CRYONICS

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Alcor New York Science Symposium

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CRYONICS

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Scholar Profile: José Luis Cordeiro

By Nicole Weinstock

It's tough to be a naysayer with Dr. José Luis Cordeiro in the room. It's not just his playful tie collection, with illustrations of Mickey Mouse, Egyptian pharaohs, Escher paintings and currencies among their frequent themes. Nor is it his humorous description of the humble beginnings of data storage, when punch cards and floppy disks offered one mere "kaka" of memory. It is his palpable zest for the future that leaves you feeling inexplicably energized about the tomorrows that lie ahead.

Dr. Cordeiro has a complex identity that defies swift characterization. The short list describes him as a futurist, transhumanist, immortalist, cryonicist, Singularitarian, Energularitarian, engineer, economist, and author. Perhaps the simplest, yet all-encompassing way to describe him is as an ardent communicator. You may recognize Dr. Cordeiro from a conference (he's presented at hundreds), or a book signing (he has written over a dozen), or a TED Talk (he has presented in seven different cities). You may even know him from the 2019 European Parliament election where he represented a new political party advocating the importance of engineering and science in curing aging and increasing longevity. His platform proposed the creation of the European Anti-Aging Agency in Spain, inspired by the National Institute on Aging in the United States.

Cordeiro holds both a Bachelor and Master of Science in Mechanical Engineering with minors in Economics and Languages from the prestigious Massachusetts Institute of Technology (MIT). He has a Masters of Business Administration in Finance and Globalization from the Institut Européen d' Administration des Affaires (INSEAD) in Fontainebleau, France. Last but not least, he earned his Ph.D. in Interdisciplinary Sciences from the Universidad Simón Bolívar (USB) in Caracas, Venezuela, which included extensive research in Tokyo, Japan. Dr. Cordeiro is a lifetime member of the scientific research honor society Sigma Xi, the engineering honor society Tau Beta Pi, and the exclusive international business honor society, Beta Gamma Sigma. He has even been listed in the Marquis edition of *Who's Who in the World*.

A self-identified global citizen, Cordeiro also supports a number of international organizations with his expertise. Among other positions, he is the Vice President of HumanityPlus, a nonprofit organization advocating the ethical use of technology to expand human capabilities. He is also a Fellow of the World Academy of Art and Science, and Director of the Millennium Project, a global think tank with a mission to enhance knowledge of the future.

As you may presume, Cordeiro's passport has no shortage of stamps. One of the latest acquisitions shows his efforts to promote the first Portuguese edition of his thirteenth book, which translates to *The Death of Death* in English. T*he Death of Death* explores the history, science, ethics, and future of aging, in addition to arguments supporting an imminent optionality of death. Despite returning from back-to-back travel, Cordeiro graciously extended his time to *Cryonics* magazine to delve deeper into this book and the history that set it in motion.

From the capital of heaven

Dr. Cordeiro was born in Caracas, Venezuela in 1962. He was the second son of Spanish parents, Pedro and María Luisa Cordeiro, who crossed the Atlantic to escape the Franco dictatorship. At the time, Venezuela was by all accounts—and certainly compared to Spain—a prosperous country. In fact, it boasted the highest standard of living in all of Latin America, thanks to its enormous oil reserves. So sweet was life, that the young Cordeiro and his childhood friends often referred to Caracas as "the capital of heaven."

The Cordeiro parents grew up with modest means that precluded formal education after the civil war in Spain (1936-1939), though this was very much a value in the household. José was encouraged to cultivate his curiosities, such as his affinity for Legos. Whenever the family went on vacation, he almost always brought his collection: the ubiquitous polymer building blocks of his next robot figurine.

Like many immigrants, Dr. Cordeiro's parents were also adamant about higher education for their children, who certainly did not disappoint. When the time came, both their children were accepted into MIT in Cambridge, Massachusetts to pursue undergraduate degrees. Their tuition was covered by the government of Venezuela, which then issued a select number of scholarships to its most promising pupils—another indicator of the country's then-thriving economy.

The youngest Cordeiro would go on to receive both his B.Sc. and M.Sc. from MIT in Mechanical Engineering, the disciplinary confluence of his enduring interests in space and robotics. Like many of his peers, he was an impressionable seven years old when the Apollo 11 moon landing made history. "That was very inspiring to me," Cordeiro recalls, "even though I watched it in black and white because there were no color TVs at the time in Venezuela."

A global citizen

Prior to MIT, Dr. Cordeiro's first computer classes relied on IBM punch cards, those telltale rectangles of cardstock encoding program instructions and data through patterns of punched out holes. When he arrived in Cambridge in 1980, however, he was met with cutting edge supercomputers and a host of faculty and classmates passionate about the future—an ocean of inspiration for engineering applications. He even had the good fortune of studying under Marvin Minsky, one of the fathers of artificial intelligence.

Cordeiro completed his B.Sc. in 1983 and immediately advanced into MIT's master's program. As he contemplated thesis ideas, President Reagan directed NASA to create a permanently inhabited orbital space station for Earth called *Freedom*. Excited by its prospect, Cordeiro created a simulation of the station through dynamic modeling for his master's thesis. In actuality, NASA's *Freedom* efforts were absorbed into what would become the International Space Station (ISS). Launched in 1998 with similar applications in mind, the new ISS served the space interests of several countries post-Soviet Union. The story could not be a more fitting evolution of Cordeiro's thesis material, as he has long been a proponent of global citizenship.

His commitment to identity sans borders was forged early on, by more than his study of *Freedom*. Cordeiro also double-minored in Economics and Languages—he learned French and German—in anticipation of travels ahead. As is expected of any student of economics, he made a sound investment. Cordeiro has now been to 137 of the world's almost 200 countries, earning him over three million American Airline miles along the way.

Like many students, some of Cordeiro's university travel experiences were the most impactful in shaping his contemporary views. His politics are a prime example. Similar to many Latin Americans of the 60s, 70s, and 80s, he was an admirer of the Argentine Marxist revolutionary, Che Guevara, and the Cuban Revolution (1953-1959). When he took on a United Nations job in Vienna during the summer of 1984, however, his beliefs were challenged by the close juxtaposition of communist and democratic cities. "...I went from Austria to Czechoslovakia and I was depressed," José recalls, "but I was even more depressed when I went to Berlin and took the train from Vienna to West Berlin. It went into East Berlin and I saw the total disaster of communism." After that fateful summer, Cordeiro abandoned his leftist ideology and began to embrace more libertarian views.

Cordeiro's Ph.D. studies also delivered some eye-opening moments. Though he completed his degree in Interdisciplinary Studies from the Universidad Simón Bolívar in Venezuela, he started his Ph.D. while still at MIT, and many years later continued his research in a program at the Institute for Developing Economies in Tokyo, Japan. During that time, one cultural difference in particular felt quite pronounced. "There is, I think, a big difference between Western mentality and Eastern mentality concerning robots and artificial intelligence. In the West, mostly because of Hollywood movies or dystopian stories, we normally think about the Terminator scenario. In the East, in Japan especially, but also in Korea and China, people love robots." Cordeiro cites the beloved cartoon series about a young android hero, Astro Boy, among others supporting this cultural phenomenon. The experience was rather affirming in terms of Cordeiro's views on not just artificial intelligence, but also on humans.

"I am a bit Japanese concerning my point of view about robots. I think robots would be fantastic and artificial intelligence as well. In fact, artificial intelligence is the greatest invention of all. It would make us more intelligent, and I think we should be more intelligent. Thus, I do not worry about becoming more intelligent and using artificial intelligence...I worry about human stupidity."

A Singularitarian

For many years, Cordeiro has described himself as a Singularitarian: someone who believes in the imminence of a technological singularity, and the importance of taking action to support its fruition. Notions of a technological singularity date back to the nineteenth century, but contemporary definitions are most often connected with Ray Kurzweil's 2005 book, *The Singularity is Near: When Humans Transcend Biology*. In it, he describes how the Singularity—an explosion of artificial intelligence far smarter than humans—will occur by the year 2045. It warrants mention that this prediction also builds upon another, that artificial intelligence will be indistinguishable from humans by 2029, when it passes the Alan Turing test.

The Singularity is Near aroused the fervor of many futurists, including José. The book was life-changing. So much so, that when Kurzweil announced the creation of an educational company focused on exponential technologies like artificial intelligence, Cordeiro immediately wrote the organizers to inquire about opportunities. His enthusiasm was greeted in kind. The company, called Singularity University (SU), hired him in time to support their very first summer program in 2009. Cordeiro would then work with SU during four summer programs, in various roles ranging from Teaching Fellow, to Team Project Lead, Energy Advisor, Energy Faculty, and Global Grand Challenges Coordinator.

Reflecting back on the experience, Cordeiro admits that it was nothing short of fantastic. Similar to his years at MIT, SU brought him in proximity to some of the most forward-thinking institutions of Silicon Valley—the NASA Ames Research Center and the Googleplex (Google's headquarters) to name just a couple—not to mention a host of brilliant entrepreneurs, eager futurists, and generally inspiring people.

The impact of the SU years has also lived on in Dr. Cordeiro's many presentations around the world. A gifted presenter, he has worked hard to develop the ideas of the Singularity and exponential technologies into accessible lectures for the public. "I just love to communicate these ideas. I want people to know that the future is changing very fast and we are living in exponential times overall."

Like many Singularitarians, Cordeiro is excited for the higher quality of life that he believes it will promise. He predicts that with human cooperation, we will acquire not just more abilities, but more profound abilities. "When we humans combine and work together, I am pretty sure we will transform into posthumans that will be incredible: super intelligent, super longevous, and super happy." Dr. Cordeiro looks forward to experiencing each quality more deeply.

An Energularitarian

In addition to a Singularitarian, Cordeiro also refers to himself as an Energularitarian. The term Energularitarian is derived from the noun Energularity, which he invented during his tenure at SU. As the pronunciation suggests, its meaning relates to two other words that saw great usage during that period: the Singularity and the Methuselarity. The Methuselarity, as popularized by Aubrey de Grey, is the point in time when people can reasonably expect to live an infinite number of years without the effects of cognitive and physiological decline caused by aging. It is expected to occur around the same time that Kurzweil predicts AI will pass the Turing test.

The defining concept of the Energularity—energy—is a significant theme in Cordeiro's life that predates Singularity University. Not only did energy shape the flourishing economy of his childhood, but it formed the field in which he first launched his career. After studying at MIT, Cordeiro worked as an engineer with oilfield services provider Schlumberger, and went on to advise major oil companies like BP, ChevronTexaco, and ExxonMobil for years. In 1996, he wrote an influential book about privatizing the huge Venezuelan oil company, PDVSA, which paved the way for his role in Venezuela's 1998 presidential election. As fate would have it, the book's readership included presidential candidate, Irene Sáez. Former Miss Universe and Mayor of Chacao (a municipality of Caracas), Sáez enthusiastically enlisted Cordeiro as her energy advisor. Had they won the election, he might also have been appointed President of PDVSA or Secretary of Energy.

In the end, Sáez lost to Hugh Chavez; however, it did not dampen Cordeiro's dedication to the field. Energy seems to run through his veins, for just over a decade later, he invented the term Energularity.

While the Energularity, Singularity, and Methuselarity all address exponentiality, the Energularity does so with respect to human energy consumption resulting from the other two. By Cordeiro's definition, the Energularity is when humanity becomes a Type I civilization, able to use and store all the solar energy that reaches Earth from the Sun. This label is derived from the Kardashev scale, named after the Soviet astronomer, Nikolai Kardashev, who introduced it in 1964. The original scale defined three types of civilization based on energy mastery of their planet (I), star system (II), or galaxy (III).

While Cordeiro has not assigned a specific date to the Energularity, he believes that it will happen by the end of this century, pending predictions of the Singularity and Methuselarity. Leading up to the Energularity, Dr. Cordeiro foresees a full transition from fossil fuels to renewable energies in the 2030s and 2040s. By 2045, he believes the whole planet will be powered by renewable energy that is predominantly solar.

This trajectory is key to one of the feats that Cordeiro looks forward to most: space travel. Like Elon Musk, he believes that the first humans will inhabit Mars within the next decade. In fact, Cordeiro participated in the first Mars simulation, "Made in Spain," with the Astroland Interplanetary Agency. "I am convinced that this will happen soon, and for that we need lots of energy. But, fortunately, we will have lots of energy." After finalizing the Spanish Mars simulation, Cordeiro is confident: "The first Martians will be humans."

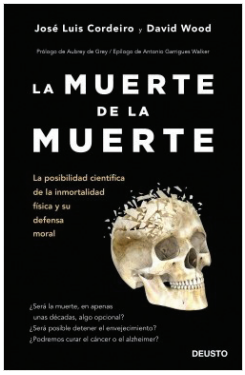
The death of death

Three years ago, Cordeiro teamed up with HumanityPlus colleague and smartphone pioneer, David Wood, to write his most ambitious book to date: *The Death of Death*. While the English version has yet to be released, the second edition in Spanish (*La muerte de la muerte*) has become a bestseller in Spain and Latin America, as has the first edition in Portuguese (*A morte da morte*) in both Brazil and Portugal.

The book's success can undoubtedly be credited back to the authors, but as Cordeiro humbly notes, the subject matter is also very unique and timely. "The death of death is the most revolutionary idea in human history. There is nothing that compares to this. Forget about Galileo. He defended something very important, that the Earth was not the center [of the universe], but not immortal. Or even Darwin, that we come from monkeys. But just the fact that we can now become immortals... This is really, really something. It's actually the first dream of humanity."

History provides ample evidence in support of this assertion, which Cordeiro readily describes. *The Epic of Gilgamesh*,

believed to be the earliest surviving piece of literature, is about a Sumerian king seeking immortality. The Egyptian *Book of the Dead*, essentially a manual for an eternal afterlife, dealt with immortality. As he so concisely puts it, "All the literature of humanity begins with immortality."



The cover of Cordeiro's thirteenth book, which translates to The Death of Death *in English.*

Going forward, Cordeiro and Wood plan to release Korean and Russian editions before moving forward into the English market. From there, they plan to break into Asian markets, starting with Japan and China. It's a lot of work, but Cordeiro is unfazed. He says, "People need to know that we believe in this so much that we are giving away all the money from the book to scientific research on longevity." Indeed, any book proceeds support local facilities in Spain and Brazil, as well as Aubrey de Grey's SENS Research Foundation in Silicon Valley.

Cordeiro holds a floppy disk at the 2017 International Longevity and Cryopreservation Summit in Madrid.

Plan B: Cryopreservation

As the eighth chapter in his book details, the death of death, like any Plan A, needs a Plan B. For Cordeiro, and many others anticipating the Singularity, this is cryonics. For him, it provides an important means of saving loved ones who may not survive the time remaining between now and the anticipated spread of anti-aging treatments. He also considers cryonics a wise safeguard against the unforeseen. "If my mother doesn't make it or even if I don't make it, I believe in cryonics. Therefore, we need to let people know that cryonics is real, is scientific, and that I support it. I want it for me, I want it for my mother, I want it for my family and friends. I want it for everybody who needs it."

Given his fervor, it might be surprising to learn that Cordeiro is not currently a member with any cryopreservation facility. He has certainly visited them all and can probably list them out faster than most. As he explains, however, geography and travel are heavy factors in his life and this decision. Cordeiro has three different country bases, none of which are in the U.S where resources are arguably strongest. He is also in a different city virtually every week.

All that said, the most significant and compelling reason behind his membership status, is this: Cordeiro wants to create the first cryonics facility in Spain. It is the country of his parentage, where most of his family still resides, and also the homebase in which he spends most of his time between trips. As fate would have it, it's also a country where cryopreservation is neither legal, nor illegal, but rather alegal.

The gray area positioning of cryonics in Spain means Cordeiro has his work cut out for him. "Laws in Spain are very restrictive, and in Spain you currently only have two choices. You now have burial and cremation." Nevertheless, Cordeiro applies a historical perspective for some fact-based optimism in this uphill battle. He explains how just fifty years ago, the rigorously Catholic Franco regime permitted burial, and burial alone, in Spain. Cremation was actually illegal. At today's accelerating rate of change, Cordeiro is hopeful that he can help bring about the legalization of cryonics in the near future, opening the doors for the creation of a Spanish facility, or helping with another one in the European Union.

In the interim however, Cordeiro has already enjoyed a great win en route to his goal. With the help of sympathetic legal and medical parties, he completed the first cryopreservation in the history of the Spanish mainland for a good friend: Javier Ruiz Álvarez. That individual's brain was declared an organ donation, and then donated to scientific research, which enabled Cordeiro

to move him from Spanish soil to a new cryopreservation facility in Dresden, Germany.

From death to life

"I'm now basically dedicating my life to curing aging, to seeing the death of death. That is my objective," says Cordeiro. In the next five years, he plans to write a fourteenth book as a counterpart to *The Death of Death*, called *The Life of Life*. The book's premise will be based on the first treatments to reverse aging, which he fully expects to appear in this same timeframe. Cordeiro believes that the emergence of these treatments will necessitate the discussion of not just life extension, but also life *expansion*: expanded capabilities, expanded dreams, and expanded ideas.

"That is why I'm dedicating my time, my money, my thinking and my writing to that, because we live in the most incredible time to be alive, and I don't want people to die. It is the worst human tragedy. Death is horrible, and we are so close to curing aging. Thus, we have to do it now, we need to act, we need to react. We are in between the last human mortal generation and the first immortal generation, and we should strive to be among the first immortals and not the last mortals." ■

To contact Dr. José Luis Cordeiro with any questions or publishing interest, please email him directly at jose_cordeiro@yahoo.com. For those readers who speak Spanish or Portuguese, he encourages you to purchase or gift a copy of *The Death of Death* on Amazon. All proceeds are being donated to longevity research.

Q&A

What was your favorite part of writing* La Muerte de la Muerte*?

Learning more and more about the rapid advances of anti-aging and rejuvenation therapies. Anyone has to learn a lot before explaining anything to anyone else, and even more in such a controversial issue as the possibility of immortality. Writing is by itself learning, and enlightening!

Many transhumanists are reticent to use the word "immortality." How do you define it and why do you use it?

In a sense, immortality is impossible to guarantee completely. Immortality means the elimination of death, but even if we stop aging completely, there will still be accidents, homicides and suicides, very sadly. Even if we become postbiological and can copy our minds and recreate them in another substrate, there will always be death lurking behind some bad scenarios. Mind uploading might not survive some cataclysms in the galaxy, like a gamma-ray burst, a neutron star explosion, or a collision with a black hole. In fact, we don´t even know for sure how the universe might end, if it ever does, or how we could avoid such ultimate tragedy with much greater intelligence. Therefore, a better word might be "amortality," but it then requires a longer explanation. Most people understand the meaning of "immortality," even if not completely accurate, but few people have heard of "amortality," even if more precise.

What was most memorable about your interview with sci-fi author Arthur C. Clarke in his last public interview before he died in 2008?

His sense of humor. As a good Englishman, even if long retired in beautiful Sri Lanka, Sir Arthur C. Clarke kept a healthy British humor, very witty and sometimes sarcastic. It was a tragedy that he believed in cryonics, and wrote about it in his books, but his death in Sri Lanka basically made it impossible to perform any real cryopreservation there at the time, unfortunately. He famously wrote, "Although no one can quantify the probability of cryonics working, I estimate it is at least 90%—and certainly nobody can say it is zero."

You have predicted that solar power will become the greatest source of energy leading up to the Energularity. Why do you think solar will win out over other renewable energies?

The sun has powered our planet since the beginning, and it will continue to do so. We receive over 8,000 times more solar energy than all of humanity uses, at current energy levels. Put another way: if we could capture all solar power reaching our planet in one hour, that would be enough to power all of humanity for one year. And still another way to think about this: if we can capture a bit less than 1% of 1% (yes, less than 0.01%) of all the energy

that reaches from the sun to the Earth, that would be enough for our current civilization. We can capture even more solar energy once we go into outer space, where the sun never sets, and where there are no clouds nor atmospheric filtering. Even fossil fuels and biofuels are derived from solar energy, and ultimately, we will be relying mostly on energy from our star.

We are already experiencing the transition from fossil fuels to renewable fuels, and solar energy is now becoming the cheapest energy source in most places around the world. Solar energy is not just more environmentally friendly, it is becoming cheaper and cheaper since the prices continue to drop, and the production keeps increasing exponentially. In the next two decades we will have finished the transition to cleaner energy, including solar energy, plus storage, and electric vehicles, and we will keep moving forward towards a civilization Type I according to the Kardashev scale, powered by more solar energy to start the colonization of space. By this time, we should also be able to produce fusion energy, which is indeed the energy of the stars.

How do you think the death of death will impact planetary population?

At the end of the eighteenth century, the British scholar Thomas Robert Malthus was worried about the population of the world when there were only about one billion people. He was even more worried about Great Britain reaching ten million people, which he considered too many for the available resources. Maybe he was right, at his time, but then the Industrial Revolution started, coupled with the mechanization of agriculture, both of which allowed us to do more with less. In fact, thanks to continuously advancing science and technology, we are continually doing much more with much less.

The problem today is actually not too many people, but too few people. Many countries are already stabilizing their populations, and most advanced countries in Europe and East Asia have declining populations. Japan is actually undergoing a population implosion, and some experts say that in two centuries there might not be Japanese people left. Germany, Italy, Russia, and several other countries also have declining populations, and soon China and Korea will join. Because of the "one child" policy in China, it is estimated that China might lose 200 million people from its peak to the end of the century. The world has never seen such a demographic contraction in times of peace. In general, the population of the world might stabilize in the coming decades and then start declining, so the problem is not overpopulation, but underpopulation in the future.

We also know today that the human brain is the most complex structure in the known universe. That is why civilization has advanced so much in the last couple of centuries with more people thinking, innovating, and creating better futures for humanity. People don't come only with a "mouth" and an "ass." We come with a brain that is able to resolve many problems as the most complex structure in the universe, as of yet. We need more brains, not less.

How likely do you think it is that posthumans will become connected to the Earth, à la Disney's Avatar?

It is impossible to imagine how we will evolve after the technological singularity, when artificial intelligence surpasses our own unenhanced human intelligence. Once we become more intelligent, augmented, we will visualize possibilities that we can't imagine now. This is like asking some bacteria what they think about our world. The evolution from human to posthuman will probably be much more transcendental than from bacteria to human. The future possibilities are almost unlimited, and we have seen nothing yet. We might in the future not only connect directly to the Earth, and to all of us, but also to the entire universe. We will soon know, as my friend Ray Kurzweil explains, hopefully by 2045, if not earlier.

What events, factors or otherwise do you believe could potentially delay or even prevent the Singularity from occurring?

There is a long list of existential risks. For example, a nuclear war would spoil the Singularity as would a comet crashing into our planet. Even though there are great risks, we need to be optimistic about a better future. As Sir Arthur C. Clarke told me in Sri Lanka: most of our ideas become self-fulfilling prophecies. If we believe that we will self-destroy, then we probably will. But if we believe that we will transcend and evolve into something much better and superior, then we will most likely become posthumans in an advanced civilization with super longevity, super intelligence, and super happiness. That is a future I can relate to. As my trekkie friends like to say: live long and prosper!

Big Chronology of Life on Earth

By José Luis Cordeiro

Two possibilities exist:
Either we are alone in the universe or we are not,
both are equally terrifying.

Sir Arthur C. Clarke, 1962

Live long and prosper.
***yIn nI' yISIQ 'ej yIchep** (Klingon pronunciation).*
dif-tor heh smusma (Vulcan pronunciation).

Commander Spock from Vulcan in the Spaceship USS Enterprise, 2260

To put into perspective a complete chronology and evolution of life on our tiny planet Earth, I summarize here what I consider the most relevant information from the very distant past to our immediate future. The objective is to reach a better understanding about the long-term evolution of life, considering also the nature of exponential changes.

Big History is a new discipline that allows us to analyze with a multidisciplinary focus the way events follow each other throughout time. Starting with a huge time scale from the faraway past to the present, we can see that there is an acceleration of the speed of changes that should continue now, thanks to exponential technologies. My futurist friend Ray Kurzweil, in his bestseller *The Singularity is Near*, explains the acceleration of these changes very well, and that is why I use some of his predictions to the end of the 21st Century.

