

The Future Of Aging? The Startups And Innovations Working To Help Us Live Longer And Better

Senolytics. Blood transfusions. Placenta stem cells. These are just some of the innovative ways that startups are tackling mortality and increasing the human lifespan. In this brief, we dive into each one and track what progress has been made in the quest to find the elusive fountain of youth.

How can we live longer? How do we become healthy enough so that we can extend our lifespans by 5, 10, or even 50 extra years?

And it's not just about living longer, but also feeling younger. For example, what if you could feel 25 at the age of 75?

These are the big questions that scientists have been trying to answer for decades, with few answers.

Understanding how we age on a physiological level is an incredibly complex topic. It shares many of the cellular and molecular processes that underlie age-related diseases like cancer or Alzheimer's, which continue to elude us in their pathology.

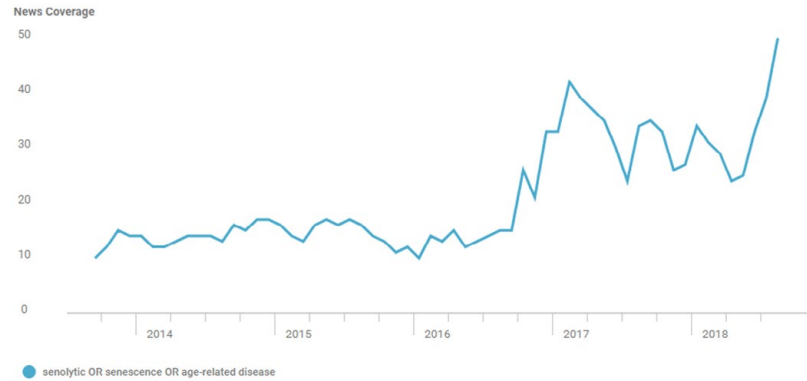
While aging itself isn't a treatable disorder or condition, companies and researchers focused on longevity are looking at bodily processes at the cellular level to see how aging progresses and trying to find the right drugs, treatments, and vitamins that might slow these processes down.

And as a result, we may discover the key to longevity, or living a longer life.

For instance, a new class of drugs known as "senolytics" are now being touted as the next big thing in anti-aging research for getting rid of decrepit (but harmful) cells that stop dividing as we age, known as senescent cells.

Interest in longevity research continue to climb

News mentions of "senolytic," "senescence," or "age-related disease" from Sept 2013 – Aug 2018



Source: cbinsights.com

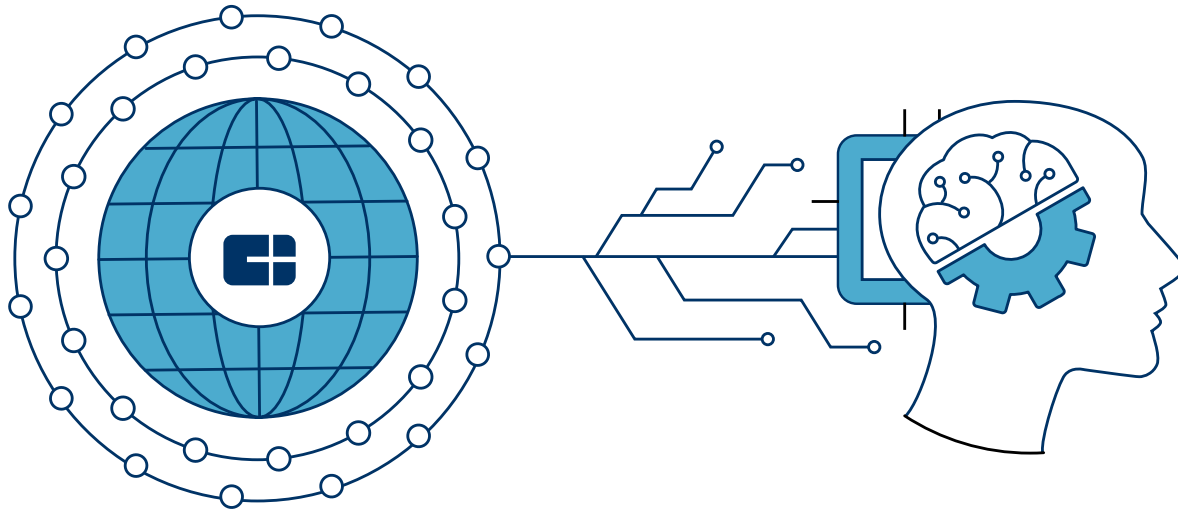
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And it's not just the biotech or pharma companies looking to combat mortality with novel drug therapies. Wellness companies are developing daily supplements that claim to prolong your lifespan. And some startups are even offering blood transfusions from younger individuals for a "rejuvenating" effect.

Below, we explore the current landscape of initiatives that aim to slow down the aging process, and in turn, reduce the likelihood of several diseases. We look at how these initiatives could promote longevity and what this market looks like for both investors and consumers.

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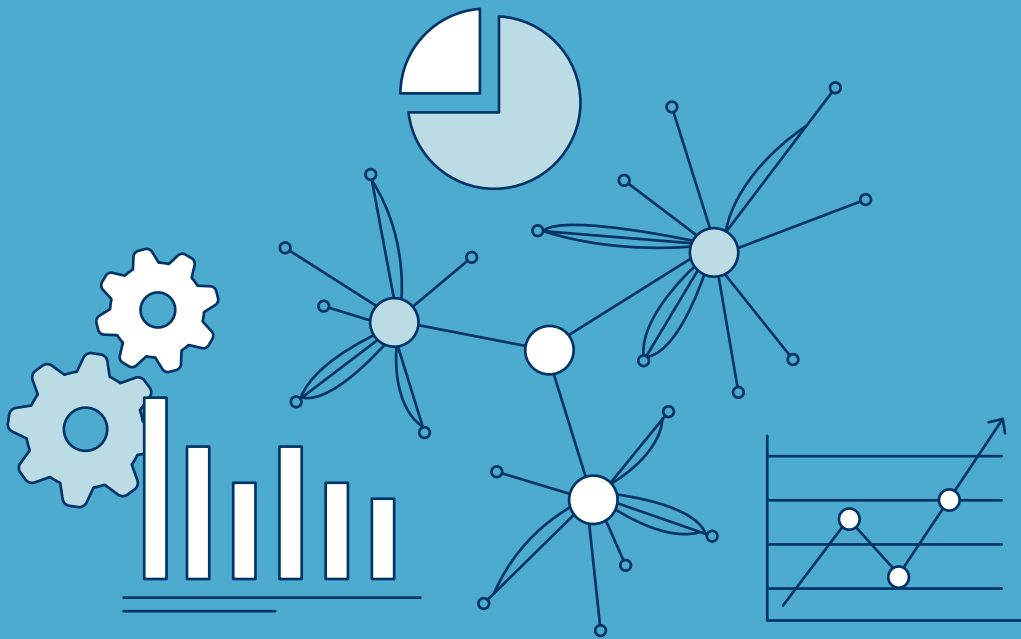
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Beti Cung,
CORPORATE STRATEGY, MICROSOFT



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1

Understanding how we age

Since the 1980s, when the first “longevity” gene was mapped by scientist Tom Johnson, there’s been more progress made in understanding how we age and how we can slow it down.

