Mitochondria in Longevity and Space Medicine

Q3 2021

Aging Analytics Agency

SpaceTech Analytics

Deep Pharma Intelligence

Deep Knowledge Analytics

www.aginganalytics.com

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Mitochondria in Longevity and Space Medicine Q3 2021 was compiled to give a detailed systematic description of the **innovative approaches for regulating mitochondrial function to control Human Longevity and treat some systemic disorders,** highlighting their practitioner application for astronauts' recovery after space flights. The report focuses on **BioTech, Pharmaceutical and Healthcare companies** and **R&D institutions** and their partnerships, predicting the development of the relevant market, and determining the degree of technology relevance. A unique database was compiled for the systematic review of key stakeholders in the industry.

All the technologies described in the analytical case study are already available, in use and ready for further research.

The Mitochondria Targets and Biomarkers are selected by their **clinical efficacy** and create the most relevant modern precedent for safe and effective human experimentation and validation within the realm of SpaceTech and Space Medicine that the Longevity Industry can apply.

Against this background, a separate chapter provides an overview of several interesting scientific and technological **convergences between ageing and the harmful effects of spaceflight,** as well as showing how the **specific therapeutic approaches that are used to protect and preserve the health of astronauts** intersect with Practical Healthy Human Longevity. Overall, this analytical case study offers a one-stop expert evaluation of a novel and dynamic industry with high growth potential.

Approach of the Report

Database

100* Companies	120 Investors	30 R&D Centers

The database was formed based on:

- the **identification of companies** that conduct or have conducted clinical or preclinical research
- the **determination of investors** that contributed money to these companies

Note: The extra 90 companies were analyzed. These companies use **AI** and they are put in the separate section "AI for Mitochondria and ageing".

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 analysis provides a comprehensive overview of the Preclinical and Clinical Trials Industry. 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

Ever since being discovered, **mitochondria – which provide the body with its main source of energy** – have played a key role in our understanding of human biology. Because of their importance in cellular physiology, defects in mitochondria are associated with various human diseases. In addition, many studies have shown that mitochondria play a central role in ageing.

Successful space exploration requires understanding and addressing the underlying causes of health problems observed in astronauts who have spent long periods of time away from Earth. These problems include loss of bone and muscle mass, immune dysfunction, and heart and liver problems. Numerous studies and clinical trials have led experts to believe that mitochondrial dysfunction is the main culprit of astronauts' premature ageing and the systematic deterioration of their health.

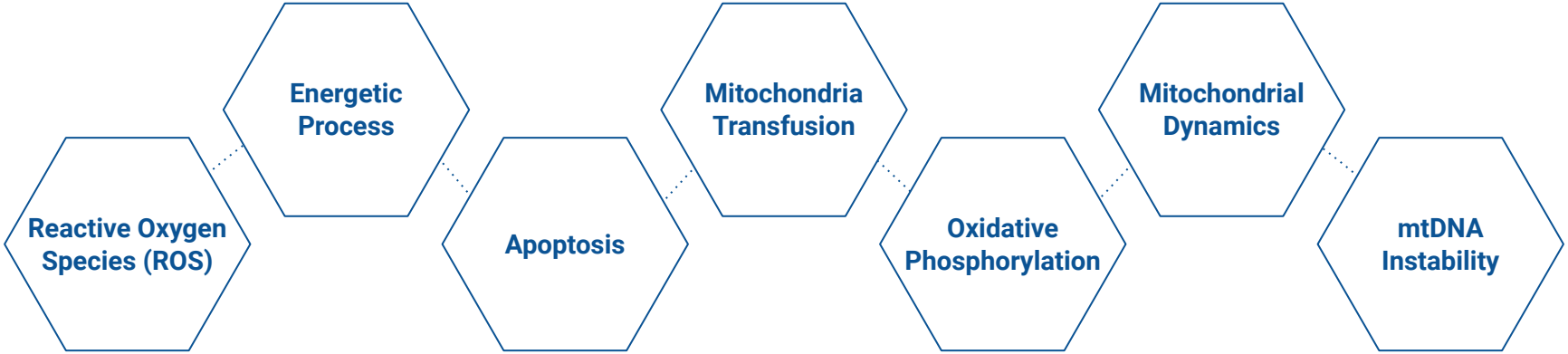
Main Features of the Analytical Case Study

- **Database of Key Market Players**
- **Overview of Clinical Trials for Mitochondria at All Phases**
- **In-depth Review of Notable Mitochondrial Trials for ageing**
- **Detailed Assessment of Mitochondria Clinical Trials**
- **Role of Mitochondria in Ageing within Clinical Trials**
- **Analysis of Mitochondrial Dysfunction after Space Flights**
- **Mitochondrial Clinical Trial Market Review and Predictions**

Mitochondrial Clinical Trials Framework

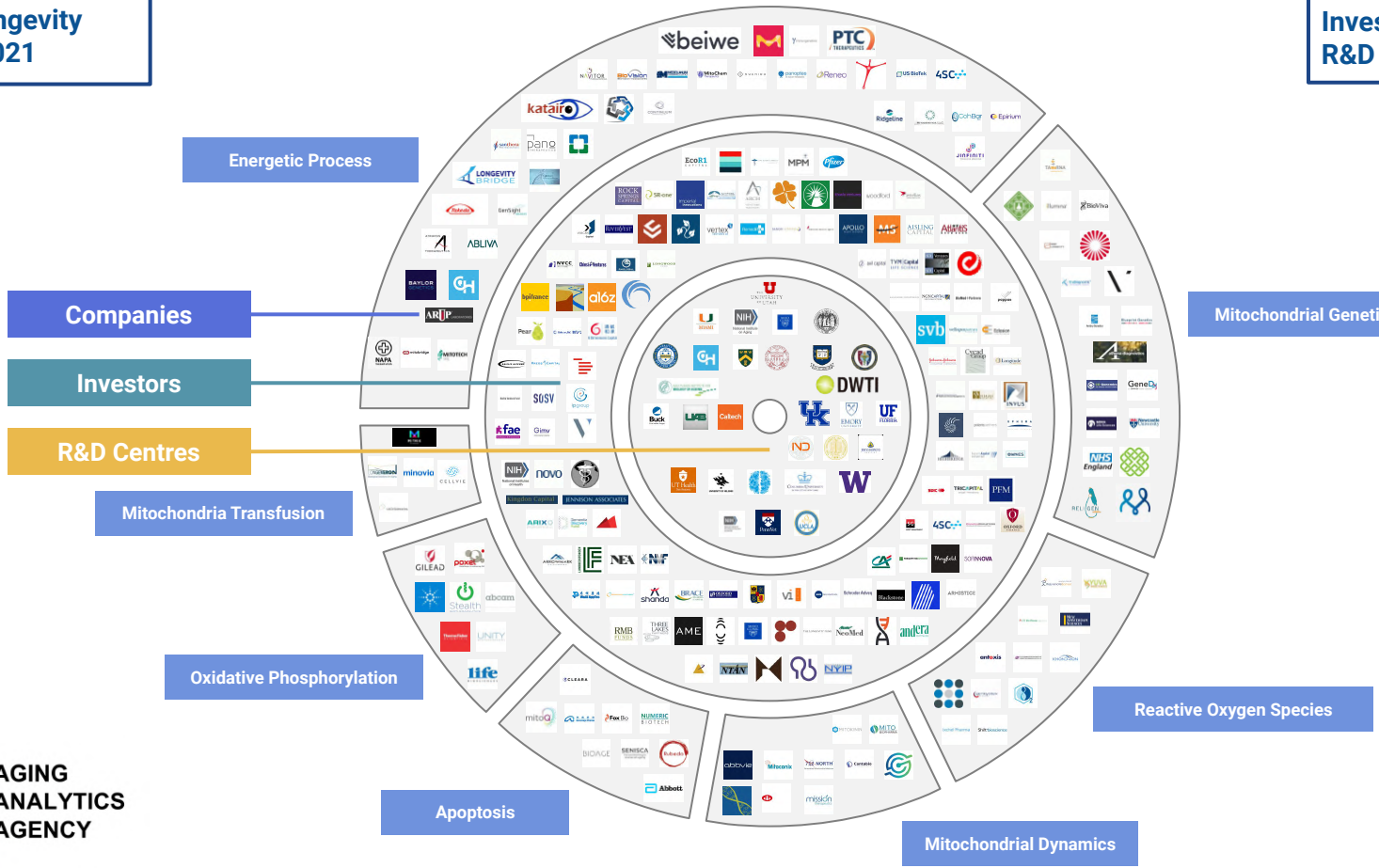
Ahead of database creation, we picked the **most significant fields of clinical studies in ageing that are related to mitochondrial function**. The categorisation of companies is based on the main mitochondrial processes involved in ageing and age-related diseases and **supported by the latest scientific evidence.** The most significant vectors of study – namely, **developing sectors such as research outsourcing** with *in silico* approaches – were distinguished. 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



Mitochondria in Longevity Q3 2021

Companies – 100
Investors – 120
R&D Centres – 30



AGING ANALYTICS AGENCY

List of Therapeutic Clinical-stage Companies*

1	4SC AG
2	Abbott
3	Abbvie
4	Abliva AB
5	Amgene
6	Beijing Tide Pharmaceutical
7	BioAge
8	GenSight Biologics
9	Gilead
10	Ixchel Pharma
11	Khondrion
12	Longeveron
13	Minovia Therapeutics
14	Mitobridge
15	MitoQ
16	Mitotech
17	Navitor Pharmaceutical
18	Numeric Biotech
19	Poxel
20	Reata Pharmaceuticals
21	Reneo Pharmaceuticals
22	Stealth BioTherapeutics
23	Takeda
24	UNITY Biotechnology
25	Yiling Pharmaceutical Group

*in alphabetical order as for 2021

List of Therapeutic Preclinical Companies*

1	712 North
2	Antoxis
3	Atropos Therapeutics
4	Beiwe Health
5	Cantabio
6	Cleara Biotech
7	Continuum Biosciences
8	Cellvie
9	FoxBio
10	Genentech
11	Guided Clarity
12	Life Bioscience
13	Longevity Biotech
14	MISSION Therapeutics
15	Mitoconix Bio
16	Mitokinin
17	Mitrix
18	Napa Therapeutics
19	Pano Therapeutics
20	Reata Pharmaceuticals
21	RejyvenataBiomed
22	Ridgeline Therapeutics
23	Rubedo Life Science
24	Senisca
25	Shift BioScience
26	Yuva BioScience

*in alphabetical order as for 2021

List of Diagnostic Companies*

1	Abcam
2	Aglient
3	Ambry Genetics
4	ARUP laboratories
5	Athena Genetics
6	BaylorGenetics
7	BioVision
8	Blueprint Genetics
9	CD-genomics
10	Centogene
11	Elysium Health
12	GeneDX
13	Jinfiniti Precision Medicine
14	Illumina
15	Longevity Bridge
16	MDNA Life Science
17	Newcastle Mitochondria
18	Prodrome
19	Religen
20	Sigma-Aldrich
21	TAmiRNA
22	Thermofisher
23	US BioTek laboratories
24	VCGS
25	Viome

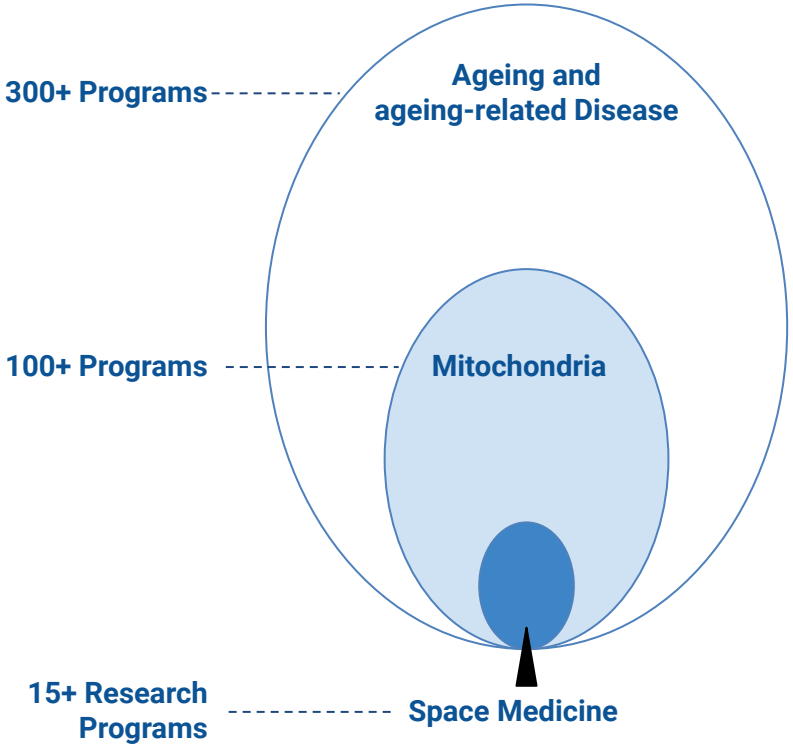
*in alphabetical order as for 2021

Market Overview

Q3 2021

AGING
ANALYTICS
AGENCY

Market at a Glance: Ageing-Related Approach



While analysing the role of mitochondria in Longevity and space medicine, it's crucial to understand the scope and impact of the aforementioned companies.

Factors include the number of existing companies within the ageing industry and the percentage of mitochondria-based programs.

As of **Q3 2021**, there are more than **300 programs targeting ageing** as a root cause of disease and not as a symptom, comprising **USD $58.5 B** in market capitalisation. Experts predict that the global anti-ageing market will reach a value of US $88.30B by 2026

Nowadays, approximately **9.5% of anti-ageing programs** address a major hallmark of ageing — **mitochondrial dysfunction**, with a total capitalisation volume of around **USD $5.5B** in value.

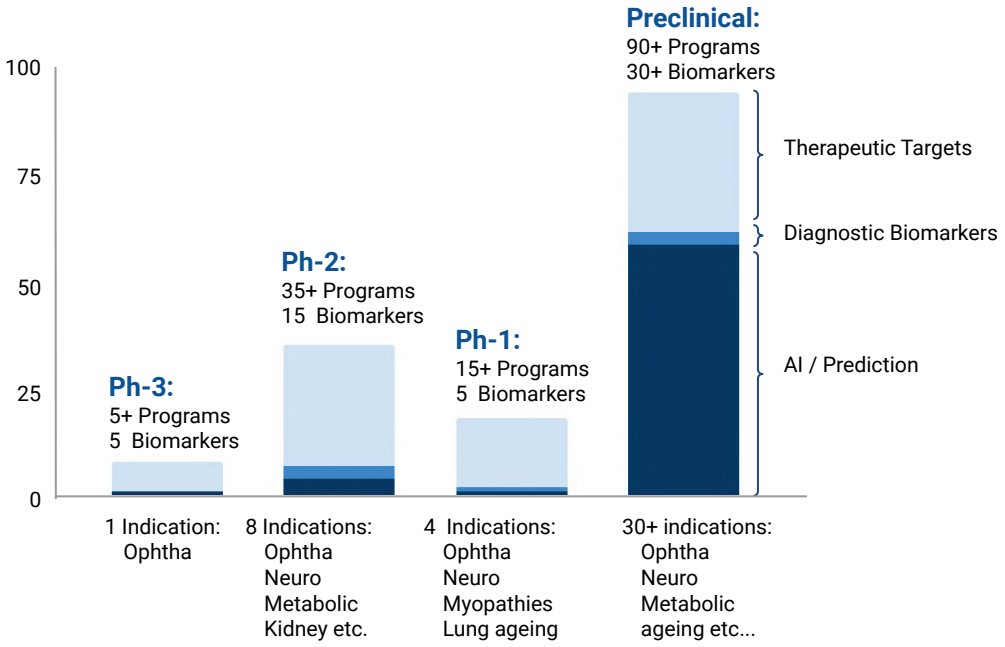
There is a niche intersection between mitochondrial programs and **space medicine**, with **15+ research programs** examined in this analytical case study.

Mitochondria in Ageing: Expansion Avenues / Directions

The BioTech industry is affected less than most by the market and logistical consequences of the COVID-19 pandemic. **BioTech companies and startups in particular just keep working through market downturns** and disruptive events, and are largely only impacted to the degree that they need to raise funding. Progress continues apace. **Mitochondria targeting approach have produced robust results in Ophthalmology.** The first human trials have been completed with promising results, and more are in progress.

The most direct and indirect approaches of mitochondria targeting are under active development, such as mitochondrial antioxidants, mTOR inhibitors, NAD+ enhancers and so on. They are essentially attempting to make the aged metabolism more resilient to underlying damage, or **override some of its reaction to damage, without actually repairing that damage.**

Mitochondria Pipeline:
100+ Programs, 100 Companies



Note: There are low numbers of clinical trial in Phase 1 due to their cancelation during the COVID 19 pandemic.

Key Market Players

Key Companies

Stealth BIOTHERAPEUTICS (25 programs)

genesight (8 programs)

LONGEVERON Biological Solutions for Aging (8 programs)

MITOTECH SKQ (7 programs)

RETROTOPE (5 programs)

mitobridge An Astellas Company (6 programs)

KHONDRION (5 programs)

CohBar INC (6 programs)

Cantabio PHARMACEUTICALS (3 programs)

Key R&D Centers *(Academia)*

MAYO CLINIC (1 program)

NIH National Institutes of Health (1 program)

COLUMBIA UNIVERSITY (2 programs)

IND Institute for Neurodegenerative Diseases (1 program)

MAX PLANCK INSTITUTE FOR BIOLOGY OF AGEING (1 program)

NIA NATIONAL INSTITUTE ON AGEING (1 program)

Caltech (1 program)

UF UNIVERSITY of FLORIDA (2 programs)

Big Pharma Players

Abbott (1 program)

abbvie (1 program)

AMGEN (1 program)

Genentech A Member of the Roche Group (1 program)

GILEAD (1 program)

Takeda (1 program)

Note: Key companies are evaluated based on the number of mitochondria-related programs. Near all of these companies are in preclinical development or in early trials, and Big Pharma has yet to become earnestly involved in the Longevity Industry. Featured Big Pharma companies are selected based on the availability of mitochondrial programs.

