about Longevity swaps is their symmetry. The risk distribution related to the Longevity swaps is much more fair in comparison to some other financial instruments on the market.

The Advantages of the Longevity Swaps

Investment and longevity risks separation

No upfront funding

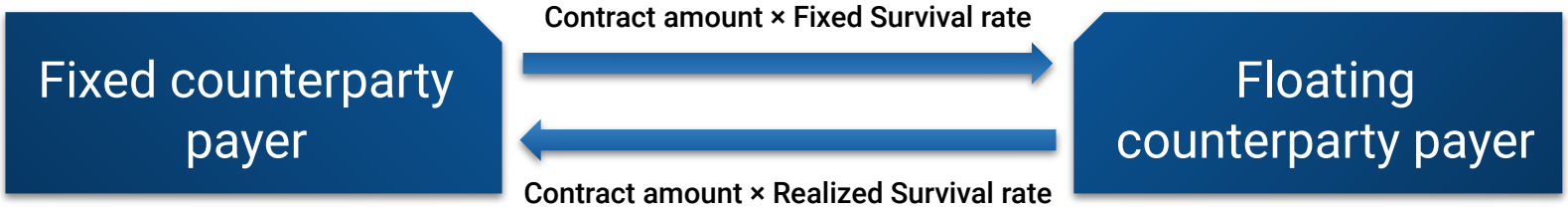
Symmetrical risk distribution among counterparties

Counterparty risk reduction

Source: Longevity Derivatives and Financial Instruments

Longevity-derived Swaps and Forwards

A survivor swap is an agreement **to exchange cash flows in the future** based on the outcome of **at least one survivor index** [Dawson, P. et al. "Survivor Derivatives: A Consistent Pricing Framework.", 2010]. It can be broken down into a collection of a more simple derivative — **the survival-forwards**. **An S-forward** is **an agreement** between two counterparties **to exchange** at a future date, an **amount equal to the realized survival rate** of a given population cohort (floating leg), in return for a fixed survival rate agreed at the inception of the contract (fixed rate payment). The use of the forward's structure is rooted in the fact that this financial instruments are well-known to be easily customizable, allowing to tailor them to a specific commodity and date.



The payoff of the S-forward is then given by:

$$Payoff\ f\ (T) = p_x - \hat{p}_x$$

Where p_x is the realized survival rate (F_T measurable), and $\hat{p}_x$ is a fixed probability of an individual aged x at time 0 to be alive at age $x + T$.

At the same time, forward contracts (Longevity forwards included) are known "to bring" higher default risk, since they tend to become incoherent to the real market as time passes.

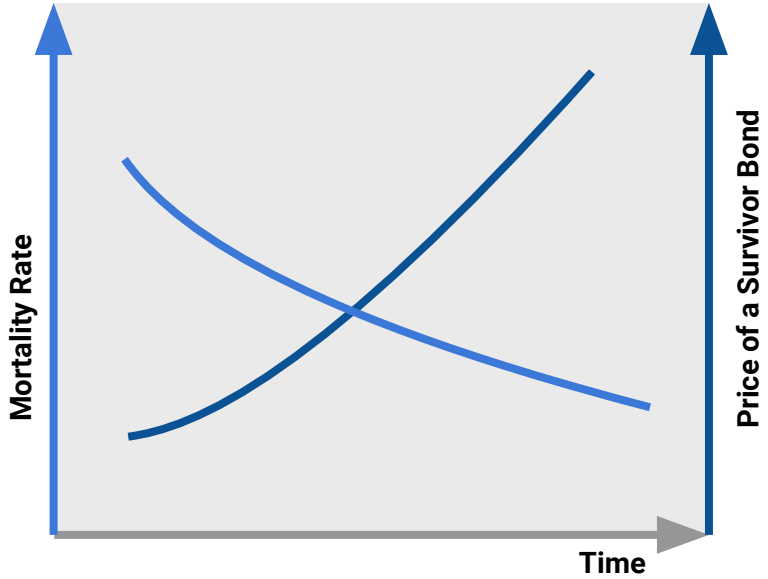
Longevity-derived Bonds

The evolution of financial market instruments has brought a number of **new risk-diversification options** to the attention of investors and new hedging options to companies that carry some specific risks, like longevity risks for insurance companies and pension funds. One of them is a survivor (longevity) bond in which coupon payments are connected to the percentage of a defined population group, especially retirees alive on the day of coupon payment. **The higher survivorship of an aging population causes higher payouts to them, and a more valuable S-bond is a suitable risk-managing instrument.**

There are also **types of longevity bonds** with conditions which can meet different needs:

- **Survivor bonds** continue to pay until the last member of the reference population dies
- **Principal-at-risk bonds** with fixed or semi-floating coupons, principal repayments are connected to a survivor index
- **Inverse bonds** whose price behavior are inversely proportional to traditional longevity bonds.