Moreover, the similarity between aging and age-related diseases is increasingly becoming the focus for many of these longevity research initiatives – many researchers studying age-related diseases like Alzheimer’s are now collaborating with researchers looking at aging more broadly.

THE BIOLOGY OF AGING

Biogerontology is the scientific discipline dedicated to the biology of aging.

Recent studies have identified key traits – referred to as hallmarks of aging – that attempt to define what aging is.

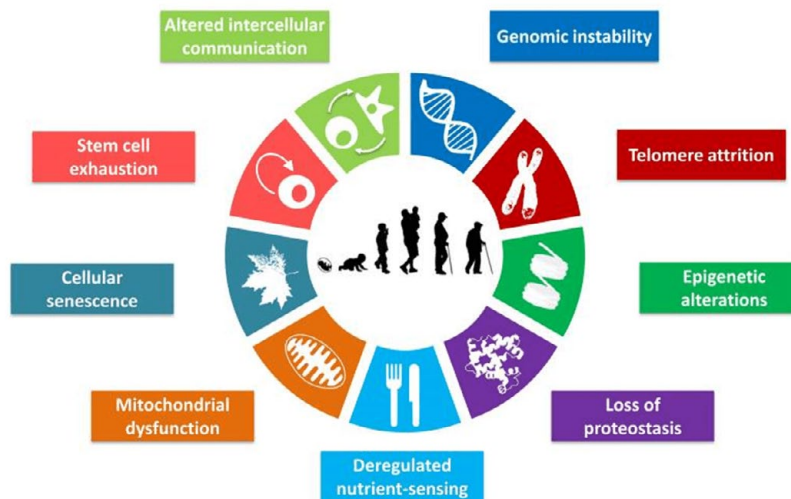


Image credit: *The Hallmarks of Aging*, PubMed

These 9 traits associated with aging include:

Genomic instability: Throughout one's life, both internal and external factors that cause genetic damage start to build up in the body. This is known to accelerate aging.

Telomere attrition: Telomeres – the protective “caps” located at the ends of our chromosomes (which house our genetic material) – start getting shorter each time a cell divides. Over time, this results in cells not being able to divide anymore, which can lead to disease.

Epigenetic alterations: There are changes in gene expression (not changes to the DNA itself) via an individual's life experiences or environmental factors which affect aging.

Loss of proteostasis: With age, cellular proteins become misfolded and therefore, lose their homeostatic functions. A build up of these damaged proteins is observed with aging or age-related diseases.

Deregulated nutrient-sensing: There are metabolism-regulating pathways, whose proteins (e.g. mTOR, sirtuins) are influenced by nutrient levels and also implicated in promoting aging.

Mitochondrial dysfunction: When the mitochondria (considered the energy powerhouse responsible for regulating metabolism in our bodies) starts to malfunction with age.

Cellular senescence: “Older” cells can't be cleared out as fast and their build up can lead to harmful health effects.

Stem cell exhaustion: Activities of the 4 types of stem cells, which all help in regenerating new tissue cells, decline with aging.

Altered intercellular communication: Communication between cells is disrupted with age, resulting in inflammation and tissue damage.

Companies focused on aging or age-related diseases are tackling one or more of these biological traits to find promising therapeutic candidates. In the next sections, we'll explore how each of these are being targeted.

THE RELATIONSHIP BETWEEN AGING & AGE-RELATED DISEASES

Longevity research on its own has seen a lot of progress, especially as we learn more about the biological processes that underlie aging.

But it's also become more intertwined with research studies focused on major diseases due to similar traits at the cellular and molecular level.

For example, there's a higher probability of lethal gene mutations as one ages that can result in diseases such as cancer or Alzheimer's. This is a big reason why many drug companies are targeting aging in an attempt to stave off other degenerative diseases.

Can cancer cures help us live longer?

Cancer begins when abnormal cells start dividing and growing at an uncontrollable rate. This can happen when the body's proper safeguards or checkpoints go awry, especially with older age.

These malignant cells continue to replicate until they've invaded other tissues, organs, or body systems. Often times, the extent of their growth is only realized after a person develops disease symptoms.

Because the median age for a cancer diagnosis is 66, understanding cancer's disease pathology could reveal new insights into what exact mechanisms also affect aging.

This is precisely why some drug companies are building out their drug pipelines to include medicines that target both cancer and aging.

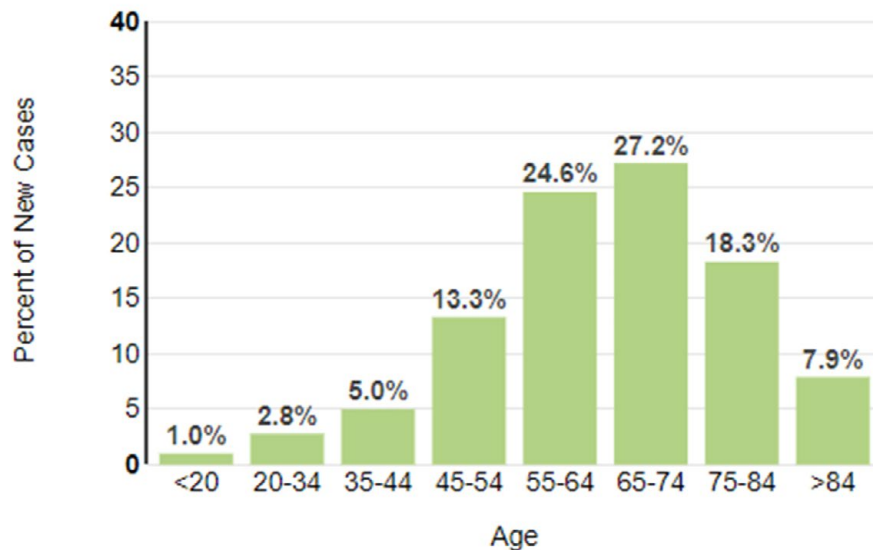


Image credit: [National Cancer Institute](#), *Percent of New Cases by Age Group: Cancer of Any Site – 2011-2015, All Races, All Sexes*

For instance, tumors start developing via two main mechanisms:

- 1 When genes known as oncogenes become active
- 2 When genes that are supposed to protect cells from becoming cancerous – known as tumor suppressor genes – become inactive

Research has shown that the somatic cells (aka non-reproductive cells) in our bodies have protective functions to prevent such tumors from forming.