Interested readers are invited to contact me directly to continue making this chronology better in the future. All comments are more than welcome, and you can find more information about my book (with my British co-author David Wood) here: https://hpluspedia.org/wiki/La_muerte_de_la_muerte

The full version of this abbreviated timeline can be found here: https://lifeboat.com/ex/big.chronology.of.life.on.earth

Millions of years ago (Ma)

~13,800 Ma	Big Bang and formation of the known Universe
~4,500 Ma	Earth formation
~ 4,000 Ma	First unicellular life (prokaryotes without cellular nucleus)
~ 250 Ma	First dinosaurs
~ 65 Ma	Extinction of dinosaurs and development of primates
~ 15 Ma	*Hominidae* family (big primates) appears
~ 0.2 Ma	*Homo sapiens* species appears
~ 0.1 Ma	*Homo sapiens sapiens* comes out of Africa and starts colonizing planet Earth

Thousands of years ago

< 40,000 BC	Rock paintings appear, symbols of deities, fertility, and death
< 4,000 BC	Possible invention of the wheel in Mesopotamia
< 3,500 BC	Egyptians invent hieroglyphs and Sumerians cuneiform writing
420 BC	Hippocrates writes the *Hippocratic Treaties* and creates the *Hippocratic oath*
350 BC	Aristotle writes about evolutionary biology and tries to classify animals

First millennium AD

400 AD	First Christian hospital founded by Saint Fabiola in Rome
870 AD	Persian doctor Ali ibn Sahl Rabban al-Tabari writes a medical encyclopedia in Arabic

1000 – 1799 AD

1030	Persian polymath Avicenna writes the *Canon of Medicine* (used until the 18th Century)
1541	Swiss doctor Paracelsus has made great progress in medicine (surgery and toxicology)
1553	Spanish doctor Miguel Servet studies pulmonary circulation (burnt at the stake for heresy)
1590	Microscope is invented in the Netherlands and makes medicine move forward faster

1665 English scientist Robert Hooke uses the microscope to identify cells

1675 Dutch scientist Anton van Leeuwenhoek starts microbiology with microscopes

1774 English scientist Joseph Priestley discovers oxygen and starts modern chemistry

1780 US polymath Benjamin Franklin writes about curing aging and human preservation

1796 English doctor Edward Jenner develops the first effective vaccine against smallpox

1800 – 1899 AD

1804 Global population reaches 1,000,000,000 people

1818 English doctor James Blundell performs the first successful blood transfusion

1842 US doctor Crawford Long accomplishes the first surgery with anesthesia

1859 English scientist Charles Darwin publishes *The origin of species* in London

1865 Austrian monk Gregor Mendel discovers the laws of genetics

1870 Scientists Louis Pasteur and Robert Koch publish the microbial theory of infections

1892 German biologist August Weismann proposes the "immortality" of germ cells

1895 German physicist Wilhelm Conrad Röntgen discovers X-rays and their medical uses

1896 French physicist Antoine Henri Becquerel discovers radioactivity

1898 Dutch scientist Martinus Beijerinck discovers the first virus and starts virology

1900 – 1959 AD

1906 German doctor Alois Alzheimer describes the disease named after him

1927 Global population reaches 2,000,000,000 people

1928 English scientist Alexander Fleming discovers penicillin (first antibiotic)

1934 Scientists at Cornell University discover caloric restriction for life extension in mice

1951 HeLa (Henrietta Lacks) cancer cells are discovered to be "biologically immortal"

1953 Scientists James D. Watson and Francis Crick demonstrate DNA's double helix structure

1954 US doctor Joseph Murray transplants the first human kidney

1959 Global population reaches 3,000,000,000 people

1960 – 1999 AD

1961 US scientist Leonard Hayflick discovers a limit on cellular division

1967 US academic James Bedford becomes the first patient in cryopreservation

1974 Global population reaches 4,000,000,000 people

1975 Different scientists finally discover the telomeres (first considered in 1933)

1978 First human being is born thanks to artificial insemination (Louise Brown in England)

1987 Global population reaches 5,000,000,000 people

1990 First gene therapy is approved to treat an immune disorder

1990 FDA approves the first genetically modified organism (Flavr Savr tomato)

1993 US biologist Cynthia Kenyon increases several times the lifespan of *C. elegans*

1996 Scottish scientist Ian Wilmut clones Dolly, first cloned mammal (a sheep)

1999 Global population reaches 6,000,000,000 people

2000 – 2019 AD

2001 US scientist Craig Venter announces his sequence of the first human genome

2009 English scientist Aubrey de Grey creates the SENS Research Foundation

2011 Global population reaches 7,000,000,000 people

2018 First commercial treatment with gene therapy using CRISPR

2018 Birth of first CRISPR babies to avoid HIV infections in China

2019	FDA approval of the first senolytics treatments for life extension

2020 AD – 2029 AD (some possibilities)

2020s	Vaccine against malaria
2020s	Vaccine against HIV
2020s	Cure for the majority of cancers
2020s	Cure for Parkinson's disease
2020s	3D bioprinting of simple human organs
2020s	First manned trips to Mars (Elon Musk)
2025	Molecular assemblers (nanotechnology) are possible (Ray Kurzweil)
2026	Global population reaches 8,000,000,000 people according to the US Census Bureau
2029	Longevity escape velocity is reached (Ray Kurzweil)
2029	An advanced AI finally passes Alan Turing's test (Ray Kurzweil)

After 2030 AD (more possibilities)

2030s	Cure for Alzheimer's disease
2030s	Consolidation of the first human colony in Mars (Elon Musk)
2039	Mental transfer from brain to brain becomes possible (Ray Kurzweil)
2042	Global population reaches 9,000,000,000 people according to the US Census Bureau
2045	Aging is cured and death becomes optional (Ray Kurzweil)
2045	The Singularity: AI surpasses all human intelligence (Ray Kurzweil)
2049	Distinction between reality and virtual reality disappears (Ray Kurzweil)
2050s	First reanimations of cryopreserved patients (Ray Kurzweil)
2072	Picotechnology starts (pico is one thousand times smaller than nano, Ray Kurzweil)
2099	Femtotechnology starts (femto is one thousand times smaller than pico, Ray Kurzweil)
2099	Lifespan becomes irrelevant in a world of "amortality" ■

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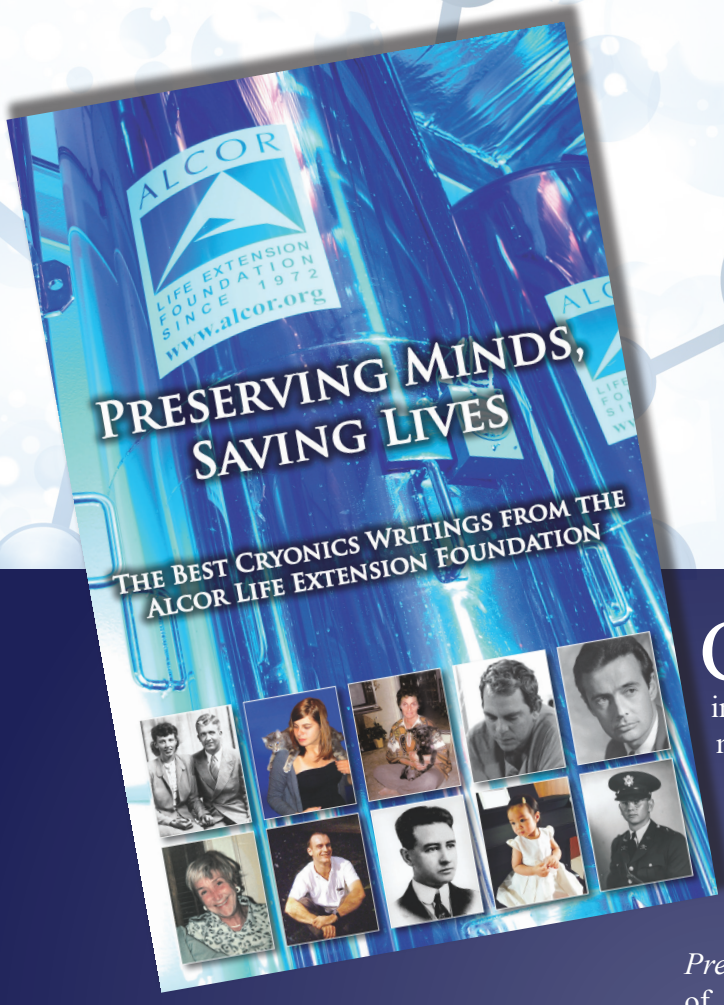

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"Society's failure to take cryonics seriously is a tragedy that is probably costing countless lives. Alcor, notably via its magazine, is leading the fight to change that."
– Aubrey de Grey, Ph.D.
Biomedical Gerontologist and Chief Science Officer of the SENS Research Foundation

"Alcor appears to be the leading organization in the application of cryonics in medicine. I'm proud to be a part of this effort."
– Michael D. West, Ph.D.
Stem Cell Scientist and Chief Executive Officer of BioTime, Inc.

Hal Finney Cryonics Research Fund

The Hal Finney Cryonics Research Fund aims to advance the technology behind cryopreservation for future revival. The fund was established in 2018 through a generous donation by Brad Armstrong, a successful cryoptocurrency entrepreneur, Alcor member, and admirer of cryoptocurrency pioneer Hal Finney.

You can read more about Hal's life and tremendous contributions to humanity below.

The fund is currently focused on research to:

- Advance the cryopreservation of brain tissue or whole brains, or
- Advance the clinical practice of cryonics, including patient stabilization, transport, and cryopreservation practices.

Project proposals of all sizes will be considered. For examples of the kinds of projects that will be considered for funding, you can read about past and ongoing Alcor-funded projects at https://alcor.org/AboutAlcor/researchcenter.html. These should be taken as indicative of topics relevant to Alcor's mission, but should not be considered exhaustive.

To be considered for funding, please submit a short (1/2 to 1 page) letter of interest to info@alcor.org that includes:

1. Principal investigator and key research personnel
2. A brief summary of the project goals, approaches employed
3. Estimated budgetary needs
4. Overall significance if the project succeeds
5. Any other information you deem worth including

Letters of interest are reviewed on a rolling basis by Alcor's research committee, and if the project is of interest you will be contacted to submit a full application. The length of a full grant application varies according to the size of the request, but it is typically shorter than government research grant proposals (e.g. NIH, NSF, CIHR) of the same scope. ■

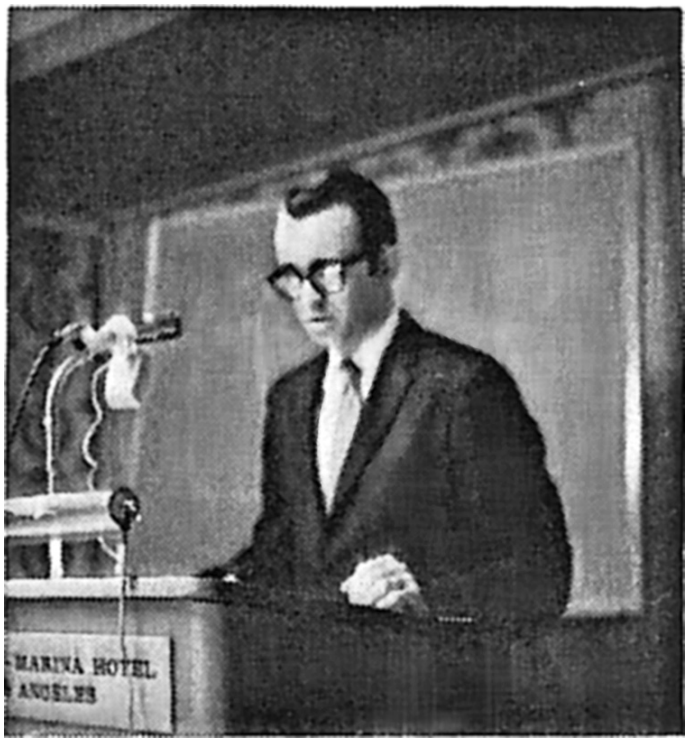
Cryonics and The Funeral Director

Address given by Joseph A. Klockgether, Jr. at the Cryonics Conference held at the Airport Marina Hotel, Los Angeles, Calif., May 15-16, 1970.

I'm going to tell you about the potential for involving funeral directors in the cryonics movement. I'll show you that they can be motivated, that their basic professional posture compels them to cooperate in the development of cryonics, and that their assistance can and will be of great value.—Where do we start?

Well, let's start with me. I'm a funeral director, and I'm extensively involved with the cryonics movement. But I didn't start out that way!

My first impression was that cryonics was some sort of hoax! Maybe these guys were trying to take over the funeral director business, I reasoned.



Klockgether delivers his address at the Los Angeles Cryonics Conference, May 1970. (Illustration from the The Outlook, *Jun. 1970, cover.)*

At any rate, I knew I had to find out more. If this was something wrong and deceitful, I knew I had to try and stop it. If it was genuine and was going to come along no matter what, I wanted to be part of it. I'd read articles by Bob Nelson and was beginning to be a little fascinated by the cryonics idea myself. It was now time for me to start talking to people, and learning more about it.

I got in touch with Bob Nelson, since he was nearby and appeared to know about as much concerning cryonics as anyone.

Bob hadn't had very favorable previous experience with funeral directors, and told me frankly they seemed complacent and unwilling to consider new ideas.

Bob and I talked about this a great deal, and began to see each other's points of view. Since then, we've become essentially members of the same team.

Let me tell you a little about the basic outlook of funeral directors. You need to understand this—their primary orientation is service—through this characteristic, they will follow you almost anywhere.

1. First of all, funeral directors are responsive to what the client wants. The funeral director has a deep respect for life; he sees, every day, the tragedy and pain loss of life brings. He values life—when he deals with persons who regard a human body as less than his values might be, he provides a service for them, one which he may not prefer nor would advise. But it's what they want that comes first with him and he does what he can to help with the same ability, responsibility and integrity as he gives to each and every one of his clients.

2. The funeral director's role of service extends into smoothing all details for persons in a state of emotional trauma. He has a deep respect for life and for individual wishes, but in addition, the funeral director above all wants to help. He can account for a myriad of details on a short scale of time. I don't need to tell you how important that capability is for a person, let's say, in a terminal condition of cancer, with dissenting friends and relatives on one side and dedicated cryonics associates on the other.

3. Funeral directors, in times past, have accommodated almost any bizarre and unusual request an emotionally distraught client can make. It's the client's feelings they're concerned with, not their own! As time goes by, funeral directors will progressively become convinced that service to persons who want cryonic suspension is fully within their legitimate

sphere of activity, and will finally realise that this area of their service is the most important extension of their roles that has ever occurred. What the funeral director must know, before he commits himself to participation in cryonics, is only that he will not become the injured object of public ridicule. Ladies and gentlemen, that's a crucial role of cryonics societies and you are all well aware of it. Cryonics societies will give cryonics a measure of respectability through public familiarity that will lead the funeral director into the kind of participation that is proper for him.

Now let me tell you why the cryonics movement needs the support of funeral directors, and how they will be able to help.

1. I will show you that funeral directors have an unparalleled knowledge of the legal expertise required for successful cryonics operations.

2. They are ideally situated for educating the great majority of uninformed persons who will not choose to energetically seek out information about cryonics.

3. Further, they have at their disposal a nationwide distribution of 24 hour facilities, that can be converted for cryonic suspension operations and maintained in constant readiness with very little investment burden.

4. The traditional services funeral directors offer are easily extended into the transitional roles required as hundreds of millions of persons become accustomed to the ideas associated with vastly extended lifetimes.

The legal problems that arise with the introduction of cryonic suspension will be extremely complicated and varied, since they will differ with each state and community in which legislation is enacted and administrative policies are formulated.

1. At the moment of clinical death, legal responsibility of care passes from the doctor's hands into those of some other organization.—Right now, 99% of those "other" organizations are run by funeral directors. Universally, funeral directors are intimately knowledgeable in the red tape involved with the handling of and transportation of the clinically dead. They know the ropes and can point the way toward whatever is required for workable cryonic suspension operations in every locality.

2. Further, as an organized whole, funeral directors can help with long term legal problems. They can help bend and retie red tape through legislative action so it fits the needs of cryonics societies and their members' needs. This influence can benefit cryonics in terms of accelerated, smooth, and well prepared growth. In another way, I guess I'm saying that you will want the majority of funeral directors on your side, and not on some other opposing side.

Across the country and around the world, in thousands upon thousands of communities where no organized cryonics movement exists, well informed funeral directors can be the first source of information for persons with a casual level of interest.

Funeral directors are usually quite active in civic affairs.—In personal contacts and in local speaking engagements, a funeral director who is familiar with cryonics will spread the idea.

Such individuals in fact may frequently turn out to be the center of community interest in cryonics. They will try to stay up to date on what is happening and may frequently be the first to start a cryonics society in their own towns.

In any case, an informed funeral director will be able to discuss cryonics frankly and openly with his friends and clients well before desperate circumstances arise. As you are well aware, by the time a point of death approaches, it is frequently too late.

The assistance of persons with advanced preparations is not a new role for funeral directors. They've been doing it for most of recorded history.

In respect for the feelings and desires of persons seeking their help, they are unlikely to make suggestions that are radically new at the last minute.

In respecting the right of each individual to determine the course of his own life, funeral directors will likely continue to offer all alternatives in the early years of cryonics. Even after a proven cryonic suspension process is available, many who are in a terminal illness may still insist on what they will refer to as a "natural" death and on burial or cremation. In other cases, uncompromising advocates of cryonic suspension may not want perfusion and full cryonics processes for a person found days after death in the woods. If this seems "overboard in all directions" to you, recognize that it is going to be part of a funeral director's normal day to day role of service.

Freezing with and without perfusion may be "technical alternatives", particularly for that guy brought in from the woods, perhaps with strong relationship to the temperature in those woods.

In any case, the funeral director's primary orientation will be—simply—service. He will try to provide what the individual says he wants, or what he has said that he wanted.

Just about anywhere you happen to be, a funeral director will be nearby—and he's available 24 hours a day.

In the cryonics context, he's going to have to be operational on an emergency, rescue basis.—Studies have shown that a cryonics rescue helicopter patrolling a one hundred square mile area can reach any inhabitant in less than five minutes after an electromagnetic alarm is initiated. This is what it will

eventually come to.—For the present, telephones and converted ambulances with 427 cubic inch engines will have to do.

At this time, a minimum change to facilities will permit funeral directors to carry out "state of the art" suspensions. As the state of the art advances, so will the required equipment, but the demand will grow too, and will finance the improvements.

As you might anticipate, a proven cryonic suspension process or even a substantial improvement in the state of the art will bring on a level of demand that will impose an overload on every competent person knowledgeable in cryonics. The more persons who become conversant with cryonics and who stay up to date on it, the better. What will we do when this explosion in demand comes? We know that we are all waiting for it! Are we even remotely prepared for it?

Assuming that the "explosion" comes through the development of some relatively sophisticated process, the demand will be primarily for that process! While a parallel effort of very rapid education, updating and retrofit will be necessary, just as important will be protection against simple incompetence and fraud. Too much is at stake for antiquated methods to be misrepresented as the product of recent discoveries. Professional standards must be established and maintained. The funeral director, with his orientation toward service and his respect for the value of human life, can and will help to assure competence and correct representation of the available processes.

When one thinks of funeral directors, the thing that sometimes comes to mind first is the viewing room and some form of ceremony. Let me assure you that until a clear and universal conviction concerning proven cryonic suspension processes is spread across the land, there will still be an extensive need for this kind of event.

Many of your friends and relatives will be fully convinced that persons suspended are gone forever. They will express their grief by a ceremony, somewhere, no matter what you believe. The cryonics oriented funeral director, by providing a service that seeks to explain how good the chances really are, can blend two very different kinds of hope and possibly influence many persons you would like to see again, to see that your choice is carefully considered, fully rational, and attractive.

The value of human life is so great, and death is such a wholesale waste, that it is always difficult to believe that a human personality has gone out of existence. That is part of the reason friends and relatives come to funerals—to face the reality of what has happened. In the cryonics context, the same feelings will crop up in a different way. Perhaps the last time you saw a person he was well and happy.—Now they tell you he is on his way to a state of full cryonic suspension. Is it really so? And how did it happen? And what level of suspension process was able to be utilized, under what circumstances? Depending on these factors, it may be a long time before you see this person again, even if a proven suspension process (under ideal circumstances) is available. In a world where cancer is not fully curable, where aging processes are not reduced to control, where people have heart attacks and are not reached rapidly, there will be some considerable uncertainty about whether you are ever going to see this person again. Just before your friend goes through final capsule insertion into a permanent storage area, you and his other friends may wish to get together for some sort of farewell event, in anticipation of the centuries that may pass before you speak again. I am not going to speculate about what, exactly, you will want to do or see. My role, as a funeral director, will be to help. Suggestions as to innovations in service, and how these may effectively be accomplished, will come from the cryonics societies' members, and will be broad in spectrum.

In the long term, over periods of centuries, the matter of custody will be important. Look around you at the short term catastrophic instabilities of current domestic and international affairs, and raise the question of how you and your trustee-protected resources will weather really extended periods of time. This is not a subject I am prepared to discuss in detail at this time, but I will simply suggest that it's a good thing to think about before you're frozen. When a proven process of cryonic suspension is perfected, the opportunities and requirements for innovation in this area will be virtually unlimited. The problems are not simply medical, although anything that shortens the required duration of suspension is of critical importance. The problems are not primarily legal, for a solution in today's legal context won't help if the ground rules are overturned. If the problems cannot be isolated from political perturbations, resign yourself to the most uncertain of outlooks. Needless to say, money alone won't solve the problem, although it may make certain solutions feasible. Think about these things—the context is wide open—I think funeral directors are going to offer some very innovative proposals in this area as cryonics seizes the imagination of the whole human race.

Finally, coming back to funeral directors' involvement with cryonics, there is an open challenge. A challenge that states funeral directors may oppose cryonics and wither with the past, or they may help roll back the doors into a fantastic future.

The funeral director who is going to survive and grow must become fully informed concerning cryonics, so that he can intelligently serve cryonics-oriented clients and help the community learn gradually about what will be the biggest jump in the evolution of life to date.

Funeral directors should add their efforts to those of cryonics societies, in emergencies, and in the long haul of transition out of the "death and taxes" orientation of society in general.

Together, funeral directors and cryonics societies can prepare for a day when their biggest challenge will be to establish and maintain the highest standards of service for people who want to extend their lives without limit. ■

Comment on Joseph A. Klockgether's "Cryonics and the Funeral Director" (2020)

By Aschwin de Wolf

Joseph Klockgether's address about the potential collaboration between funeral directors and cryonics organizations is a product of its time in terms of optimism about the growth of cryonics but remarkably up-to-date in terms of what funeral directors can do to assist in a successful human cryopreservation.

Funeral Director assistance in cryonics can come roughly in three forms:

1. Ad-hoc utilization of cooperating funeral directors to assist in procedural, logistical, and regulatory aspects of a cryonics case. Often these funeral homes are identified after contacting several of them in the course of managing a cryonics case.

2. Repeated cooperation with a known funeral director. In such cases, a cooperating and dependable funeral director was identified prior or during a case and this relationship is continued in future cases.

3. The cryonics organization has a close relationship with a funeral director. In the most favorable situation, the funeral director is strongly supportive of cryonics or even has cryonics arrangements himself. The funeral director (or his staff) attends cryonics meetings and training and actively collaborates to optimize his role in a cryonics case.

Funeral director cooperation of the first kind cannot always be avoided but basically reflects poor planning of the cryonics organization or regional group. Or perhaps one might say that it reflects a lack of interest of the cryonics organization to encourage local groups or individuals to establish enduring and productive relationships with local funeral directors. In cases of ad-hoc or sporadic contact, a funeral director cannot be expected to correctly comply with any kind of cryonics logistical or shipping procedures unfamiliar to him. This is not a fault of the funeral director; it is simply unrealistic for a new funeral home to properly educate themselves about cryonics procedures and shipping instructions. Such circumstances call for detailed documentation, good communication, and having (local) people onsite to ensure compliance with cryonics organization directions.

If a funeral director is well known to the cryonics organization, such requirements can be somewhat relaxed but having people onsite and providing photographic evidence of proper compliance and local verification remains a must.

