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CRYONICS

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George Church on Genome Editing and Transforming Human Aging

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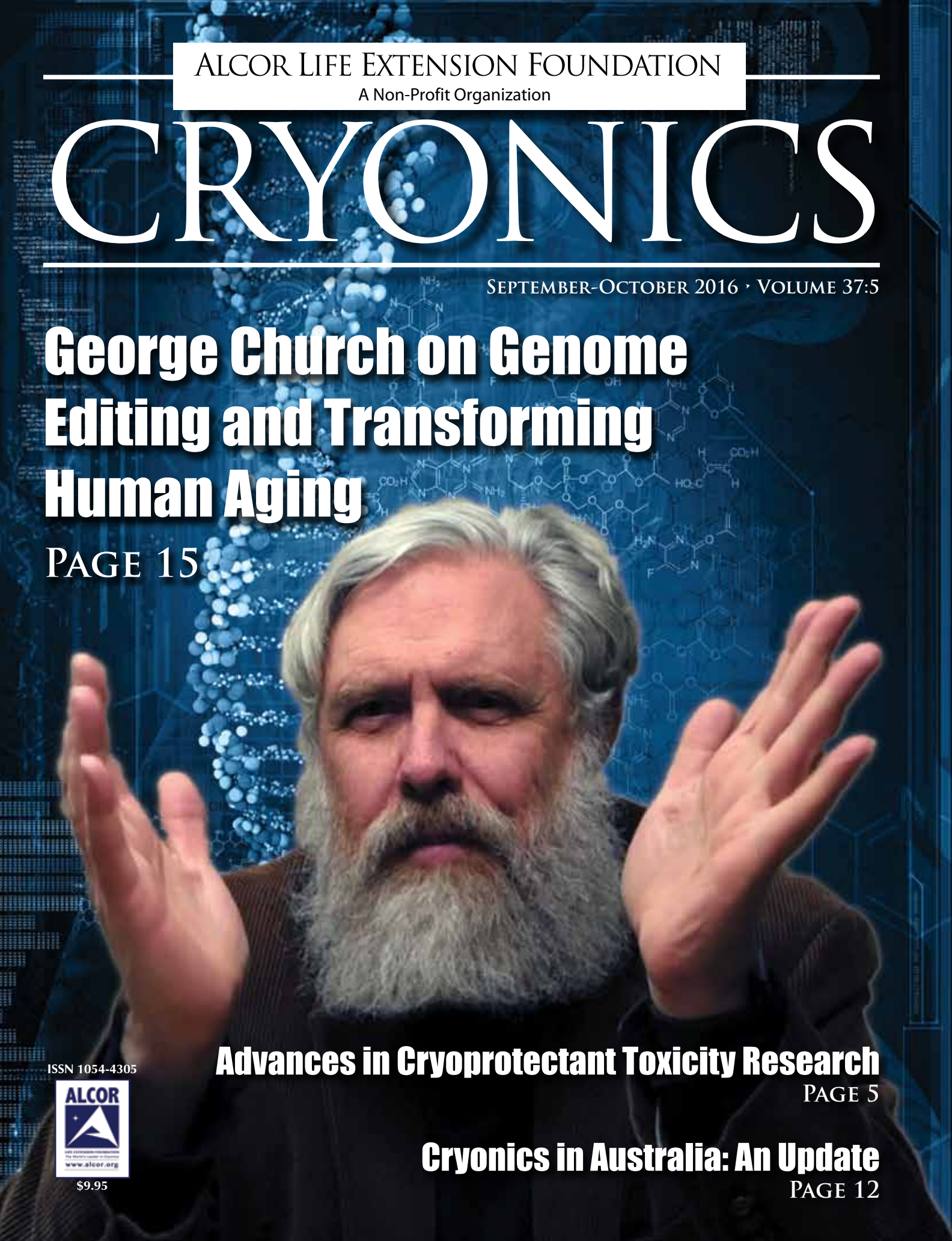

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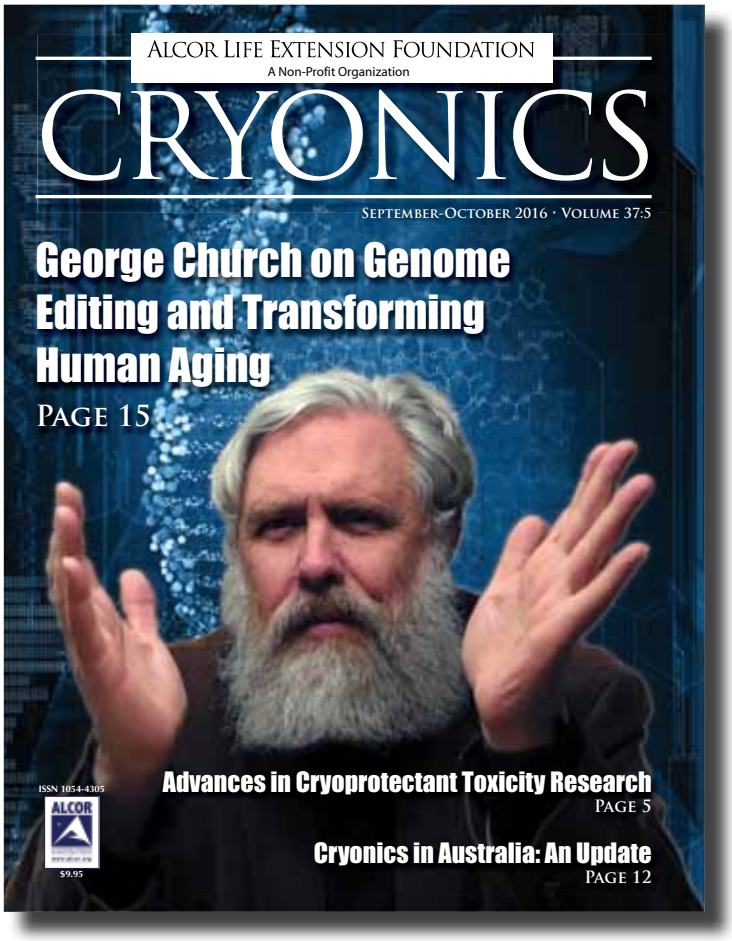

On the cover: *George Church, Ph.D.*

COVER STORY: PAGE 15

George Church on Genome Editing and Transforming Human Aging

There are a lot of exciting developments going on in aging research and a number of different proposals have been suggested for extending the human lifespan. One of these approaches is gene therapy, and rapid advances in gene delivery and replacement methods such as CRISPR are creating a lot of optimism. With permission of the Life Extension Foundation we are publishing the complete transcript of an interview with gene therapy pioneer George Church, conducted by cryobiologist and bio-gerontologist Greg Fahy. We think this is one of the most inspiring articles about the prospects of conquering aging that we have published in awhile.