R&D Centres by Area of Study*

Fundamental Research / Biology

- Burke Neurological Institute (USA)
- Caltech (USA)
- Children Hospital of Philadelphia, Wallace Lab (USA)
- Columbia University (USA)
- David Geffen School of Medicine at UCLA (USA)
- Institute for Neurodegenerative Disorders (USA)
- Johns Hopkins Medicine (USA)
- Max Planck Institute for Biology of Ageing (Germany)
- National Institutes of Health (USA)
- PennVet (USA)
- University of Cologne (Germany)
- University of Miami (USA)
- University of Pittsburgh (USA)
- University of Southern California (USA)

Therapy

- D. Western Therapeutics Institute (Japan)
- Columbia University (USA)
- Mayo Clinic (USA)
- National Institute of Neurological Disorders and Stroke (USA)
- National Institute on ageing (USA)
- The University of Texas (USA)
- University of Alabama at Birmingham (USA)
- University of Florida (USA)
- University of Helsinki (Finland)
- University of Kentucky (USA)
- USC Leonard Davis (USA)
- University of Regina (USA)
- University of Utah (USA)
- Yale University (USA)

Diagnostic

- Columbia University (USA)
- Copenhagen University (Denmark)
- Institute for Neurodegenerative Disorders (USA)
- National Institutes of Health (USA)
- NHS Foundation Trust (USA)
- University of Pisa (Italy)
- University of Southern Denmark (Denmark)
- Wuhan University (China)

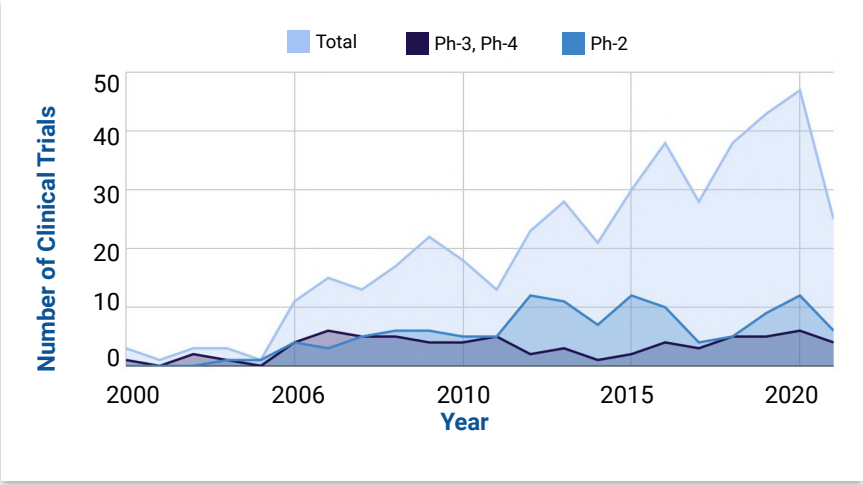
AI / Machine Learning

- University of Copenhagen (Denmark)
- George Mason University (USA)
- Buck Institute of ageing (USA)
- Georgia Institute of Technology (USA)
- University of Oxford (UK)

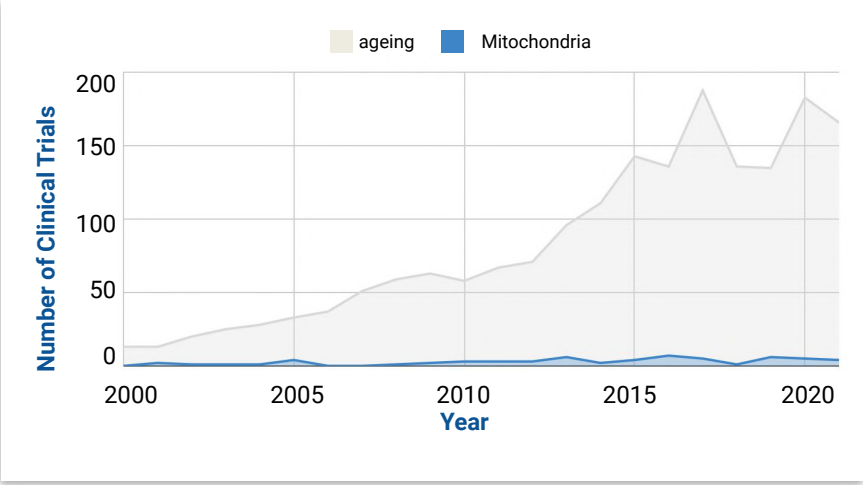
*in alphabetical order as for 2021

Mitochondrial Clinical Trials vs. Ageing Clinical Trials

Total Number of Mitochondrial Clinical Trials (630 trials)



Share of Mitochondrial Trials in Ageing (2,100 trials)



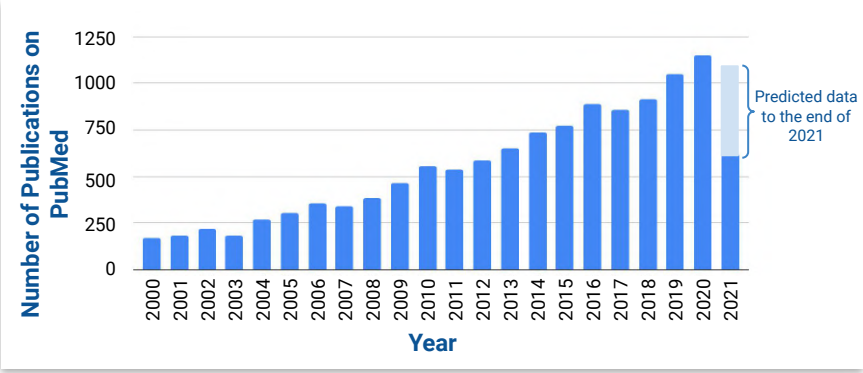
As of 2021, the percentage of clinical trials related to mitochondrial dysfunction is **negligible compared to trials focused on other hallmarks of ageing (~3% of the total amount)**. Of these, only 16% have reached Phases 3 and 4, the stages at which industry-ready products are feasible in the near future.

The majority of other BioTech companies are focussing on reparation energetic processes (37 programs) in mitochondria and reduction of oxidative stress (10 programs).

Source: ClinicalTrials.gov Longevity Clinical Trials Tracker

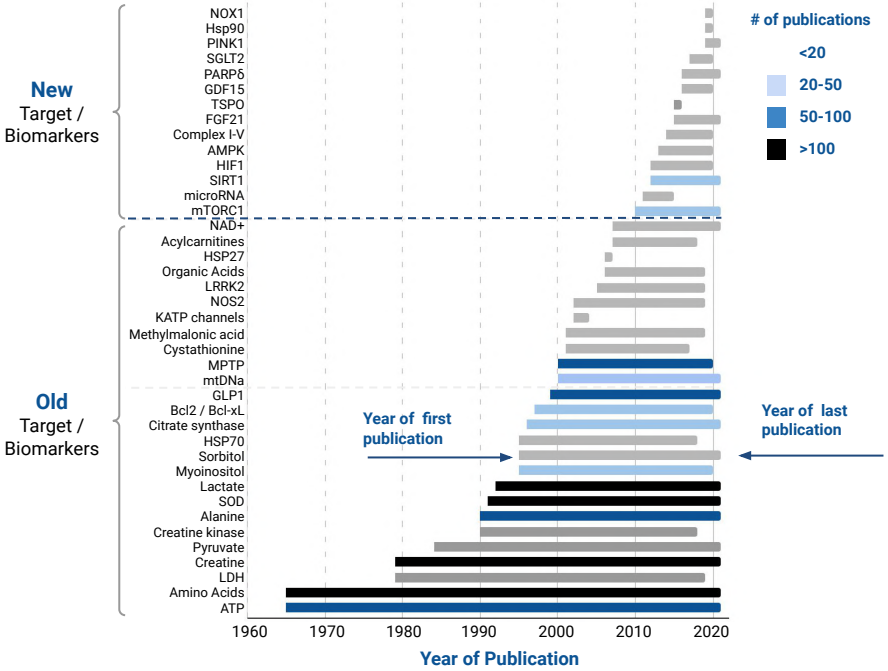
Growth of Scientific Interest in the Role of Mitochondria in Ageing

Total Scientific Interest in the Role of Mitochondria in Ageing



Broadly speaking, scientific interest in the role of mitochondria in ageing is now 10 times greater than it was in the early 2000s. **The most reliable mitochondrial biomarkers,** such as concentration of **amino acids, creatinine level, lactate and SOD** in biological samples, are a "golden standard" for clinical trials. The **new diagnostic biomarkers** are **GDF15 and FGF21**.The other one is **miRNA** which used for diagnostic of mitochondrial disease (TamiRNA). Among the newest mitochondrial therapeutic targets, **the most promising** are **TSPO** for imaging and **SIRT1** and **mTOR** for regulation of energetic processes.

Popularity of Mitochondrial Targets / Biomarkers in Time

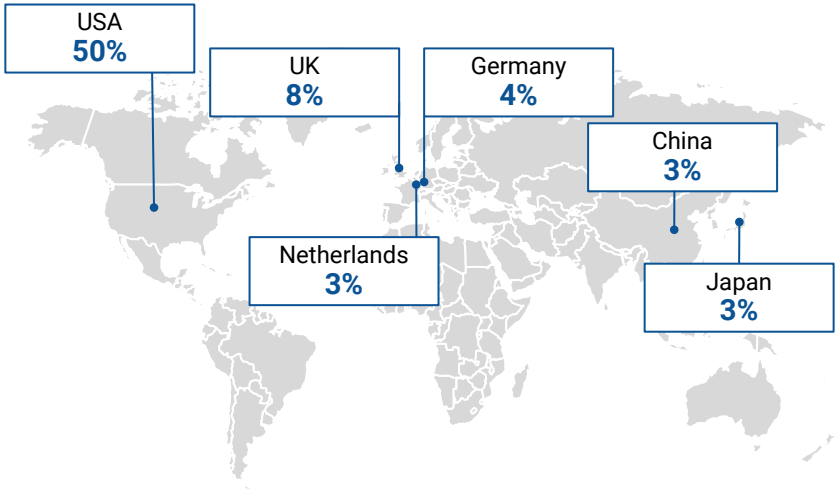


Search Terms
Keywords: "target name" + ageing
Article Type: Clinical Trials

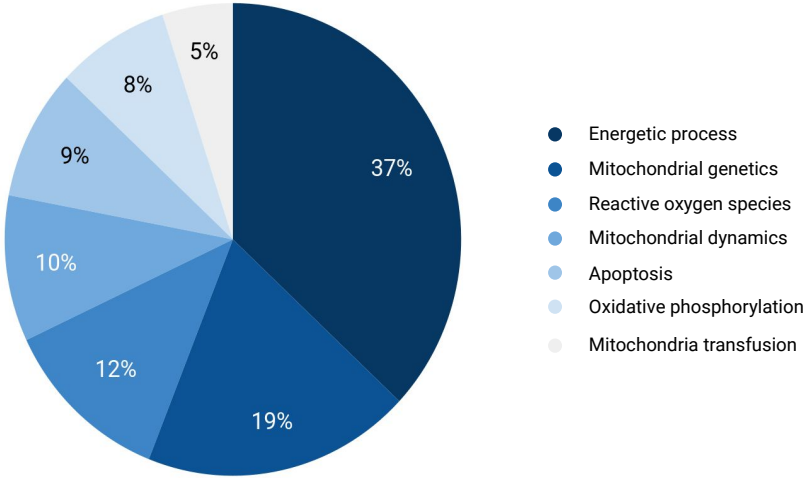
Source: PubMed database

Market at a Glance: BioTech Companies

Distribution of Companies by Country, %



Distribution of Companies by Category, %

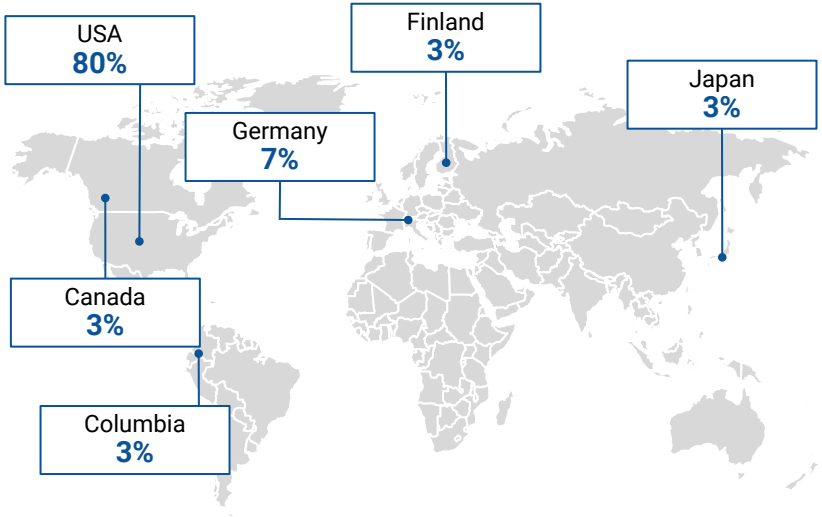


The **majority** of companies conducting mitochondria research are located in the **United States**, which accounts for **50%** of the entire range of analysed companies. The United States is distantly followed in this regard by the **United Kingdom** and **Germany**, which together account for 12% of the total number of companies analysed.

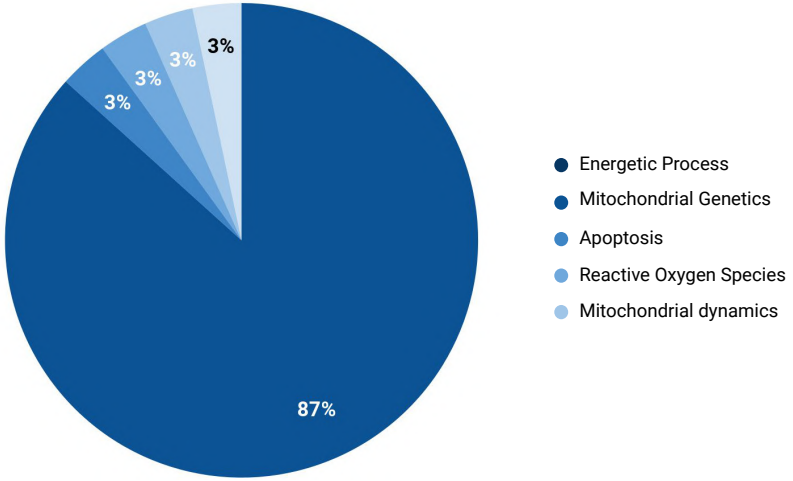
The main domains in which companies are being conducted are **energetic process**, **mitochondrial genetics** and **reactive oxygen species** which account for **37%**, **19%** and **12%** of all companies **respectively**.

Market at a Glance: R&D Centres

Distribution of R&D Centres by Country, %



Distribution of R&D Centres by Category, %



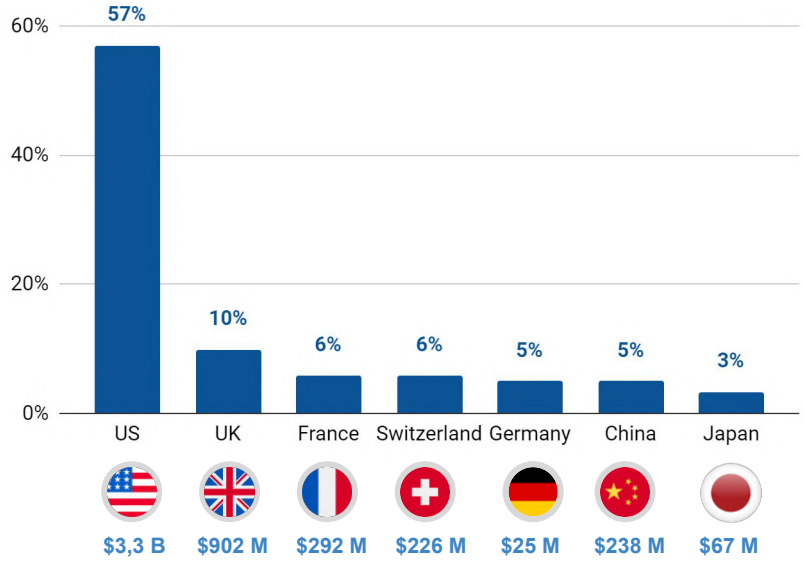
The **vast majority of R&D Centres** that conduct mitochondria research are located in the **United States**, where **80%** of the whole range of analysed R&D Centres are located. The United States is distantly followed by **Germany** and **Finland** which together make up **10%** of all R&D Centers.

The major domain in which mitochondria research are being conducted is **energetic process - more than 85%** of centers conduct research in this field.

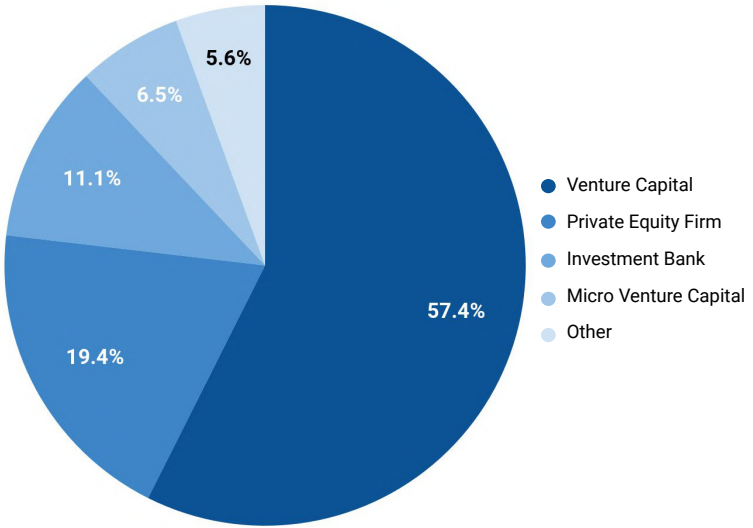
Source: Aging Analytics Agency analysis

Market at a Glance

Top Countries by Number of Investors, % of Total



Main Type of Investors, %



More than half (around **57%)** of investors in Mitochondria research are in the **United States. An additional 32%** of investors are located in **Europe**, including 10% in the UK, 6% each in France and Switzerland, 5% in Germany and 5% in other European countries**.** Only **around 8%** of investors are **in Asia**.
Most investors are **Venture Capitals,** which constitute more than half of all investors (**57.4%**). The other main types are **Private Equity Firms** (**19.4%**), **Investment Banks and Micro Venture Capitals** (**6.5% each**).