If a cryonics organization has a strong, enduring, relationship with a funeral director (or the funeral director is a cryonicist himself) the kind of scrutiny that would be proper would be similar to the kind of scrutiny that would be recommended for cooperating with existing SST (Standby, Stabilization and Transport) organizations.

Three issues that need considerable attention in cooperating with funeral directors are (1) transport from the hospital (or hospice) to the funeral home (2) surgical assistance (3) shipping of the patient. There is such a vast difference between comprehensive cryonics stabilization procedures (rapid cooling, cardiopulmonary support, and medications administration) that basic patient pick-up and transport would only be an option in case the cryonics organization (or its contractors) cannot arrive in time and local assistance is not available. The only exception to this rule is where a funeral home is an active, well-staffed, component of existing SST operations (a rarity). A similar argument applies to surgical assistance. If no appropriate medical staff can be deployed in time, a funeral director can be asked to assist in establishing vascular access under the supervision of the cryonics organization and on-site team members. This would usually entail neck vessel or femoral surgery to assist in washout or field cryoprotection.

One of the most important and sensitive topics is the assistance of a funeral director in cooling and shipping. These tasks often seem so intuitively simple that there is a tendency to trust funeral directors to comply with the cryonics organization's directions. Unfortunately, cryonics organizations have learned the hard way that verbal directions or even detailed written instructions are not sufficient to ensure compliance. As much as there are overlapping areas of interest of funeral directors and cryonics organizations, funeral directors are usually not in the business of applying rapid (emergency) procedures. One issue of particular concern is a misunderstanding of ice packing instructions (too little, too late, water ice vs dry ice) and long-distance shipping requirements (insulation, leaking prevention, replenishing the ice used during the cooling process prior to shipping). Local assistance, oversight, and

photographic documentation prior to authorization shipment are essential to avoid disastrous outcomes (warming or thawing of the patient).

The observations above may make it seem that the productive relationship between funeral directors and cryonics organizations is more akin to getting out of each other's way than the magnificent cooperation envisioned in the Klockgether article. Given the low popularity of cryonics it is not likely that any funeral home can expect to substantially grow its operations and profits in dealing with cryonics organizations. Carefully nurturing enduring (local) cooperation between cryonics organizations and cryonics providers remains important, however, and avoiding last-minute, ad-hoc utilization of funeral directors should be a last resort. In smaller countries having an actively interested and proactive funeral director can be key for delivering cryonics services in particular. ■

Joe Klockgether receives award from Jan Jewell for long service to Alcor at conference in Nov. 2002 (Reference: Cryonics 23(4) (4Q 2002), esp. 10-11)

FOR THE RECORD

Cryonics in New York: Years with Alcor, 1986-1994 (Part Seven of an Ongoing Series)

By R. Michael Perry, Ph.D.

Introduction

Readers may remember that, in 2013, we ran a series of articles on the early history of cryonics in New York (six articles in all).[1] Our coverage mainly focused on the crucially important decade that started in 1964 with the publication of Robert Ettinger's book, *The Prospect of Immortality*, that largely started the cryonics movement.

Affairs with the New York cryonics group entered a "twilight" phase following their last freezing, which occurred in April 1974. Many of the important, early players had either dropped out or gone elsewhere. One who stayed, though, was Curtis Henderson. An attorney by profession, Curtis had been the principal organizer of the Cryonics Society of New York and his presence in the area, extending to 1998,[2] provided continuity and encouragement to others. So, in fact the New York group continued to exist, and (though Curtis himself was cryopreserved in 2009[3]) still persists today.

The earlier series on cryonics did cover events after 1974; however, there was much that was unreported which can be reconstructed from newsletters and the other usual sources. Here, in "part seven," we summarize the activities of the New York group during an interesting time period, extending from 1986 to 1994, when mainly they had become an Alcor group. It starts (after some preliminaries) with the efforts of Mike Darwin, then president of Alcor, to organize a group in New York, and ends with the cryopreservation of "Mrs. Stone" in 1994, where volunteers of the now organized Alcor New York played an important role. Covered is a most interesting report by Brenda Peters on the successful (for its time) struggle to organize a group with the capability to handle a local case, an issue very pertinent today.

Passing the Torch: Curtis Henderson over to Mike Darwin[4]

Mike Darwin tells us that he first met Curtis Henderson in 1971 when Curtis was on his way to Los Angeles, and from there, to the National Cryonics Conference, held that year in San Francisco. Mike was then about 16, living in Indianapolis. His impression of Curtis was "that he was a cross between Machiavelli and Mephistopheles," an opinion he would change. Just before meeting him, Mike had called "and asked many probing questions about how [Curtis] was storing patients for the Cryonics Society of New York." Curtis's response was well, come and see for yourself, and Mike paid a visit that summer.

The years passed. Mike and Steve Bridge in Indianapolis founded the (ambitiously named) Institute for Advanced Biological Studies in 1977 to further the practice of cryonics. Five years later IABS would merge with Alcor in southern California and Mike would go there and become its president.[5]

Backtracking a little, in a 1981 article Mike would describe Curtis Henderson as

> something rare and precious, far from my sinister first impressions. Above all Curt is an honest, reliable, and unfailing friend. … Perhaps the most valuable and important thing about Curt is his honesty and his advice. I have found both to be of the highest quality. … Curtis Henderson has taught me much of what I know about cryonics and has saved me an incredible amount of grief with good advice and stern admonitions. He has also taught me that sometimes you have to stand up like a man and say what you think regardless of what the timid tell you. He taught me that you must always stand by a friend, for if you can't do that, then even immortality isn't worth a damn. For that last lesson I am eternally grateful.

NY Training Session and Seminar: 1986[6]

With Mike in control of Alcor and Curtis still prominent in the remaining New York group, major contacts were relatively frequent. The first reported was a weekend affair at the beginning of March 1986. Mike's summary of this event starts with another, preliminary trip to enlist a colleague. It continues with the main events, including, finally, "starvation relief" for the hard-working, hungry participants at the close. As an afterword, another important issue is raised: preserving cryonics history; specifically, the records of the former, now inactive, New York organization.

> On Tuesday, February 25th, I flew to Gaithersberg, Maryland to meet with ALCOR Coordinator Bob Abernathy and provide some on-site instruction on use of the ALCOR rescue kit which was deployed with Bob several months ago. On Thursday the 27th, Bob and I drove up to Sayville, Long Island to meet

> with Curtis Henderson, former President of the now inactive Cryonics Society of New York, and to set up the training sessions and public seminar which were to [be] held that Saturday and Sunday at the Holiday Inn at nearby MacArthur Airport.

(Note: "Bob Abernathy" is a pseudonym.) Who attended the event? From the New York area Mike lists Curtis Henderson, Ruth Sears, Irving Rand, and Cindy Magellan. From elsewhere there was Glen Tupler (Florida), Andrea Hines (Virginia), and Jerry Cullins (North Carolina). Mike then goes into details:

> The training sessions were both grueling and productive. Every aspect of initial transport and stabilization of suspension patients was covered in the 16 hours or so of sessions. Both of the ALCOR Coordinators who attended, Bob Abernathy and Glen Tupler, had had some previous training or experience in the medical/cryonics area, so the sessions for them acted primarily to polish skills and learn newly formulated ALCOR administrative and technical policy. Issues such as when not to apply CPR, how to deal with hospital personnel, coroners, and so on were among the "new" material covered.

Mike notes the first use of a new, unpublished Alcor training manual, "a document of basic standards for transport cryonic care and [for use] as a teaching manual." Feedback was sought during the sessions, with "a lot of useful suggestions and questions from attendees" for improvements when the manual would be released later that year. Then:

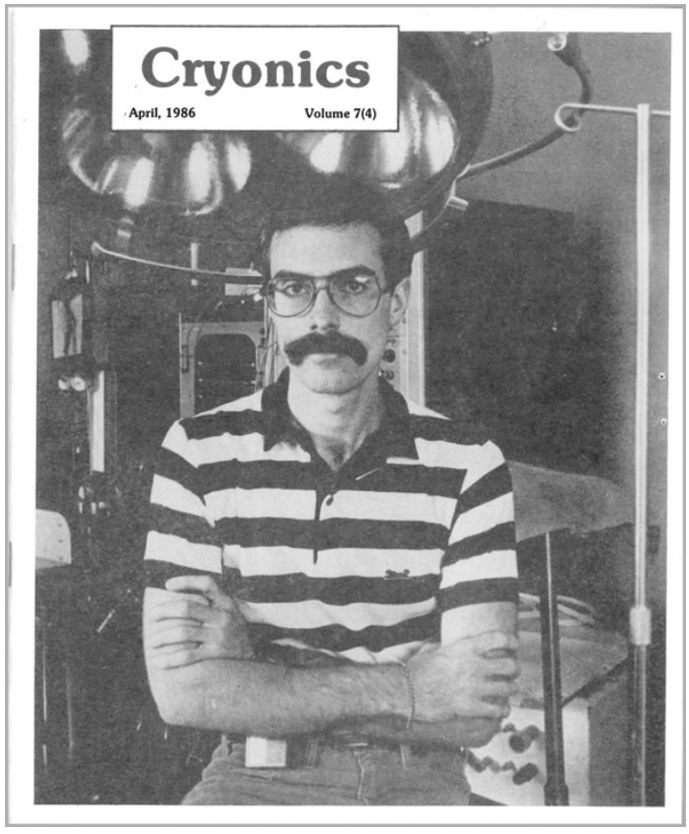
> A very gratifying aspect of the weekend was the opportunity to meet and work with people whom we have had little or no contact with before. Ruth Sears, Andrea Hines, Irving Rand, and Cynthia Magellan are all relative newcomers to cryonics who we hope will become more actively involved with ALCOR in the coming months. It was especially nice to get to meet ALCOR Suspension member Jerry Cullins who, until these sessions, had been just a voice on the telephone.

The sessions extended over a two-day weekend (Mar. 1-2, 1986). At the end of the day on Sunday, a slide show on cryonics was offered to the public, though only a few besides the regular attendees showed up, to make an audience of 12. But the discussion at the end was long and lively, so much that the time of the evening dinner reservation went by, and the hungry audience had to wait nearly two extra hours to be served at a local restaurant. It all went well in the end, however, with everyone getting their fill: "By the end of the evening a stuffed, happy, and relaxed crowd spilled out into the cold Long Island night with warm goodbyes and promises to keep in touch."

At the end of his article Mike notes another, unexpected bonus: "the boxing and relocation of the majority of the archives and records of the Cryonics Society of New York (CSNY)." Curtis was storing these records in his garage, but agreed to transfer them to Alcor's custodial care, at Mike's insistence. Mike, in fact, had a keen interest in preserving historical materials, and his interest helped establish a tradition of historical preservation at Alcor which continues today. Mike concludes:

> The job of doing a preliminary inventory, boxing, and shipping this material was yet another demand on already short time. Bob Abernathy, Curtis Henderson, and I worked long and hard to pack and ship all 21 boxes of archival material. This material is of absolutely critical importance to any understanding of the history of cryonics. The photographs, film, letters, financial records, and other documents, much of it quite amazing and unbelievable, comprise the history of the very first cryonics society. It is an irreplaceable treasure which ALCOR is proud to act as the custodian of, and it complements the archives of the Cryonics Society of California material which came into our possession several years ago.

(Most of these materials are presently stored with Underground Vaults and Storage in Hutchinson, Kansas. Some have been used with the many articles on cryonics history that have appeared in this magazine.)



Mike Darwin, cover of April 1986 Cryonics

New York Discussion Group: 1988[7]

Mike Darwin reports in the May 1988 *Cryonics* that "a number of New York Alcor members have been agitating to form a group – and have succeeded in doing so." The report notes that cryonics largely got its start in New York City in the 1960s. (Indeed, the term "cryonics" was coined by one of the activists there at the time, Karl Werner). By the late 1970s, however, cryonics activity in the area had nearly died out, compared with other major population centers (Los Angeles, San Francisco, Miami) in which, or nearby, cryonics groups were thriving. A decade later, however, there is finally more encouraging news:

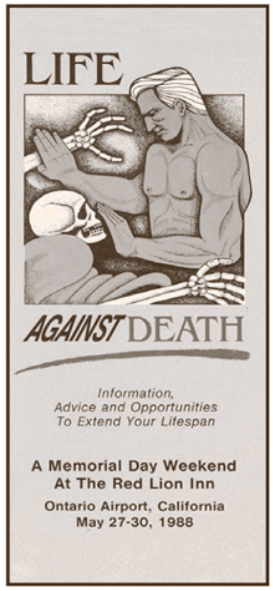
> On March 19th the first meeting the New York Cryonics Discussion Group was held and five people attended. On April 16th a second meeting was held with eight people in attendance. The concentration of Alcor suspension members in the New York City/Long Island area has been rising sharply and the odds look good for the beginnings of a renaissance of New York cryonics.
>
> The principal leaders of this effort have been Jerry Arthus, Curtis Henderson (the former president of the Cryonics Society of New York), and Al Roca. A more recent addition to the Alcor contingent is trust and estate planning attorney Charles Butin, who recently became an Alcor Suspension Member.

The group planned to meet monthly and to establish a Coordinator capability for full emergency response (medications, heart-lung resuscitator, and related transport equipment). A member needing cryonics services in the area could then undergo body washout and preliminary cooling to near water-ice temperature, and as soon as possible be transported by air shipment to Alcor's main facility for cryoprotective perfusion and cooldown to cryogenic temperature. The New York group in addition intended to hold informal discussions and establish a resource database for inquiries about cryonics and Alcor.

There is a further, follow-up notice in the next (June 1988) *Cryonics* to the effect that a regular time and place for monthly meetings has been established, and giving contact information.[8]

Life Against Death Conference in New York: 1988[9]

Saul Kent, who got his start in cryonics with the early New York group, did not end his involvement when he decided to relocate to Florida in 1971. Instead he ended up working with Bill Faloon to form the Life Extension Foundation, selling dietary supplements and using the revenues to fund research and other activities relating to cryonics and life extension. Saul was instrumental in organizing several conferences in the 1980s and 1990s with life extension themes.[10] In 1988 alone there were not one but three such conferences, all titled "Life against Death," all at airport hotels: Ontario, California (May 27-30); San Francisco (Sep. 2-5); and finally, New York City (Oct. 30). Details of exactly what transpired are somewhat scanty, but it appears that the first two conferences had two main days of presentations, Saturday and Sunday. The Saturday sessions emphasized such areas as dietary and antiaging approaches to life extension, along with nanotechnology, and the Sunday sessions, cryonics. The last conference, on a Sunday at the La Guardia Airport Holiday Inn, focused more exclusively on cryonics. As noted in the report, it was abbreviated from the usual 4-day length due to preoccupation with legal challenges in Alcor's then home state of California, testing whether cryonics would be allowed to continue in that state. (Fortunately there would be a happy outcome of the long, expensive struggle and cryonics would indeed continue and be recognized as legitimate.[11])



Life Against Death Conference brochure

The previous Friday, October 28, Mike Darwin, Saul Kent, Brenda Peters, and Jo Ann Martin had flown to New York City to coordinate the event. Saturday saw them meeting with several key people and making an effort afterward "to take in a little of the Big Apple's sights, including a shopping/dining/theater trip to Greenwich Village." Mike Darwin continues:

> Sunday, the conference ran from 9 AM to 11 PM. Approximately 30 people attended. Considering the lack of advanced promotion and the rocky course of events in California, we were lucky to have anyone there! The constant state of crisis in Los Angeles had caused a sweeping curtailment of the program and delayed and telescoped promotional efforts. Nevertheless, despite the limitations, the conference was considered a success. It resulted in three new people beginning the sign-up process and provided Alcor with an opportunity to meet with a number of people we had never seen before, including some long-time cryonics enthusiasts like Janet Pinkney from New Jersey. Miss Pinkney has had a 20 year long interest in cryonics

> and only recently decided to get more involved. There were many new faces at the conference and about six subscribers to *Cryonics* who were just faceless names before the weekend. It was a real pleasure to actually meet some of the people who read what we write!

As for just what was covered, the report is silent beyond the above, but we can approximately reconstruct the likely events by studying the published material on the other two conferences, where the coverage was more complete. Probably what happened was similar to the reported events for the May event at Ontario Airport (Sunday, May 29), which was also a close match to the published program for the Sunday, September 4 session of the conference in San Francisco. At the May conference Saul Kent and several others from Alcor first talked about how Saul's mother Dora was narrowly saved from a brain autopsy through their strenuous legal efforts in the face of determined opposition from the Riverside, California coroner.

Next, Mike Darwin talked about the value of cryonics, why it could work even though it had not yet been proven workable, and how Alcor offered the best available cryonics services. While eventually science should find the means to extend the lifespan through aging control, *we aren't there yet*, and thus cryonics is worth pursuing and should be the top priority for anyone who is seriously interested in life extension. Saul then briefly spoke about a new trust agreement he was working on "to protect the assets of individuals after they are frozen."

Next: "For the rest of the afternoon, the conference participants were given the opportunity to sign up for cryonic suspension services with Alcor and to ask questions about any aspect of cryonics." At an evening session, Saul talked briefly about making investments in life extension. Then there was an impromptu panel discussion that covered various topics relating to cryonics, including issues of personal identity and survival. Finally, several members of the audience talked about their personal interest in life extension and why they had signed up with Alcor. Again, this was what happened at the cryonics portion of the May conference in Ontario, but probably something similar occurred at the October conference in New York, particularly the signup session.

New York Gets Coordinator Status: 1989[12]

Coordinator status, as we noted above, would mean that the New York group would have full emergency response capability and could do the initial stages of preparation for cryopreservation (body washout, cooldown to near water-ice temperature, transport to Alcor's main facility to complete the cryopreservation). Members in the area could expect more rapid response in their time of need and a better cryopreservation. Coordinator status was not given lightly but only to groups which had been trained in the use of the equipment that would be needed and who had passed an exam in its use. Mike Darwin here reports on a training session held at the Islip Airport over the weekend of July 15-16, 1989, with the result that the New York group was granted the sought-for status.

> The training session began on Saturday morning and was well attended. All of the core members of the N.Y. group were present, including Gerry Arthus, Curtis Henderson, Phil Kirschner, Kevin Brown, Al Roca, Janet Pinkney, Alvin Steinberg and Phillip Marden. Alcor Suspension Member (and Emergency Medical Technician and nursing student) Jerry Cullins also made the trip up from North Carolina to participate in the session. This was [the] second session for Jerry Cullins and Curtis Henderson, as they had attended the one held on Long Island almost four years ago.
>
> The session was a grueling one, covering as it did all aspects of Alcor's transport protocol in only two days. This included the use of new medications and the Pizer Tank Portable Ice Bath (PIB) (which the N.Y. group will shortly be issued as part of their rescue kit).
>
> The session went well, although there were a few rocky moments. The scores on the final exam were mostly in the very respectable mid to high 80s and the bottom line is that the New York group was issued a rescue kit. As a result, Alcor now has a new Coordinator location providing coverage to the Northeastern U.S.

A Reported Setback[13]

A short article by Mike Darwin in the March 1991 *Cryonics* reports: "N.Y. transport capability withdrawn." Mike Explains:

> Recently we made a decision to upgrade the status of Coordinators in the field and go to "certification." Certification means that the Coordinator must go through basic training on his/her own (usually EMT certification) and then complete Alcor's certification course successfully. Refreshers are required on an annual basis. We are also trying to put the Coordinator program on a more organized and formal footing and plan to have a model agreement ready for use with local groups sometime in the next few months.
>
> The start of the implementation of the certification program prompted a careful reassessment of our field capability. A decision was made to withdraw equipment from areas where there was not a sufficiently broad base of support and/or adequately skilled people.
>
> Despite the fact the New York and Eastern Seaboard region is a high growth area, we have had very, very few people from that region willing to "get their hands dirty." Almost everyone from that area wants to be a "customer" as opposed to an involved member. The problem is, that simply isn't possible at this time.

> An added problem is that customers demand a high level of service. And we know from experience that they are relying on our Coordinators to at least be able to respond in an organized fashion. After careful assessment it was decided that the level of capability we had to offer in New York was sufficiently low that it represented a potential liability rather than an asset; we would rather people be clearly informed that we do not have any quick-response service in their area.

Emergency response in the New York area will now be handled by the Indiana and Florida Coordinators, Mike Says. (But there is more to this story, as follows.)

The Big Apple Bites Back[14]

In the November 1991 *Cryonics* there is an article by Brenda Peters, then an Alcor Board member, "The Big Apple Bites Back, Or, 'Brenda's New York Diary.'" Brenda at that point had been active in the New York group and deeply resented the decision by Mike Darwin to rescind the Coordinator status she and others desired for their area and had worked hard to obtain. It opens with a list of some thirty "achievements of Alcor New York members," of which the first three are "2 members with State EMT Certification," "2 members Alcor Transport Technician Certified," and "1 member with advanced EMT training." Eighth on the list, the New York group is noted as the "fastest growing area in the U.S. in terms of Alcor membership." Last but we may imagine not least is "Instrumental in Dr. Gregory Fahy's article appearing in Mount Sinai Journal of Medicine." The rest of Brenda's story, in more usual prose format, is fascinating but very long; I've excerpted some of the more salient points here. Interested readers can, as usual with *Cryonics* back issues, find the entire text online in Alcor's archive. (Brenda refers to "Courtney" who was her then husband, Courtney Smith.)

Brenda Peters

"… what if you are involved in an accident, or some other emergency situation?… (and) Alcor is 3000 miles away. Alcor technicians giving instructions over the phone is not my idea of an optimum rescue situation and I'm sure it's not yours either. It is for that very reason that we must not rest… until we know that if we become victims of an emergency situation, we have highly skilled Alcor technicians who are local to our area, who are on call at all times, and who have the finest equipment possible in order to help us."

The above quote is from a fund-raising letter I sent out recently. After 15 years of Los Angeles living and 8 years of being Alcor active, I moved, with some apprehension, to New York City in June 1990. Since I was relocating anyway, my hope was that the presence of a Board member in New York would prove to be useful for growth and activity. The subsequent events are something I never could have predicted. As I sit down and put fingertip to keyboard, I reflect upon my 15 months here in the wilds of New York.

Let's Get Physical

The New York Discussion Group provided information dissemination and a forum for discussion. Kevin Brown had even established the successful electronic cryonics mailing list, referred to as "Cryonet." Attendance had been steady at the Manhattan meetings for over a year and the group had flown Mike Darwin out to conduct a training session. But I found the meetings, like the group's title (The New York Cryonics Discussion Group of Alcor Life Extension Foundation) to be lengthy and disappointingly unproductive. […]

As far as I could see, there were no activities to attend or participate in and no well-focused goals. […] Only two people had put forth real effort to respond should there be a local member who needed help. I feel these efforts were extraordinary considering the malaise which had set in.

Those two people were Gerry Arthus, the New York Coordinator, who had completed his State EMT Certification course when I arrived, and Curtis Henderson, who completed his State Advanced EMT Certification course a few months later.

[…].

From Donuts to Dollars

[…]

I attended the 1990 European Cryonics Conference in October and, shortly after my return, we had our

November meeting. The $1200 [the New York group owed Alcor for expenses relating to Mike Darwin's training session in 1989] was going to be a challenge to our progress[. I]t had been disheartening to discover its existence, but since everyone else's morale was so high, I didn't wallow in a mire for very long. Fifteen people came to that meeting (a 50% improvement in attendance)! We decided to have more formal agendas at the meetings, which would be more conducive to action. We also decided to purchase Steve Bridge's wonderful Alcor/cryonics slideshow/lecture for special events. People donated the $200 on the spot to purchase the slideshow. It was a good indicator of renewed commitment.

We were planning for upcoming events, gathering ideas for advertising, and getting information on a possible seminar at continuing education schools. Alvin Steinberg, in an outreach effort to scientists regarding cryonics and nanotechnology, was writing to his congressman, Dr. Linus Pauling, and others. Alvin's efforts, including replies he received from Dr. Pauling and the National Institute[s] of Health resulted in Dr. Gregory Fahy's article in the Mount Sinai Journal of Medicine and Dr. Fahy's presentation at the American Aging Association.

The New York Group had made some very good decisions regarding officers. Janet Pinkney (a writer and researcher at heart) had been appointed Secretary. Janet is relentless when it comes to getting the data. She's not shy about asking for clarification and always has a tape recorder going as a backup. Kevin Brown became Treasurer and does a stellar job, another one for clarity, he's also frugal and diplomatic. We're very fortunate to have them.