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CRYONICS

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QUOD INCEPIMUS CONFICIEMUS

Photo: Cryo-Care Equipment Corporation at 2340 E. Washington St., Phoenix, AZ. Dr. Bedford's "home" about 1970.

ADVANCES IN CRYOPROTECTANT TOXICITY RESEARCH By Aschwin de Wolf

There is little disagreement among cryobiologists that the biggest limiting factor to reversible organ cryopreservation is cryoprotectant toxicity. It is actually not that hard to create vitrification solutions that completely inhibit ice formation at even the slowest cooling rates. The problem is that such highly concentrated vitrification solutions are too toxic to permit recovery of complex tissues. The least toxic vitrification solution for complex mammalian organs as of writing is M22. M22 is the culmination of many years of experimental and theoretical work by cryobiologist Greg Fahy and colleagues using rabbit kidney slices. Studying selected cryoprotectant mixtures on rabbit kidney slices, Fahy and colleagues came to the following conclusions:

1. High concentrations of a cryoprotective agent (or a mixture of different cryoprotective agents) can prevent ice formation during cooldown and warming.
2. The toxicity of some cryoprotectants can be neutralized by combining them with other cryoprotective agents.
3. The non-specific toxicity of a cryoprotectant solution can be predicted by calculating a quantity ("qv*") which is intended to measure the average hydrogen-bonding strength of the cryoprotectant polar groups with the water molecules in the solution.
4. Within limits, non-penetrating agents can reduce the exposure of cells to toxic amounts of cryoprotectants without reducing vitrification ability.
5. Synthetic "ice blockers" can be included in a vitrification mixture to reduce the concentration of toxic cryoprotective agents necessary to achieve vitrification.

While M22 is a low toxicity solution, its toxicity profile still necessitates minimizing exposure time and introduction and removal at low (subzero) temperatures.

While M22 is a low toxicity solution, its toxicity profile still necessitates minimizing exposure time and introduction and removal at low (subzero) temperatures. If we had a better understanding of the mechanisms of cryoprotectant toxicity, vitrification solutions with no toxicity at all could be introduced at higher temperatures and exposure times could be increased to optimize complete equilibration of the tissue with the cryoprotectant.

Two major reviews of cryoprotectant toxicity were published in the last 5 years; Gregory Fahy's"Cryoprotectant Toxicity Neutralization" (*Cryobiology*, 2010) and Benjamin Best's "Cryoprotective Toxicity: Facts, Issues, and Questions" (*Rejuvenation Research*, 2015).

Greg Fahy's paper is a rigorous exposition of experimental results concerning the phenomenon of cryoprotectant toxicity neutralization. The paper is mostly limited to the discovery that DMSO can block the toxic effects of amides such as formamide. The combination of DMSO and formamide (or other amides such as urea and acetamide) is indeed one of the building blocks of M22 but this combination cannot be used without limit and the paper includes data that indicate the maximum molar concentrations (and ratios) that still permit full viability. In theory, if two (or more) cryoprotectants would completely neutralize each other's toxicity they could be the sole components of a vitrification solution. But as the

formulation of M22 shows, it is still necessary to add weak glass formers such as ethylene glycol, extracellular CPA's, and "ice blockers" to supplement the toxicity neutralization obtained with formamide and DMSO. An important finding in Fahy's paper is that n-methylation abolishes toxicity neutralization for amides and combining methylated amides also does not lead to toxicity neutralization between them. In fact, Fahy found that the presence of n-methylated compounds renders even small amounts of DMSO toxic. The remainder of the paper discusses the mechanisms of cryoprotectant toxicity and Fahy now favors protein denaturation as a plausible mechanism of (non-specific) toxicity. While other cases of toxicity neutralization have been reported in the literature, no rigorous studies have been done to produce a body of knowledge that is comparable to what we know about amide-DMSO interactions.

While other cases of toxicity neutralization have been reported in the literature, no rigorous studies have been done to produce a body of knowledge that is comparable to what we know about amide-DMSO interactions.

Benjamin Best's paper is more general in scope but presents a lot of experimental data and also critically discusses Fahy's work on cryoprotectant toxicity. As Ben Best points out, different (and seemingly contradictory) results do not necessarily mean that cryoprotectant toxicity is a species or cell-type dependent phenomenon. One could imagine a meta-analysis of cryobiology data in which variables such as concentration, loading and unloading protocols, exposure temperature, exposure time, and the type of viability assay are matched to ensure methodological consistency. It is also important to compare cryoprotectants at their minimum concentration to vitrify to make meaningful toxicity comparisons. If the work at 21st Century Medicine is an indication, universal low-toxicity cryoprotective solutions should be feasible. Perhaps the most interesting part of the paper is where Best offers a critique of Grag Fahy's "qv* hypothesis of cryoprotectant toxicity," which aims to show that non-specfic toxicity concerns the degree to which cryoprotectants leave water available to hydrate macromolecules. This discovery allowed for the substitution of ethylene glycol for propylene glycol in Fahy's lower toxicity vitrification solutions, despite the resulting higher CPA concentrations. Best observes, "it seems contradictory that water remains available for hydration, but not available for ice formation." A potential rejoinder to this observation is that so called "bound water" does not participate in ice formation but can be disturbed by strong glass formers. Best also suggests a potential refinement of qv* that allows for more precise calculation of the hydrogen bonding strength of the polar groups that are used to calculate qv*. It is conceivable that such a refinement would eliminate the few remaining outliers in the data that support the qv* hypothesis. The paper also draws attention to the possibility of kosmotropic co-solvents and changes of pH and microenvironment polarity to mitigate cryoprotectant toxicity.

Conventional cryoprotective agents such as PG, EG, and DMSO have poor blood brain barrier penetration and the brain may not tolerate the CPA exposure times that other organs do.

Neither of the papers discusses cryopreservation of the mammalian brain, but there is good reason to believe that in the case of this organ modification of low-toxicity vitrification solutions is required. Conventional cryoprotective agents such as PG, EG, and DMSO have poor blood brain barrier (BBB) penetration and the brain may not tolerate the CPA exposure times that other organs do. For example, while M22 can be used for cryopreservation of the brain, many of its component have poor BBB penetration and PVP and the ice blockers (X-1000 and Z-1000) are assumed not to cross the (non-ischemic) BBB at all. One potential solution is to (reversibly) open the BBB with so-called BBB modifying agents like detergents or perhaps to search for cryoprotective agents that *can* cross the BBB.