But, over time, these cells age, lose their functions, and build up in the body. And although they're technically dead, they're still metabolically "active." This means that they can secrete immune cells like cytokines that increase the likelihood of abnormal growths of tissue.

Identifying these pathways to disease could result in a future in which an anti-aging treatment could also prevent certain tumors from growing.

Aging poses biggest risk to neurodegeneration

The biggest risk factor for neurodegenerative diseases (NDDs) such as Alzheimer's or Parkinson's is aging.

For instance, symptoms for Alzheimer's disease – a progressive degenerative disorder of the brain resulting in dementia – start appearing in people in their mid-60s.

One of its key features is the abnormal buildup of amyloid plaque or tau tangles in the brain. The condition results in the nerve cells in the brain losing their ability to communicate with each other and with different parts of the body.

It currently remains incurable, like other neurodegenerative disorders.

NDDs share cellular and molecular mechanisms commonly seen in aging cells such as mitochondrial dysfunction, oxidation stress, and inflammation.

In fact, a **research study** published in September from the Mayo Clinic removed senescent cells in mice, which ended up preventing brain degeneration. More research efforts could provide detailed insights into the relationship between cellular aging and neurodegeneration.

2

Slowing down the aging process

So, how do we slow down aging?

It's a complex question without definitive answers. However, more advances are being made here than ever before, from creating novel drug therapeutics to blood plasma transfusions and more.

PHARMACEUTICALS

Drug therapies make up the vast portion of potential treatments in this area. Below, we highlight some of the prominent types of drugs that could help slow aging.

Senolytics

One of the most popular areas of research is around senolytics – a class of drugs that target aging (or senescent) cells and destroy them via induced cell death.

It's part of a new, emerging area of research known as “senotherapy,” in which senolytics is a key class of therapeutics. Senotherapeutics include geroprotectors – drugs that are supposed to be able to prevent or reverse aging by targeting its cellular triggers such as damage to the DNA.

These drugs are in the early stages of development and if approved by the FDA (which does not recognize “aging” as a standalone disease) would be prescribed to target a specific condition or disease, but would carry the secondary impact of slowing down aging.

One example here is **Juvenescence AI** and its joint venture with deep learning drug discovery company **Insilico Medicine**. They're working on developing both pharmaceutical and nutraceutical products that target senescent cells.



As we age, cells stop working as efficiently as they once did and lose their ability to carry out their normal functions.

And when these senescent cells start accumulating in the body, they can secrete pro-inflammatory signals to the immune system. Essentially, they can still be "active" even when they've lost their functions, and the molecules they secrete can result in cell damage and ultimately, disease.

Rapamycin (aka sirolimus)

Compounds known as rapamycin were originally extracted from soil bacteria native to the Easter Islands (native name: Rapa Nui) and are proving to be important for anti-aging research.

Rapamycins are naturally-derived and considered multi-functional in medicine due to their effects on immune cells. They're often used as immune suppressants during organ and bone marrow transplants to prevent rejections.

They primarily act by targeting the mTOR (or mechanistic target of rapamycin) pathway, which ultimately blocks a key protein involved in cell division.

Using rapamycin has now been linked to prolonged lifespan, along with other enhanced cognitive and immune functions. Early research studies have shown increased lifespans of mice treated with the compound. However, this is still a nascent area of research.

Metformin

Metformin (also known as Glucophage) — a cheap, generic drug to treat type 2 diabetes — has emerged as a possible drug for promoting longevity.

Currently, it is prescribed to only type 2 diabetes patients in order to lower the amount of sugar produced in the liver, which can delay the disease's progress.

Aside from its effect in glucose metabolism, it has captured the attention of longevity researchers because of its effects in reducing oxidation stress and inflammation — both associated with aging.

Key academic institutions or hospitals have begun conducting clinical trials using metformin for age-related conditions such as pre-diabetes, frailty, inflammation, muscle atrophy, and insulin resistance.

For example, Mayo Clinic is currently recruiting patients for a **trial** that will study metformin's effects on frailty in 12 subjects 60 years old and up. It will study if a chronic administration of metformin may augment cellular regeneration and reduce senescence, thereby improving frailty and physical functioning.

REGENERATIVE MEDICINE

Regenerative medicine has been a big area of interest for restoring the structure and function of damaged tissues or organs. And this could be a crucial part of increasing longevity as individuals replace damaged body parts with new ones.

Stem cells

Stem cell research is one of the most promising areas in regenerative medicine.

Because stem cells can differentiate and produce specific cells and tissues, they may hold the key to treating age-related issues.

Here's how it works: researchers can manipulate a given set of stem cells under a controlled setting and stimulate them to differentiate into the desired cells they want. In particular, stem

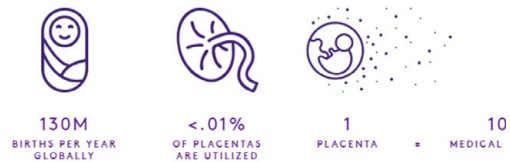
cells taken from an embryo can be very useful, as these can be induced to become virtually any cell – a key difference from adult stem cells.

This type of technology could give way to a new frontier for anti-aging research, using stem cells to regenerate cells or tissues that have lost functions.

Therapeutics derived from placenta stem cells is one example of this growing area of research, and startup **Celularity** is striving to make this happen.

why the placenta?

Celularity is the only company to use an **allogenic** placental platform. Because stem cells derived from the placenta are intrinsically safe, they can be taken from any placenta and injected into any human without the risk of rejection. These cells are also incredibly abundant, making treatments more **affordable** and **immediate**.



It seeks to “make 100 years old the new 60” with stem cells taken from the placenta to create drug therapeutics for diseases from cancer to Crohn’s disease to diabetic peripheral neuropathy.

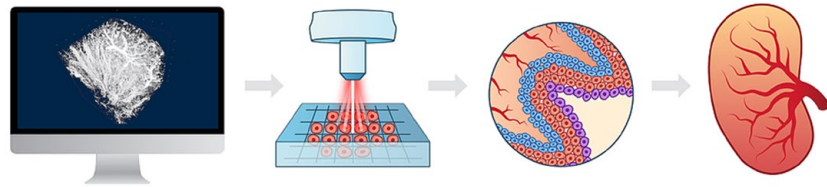
Organ regeneration

As a vital part of regenerative medicine, 3D bioprinting of tissues and organs present a novel way to restore lost structures or functions.

These would replace damaged counterparts, potentially prolonging an individual’s lifespan. This type of technology could be able to create more robust tissues and organs that naturally deteriorate as people age.