[…]

Courtney and I went to California in late December and spent time discussing the situation in New York with Alcor staffers and other members. As I'm sure most remote groups do, we lamented a slow rate of progress and isolation syndrome but received encouragement and advice. […] We received word that the December meeting had been well attended in our absence, (11 people, even without us and only a few days before xmas/winter solstice – it was a very good sign), a new meeting time (Sundays at 2PM) had been successfully voted in (even without our votes!), Membership dues were established at the meeting, people had begun to generously contribute toward the $1200 debt, the New York group was opening its own bank account, people had already begun paying their yearly dues ($25), Kevin sent off the first payments to Alcor for the $1200, he mailed a check to Steve Bridge, and the slide show was on its way. So, we returned to New York with renewed enthusiasm and determination.

The Curtain Rises or Curtains for Us?

[…]

One day early in February [1991], we got a fax from Mike Darwin informing us that he had made a decision to pull all the stabilization equipment from New York. I couldn't believe it. Courtney and I were stunned. Gerry, Kevin, and Janet were dismayed and deeply disappointed. We had been reassured by Mike and other staffers, while in California only weeks before, that Alcor supported the New York group and what we were trying to do. It was clear that Mike was disappointed (we all were, especially the people who had been pulling for years to make things happen here) in the progress toward an emergency response capability in the northeast. Progress is never fast enough for cryonicists, that's an integral part of our nature.

Some of the New York group. From left: Alvin Steinberg, Kevin Brown, Steven Berger, Stanley Gerber

Curtis Henderson and Janet Pinkney

Just as impatience is part of our nature, so is determination. We weren't going to take this lying down. We couldn't… our lives might depend upon it. We insisted upon a vote by the entire Board on this issue. They were uninformed as to the situation and progress that was taking place in New York. At a special Board meeting which I attended by "conference call", once the facts were presented, it was decided that the equipment would be left in New York.

[…]

The Membership Meeting was approaching. I was given a budget for refreshments and Courtney and I bought the food the day before, carried it home in two trips, then taxied it up to the dance studio next day. For this meeting we were paying $26 an hour for their largest room. Our ad had been appearing in the Village Voice. The Life Extension Foundation sent out fliers with their monthly report to Life Extension members in the area, and Janet made an announcement in her monthly invitation which goes to the 79 mysterious people who never show up. We were ready as far as food was concerned, nervous as far as the slide show and lecture was concerned, and excited at the prospect of getting some new members.

A business meeting was scheduled for 4PM and the "event" for 5PM on March 17th. By 3:30 we had run out of chairs. There were over 60 people trying to squeeze into the room. I was smiling all over. We dispensed with the business meeting and proceeded with the "event." I believe we had a bigger turnout than any cryonics membership meeting in the history of cryonics, even bigger than some of the conferences.

After our stunningly successful membership meeting, I was handed a copy of the new issue of *Cryonics* Magazine [March 1991, see above], in which it was announced that we "represented a potential liability" and that "very, very few people from (our) region were willing to get their hands dirty." The "N.Y. Transport Capability Withdrawn" headline was a heartbreak to say the least. We all felt… it's difficult to express what we felt. We will never know how many people had read those words and decided that they made the right decision when they did not attend our meetings and did not get involved.

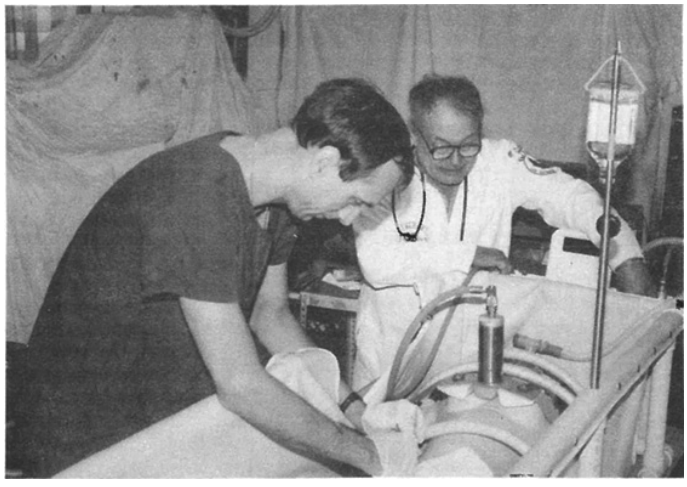
I told myself that it must have gone to press before the special February meeting of the Board. Even at that, it was in my opinion presumptuous and premature. But I decided not to worry, because at the very least, there would be a correction in the next issue of the magazine. Wrong. A few days later I asked Mike Darwin if there was a retraction in the April issue. I was told that there was not a retraction. Mike said there had not been room because of more pressing news. I've examined the next issue and I can only surmise that advising Alcor Members of the holdup in the release of the movie *Late For Dinner*, or the large blank spaces on pages 5, 11, 16, 23, and 24 were considered to be more pressing news. Pulling the stabilization equipment was newsworthy but keeping east coast members informed and the correction of a serious error was not? It was May before one tiny paragraph appeared in Cryonics (which by the way would have fit into any of the aforementioned blank spaces) stating that the New York group would retain the "kit."

[…]

Roads are Made by Walking

[…]

At the August [1991] meeting we began to show cryonics videos as the last item on the agenda. Curtis and Gerry bought a $42 inflatable woman, which they donated for training sessions. I wish I had a video tape of them walking into the porno shop and telling the owner they wanted the doll to use in an experiment. In the ledger, Kevin calls it the "inflatable transport training and experimentation module." Curtis and Gerry bought the doll, but somehow I don't think the porno shop owner bought their story. "Zsa Zsa" or "Miss IceCapades 1992," as Curtis calls her, will be filled with water and used as a "patient" for "practice cooldown" training until we are financially flush to purchase a Resusci-Anne.



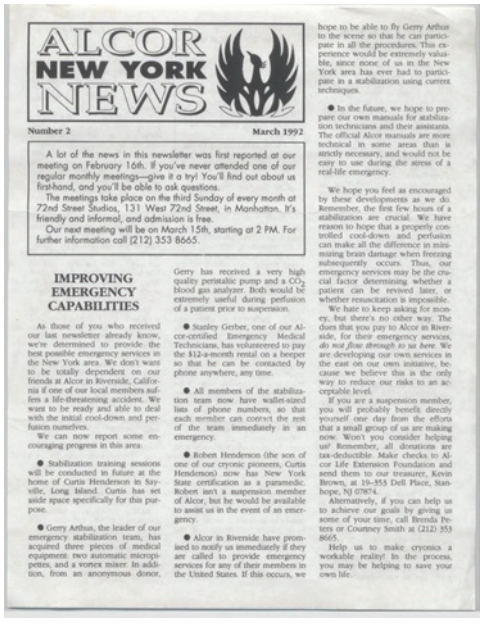
Gerry Arthus (left), Curtis Henderson, and "Miss IceCapades 1992"

One of our new members, Stanley Gerber, enrolled in the State EMT Certification Course. We would soon have a new member on our Transport and Stabilization Team! On September 3rd, I drafted and received approval for a follow-up fund raising letter.

[…]

And now I have to go, there's someone on the phone who says he once attended an Alcor meeting in New York and he keeps getting letters from some stranger named Brenda.

Alcor New York News: 1992



ALCOR NEW YORK NEWS

Number 2 March 1992

A lot of the news in this newsletter was first reported at our meeting on February 16th. If you've never attended one of our regular monthly meetings—give it a try! You'll find out about us first-hand, and you'll be able to ask questions.

The meetings take place on the third Sunday of every month at 72nd Street Studios, 131 West 72nd Street, in Manhattan. It's friendly and informal, and admission is free.

Our next meeting will be on March 15th, starting at 2 PM. For further information call (212) 353 8665.

IMPROVING EMERGENCY CAPABILITIES

As those of you who received our last newsletter already know, we're determined to provide the best possible emergency services in the New York area. We don't want to be totally dependent on our friends at Alcor in Riverside, California if one of our local members suffers a life-threatening accident. We want to be ready and able to deal with the initial cool-down and perfusion ourselves.

We can now report some encouraging progress in this area.

● Stabilization training sessions will be conducted in future at the home of Curtis Henderson in Syosset, Long Island. Curtis has set aside space specifically for this purpose.

● Gerry Arthus, the leader of our emergency stabilization team, has acquired three pieces of medical equipment: two automatic micropipettes, and a vortex mixer. In addition, from an anonymous donor, Gerry has received a very high quality peristaltic pump and a CO_2 blood gas analyzer. Both would be extremely useful during perfusion of a patient prior to suspension.

● Stanley Gerber, one of our Alcor-certified Emergency Medical Technicians, has volunteered to pay the $12-a-month rental on a beeper so that he can be contacted by phone anywhere, any time.

● All members of the stabilization team now have wallet-sized lists of phone numbers, so that each member can contact the rest of the team immediately in an emergency.

● Robert Henderson (the son of one of our cryonic pioneers, Curtis Henderson) now has New York State certification as a paramedic. Robert isn't a suspension member of Alcor, but he would be available to assist us in the event of an emergency.

● Alcor in Riverside have promised to notify us immediately if they are called to provide emergency services for any of their members in the United States. If this occurs, we hope to be able to fly Gerry Arthus to the scene so that he can participate in all the procedures. This experience would be extremely valuable, since none of us in the New York area has ever had to participate in a stabilization using current techniques.

● In the future, we hope to prepare our own manuals for stabilization technicians and their assistants. The official Alcor manuals are more technical in some areas than is strictly necessary, and would not be easy to use during the stress of a real-life emergency.

We hope you feel as encouraged by these developments as we do. Remember, the first few hours of a stabilization are crucial. We have reason to hope that a properly controlled cool-down and perfusion can make all the difference in minimizing brain damage when freezing subsequently occurs. Thus, our emergency services may be the crucial factor determining whether a patient can be revived later, or whether resuscitation is impossible.

We hate to keep asking for money, but there's no other way. The dues that you pay to Alcor in Riverside, for their emergency services, *do not flow through to us here*. We are developing our own services in the east on our own initiative, because we believe this is the only way to reduce our risks to an acceptable level.

If you are a suspension member, you will probably benefit directly yourself one day from the efforts that a small group of us are making now. Won't you consider helping us? Remember, all donations are tax-deductible. Make checks to Alcor Life Extension Foundation and send them to our treasurer, Kevin Brown, at 19-355 Dell Place, Stanhope, NJ 07874.

Alternatively, if you can help us to achieve our goals by giving us some of your time, call Brenda Peters or Courtney Smith at (212) 353 8665.

Help us to make cryonics a workable reality! In the process, you may be helping to save your own life.

In January 1992 the group started publishing a newsletter: *Alcor New York News*. Due to space and other limitations we limit our coverage here to one article describing some research of Gerry Arthus, reported in issue no. 4 (May 1992) under the heading, "Cryonic Research: The Worms That Turned."[15]

Gerry Arthus, our New York Coordinator, has announced preliminary results of an experiment which was designed to investigate whether memories will survive cryonic suspension.

For his experiment, Gerry used *Caenorhabditis elegans*, a nematode (tiny worm) that's one of the simplest living creatures. It has a complete nervous system, however, and can be "trained" in a rudimentary way. Worms that are raised in a warm environment will "remember" it and will prefer it if they are given the choice. Conversely, worms that were raised in a cooler area will tend to prefer that environment.

Gerry placed a small number of worms in a cryoprotective solution and froze them to -80 degrees Celsius for two hours. After he revived the worms, the ones that survived the experience still "remembered" their former environmental preferences. So far as we know, this is the world's first experiment designed to verify that memory is chemically encoded and will survive the freezing process.

The sample that Gerry used is too small to prove anything conclusively. Soon, however, Gerry hopes to repeat the experiment with a larger sample. He also intends to devise tests to eliminate the possibility that the worms changed physiologically to adapt themselves to warmer or cooler environments.

We're excited by Gerry's work, which was done on a tiny budget but was rigorous and professional in its execution. Gerry believes that there are many other simple experiments which could be done, with a minimal investment, to verify the feasibility of cryonics and help us to refine our methods of cryopreservation.

Will some of these experiments be conducted at Riverside, if the staff there has time between fighting lawsuits and debating whether to move to Arizona? We hope so!

(Note: no follow-up of the above was done, either in New York or at Alcor's then headquarters in Riverside, California. Such work was finally completed in 2015, however, using Alcor's laboratory facilities at their new location in Scottsdale, Arizona, by Natasha Vita-More and Daniel Barranco.[16] It conclusively established that *C. Elegans* can survive cooldown to liquid nitrogen temperature and be warmed up with memory intact. Gerry's results are a remarkable near-anticipation of this later work, unfortunately stymied in the end by limitations of budget and other constraints. – R.M.P.)

The Cryopreservation of James Hourihan[17]

James Hourihan

A 28-year-old cancer patient living in the Boston area, James Hourihan first contacted Alcor in February 1992, when he thought he had maybe at least 12-24 months before he might need Alcor's services. It didn't work out that way, and by the following June James was in an emergency room. The cancer had invaded the wall of his stomach, causing internal bleeding, and he had maybe 48 hours left, if the cancer did not abate. At that point he had not even completed his paperwork, and his funding had not been approved. Moreover, right then Alcor's primary Remote Standby Team was occupied with a case in Colorado (Jim Glennie) and would be unavailable to help him.

The paperwork/funding issues were dealt with. As for the standby, the main responsibility fell to the New York group, since they were by now well-prepared and also not far away. (Back then, of course, there were no third-party organizations handy to regularly provide services to Alcor members at remote locations.) Quoting from the report by Tanya Jones on this case (as throughout this section):

> Alcor New York team members Stanley Gerber, Gerry Arthus, and Curtis Henderson prepared for the four-hour drive to Jim's hospital, on what could be the very first application of their cryonic suspension skills (beyond a multitude of training sessions). Upon arrival, they made the first contact and initial arrangements inside the hospital where Jim was receiving critical care. (with later assistance from Tony Reno, K. E. Nelson, Walter Vaninni, and Dr. David Greenstein of the Boston area.)
>
> Stanley Gerber was designated the hospital/family liaison, and he quickly obtained permission to set up the emergency response equipment (which had been brought from New York by van) in an unoccupied Critical Care Ward directly across the hall from Jim's room. Shortly after their arrival, Arel Lucas was deployed from northern California. About 16 hours after the New York Team arrived, Arel joined them. The four of them maintained a constant watch for another two days before being joined by Michael Darwin and Tanya Jones, both of whom had departed for Boston from Riverside just before the completion of Jim Glennie's suspension.
>
> Greeted at the airport by a somewhat disheveled Stan and Curtis, Mike and Tanya were then briefed on the rather tense situation that faced them at the hospital. Jim's family, although familiar with the concept of cryonics, had been unaware of Jim's strong desire to sign up for suspension. It came as something of a shock. Compounding their distrust of Jim's unexpected request for suspension was the appearance of the New York team. The dedicated New Yorkers, well-spoken and polite, had worked furiously and round-the-clock to prepare the Critical Care Ward for the impending (or so it seemed) transport, in the process neglecting little things, like showering, shaving, and shut-eye. Their efforts were in Jim's best interests, but the family would have preferred to see dapper, professional-looking representatives working 8-hour shifts.
>
> So Stan, Curtis, and Gerry were dispatched to get some well-deserved rest while Arel gave Mike and Tanya a brief tour and introductions to the family and some of the hospital staff. Jim's mother and his fiancée, Devra, became our primary points-of-contact. They were cool and distant and seemed reluctant to talk with us at first. They expressed concerns about cryonics and were worried that this whole thing might be a scam. Once Mike and Tanya explained that the team from New York [consisted] of *volunteers*, more concerned with preparedness than appearance, the atmosphere began to lighten. […]
>
> Jim recovered from the internal bleeding. It was the hospital's policy to use extraordinary measures to save the life of every patient in their wards, even if it meant pumping multiple liters of blood products into the patient on a daily basis, which is the course of care that Jim required. Despite his surprising recovery, though, Jim's situation was still delicate enough that the full team stood by for several days, even going so far as to recruit Steve Bridge from Indiana for a weekend when Stan, Gerry and Curtis were sent home. Stan's dedication in assisting with this transport nearly cost him his job as an EMT, due to his extended absence.
>
> Tanya and Arel left Boston a week into the standby. But just hours after they left to return home, the call came through that Jim's condition had taken a drastic turn for the worse. In an attempt to get sufficient trained personnel on-site for the transport, as only Mike Darwin and the local members were remaining, Naomi Reynolds was sent on the first available flight from northern California to Boston. Little did any of us know, Jim was going to rally yet again.
>
> One of the things Stan had done, prior to the arrival of Mike and Tanya, was go through the Boston yellow pages line by line, trying to locate a mortuary which would be willing to work with us. He found one which was a thirty minute drive from the hospital. This mortuary backed out of their verbal contract with us, on the night Tanya and Arel left: just when their services could be needed the most (when Jim gave us a scare!). They did, however, recommend another mortuary which could assist us with the rather special requirements of Massachusetts law. (A body cannot be shipped out of Massachusetts unless it's embalmed!)

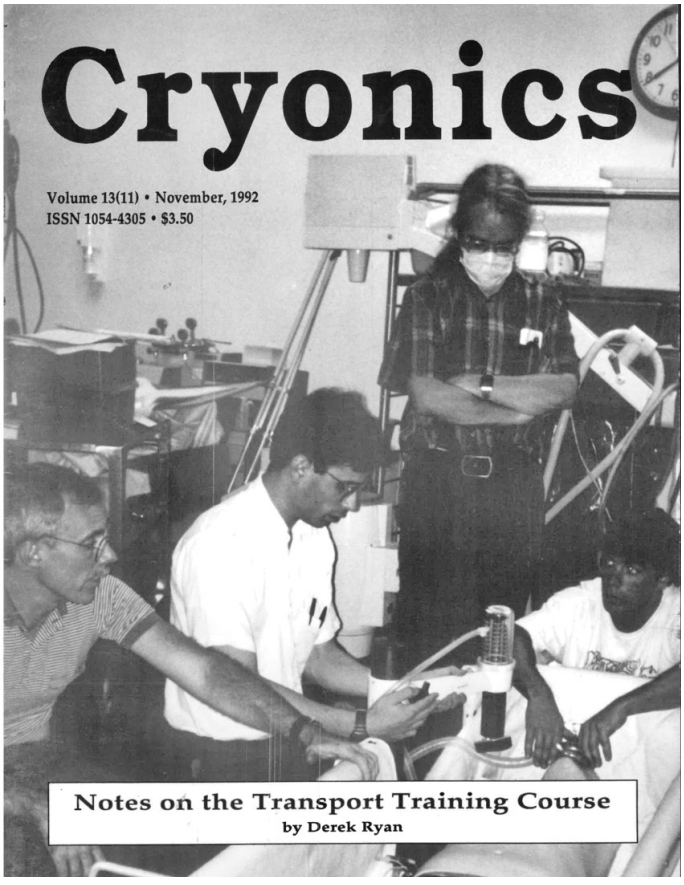
In the end, Jim rallied, and the standby team members all went home, while Jim went to home hospice care. Plans were developed to have Jim move near Alcor, then in Riverside, California, to avoid the difficulties of remote standby when arrest was finally imminent. However, when it came time to make the flight out to California, Jim "didn't quite feel able to leave his family and friends, given the circumstances," and it didn't happen. What to do? Up to then heroic measures had been taken at the hospital when arrest seemed imminent (and it had worked). The Alcor team was assured that such measures would no longer be taken, before agreeing to redeploy. Mike Darwin,

Tanya Jones, and Naomi Reynolds arrived at the hospital on the evening of the 26th, finding Jim looking well and showing good oxygen saturation levels. The next morning he arrested. The three Alcor members were not on site at that point, having thought it safe to get a night's rest nearby, but arrived quickly to begin the washout procedure. (There were some delays but it seemed to go well.) After this, Jim at water ice temperature was flown to Riverside and cryoprotection and cooldown (as neuro) were completed.

In all, the New York group's involvement in this case had been a "dry run" due to the hospital's approach to managing the illness. But what a dry run! And I think Stanley Gerber especially distinguished himself by his dedicated efforts over a long enough period that he could have lost his job. (Fortunately his employer was understanding.)

Training Course in Riverside[18]

A little more than a year after the Hourihan case a transport training course was organized by Mike Darwin and held at Alcor's headquarters in Riverside, California. Stan Gerber and Robbie Henderson (son of Curtis) from the New York group attended the five day session (Sep, 6-10, Mon.-Fri, 1992).



Cryonics Nov. 1992 cover showing training course attendees. From left: Mike Darwin, Stanley Gerber, Keith Lofstrom, Robbie Henderson.

The Cryopreservation of "Mrs. Stone":1994[19]

The first cryopreservation that the New York volunteers played a part in when it actually occurred was in April 1994. Two months before, Alcor had moved to their present location in Scottsdale, Arizona. Steve Bridge was president, and Mike Darwin had (temporarily) left the organization. "Mrs. Stone," The 91-year-old mother of an Alcor member in the NYC area, suffered a nonfatal but serious heart attack and the son called Alcor. A little later the woman's physician called from the hospital, spoke to Steve Bridge, and said she was in a coma and not likely to survive the night. It was time to act.

Unfortunately, the main Alcor team members were then at a conference in Sunnyvale, California (Extro 1). Tanya Jones in her article on the case relates what happened next:

> Within two hours of Steve's speaking with the physician, Hugh Hixon and I were being rushed to the airport by Keith Henson (who was also attending the conference) to catch the next flight to New York. Steve Bridge had arranged for Scott Herman to take Alcor's transport kit, custom shipping container, and supply of ViaspanTM (a blood replacement solution used commercially in stabilizing transplant organs) to the Phoenix Sky Harbor Airport, where they were awaiting shipment to New York. Additionally, the New York Transport Team Members had been notified of the impending suspension and dispatched to the hospital to await deanimation.
>
> Once the stabilization equipment shipment and local emergency response had been coordinated, Steve's next step was to contact the New York City mortician who'd been contacted to assist with the transport. At about 1:30pm, the mortician and Steve had completed the negotiations regarding the use of the mortician's facility and services. They were discussing logistical details, when the mortician took another call. It was Mrs. Stone's son, calling to say that his mother had deanimated and was awaiting removal from the hospital. Hugh and I were somewhere over Nevada when this call came. After discussing several probable transport scenarios with Hugh, I asked Steve to stop the transport kit shipment to New York, as it appeared unlikely that we'd use it. (We expected that no blood replacement would be possible due to the excessive clotting which occurs to people when their circulatory system shuts down, a decision based on the fact that Hugh and I were hours distant, and the local Transport Team members had not yet arrived at the hospital.) We could attempt the washout with the local equipment, but were expecting blood clots to prevent any significant circulation of the washout solution. With further consideration, we changed our minds—sending

the transport kit was probably a good idea, as there were many items in it that were not in the local kit, and depending on how the circumstances developed, some of these items might be useful. Twenty minutes passed between these decisions, and they were poorly timed. The only flight which would get the kit to New York before late Sunday morning (this was Saturday) had been the plane from which the kit had been off-loaded, and it had just left.

Meanwhile, the New York Transport Team volunteers had been sent to the hospital with their transport equipment. Stan Gerber went straight to the hospital from his apartment in New York City [actually Flushing/Queens – R.M.P.], while Gerry Arthus and Curtis Henderson were traveling from Long Island. Gerry and Curtis were given permission by Steve to locate a back-up van for their equipment, as Curtis' van was old and possibly unreliable for long trips, but Steve also said that this wasn't critical, and that any search for a van should not delay the deployment of the equipment to the hospital. Gerry called one rental company who claimed to have a van immediately available, so he and Curtis went to pick it up. Unfortunately, they didn't take the equipment with them, and subsequently, had to return to Curtis' home to pick it up when they found that the rental company was mistaken and no van was on the lot. This, in conjunction with the standard snarls of New York City traffic culminated in several hours' delay.

Stan Gerber arrived at the hospital shortly after the patient was pronounced. The patient's physician had allowed the patient's son to pack her head in ice, and informed Stan that he could perform cardiopulmonary resuscitation (CPR) (which he did, manually) and administer the transport medications, but that the hospital would not provide him with medications from their inventory. Much to Stan's frustration, he had no medications with him, since the transport medications kit was still en route with Gerry and Curtis.