The most fundamental question in the design of vitrification solutions remains whether it is possible at all to introduce high concentrations of cryoprotectants without creating *any* kind of *irreversible* molecular and ultrastructural adverse effects. Understanding what specific and non-specific cryoprotectant toxicity exactly is should enable us to answer this question. ■

CEO Update

By Max More

CORPORATE MEMBERSHIP RATE

In 2015, *Cryonics* editor Aschwin de Wolf wrote a column about "cryonics as an employee benefit." We have received a few requests for this option, which would involve a company securing reduced membership dues for interested staff in return for simplified billing on our part. In discussing this at the July board meeting, management and board decided to treat corporate membership as much like the family discount policy.

A minimum of five individuals would need to be included, and all would be charged the current rate applied to second family members. To simplify administration, Alcor will bill the corporation annually. (The corporation can decide whether to cover all, some, or none of the amount of the dues.)

NEW MEDICAL RESPONSE DIRECTOR

On July 18, Josh Lado joined Alcor as our new Medical Response Director. Josh comes to us from John C. Lincoln hospital where he had a range of roles and responsibilities. In addition to having been an EMT for over 10 years, he assisted the nurses in Pre-Op and Post-Anesthesia Care Unit (PACU) with patient care, recovery of patients after anesthesia and assisting family members to answer questions they have. He also operated the Stealth Machine. This is a navigation unit surgeons use to help place screws into vertebra, assist in brain tumor resections, and manage placement of shunts into a patient's brain.

He has also been in charge of Human Tissue Tracking for the hospital's In-Patient and Out-Patient Surgery. He maintained a database that controls inventory and helped the hospital stay compliant with federal laws and competed a weekly inventory for all tissue in the hospital and worked with vendors for outdated product.

He also worked with the Emergency Preparedness Coordinator and Trauma Service personnel to train hospital employees for emergencies including Chemical, Biological, Radiological, Nuclear and Explosive (CBRNE) events. He has an Applied Science Degree in Paramedic Studies, and Applied Science degree in Fire Science, with numerous FEMA and related certificates.

Corporate membership...would involve a company securing reduced membership dues for interested staff in return for simplified billing on our part.

During his time at John C. Lincoln, Josh was exposed to many different areas and, by all accounts, was highly proactive in solving problems beyond his required role. While working in surgery, he became very familiar with many instruments used and how to pass them to a surgeon. He assisted anesthesiologists with intubation of patients and IV access points. He has worked in high stress areas such as the trauma room in the Emergency Department and the OR Trauma Room and helped in the ICU with critical patients.

In talking with Josh, we were impressed not only by his range of skills but also by his attitude and interest in learning more about the science behind cryonics. Josh will receive thorough training by his predecessor, Aaron Drake. (We are also bringing in several other individuals to refresh and update their training.) Aaron will continue to be available to consult with Alcor during parts of the year, to take on special projects, and to provide relief to Josh so that he is not on-call 24/7/365.

GROWTH

A quick update to last issue's membership growth rate numbers. The annualized growth rate as of May 27 was 4.55%. As of June 30, it is up to 5.9%. With the strong gain in June, we now have 1,085 full cryopreservation members – a net gain of 31. We cannot guarantee that terminations won't pull that number down, but it's an encouraging sign of slowly accelerating growth.

At mid-year, in addition to 1,085 full members, we had 146 patients, and 316 associate members, for a "total membership" of 1,547.

If we had lost *no* members this year, growth would have been 8.5%. (14 memberships have been terminated so far this year.) In 2015, 40 members were terminated. If terminations had been zero in 2015, membership growth would have been 8.32%. Some attrition is inevitable and unavoidable. But what this shows is that membership retention matters as much as new-member acquisition.

We can address this by maintaining slow but steady downward pressure on membership dues; by engaging more fully with members (such as through annual surveys and other means); and by improving

the odds that new members are the kind of people who will be able to sustain their membership. The latter factor could be addressed by requiring a larger application fee (credited against dues), by offering an option of Lifetime Membership, and other ways.

In talking with Josh, we were impressed not only by his range of skills but also by his attitude and interest in learning more about the science behind cryonics.

Despite this growth, growth in staff has been modest. While researching some Alcor history recently, I came across a *Cryonics* magazine article from 1990. At a time when Alcor had just 172 Suspension Members and 16 cryopreserved members, we had five full-time employees and one part-time. That's 1 staff member per 30.9 members. As of today, we have 8 full-time staff and one part-time. That's 1 staff member for 127 members. A direct comparison is difficult because the number of volunteers and contractors has changed over the years. But it's an encouraging sign of economies of scale.

WHAT'S NEW AT ALCOR?

Here's a grab-bag of brief updates:

In reviewing our liquid nitrogen costs, I was pleasantly surprised to see that they have not gone up since we got a new contract 3.5 years ago – even though a limited annual escalation is allowed. In fact, it looks like Hazmat and delivery charges have gone down. Another supplier is hungry for our business and may actually enable us to further reduce our costs once our current contract term expires. Combined with the new dewar design (yet to be tested), this could lead to a significant decrease in our liquid nitrogen costs for years to come.

On the physical plant and facility front: We have upgraded to a newer, better BizHub copier/printer from Konica-Minolta. This was an easy choice: The improved capabilities (such as ability to fax from our computers) come at a lower cost than the previous lease. We are currently awaiting a quote on moving the server and phone system into a new, secure location. The IT expert who came in to see what we were planning was clearly delighted with the proposed new location.

Two Bigfoot dewars were delivered on Wednesday July 6. We are expecting delivery of the new, 9-patient (if all whole body patients) around mid-September. This new design by Steve Graber (which I like to call the "Superdewar") should dramatically reduce boiloff. As our patient population grows, we need to plan ahead to expand the Patient Care Bay. We met with our architect again on June 15. We aim to secure all necessary permits and get work underway ASAP.

...membership retention matters as much as new-member acquisition.

There are many other technical improvements and innovations either already implemented or in the design stage (mostly by Steve Graber) that I will not even attempt to list them here. Look for a feature on his work (and some other advanced) in a forthcoming issue of this magazine.

Several new case summaries have been posted on the blog and from the list of cases on Alcor's website. We are now all caught up with case summaries, and good progress is being made with several detailed case reports. Case report writers are now regularly reviewing video of the various stages of the stabilization, transport, surgery, and perfusion procedures. This provides extremely valuable information and input to quality control. It will also be invaluable for training.

We are printing 2,000 extra copies of the July/August issue of *Cryonics*, since it includes by special arrangement Tim Urban's exceptionally good and persuasive "Why Cryonics Makes Sense." This will be a perfect issue to include in information packets and the forthcoming new member packet.