Mitochondria Treatment Targets

Energetic Processes	Apoptosis	Mitochondrial Dynamics	Reactive Oxygen Species	Oxidative Phosphorylation
AMPK DOHD GIP ATPase ND1	BCL-XL BCL-2 ROS	USP 30 LRRK2 DJ1 MCS	NOX1 NOX2 NOX4 ROS	Mitochondrial uncouplers
ICT KATP PARP delta Prostaglandin-E	foxo4-p53 FOXO p53	HSP90 HSP27 HSP 70	SOD Frataxin STAT3	FRX ACC GLP1R
mTOR(1,C1) NAD+ NNMT SIRT1	HIF1 ERR	PINK1 OMA1 SGLT2	NOS II NF-E2	Mitochondrial pyruvate carrier

Treatment products

4SC EpiScience for Life, katairo therapeutics in sight®, Ridgeline Therapeutics, CohBar, mitobridge, antoxis, MITOTECH SKQ, NAPA THERAPEUTICS, NAVITOR PHARMACEUTICALS, CONTINUUM, ATROPOS THERAPEUTICS, RETROTOPE, ABLIVA, pano THERAPEUTICS, beiwe, minovia, MAYO CLINIC, CYTEGEN, KHONDRION

Treatment products

MAYO CLINIC, Rubedo, Abbott, SENISCA, NUMERIC BIOTECH, mitoQ, Fox Bio, CLEARA

Treatment products

712 NORTH Personalized Mitochondrial Medicines, MITOKININ, mission therapeutics, REATA, わかもと製薬株式会社 WAKAMOTO PHARMACEUTICAL CO., LTD., Genentech, Cantabio PHARMACEUTICALS, YILING, GUIDED CLARITY

Treatment products

genkyotex the nox company, NEW AMSTERDAM SCIENCES, REATA, TIDE, 泰德制药 TIDE PHARMACEUTICAL, HEALTHY FOR LIFE RejuvenateBiomed, Shift bioscience, Ixchel Pharma, YUVA BIOSCIENCES

Treatment products

Stealth BIOTHERAPEUTICS, life BIOSCIENCES, poxel

Note: Therapeutic target medicines that are in development or are currently on the market are presented here. It is evident that energetic processes are the primary focus of study and development. Other fields are actively growing, but because of the high complexity, most of them are not yet marketed.

Source: aginganalytics.com

Diagnostic Biomarkers

Mitochondrial Genetics

- Single nucleotide polymorphisms
- Deletions, Gene expression, Insertions
- Mitochondrial DNA copy number

Biomarkers products, tests, panels

NHS, VIOME, MAYO CLINIC, illumina, CENTOGENE, GeneDx, athena diagnostics, RELIGEN, BAYLOR GENETICS, Ambry Genetics, MDNA Life Sciences, ARUP LABORATORIES, VCGS, Blueprint Genetics

Metabolic Biomarkers

- Lactate, Pyruvate, Orotic Acid
- Beta-Hydroxybutyric Acid
- Carnitine, Acylcarnitine, Creatine
- Fatty Acids, Organic Acids, Amino Acids

Biomarkers products, tests, panels

MOLECULAR SYNTHESIS, MAYO CLINIC, US BioTek LABORATORIES, BAYLOR GENETICS, ARUP LABORATORIES, Cleveland Clinic Laboratories

Oxidative Phosphorylation

- Pyruvate dehydrogenase complex
- Complex I-V, H+ (proton) leak
- Endpoint relative mitochondrial membrane potential
- Dynamic changes in relative mitochondrial membrane potential

Biomarkers products, tests, panels

ThermoFisher SCIENTIFIC, BAYLOR GENETICS, RELIGEN, SIGMA-ALDRICH, MAYO CLINIC, abcam discover more, Agilent Technologies

Mitochondrial Dynamics

- Mitochondrial outer membrane integrity
- Mitochondrial permeability transition
- Muscle biopsy examination, Cardiolipins

Biomarkers products, tests, panels

MAYO CLINIC, ThermoFisher SCIENTIFIC, NHS, BAYLOR GENETICS, abcam discover more, SIGMA-ALDRICH

Energetic Process

- ATP-linked respiration, ADP/ATP ratio
- Maximal respiration, NAD/NADH ratio
- Spare respiratory capacity

Biomarkers products, tests, panels

NHS, JINFINITI PRECISION MEDICINE, abcam discover more, BioVision, ThermoFisher SCIENTIFIC, SIGMA-ALDRICH, Agilent Technologies

Note: Biomarkers that currently available on the market both for diagnostics and research are presented here. The most attention is paid to mitochondrial genetics, while mitochondrial dynamics biomarkers are less present in the market due to high complexity of the tests.

Source: Longevity Biomarkers Ecosystem

Diagnostic Biomarkers*

Diagnostic Tools

athena diagnostics
Ambry Genetics
A Konica Minolta Company
RELIGEN
ARUP LABORATORIES
BAYLOR GENETICS
MAYO CLINIC
Cleveland Clinic Laboratories
VCGS
leaders in genetic health
CENTOGENE
THE RARE DISEASE COMPANY
Blueprint Genetics
MDNA Life Sciences
NHS
US BioTek LABORATORIES

Research Tools

Agilent Technologies
BioVision
BioVision Incorporated
illumina
SIGMA-ALDRICH
abcam
discover more
ThermoFisher SCIENTIFIC

Preventative Medicine Tools

JINFINITI
PRECISION MEDICINE
VIOME

Note: Mitochondria biomarkers are mostly used for the mitochondrial disease diagnostics, while only few companies offer mitochondrial function preventive screening tests. The most popular biomarkers used for diagnostics are mtDNA examination and metabolites evaluation, as they are relatively cheap or more accessible. Other biomarkers test and test panels are used mostly for research only, due to their high complexity and problems with sample storage.

*in alphabetical order as for 2021

Reactive Oxygen Species Pathways Longevity Research

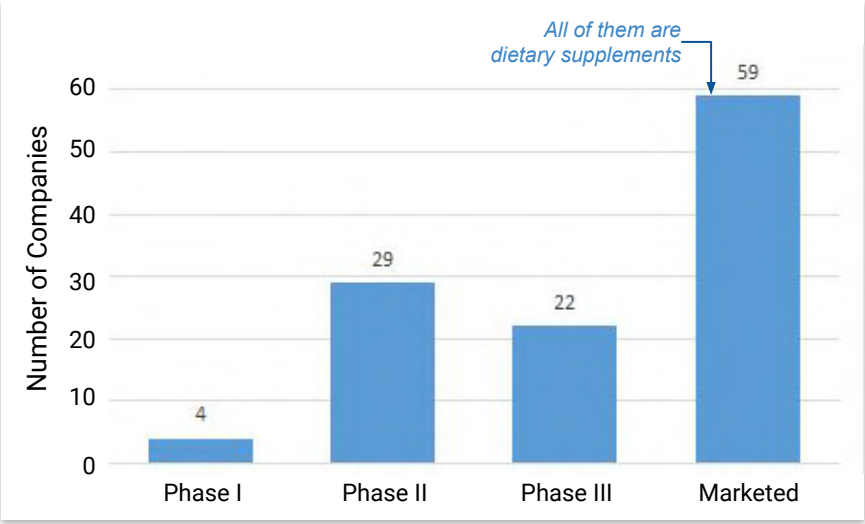
Reactive oxygen species (ROS) are highly reactive chemicals formed from oxygen. They are primarily generated during mitochondrial oxidative metabolism and in cellular response to xenobiotics, cytokines, and bacterial invasion. Overproduction of these molecules causes oxidative stress.

Oxidative stress has been linked to various illnesses, including atherosclerosis, chronic obstructive pulmonary disease (COPD), Alzheimer's disease and cancer, revealing the multiple ways by which oxidants cause cellular damage. However, the degree to which oxidative stress contributes to disease pathogenesis varies widely. Therefore, boosting antioxidant defense may be ineffective in some conditions.

There are two main ways that oxidative stress leads to illness. The first includes the generation of reactive oxygen species that directly oxidize macromolecules, while the second incorporates the intervention of ROS signaling.

Antioxidants are chemicals that can prevent or delay the damage caused by free radicals. For a long time, antioxidants were a promising field of therapeutics, **which potentially could increase lifespan and life quality in the elderly.**

Number of Companies by Product Development Stage



Note: ROS and the oxidative stress induced by it are key reasons for uncontrolled cellular damage, which leads to ageing. For that reason, there is a huge number of studies in this area. Most modern solutions are already marketed, yet some are undergoing clinical trials. As can be seen in the figure above, the number of clinical trials in Phase I is relatively small, which indicates a loss of interest in developing such products.

Source: aginganalytics.com

Reactive Oxygen Species Pathways Longevity Research

Today the two most common approaches to ROS pathway therapy are **antioxidant treatment** and **internal antioxidant system stimulation.** Antioxidant treatment is more highly developed and studied due to the higher complexity of potential drugs for the internal antioxidant system.

Several antioxidant enzyme mimics have been developed and are now being tested in clinical studies. Many of these substances are protective in non-human animal research and even in clinical trials. The **small molecules treatment approach is the most popular** because it is primarily supplementary and does not always require clinical trials for validation.

Nonetheless, there are many constraints that restrict capacity to use antioxidant methods therapeutically. The amount to which oxidative stress plays a role in disease limits the efficacy of antioxidant defenses. The insignificant action of scavenging by tiny molecules is a significant restriction in antioxidant defense. In addition, **a lot of antioxidants can't perform significant results in vivo.**

Due to low end-point efficiency and a variety of marketed solutions, interest in ROS pathways is declining.

Genkyotex has built a diverse pipeline of NOX inhibitors. Preclinical studies show that NOX1&4 inhibitors have broad treatment potential across fibrotic and inflammatory diseases of the liver, kidney, lungs and skin.

Yuva Biosciences has a mission to use mitochondrial science to develop cosmeceuticals and pharmaceuticals that can provide Youthfulness for Life. Their products include antioxidants.

LTT Bio-Pharma works with laboratories at medical schools in Japan, mainly researching, developing and selling DDS. Company has multiple solutions for various conditions.

Source: aginganalytics.com

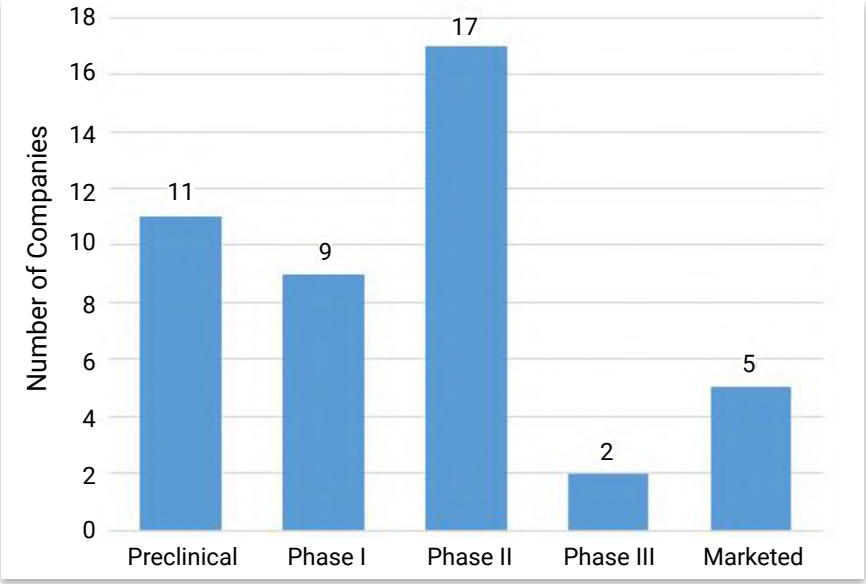
Energetic Process Pathways Longevity Research

Maintaining energy metabolism to allow Longevity is one of the key principles of the modern approach. It is proven that with ageing a huge number of metabolism dysfunctions accumulate as in organism as in individual body cells. Most of them are associated with disbalances in metabolites, which can be abundant due to mitochondrial dysfunctions.

Mitochondria have been recognized to be a central player in ageing for over five decades, and are considered to be the **organelle that is most affected by ageing.** Many aspects of mitochondria change as mammals age, including respiration rate, enzyme levels, overall mitochondrial mass, and morphology. For example, 95% of mitochondria in the muscle tissue of a healthy 90-year-old man were found to be damaged, compared to no detectable damage in the muscle tissue of a 5-year-old child.

Dysfunctions in energetic processes are the root cause of many illnesses, including muscular dystrophy, epilepsy, Parkinson's disease, and cardiomyopathy. Because there are so many of these conditions, there has been a large number of studies undertaken in this area, and some of the disorders have marketed therapies.

Number of Companies by Product Development Stage



Note: Mitochondria and their role in metabolism has been in focus of studies for decades; that is why therapeutic products that target them are already available on market. A lot of these studies are ongoing and have the potential to result in therapeutics with multiple applications.

Source: Longevity Clinical Trials Q3 2021

Energetic Process Pathways Longevity Research

Most modern studies are focused on developing ways of restoring normal activity of energetic processes in mitochondria in cases of impairment. Multiple approaches are being used, including **metabolite balance restoration by modulating enzyme activity; modulating mitochondrion membrane throughput; mitochondrion rejuvenation;** and **mitochondrial stimulation.**

The most common method of energetic process restoration is **metabolism restoration via food supplements.** It is used due to the optionality of conducting clinical trials. It is believed that lack of metabolite balance in energetic pathways can be restored by dietary supplements, but some of the marketed solutions have no clinical evidence of efficiency.

A cohort of studies demonstrate the **beneficial effects of exercise, which is associated with an increase in ATP metabolism.** Although it is only a preventive method, most experts still recommend physical exercise.

Energetic process pathway modulation was and will be the main target of treatment of mitochondrial disorders; thus this market will soon develop more therapies and approaches.

Mitotech – mitochondria addressed cardiolipin peroxidation inhibitors. Mitotech is developing several drug formulations of SkQ1 covering a variety of therapeutic areas and methods of administration.

Mitobridge discover and develop a pipeline of therapeutics to improve mitochondrial function for patients, including in kidney and muscle diseases. The company's lead drug development programmes are focused on modulation of PPARδ.

Katairo has developed Remofuscin, which has the surprising characteristic of removing lipofuscin from living cells in the retinal pigment epithelium. This paradigm-breaking effect was previously believed to be impossible.

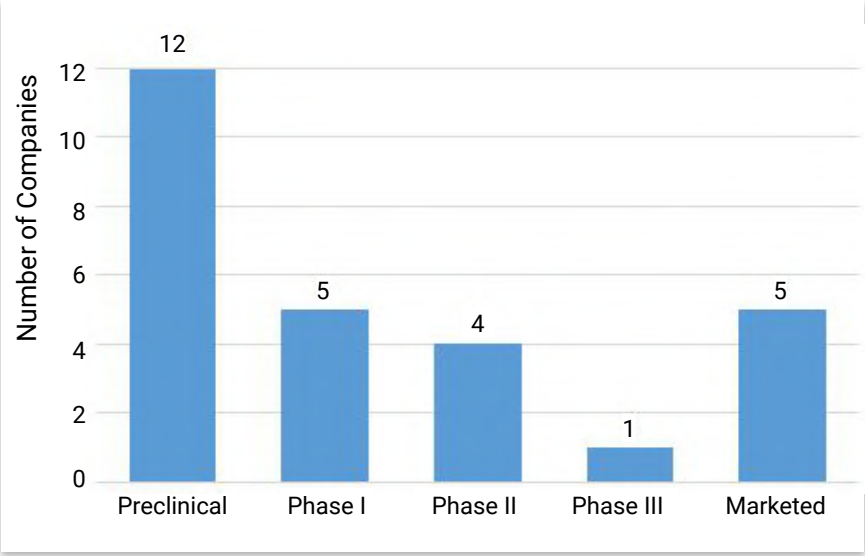
Source: Longevity Clinical Trials Q3 2021

Mitochondrial Dynamics Longevity Research

Mitochondrial dynamics impairment is one of the key processes that leads to cell ageing and, as a result, mitochondrial dysfunction-related illnesses. As a result, much work is being expended in determining the system's malfunctions. At the time, **mitochondrial fusion is the most difficult challenge for researchers to solve.** This subject has attracted a lot of interest since it could be the cause of several cardiovascular and neurological illnesses. Although the majority of illnesses caused by this abnormality are genetically inherited, there is a small group of age-related disorders caused by it, as well as loss of tissue and organ function, loss of immunological potential, and a rise in global inflammation.

At present, most of the companies are conducting their preclinical experiments, but there are some marketed solutions which are mostly represented by small molecule drugs aimed to promote fused mitochondria degeneration. As well as that, there are **drugs in development that are positively influencing mitochondrial relocation in the cell.**

Number of Companies by Product Development Stage



Note: The graph shows that the field of mitochondrial dynamics-targeting drugs is currently in active development. The use of this approach can in future lead to discovering ways of fighting such disorders as arteriosclerosis and Parkinson's disease.

Source: Longevity Clinical Trials Q3 2021

Mitochondrial Dynamics Longevity Research

At present, **biomarkers search is the most common approach** to the diagnostics of mitochondrial dynamics, which is a very difficult endeavour. But due to the complexity of mitochondrial processes and their in-cell localisation, finding a comprehensive biomarker remains a key goal.

Newly discovered alternative approaches to diagnostics may open a way to practise early identification of some diseases offstes. One such innovation in the field is **mitochondrial visualisation**. This is a technique based on labeling mitochondria in dead or living cells with the intention of counting them or their dynamics in individual cells.