The mortician arrived about an hour later and submitted the paperwork for the removal of the patient, which was then accomplished in short order. Upon arriving at the mortuary, Stan once again began manual chest compressions, and performed CPR (without ventilation, as our protocol requires) until shortly before the arrival of Gerry and Curtis at 8:15pm (EST). Stan had to stop CPR in order to head for the airport as Hugh and I were arriving. He was accompanied by the patient's son.

About the time Hugh and I landed at JFK Airport, Gerry and Curtis arrived at the mortuary. Once the equipment was unloaded, they began to implement the transport protocol. The mechanical CPR device was placed and started. An IV was in place, but no fluid could be pushed through the clotted line. Of all the transport medications, only Maalox could be administered at this time.

Tanya and Hugh arrived at the mortuary, and made the decision to attempt a body washout, using Viaspan™ sent from Florida. In the end it was partly successful and judged to have been worth the effort. Various other problems were solved, and the patient near water ice temperature was flown back to Alcor, perfused, and cooled to liquid nitrogen temperature (whole body).

Tanya Jones at the cryopreservation of Mrs. Stone

So this time the New York group assisted with a cryopreservation in their area. Mistakes were made, and it was a difficult case to begin with due to the shortness of time between recognizing that standby should begin and the member's arrest. But an important milestone had been passed with this case and the one before it. New York's volunteers were far from perfect but could ably and competently assist with emergencies in their area. ■

Image Credits

Photos shown in "The Big Apple Bites Back" are from the magazine article (BP). The photo of Brenda Peters is unattributed. The photo showing "Miss Icecapades 1992" is by Huiying Wei; the others are by Courtney Smith.

James Hourihan and Tanya Jones are from Alcor archives.

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Notes on the 1st Alcor New York Science Symposium

Adapted from a review by Reason and expanded by R. Michael Perry

Saturday, Nov. 23, 2019 was the occasion in New York City for a symposium on cryonics and life extension organized by Alcor member and editor of *Cryonics* magazine Aschwin de Wolf. In his introduction to the meeting, Aschwin noted that New York, and specifically the NYC area, was important in early cryonics history (1960s and '70s). During this time there was a Cryonics Society of New York (CSNY) which was among the first to carry out cryopreservations of legally deceased people in hopes they might be revived in good health someday, when more advanced technology would be available. Working with the present group of Alcor members in the vicinity, Aschwin hopes to create well-organized standby capabilities to handle the initial stages of cryopreservation for people in the surrounding areas, most notably the New York tri-state area and the Northeast US.

The talks at the meeting were divided between discussions of cryonics and of progress toward slowing or reversing aging. In general, cryonicists have a strong interest in just staying healthy and not having to be cryopreserved after all, and thus are quite interested in what is going on in the newly formed longevity industry. The weight given to cryonics is tempered by expectations as to how soon rejuvenation therapies will arrive, and how effective they will be over time.

João de Magalhães was the first presenter, calling in remotely from the UK. He gave his view on the present state of progress toward therapies to slow and reverse aging. He concluded, conservatively, that it is not likely that "actuarial escape velocity" or essentially curing aging will occur in our lifetime. He does however think we will see a slowing of aging in our later lives. Still, cryonics for those living today is very important. For this reason, it is especially important to achieve for cryonics what has already been achieved for work on the treatment of aging – to move it from a small, not-well-regarded fringe concern to a field with notable technical successes and greater financial support. In accomplishing this there is little substitute for the hard work of bootstrapping, advocacy, research in a resource-constrained environment, and so on. De Magelhaes himself is involved, on the cryonics end of life extension, in setting up the *UK Cryonics and Cryopreservation Research Network*, to spur more academic research into relevant technologies.

Ben Best next spoke about NAD+ upregulation and senolytics. He works at the *Biomedical Research and Longevity Society* (BRLS, formerly *Life Extension Foundation* or LEF), and the principals there have recently started to heavily promote these approaches to treating aging. To the extent that they work, this is an example of what will happen to the "anti-aging" industry that is often accused of being rife with fraud, false hope and supplements that do little good. Even if so, it does not mean all is bad or hopeless. Many of the people involved are motivated to do something about aging, and thus the good should chase out the bad, given time and therapies that actually work. Ben has experimented with these approaches himself. One of the physicians connected with BRLS is willing to prescribe the senolytic dasatinib and NAD+ infusions, but committed the cardinal sin of not keeping good records of the condition of the subject before and after treatments, using appropriate metrics. This is sadly prevalent in the self-experimentation community. If you don't measure, nothing happened. Still, there is evidence

Aschwin de Wolf, CEO of Advanced Neural Biosciences and co-organizer of the Alcor New York group.

that both NAD+ upregulation and senolytics are beneficial in older people, and sooner or later ever more physicians will become comfortable enough with the evidence to prescribe these therapies to the many who might benefit.

Mike Perry then gave a fascinating talk on the early history of cryonics, starting in the mid-1960s. It is eye-opening just how much information can be lost even at a distance of a mere fifty to sixty years. For example, James Bedford was not the first preserved individual, but only the second. The first was a woman apparently named Sarah Gilbert; details of her case are still under investigation. But of the seventeen people cryopreserved from 1966 to 1973, only Bedford remains. All the others were lost to the haphazard, unprofessional nature of the early initiatives. Perry exhibited a short film made in 1968 by Karl Werner, who was a member of the Cryonics Society of New York and the one who coined the term "cryonics." It shows the process of cryopreservation in one of the dewars of the time and is quite an artifact of its era.

The next presentation was by Chana Phaedra of Advanced Neural Biosciences (ANB) on paths toward optimization of brain cryopreservation. The success of brain vitrification depends on efficient and rapid delivery of cryoprotectant to the brain. At present, even in the best of circumstances the perfusion of cryoprotectant isn't optimal. This is challenging on several fronts: the skull can cause sub-optimal perfusion during swelling; pressure needs to be carefully controlled; the blood-brain barrier limits penetration of most cryoprotectants to some degree. Based on work at ANB, the low-hanging fruit here is finding ways to bypass or open the blood-brain barrier. That may mean new cryoprotectants, or some chemical way of disrupting the blood-brain barrier rapidly and selectively. Other options to improve the situation: faster perfusion, less ischemia, and better assays that can be used in animal studies or on preserved human brains to reliably establish the quality of the preservation.

Aschwin de Wolf then discussed the prospects for revival of patients who were frozen rather than vitrified, in part or in whole. Today there are many who are cryopreserved by straight freezing because there is too much delay after arrest for vitrification perfusion protocols to be applied. It often happens also, even with perfusion, that there is uneven distribution of the cryoprotectant so that some areas of the brain are essentially just straight frozen. Present wisdom holds that straight freezing is highly destructive and causes large amounts of ice crystal formation. Can people with this sort of damage be repaired? De Wolf argued that the best approach, conceptually, is some form of low-temperature repair, via nanomachinery capable of operating in a preserved tissue at liquid nitrogen temperatures. The more interesting part of the discussion was a presentation of straight frozen and then thawed brain tissue that doesn't appear to have anywhere near as much damage as we might expect. The state of the tissue is worse than the same case for vitrification, but perhaps not as much worse as thought, and might lead to a lower-cost form of acceptable cryopreservation. More work is needed to assess this conjecture, but the findings are hopeful so far. He emphasized the point that freezing causes damage but that by also lowering the temperature identity-critical information may be preserved by inhibiting diffusion-based chemistry.

Michael Benjamin of Advanced Neural Biosciences then gave a talk on "comprehensive meta-analysis, modelling, and experimental validation of Alcor cases." This is an ambitious project-to-be-completed that is intended to create a comprehensive database of Alcor cryopreservation cases, with a view toward developing better protocols for cryopreservation. When the treatment effect (or effect size) is consistent from one study to the next, meta-analysis can be used to identify this common effect. When the effect varies from one study to the next, meta-analysis may be used to identify the reason for the variation. Understanding how the different variables cause the variation in results will make it possible to assign a value or weight to each variable. From there it should be possible to assign a quality score to existing and new cases, and tweak procedures in real time based on inputs pertaining to each case such as age, weight, medical history, and time from pronouncement. Assessments will be made of such issues as (1) effects of medications on perfusion, (2) effect of cooling rates on preservation quality, and (3) quality/effect of tissue preservation at the cellular and molecular levels for the various cryoprotectants.

Alcor member Michael Benjamin talks about the Alcor case meta-analysis project.

Since one of the presenters was ill, Reason then filled in and gave an impromptu talk on self-experimentation: how to do it responsibly and effectively. We might consider four classes of self-experimentation at increasing levels of sophistication. Class 1: the sort of thing that everyone does with dieting for weight loss or eating foods and supplements for benefits. Class 2: compounds that are easy to obtain, easy to use, have great human safety data, and that may have effects on aging, such as metformin (a poor idea, the speaker thought) or senolytics (a better prospect). Class 3: treatments that are logistically challenging, and that may need a personal lab. Few people would be able to safety inject themselves with myostatin antibodies, for example. Get that wrong, and you die. But it is technically plausible, and helpful in terms of spurring muscle growth, given the evidence. Class 4: treatments that require a company or other significant effort to create. Liz Parrish's efforts with Bioviva, in order to self-experiment with telomerase gene therapy, are an example. Another, for that matter is cryonics. In nearly all cases, from dieting to quite sophisticated efforts, people tend to self-experiment poorly. They do not do the one fundamental thing, which is to measure the effects.

Reason of Fight Aging! And Repair Biotechnologies talks about the proper way to do anti-aging self-experimentation.

The next speaker was Dr. Ralf Spindler whose topic was the functional evaluation of brain preservation protocols. An interesting method was outlined that was not limited to cryopreservation. Essentially it involved examining labelled dendritic spines in neural tissue. This can be done before and after an experimental preservation to see how well the fine structure survives. In principle it could also be done in a whole brain, rather than just in sections of brain tissue.

Cryobiologist Ralf Spindler presents on novel methods to assess the quality of brain preservation.

Dr. Roman Bauer of Newcastle University (UK) spoke next, on the use of computer modeling and machine learning to optimize cryopreservation procedures. There are many variables that can be tweaked, from cooldown trajectory to type and mix of cryoprotectants. Modeling could be used to find optimal parts of this large state space more effectively than other forms of experimentation. He also mentioned the desirability of using more sophisticated viability assays such as measuring electrical activity in the brain or LTP (long-term potentiation).

Cryobiologist Roman Bauer about the potential use of computer modelling in cryobiology.

Dr. Emil Kendziorra, board president of the European Biostasis Foundation (EBF) spoke next, outlining the EBF's efforts to build a professional cryonics provider in Switzerland. This, if successful, would be the first in Europe. Customer focus and scalability are the weak points of the present cryonics industry, says Dr. Kendziorra, given its non-profit roots. Thus one of the initial projects is to ramp up the professionalization of signup and standby. Toward this end, the EBF is launching a project called Tomorrow, which streamlines the process of signing up for cryopreservation, making it an entirely online process that runs more smoothly and requires less work on the part of the individual. They are also looking into how to make a for-profit cryonics organization viable through the path of long-term asset management, meaning partnership with life insurance companies. Most cryopreservations currently are funded by life insurance policies, making it quite cost-effective, particularly if started at a younger age. Middlemen in the life insurance industry are a well-established business model, and so this might be a path towards for-profit cryonics. Beyond these early stage efforts, EBF supports research efforts to improve the quality and reliability of cryopreservation, and is planning a storage facility, but this will be contingent on success in the initial for-profit path, opening the door to capital investment.

Emil Kendziorra, president of the European Biostasis Foundation (EBF), talks about a new European cryonics organization.

Dr. Robin Hanson of George Mason University then gave the keynote address and final talk of the event, on how hidden motives help explain why cryonics isn't popular. Dr. Hanson has just co-authored a book, with Kevin Simler, *The Elephant in the Brain: Hidden Motives in Everyday Life*. Many pursuits in life show hidden motives. Examples include laughter, body language, conversation, consumption, art, charity, education, medicine, religion, and politics. People are trying to show their "stage presence," impress others with their possessions, flirt, feel cared about, feel like they belong, prove to others they are generous, and so on. Often these motives are hidden – from others and even themselves. They don't always fit with social norms nor are things we want to believe about ourselves. Applying this to cryonics, we note in the first place that it is a "far" concern, remote from everyday experience with its complicated behavior driven by hidden motives. A simple motive to live in a more distant future with possible options beyond this life is overridden by the complex of often hidden motives that dominate the behavior of people today. What people say they want is often not in good alignment with what they really want. For example, they might claim that there is no scientific proof for cryonics but really are concerned about family cohesion and losing all they care for. How can we engage the "elephant in the brain" to get more people moving toward signing up for cryonics? This is a difficult, perplexing issue. In some way however we must make the prospect of "coming back" through cryonics seem attractive. We need to help people appear to want what they say they want, while actually giving them more of what they really want.

Robin Hanson delivers the keynote speech about his new book and what it means for effectively communicating cryonics.

In closing, the cryonics community needs to grow and find success. We live in a strange world, in which there is an alternative to oblivion and the grave, but it is poorly capitalized, poorly supported, and rarely used. Cryonics, as happened for the treatment of aging as a medical condition, must find its way to success and growth. This may be achieved in part by the slow process of building technologies that work, such as reversible vitrification of donor organs, carried out in research communities that presently have little funding for rapid progress. Another important contribution could come from initiatives such as those of the EBF, the process of discovery in business models and persuasion. Finally, and most importantly, we need to convince people that they have good reason to want to have more of life, and a life in the future which in many ways should be better than our life today. To that end, Alcor aims to put more emphasis on rebuilding the kind of regional communities that drew so many people into cryonics in the first place. ■

Fight Aging!

Reports From the Front Line in the Fight Against Aging

Reported by Reason

Fight Aging! exists to help ensure that initiatives with a good shot at greatly extending healthy human longevity become well known, supported, and accepted throughout the world. To this end, Fight Aging! publishes material intended to publicize, educate, and raise awareness of progress in longevity science, as well as the potential offered by future research. These are activities that form a vital step on the road towards far healthier, far longer lives for all.

A Skeptical Review of the Evidence for Metformin

September, 2019

This review paper more or less leans towards my thoughts on metformin as a treatment to slow aging: the animal data is not great, the human data is a single study, the effect size on life span is far too small to care about, and the detrimental side effects are large in comparison to that effect size. The strategy of upregulating stress response mechanisms via drugs such as metformin is a poor strategy for long-lived species, as we clearly don't exhibit the sizable gains in life span that occur in short lived species such as mice under these circumstances. Metformin, in turn, is a low performance example of this strategy, much worse than, say, the practice of calorie restriction or mTOR inhibitors.

Metformin is sometimes proposed to be an "anti-aging" drug, based on preclinical experiments with lower-order organisms and numerous retrospective data on beneficial health outcomes for type 2 diabetics. Large prospective, placebo-controlled trials are planned, in pilot stage, or running, to find a new use (or indication) for an aging population. In 2015, Nir Barzilai met with regulators from the FDA to discuss the now famous phase III multi-site TAME (Targeting Aging with Metformin) trial. The acronym chosen and the intention behind it – namely, that aging is a "disorder" that can be treated like any other disease – was a clear provocation. The FDA's mandate is to regulate medications and devices to cure diseases or aid in their diagnosis, but aging is not (yet) an indication. Interestingly, frailty is missing from the proposed composite outcome. Other ongoing trials (e.g., NCT02570672) with metformin provide arguments that frailty may be an important endpoint. It will be interesting to compare the results with the ongoing fisetin trial (NCT03675724).

Although widely cited as evidence for the small effects of 0.1% metformin in the diet on the lifespan of older male inbred mice, earlier results obtained by researchers should be dismissed: the National Institute on Aging Interventions Testing Program could not replicate the findings regarding an extension of the lifespan with 0.1% metformin. The negative results were obtained at three different locations using genetically heterogeneous female and male mice.

The rationale for the ongoing or planned metformin trials is almost exclusively based on observations (associations) of potential benefits in a diabetic (or prediabetic) population. Its efficacy even in an at-risk cohort of aged people has not yet been proven. Metformin is associated with a higher risk of vitamin B12 and vitamin B6 deficiency, which may result in an increased risk of cognitive dysfunction. Supplementation is strongly recommended to metformin users.

Of greater concern are the results of small trials in which the effects of metformin on metabolic responses to exercise or on cardiorespiratory fitness were tested. In a placebo-controlled, double-blind, crossover trial with healthy young subjects, metformin caused a small but significant decline in maximal aerobic capacity. A double-blind, placebo-controlled landmark trial with older adults with one risk factor for type 2 diabetes investigated the effects of metformin and 12 weeks of aerobic exercise. Contrary to expectations – namely, that the effects of exercise and the drug would be additive – "metformin attenuated the increase in whole-body insulin sensitivity and abrogated the exercise-mediated increase in skeletal muscle mitochondrial respiration."

Link: https://doi.org/10.1159/000502257

Intervene Immune Publishes Thymus Regrowth Trial Results

September, 2019

Intervene Immune is the company formed to commercialize the methodology for regrowth of thymic tissue used in the small TRIIM (Thymus Regeneration, Immunorestoration, and Insulin Mitigation) trial, a combination of growth hormone, DHEA, and metformin. As I've noted in the past, that the approach involves the use of human growth hormone over an extended period of time makes it less desirable as an intervention, but if one can gain an expectation of some thymic regeneration, leading to an extended improvement in immune function that lasts for years beyond the treatment period, then it might be worth the trade-off. In general, higher growth hormone levels are associated with a worse outcome in the study of aging, while lower levels are associated with a slowing of aging. Using growth hormone for anything other than treating rare clinical conditions of deficiency is something like burning the candle at both ends.

The thymus is an inaccessible organ in the chest responsible for transforming thymocytes created in the bone marrow into T cells of the adaptive immune system. This complicated process takes place in thymic tissue that, unfortunately, atrophies with age, becoming replaced with fat. The less tissue, the fewer T cells are generated, and the worse the function of the immune system over time. The thymus loses much of its mass quite early in life, following childhood, but the later, slower decline over the course of adult life is a different process mediated by chronic inflammation and other factors that arise with old age. The adaptive immune system is vital to health, and thus a great deal of research has taken place over the past few decades into means of thymic regeneration: upregulation of FOXN1 or related genes such as BMP4; engineering of new thymic tissue; delivery of recombinant KGF, delivery of growth hormone; sex steroid ablation; and so forth. Some are more reliable than others, and some, such as KGF, have succeeded in mice and failed in human trials.

The Intervene Immune team has presented a fair amount of data on the results from their trial at recent conferences, including epigenetic age changes, and you'll find it all in the open access paper noted here. The results unfortunately don't include all of the assays of immune cell characteristics one might want in order to be able to compare directly with the effects of sex steroid ablation in human patients, but are intriguing. (In turn the sex steroid ablation trials didn't look at thymic mass in CT scans, an unfortunate omission). Further, it isn't possible to clearly associate all of the outcomes with regrowth of thymic tissue, particularly the epigenetic age effects, given everything else the treatment might be doing. Nonetheless, taken as a whole this is good supporting evidence for those groups working on more direct approaches to the problem of the atrophied thymus, such as Lygenesis and the company Bill Cherman and I founded last year, Repair Biotechnologies.

First hint that body's 'biological age' can be reversed

A small clinical study has suggested for the first time that it might be possible to reverse the body's epigenetic clock, which measures a person's biological age. For one year, nine healthy volunteers took a cocktail of three common drugs – growth hormone and two diabetes medications – and on average shed 2.5 years of their biological ages, measured by analysing marks on a person's genomes. The participants' immune systems also showed signs of rejuvenation.

The latest trial was designed mainly to test whether growth hormone could be used safely in humans to restore tissue in the thymus gland. The gland, which is in the chest between the lungs and the breastbone, is crucial for efficient immune function. White blood cells are produced in bone marrow and then mature inside the thymus, where they become specialized T cells that help the body to fight infections and cancers. But the gland starts to shrink after puberty and increasingly becomes clogged with fat. Evidence from animal and some human studies shows that growth hormone stimulates regeneration of the thymus. But this hormone can also promote diabetes, so the trial included two widely used anti-diabetic drugs, dehydroepiandrosterone (DHEA) and metformin, in the treatment cocktail.

Checking the effect of the drugs on the participants' epigenetic clocks was an afterthought. The clinical study had finished when geneticist Steve Horvath conducted an analysis. Four different epigenetic clocks were used to assess each patient's biological age, and he found significant reversal for each trial participant in all of the tests. "This told me that the biological effect of the treatment was robust. The effect persisted in the six participants who provided a final blood sample six months after stopping the trial. Because we could follow the changes within each individual, and because the effect was so very strong in each of them, I am optimistic."

Reversal of epigenetic aging and immunosenescent trends in humans

Thymus regeneration and reactivation by growth hormone administration have been established in aging rats and dogs by restoration of youthful thymic histology and by reversal of age-related immune deficits. The present study now establishes highly significant evidence of thymic regeneration in normal aging men accompanied by improvements in a variety of disease risk factors and age-related immunological parameters as well as significant correlations between thymic fat-free fraction (TFFF) and favorable changes in monocyte percentages and the lymphocyte-to-monocyte ratio (LMR), independent of age up to the age of 65 at the onset of treatment. These observations are consistent with the known ability of growth hormone to

stimulate hematopoiesis and thymic epithelial cell proliferation. Our finding of an increase in FGF-21 levels after 12 months of treatment suggests that thymic regeneration by the present treatment may be mediated in part by this cytokine, which we believe is a novel finding.

Treatment-induced increases in naïve CD4 and naïve CD8 T cells were relatively small compared to changes reported in recombinant growth hormone treated HIV patients, but our volunteer population was pre-immunosenescent and not depleted of naïve CD4 and naïve CD8 T cells at baseline. Positive responses also occurred despite potential complications caused by lymph node aging. Therefore, the small increases observed in these cells and in CD4 T-cell recent thymic emigrants are consistent with the ultimate goal of preventing or reversing the normal age-related collapse of the TCR repertoire at ages just above those of our study population.

There may be both immunological and non-immunological mechanisms of epigenetic aging reversal. Growth hormone, DHEA, and metformin have unique effects that are in opposition to aging, and it is possible that the specific combination of these agents activates a broad enough range of therapeutic pathways to account for the previously unpredictable reversal of epigenetic aging, even independently of the immunological markers we have measured.

An Investigation of Adverse Effects of Nicotinamide Riboside Supplementation

November, 2019

Nicotinamide riboside is so far the only approach to NAD+ upregulation for which there is published human trial data, though other trials for other approaches are underway at the present time. NAD+ declines with age, for reasons that remain comparatively poorly understood, and this has a negative impact on mitochondrial function. Thus there is considerable enthusiasm at the moment for intervening in this known manifestation of aging by tackling the proximate causes, raising NAD+ levels, but without addressing underlying causes.

Researchers here find the potential for adverse effects on glucose metabolism and white adipose tissue function to result from nicotinamide riboside supplementation, but there are a great many details involved: dietary differences and genetic differences in mice appear important as to whether problems arise, and the final sections of the discussion in the paper are worth reading closely. It is hard to say whether or not the discoveries made in mice that are reported in this open access paper will apply to humans, but the specific details suggest that investigation is warranted.

Nicotinamide riboside (NR) is a nicotinamide adenine dinucleotide (NAD+) precursor vitamin. The scarce reports on the adverse effects on metabolic health of supplementation with high-dose NR warrant substantiation. Here, we aimed to examine the physiological responses to high-dose NR supplementation in the context of a mildly obesogenic diet and to substantiate this with molecular data. An 18-week dietary intervention was conducted in male C57BL/6JRccHsd mice, in which a diet with 9000 mg NR per kg diet (high NR) was compared to a diet with NR at the recommended vitamin B3 level (control NR). Both diets were mildly obesogenic (40 en% fat). Metabolic flexibility and glucose tolerance were analyzed and immunoblotting, qRT-PCR, and histology of epididymal white adipose tissue (eWAT) were performed.

Mice fed with high NR showed a reduced metabolic flexibility, a lower glucose clearance rate and aggravated systemic insulin resistance. This was consistent with molecular and morphological changes in eWAT, including sirtuin 1 (SIRT1)-mediated PPARγ (proliferator-activated receptor γ) repression, downregulated AKT/glucose transporter type 4 (GLUT4) signaling, an increased number of crown-like structures and macrophages, and an upregulation of pro-inflammatory gene markers. In conclusion, high-dose NR induces the onset of WAT dysfunction, which may in part explain the deterioration of metabolic health.