Another benefit here is that those waiting for organ transplants could have access to specific organs that won’t get rejected, which could possibly prolong their lives.

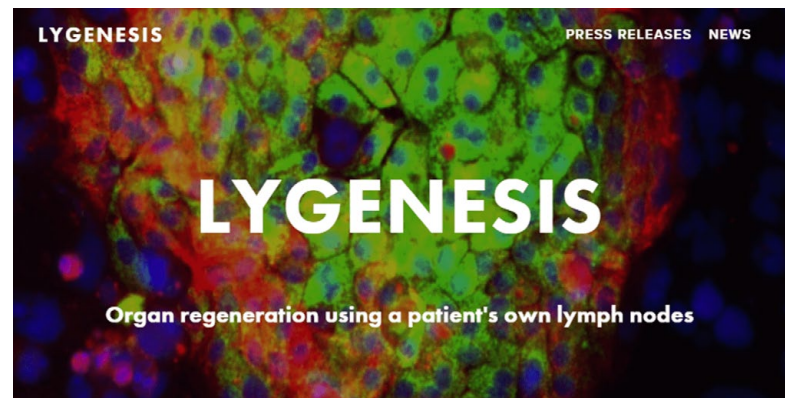
While the progress has been relatively slow here due to the complexities in creating a human organ composed of interconnecting tissues, companies like **Prellis Biologics** are working in the space to make this a reality.



In June, the company announced it could print human tissue with viable capillaries, which is a promising signal for being able to print organs.

LyGenesis is another company working towards organ regeneration.

It wants to use a patient's lymph nodes as bioreactors to regrow organs there. For instance, it would transplant liver cells into the lymph nodes, where they would essentially become "miniature ectopic livers."



Its current focus is on liver regeneration for patients with end stage liver disease (ESLD) with plans to expand to the thymus, pancreas, and kidney. It raised a \$3M Series A financing round from Juvenescence AI in May 2018.

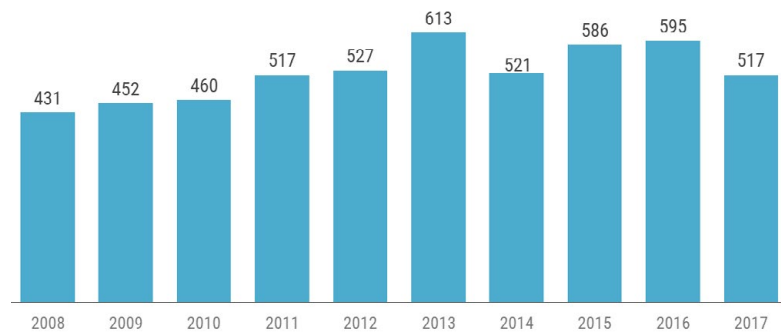
CALORIC RESTRICTION

There's a recent wave of research looking at the role that caloric restrictions play in promoting longevity. This consists of reducing overall caloric intake with a carefully maintained diet to avoid malnutrition.

Such efforts have proven to dramatically increase lifespans in rodents and nematode worms in past laboratory studies. Studies have also **shown** that it can prevent or delay age-related diseases from manifesting – a key example being cancer.

Caloric restriction studies maintain a steady increase

Number of published research studies looking at caloric restriction (2008 – 2017)



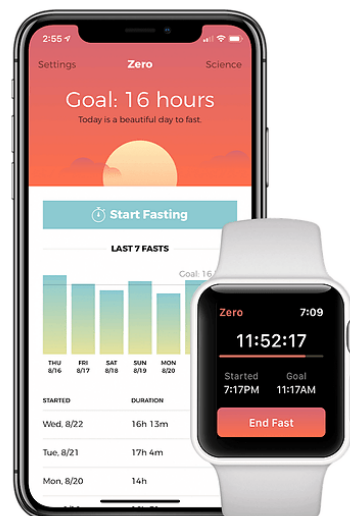
Source: cbinsights.com

*Data taken from PubMed.Gov, US National Library of Medicine, National Institutes of Health

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A **study** published in January 2017 looked at the effect of caloric restriction in rhesus monkeys.

It compared longitudinal data from two studies that sought to answer if reasonable calorie restriction really extended the lives of these monkeys. The results showed that it improved both the health and survival in this population and suggested that it could be “translatable” to humans.



A **study published** in the Cell scientific journal in March 2018 further underscored this conclusion. It showed that cutting back calories by 15% for 2 years slowed down the metabolic processes involved in aging and in age-related diseases. However, the long-term effects are still largely unknown.

Intermittent fasting is one way to adhere to this dietary regimen. There are even some

studies that have looked at specific eating time windows in order to optimize body's energy metabolism. This time-restricted eating could help cut back calorie consumption.

A startup working in this area is **Zero Fasting**, which allows consumers to choose their respective fasting methods with goal tracking. It recently raised \$1.2M in seed financing from investors such as Trinity Ventures and True Ventures.

Such methods of caloric restriction still have a ways to go before being legitimized in the scientific community as a potential intervention for aging or age-related diseases. However, more research in this area may help us better understand how eating impacts our lifespans.

DIETARY SUPPLEMENTS

Dietary supplements in the form of NAD⁺ (nicotinamide adenine dinucleotide) – or its precursors NMN (nicotinamide mononucleotide) and NR (nicotinamide riboside) – have become a focus in the longevity space.

They are all forms of the vitamin B3 – also known as niacin – which has digestive, skin, and mental health benefits.

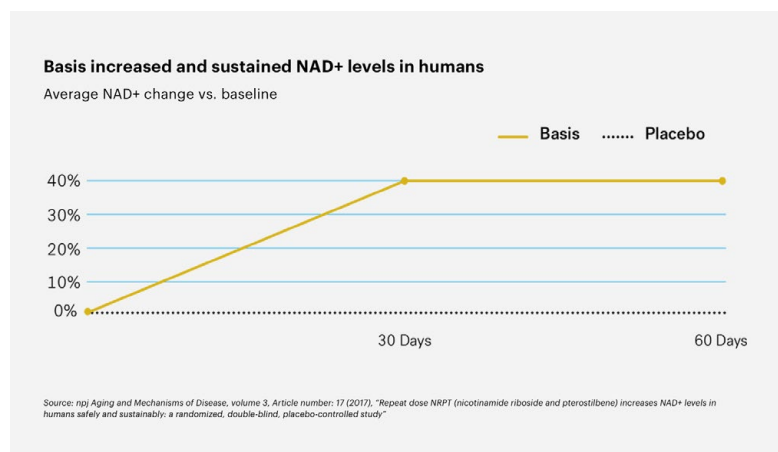
In particular, NAD⁺ has been receiving a lot of attention recently. It is a naturally occurring key molecule known as a coenzyme that regulates healthy metabolism and other biological processes in the body. It exists in every cell in the body because it impacts everything from DNA repair to creating energy needed to conduct vital cellular processes.