I have been working with Marji to provide material to Christine Gaspar. Christine has been tremendously helpful in making progress with writing case reports – as well as with ensuring greater consistency and completeness. At the same time, Linda Chamberlain has steadily and relentlessly been going through the "Red Books" that contain all patient information, improving their organization and moving mis-located items to their proper folders. Once we catch up more with both case reports and the historical information in the Red Books, we can distill core demographic, medical, and circumstantial data about our patient population.

Independently, both Suspended Animation and Diane and Marji at Alcor discovered a problem with our emergency line. It turns out that the fault lay with Cox, not our emergency service. It was a case of a fix breaking something else. We were concerned that the emergency number gets forwarded through our box at Alcor, and that box can break down (and has). We therefore had Cox install a separate line that doesn't run through the system. Cox should have immediately changed the forwarding, but failed to do so – until we called them about it. The problem has been resolved, and the new line should ensure that emergency calls get through even if our in-house phone system goes down.

In reviewing our liquid nitrogen costs, I was pleasantly surprised to see that they have not gone up since we got a new contract 3.5 years ago.

PUBLIC EDUCATION AND MEDIA:

Over the past month, I have turned down many media requests, due to other priorities. One request that I did grant

led to filming on June 6 for the Spanish-language station Univision. My thanks to Linda Chamberlain for giving her time to provide a second voice for the piece. This resulted in three TV reports (shown July 11 through Wednesday July 13) plus a written article by Daniela Zavala. Ms. Zavala was able to persuade the station to give the cryonics story more air time for each part, meaning that it's more likely to be aired by the network and other local stations around the country. If you play part one, you should automatically be led to the following two segments.

Part 1: "Is it possible to return from the dead?" (3:28)

http://www.univision.com/arizona/ktvw/noticias/ciencia/es-posible-regresar-de-la-muerte-video

Many of you may be familiar with the excellent weekly roundup of life extension news, Fight Aging, gathered and written by Reason. Reason has long recommended cryonics but only recently signed up. Here's his July 15 piece: "Finally Signed Up for Cryopreservation: the Existence of a Fallback Plan is Great, but Only if You Actually Take Advantage of It."

https://www.fightaging.org/archives/2016/07/finally-signed-up-for-cryopreservation-the-existence-of-a-fallback-plan-is-great-but-only-if-you-actually-take-advantage-of-it/

Case report writers are now regularly reviewing video of the various stages of the stabilization, transport, surgery, and perfusion procedures.

Among several other good pieces of exposure, an especially strong one was a set of several articles in the UK's *New Scientist* feature, dated June 29. Helen Thomson's work was sympathetic and informative and can only help cryonics move closer to mainstream acceptance. The main page is here: https://www.newscientist.com/article-topic/cryogenics/

We are now all caught up with case summaries, and good progress is being made with several detailed case reports.

This leads to several articles, including: "I want to put your death on ice so that you can live again." Max More cryogenically preserves people's bodies and heads in the hope that one day they can be brought back to life. It doesn't make him popular. "9 things you need to know about cryogenically freezing your body." Fancy freezing your body after death? This is what you're dying to know about what it involves, what it costs and the chances of reanimation. "Ark of the immortals: The future-proof plan to freeze out death." In Comfort, Texas, a disaster-proof complex will house 50,000 frozen people with plans to bring them back from the dead – and will help others to stay alive. "Some people choose to be frozen at death. Here's how it happens." How do you freeze a body so that one day it could come back to life? Here's how the experts intervene within seconds to stop nature taking its course.

Australia's Channel 7, "Sunday Night," produced a solid and supportive piece (an article with two 8-minute videos), "Cryonics: Kim's Plan for Life After Death", produced by Naima Lynch and hosted by Denham Hitchcock. (Scroll down for the second video.)

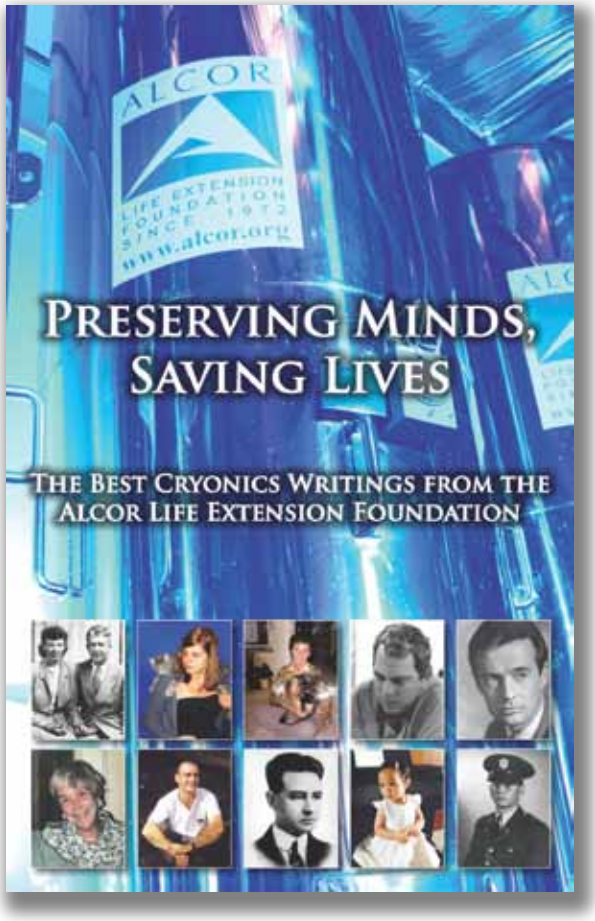
https://au.news.yahoo.com/sunday-night/features/a/31861024/cryonics-kims-plan-for-life-after-death/#page1

This can also be found here:

http://canmua.net/arizona/kim-suozzis-cryogenically-frozen-future-as-boyfriend-delivers-her-belongings-for-the-next-life-946361.html ■

Why You Want to Read Alcor's New Book

By Stephen Bridge, co-editor



So perhaps you're fairly new to Alcor and cryonics. You're pretty sure this technology might be worth investigating; maybe you've even gotten signed up. But there's a lot you don't know. When your friends and relatives ask you those awkward questions about WHY you're doing this and what makes you think it will work, you haven't figured out solid answers yet. Especially if you live in an area without many other people involved in cryonics, you may really need solid ideas. You may even wish you have a book you could hand some of them, something that might make all of these ideas clear.

We have that book – *Preserving Minds, Saving Lives: The Best Cryonics Writings from the Alcor Life Extension Foundation*. We have been working on those answers for more than 35 years, often in the pages of our magazine, *Cryonics*. This book takes many of those great answers and puts them together in one volume for you.

Why do we preserve patients in liquid nitrogen? How might that change in the future?

What is the difference between freezing and vitrification? Why is vitrification better?

How does cryonics connect with religious beliefs?

What kind of research has been done in the past and what is needed for the future?

Why do some people choose whole body preservation and some choose to only preserve their brains?