Link: https://doi.org/10.3390/nu11102439

A Biomarker of Aging Based on Blood Protein Levels

December, 2019

A robust, reliable, low-cost biomarker of aging that measures the burden of damage that causes aging would be of great value to the field. It would allow rapid testing of potential rejuvenation therapies, given the capacity to show how effective a treatment is in only a short period of time: test once, apply the therapy, test again a few days or a month later. Most of the work aimed at producing and proving such a biomarker is focused on assessment of epigenetic changes that are characteristic of aging. This is not the only approach, however. Research groups are also attempting algorithmic combinations of very simple assessments such as grip strength and skin elasticity, while others, as is the case here, are focused on measuring protein levels in blood samples.

At the end of the day, however, it is still far from clear as to how all of these potential biomarkers relate to the underlying damage that causes aging. It is quite possible that they are strongly dependent on only a fraction of the full range of types of damage, for example. A rejuvenation therapy might not change the biomarker as much as it should. Or perhaps more than it

should. Thus proving out biomarkers must proceed in parallel with proving out rejuvenation therapies based on damage repair. At the present time one cannot just blindly use any of the existing biomarkers and assume the results to be useful in the matter of assessing interventions.

One interesting outcome from the work noted here is that it shows staged alterations in the biomarker, rather than a smooth progression of changes. The first such change occurs quite early, in the 30s. One might compare that result with recent work on changes in the gut microbiome that also shows alterations in gut microbe populations that are relevant to health, due to a loss of beneficial compounds produced by these microbes, taking place during the 30s – at exactly the same average age in the mid-30s, in fact, which is most intriguing.

Stanford scientists reliably predict people's age by measuring proteins in blood

Researchers analyzed the levels of proteins circulating in plasma – the cell-free, fluid fraction of blood – from 4,263 people ages 18-95. On measuring the levels of roughly 3,000 proteins in each individual's plasma, researchers identified 1,379 proteins whose levels varied significantly with participants' age. A reduced set of 373 of those proteins was sufficient for predicting participants' ages with great accuracy. In fact, a mere nine proteins were enough to do a passable job, and adding more proteins to the clock improves its prediction accuracy only a bit more.

The study's results suggest that physiological aging does not simply proceed at a perfectly even pace, but rather seems to chart a more herky-jerky trajectory, with three distinct inflection points in the human life cycle. Those three points, occurring on average at ages 34, 60 and 78, stand out as distinct times when the number of different blood-borne proteins that are exhibiting noticeable changes in abundance rises to a crest. This happens because instead of simply increasing or decreasing steadily or staying the same throughout life, the levels of many proteins remain constant for a while and then at one point or another undergo sudden upward or downward shifts. These shifts tend to bunch up at three separate points in a person's life: young adulthood, late middle age and old age.

The investigators built their clock by looking at composite levels of proteins within groups of people rather than in individuals. But the resulting formula proved able to predict individuals' ages within a range of three years most of the time. And when it didn't, there was an interesting upshot: People whose predicted age was substantially lower than their actual one turned out to be remarkably healthy for their age.

Undulating changes in human plasma proteome profiles across the lifespan

Aging is a predominant risk factor for several chronic diseases that limit healthspan. Mechanisms of aging are thus increasingly recognized as potential therapeutic targets. Blood from young mice reverses aspects of aging and disease across multiple tissues, which supports a hypothesis that age-related molecular changes in blood could provide new insights into age-related disease biology. We measured 2,925 plasma proteins from 4,263 young adults to nonagenarians (18-95 years old) and developed a new bioinformatics approach that uncovered marked non-linear alterations in the human plasma proteome with age. Waves of changes in the proteome in the fourth, seventh and eighth decades of life reflected distinct biological pathways and revealed differential associations with the genome and proteome of age-related diseases and phenotypic traits. This new approach to the study of aging led to the identification of unexpected signatures and pathways that might offer potential targets for age-related diseases.

A Look Back at 2019: Progress Towards the Treatment of Aging as a Medical Condition

December, 2019

It is that time again, an arbitrary midwinter point in the annual pilgrimage around the sun at which we take a look back to summarize some of the high points of the past year. As has been the case for a few years now, progress towards the implementation of rejuvenation therapies is accelerating dramatically, ever faster with each passing year. While far from everyone is convinced that near term progress in addressing human aging is plausible, it is undeniable that we are far further ahead than even a few years ago. Even the public at large is beginning to catch on. While more foresightful individuals of past generations could do little more than predict a future of rejuvenation and extended healthy lives, we are in a position to make it happen.

The State of Funding

A great deal of venture funding is arriving or preparing to arrive to support biotech startups that are working on means to treat aging. This year saw the launch of the Longevity Vision Fund, among others. I can think of three groups presently working to launch new mid-sized longevity-focused venture funds in 2020, and this is as seen from my fairly sedate perch of observation, without any great attempt to reach out and ask folk for a census. This activity will have a beneficial influence on public and private funding available for fundamental science in this part of the field. It also influences non-profit advocacy, as new organizations such as the Academy for Health and Lifespan Research are created. New governmental initiatives are also emerging, such as the Healthy Longevity Global Grand Challenge, and not just in the US: the UK government is putting out position statements on health longevity. Regulators are being petitioned by the scientific

community to approve treatment of aging as a recognized goal for medicine. We should expect this trajectory to continue, though beyond the clearance of senescent cells, where development of therapies is very much a going concern, few approaches to rejuvenation are very close to making the leap from laboratory to clinical development.

There is no shortage of new companies targeting aging, many of which are (unfortunately, I think) focused on manipulation of stress responses rather than rejuvenation. BHB Therapeutics works on ketosis mechanisms. Turn.bio aims to produce a safe way to partially reprogram cells in vivo, restoring youthful function. Samsara Therapeutics works on autophagy enhancement. Rejuvenate Bio works on gene therapies to slow aging, initially in dogs. My own company, Repair Biotechnologies, still young, raised a seed round to fund our work on thymic regeneration and reversal of atherosclerosis. The Oisin Biotechnologies spinoff OncoSenX also raised a seed round this year to deploy their suicide gene therapy in cancer patients, and LIfT Biosciences raised funds to develop immune cell transplants that have been shown to do very well against cancer in animal models. Underdog Pharmaceuticals is the SENS Research Foundation spinout targeting 7-ketocholesterol (which may be important in more than just atherosclerosis). They raised a seed round this year and are well on their way. Nanotics has launched a senolytics program based on interfering in mechanisms that senescent cells used to evade immune surveillance. For more you might look at the recently created Aging Biotech Info and its curated list of companies in the longevity industry.

Speaking of funding, the SENS Research Foundation year end fundraiser is coming to a close. More than three quarters of a million dollars was donated last year. I hope that you all did your part and contributed this year – helping this form of research is the most effective form of altruism, given the size of the potential benefits. The SENS Research Foundation remains one of the most important organizations in research aimed at treating aging. Just because senolytics to clear senescent cells is a going concern, we cannot ignore the fact that the rest of the rejuvenation research agenda is nowhere near as advanced. It still needs funding, and near all funding for many of these vital projects remains philanthropic. We fund it. We are the people who make that difference, ensuring that important research projects can advance to the point at which they attract the support of more conservative, mainstream sources of large-scale funding.

Conferences and Community

These days, I'm as often as not out and about in the world raising funding or reporting on progress for a startup biotech company, Repair Biotechnologies. I'm found at many more conferences than would otherwise be the case. Side-effects of the growth of the longevity industry over the past few years include a change in the tenor of existing scientific conferences, as well the addition of new conference series on aging that are focused as much on industry as on academia. This past year, I attended and wrote up a few notes on the following events: the SENS Research Foundation / Juvenescence gathering in San Franscisco held alongside the big JPM Healthcare conference; the first Longevity Therapeutics event, also in San Francisco; the Longevity Leaders conference in London; the vitally important Undoing Aging in Berlin; Biotech Investing in Longevity in San Francisco; the Ending Age-Related Diseases conference organized by LEAF in New York; BASEL Life, Founders Forum, LSX USA, and Giant Health in quick succession later in the year; the Alcor New York Science Symposium; and the Longevity Week events in London coordinated by Jim Mellon and his allies.

Many conference presentations and interviews with members of the growing community have been published over the past year, too many to note each and every one.

Clinical Development

Drug development pipelines are moving forward, though not always smoothly. There is a high failure rate in the development of medical biotechnology. Eidos Therapeutics announced Phase II results for their approach to preventing transthyretin amyloid aggregation. Gensight is presently struggling with phase III for allotopic expression of mitochondrial genes – the mechanism works, the earlier trials passed, and now reaching sufficient efficacy is proving to be a challenge. Intervene Immune published interesting results from their small thymic regeneration trial, while Libella Gene Therapeutics is launching a patient paid trial for telomerase gene therapy. The resTORbio approach to inhibition of mTORC1 failed a phase III trial for immunosenescence, which may or may not cast a pall over that part of the industry. The TAME clinical trial for metformin, using a new composite endpoint as a surrogate for aging, was funded this year and will start soon. This despite the point that metformin remains a terrible choice of intervention, picked because the FDA couldn't object to it on technical grounds, not because anyone thinks that it will produce meaningful results for patients. Opinions are mixed on this topic.

The first human trials of senolytic therapies to clear senescent cells reported results this year, starting with promising results for lower dose dasatinib and quercetin versus idiopathic pulmonary fibrosis. Data from an as yet incomplete trial of dasatinib and quercetin versus chronic kidney disease has confirmed that these senolytics do clear senescent cells in humans in the same way as in mice. Unity Biotechnology announced results from their first trial of senolytics for osteoarthritis of the knee, and is moving on to phase II. There are those who think that there is still a long road ahead to the clinic. A trial of fisetin by the Mayo Clinic has yet to publish results, but for those who'd like to follow along at home in advance of data, the Forever Healthy Foundation published a risk/benefit analysis covering what is known of fisetin as a senolytic.

Cellular Senescence

Senescent cells accumulate with age and contribute to degenerative disease, despite their many beneficial roles earlier in life. Senolytics to selectively destroy lingering senescent cells continue to show great promise in animal models, and as a class of therapy appear about as close to a panacea as it is possible to be. New supporting evidence published over the course of 2019 offers the potential of effective treatment for a range of conditions: Alzheimer's disease, osteoporosis, osteoarthritis, rheumatoid arthritis, atherosclerosis, cardiac fibrosis and hypertrophy, periodontitis, pulmonary fibrosis, cataracts, aortic aneurysm, acute kidney injury, chronic kidney disease, heart failure, type 1 diabetes, type 2 diabetes, thrombosis, degenerative disc disease, immunosenescence due to changes in hematopoiesis, pulmonary disease resulting from smoking, age-related loss of liver function, neurodegeneration through astrocyte senescence, recovery from heart attack, and recovery from chemotherapy. The accumulation of senescent T cells is an important component of immune aging and chronic inflammation, including some of the issues observed in type 2 diabetes. Visceral fat tissue produces many of its harmful effects via the generation of more senescent cells than would otherwise be created.

Any number of compounds are under evaluation as potential senolytics, though we should always be skeptical of effect size until animal data is in hand, particularly when the compounds include those already in widespread use, as drugs, supplements, or components of diet. Compounds recently examined for senolytic effects include circumin analogs, the fibrate class of drugs used to treat raised blood lipid levels, cardiac glycosides used in treatment of aspects of heart disease, and quercetin coated nanoparticles. Other approaches also exist: exosomes from embryonic stem cells clear senescent cells, and it may be possible to interfere in the mechanisms that senescent cells use to evade the immune system. Further, designed compounds that are transformed into toxins by senescence-associated β-galactosidase, which is upregulated in senescent cells, appear a promising line of attack.

A great deal of research is ongoing into the biochemistry of cellular senescence, not least because any particular mechanism might turn out to be the basis for therapies that meaningfully turn back aging – there is a little of the element of a gold rush to the work. Senescent cells are large because they produce too much protein in expectation of cell division that doesn't occur – or possibly also because they consume neighboring cells. The ceremides found in extracellular vesicles increase senescence. Versican may link the hyperglycemic diabetic metabolism to increased vascular calcification via cellular senescence. The harmful secretions of senescent cells, the senescence-associated secretory phenotype (SASP) depend on certain aspects of the heterochromatin. The activity of L1 retrotransposons also appears relevant to the SASP. Naked mole-rat senescent cells do not exhibit the SASP, which goes a long way towards explaining how this species can exhibit robust good health even while accumulating senescent cells just like other mammals. Meanwhile, researchers are producing a comprehensive map of all of the molecules making up the SASP, many of which are conveyed via exosomes. Another group has published a database of senescence-associated genes. Acute myeloid leukemia turns out to produce senescent cells to aid its own growth. The gene ccna2 is a regulator of the senescent state. Rising levels of aneuploidy may be important in increasing numbers of senescent cells. Upregulation of CBX4 or DGCR8 reduces senescence in mice. Melanocytes are the only epidermal cell type to exhibit senescence. Age-related AT1 autoimmunity may spur generation of senescent cells in vascular tissue, and consequent vascular dysfunction.

An important part of the senolytics industry, and one that has so far lagged behind, is the ability to quantify the number of senescent cells in different tissues by age, along with their pace of creation. A start on senescence burden by tissue and age was published this year for mice, accompanied by a good review on the far patchier data for humans. Are these errant cells lingering for years on end, or is turnover and clearance still happening in very old people, and just needs a helping hand? Recent work on topical rapamycin for skin aging and the speed of senescent cell clearance by age suggests that the latter model is more the case. Answering these questions robustly will require better means of quantifying senescence in patients without resorting to a biopsy. This might be achieved via fluorescent reporter genes, or, for senescence in the kidney, by suitable urinalysis. It will likely also require better and more consistent signatures of cellular senescence.

Mitochondria in Aging

Mitochondrial function is clearly important in the progression of aging. Why does it falter consistently in cells throughout the body? Proximate causes appear to involve a loss of fission, leading to worn and damaged mitochondria that are too large to be effectively cleared by mitophagy; this appears to be related to changing expression of PUM2 and MFF, but how that relates to the underlying molecular damage of aging remains a question.

A method of enhancing mitophagy has been shown to improve mitochondrial function in old humans. Other approaches to mitochondrial decline are at various stages of development, such as delivering entire mitochondria that are taken up by cells and put to work. The SENS Research Foundation team continues to work on allotopic expression of mitochondrial genes as a way to prevent certain forms of mitochondrial DNA damage from causing cells to become pathological, and crowdfunded one of the next steps in their program this year.

Efforts to increase NAD+ levels in old mitochondria are enjoying considerable support at present, though it remains to be proven rigorously that they are producing benefits in the many people who are chosen to employ the various supplements. Animal studies and human trials continue, as does the more fundamental research into the biochemistry of NAD+ in mitochondria. An NMNT

inhibitor improves NAD+ salvage to increase stem cell function. Nicotinamide riboside improves intestinal stem cell function. The levels of eNAMPT may be important in the way nicotinamide mononucleotide supplementation increases NAD+. Increased NAD+ levels also slows age-related hearing loss in mice.

Nuclear DNA Damage

Random mutations can spread through a tissue when they occur in stem cells or progenitor cells. There are also epigenetic mutations to consider, persistent and aberrant changes in epigenetic markers that alter the production of proteins. Is this damage a meaningful cause of aging beyond its contribution to cancer risk, though? Most mutations happen in genes that are turned off in tissues. There was a discussion earlier this year of the evidence for this sort of clonal expansion of mutations to be involved in neurodegeneration.

The most interesting new work to emerge this year suggests that repair of certain types of DNA damage causes the epigenetic changes observed to take place with age. Since this mechanism doesn't depend on the mutation of specific genes, and the effect arises wherever the DNA damage occurs in the genome, this is a viable alternative to explain how mutational damage can contribute to aging in a way that is very similar in every cell, despite the random nature of the damage, and the fact that the damage largely occurs to irrelevant portions of the genome. It also has implications for the viability of epigenetic reprogramming as an intervention. That the pathological outcomes of the DNA repair deficiency Werner syndrome were shown this year to be strongly dependent on mitochondrial dysfunction, which itself emerges from changes in gene expression mediated by epigenetics, might be taken as somewhat supportive of this new line of work.

Cross-Links

There has been little further progress towards bringing approaches to cross-link breaking into a new generation of startup companies this year. Revel Pharmaceuticals, spinning out from the Spiegel Lab at Yale, has yet to raise seed funding to progress beyond initial setup – this is taking far too long, for reasons that have little to do with the technical details. An interesting unrelated advance relates to cross-links in the lens of the eye, which are completely different from those in other tissues in the body and thus require a different approach. A cross-link breaker for these forms of cross-link was trialed for age-related presbyopia, and the results were good.

Neurodegeneration

In neurodegenerative research, the concept that failing drainage of cerebrospinal fluid from the brain is an important component of these conditions is gaining support. Cerebrospinal fluid drainage clears metabolic waste from the brain – and this clearance fails with age as the channels are disrupted by tissue dysfunction. Researchers have suggested that hypertension may contribute to the effect, along with age-related declines in lymphatic vessel function, and have provided evidence for reduced flow to correlate with cognitive decline.

Another growing theme in the study of neurodegenerative conditions is the importance of chronic inflammation. This is thought to be the mechanism by which gum disease is linked to Alzheimer's risk, for example. The neuroinflammation model of Alzheimer's disease inverts the first two steps in the amyloid cascade hypothesis: instead of amyloid aggregation causing chronic inflammation, which in turn produces tau aggregation, the chronic inflammation is the whole of the cause of the early stages of the condition, with amyloid as a side-effect. Much the same view is argued for Parkinson's disease and its protein aggregates. The infection hypothesis is a different aspect of this view, in which amyloid aggregation and chronic inflammation both arise from persistent viral infection. A variant of this hypothesis places more emphasis on the way in which infection generates senescent immune cells in the brain, promoting inflammation via that path. In any of these possibilities, dysfunction in glial cells is an important part of the inflammatory process, and depleting these cells reduces inflammation and consequent tau pathology. There is evidence in mice for herpesviruses to accelerate amyloid buildup. Whatever the order of causation, there is good evidence for amyloid and tau aggregates to synergize with one another in degrading neural function.

The evidence for CMV to generate chronic inflammation and otherwise impact immune function suggests that persistent viral infection is harmful in general, not just when it comes to the brain. The immune system and its decline is an important determinant of aging, and chronic inflammation is the proximate cause of a sizable fraction of age-related disease. Complicating matters, chronic inflammation might even contribute to thymic involution, an important cause of immune aging.

The Alzheimer's community is looking for new approaches. There is an increasing focus in the Alzheimer's research community on targeting tau rather than amyloid-β. A variety of methods are under exploration. An existing farnesyltransferase inhibitor drug was found to reverse tau aggregation in a mouse model. Approaches aimed at clearance of amyloid-β have not gone away, of course, and are still very actively developed. The use of affibodies is becoming explored, to pick one example. Clearance of protein aggregates is still a comparatively underutilized approach for other neurodegenerative conditions, however. There is still work taking place, such as small molecule discovery to interfere in α-synuclein aggregation in Parkinson's disease, or catching α-synuclein aggregation in the gut before it spreads to the brain. Researchers are also investigating the heat shock response as a way to direct greater clearance of protein aggregates, as well as the far more promising use of catabodies as pioneered by Covalent Bioscience.

The blood-brain barrier has long been thought important in neurodegeneration. Dysfunction in the barrier is an early leading indicator of larger neurodegeneration, though, confusingly, amyloid aggregation can cause blood-brain barrier leakage. This dysfunction is centered around the tight junction structures of the barrier, and it isn't just neurodegenerative conditions in which this is a factor. Many forms of damage to the brain are characterized by leakage of the blood-brain barrier. Early disruption of the barrier might be due in part to increased levels of acid sphingomyelinase. The primary contribution of blood-brain barrier dysfunction to neurodegeneration may well be that a leaking barrier allows the passage of cells and molecules that drive chronic inflammation in brain tissue, such as fibrinogen.

Upregulation of Cell Maintenance

Upregulation of the various cell maintenance processes in order to modestly slow aging, particularly autophagy (a process that shows up everywhere in aging) and the ubiquitin-proteasome system, is an area of active research. Autophagy is known to decline with age for a variety of reasons, such as progressive failure to form autophagosomes. Recent evidence links this decline to aging in skin, and accumulation of senescent cells in the brain.

Strangely, there hasn't been all that much progress towards the clinic over the past decade, despite all of this ongoing activity. Restoration of mitophagy has been proposed as a potential treatment for neurodegenerative conditions. Upregulation of autophagy in general has recent evidence supporting its use in slowing the progression of sarcopenia, memory B cell decline, and atherosclerosis. Researchers have also proposed altering the behavior of the proteasome to target unwanted molecules, such as those altered by misfolding, or achieving a similar effect by binding unwanted proteins to component parts of the autophagosome, ensuring they get dragged along to the lysosome for disassembly. Targeting the GATA transcription factor can upregulate autophagy. The proteasome can be made more active by increasing production of one of its component parts, which is an interesting potential strategy that is gaining some support in the research community. Improving cellular maintenance in intestinal stem cells extends life in flies, a species in which intestinal function is particularly important in aging.

In Vivo Cell Reprogramming

A number of groups are working on in vivo cell reprogramming, applying similar strategies to that used to produce induced pluripotent stem cells, but in a living animal. Turn.bio launched this year to work on a method of partial reprogramming, and another group has demonstrated regeneration from optic nerve injury. The challenge here is cancer risk, and the gains appear at this point to be some combination of restoring more youthful mitochondrial function and epigenetic control of gene expression.

Parabiosis

Work on parabiosis continues apace, linking the circulatory systems of an old and a young animal and observing the results on each. It is a way to identify factors in young blood and tissue or old blood and tissue that can slow or accelerate aging, for all that the evidence is somewhat confusing and contradictory at this time. The two companies in the space in recent years, Ambrosia and Alkahest have produced only marginal results in human trials. Researchers have found MANF as a possible factor in young blood, associated with liver function. Factors in young blood appear to influence kidney function via upregulated autophagy. It is argued that most of the effects of parabiosis are mediated by the contents of extracellular vesicles, not individually secreted proteins. Beyond parabiosis, there are other approaches that involve introducing young tissue into old animals. Researchers have shown that transplanting young bone marrow into old mice is beneficial, resulting in extended life span.

The Gut Microbiome in Aging

Research into the role of changes in the gut microbiome in aging seems to be hitting its stride. The effect size of the loss of beneficial bacteria and gain in harmful bacteria is an open question, but studies in short-lived animals suggest it might be in the same ballpark as that of exercise. Certainly, healthier older people tend to have more youthful-appearing microbial populations, and this is true for thinner, fitter individuals as well. Changes in the microbiome are shown to contribute to inflammation and vascular dysfunction, as well as neurodegenerative conditions. Further, a number of quite concrete, actionable discoveries have been made in the past few years. The secretion of proprionate improves exercise capacity, and the microbes responsible are found in athletes. Optimizing gut microbial populations for greater butyrate production is beneficial to cognitive function. The populations responsible for providing tryptophan and indole decline precipitously in the mid 30s in humans, indicating supplementation of these metabolites or restoration of the lost microbes will be beneficial when started comparatively early in adult life, well ahead of most signs of aging.

Calorie restriction slows changes in the gut microbiome, but can these age-related changes be reversed? The answer is yes: transplantation of young microbes into old animals has produced good results in animal studies. Fecal microbiota transplantation is an established procedure in human medicine for conditions in which the gut is overtaken with pathological microbes, so perhaps it would not be a huge leap to extend it to improving the elderly gut microbiome. There are other approaches: limiting energy generation by pathological bacteria can diminish these populations; immunization against flagellin causes the immune system to more aggressively cull harmful gut microbes.

Biomarkers of Aging

The measurement of aging is an important goal. Quick, low-cost, reliable assessments that can be used shortly before and shortly after application of a potential rejuvenation therapy would greatly speed development of the field. Epigenetic clocks based on DNA methylation are the best known of present development programs aimed at producing biomarkers of aging. These clocks are multiplying rapidly, and do a fair job of predicting disease risk and mortality. Epigenetic age correlates with cancer risk, for example. The GrimAge clock was announced this year, as was a ribosomal DNA focused clock. In a related part of the field of epigenetic research, it was recently found that CpG site density in the genome correlates with species life span.