It plays an important role in facilitating key biochemical pathways that need to function properly in order to avoid disease. And it's been shown that NAD⁺ levels start to fall with age.



Elysium Health's daily supplement, Basis, seeks to elevate these NAD+ levels in the body in order to prolong one's lifespan. Its formulation consists of crystalline NR and pterostilbene.

This compound claims to increase NAD+ levels while also activating sirtuins (a class of proteins also associated with aging and metabolism), which can help improve cellular health.



The above graph shows results from the company's clinical trial, which studied people who took the supplements vs. those who did not (placebo): There was an average of 40% increase in NAD+ levels with Basis.

But, while it was able to increase NAD levels using the supplement, it remains to be seen if this may have the long-term effect it desires. For one, studying longevity is difficult because

it requires decades-long investigation into proving its intended effect. Another reason is that dietary supplements are not regulated by the FDA and therefore, don't have to be controlled.

ARE 'BLOOD BOYS' A POSSIBILITY?

As depicted in the TV show Silicon Valley, longevity-promoting blood transfusions from a younger individual to an older one could soon become a reality.

Such blood transfusions – known as “parabiosis” – have been a pillar of anti-aging research due to the rejuvenating effects for the aged animal. This concept traces back to the 1950s, when Cornell scientists joined two rats' circulatory systems together.

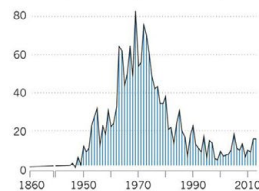
The following graphic from [Nature](#) in 2014 illustrates how this was done via the joining of the two bloodstreams through a capillary network.

Share and share alike

Parabiotic experiments, in which two animals share a common bloodstream, were first attempted in the 1860s. By connecting animals with different qualities or conditions, scientists can investigate how blood factors, such as cells, proteins or hormones, influence health. In recent years, a few researchers have looked at heterochronic (old and young) mouse pairs to understand how young blood helps to repair many tissues.

Publications on parabiosis

Parabiosis gained popularity during the 1960s and 1970s, but eventually fell out of wide practice.



A simple surgery

A veterinary surgeon will anaesthetize the animals, peel away a thin layer of skin along their sides and stitch or staple the exposed surfaces together. Wound-healing processes join the bloodstreams through a capillary network, and in one to two weeks, the animals are pumping each other's blood.

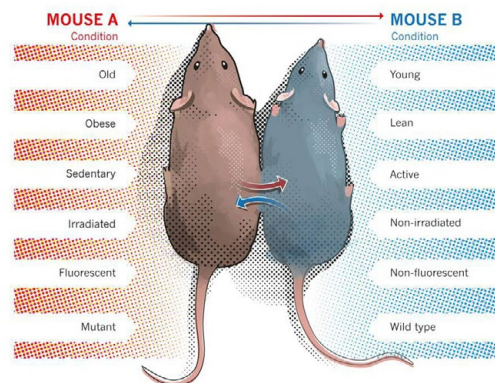


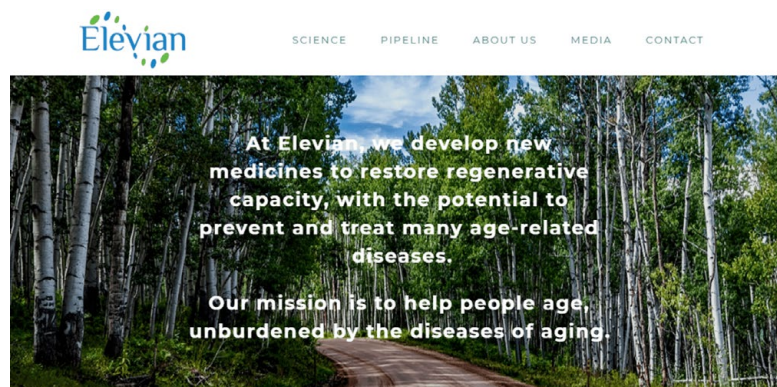
Image credit: Nik Spencer/Nature; Chart Data: A. Eggel & T. Wyss-Coray Swiss Med. Wkly 144, W13914 (2014)

Parabiosis is an experimental procedure that circulates shared blood between a younger and an older animal, according to the National Institute of Aging (part of NIH). The resulting benefits have included brain and muscle tissue improvements in older mice.

However, there's also contrasting evidence according to a **2016 parabiosis study** done at UC Berkeley, which showed older mice injected with younger blood had "slight or no significant improvements." But, younger mice injected with blood from older mice saw tissue and organ declines.

One startup working in this area is **Elevian**, using its GDF11 (Growth Differentiation Factor 11) protein – a naturally occurring circulating factor that may decline in elderly people, although this hasn't been verified yet.

Elevian claims that daily GDF11 injections from younger to aged animals can ultimately treat age-related diseases. Its current pipeline targets coronary artery disease, type 2 diabetes, Alzheimer's disease, and sarcopenia (loss of muscle mass). The company has not yet announced any clinical trials, as they are still in the early stages of research.



Elevian raised \$5.5M in seed funding in September 2017 from industry investors such as the Longevity Fund.

One particular startup that has stirred up a bit of controversy recently is **Ambrosia**, which is a private clinic where patients aged 30 – 80 can pay \$8,000 to get blood plasma from younger individuals.

Its **clinical trial** began in June 2016, enrolling 200 patients aged 35 and up to receive blood plasma from young donors (ages 16-25). It monitored blood biomarkers before the treatment and 1 month after. This concluded in January 2018, and the study results have not been published.

While this may conjure up unsavory or sci-fi images, it continues to carry an intrigue among researchers and healthcare companies.

For instance, Spain-based pharmaceutical company Grifols acquired a 45% stake in **Alkahest** – which develops blood plasma-derived therapies targeting aging – for \$37.5M in March 2015. Its main pipeline focus is on cognitive decline in aging such as dementia along with neurodegenerative disorders like Alzheimer's.

Pipeline

Therapeutic Modality	Indication	Research	IND Enabling	Phase 1	Phase 2	Phase 3
Plasma Proteins	Alzheimer's Disease – Mild to Moderate	██████████	██████████	██████████	██████████	
	Alzheimer's Disease – Advanced	██████████	██████████	██████████	██████████	
	Parkinson's Disease	██████████	██████████	██████████	██████████	
	Undisclosed Disease	██████████	██████████	██████████	██████████	
CCR3 Antagonist	WetAMD	██████████	██████████	██████████	██████████	
	Neurodegenerative Disease	██████████	██████████	██████████	██████████	
	Inflammatory Disease	██████████	██████████	██████████	██████████	
TIMP2	Neurocognitive Disease	██████████				
Extracorporeal Therapy	Dialysis Related Dementia	██████████	██████████			
Novel Factors		██████████				

Currently, it has 3 clinical trials that are recruiting for patients. In February 2017, it completed **its trial** using blood plasma from young donors to those aged 50 to 90 years old with mild to moderate Alzheimer's disease. No results have been posted yet.