This field of research is being actively studied due to its clear interconnection with the field of reproductive medicine. Those modern reproductive approaches aim to maximise fertility, which strongly depends on the normal functioning of the mother's mitochondria.

The manipulation of mitochondrial dynamics is a promising field of scientific research. Its novelty is pushing the market forward but time is needed for the desired outcomes to appear.

712 NORTH
Personalized Mitochondrial Medicines

712 North is a pre-clinical stage pharmaceutical company that develops modulators of the dynamic mitochondrial network for patients with Alzheimer's and other diseases.

abbvie

Abbvie is developing innovative candidate compounds that specifically enhance PINK1 enzyme activity, addressing mitochondrial malfunction that leads to the progression of Parkinson's disease.

MITO BIOPHARMA

Cantabio's core research strategy focuses on the development of a pipeline of therapeutic candidates with novel mechanisms of action for preclinical testing and clinical development for Alzheimer's, Parkinson's diseases and diabetes.

Source: aginganalytics.com

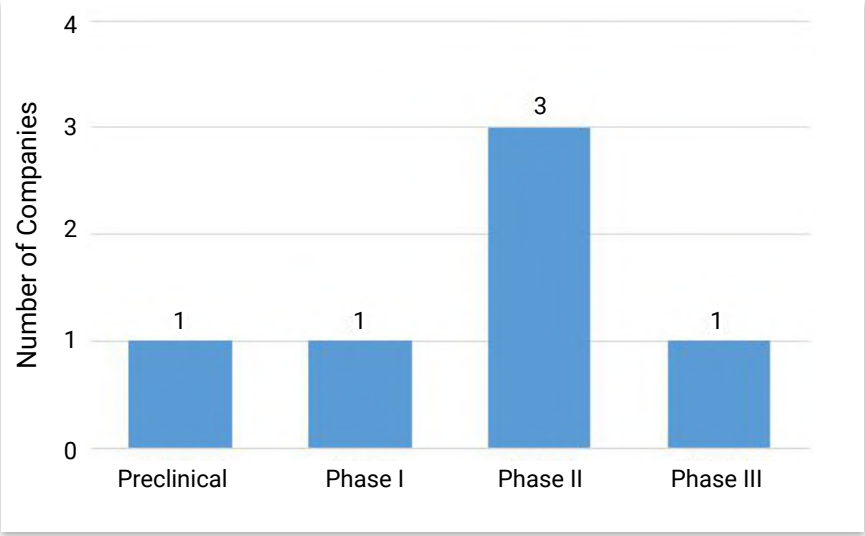
Mitochondrial Induced Apoptosis Longevity Research

Mitochondrial induced apoptosis is an emerging field of studies which can potentially have a huge field of clinical implementations. Due to the novelty of the field, researchers are still working on approaches to achieve the desired result. Mitochondrial-induced apoptosis drugs that selectively disrupt malfunctioning mitochondria could be created by designing molecules that act on the malignant mitochondria by, for instance, inhibiting glycolysis, depolarizing the membrane potential, and inhibiting the mitochondrial permeability transition pore.

Most of the promising drug candidates represent small lipophilic molecules which can penetrate cell and mitochondrial membranes. A crucial factor for developing such medication is the **selectivity of the drug.** This can be achieved by various approaches, but, as of yet, none of them has been approved for clinical use.

At present, most clinical trials are focusing on age-related diseases but these medications also have the potential for curing some kinds of cancer and other complex metabolic disorders.

Number of Companies by Product Development Stage



Note: The graph indicates that, at present, drugs targeting mitochondrial-induced apoptosis are mostly undergoing Phase II of clinical research. The total amount of studies in this field is small; nonetheless, despite the current lack of marketed solutions, these drugs have the potential to provide for a lot of medical implementations.

Source: aginganalytics.com

Mitochondrial Induced Apoptosis Longevity Research

It has been proven that mitochondria clearance in cells during ageing is impaired. Due to the fact that mitochondria accumulate damage during a person's lifetime and can't be normally utilized from the cell, accumulation of such impaired mitochondria leads to cell dysfunction. Thus, for treatment of impaired mitochondria, the cells with them should be removed.

The approach of targeted promotion of-mitochondria induced apoptosis has promising anti-ageing applications, but at the moment research is focused only on age-related diseases.

Chronic age-related diseases such as **sexual dysfunction, chronic kidney disease and myelofibrosis** are the targets of **Phase II** clinical trials. However, recent research is developing a broader application range, such as therapies for fighting immune and muscle ageing, cell senescence and inflammatory background.

Research in the field of mitochondrial-induced apoptosis is not only benefiting the development of medication but also the development of the wider sphere of diagnostics due to the discovery of new biomarkers and targets. Those discoveries are mostly achieved by **software and AI analysis.**

Abbvie has developed Navitoclax, which is a BCL-XL/BCL-2 inhibitor. It is being investigated for the treatment of myelofibrosis but potentially has many more applications. It is currently at Phase III of clinical studies.

The **Mayo Clinic** has a Phase II clinical trial investigating possible use of dasatinib and quercetin for treating senescence in the case of chronic kidney disease by inducing apoptosis in senescent cells.

Human Longevity inc. is developing a Health Nucleus – a complex approach for ageing diagnostics, which includes markers of mitochondrial-induced apoptosis.

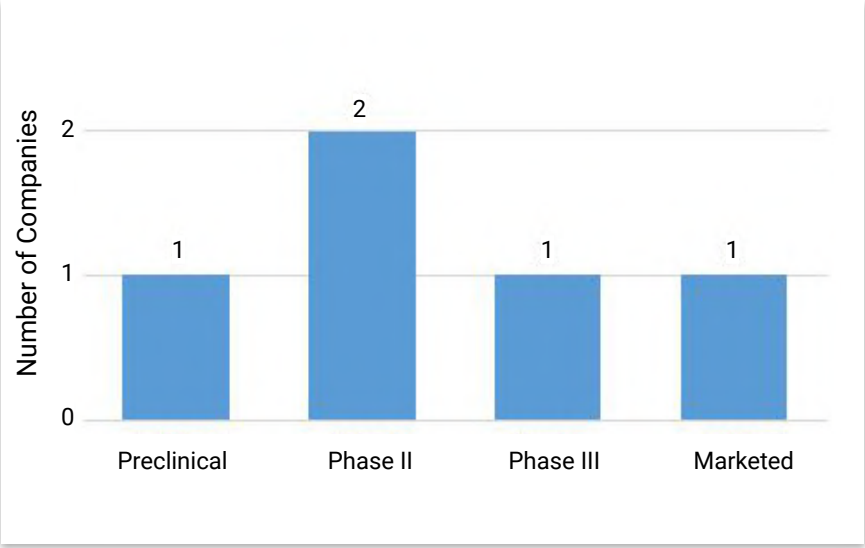
Source: aginganalytics.com

Oxidative Phosphorylation Pathways Longevity Research

Oxidative phosphorylation (OXPHOS) is responsible for producing the majority of the ATP required for normal cellular function. This system is the key energy factor for every cell in human body; thus its dysfunction can have substantial effects on the functioning of an entire organism. Tissues with a high energy demand, such as brain, nerves, retina, skeletal and cardiac muscle, are particularly vulnerable to defects in oxidative phosphorylation. It is a fact that mitochondria accumulate different function mistakes during their existence, which leads to decrease of efficiency. Depending on the level of dysfunction, different kinds of local or global cellular malfunctions can occur. These malfunctions cause a loss of efficiency of different organs and systems. OXPHOS dysfunction has also been implicated in a number of diseases of ageing such as Parkinson disease, Alzheimer disease, diabetes, deafness and cancer.

The significance of this system is driving research, but the complexities of its operation are stifling therapy development. **AI and modelling breakthroughs** are promising for this sector. New research methods could result in the exponential growth of the number of new studies in this field.

Number of Companies by Product Development Stage



Note: The graph shows that drugs targeting OXPHOS are currently at a low level of development. Although there are marketed solutions, overall research coverage is small. The importance of this system is underestimated by the community and, due to its complexity, studies in this field are only just beginning to develop.

Source: aginganalytics.com

Oxidative Phosphorylation Pathways Longevity Research

Modern approaches for curing OXPHOS dysfunction are focused on certain diseases. But their development has a wide range of potential applications as treatment for other types of disorders as well as treatment of ageing.

One of the most important topics at present is diagnostics of **OXPHOS dysfunction.** OXPHOS is found inside mitochondria, which makes this work difficult and, at the moment, necessitates a particular examination of a patient's separated mitochondria. The **emerging area of biomarkers** is currently looking for **particular molecules that can identify OXPHOS dysfunction without the need for time-consuming and resource-intensive techniques.**

Approaches to treatment are centered on developing methods of targeted drug delivery. Researchers are interested in two sorts of therapeutic approaches: **regulating mitochondrial enzyme activity** and **targeted delivery of active substances for restoration of metabolic balance.** The advancement of precision medicine is delayed due to the complexity of mitochondrial genetics and interactions. Nevertheless this area of mitochondria-focused treatment is one of the most promising for the Longevity sector.

Stealth bio is developing a Mitochondrial Carrier Technology (MCT) platform to utilise the unique ability of proprietary compounds to deliver biologically active cargo to mitochondria.

Gilead discover,s identifies and evaluates investigational compounds that show potential to advance the treatment of life-threatening diseases.

Poxel is a clinical stage biopharmaceutical company developing innovative treatments for serious chronic diseases with metabolic pathophysiology, including non-alcoholic steatohepatitis (NASH) and rare disorders.

Source: aginganalytics.com

Role of Mitochondria in Longevity

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Mitochondrial Dysfunction Among Other Hallmarks of ageing

Genomic Instability

Ageing 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 remodelling.

Loss of Proteostasis

Proteostasis involves mechanisms for the stabilization of correctly folded proteins, and the heat-shock family of proteins, as well as mechanisms for the degradation of proteins. These processes tend to change during ageing.

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 ageing.

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

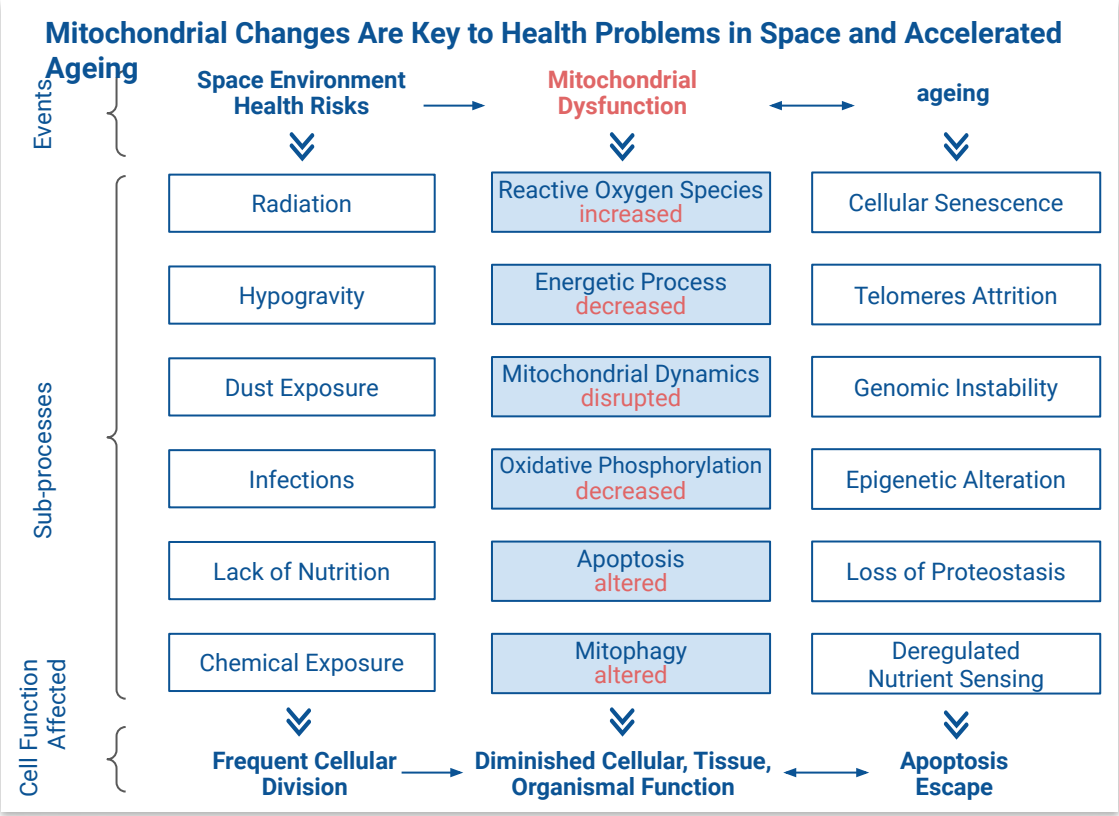
Stem cells are cells from which all other cells with specialized functions are generated. There is a substantial decrease in the number of stem cells during life. Recent studies suggest that stem-cell rejuvenation may reverse the ageing phenotype.

Altered Intercellular Communication

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

Role of Age-Related Mitochondrial Dysfunctions in Space Medicine

The latest studies have shown that the **Km and Vmax of complexes I, III, and IV** of the mitochondrial electron transport chain all **decline with age**. In addition, the abundance of both **ubiquinone and cytochrome c**, two mobile electron carriers within the chain, **decreases**; and **ATP production decreases** at the expense of elevated reactive radical species production. Whether causative or consequential, age-associated **mitochondrial dysfunction is linked with many diseases** that limit life expectancy in humans, including Type II diabetes, metabolic syndrome, Alzheimer's disease, Parkinson's disease, depression, and blindness. The role of mitochondria in the pathogenesis of multiple diseases is a consequence of their role in the **generation of up to 90% of cellular ATP**. Other important functions of mitochondria include calcium sequestration, Fe-S cluster formation, nucleotide biosynthesis, infection signalling, stem cell maturation, apoptosis signalling, oxidative stress signalling, steroid biosynthesis, and xenobiotic detoxification.



Prognosis of Treatment Efficacy

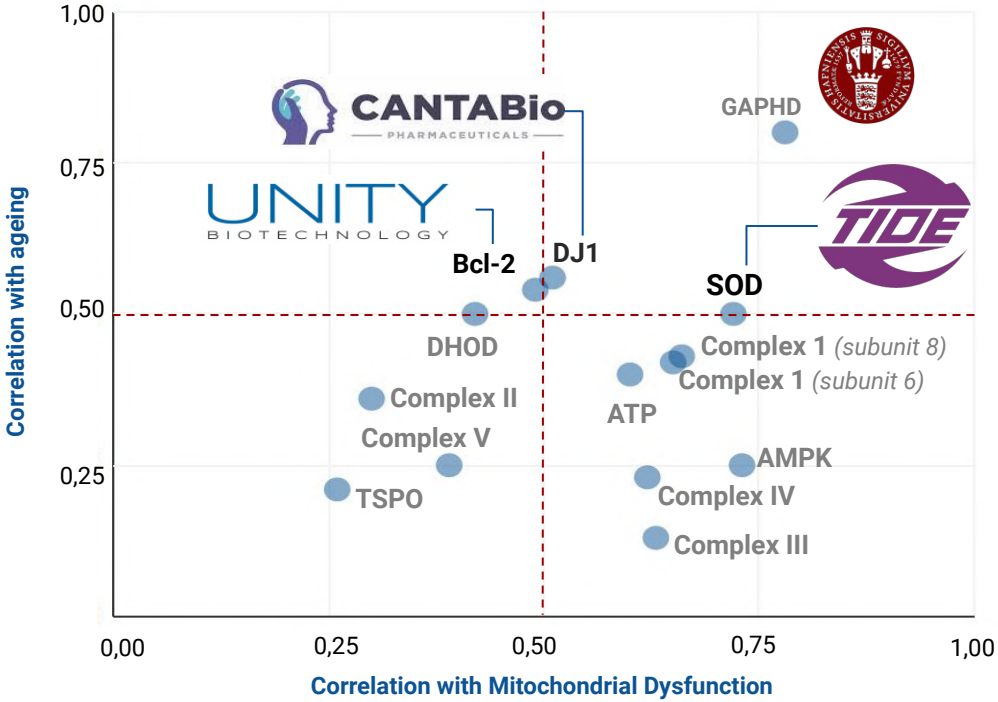
The new direction in ageing treatment is the development of **molecular targeted therapy**, in which mitochondrial processes are regulated by interfering with specific molecules that are necessary for cellular energetic processes and cell death control.

For this purpose, selected mitochondrial targets are validated by their association with ageing and mitochondrial dysfunction.

Data is based on clinical studies of ageing groups (>65 years) vs. young patients (16-50 years).

For analysis of target correlation with mitochondrial dysfunction, we select publications with studies on age-related disease, where patients are compared with a healthy control group of people in the same age range.

Ranking of Therapeutic Targets

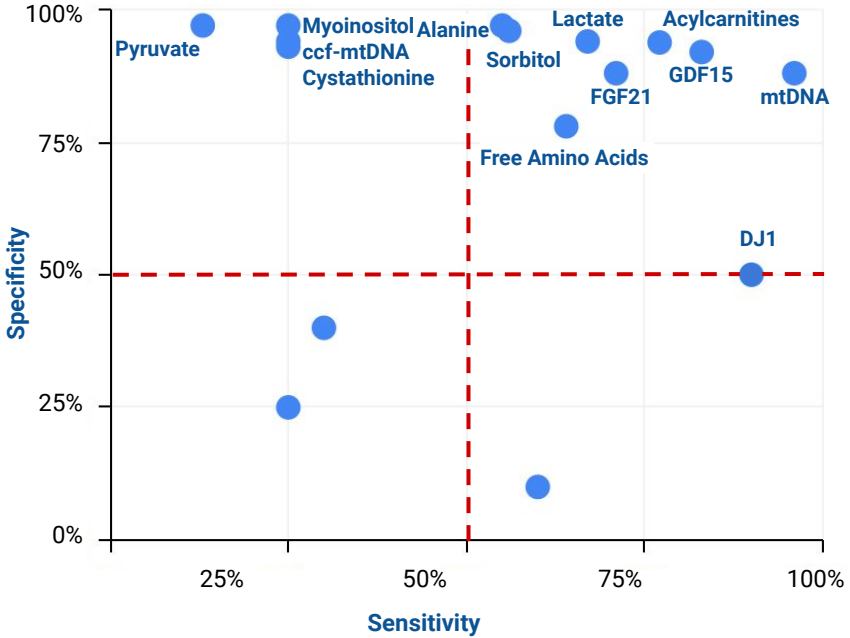


Note: Pearson correlation coefficients with P-value <0.05

Source: PubMed Database

Diagnostic Accuracy Biomarkers with Ageing in Patients

Ranking of Diagnostic Biomarkers



Acylcarnitine, GDF-15 and mitochondrial DNA copy number (mtDNA) are the best biomarkers up to date. All three measured biomarkers correlate with chronological age and can be used as Longevity biomarkers, which help in mitochondrial function evaluation.