The clocks are not without their challenges. We don't know what they are actually measuring, and there is no guarantee that the results will be useful for any given therapy. Troubling results have been reported, the most recent of which include the inability of the clocks to distinguish between sedendary versus active twins, and lack of correlation between telomere length measures and epigenetic clocks.

Epigenetic measures are far from the only area of focus. Other groups are set on constructing biomarkers of aging from algorithmic combinations of simple measures such as grip strength, or from the gut microbiome. In the past year, other researchers have proposed intron retention via alternative splicing, the fundamentals of systems biology, measurement of protein levels in blood, and immune system metrics as potential foundations for a biomarker.

Cancer

I don't watch cancer research in as much detail as I did in past years. There is a lot of very interesting work taking place, nonetheless, and the outlook is favorable for those of us who are expecting to tackle our own cancers two decades or more in the future – survival rates continue to improve, and the technologies presently in trials or development are considerably better than past therapeutic approaches. Much of the focus these days is on the refinement of ways to unleash the immune system, removing suppression mechanisms that are preventing it from vigorously attacking tumors. For example by interfering in CD47 signaling or the newly discovered similar role for CD24. There are also more speculative early stage approaches such as permanently increasing the number of natural killer cells to reduce cancer risk, or clearing out subsets of tumor associated macrophages that appear to be suppressing anti-tumor immune function.

That said, some more exciting work turns up at early stages, such as a potentially safe way to suppress telomerase activity. All cancers require lengthening of telomeres, via telomerase or ALT. Turning that off could be a universal cancer therapy. On the ALT side of the house, researchers have found that inhibition of FANCM activity is a potential point of intervention.

The Genetics of Longevity

All things genetic continue to attract a great deal of funding. This is an age of low-cost, high-capacity genetic tools – but given a hammer, perhaps too many things start to look like a nail. Studies of recent years have shown over and again that genetic contributions to human variance in aging are near entirely some combination of rare and inconsistent, small in effect size, and overall not all that important. Essentially, we all age in the same way, because of the same causes, and the observed variance is largely down to environment, chance, and choice. Based on this, I predict, and we can come back and look at this prediction in a few years, that the benefits produced by senolytic rejuvenation therapies will be very little affected by human genetic variation, as this form of therapy targets a mechanism in which the size of effect is significantly larger than the variance in that effect.

Regenerative Medicine

Efforts are underway to replace first generation cell therapies of many sorts, some of which were never even deployed to the clinic, with the delivery of extracellular vesicles harvested from those cells. This appears a very promising line of work. Development is underway aimed at skin regeneration, such as via increased collagen production, as well as osteoporosis and thymic regrowth. One can also mix and match: use exosomes to make a cell therapy more effective. Another possible approach to the replacement of cell therapies is reprogramming of cells in situ, such as to make astrocytes or glial cells become neurons in the brain, or turning supporting retinal cells into photoreceptors, heart fibroblasts into cardiomyocytes, or inner ear cells into sensory hair cells to replace losses. There is also considerable interest in rejuvenating stem cell populations in situ via signaling molecules, gene therapies (such as upregulation of GAS1 in muscle stem cells, or Nrf2 for degenerative disc disease), or other strategies.

Cell therapies are of course still very much a going concern, for all that their implementation in the clinic has proven to be challenging. There are some surprising successes in animal models, such as the use of a stem cell therapy to restore lost sense of smell in mice. Researchers are working on ways to replace lost cell populations or influence disease processes in Parkinsons's disease, atherosclerosis, corneal damage, and hearing loss, just to list a small selection of work from the past year. A large part of working towards success in this goal is to ensure that more cells survive and engraft, and that might be achieved by as simple an approach as culling less healthy cells prior to transplant. The march towards more cost-effective means of cell therapy continues, with the creation of cell lines that can be used in every patient being a priority. That reprogramming cells into induced pluripotent stem cells reverses epigenetic

signatures of aging seems like a good reason to put more effort into using these cells as a basis for therapy.

In the tissue engineering space, the research and development community continues to move towards the growth of human organs in animals as a source for transplantation. Meanwhile, organoids are being generated for many tissue types; work on the kidney is being carried out by numerous research groups. Further, some organs are simple enough that simpler, artificial versions are useful – artificial lymph nodes, for example, are a popular topic. Or bioprinted corneal tissue. Arguably the biggest advances of the past year have been demonstrations of printed tissue incorporating microvasculature, either directly printing vascular channels, via a form of sacrificial embedded printing, or by providing a mix of cells that generates a vasculature in and of itself, potentially working around the limits to size on engineered tissues. Justifiably, these advances received considerable attention.

Odds and Ends

As is usually the case, a range of scientific work was published this year relating to approaches that could in principle lead to enhancement biotechnologies that would improve health and capabilities for everyone, not just sick people. There is, sadly, near zero chance that most such approaches will be developed to the point of robust function and widespread availability, given the present regulatory environment. To pick a few examples: symbiotic bacteria that increase oxygen availability in tissues; CXCL12 promotes small artery growth, providing alternative paths for the bloodstream that can reduce mortality and harm from heart attacks and similar blood vessel blockages. One of the possible exceptions to the absence of development efforts is delivery of soluble klotho, which has been picked up by Unity Biotechnology to expand their pipeline beyond senolytics.

There are of course any number of other topics I could have discussed at greater length and chose to skip over for the sake of time. Destruction and recreation of the immune system as a way to put autoimmunity into remission continues to be promising, and continues to need a better, safer approach than hematopoietic stem cell transplantation. Age-associated B cells are a good target for more selective destruction, though, as ever, it doesn't fix as many problems as we'd like it to. Being fit is good for you, and in a world without rejuvenation therapies, exercise capacity is a better predictor of mortality than chronological age. Reversal of atherosclerosis is ever an interesting topic, and earlier this year I summarized some of the past work in this part of the field in the context of nattokinase. In this context, it is fascinating that humans seem to need far less cholesterol than we actually have in our bloodstreams, even in a healthy state. Naked mole-rats have a far more effective and resilient metabolism than other mammalian species, and it is possible that improved mitochondrial antioxidants might be a part of that general superiority – though this is a species that thrives under high oxidative stress. There was a sizable debate over whether or not Jeanne Calment was actually aged 122 at death. Late life mortality is in general tough to examine because the data is of a terrible quality, which makes it difficult to debate propositions such as whether or not there is a limit to human longevity in the present environment of slowly increasing life spans. Does obesity actually accelerate aging? Quite likely yes. Declines in the density of microvasculature may be an important mediating process in aging, linking fundamental molecular damage to declining tissue function as a consequence. TDP-43 protein aggregation is a comparatively newly discovered form of proteopathy causing neurodegeneration, and researchers continue to explore the implications. Human cell division rates decrease with age, which might explain why cancer risk actually declines in very late life. Amyloid buildup in the heart correlates with the risk of atrial fibrillation, adding to data from past years showing that amyloid contributes to heart disease and cardiac mortality. Dogs are a possibly underused model for aging research; that underuse might change with the growth of the Dog Aging Project.

Short Articles

As usual, a number of short articles were written over the past year, though it seems I'm doing this less often than used to be the case. Time is ever fleeting.

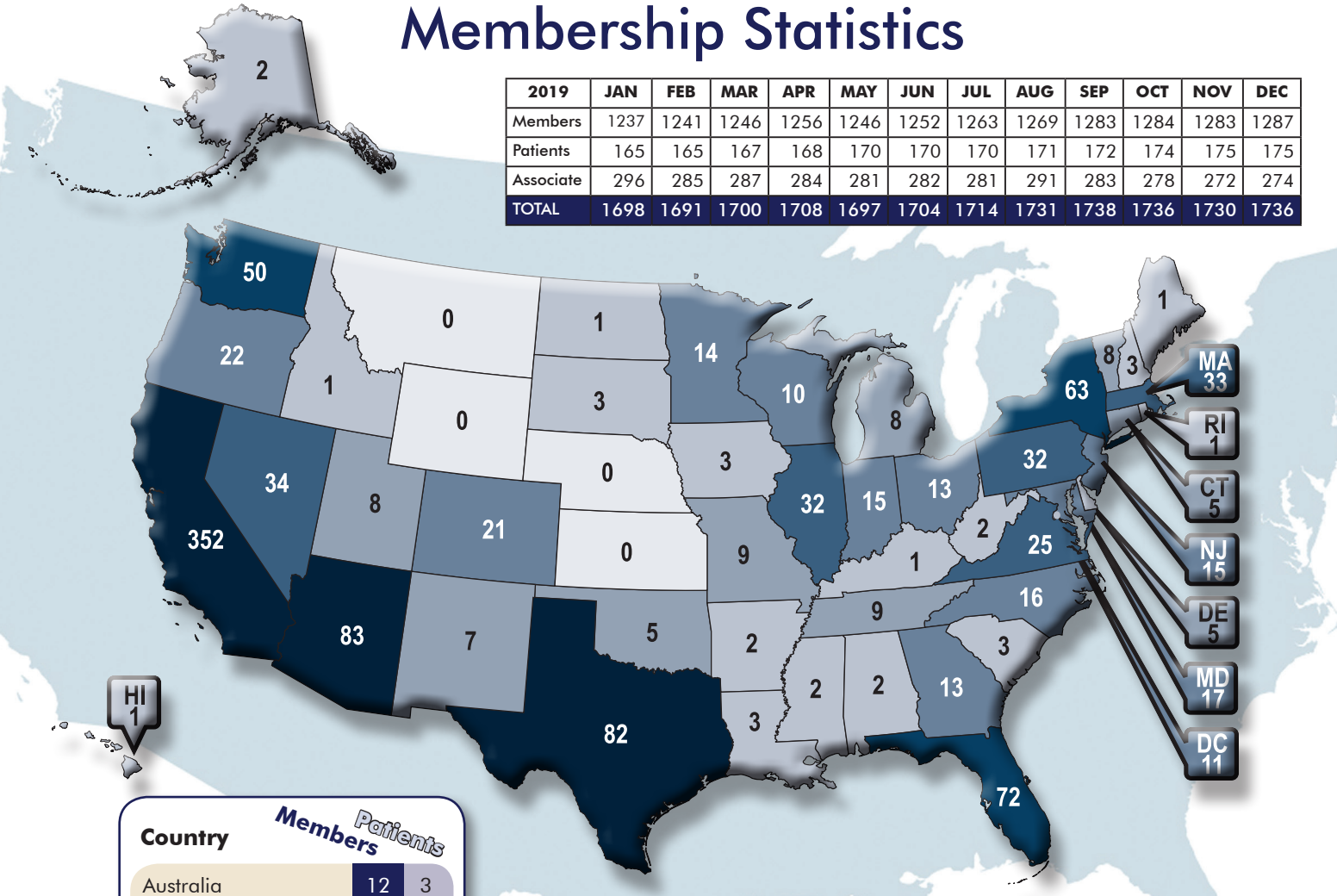
- Request for Startups in the Rejuvenation Biotechnology Space, 2019 Edition
- Rejuvenation Therapies Will Also Have Cycles of Hope and Disillusionment
- The Cosmological Noocene
- Taking the Founders' Pledge to Donate to Charity Following a Liquidity Event
- How to Start a Biotech Company in the Longevity Industry

In Conclusion

A great deal of progress is being made in the matter of treating aging: in advocacy, in funding, in the research and development. It can never be enough, and it can never be fast enough, given the enormous cost in suffering and lost lives. The longevity industry is really only just getting started in the grand scheme of things: it looks vast to those of us who followed the slow, halting progress in aging research that was the state of things a decade or two ago. But it is still tiny compared to the rest of the medical industry, and it remains the case that there is a great deal of work yet to be done at all stages of the development process. Senolytics must reach the clinic and widespread availability, and that will involve the deployment of vast amounts of funding. At the same time, however, numerous other equally important lines of rejuvenation research are still largely stuck in the labs or in preclinial development at best. There is much left to accomplish. ■

Membership Statistics

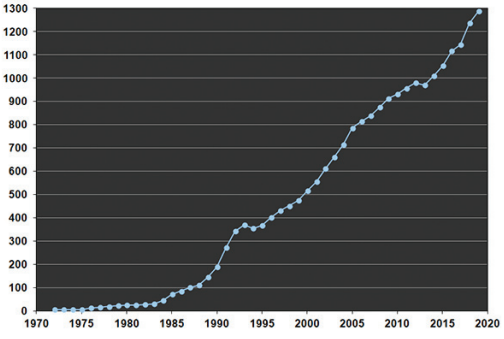
2019	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Members	1237	1241	1246	1256	1246	1252	1263	1269	1283	1284	1283	1287
Patients	165	165	167	168	170	170	170	171	172	174	175	175
Associate	296	285	287	284	281	282	281	291	283	278	272	274
TOTAL	1698	1691	1700	1708	1697	1704	1714	1731	1738	1736	1730	1736



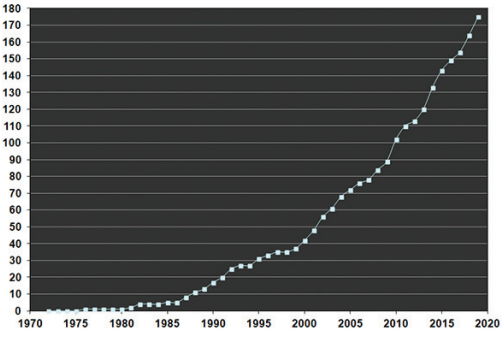
International Members & Patients

Country	Members	Patients
Australia	12	3
Austria	1	0
Belgium	1	0
Brazil	1	0
Bulgaria	1	0
Canada	62	4
China	0	1
Finland	1	0
France	0	1
Germany	18	0
Hong Kong	1	0
Israel	1	1
Italy	2	0
Japan	5	0
Luxembourg	1	0
Mexico	5	0
Monaco	1	0
Netherlands	1	0
New Zealand	1	0
Norway	2	0
Portugal	4	1
Puerto Rico	1	0
South Korea	1	0
Spain	5	1
Taiwan	1	0
Thailand	2	1
United Kingdom	40	3
TOTAL	170	16

- 0 Members
- 1–4 Members
- 5–9 Members
- 10–24 Members
- 25–49 Members
- 50–74 Members
- 75+ Members



Number of Alcor members



Number of Alcor patients

Alcor Associate Membership

Supporters of Alcor who are not yet ready to make cryopreservation arrangements can become an Associate Member for $5/month (or $15/quarter or $60 annually). Associate Members are members of the Alcor Life Extension Foundation who have not made cryonics arrangements but financially support the organization.

Associate Members will receive:

- ***Cryonics* magazine by mail**
- **Discounts on Alcor conferences**
- **Access to post in the Alcor Member Forums**
- **Access to local Alcor meetings and training events**

ALCOR
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The World's Leader in Cryonics
www.alcor.org

To become an Associate Member send a check or money order ($5/month or $15/quarter or $60 annually) to Alcor Life Extension Foundation, 7895 E. Acoma Dr., Suite 110, Scottsdale, Arizona 85260, or call Marji Klima at (480) 905-1906 ext. 101 with your credit card information.

Or you can pay online via PayPal using the following link: http://www.alcor.org/BecomeMember/associate.html *(quarterly option is not available this way)*.

Associate Members can improve their chances of being cryo-preserved in an emergency if they complete and provide us with a Declaration of Intent to be Cryopreserved (http://www.alcor.org/Library/html/declarationofintent.html). Financial provisions would still have to be made by you or someone acting for you, but the combination of Associate Membership and Declaration of Intent meets the informed consent requirement and makes it much more likely that we could move ahead in a critical situation.

Revival Update

Scientific Developments Supporting Revival Technologies

Reported by R. Michael Perry, Ph.D.

Translational Regulation of Non-autonomous Mitochondrial Stress Response Promotes Longevity

Lan J, Rollins JA, Zang X, Wu D, Zou L, Wang Z, Ye C, Wu Z, Kapahi P, Rogers AN, Chen D

PubMed, Cell Rep. 2019 Jul 23;28(4):1050-1062, https://www.ncbi.nlm.nih.gov/pubmed/31340143, accessed 20 Jan. 2020

Abstract

Reduced mRNA translation delays aging, but the underlying mechanisms remain underexplored. Mutations in both DAF-2 (IGF-1 receptor) and RSKS-1 (ribosomal S6 kinase/S6K) cause synergistic lifespan extension in *C. elegans*. To understand the roles of translational regulation in this process, we performed polysomal profiling and identified translationally regulated ribosomal and cytochrome c (CYC-2.1) genes as key mediators of longevity. cyc-2.1 knockdown significantly extends lifespan by activating the intestinal mitochondrial unfolded protein response (UPR^{mt}), mitochondrial fission, and AMP-activated kinase (AMPK). The germline serves as the key tissue for cyc-2.1 to regulate lifespan, and germline-specific cyc-2.1 knockdown non-autonomously activates intestinal UPR^{mt} and AMPK. Furthermore, the RNA-binding protein GLD-1-mediated translational repression of cyc-2.1 in the germline is important for the non-autonomous activation of UPR^{mt} and synergistic longevity of the daf-2 rsks-1 mutant. Altogether, these results illustrate a translationally regulated non-autonomous mitochondrial stress response mechanism in the modulation of lifespan by insulin-like signaling and S6K.

From: MDI Biological Scientists Identify Pathways That Extend Lifespan by 500 Percent (unattributed), MDI Biological Laboratory, 08 Jan. 2020, https://mdibl.org/press-release/mdi-biological-scientists-identify-pathways-that-extend-lifespan-by-500-percent/, accessed 20 Jan. 2020

Scientists at the MDI Biological Laboratory, in collaboration with scientists from the Buck Institute for Research on Aging in Novato, Calif., and Nanjing University in China, have identified synergistic cellular pathways for longevity that amplify lifespan fivefold in *C. elegans*, a nematode worm used as a model in aging research.

The increase in lifespan would be the equivalent of a human living for 400 or 500 years, according to one of the scientists.

The research draws on the discovery of two major pathways governing aging in *C. elegans*, which is a popular model in aging research because it shares many of its genes with humans and because its short lifespan of only three to four weeks allows scientists to quickly assess the effects of genetic and environmental interventions to extend healthy lifespan.

Because these pathways are "conserved," meaning that they have been passed down to humans through evolution, they have been the subject of intensive research. A number of drugs that extend healthy lifespan by altering these pathways are now under development. The discovery of the synergistic effect opens the door to even more effective anti-aging therapies.

The new research uses a double mutant in which the insulin signaling (IIS) and TOR pathways have been genetically altered. Because alteration of the IIS pathways yields a 100 percent increase in lifespan and alteration of the TOR pathway yields a 30 percent increase, the double mutant would be expected to live 130 percent longer. But instead, its lifespan was amplified by 500 percent.

"Despite the discovery in *C. elegans* of cellular pathways that govern aging, it hasn't been clear how these pathways interact," said Hermann Haller, M.D., president of the MDI Biological Laboratory. "By helping to characterize these interactions, our scientists are paving the way for much-needed therapies to increase healthy lifespan for a rapidly aging population."

The elucidation of the cellular mechanisms controlling the synergistic response is the subject of a recent paper in the online journal Cell Reports entitled "Translational Regulation of Non-autonomous Mitochondrial Stress Response Promotes Longevity." The authors include Jarod A. Rollins, Ph.D., and Aric N. Rogers, Ph.D., of the MDI Biological Laboratory.

"The synergistic extension is really wild," said Rollins, who is the lead author with Jianfeng Lan, Ph.D., of Nanjing University. "The effect isn't one plus one equals two, it's one plus one equals five. Our findings demonstrate that nothing in nature exists in a vacuum; in order to develop the most effective anti-aging treatments we have to look at longevity networks rather than individual pathways."

Optimal Solid State Neurons

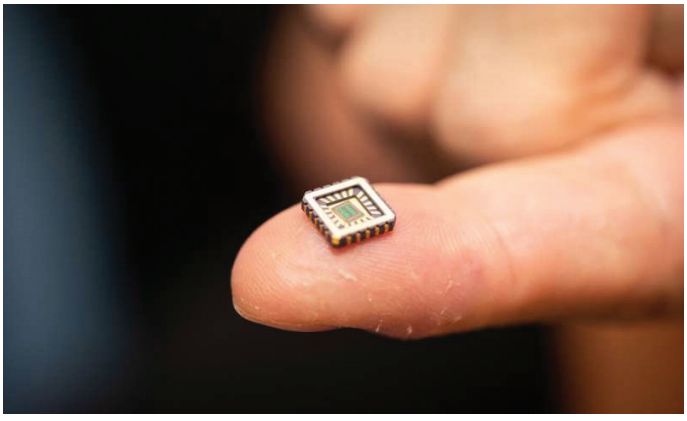
Kamal Abu-Hassan, Joseph D. Taylor, Paul G. Morris, Elisa Donati, Zuner A. Bortolotto, Giacomo Indiveri, Julian F. R. Paton, and Alain Nogaret

Nature Communications 10, Article 5309, 3 Dec. 2019, https://www.nature.com/articles/s41467-019-13177-3, accessed 4 Dec. 2019

Abstract

Bioelectronic medicine is driving the need for neuromorphic microcircuits that integrate raw nervous stimuli and respond identically to biological neurons. However, designing such circuits remains a challenge. Here we estimate the parameters of highly nonlinear conductance models and derive the ab initio equations of intracellular currents and membrane voltages embodied in analog solid-state electronics. By configuring individual ion channels of solid-state neurons with parameters estimated from large-scale assimilation of electrophysiological recordings, we successfully transfer the complete dynamics of hippocampal and respiratory neurons in silico. The solid-state neurons are found to respond nearly identically to biological neurons under stimulation by a wide range of current injection protocols. The optimization of nonlinear models demonstrates a powerful method for programming analog electronic circuits. This approach offers a route for repairing diseased biocircuits and emulating their function with biomedical implants that can adapt to biofeedback.

From: World First as Artificial Neurons Developed to Cure Chronic Diseases (unattributed), University of Bath, 3 Dec 2019, https://m.techxplore.com/news/2019-12-world-artificial-neurons-chronic-diseases.html, accessed 6 Dec 2019.



One of the artificial neurons in its protective casing on a fingertip. Credit: University of Bath

Artificial neurons on silicon chips that behave just like the real thing have been invented by scientists—a first-of-its-kind achievement with enormous scope for medical devices to cure chronic diseases, such as heart failure, Alzheimer's, and other diseases of neuronal degeneration.

Critically the artificial neurons not only behave just like biological neurons but only need one billionth the power of a microprocessor, making them ideally suited for use in medical implants and other bio-electronic devices.

The research team, led by the University of Bath and including researchers from the Universities of Bristol, Zurich and Auckland, describe the artificial neurons in a study published in *Nature Communications.*

Designing artificial neurons that respond to electrical signals from the nervous system like real neurons has been a major goal in medicine for decades, as it opens up the possibility of curing conditions where neurons are not working properly, have had their processes severed as in spinal cord injury, or have died. Artificial neurons could repair diseased bio-circuits by replicating their healthy function and responding adequately to biological feedback to restore bodily function.

In heart failure for example, neurons in the base of the brain do not respond properly to nervous system feedback, they in turn do not send the right signals to the heart, which then does not pump as hard as it should.

However developing artificial neurons has been an immense challenge because of the challenges of complex biology and hard-to-predict neuronal responses.

The researchers successfully modelled and derived equations to explain how neurons respond to electrical stimuli from other nerves. This is incredibly complicated as responses are 'non-linear'—in other words if a signal becomes twice as strong it shouldn't necessarily elicit twice as big a reaction—it might be thrice bigger or something else.

They then designed silicon chips that accurately modelled biological ion channels, before proving that their silicon neurons precisely mimicked real, living neurons responding to a range of stimulations.