When will the cryopreserved patients be brought back to life? Wait – should we even call them "dead" or are they already "alive" in some way? And who will pay for it?

How did this odd idea get started in the first place? What has Alcor gone through to get to this point? What mistakes were made along the way and how do we know cryonicists have learned from those mistakes? Why the heck isn't cryonics wildly popular?

It's all here, along with many other discussions, by the best writers Alcor has had to offer for more than three decades. There are a handful of technical articles, because we want to make sure that the bases for this technology are readily available for future researchers. But most of the articles are accessible to anyone.

This is the book you need. We have both hardcover and paperback copies, and we're working on an e-book version. The book is printed on very high-quality paper and will last a long time. It ought to say something worth lasting as long as the paper.

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http://www.alcor.org/book/index.html

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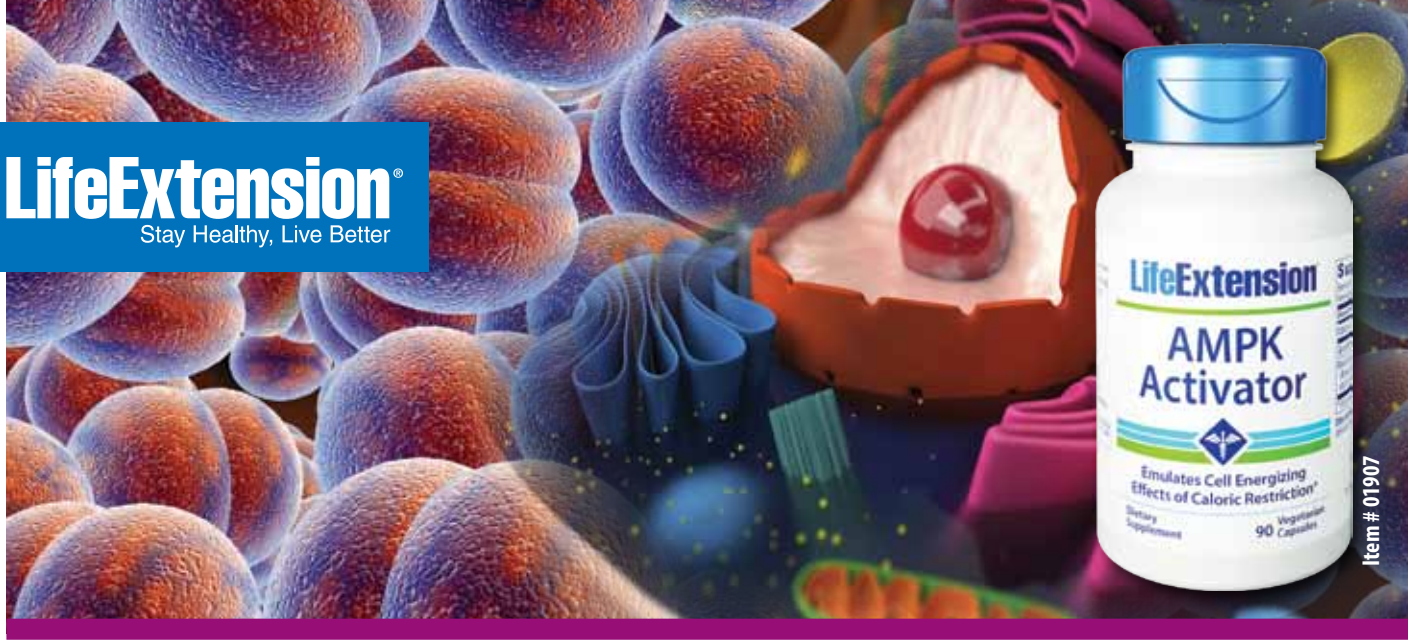

AMPK Activator

A New Paradigm in Controlling Aging

AMPK is an *enzyme* that serves as the body's "**master regulating switch**." It inhibits multiple degenerative factors by *revitalizing* aging cells.[1]

Found in every cell,[2,3] **AMPK** promotes ***longevity factors*** that have been shown to extend life span in numerous organisms.[1,4] Increasing AMPK signaling "turns off" many damaging effects of aging, thus enabling cells to return to their youthful vitality.[5]

Life Extension® scientists have compiled years of research to create **AMPK Activator**, a specialized *dual-extract formulation* that supports **AMPK** activation for health optimization. This natural formula supports AMPK enzymatic activities required to safely support a more youthful cellular environment.

Importance of AMPK

Greater **AMPK** (*adenosine monophosphate-activated protein kinase*) activation has been shown to help target damaging factors of aging.[5] Studies show **increased** AMPK activity supports reduced fat storage,[6] new mitochondria production,[7] and the promotion of healthy blood glucose and lipids already within normal range.[4]

Gynostemma Pentaphyllum

An extract of the plant *Gynostemma pentaphyllum* was traditionally used in Asian medicine to promote longevity and scientists now know why — *G. pentaphyllum* promotes **AMPK** activation![8-10] In one of many studies showing a wide variety of benefits, researchers documented a one-inch reduction in **abdominal circumference** in overweight individuals who took **450 mg** daily of *G. pentaphyllum* extract for 12 weeks.[11]

Trans-Tiliroside

Trans-tiliroside, extracted from plants such as **rose hips**, also boosts **AMPK** activation, but triggers different downstream metabolic benefits than *G. pentaphyllum*.[12-14] Among its many benefits, a low human equivalent dose of **56 mg** daily *trans*-tiliroside has been shown by researchers in preclinical studies to promote healthy blood glucose levels and body weight already within normal range.[15]

The suggested daily dosage of **AMPK Activator** is to take two capsules with the first meal of the day and one capsule with the second meal. Three vegetarian capsules provide:

ActivAMP™ *Gynostemma pentaphyllum* extract (leaf)	**450 mg**
Rose hip extract	**1,120 mg**
Standardized to ***trans*-tiliroside**	**56 mg**

Anti-Aging Discovery That Cannot Be Overlooked

Scientists uncovered the cell-energizing effect of **AMPK** in the 1970s. Since then, an exponential volume of data (over 7,500 published studies) has documented the critical role that activated **AMPK** plays in maintaining life-sustaining cellular functions.

Those seeking to meaningfully extend their healthy life span should ensure they optimally activate their cellular **AMPK**. The reason this is so important is that in response to aging, excess calorie consumption, and/or low levels of physical activity, AMPK activity markedly declines.

A targeted way of **reversing** cellular depletion of this critical enzyme is to take the new **AMPK Activator** formula that comprises a dual-extract, plant-based formulation.

A bottle of 90 vegetarian capsules of **AMPK Activator** retails for $48. If you purchase four bottles, the price is reduced to **$33** per bottle.