Correlation between the Mortality Rate and the Price (Coupon) of a S-Bond



In 2003, for the first time in history, Swiss Re issued Longevity principal-at-risk bonds, with a coupon pegged to LIBOR, and a principal pegged to a weighted index of mortality rates in its countries.

Source: Blake, David, et al. "Longevity bonds: financial engineering, valuation, and hedging.", 2006.

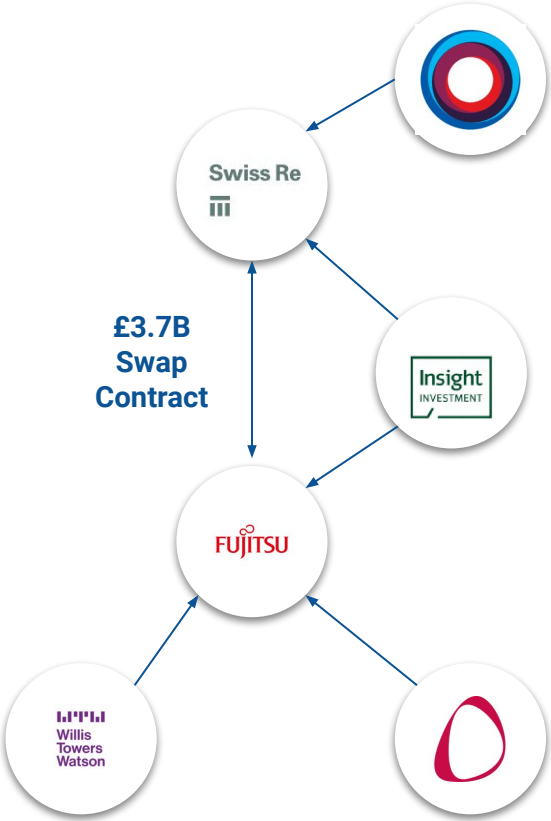
Examples of Longevity Derivatives Users' Activities

Financial institutions which wanted to make a profit from arbitrageurs fees have started to issue longevity derivatives in 2003. Global reinsurer **Swiss Re** offered a three-year mortality bond whose principal payment was tied to an international mortality index. Swiss Re continues making big deals on the longevity derivatives market.

The last deal using longevity swap was signed in May 2021 between **Swiss Re as an arbitrageur** and **The Trustee of the ICL Group Pension Plan, a Fujitsu** pension scheme, **as a hedger.** This longevity risk transfer insured **£3.7 billion of hedgers' liabilities** and covers pensions in payment for approximately 9,000 members. **Other institutions o**f the swap deal infrastructure include:

- **Willis Towers Watson** as actuarial and transaction adviser to the hedger.
- **Gowling WLG LLP and Momentum Investment Solutions and Consulting** as legal and investment adviser to the hedger.
- **Pinsent Masons LLP** as legal adviser to the hedger.
- **Insight Investment** as calculation agent, collateral manager, and collateral valuation agent.

Daniel Harrison, Global Head of Longevity Solutions at Swiss Re says: 'There is a compelling rationale for pension plans and insurers to transfer their longevity risk to reinsurers. We have a natural offset with our mortality business, the capacity to write the business onto our balance sheet, and the expertise to tailor the transaction to meet our client's needs.'



Longevity Biomarkers Financial Applications

Longevity Biomarkers show a great value for financial market, allowing engineering of optimized financial instruments and implementation of the biomarkers-based due diligence and valuation

As was shown, many financial instruments can be formulated in terms of the Longevity. This implies the importance of the development different quantifiable biomarkers' assessment approaches. As a result, such approaches can be used for:

1. Longevity Risks Hedging
2. Investment Risks Reduction
3. Personal Financial Risks Optimization

It is important, that use of biomarkers in financial areas will positively affect not only institutional or other “big” players. Biomarkers can become a feasible solution for personal risk management too. Additionally, the active implementation of the biomarker-derived data will provide sufficient means for investment risks management, which will optimize the effectiveness of the allocation process. This, in turn, can provide better and more efficient Longevity solutions for the public.

When time is money, biomarkers are the means for wealth management.

Biomarker Panels Actionability

Biomarker Panels: Overview

Genomics, metabolomics, proteomics, microbiomics and so forth, but fundamentally novel multi-omics approaches, are offering thumping amounts of biological data and ultra-modern insights on disease trajectories. These are all concise examples of **Comprehensive Panels of Biomarkers**.