Acylcarnitine takes part in the transport of free fatty acids into mitochondria. It comes from muscles, the brain, and less from other tissues. This molecule is a good biomarker of **earlier changes in mitochondrial function.**

mtDNA copy number reflects the number of mitochondria and their function, and it is good for **predicting both age-related and mitochondrial diseases**. It also has a strong correlation with chronological age and age-related decline.

Another biomarker, known as **Growth Differentiation Factor 15 (GDF-15),** has a positive correlation with age and negative correlation with telomere length. It is more reliable for the detection of mitochondrial disease.

Note: The sensitivity and specificity of selected biomarkers are measured for to evaluate the accuracy metrics for the detection of specific conditions. These parameters were assessed for the detection of mitochondria or age-related diseases.

Mitochondrial Function During Space Flights

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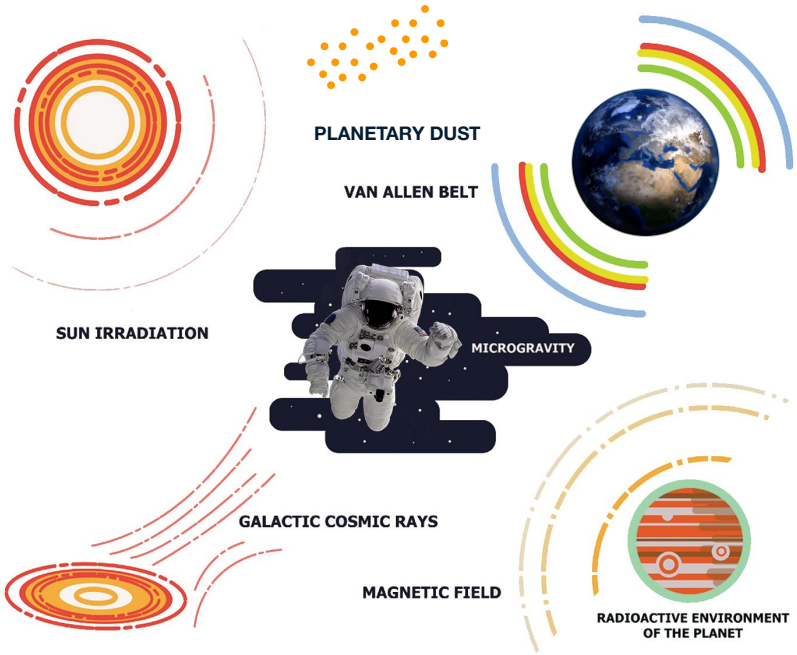
The Issue of Ageing in Space



Spaceflight presents immensely difficult challenges. **Microgravity**, **planetary dust** and **space radiation** pose a significant threat to manned space flights and planetary habitats, resulting in the development of life-threatening diseases in astronauts. In addition to this, the closed environment astronauts live creates additional pressure on crew work performance and mental health.

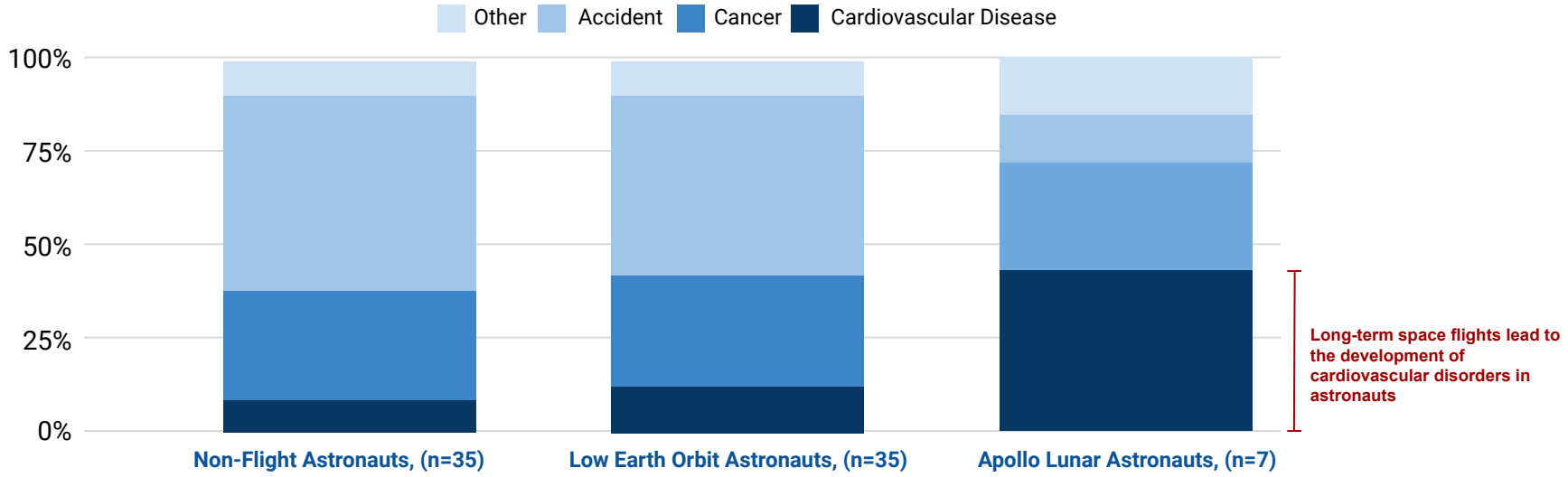
Advances in Longevity are crucial for the future of space exploration. As more private companies enter into the expanding space economy, the viability of space Longevity research substantially increases. Space tourism is gaining popularity, and new powerful heavy-lift launch vehicles are being developed with an with unprecedented speed. However, humanity needs to develop new personalised medicine approaches that can be applied in space in order to protect astronauts' health and become a multi-planetary civilization.

Fresh studies indicate that **breakdowns in mitochondrial activity** might play a crucial role in the health and performance challenges faced by humans in space. A detailed description of mitochondrial dysfunction and the affected organs will be given in the following chapter. There will also be an analysis of key companies and the private research that is carried out on the International Space Station to mitigate these problems.

Sources: SpaceTech Analytics; da Silveira et al., 2020. Cell.

Health Risks for Astronauts

Proportional Mortality Rates (%) Among Astronauts

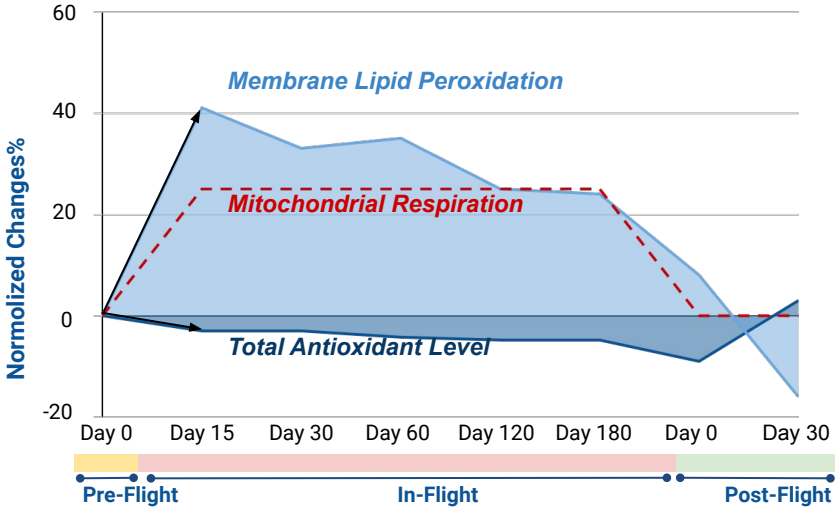


As multiple spacefaring nations contemplate extended manned missions to Mars and the Moon, health risks could be elevated as travel goes beyond the Earth's protective magnetosphere into the more intense deep space radiation environment. There are no differences in CVD mortality rate between non-flight (9%) and LEO (11%) astronauts. However, the CVD mortality rate among Apollo lunar astronauts (43%) was 4–5 times higher than in non-flight and LEO astronauts.

Source: M. Delp at al. (2016) Scientific Reports, 6, Article number: 29901

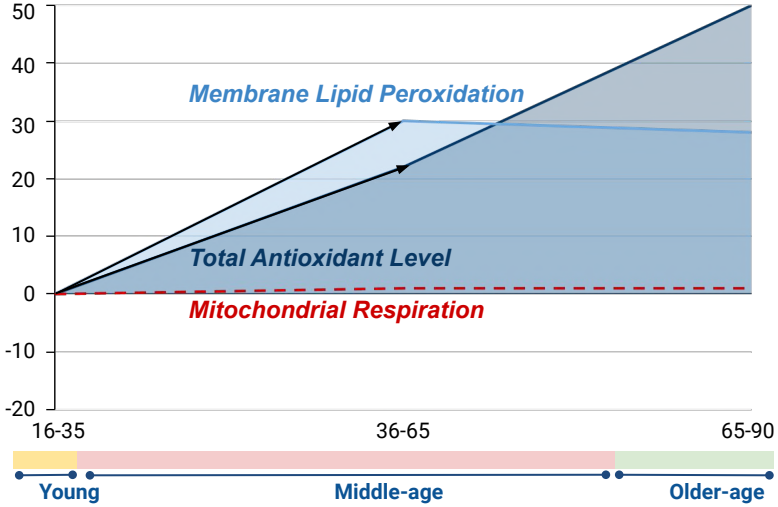
Mitochondrial Respiration and Redox Status in Astronauts vs. Ageing

Astronauts: Alterations of Antioxidant Status



Source: da Silveira et al., 2020, Cell 183, 1185–1201

Healthy ageing: Alterations of Antioxidant Status

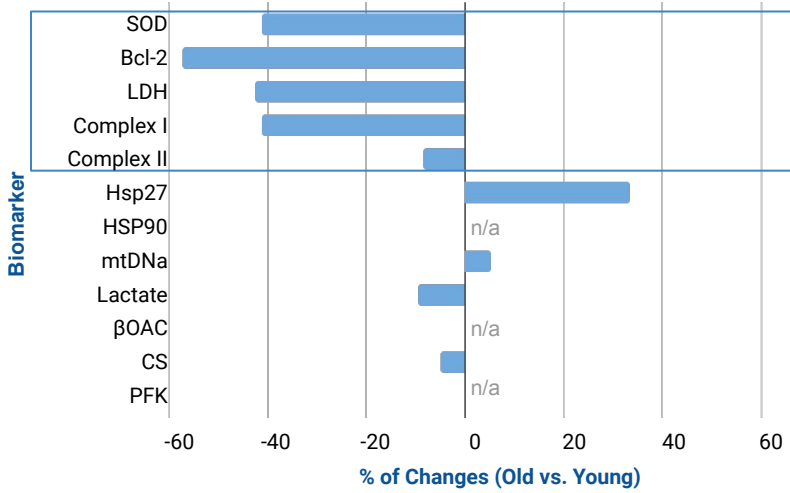


Source: M. Kasapoglu, T. Ozben, 2001, Experimental Gerontology 36, 209-220
E. Limberaki et al., 2012, Hippokratia, 16(2), 118-123
O. Miro et. al, 2000, Cardiovasc Res.. 18;47(3):624-31

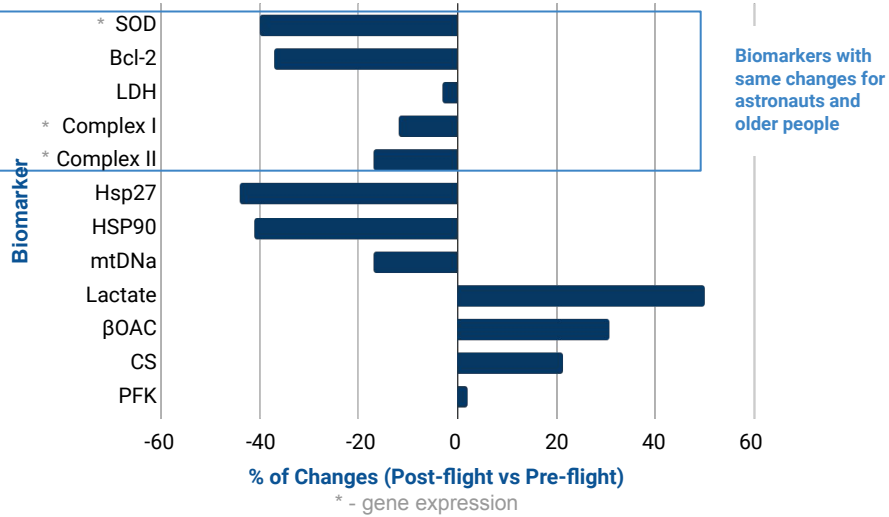
Long space flights lead to **~25% activation of mitochondrial respiration** and **~30% growth of membrane lipid peroxidation** compared to pre-flight levels. In addition, **antioxidant levels in astronauts is 4-10% lower** in space flight compared to pre-flight levels. Oxidative membrane damage was evaluated through the assessment of lipid peroxidation. This damage is also observed in elderly people, but they have increased level of antioxidants and, for that reason, there are no any changes in mitochondrial respiration.

Mitochondrial Biomarkers Changes: Space Flights vs. Ageing

Ageing: Biomarker Level Changes in Older vs. Young People, %



Astronauts: Biomarker Level Changes in Post-flight vs. Pre-flight, %

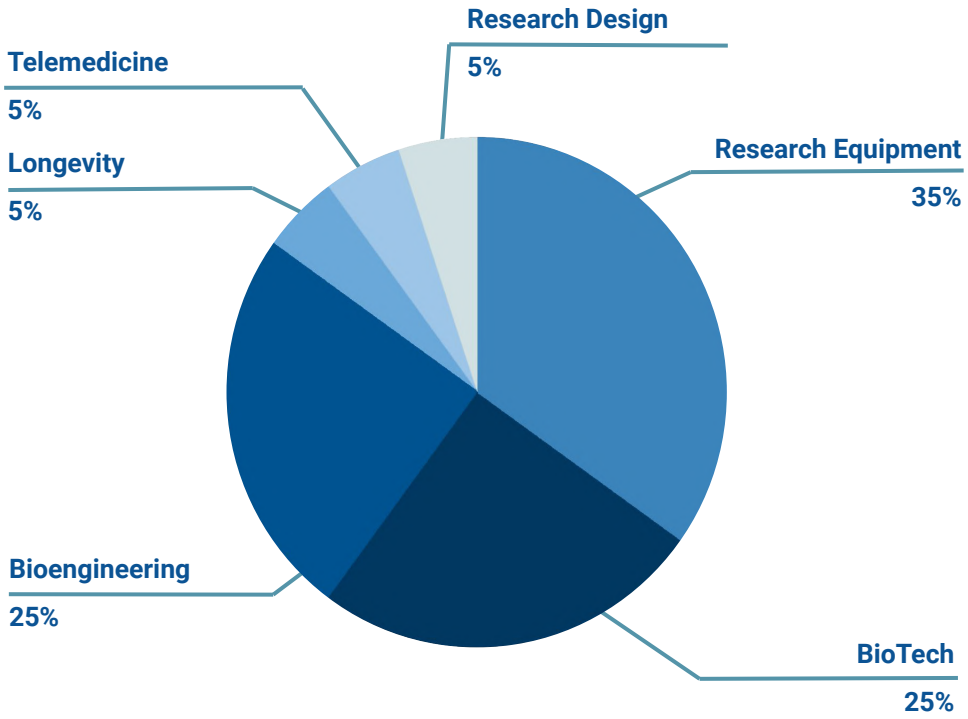


The NASA Twin Study provided useful results, looking at the same variables in an astronaut on a year-long mission. A number of mitochondria-related changes at the genomic and functional levels related to the one-year mission have been identified.

Unfortunately, studies of space-related stress in whole organism of astronauts are different compared to isolated cells. **Only five mitochondrial biomarkers, as SOD, Bcl-2, LDH, Complex I and Complex II have same changes** in astronauts after space flights (>6 months) and ageing.

Services to Enhance the Space Medicine Industry

Number of Companies in Each Sector



25% of the Space Medicine Industry is dedicated to **bioengineering** solutions to adverse age-related degenerative conditions in astronauts. These solutions include eye and bone implants and medical hardware to analyse and support astronauts health. An additional **25%** of the industry is focused on **biotechnology** dealing with space related disorders and *in situ* amino acid production.

More than **35%** of space related companies **provide research equipment for the ISS**.

Five percent is dedicated directly to Human Longevity in space. In particular, a new venture capital fund called **SP8CEVC** is placing a laser-tight focus on the intersection between SpaceTech and Human Longevity.

Sources: SpaceTech Analytics

Timeline of Private Biological Research at the International Space Station

The International Space Station (ISS) became available for private research from the beginning of 2016.

Most investigations were carried out by pharmacological companies and studies were related to pharmacokinetics and drug delivery systems.

Due to the COVID-19 pandemic, no private research was carried out in 2020.