ActivAMP™ is a trademark of Gencor.

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Cryonics in Australia: *An Update*

By Carrie Wong

INTRODUCTION

There are cryonicists spread out all around the world, but most of us here in North America seldom make contact with cryonicists from other countries. Earlier this year, at the young cryonicist conference, I got to meet an Australian cryonicist for the first time. In the past, the most far-flung cryonicists that showed up were Russians from KrioRus. There are a few different Cryonics Associations in Australia, but no "full service" organizations currently exist. Most cryonicists in Australia are signed up with Alcor or Cryonics Institute. However, there have been a number of very interesting developments in the last few years that may lead to fully developed cryopreservation capabilities and facilities in Australia. In this article, I explore the options available today in Australia through email correspondence with Peter Tsolakides, Director at Cryonics Services of Australia and co-founder of Stasis Systems Australia.

There are three separate cryonics organizations in Australia: Cryonics Association of Australasia, Cryonics Services of Australia and Stasis Systems Australia. The Cryonics Association of Australasia (CAA) is a non-profit organization that offers support for residents of Australia, New Zealand and other countries in the region. CAA helps Australians make cryonics arrangements with any US Cryonics organizations and promotes the concept of cryonics in Australia. CAA is the oldest organization in this group and historically assisted with standby training and transportation. It was managed by the members to help other members and operated on a volunteer basis. CAA is now evolving into a body to maintain cryonics membership and to act as a self-regulatory authority for other cryonics facilities that are developing in Australia today.

The second organization, Cryonics Services Australia (CSA) is not a membership-based organization; it exists to coordinate cryonics services for cryonics clients. Compared to the United States, it is not straightforward in Australia to set up appropriate life insurance arrangements with overseas cryonics organizations. CSA is a client service that puts its clients in contact with appropriate licensed professionals that handle life insurance and trust and estate planning in the context of cryonics. CSA identifies its clients' exact needs and put them in contact with the most cost-efficient plans for an upfront fee. In addition, CSA is currently setting up a professional standby and transportation process through a network of funeral directors for transportation requirements both for overseas and for within Australia when Stasis Systems is operational. CAA, the first organization mentioned, also had a membership-based network for standby and transportation, but it was less formal and run on a mostly volunteer basis.

Last but not least, there is Stasis Systems Australia (SSA), a non-profit organization formed to build and operate Australia's first cryonic storage facility. SSA is the newest and most ambitious organization in Australia today. They intend to serve cryonics clients in all of Australia, Tasmania and New Zealand.

Stasis Systems Australia's Mission Statement:

1. Provide a professional 'one stop' service to make cryogenic suspension affordable and readily available in Australia
2. Create a positive consumer awareness for scientifically-based cryogenic suspension
3. Promote scientific research into cryogenic suspension, revival, and life extension

SSA incorporated in 2012 in New South Wales, Australia and spent the next few

years gathering up the initial investors to make this facility a reality. Stasis Systems has ten founding members (investors) who have each committed $50,000 (AUD) to build the facility. In 2015 they identified the ideal place to build the facility and have purchased the land in a town called Holbrook, located between Sydney and Melbourne. SSA is currently working on construction plans for the new facility. After moving forward with their land purchase, more investors have become interested and are waiting on further developments. Stasis Systems is the incorporated name, but they will be operating under the name Southern Cryonics once the facility is up and running. Currently, the work of creating Southern Cryonics is done on a volunteer basis by Mark Milton (coordinating the building of the facility), Matt Fisher (Media Coordination), Peter Tsolakides (Standby/Transportation) and Marta Sandberg (volunteer, also a Cryonics Institute Director).

Building Concept for Stasis System's Facility

INTERVIEW WITH PETER TSOLAKIDES (FOUNDING DIRECTOR OF BOTH SSA AND CSA)

1. **What are the main projects that Stasis Systems is currently undertaking? From the website Stasis Systems serves an important role in helping Australians sign up with Alcor or CI and also undertaking a big project to build a long-term patient storage facility in Australia.**

Stasis Systems Australia, a non-profit organization, will be operating under the name Southern Cryonics. Its aim is to build and then operate a cryonics patient storage facility in Australia. Stasis Systems Australia have, in May 2016, purchased a block of land in a rural town called Holbrook, which is located approximately midway between Australia's largest cities, Sydney and Melbourne. It is near the large inland state border towns of Albury and Wodonga, and is on a main route for liquid nitrogen deliveries. Current plans are to complete building this facility by year-end 2017. Stasis Systems Australia, as such, is not directly involved with helping Australians sign up with Alcor or CI, although they do, on their website, refer any one currently interested in cryonics to those organisations. Stasis Systems Australia has a sister organisation called Cryonics Services Australia, who are involved in assisting with cryonics related requirements, including financial, administrative, and standby/transportation. As well, they provide help to those wishing to join cryonics organisations, whether they be Alcor, CI or Stasis Systems Australia, when operating. So there are two new cryonics organizations in Australia, namely Stasis Systems Australia to build and operate the cryonics facility and Cryonics Services Australia to assist with all other aspects of cryonics.

2. **What emergency standby personnel or equipment is available with Stasis Systems or for cryonics in Australia as a whole? It is great that Stasis Systems currently has contracts with funeral directors for transportation, but is there an emergency response team? Cryonicists in many parts of the world lack an emergency response team.**

Historically, Cryonics Association of Australasia handled transportation and standby. Cryonics Association of Australasia has been around for many years in Australia. It offers membership and is a cryonics community association for sharing of ideas and to actively progress cryonics. Because there was no other organisation available, Cryonics Association of Australasia also historically assisted with standby/transportation. It was handled by the members to help other members. The plan now is for this organisation to evolve to a more peak body. They will continue to maintain the membership and sharing of ideas role to progress cryonics. In addition however, as a peak body, they will assist other cryonics and similar organisations in Australia with standards and consistent processes. It is unlikely that this organisation will continue in the future with standby/transportation, except where members may assist in emergency situations.

Cryonics Services Australia will gradually take over the standby and transportation role. They are now developing a network of funeral directors, assisted by volunteers, to handle the emergency response. This network of funeral directors will also be involved with the preparation and transportation of patients, either overseas or within Australia. The aim is to have this in place over the next eighteen months. Due to Australia's large geographic size and relatively small population, it is planned that this network will be represented in all the major cities where Australia's population is concentrated. The actual emergency response for a geographic area as large as Australia is still a challenge, especially since, with the relatively low population, the frequency of patients may initially be extremely low, requiring the network to be in place, through perhaps years of no activity. By way of comparison, Australia is about the same size as continental USA, but with a population of only about 23 million. Of note, one major logistical advantage of the location of the proposed Stasis Systems Australia facility is that it is between Australia's two largest cities, which have a total population of about 10 million, over 40% of Australia's population.