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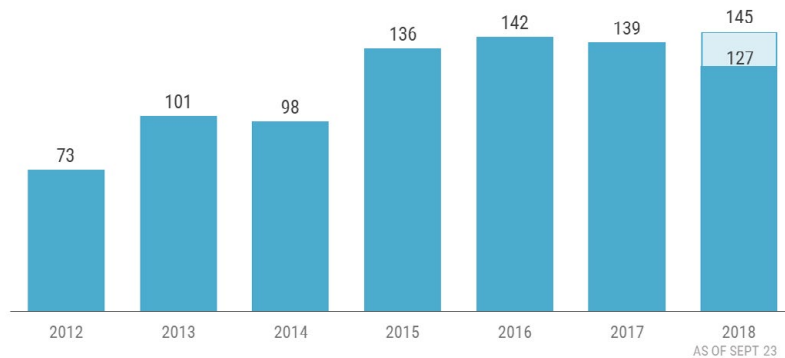
Who's interested in longevity

Anti-aging research had been a slow area for deal activity even 5 years ago. However, recent deals indicate that more investors may be making bets on this nascent market.

The increasing number of clinical trials targeting aging is another indicator that this area is garnering more interest.

Clinical trials targeting aging see a steady growth

Number of clinical trials for condition "Aging" by study start date (2012 – 2018)



Source: cbinsights.com

*Data taken from ClinicalTrials.gov; light blue indicates trials that are slated to begin in 2018 but have not started yet

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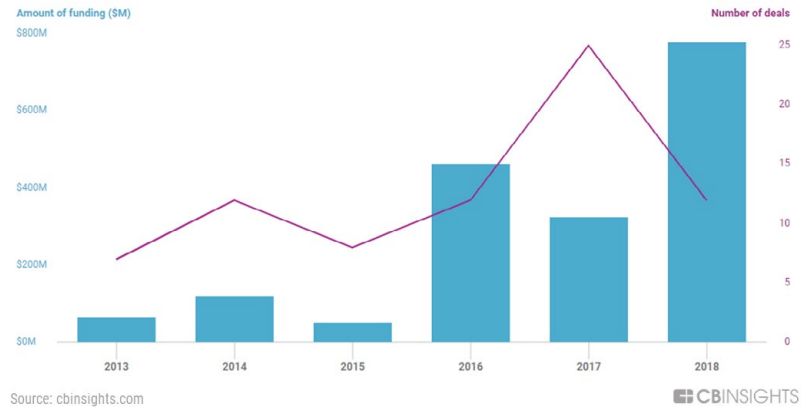
INVESTMENT LANDSCAPE

Funding to longevity startups has seen a huge uptick in the last 3 years. In particular, 2017 saw an unusual spike in the number of deals, with both follow-on and new rounds contributing to an all-time high.

Some companies even saw multiple funding rounds in 2017, including Juvenescence and Insilico Medicine.

CB Funding to longevity startups sees a huge jump

Amount of funding (\$M) and number of deals from 2013 – 2018 (as of 9/25/2018)

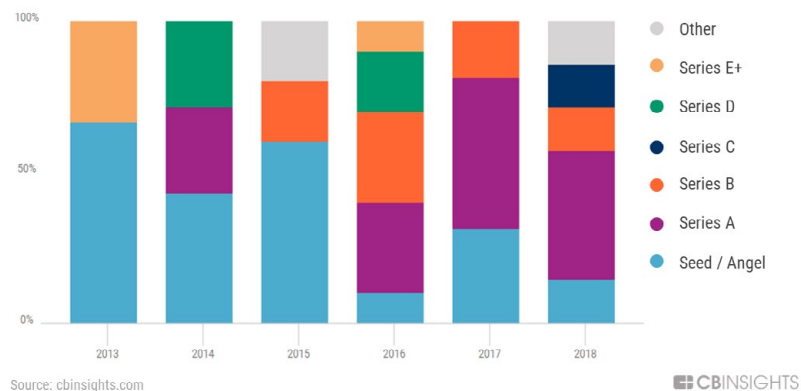


And 2018 has already seen record-high financing into the sector. This increase has been largely due to mega-deals like **Samumed's** \$438M financing round in August and Celularity's \$210M Series A round in February.

The market is also beginning to see some slight maturation, as witnessed by the distribution of deal share over the past 6 years.

CB The longevity startup ecosystem starts maturing

From 2013 – 2018 as of 9/25/2018



The share of seed/angel deals, for example, has steadily gone down in the last 5 years as other funding rounds such as Series A have started to take an increasing share of deals.

KEY INVESTORS

One VC firm specifically dedicated to funding startups in the longevity space is The Longevity Fund by Laura Deming.

Its notable portfolio companies include UNITY Biotechnology, Metacrine, ALX Oncology, and Precision Biosciences. The firm invests in seed and Series A startups and has \$37M under management.

Another notable investor in the space is Kizoo Technology Ventures, which has invested in 4 longevity startups since 2013: AgeX Therapeutics, CellAge, Antaxerene, and Elevian.

Jim Mellon is also a prominent angel investor in longevity startups. His investments include Juvenescence, Insilico Medicine, and AgeX Therapeutics.

NOTABLE LONGEVITY-FOCUSED COMPANIES

Although a nascent space, several startups are emerging to target anti-aging remedies in the hopes of increasing longevity.

Samumed, a regenerative medicine company, raised \$438M in August, bringing its valuation to \$12B.

It's developing drug therapeutics that target key proteins in the WNT pathway, which helps with regulating tissue health. Essentially, when something goes wrong in the WNT pathway, it leads to disease in a given tissue.

The company claims that WNT levels "get out of balance" with age, resulting in disease. Samumed's current pipeline targets diseases associated with aging such as osteoarthritis — a degenerative joint disease where the cartilage at the ends of bone wear down — and degenerative disc disease.

The company **announced** a successful completion of its phase 2 clinical trial involving lead drug SM04690.

“The completion of our Phase II clinical trial of SM04690 for the potential treatment of OA of the knee marks an important milestone for physicians, patients, and our development program ... While the current standard of care is focused on relieving signs and symptoms of the disease, SM04690 has the potential to be the first disease modifying treatment approved for OA of the knee.”

– DR. YUSUF YAZICI, SAMUMED’S CHIEF MEDICAL OFFICER.

Osteoarthritis seems to be a key target for many drug companies looking to develop therapies for age-related diseases.