These uses of numerous biomarkers assembled in Panels including multi-omics data and their deep analysis by AI platforms push back the boundaries of biomedical knowledge, health status characterization, diagnosis and early detection, and opens new doors for Precision, Preventive, Personalized and Participatory interventions; for **P4 Medicine**.

The use of Biomarker Panels means more granular data, and more granular data translates into more finely tuned ways of performing risk and disease progression stratification for assignment to different care regimens and shift from late stage care to preventive medicine. This shift from treatment to prevention is ultimately leading to a coming age of Preventive Treatments and Precision Health, where patients are empowered with the tools necessary to become the drivers and engineers of their own health status; i.e., through the application of P4 Medicine in response to continuous monitoring of fluctuations in these Biomarkers of Aging.

A list of **100 key biomarker panels** currently on the market was developed for our report.

Indexes for Scoring Biomarkers

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 evaluating 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

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**

Index Values for Single Biomarkers of Aging 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.

Possibilities for Further Improvements

The number of biomarkers of aging and their association with various diseases increases each year but a critical review of each of them is needed. Understanding that biomarkers of aging Industry development is an ongoing process means that the project needs to be further improved and monitored. For instance, new analytical reports need to be done for creating new accurate and current databases.

The database of firms, investors, and R&D facilities will be enlarged to accommodate new startups and established companies looking to increase their longevity products rollout efforts.

New techs like AI, Omics, and Digital monitoring gadgets assessment in biomarkers of aging Industry will be done to understand their impact on Biomarker Industry advances in general.

An extensive study on products and treatment methods to promote longevity or decrease rates of development of age-related diseases will be undertaken as well.

Multiple forecasts concerning biomarkers of aging Market trends are required to identify all aspects and further development of companies in longevity field. They are also needed to understand which forecasts were proven to be true in order to optimize the our analyzing strategy.

Avenues for Further Improvement in the Second Iteration of the Project

- Database Expansion
- TRL analysis of each documented test or platform
- Updates on the Most Notable Longevity Companies
- Follow-up on Predictions Made in the Previous Iteration
- Increase Number of Deeply Studied Cases
- Separate Research on Longevity Biomarkers Development
- Deep Analysis of AI and Omics-tech Implementation
- Broad Assessment of New Longevity Startups
- Current Monitoring of Longevity Biomarkers Trends

Conclusions

Conclusions

High demand for personalized medicine leads to rise in commercial interest and government support for Age-related Biomarkers and AI-technologies for Longevity. That trend accelerates strong funding of Longevity sector thus promoting faster innovation.

The amount of **clinical and biological data** in the world is steadily rising, with a projected **CAGR** of more than **30%.** The n**umber of datapoints** for clinical usage is **rapidly increasing**, and the only option to optimize their utilization is to create **digital avatars**. A **digital avatar is a forerunner in the field of personalized medicine**, which is still in its early stages. Because of the massive amounts of data, clear **analysis of such avatars is only feasible with the help of AI**.

The ability to monitor health status with accurate and trustworthy lab findings explains the market's significant appeal for the **at-home tests**. This **trend emerges** as a result of the **simplified procedure of ordering tests, collecting samples, and obtaining results**. Typically, such solutions arise as a result of the probable **removal of the need for hospital/lab visits,** making such tests an ideal solution for modern people. **This tendency is about to take off on a massive scale, and traces of it can already be observed.**

The **increasing popularity of Artificial Intelligence** leads to the creation of innovative techniques and the digitization of healthcare services. The **use of Artificial Intelligence** possibilities in both **preventative and therapeutic medicine** is a **major trend in the industry**. It is now evident that **AI can be used to augment many operations** in order to **save costs and enhance overall results**.

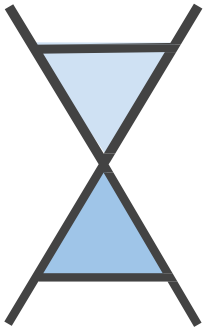
AI for Longevity will become one of the most impactful sectors within the industry in the next several years, and make its potential to accelerate the continued development of the industry in almost every sector, such as **Longevity R&D, therapeutic development, P4 Medicine, biomarker discovery**, and even non-biomedical sectors such as the **Longevity Financial Industry**.

Longevity risks are an important component of the **financial sector**, and as the **population ages**, their prevalence grows larger and more impactful. Because of the progression of the longevity industry, a lot of **innovation is altering the paradigm of longevity risk assessment**, which might possibly **lead to significant changes in the longevity financial sector**. As a first sign of such transformation, new derivatives and risk assessment approaches are developing.