Source: The Scientist.com

Private Age-Related Research In Space

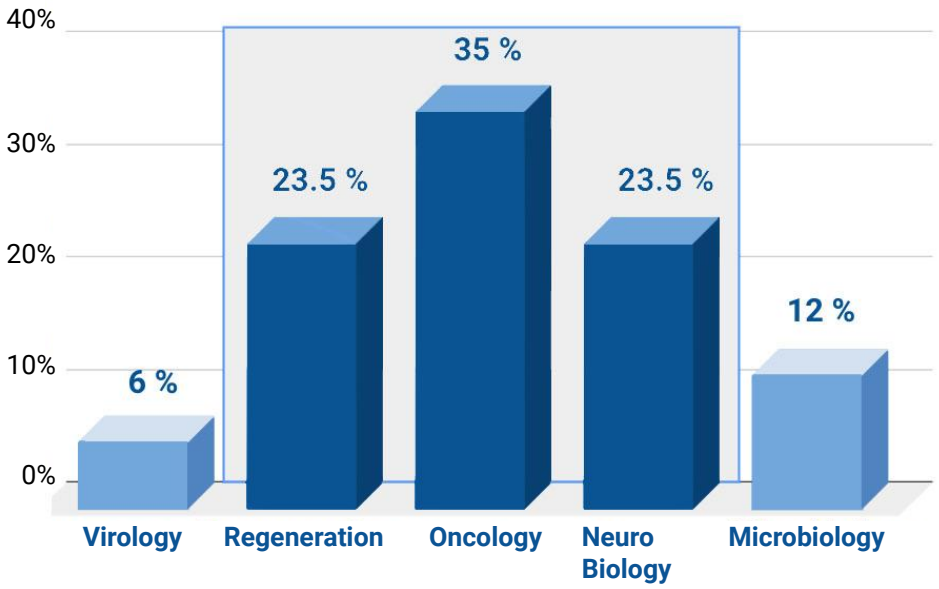
Low Earth orbit is a unique environment for the investigation of novel approaches for mitigating age-related disorders.

Thirty-five percent of all private research on the ISS is dedicated to drug delivery systems to overcome **cancer**.

A combined **47%** of applied sciences are focused on **neurodegenerative disorders therapy,** mainly for Alzheimer's disease, and **regenerative medicine**: muscle and bone restoration using human cell cultures. The gray background in the graph opposite highlights the age-related fields.

As microbes in space change their metabolism and cause serious harm to astronauts, almost 12% of private research is dedicated to microbiology and 6% to the study of viral replication and production study, including vaccine development for space.

Main Research Fields



Top Companies Advancing in Space Medicine

United States

Biogen Inc
Cambridge, Massachusetts, United States

Amgen
Thousand Oaks, California, United States

RevBio
Lowell, Massachusetts, United States

Angiex
Cambridge, Massachusetts, United States

Kernal Biologics
Cambridge, Massachusetts, United States

Merck
Kenilworth, New Jersey, United States

MicroQuin
Cambridge, Massachusetts, United States

490 BioTech
Knoxville, Tennessee, United States

Tympanogen, Inc.
Richmond, Virginia, United States

Eli Lilly
Indianapolis, Indiana, United States

SP8CEVC, Venture Capital
New York, New York, United States

Israel

SpacePharma
Herzliya Israel, Courgenay Switzerland

Pluristem Therapeutics Inc.
Haifa, Israel

France

Sanofi
Paris, Ile-de-France, France

Medes
Toulouse, Midi-Pyrenees, France

United Kingdom

AstraZeneca
Cambridge, Cambridgeshire, United Kingdom

Netherlands

OrgaNext Research
Arnhem, Gelderland, The Netherlands

Italy

Kayser Italia
Livorno, Toscana, Italy

Switzerland

Nova Space Biotechnology
Zürich, Zurich, Switzerland

Novartis
Basel, Basel-Stadt, Switzerland

Sixty percent of all private companies with space medical research presented here have their headquarters in the **US**. An additional **30%** are located in **Israel, France or Switzerland**. Other companies are distributed equally between **UK, Netherlands** and **Italy**.

To find more about leading SpaceTech companies, visit the SpaceTech Industry 2021 / Q2 Landscape Overview.

AI for Mitochondria and Ageing

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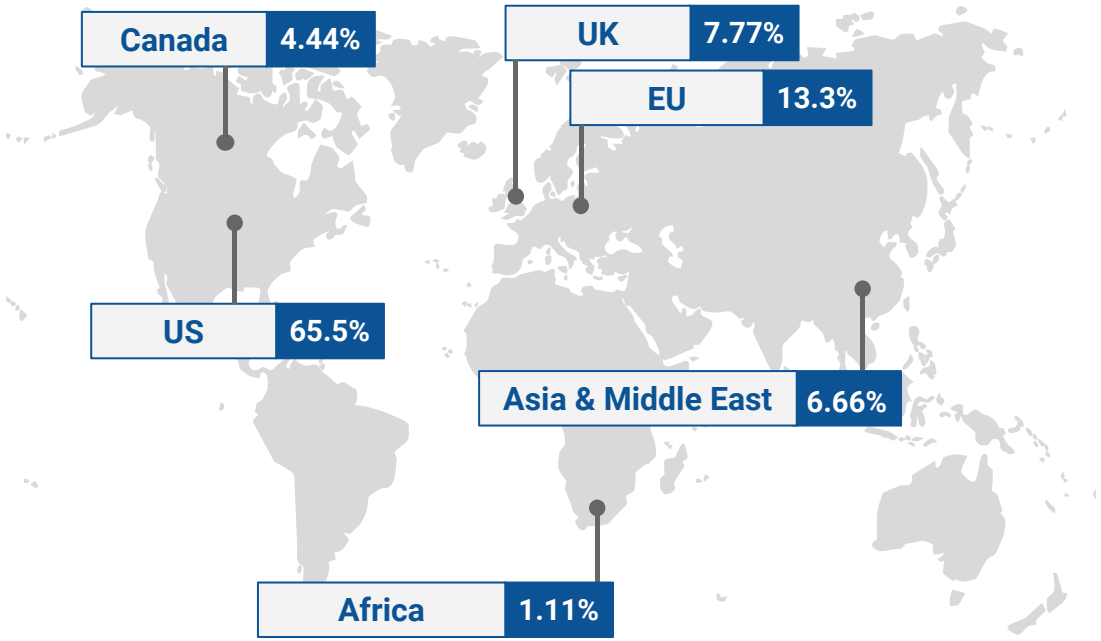
PHARMA
INTELLIGENCE

90 AI Companies: Regional Proportions

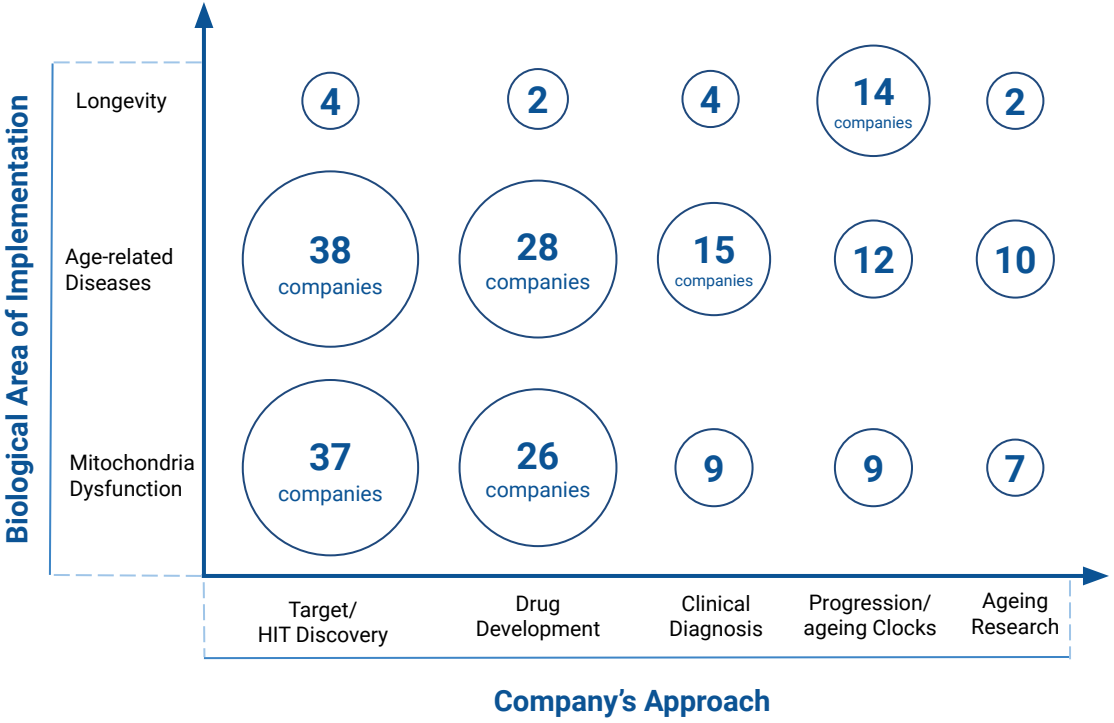


Analysis of **90 companies** by the location of their headquarters showed that the **US** is a leader (**65.5%**) in the number of companies that implement AI for the treatment, diagnosis and research of age-related and mitochondrial dysfunction-related diseases and Longevity in general. The leading state is California – 25 of 59 US companies are located there. The second most prominent region is the **European Union** (**13.3%**) – the leaders in the EU are France, Denmark and Switzerland. The **UK** takes third place worldwide (**7.77%**).

To find out more about AI in drug development, see the DPI report "AI for drug discovery, biomarker development and advanced R&D landscape overview Q2 2021"

Implementation of Artificial Intelligence

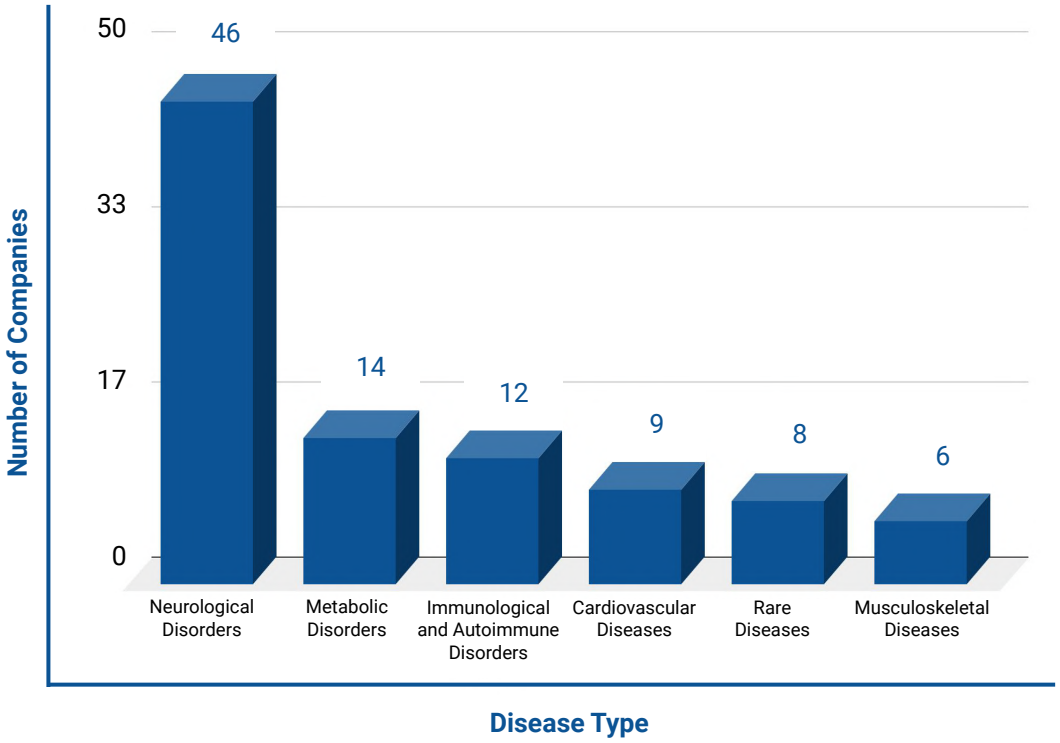
The **90 companies that use AI** were selected, analysed and distributed to certain categories by their **approach** (drug development [early and clinical], diagnosis, risk predictions, research) and **biological focus** (age-related diseases, mitochondria dysfunction-related diseases and longevity in general). The leading area is **drug development.** AI can be used at every step of this process: **target identification, drug design and lead optimization, preclinical and clinical development.** The important future direction of AI implementation is in **clinical diagnosis**. Companies apply AI to **search for disease biomarkers**. Mainly, they operate with machine learning methods for "omics" data processing. Additionally, some companies search for markers for **ageing prognosis prediction, ageing clocks creation, disease progression risk assessment**, etc. For this research, AI is used for **intelligent image processing** (clinical images such as MRI and research images such as mitochondria morphology studying), **clinical data organization**, etc.



To find out more about AI in drug development, see the DPI report "AI for drug discovery, biomarker development and advanced R&D landscape overview Q2 2021"

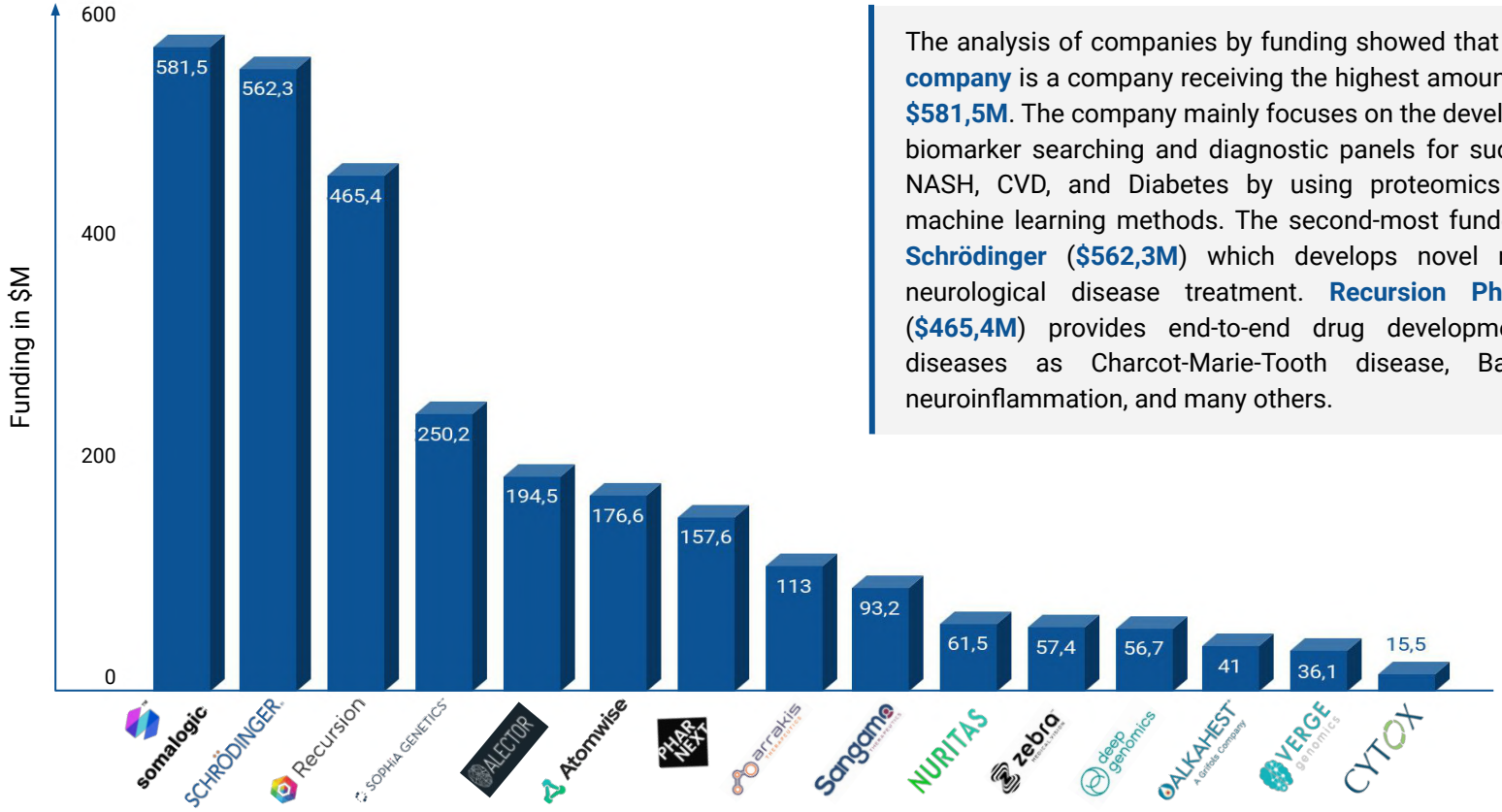
Biological Focus of AI for Drug Discovery in Age-Related Diseases

Drug discovery is the most significant area of AI implementation for ageing mitochondrial dysfunction-related diseases. **Neurological disorders** are the leading area. The brain is highly dependent on mitochondrial energy metabolism, and mitochondrial dysfunction is the main reason for many adult-onset neurological diseases, including **Alzheimer's, Parkinson's, amyotrophic lateral sclerosis, frontotemporal dementia**, etc. The basis of such focus on neurological disorders is that, according to the WHO, 50 million people have dementia worldwide, and most of them are over 65 years old. And this trend is increasing – nearly 10 million new cases of dementia appear every year, and the World Health Organisation has projected that the number of people with dementia will reach 150 million by 2050. An additional factor is that such disorders affect not only patients but also their families, which have to provide them with proper care, often to the detriment of their interests.



Sources: WHO, Neuroepidemiology

20 Companies that Use AI Treat/Diagnose Mitochondrial Dysfunction-related Diseases by Funding Amounts



The analysis of companies by funding showed that the **Somalogic company** is a company receiving the highest amount of funding, at **$581,5M**. The company mainly focuses on the development of new biomarker searching and diagnostic panels for such diseases as NASH, CVD, and Diabetes by using proteomics coupled with machine learning methods. The second-most funded company is **Schrödinger** (**$562,3M**) which develops novel molecules for neurological disease treatment. **Recursion Pharmaceuticals** (**$465,4M**) provides end-to-end drug development for such diseases as Charcot-Marie-Tooth disease, Batten disease, neuroinflammation, and many others.