Pipeline

Samumed continues to invest in preclinical research, expanding its technology platform while deepening its primary focus on the Wnt pathway. Thus, the company now claims a diverse pipeline of programs in different stages of clinical readiness.

Lead Compound	Disease Area	Preclinical	Phase 1	Phase 2	Phase 3
SM04690	Osteoarthritis	[Progress bar spanning Preclinical, Phase 1, and Phase 2]			
SM04690	Degenerative Disc Disease	[Progress bar spanning Preclinical and Phase 1]			
SM04646	Idiopathic Pulmonary Fibrosis	[Progress bar spanning Preclinical and Phase 1]			
SM04755	Psoriasis	[Progress bar spanning Preclinical and Phase 1]			
SM04755	Tendinopathy	[Progress bar spanning Preclinical and Phase 1]			
SM04554	Androgenetic Alopecia	[Progress bar spanning Preclinical, Phase 1, and Phase 2]			
SM08502	Oncology	[Progress bar spanning Preclinical and Phase 1]			
SM07883	Alzheimer's Disease	[Progress bar spanning Preclinical]			

UNITY Biotechnology, which went public this May at a valuation of \$712M, is also active in this area.

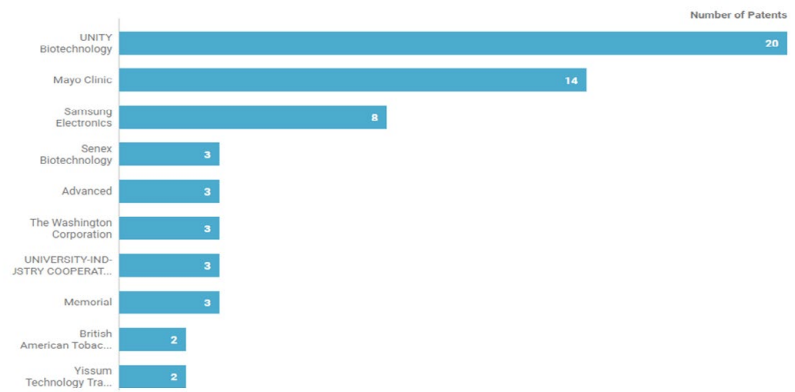
The company has had many notable healthcare investors including ARCH Venture Partners, Mayo Clinic Ventures, and WuXi Healthcare Ventures. Jeff Bezos' Bezos Expeditions and Peter Thiel's Founders Fund have also invested in UNITY.

Its current pipeline includes senolytic drug candidates targeting musculoskeletal, ophthalmology, and pulmonary diseases. In May, it began its first **clinical trial** using its senolytic drug candidate UBX0101 for treating osteoarthritis.

Most notably, UNITY leads with senescence- or senolytic-related patent applications from the last 5 years, according to our Patent Analysis tool.

UNITY Biotechnology leads with most senolytic patents

of patent applications involving "senescence" or "senolytic" (2013 – 2018*)



Source: cbinsights.com
*As of 9/24/2018

 CBINSIGHTS

Mayo Clinic filed 12 out of 14 of its senolytic patents jointly with UNITY.

WHERE BIG PHARMA IS PLACING ITS BETS

Pharmaceutical companies have had mixed success in the longevity market.

For example, GlaxoSmithKline (GSK) shut down the aging-focused drug discovery company Sirtris Pharmaceuticals in 2013. This came roughly 5 years after GSK acquired Sirtris for \$727M.

However, that hasn't stopped other big pharma players from getting involved.

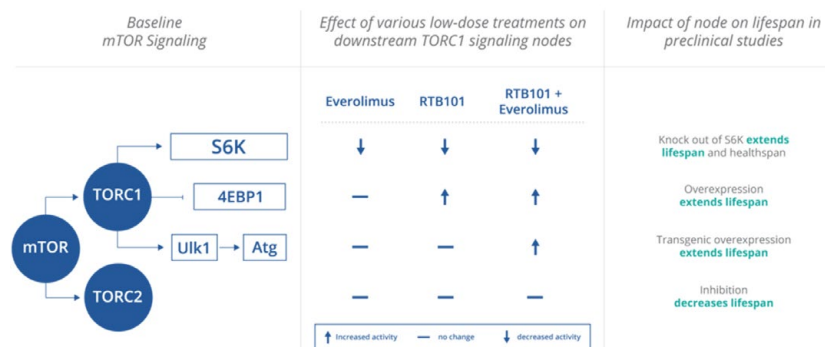
Novartis

In particular, Novartis has been a relatively early contributor to this space, beginning with its 2014 study looking at rapamycin's surprising effect on boosting the immune system in elderly people. Its most recent [paper](#) from July demonstrated its 2 drugs being used to block the **mammalian target of rapamycin (mTOR)**, reducing infections in elderly volunteers.

In March 2017, Novartis announced it would sell its two clinical-stage programs for aging-related disorders. Under the agreement, buyer PureTech Health has plans for its subsidiary [resTORbio](#) to develop these drug candidates to focus on immuno-senescence (age-related decline in immune function).

Novartis has a 15% stake into those candidates.

Before resTORbio went public in January, it had raised a \$40M Series B from investors such as Fidelity Investments and OrbiMed Advisors.



As seen in the above graphic, resTORbio's drug candidates target the mTOR pathway in order to ultimately extend lifespan.

In its Phase 2b trial using its lead drug RTB101, a TORC1 (rapamycin complex 1) inhibitor, showed a **30.6%** decrease in respiratory tract infections (RTIs) compared to those who received the placebo. This clinical trial was done with 652 elderly patients at risk of RTIs.

Celgene

Alongside Novartis, other pharma companies are also looking at this market.

Celgene has been involved in furthering Celularity's longevity R&D pipeline. Spun out of Celgene Cellular Therapeutics in June 2017, Celularity develops anti-aging therapeutics derived from placental stem cells. It last raised a \$210M Series A financing in February with Celgene participating.

Others

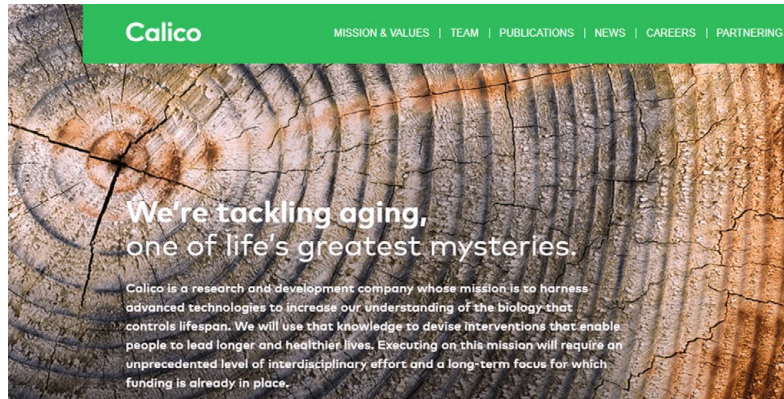
The innovation arm of Johnson & Johnson has invested in 2 vision startups: ReVision Optics and Powervision, both of which focused on ophthalmology disorders such as age-related macular degeneration. ReVision shut down in January.