Longevity Investment: Big Data Analytics Dashboard

Source: Longevity Investment Big Data Analytics Dashboard

About Aging Analytics Agency



AGING
ANALYTICS
AGENCY

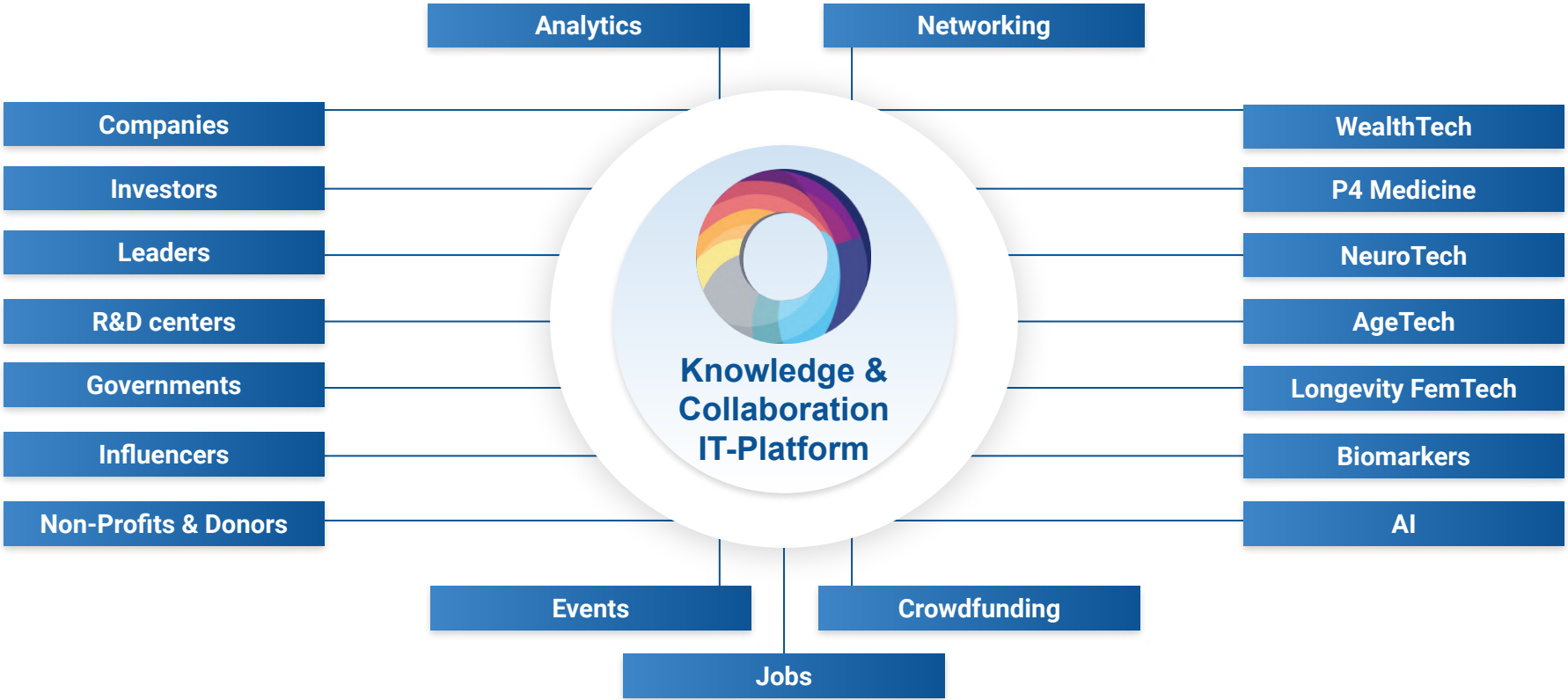
Aging Analytics Agency is primarily interested in strategic collaboration with international corporations, organizations, and governments in Longevity-related projects and initiatives.

Aging Analytics Agency is open to cooperation with strategic clients via a variety of approaches, including:

- Conducting customised case studies, research and analytics for internal (organizational) use, tailored to the precise needs of specific clients.
- Producing open-access analytical reports.
- Offering customised analysis using specialised interactive industry and technology databases and IT-Platforms.

In certain specific cases, if it meets our interests, Aging Analytics Agency is open to co-sponsoring research and analytics for the production of internal and open-access industry reports, as well as special case studies for a variety of governmental, international, and corporate clients. Their topics of interest may include Longevity, the Longevity Financial Industry, Longevity Policy and Governance, and the development and execution of fully-integrated National Healthy Longevity Development Plans tailored to the specific needs of national governments and economies.

Longevity.International: One-Stop Platform for Longevity Industry Knowledge



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