Overview of Five Companies that Implement AI in their Work

Company	Insilico Medicine	DEEP LONGEVITY	deep genomics	NANNA THERAPEUTICS	BIOAGE
Approach	Biological age calculator	Biological age calculator	Identifying novel targets and searching for the best Steric Blocking Oligonucleotide (SBO) for their treatment	Early drug development for mitochondrial dysfunction-related diseases	Identification of key drug targets that impact ageing
Input Data	Blood test parameter	Lifestyle data, photo, blood test, epigenomics and transcriptomics data, microbiome data, HRV, psychological test	Whole-genome sequence	Chemical design of compound	Blood test parameters, omic data, and medical records
Output Data	Biological age and lifestyle recommendations	Ageing clocks, biological age and personalized longevity plan	Mutations that might be targets and SBOs for them	Drug efficacy, Structure Activity Relationships (SAR), selectivity, toxicity, other drug properties	Novel ageing targets

Market and Tech Trends

Q3 2021

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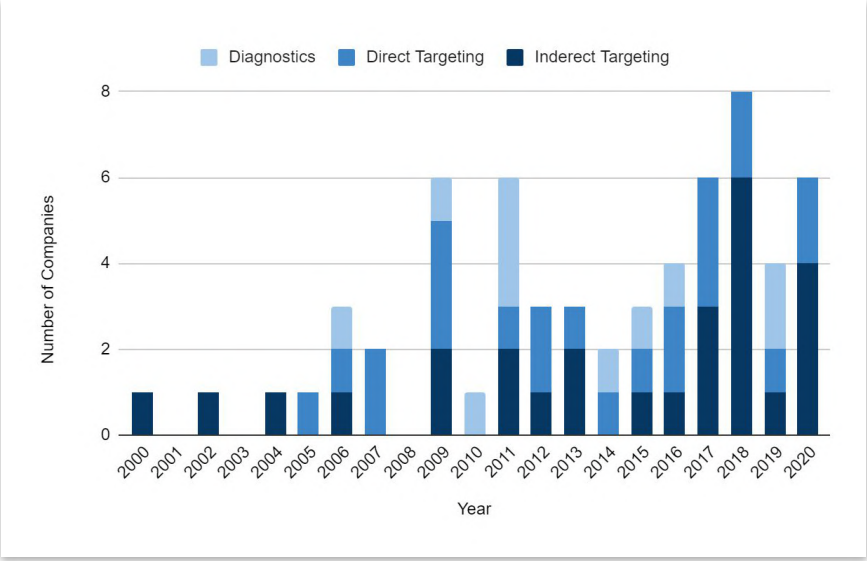
Market Trends

The graph opposite illustrates the growth in the number of companies on the market since 2000. Recently, the increase in the number of projects working on mitochondria for longevity has been **caused by the synergy of four key factors**:

Key Market Trends	Determinant
Focus on precision drug delivery	Therapy
Mitochondria transfusion research	
Mitochondrial metabolism	Diagnostic
New Applications of AI	Digitalization

New Companies: Mitochondria Targeting for ageing Treatment

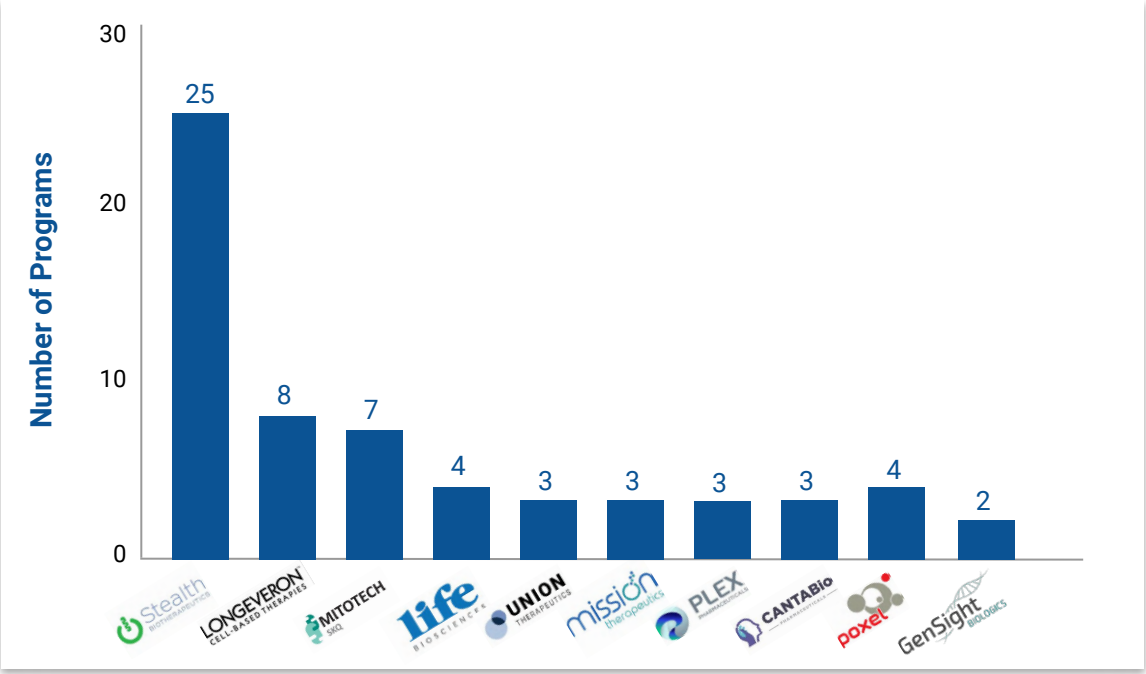


Note: Perhaps ~100 BioTech companies and startups are carrying out work that may lead to a form of rejuvenation or are focused on interventions that target the mechanisms of ageing. Nearly all of these companies are at most a few years old, in preclinical development or in early trials, and Big Pharma has yet to become earnestly involved in the Longevity Industry.

Source: ClinicalTrials.gov

Top 10 BioTech Companies in Mitochondria Treatment and Diagnostics

Ranking of Companies by Number of Programmes



Brief review of leader BioTech companies. These companies are all quite young and focused on various means of the selective targeting of mitochondria in ageing and Age-related diseases.

Stealth is way ahead of the pack: no other company has more than 10 programs. This company proposes a unique approach of **precise drug delivery to mitochondria**.

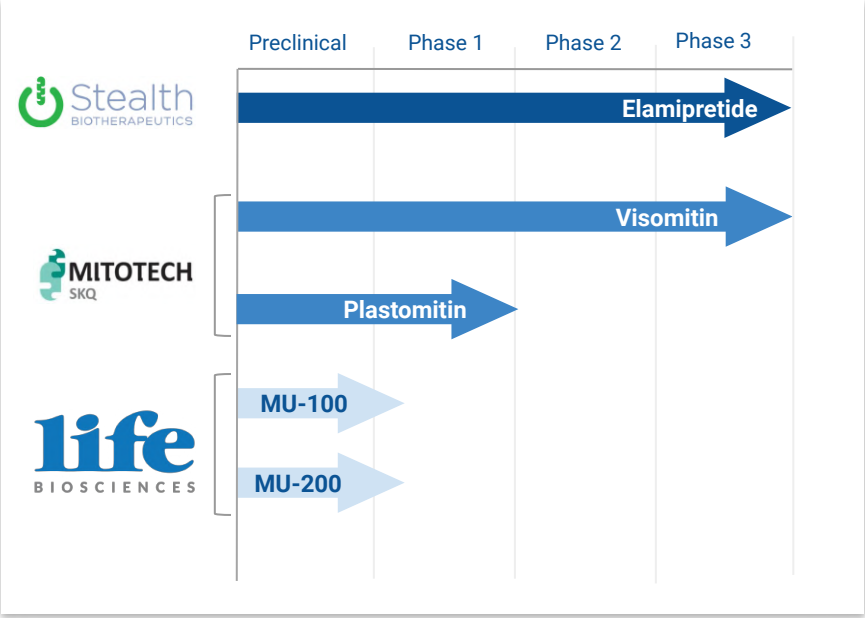
Longevron is a company with a cell-based approach that embarks on its mission to develop a "whole-body mitochondrial transfusion" technology.

The majority of other BioTech companies are focusing on reparation Oxidative Phosphorylation and Energetic Processes in mitochondria.

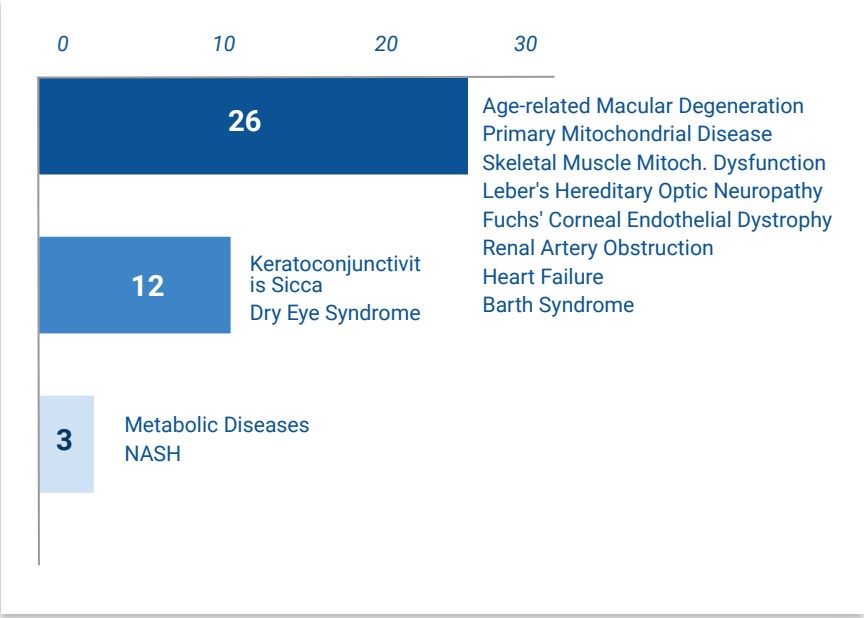
Note: Antioxidative therapies and reactive oxygen species stress management were not covered in the analysis: ROS scavengers (30 programmes), SOD modulators / mimetics (30 programmes) / antioxidants (>300 programmes).

Most Promising Mitochondria Technology

Technology Clinical Trial Phase



Number of Clinical Trials



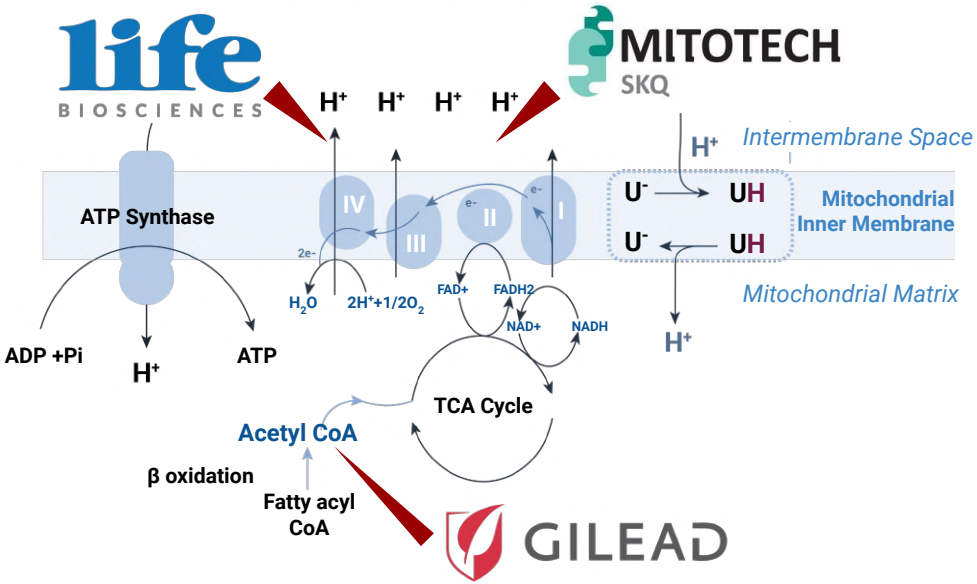
Out of the several dozen companies focused on mitochondrial Longevity, three companies stand out in their innovative approach and efficacy. These are **Stealth BioTherapeutics, Life Blosciences, and Mitotech.** These companies have carried out 26, 12 and three trials, respectively.

Approach Review: Mitochondrial Uncoupling

Mitochondrial uncoupling is a process that decouples mitochondrial oxidation from ATP synthesis. It is mediated by proton influx across the mitochondrial inner membrane without passing through ATP synthase. Mitochondrial uncoupling occurs naturally in mammals, induced by mitochondrial uncoupler proteins, or UCPs. While the first uncoupling proteins were discovered more than 15 years ago, utilizing the process in mitochondria for commercial use.

While there are only a couple of companies working on this research avenue, the need for novel therapeutic solutions for such age-related diseases as Type 2 diabetes, cancer, and NASH, is **expected to attract more interest in the near future.** Since the BioTech Industry is one of the industries least disrupted by the COVID-19 pandemic, investors' attention will be drawn to Mito BioPharma, Life Bioscience, and other companies following their footsteps in mitochondrial uncoupling programs.

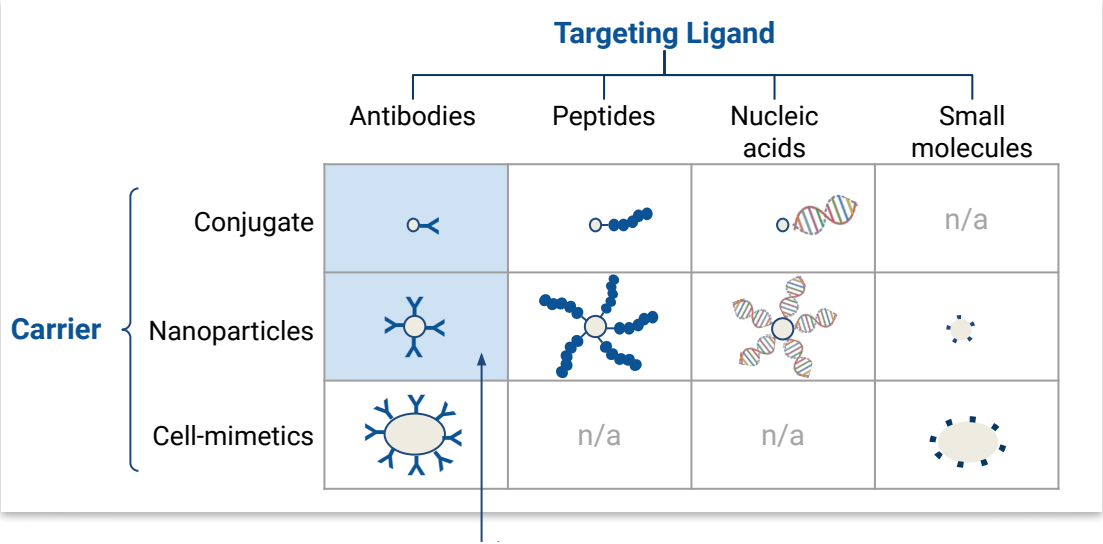
Processes of Oxidative Phosphorylation and Mitochondrial Uncoupling Induced by Mitochondrial Uncouplers



Sources: Mito BioPharma LLC,

Approach Review: Mitochondrial Drug Delivery

The Mitochondrial Targeted Drug Delivery System



Note: The Guilarte laboratory has pioneered the validation and application of Translocator Protein 18 kDa (TSPO) as an early, sensitive and predictive biomarker of brain disorders and has been a leader in determining the function of TSPO in glial cells. NASA seeks *"[a]n approach… to extrapolate existing observations to possible cognitive changes, performance degradation, or late CNS effects in astronauts. We believe non-invasive TSPO imaging may help provide a method and approach that could be utilized today, in pre-flight and post-flight testing of astronauts…"*.

Precise targeting of mitochondria and **direct drug delivery** to this organelle is the most promising widely-used approach for the treatment and diagnosis of various diseases. There are several variations for the ideal design and development for mitochondrial-targeted drugs, such as the selection of **suitable ligand and linker targets** or **delivery in nanocarriers**. In an ideal world, nanoparticles with targeting ligands can solve some challenges related to drug solubility and the selectivity of therapeutic drugs, and they offer elegant platforms for mitochondria-specific drug delivery. Unfortunately, the direct delivery of therapeutic molecules is **not sufficiently reflected in the treatment and diagnosis of ageing**. Only a few R&D Centres are trying to develop this approach.

Sources: 23rd Annual NASA Space Radiation Investigators' Workshop (2012)

Approach Review: Mitochondria Transfusion Research

Transplantation of functional mitochondria directly into defective cells is a novel approach that has recently caught the attention of scientists and the general public alike. The company **Mitrix** is actively developing **a whole-body mitochondria transfusion** to cure a variety of mitochondrial dysfunction that are generally correlated with ageing.

Mitrix is still a company in its earliest stages, and what it is proposing is the only theory at this point, but the progress made in the understanding of mitochondria over the past 10 years makes it a theory worth pursuing.

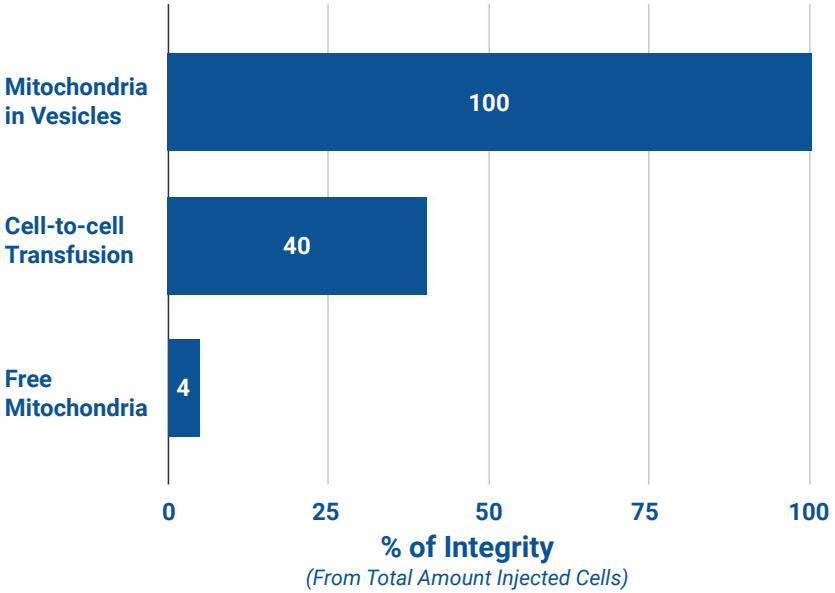
Mitrix

News

Mitrix wants to create biobanks of our "young mitochondria" that we can use to help our cells regenerate as we age.