GOOGLE'S CALICO LOOKS TO THE NAKED MOLE RAT

Google's anti-aging spinout **Calico Life Sciences** is one of the most talked about companies in the longevity space. It seeks to understand the biology that controls lifespan and find interventions.

In June, it extended a collaboration with pharma giant AbbVie for their joint venture to develop drug therapeutics targeting aging and age-related diseases including neurodegeneration & cancer. Each party is contributing an additional \$500M, further building on their collaboration that started in 2014.

According to Calico's press release, it has produced "more than two dozen early-stage programs addressing disease states across oncology and neuroscience and yielded new insights into the biology of aging."



This announcement follows its **January publication** which studied naked mole rats, rodents the same size of a lab mouse but can live up to 10x as long. Its long lifespan along with its ability to ward off cancer has fascinated researchers.

As seen in the figure below taken from the paper, the naked mole rat mortality hazard is distinct from that of other mammals in its stability as they age.

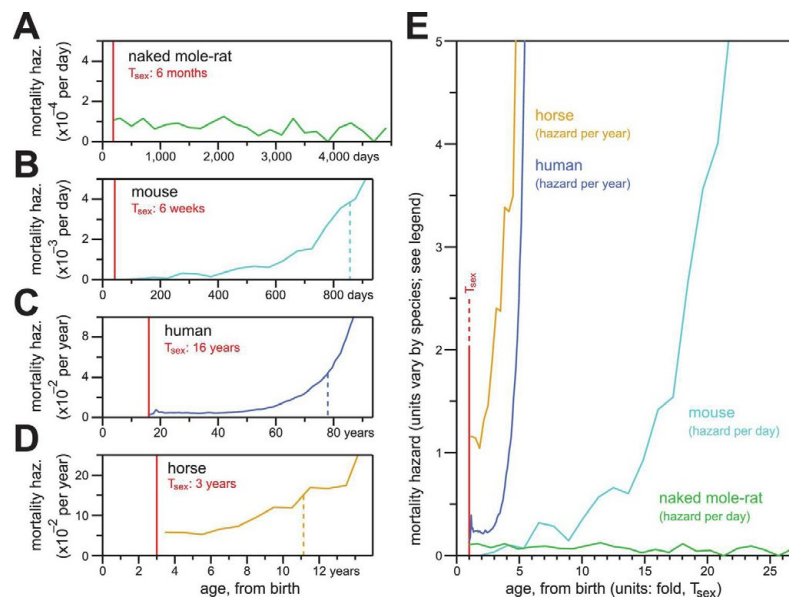


Image credit: Calico Life Sciences

Key takeaways from this paper included:

- Naked mole rats do not age as other mammals do, with little to no signs of aging
- Their risk of death doesn't increase even at 25x past their time to reproductive maturity

Calico also has a 5-year strategic partnership with cancer therapeutics company **C4 Therapeutics** that began in March 2017. The goal is to discover and develop small molecule protein-degrading therapies that can treat aging, including cancer. This would work by removing certain disease-causing proteins.

C4 last raised a \$73M Series A round in 2016 with participation from Novartis Venture Funds & Roche Venture Fund.

These partnerships with pharmaceutical companies show that longevity could see new therapeutics emerge. Going beyond just targeting senescent or aging cells, these therapies could work in a dual fashion – staving off aging while also fighting chronic diseases like diabetes and neurodegeneration. However, it will be an uphill battle for the FDA to approve medicines designed to stave off aging before a chronic disease has manifested itself.

4

Challenges & controversies

Inevitably, when it comes to an idea like fighting mortality, there are certain risks and controversies associated with it.

SKEPTICISM & RISKS

The discussions on extending longevity can spark moral, ethical, or religious concerns about taking “magic pills” or injections to keep death at bay.

Some scientists are now questioning whether this may even be a feasible task, and perhaps a gateway to potentially endangering our health further.

With any new technology used in human health, there are unintentional downstream effects to think about – especially since aging or age-related diseases can be difficult to study due to the length of time needed to fully evaluate a therapy's full range of effects, both in the short- and long-term.

In fact, there was a **study** published in December 2017 titled “*Intercellular competition and the inevitability of multicellular aging,*” which looked at the cellular processes underlying aging.

The researchers concluded that aging cannot be stopped in multicellular organisms (i.e. any organism which has more than 1 cell). This is due to the fact that it presents a “catch-22” scenario where targeting one mechanism underlying aging could affect others, thereby potentially causing disease in other ways.

This study illustrated that even if we were able to target one hallmark of aging, we may also simultaneously be stimulating other processes that speed up our aging and could even cause diseases in the process.

“Aging is mathematically inevitable – like, seriously inevitable. There’s logically, theoretically, mathematically no way out.”

– **JOANNA MASEL**, UNIVERSITY OF ARIZONA PROFESSOR OF ECOLOGY & EVOLUTIONARY BIOLOGY

CONTROVERSIES

Possessing the power to extend one's life comes with a host of controversies. But the two biggest ones include how such a technology will influence the global population and resources along with the creation of social inequities between different socioeconomic classes.

1. Overpopulation

If these anti-aging therapies enter the market, some fear that overpopulation may indeed become a reality.

The current assumption goes that if we are able to increase the human lifespan, it could result in more people living with limited resources (e.g. food, land, etc). But, critics to this scenario say that it would not cause overpopulation if more technological innovations resulted in an increase of these resources for everyone globally.

2. Social inequities

This type of treatment could also cause more inequities between different socioeconomic classes. For example, if such treatments come at a premium price then presumably, only the wealthy would be able to afford them and ultimately live longer. It could usher in a dystopian world where human lifespans vary even more widely across different geographical landscapes or levels of wealth.

On the other hand, some would argue, current forms of medicine are costly and bring incremental improvements especially at an older age. If these anti-aging therapeutics were provided at a one-time or a fixed number of sessions, would the cost end up being cheaper than that of other extensive medical procedures or drugs?

5

Looking forward

New anti-aging research efforts are gaining traction. And with technology continuing to provide novel solutions, finding ways to extend our lifespans may not be so far away.

In fact, a leading figure in this space, Aubrey de Grey, chief science officer of SENS Research Foundation, states that human experimentation with these therapies may be possible within the next 20 years.

While we're still far away from these fountain of youth treatments on drugstore shelves, we may be seeing the first wave of what could ultimately redefine the human experience.