3. **Has Cryonics Services Australia or Cryonics Associate of Australasia handled an emergency de-animation recently?**

Although I do not have the exact timing, I believe, the last emergency de-animation in Australia was handled by Cryonics Association of Australasia over 10 years ago. Cryonics Services Australia is not yet operational to handle emergency de-animations. In early 2014, Aaron Drake, at that time Alcor's Medical Response Director, visited Australia and provided training. In addition, I have personally visited Alcor, CI and UK cryonics and they have provided us with very valuable and generous assistance. Let me also add that I was very impressed by the dedication and the operating practices of the people at all locations I visited. We have a vast amount of very professional knowledge to draw from.

4. **Is there an Australian surgeon and medical team that Alcor contracts out to at the present moment or does Alcor have to send their team to Australia to vitrify the patient?**

I am not aware of the specific arrangements Alcor currently has in Australia. My impression was that they send a team to handle the standby and transportation. Of course, I cannot speak for Alcor so this would need to be confirmed by them. When Cryonics Services Australia is fully operational, our aim is to reach out to Alcor and see if they need someone on the spot on a timely basis who could then hand over to the Alcor team at the appropriate point, which may be in Australia when their team arrives. Similarly CI patents may use Cryonics Services Australia for standby and then transportation to the US. This coordination has yet to be fully explored, but it would make sense.

5. Overall, how does the average Australian react to cryonics? Would you say the media attention has been mostly positive, lukewarm or even negative?

The average Australian is very open-minded to cryonics. This is generally the Australian way, to be open to new ideas. When we talk to people who are not involved with cryonics, they are typically very interested in what we are doing. Perhaps they may not want to join, but they are nonetheless intrigued by the concept. The media attention has surprised us by being very upbeat and extensive. Coverage has been very positive by major television networks and newspapers and they have followed up with coverage at each of Stasis Systems Australia's major milestones. To date there have not been any negative media reports.

6. How many members are there currently in Stasis Systems, including volunteers and investors?

Stasis Systems Australia has 10 official members at the moment who are also the "investors". They have each committed Aust$50,000 to the project and are each entitled to one suspension when Stasis Systems Australia is operating. With the recent positive milestone of buying land, another 4 potential "investors" are actively making inquiries to join Stasis Systems Australia. When Stasis Systems Australia is nearing operational capability the option of becoming an "investor" member will likely be closed off. Once operational, prospective members will be those who will have suspension and storage agreements with financial arrangements primarily through life insurance, very similar to what Alcor and CI do now.

As well as the "investors", Stasis Systems Australia has had up to about 5 individuals providing volunteer help. The numbers vary over time and depend on the work needing to be done.

7. Are there any recent developments in the field of biomedical technology or cryonics as a whole that you personally find interesting and promising?

None of what I am going to refer to is strictly cryonics, but there are just so many tantalizing developments out there. More specifically activities like that brain preservation prize, hypothermia surgery, low temperature trauma surgery, use of low temperatures for storing human tissues and the ongoing research to expand the range of tissues and organs that may be stored. Then, more generally, progress with computing, AI and significant advances in understanding the brain, extending the life span, continual progress in tackling illness, and strides in organ regeneration research. I could name many more. It is like being around a few hundred years ago and seeing all the very early work in physics, thermodynamics and electricity, and, not even in our wildest dreams imagining what they would all lead to. I believe we are standing at the same point now. Almost every development will coalesce into something needed for the future by cryonics.

8. What is the biggest barrier for Australians signing up with Stasis Systems?

I believe it is being aware that cryonics is a credible option and it is affordable. We need to get that message out there, especially when Stasis Systems Australia is operating. But, even for those that know it exists and want to join, it is not that easy in Australia, especially the life insurance aspects. Very many people had told me they are interested in cryonics, but don't know how to do all the arrangements necessary. That is what we are trying to do through Cryonics Services Australia. To provide those interested with options as to what they could do and then "hand hold" them through the whole process.

CONCLUSION

There are very exciting developments in Australian Cryonics today. In many ways, Australia is comparable to Canada when it comes to the challenges of cryonics; both countries have large landmasses with smaller, spread-out population centers. There are only 13 Alcor members in Australia, while Canada has 49, according to *Cryonics* magazine's latest issue. Standby in Western Canada is less developed despite having a greater number of members, but that will change in the near future. In Eastern Canada, especially in the greater Toronto area, standby is in a more advanced state, with trained volunteers, appointed funeral directors and emergency cryo-preservation kits. As a Canadian cryonicist, I am inspired by the progress Australia has made in developing their facilities despite facing similar challenges. ■

ABOUT THE AUTHOR

Carrie Wong is a young Canadian cryonicist. She graduated in 2011 with a degree in geology from The University of British Columbia and worked in gold exploration for a few years. In addition to writing for *Cryonics* magazine, she is also writing for geologyforinvestors.com and running a cartography business.

George Church on Genome Editing and Transforming Human Aging

Introduction by William Faloon

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HUMAN AGE REVERSAL AT HARVARD UNIVERSITY

When I incorporated the **Life Extension Foundation**, I envisioned a time when human longevity would not be constrained to a finite number of years.

I was confident technology would emerge to enable science to gain control over pathological aging. When this biomedical turning point occurs, healthy life spans will extend beyond what anyone imagines today.

Over the past two years, our hypotheses in the **1970s** have emerged into scientific probability. I am pleased that ***Life Extension***® was able to contribute in a small way to an emerging gene editing technique that may enable age reversal to transform soon into clinical reality.

"Editing" Our Human Genome *In Vivo*

As we age, genes that maintain cellular health and vitality are down regulated, while genes that promote disease and senescence become overexpressed.

Once physicians are able to regulate or **"edit"** cellular genes, then youthful health may be restored to the entire individual.

Articles in this month's issue of ***Life Extension***® magazine describe a technology called **CRISPR** that has been developed and is being improved and extensively used at **Harvard University** and other institutions.

Although most readers will find it difficult to comprehend, what's important to know is that **CRISPR** (*clustered regularly interspaced short palindromic repeats)* also offers a new way to rapidly transform **senescent cells** to regain ***youthful*** function and structure.

CRISPR/Cas is a DNA cutting system originally developed in nature by bacteria as a way to destroy the DNA of viruses that frequently attack them. A natural version of CRISPR has been adapted by scientists to enable the **reprogramming** of cellular DNA to rid cells of unfavorable genetic changes. Once perfected, old cells may be rejuvenated and **never age again**.