Blocking the Thrombin Receptor Promotes Repair of Demyelinated Lesions in the Adult Brain

Hyesook Yoon, Chan-Il Choi, Erin M. Triplet, Monica R. Langley, Laurel S. Kleppe, Ha Neui Kim, Whitney L. Simon and Isobel A. Scarisbrick

Journal of Neuroscience 7 January 2020, 2029-19; DOI: https://doi.org/10.1523/JNEUROSCI.2029-19.2019

Abstract

Myelin loss limits neurological recovery and myelin regeneration and is critical for restoration of function. We recently discovered that global knockout of the thrombin receptor, also known as Protease Activated Receptor 1 (PAR1), accelerates myelin development. Here we demonstrate that knocking out PAR1 also promotes myelin regeneration. Outcomes in two unique models of myelin injury and repair, that is lysolecithin or cuprizone-mediated demyelination, showed that PAR1 knockout in male mice improves replenishment of myelinating cells and remyelinated nerve fibers and slows early axon damage. Improvements in myelin regeneration in PAR1 knockout mice occurred in tandem with a skewing of reactive astrocyte signatures towards a pro-repair phenotype. In cell culture, the pro-myelinating effects of PAR1 loss-of-function are consistent with possible direct effects on the myelinating potential of oligodendrocyte progenitor cells (OPCs), in addition to OPC-indirect effects involving enhanced astrocyte expression of pro-myelinating factors, such as BDNF. These findings highlight previously unrecognized roles of PAR1 in myelin regeneration, including integrated actions across the oligodendrocyte and astroglial compartments that are at least partially mechanistically linked to the powerful BDNF-TrkB neurotrophic signaling system. Altogether findings suggest PAR1 may be a therapeutically tractable target for demyelinating disorders of the CNS.

Significance Statement

Replacement of oligodendroglia and myelin regeneration holds tremendous potential to improve function across neurological conditions. Here we demonstrate Protease Activated Receptor 1 (PAR1) is an important regulator of the capacity for myelin regeneration across two experimental murine models of myelin injury. PAR1 is a G-protein coupled receptor densely expressed in the CNS, however there is limited information regarding its physiological roles in health and disease. Using a combination of PAR1 knockout mice, oligodendrocyte monocultures and oligodendrocyte-astrocyte co-cultures, we demonstrate blocking PAR1 improves myelin production by a mechanism related to effects across glial compartments and linked in part to regulatory actions towards growth factors such as BDNF. These findings set the stage for development of new clinically relevant myelin regeneration strategies.

From: Mayo Clinic Research Discovers a Molecular Switch for Repairing Central Nervous System Disorders by Susan Buckles, Mayo Clinic News Network, 10 Jan. 2020, https://newsnetwork.mayoclinic.org/discussion/mayo-clinic-research-discovers-a-molecular-switch-for-repairing-central-nervous-system-disorders/, accessed 20 Jan. 2020.

A molecular switch has the ability to turn on a substance in animals that repairs neurological damage in disorders such as multiple sclerosis (MS), Mayo Clinic researchers discovered. The early research in animal models could advance an already approved Food and Drug Administration therapy and also could lead to new strategies for treating diseases of the central nervous system.

Research by Isobel Scarisbrick, Ph.D., published in the Journal of Neuroscience finds that by genetically switching off a receptor activated by blood proteins, named Protease Activated Receptor 1 (PAR1), the body switches on regeneration of myelin, a fatty substance that coats and protects nerves.

"Myelin regeneration holds tremendous potential to improve function. We showed when we block the PAR1 receptor, neurological healing is much better and happens more quickly. In many cases, the nervous system does have a good capacity for innate repair," says Dr. Scarisbrick, principal investigator and senior author. "This sets the stage for development of new clinically relevant myelin regeneration strategies."

Myelin acts like a wire insulator that protects electrical signals sent through the nervous system. Demyelination, or injury to the myelin, slows electrical signals between brain cells, resulting in loss of sensory and motor function. Sometimes the damage is permanent. Demyelination is found in disorders such as MS, Alzheimer's disease, Huntington's disease, schizophrenia and spinal cord injury.

Thrombin is a protein in blood that aids in healing. However, too much thrombin triggers the PAR1 receptor found on the surface of cells, and this blocks myelin production. Oligodendrocyte progenitor cells capable of myelin regeneration are often found at sites of myelin injury, including demyelinating injuries in multiple sclerosis.

"These oligodendroglia fail to differentiate into mature myelin regenerating cells for reasons that remain poorly understood," says Dr. Scarisbrick. "Our research identifies PAR1 as a molecular switch of myelin regeneration. In this study, we demonstrate that blocking the function of the PAR1, also referred to as the thrombin receptor, promotes myelin regeneration in two unique experimental models of demyelinating disease."

The research focused on two mouse models. One was an acute model of myelin injury and the other studied chronic demyelination, each modeling unique features of myelin loss present in MS, Alzheimer's disease and other neurological disorders. Researchers genetically blocked PAR1 to block the action of excess thrombin.

The research not only discovered a new molecular switch that turns on myelin regeneration, but also discovered a new interaction between the PAR1 receptor and a very powerful growth system called brain derived neurotropic factor (BDNF). BDNF is like a fertilizer for brain cells that keeps them healthy, functioning and growing.

A Scalable Pipeline for Designing Reconfigurable Organisms

Sam Kriegman, Douglas Blackiston, Michael Levin, and Josh Bongard

PNAS first published 13 January, 2020 https://doi.org/10.1073/pnas.1910837117, accessed 19 Jan. 2019.

1. Edited by Terrence J. Sejnowski, Salk Institute for Biological Studies, La Jolla, CA, and approved November 26, 2019 (received for review June 24, 2019)

Abstract

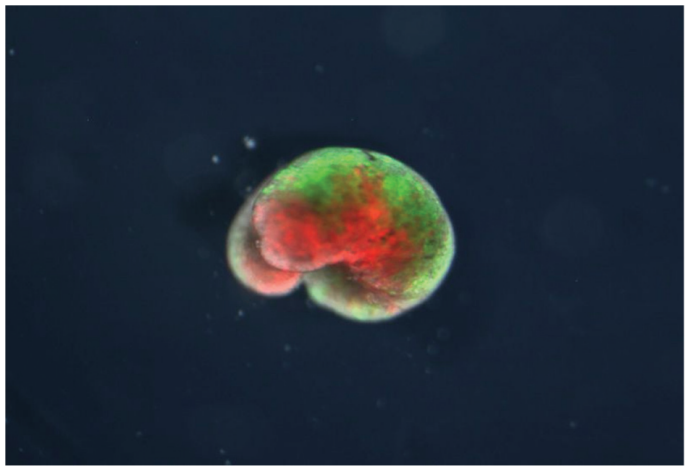
Living systems are more robust, diverse, complex, and supportive of human life than any technology yet created. However, our ability to create novel lifeforms is currently limited to varying existing organisms or bioengineering organoids in vitro. Here we show a scalable pipeline for creating functional novel lifeforms: AI methods automatically design diverse candidate lifeforms in silico to perform some desired function, and transferable designs are then created using a cell-based construction toolkit to realize living systems with the predicted behaviors. Although some steps in this pipeline still require manual intervention, complete automation in future would pave the way to designing and deploying unique, bespoke living systems for a wide range of functions.

Significance

Most technologies are made from steel, concrete, chemicals, and plastics, which degrade over time and can produce harmful ecological and health side effects. It would thus be useful to build technologies using self-renewing and biocompatible materials, of which the ideal candidates are living systems themselves. Thus, we here present a method that designs completely biological machines from the ground up: computers automatically design new machines in simulation, and the best designs are then built by combining together different biological tissues. This suggests others may use this approach to design a variety of living machines to safely deliver drugs inside the human body, help with environmental remediation, or further broaden our understanding of the diverse forms and functions life may adopt.

From: Scientists Assemble Frog Stem Cells Into First 'Living Machines' by Katherine J. Wu, Smithsonian Magazine, 13 Jan. 2020, https://www.smithsonianmag.com/innovation/scientists-assemble-frog-stem-cells-first-living-machines-180973947/, accessed 19 Jan. 2020.

In Michael Levin's laboratory at Tufts University, cells can expect to find themselves in unusual company. Here, the precursors of



A "living machine" containing frog stem cells in a new configuration designed by a computer algorithm. Parts shown in green are made up of frog skin cells, while parts in red are frog heart cells. (Kriegman et al., PNAS, *2020).*

frog skin sidle up to cells that, in another life, might have helped an amphibian's heart beat. They're perfect strangers: biological entities that, up until this point, had no business being together. And yet, Levin and his colleagues have found that skin cells and heart cells can be coaxed into coalescing. Placed side by side, they will self-organize into intricate, three-dimensional mosaics of frog cells that aren't actually frogs.

Designed by a computer algorithm and surgically shaped by human hands, these skin-heart hybrids, each roughly the size of a grain of sand, don't resemble anything found in nature. But the tasks they accomplish are eerily familiar: Without any external input, they can zoom around Petri dishes, push microscopic objects to and fro, and even stitch themselves back together after being cut.

Levin calls these clusters of cells a "new form of life"—one that's not quite an organism and not quite a machine, but perhaps somewhere in between. Named "xenobots" in honor of the *Xenopus laevis* African clawed frogs from which their cells derive, they have enormous potential to reveal the rules that govern how the building blocks of life assemble.

The team's approach, which relies on a mashup of computational and biological techniques, resembles other technologies that have rejiggered the known building blocks of life, says Deans. But rather than tweaking a known template like DNA, the team's technique—which simply rearranges existing cells into new configurations—feels more organic, she says. "This process … has a resounding respect for the biology that's involved."

At just a millimeter or so across, the xenobots aren't capable of much yet. Devoid of mouths or digestive systems, they're fueled exclusively by the bits of embryonic yolk they came with, and die after about a week when that juice runs dry, Bongard

says. But he and his colleagues think the bots could someday be used to deliver drugs into human bodies, or scrape plaque out of arteries. Released into the environment, they could quantify toxins, or sweep microplastics out of oceans.

The team is already experimenting with different sorts of cells, tasked with new types of chores. In a haunting echo of their particle-herding behavior, their xenobots also seem capable of making new versions of themselves, corralling single cells together until they start to coalesce, Levin says. They're also resilient: When sliced open, the bots simply repair their wounds and carry on.

While a lot of good could come out of this technology, it's also important to consider potential downsides, says Susan Anderson, a philosopher and machine ethics expert at the University of Connecticut who wasn't involved in the study. In the wrong hands, the power of xenobots could easily be exploited as a bioweapon, ferrying poisons instead of medicines into people. There's also cultural acceptance to consider: The mere idea of reassembling existing life forms could be troubling to some, evoking thoughts of Frankenstein's monster or the experimental vivisection in H.G. Wells' 1896 science fiction novel *The Island of Doctor Moreau.*

VEGF-C-Driven Lymphatic Drainage Enables Immunosurveillance of Brain Tumours

Eric Song, Tianyang Mao, Huiping Dong, Ligia Simoes Braga Boisserand, Salli Antila, Marcus Bosenberg, Kari Alitalo, Jean-Leon Thomas & Akiko Iwasaki

***Nature* 15 Jan. 2020, https://www.nature.com/articles/s41586-019-1912-x, accessed 20 Jan. 2020.**

Abstract

Immune surveillance against pathogens and tumours in the central nervous system is thought to be limited owing to the lack of lymphatic drainage. However, the characterization of the meningeal lymphatic network has shed light on previously unappreciated ways that an immune response can be elicited to antigens that are expressed in the brain. Despite progress in our understanding of the development and structure of the meningeal lymphatic system, the contribution of this network in evoking a protective antigen-specific immune response in the brain remains unclear. Here, using a mouse model of glioblastoma, we show that the meningeal lymphatic vasculature can be manipulated to mount better immune responses against brain tumours. The immunity that is mediated by CD8 T cells to the glioblastoma antigen is very limited when the tumour is confined to the central nervous system, resulting in uncontrolled tumour growth. However, ectopic expression of vascular endothelial growth factor C (VEGF-C) promotes enhanced priming of CD8 T cells in the draining [of] deep cervical lymph nodes, migration of CD8 T cells into the tumour, rapid clearance of the glioblastoma and a long-lasting antitumour memory response. Furthermore, transfection of an mRNA construct that expresses VEGF-C works synergistically with checkpoint blockade therapy to eradicate existing glioblastoma. These results reveal the capacity of VEGF-C to promote immune surveillance of tumours, and suggest a new therapeutic approach to treat brain tumours.

From: Scientists Breach Brain Barriers to Attack Tumors by Bill Hathaway, YaleNews, 15 January, 2020, https://news.yale.edu/2020/01/15/scientists-breach-brain-barriers-attack-tumors, accessed 20 Jan. 2020.

The brain is a sort of fortress, equipped with barriers designed to keep out dangerous pathogens. But protection comes at a cost: These barriers interfere with the immune system when faced with dire threats such glioblastoma, a deadly brain tumor for which there are few effective treatments.

Yale researchers have found a novel way to circumvent the brain's natural defenses when they're counterproductive by slipping immune system rescuers through the fortresses' drainage system, they report Jan. 15 in the journal *Nature*.

"People had thought there was very little the immune system could do to combat brain tumors," said senior corresponding author Akiko Iwasaki. "There has been no way for glioblastoma patients to benefit from immunotherapy."

While the brain itself has no direct way for disposing of cellular waste, tiny vessels lining the interior of the skull collect tissue waste and dispose of it through the body's lymphatic system, which filters toxins and waste from the body. It is this disposal system that researchers exploited in the new study.

These vessels form shortly after birth, spurred in part by the gene known as vascular endothelial growth factor C, or VEGF-C.

Yale's Jean-Leon Thomas, associate professor of neurology at Yale and senior co-corresponding author of the paper, wondered whether VEGF-C might increase immune response if lymphatic drainage was increased. And lead author Eric Song, a student working in Iwasaki's lab, wanted to see if VEGF-C could specifically be used to increase the immune system's surveillance of glioblastoma tumors. Together, the team investigated whether introducing VEGF-C through this drainage system would specifically target brain tumors.

The team introduced VEGF-C into the cerebrospinal fluid of mice with glioblastoma and observed an increased level of T cell response to tumors in the brain. When combined with immune system checkpoint inhibitors commonly used in immunotherapy,

the VEGF-C treatment significantly extended survival of the mice. In other words, the introduction of VEGF-C, in conjunction with cancer immunotherapy drugs, was apparently sufficient to target brain tumors.

"These results are remarkable," Iwasaki said. "We would like to bring this treatment to glioblastoma patients. The prognosis with current therapies of surgery and chemotherapy is still so bleak."

Caloric Restriction Reprograms the Single-Cell Transcriptional Landscape of *Rattus Norvegicus* Aging

Shuai Ma, Shuhui Sun, Lingling Geng, Moshi Song, Wei Wang, Yanxia Ye, Qianzhao Ji, Zhiran Zou, Si Wang, Xiaojuan He, Wei Li, Concepcion Rodriguez Esteban, Xiao Long, Guoji Guo, Piu Chan, Qi Zhou, Juan Carlos Izpisua Belmonte, Weiqi Zhang, Guang-Hui Liu

***Cell*, https://www.cell.com/cell/fulltext/S0092-8674(20)30152-5?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867420301525%3Fshowall%3Dtrue#%20, accessed 2 Mar. 2020.**

Summary

Aging causes a functional decline in tissues throughout the body that may be delayed by caloric restriction (CR). However, the cellular profiles and signatures of aging, as well as those ameliorated by CR, remain unclear. Here, we built comprehensive single-cell and single-nucleus transcriptomic atlases across various rat tissues undergoing aging and CR. CR attenuated aging-related changes in cell type composition, gene expression, and core transcriptional regulatory networks. Immune cells were increased during aging, and CR favorably reversed the aging-disturbed immune ecosystem. Computational prediction revealed that the abnormal cell-cell communication patterns observed during aging, including the excessive proinflammatory ligand-receptor interplay, were reversed by CR. Our work provides multi-tissue single-cell transcriptional landscapes associated with aging and CR in a mammal, enhances our understanding of the robustness of CR as a geroprotective intervention, and uncovers how metabolic intervention can act upon the immune system to modify the process of aging.

From: Eat Less, Live Longer: Salk Scientists Show How Caloric Restriction Prevents Negative Effects of Aging in Cells (unattributed), 27 Feb. 2020, *Salk News*, https://www.salk.edu/news-release/eat-less-live-longer/, accessed 2 Mar. 2020.

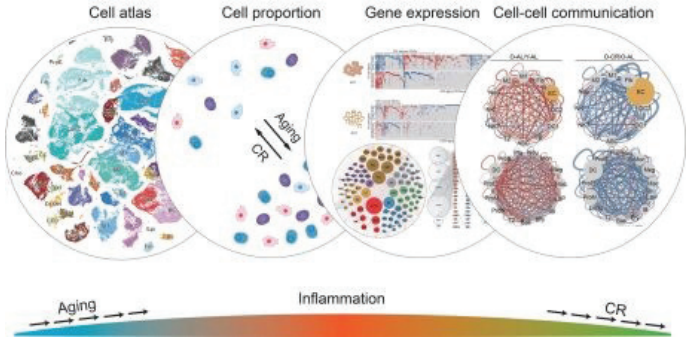
If you want to reduce levels of inflammation throughout your body, delay the onset of age-related diseases and live longer—eat less food. That's the conclusion of a new study by scientists from the US and China that provides the most detailed report to date of the cellular effects of a calorie-restricted diet in rats. While the benefits of caloric restriction have long been known, the new results show how this restriction can protect against aging in cellular pathways, as detailed in *Cell* on February 27, 2020.

"We already knew that calorie restriction increases life span, but now we've shown all the changes that occur at a single-cell level to cause that," says Juan Carlos Izpisua Belmonte, co-corresponding author of the new paper, a professor in Salk's Gene Expression Laboratory and holder of the Roger Guillemin Chair. "This gives us targets that we may eventually be able to act on with drugs to treat aging in humans."

Aging is the highest risk factor for many human diseases, including cancer, dementia, diabetes and metabolic syndrome. Caloric restriction has been shown in animal models to be one of the most effective interventions against these age-related diseases. And although researchers know that individual cells undergo many changes as an organism ages, they have not known how caloric restriction might influence these changes.

In the new paper, Belmonte and his collaborators—including three alumni of his Salk lab who are now professors running their own research programs in China—compared rats who ate 30 percent fewer calories with rats on normal diets. The animals' diets were controlled from age 18 months through 27 months. (In humans, this would be roughly equivalent to someone following a calorie-restricted diet from age 50 through 70.)

At both the start and the conclusion of the diet, Belmonte's team isolated and analyzed a total of 168,703 cells from 40 cell types in the 56 rats. The cells came from fat tissues, liver, kidney, aorta, skin, bone marrow, brain and muscle. In each isolated cell, the researchers used single-cell genetic-sequencing technology to measure the activity levels of genes. They also looked at the overall composition of cell types within any given tissue. Then, they compared old and young mice on each diet.



The illustration represents the ways in which caloric restriction affects various aspects of cellular function, with the overall result of reducing inflammation and the activity of many aging-related genes. Credit: Salk Institute

Many of the changes that occurred as rats on the normal diet grew older didn't occur in rats on a restricted diet; even in old age, many of the tissues and cells of animals on the diet closely resembled those of young rats. Overall, 57 percent of the age-related changes in cell composition seen in the tissues of rats on a normal diet were not present in the rats on the calorie restricted diet.

"This approach not only told us the effect of calorie restriction on these cell types, but also provided the most complete and detailed study of what happens at a single-cell level during aging," says co-corresponding author Guang-Hui Liu, a professor at the Chinese Academy of Sciences.

Some of the cells and genes most affected by the diet related to immunity, inflammation and lipid metabolism. The number of immune cells in nearly every tissue studied dramatically increased as control rats aged but was not affected by age in rats with restricted calories. In brown adipose tissue—one type of fat tissue—a calorie-restricted diet reverted the expression levels of many anti-inflammatory genes to those seen in young animals. ■

A Roadmap to Revival

Successful revival of cryonics patients will require three distinct technologies: (1) A cure for the disease that put the patient in a critical condition prior to cryopreservation; (2) biological or mechanical cell repair technologies that can reverse any injury associated with the cryopreservation process and long-term care at low temperatures; (3) rejuvenation biotechnologies that restore the patient to good health prior to resuscitation. OR it will require some entirely new approach such as (1) mapping the ultrastructure of cryopreserved brain tissue using nanotechnology, and (2) using this information to deduce the original structure and repairing, replicating or simulating tissue or structure in some viable form so the person "comes back."

The following is a list of landmark papers and books that reflect ongoing progress towards the revival of cryonics patients:

Jerome B. White, "**Viral-Induced Repair of Damaged Neurons with Preservation of Long-Term Information Content**," Second Annual Conference of the Cryonics Societies of America, University of Michigan at Ann Arbor, April 11-12, 1969, by J. B. White. Reprinted in *Cryonics* 35(10) (October 2014): 8-17.

Michael G. Darwin, "**The Anabolocyte: A Biological Approach to Repairing Cryoinjury**," *Life Extension Magazine* (July-August 1977):80-83. Reprinted in *Cryonics* 29(4) (4th Quarter 2008):14-17.

Gregory M. Fahy, "**A 'Realistic' Scenario for Nanotechnological Repair of the Frozen Human Brain**," in Brian Wowk, Michael Darwin, eds., *Cryonics: Reaching for Tomorrow*, Alcor Life Extension Foundation, 1991.

Ralph C. Merkle, "**The Molecular Repair of the Brain**," *Cryonics* 15(1) (January 1994):16-31 (Part I) & *Cryonics* 15(2) (April 1994):20-32 (Part II).

Ralph C. Merkle, "**Cryonics, Cryptography, and Maximum Likelihood Estimation**," First Extropy Institute Conference, Sunnyvale CA, 1994, updated version at http://www.merkle.com/cryo/cryptoCryo.html.

Aubrey de Grey & Michael Rae, "**Ending Aging: The Rejuvenation Breakthroughs That Could Reverse Human Aging in Our Lifetime**." St. Martin's Press, 2007.

Robert A. Freitas Jr., "**Comprehensive Nanorobotic Control of Human Morbidity and Aging**," in Gregory M. Fahy, Michael D. West, L. Stephen Coles, and Steven B. Harris, eds, *The Future of Aging: Pathways to Human Life Extension*, Springer, New York, 2010, 685-805.

Chana Phaedra, "**Reconstructive Connectomics**," *Cryonics* 34(7) (July 2013): 26-28.

Robert A. Freitas Jr., "**The Alzheimer Protocols: A Nanorobotic Cure for Alzheimer's Disease and Related Neurodegenerative Conditions**," *IMM Report* No. 48, June 2016.

Ralph C Merkle, "**Revival of Alcor Patients**," *Cryonics*, 39(4) & 39(5) (May-June & July-August 2018): 10-19, 10-15.

What is Cryonics?

Cryonics is an attempt to preserve and protect human life, not reverse death. It is the practice of using extreme cold to attempt to preserve the life of a person who can no longer be supported by today's medicine. Will future medicine, including mature nanotechnology, have the ability to heal at the cellular and molecular levels? Can cryonics successfully carry the cryopreserved person forward through time, for however many decades or centuries might be necessary, until the cryopreservation process can be reversed and the person restored to full health? While cryonics may sound like science fiction, there is a basis for it in real science. The complete scientific story of cryonics is seldom told in media reports, leaving cryonics widely misunderstood. We invite you to reach your own conclusions.

How do I find out more?

The Alcor Life Extension Foundation is the world leader in cryonics research and technology. Alcor is a non-profit organization located in Scottsdale, Arizona, founded in 1972. Our website is one of the best sources of detailed introductory information about Alcor and cryopreservation (www.alcor.org). We also invite you to request our FREE information package on the "Free Information" section of our website. It includes:

- A fully illustrated color brochure
- A sample of our magazine
- An application for membership and brochure explaining how to join
- And more!

Your free package should arrive in 1-2 weeks. (The complete package will be sent free in the U.S., Canada, and the United Kingdom.)

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To become an Associate Member send a check or money order ($5/month or $15/quarter or $60 annually) to Alcor Life Extension Foundation, 7895 E. Acoma Dr., Suite 110, Scottsdale, Arizona 85260, or call Marji Klima at (480) 905-1906 ext. 101 with your credit card information. You can also pay using PayPal (and get the Declaration of Intent to Be Cryopreserved) here: http://www.alcor.org/BecomeMember/associate.html

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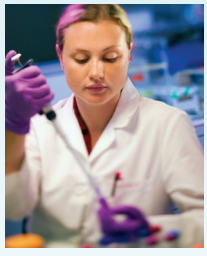

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