Californian start-up Mitrix this week secured $250,000 in pre-seed funding to embark on its mission to develop a "whole body mitochondrial transfusion" technology. The company is the first investment of Ronjon Nag's R42 AI and Longevity Fund, which split the round 50/50 with Petr Sramek's Longevity Tech Fund.

Effectiveness of Donor Mitochondria Transfer into Host Cells
(Animal Studies)



Cell-to-cell Transfusion — mitochondria transferred from Mesenchymal Stem Cells to T cells; **Mitochondria in Vesicles** — mitochondria transferred in Asialo Orosomucoid-Polylysine with Listeriolysin O capsules into hepatocytes.

Source: Longevity Technology

Approach Review: Gene Therapy

NASA is currently pursuing a **three-year mission to Mars**, which is much further away than the ISS, which orbits at a height of about 200 miles.

NASA named **radiation as one of its top research priorities** last year, stating: "Though far off, a medication that would counteract some or all of the health effects of radiation exposure would make it much easier to plan for a safe journey to Mars and back."

Scientists in this field of study are proposing to build upon knowledge already gained in the study of human ageing. Part of the plan is to **make some human cells radio-resistant**.

Scientists want astronauts to have **personalised drugs** tailor-made for their own bodies. To do this, they will have to use AI to pinpoint which cells are more resistant than others and fortify them using gene therapy.

Search The Guardian For 200 years US edition

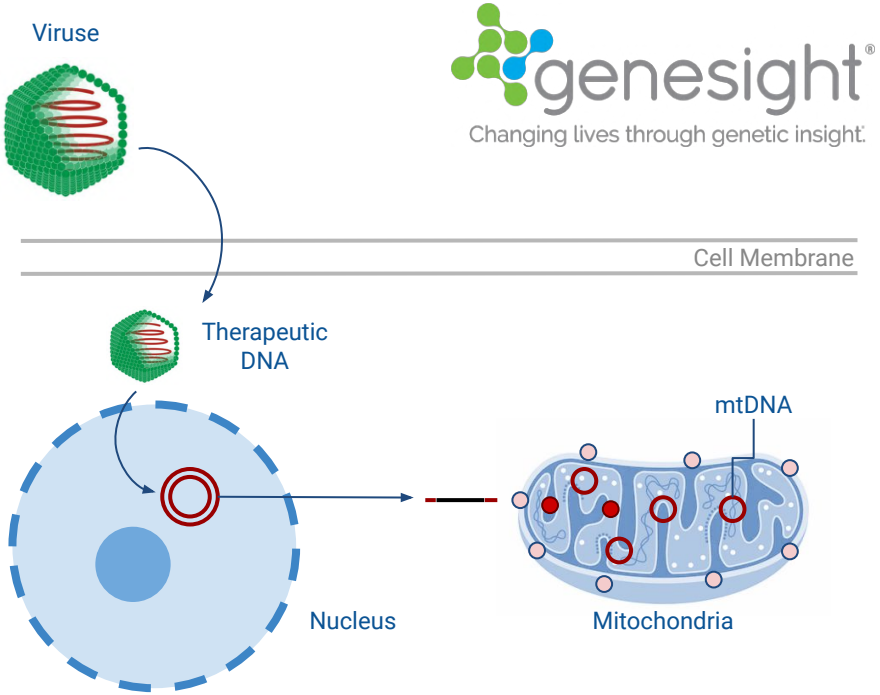
Space

This article is more than **3 years old**

Gene therapy may help astronauts going to Mars resist deadly radiation

Researchers and scientists say new discoveries and drug creation could be beneficial to future astronauts on deep space missions

How Can Gene Therapy Improve Mitochondria in Astronauts?



Note: The GS010 product candidate for ND1 gene in mtDNA (NADH dehydrogenase subunit 4 replacements) is now in late Phase III trials.

Source: The Guardian

New Technologies in Mitochondrial-based Therapeutics

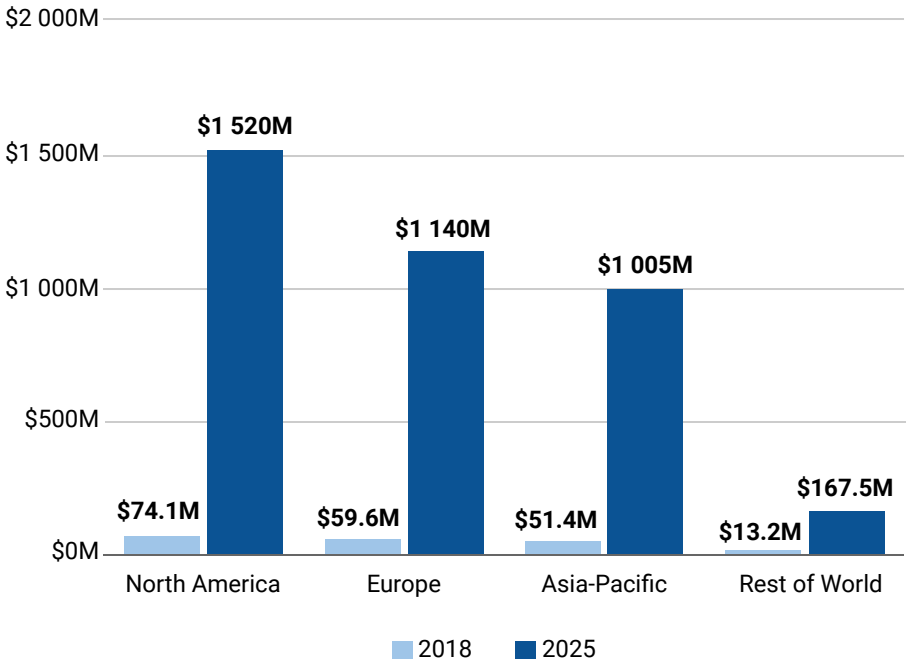
Some of the novel drugs that are currently being assessed include **mitochondrial biogenesis enhancers** (bezafibrate, epicatechin, and RTA 408), **antioxidants** (RP 103 and EPI-743), and **cardiolipin protector** (elamipretide).

At the same time, with traditional therapy, some outstanding approaches have been developed, including **mitochondria transfusion** and **mitochondria-targeting drug delivery**.

Gene therapy has shown positive results in the treatment of LHON, and the first successful gene therapy based on editing of the mtDNA in vivo has brought hope of curing mitochondrial diseases. Moreover, other potential therapeutic methods are expected to provide more treatment options for mitochondrial diseases.

One of the most-used **AI-driven software solutions** for developing mitochondrial therapeutics is machine learning. Supervised machine learning algorithms underlie novel tools that enable automated, high throughput and unbiased screening of changes in mitochondrial morphology and biochemistry.

AI Market in the Global Biopharma Industry in 2018 and a Projection for 2025, by Region



Sources: Digitalisation of clinical trials , Artificial intelligence market in the global biopharma industry, Statista

Conclusions

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Key Takeaways

Despite a relatively small number of programmes of mitochondria in ageing and mitochondria in Space Medicine, there is a noticeable overlap that is of particular importance for this analytical case study. Being at the intersection of two frontiers of the modern medicine simultaneously, these programs **hold the most promise in discovering how spaceflight conditions reveal the causes of accelerated ageing**.

Due to their presence in every cell of the body and every energy production function, **mitochondria are recognized as a key research target both in ageing and the Space Medicine Industry**. This is a relatively new field as these organelles are harder to alter in a precise manner. It is hypothesised that mitochondrial medicine will undergo a similar boom to genetic medicine in the coming years.

The most recent studies indicate that breakdowns in mitochondrial activity might play a crucial role in health and performance challenges faced by humans in space. Programs working on this opportunity are discussed in detail. The **findings are transferrable to the Earth-bound population, which undergoes similar environmental impacts** (radiation).

The recent exponential growth of the mitochondria industry is driven by the synergy of four factors — **a focus on precision drug delivery, mitochondrial transfusion, mitochondrial metabolism diagnostics, and the broad adoption of AI** in R&D. All four market trends show no sign of slowing down, with projected innovation emerging in the next few years.

Among the Top 10 BioTech companies focusing on mitochondrial health, **Stealth Biotherapeutics is leading with 25 programs** working on this organelle dysfunction. Longeveron and Genesight are closely following, with 8 programs each. It is predicted that more startups and well-established BioTech companies will join the field in the near future.

Key Takeaways

The most prominent research vectors in the field of **treating mitochondrial dysfunctions** are aimed at **restoring energetic pathway function, modifying mitochondrial dynamics, triggering apoptosis, restoring oxidative phosphorylation pathways, and decreasing the effects of reactive oxygen species on cells**. The majority of biomarker research for diagnostics concentrates on metabolic anomalies and irregularities in dynamics.

Biomarkers are robust indicators for the evaluation of mitochondrial health in Longevity and Space Medicine**. Acylcarnitine, GDF-15 and mitochondrial DNA copy number (mtDNA)** are the best up-to-date biomarkers. All three measured biomarkers correlate with chronological age and can be used as Longevity biomarkers, which help in mitochondrial function evaluation.

Five percent of the Space Medicine Industry is focusing its efforts on Longevity, compared to 25% of the BioTech Industry. This showcases an **increased interest in healthy lifespan extension in Space Medicine** compared to Earth-bound development, with a significant proportion of research dedicated to mitochondria.

Drug discovery is the largest area of AI implementation for ageing mitochondrial dysfunction-related diseases. **Neurological disorders are the leading area**, closely followed by metabolic disorders. Mitochondria plays an important role in both areas.

Mitochondria are powering the future of space biology and Longevity research, pointing the way toward discoveries that will help astronauts live safely in orbit and beyond, as well as Earth-bound people suffering from mitochondrial dysfunction.

Biomarkers of Longevity

Approved for Clinical Use — 41
Research Use Only — 45
Healthcare-Ready — 33

2nd edition.
Current Status, 2021

Approved for Clinical Use

Healthcare-Ready
(waiting for clinical approval)

Research Use Only

Biomarker Panels

- InsideTracker Inner Age
- InsideTracker Ultimate Plan
- RGCC aCGH RGCC
- RGCC Immune-Frame
- GENOVA DIAGNOSTICS Comprehensive Adrenal Stress Profile
- ARUP B-Cell Memory and Naive Panel
- ARUP Natural Killer Cell and Natural Killer T-Cell Panel
- Health + Ancestry Service
- ARUP Carnitine Panel
- ARUP Cytokine Panel, TH1
- ARUP Hepatic Function Panel
- ARUP Regulatory T-Cell Panel
- ARUP Cytokine Panel
- GENOVA DIAGNOSTICS Oxidative Stress Analysis 2.0
- FLUIDS iQ Adrenal Check
- Adrenal Stress Profile
- Advanced MethylDetox Profile
- Advanced MethylDetox Profile + Thelomere Length
- Diagnoptics AGE-Reader mu Test
- Cytokine Panel
- biobank Biomarker Panel
- WellnessFX Premium
- Aging Theranostic 1.0
- Labrix 10 Hormone Saliva Test Kit
- Wellness Lab Anti-Aging #4 Comprehensive Blood and Urine Test Panel
- Female/Male Saliva Profile II - Test Kit for 6 Hormone Level Imbalances
- LifeExtension Healthy Aging Panel (Comprehensive)
- GENOVA DIAGNOSTICS CardioGenomic Plus Profile
- GENOVA DIAGNOSTICS ImmunoGenomic Profile
- NeuroGenomic™ Profile
- GENOVA DIAGNOSTICS Metabolic Analysis Profile (Organic Acids)
- PhysioAge Biomarkers of Aging Test
- smartDNA smartGUT™ Microbiome Test
- cerascreen Genetic Age Test
- VIOME Viome Gut Intelligence™ Test
- MICROBA Microba Insight™
- GLYCANAGE GlycanAge Test
- TFTAK Gut Microbiota Biohacker
- TAmiRNA toxomiRTM biomarkers of toxicity
- TAmiRNA osteomiRTM validated bone biomarkers
- TAmiRNA thrombomiRTM biomarkers of platelet function
- Glick Proteomics Metabolism Panel
- Glick Proteomics Immune Response Panel
- Glick Proteomics Inflammation Panel
- Glick Proteomics Organ Damage Panel
- Glick Proteomics Cardiovascular II Panel
- Glick Proteomics Cardiometabolic Panel
- Glick Proteomics Oncology III Panel
- Glick Proteomics Oncology II Panel
- Glick Proteomics Neurology Panel
- Glick Proteomics Neuro Exploratory Panel
- Glick Proteomics Cell Regulation Panel
- Glick Proteomics Cardiovascular III Panel
- myriad HumanMAP v.2.0
- myriad MetabolicMAP v.1.0
- myriad CardiovascularMAP v.3.0
- myriad DiscoveryMAP v.3.3 Panel
- myriad AngiogenesisMAP v.1.0
- myriad NeuroMAP v.1.0
- myriad ImmunoMAP v.1.0
- myriad Explorer MAP v.1.0
- myriad InflammationMAP v.1.0
- myriad CytokineMAP B
- myriad CytokineMAP A
- BioLegend LEGENDplex Human CD8/NK Panel
- BioLegend LEGENDplex Human B Cell Panel
- MIRXES MIRXES ID3EAL miRNA Assay
- cisbio Phospho-H2AX (Ser139) Cellular Kit
- Senescence Detection Kit
- SPIDER-βGal
- Cytometry OMIP-004
- Cytometry OMIP-018
- Cytometry OMIP-039
- Salivary Cytokine Panel
- BioLegend LEGENDScreen Human PE Kit
- BioLegend LEGENDplex Human Th Cytokine Panel
- Cytometry OMIP-027
- Cytometry OMIP-007
- Cytometry OMIP-029
- Human v3 miRNA Assay

Digital Panel Platforms

- babylon Babylon Health Platform
- ada Ada Symptom Checker app
- CarePredict CarePredict Platform
- Health Reviser Platform
- Google DeepMind Google's DeepMind Health AI Platform
- Centers for Age Control AgeMeter
- nourish balance thrive Blood Chemistry Calculator
- zebra AI-Powered Radiology Assistant
- MEDIAGE MEDIAGE™ Biological Age Measurement System
- KenSci KenSci Platform
- enlitic Enlitic Platform
- Aging.AI
- YOUNG.AI
- PathAI PathAI Platform
- buoy Buoy Health Platform
- Haut.AI PhotoAgeClock
- Haut.AI Haut.AI Skin Health
- zipongo Digital Nutrition Platform
- PROSCIA Proscia Platform
- freenome Freenome Platform
- BenevolentAI Platform
- Better Better Therapeutics Platform
- Tempus Platform
- CarbonX ICabonX Platform

Single Biomarkers

- ARUP LABORATORIES CD4+ T-Cell Recent Thymic Emigrants
- ARUP LABORATORIES CD21 (Dendritic Cell) by Immunohistochemistry
- TruDiagnostic TruAge™ Epigenetic Test Kit
- CHRONOMICS EpiHealth
- TELOYEARS TeloYears + Advanced Ancestry Tests
- HCPI Targeted Seq. for DNA Methylation Analysis

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Sources: Biomarkers 2021

Longevity Investment: Big Data Analytics Dashboard

Sources: Longevity Investment Big Data Analytics Dashboard

About Aging Analytics Agency

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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.

About Deep Pharma Intelligence

Deep Pharma Intelligence produces regular analytical reports on areas of high potential in the pharmaceutical and healthcare industries. It maintains ratings of companies and governments based on their innovation potential and business activity in the BioTech space, and it provides strategic consulting and investment intelligence services to top-tier clients. Our clients include major investment funds and banks, family offices, insurance companies, government organizations, and Big Pharma companies, among others. The company is a joint venture between the two highly specialized UK-based market intelligence hubs in the Pharma / BioTech space:

Pharma Division of Deep Knowledge Analytics (PD-DKA), a specialised subsidiary of Deep Knowledge Analytics (DKA), the leading analytical entity focused on deep intelligence regarding the high-potential areas in the pharma industry, including artificial intelligence (AI) for the drug discovery sector.

Deep Knowledge Analytics' Pharma Division serves as the main source of investment intelligence and analytics for AI-Pharma, a specialised index hedge fund for AI in the drug discovery sector. PD-DKA's insights are frequently covered by top media outlets such as Forbes and the Financial Times and acknowledged by top pharma executives.

Recently, MIT named this division a top technology think tank, acknowledging the AI ranking framework it has developed.

BPT Analytics (BiopharmaTrend) is a rapidly growing analytical portal and media resource dedicated to tracking emerging companies (startups/scaleups), innovations, investments, and trends in the pharma and BioTech space.

BiopharmaTrend's reports and articles have been referenced by Deloitte, Forbes, and other high-profile media and consulting companies.

BiopharmaTrend is a media partner to several top-tier conferences and symposia in preclinical, clinical, and healthcare research.

About SpaceTech Analytics

SpaceTech Analytics

SpaceTech Analytics is a strategic analytics agency focused on markets in the Space Exploration, Spaceflight, Space Medicine, and Satellite Tech industries.

Its range of activities includes conducting research and analysis on major areas of high potential in the SpaceTech industry; maintaining profiling of companies and government agencies based on their innovation potential and business activity; and providing consulting and analytical services to advance the SpaceTech sector.

Our IT-Platform is designed to make key strategic recommendations and guidance regarding space-related technologies and techniques within reach of companies, other entities, and nations to assist them in optimising their action plans and strategies, providing specialized guidelines for business, and making core investment decisions.

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