Programming Our Cellular Genes like Computers

The CRISPR/Cas system is empowering scientists to do very controlled **gene editing**, which means adding, disrupting or changing the sequence of specific genes. This has led to exciting new methods of transiently or permanently modifying gene action, either to increase or decrease the activities of targeted genes in a controllable way, potentially anywhere in the body and anywhere in one's complete set of genes and DNA (our genome).

Since key features of aging are powerfully controlled by how genes are activated or inactivated (expressed or suppressed) in the body, these are critically important developments.

Introducing the Harvard Pioneer of CRISPR

Dr. George Church is a pioneer in the area of genome engineering and the

Life Extension Foundation Funding of CRISPR Research

By Ben Best

The May 2013 issue of this publication reported on how the **Life Extension Foundation** was funding the collection and analysis of ***genes*** of **supercentenarians** (people living to age 110 or older) to discover protective genes that allow them to live so long.

This funding was provided to a group called Androcyte LLC that initially consisted of CEO James Clement and his assistant, Parijata Mackey. They travelled the world to collect tissue samples from approximately 60 supercentenarians and their family members. Harvard Medical School geneticist, Dr. George Church, was collaborating with Androcyte to analyze the genes.

Since then, Dr. Church has achieved additional fame as a co-inventor and pioneer in the new CRISPR gene-editing technology. Also since then, the Life Extension Foundation has continued to fund Androcyte to open a laboratory in California dedicated to applying CRISPR to deliver longevity genes, initially to mice. Androcyte CEO James Clement continues to work with Dr. Church in doing this research.

Androcyte currently has a colony of 300 mice, and growing. Sixty of these mice were received from the National Institutes of Aging, and are between 26 and 36 months of age—the equivalent of very old humans.

Androcyte has targeted about 25 promising longevity genes that are being tested in the mice via CRISPR/Cas9 gene therapy. Particular attention is being paid to the elderly mice to see if they can be restored to youth and good health.

To keep costs low, Androcyte purchased a one-acre property with an existing 1,500 square-foot building that is an hour's drive from costly Los Angeles. As it outgrew its initial vivarium (housing for mice), it added two office trailers to the property to provide additional vivarium and laboratory space.

In addition to Dr. Church and other expert consultants, Androcyte CEO James Clement has acquired the assistance of two new interns: Ellie Dubrovina and David Falzarao, who were referred by Aubrey de Grey's **SENS Foundation**. Ellie assists with the scientific work, whereas David assists with the care of the mice.

Androcyte has also received two elderly Arabian mares 28 and 30 years old (age-equivalent to 80-year-old humans) from a sanctuary. If genes delivered by CRISPR to the mice are able to restore youth and health, CRISPR delivery of those genes will be tested on the horses to show that large animals can also benefit. Success with the horses could pave the way for using CRISPR to bring better health and greater longevity to humans.

development of gene editing tools based on the CRISPR/Cas9 system (referred to as **CRISPR** here).

Dr. Church has already been able to ***reverse aging*** in human cells using CRISPR technology, and expects the first clinical trials of this technology to begin within as little as one year.

In response to these breakthroughs, ***Life Extension***® magazine sent Dr. Gregory M. Fahy to **Harvard University** to interview Dr. Church. We needed to clarify the opportunities for reversing human aging to save the lives of most of those reading this article now.

These articles/interviews are written to enlighten our scientific supporters about this new **age reversal** modality. All readers should appreciate that this novel technology is being developed for the purpose of rapid integration into the human clinical setting.

Opening Comments by Dr. Greg Fahy…

IS THE END OF AGING NEAR AT HAND?

As a student of the aging process, I have been attending scientific meetings devoted to aging since the early 1980s, and have seen and heard a lot of very exciting things. But when I attended George Church's talk at a conference sponsored by Aubrey de Grey's **SENS Foundation** near the end of 2014, I realized that I had just heard the most remarkable talk in my life.

Why? For three very simple reasons.

First, as Dr. Church's talk highlighted, aging seems to be controlled to a large extent by the action of a rather small subset of your genes, and especially by master genes that control large numbers of other genes. Your genes, of course, are areas of your DNA that determine your eye color, your hair color, your sex, your height, and other characteristics of your body. But what is becoming increasingly clear is that genes also determine how you age—and maybe even whether you age.

Second, Dr. Church described how technologies have advanced to the point where the activity of your genes—whether the genes are "turned on" (expressed) or "turned off" (repressed, or down regulated)—can increasingly be controlled. And this is not happening in just a test tube, but in whole bodies, and even in the brain.

Dr. Church's focus is on CRISPR *(clustered regularly interspaced short palindromic repeats)* technology, which is a relatively new and particularly powerful method for adjusting gene activity in many different ways.

CRISPR can "edit" or change genes for the purpose of correcting deleterious mutations, or to create deliberate mutations that can have positive effects (such as in knocking out the effects of pro-aging genes). So the implication is very clear: If aging is controlled by master genes, and if the activity of such genes can now be intentionally controlled, then we are beginning to approach the control of aging on a very fundamental level. And the same technology can be applied to the correction of many diseases as well, whether age-related or not.

Finally, it would be of no use just to have the power to control aging if there was no will to utilize that power and move aging control to the clinic. Fortunately, Dr. Church wants his achievements to be rapidly translated into the clinical arena. He wants to make the control of aging a practical reality—and soon. And Dr. Church, as a highly distinguished professor of genetics and major figure at Harvard Medical School, is in an excellent position to make his wishes come true.

Gene Editing with CRISPR

Fahy: Just how efficient is CRISPR at editing targeted genes?

Church: Without any particular tricks, you can get anywhere up to, on the high end, into the range of **50%** to **80%** or more of targeted genes actually getting edited in the intended way.

Fahy: Why not **100%**?

Church: We don't really know, but over time, we're getting closer and closer to **100%**, and I suspect that someday we will get to **100%**.

Fahy: Can you get a higher percentage of successful gene edits by dosing with CRISPR more than once?

Church: Yes, but there are limits.

Fahy: How does CRISPR edit genes?

Church: The way CRISPR works, classically, is by cutting DNA so many times in a specific place that eventually an error in DNA repair is made at the location of the cut, and you end up with a random change in the DNA—a mutation—at that location. For that kind of change, the longer CRISPR is around, the more likely you are to accomplish a random mutation, and that can be good if you want to inactivate a troublesome gene, since usually a random mutation will in fact inactivate the gene.

But newer versions of CRISPR are more interesting because they allow you to not just make cuts in DNA that get misrepaired, they allow you to splice a particular new piece of DNA, which can do new things, into your genome at a precise location. The trouble there is that it's possible the first round of treatment might have altered the site where you want to insert your new DNA in some of the cells, such that the site of interest can no longer be edited in those altered cells.

Fahy: Can you remove DNA also?

Church: Yes, you can delete a specific piece of DNA cleanly by making cuts not just in one place, but in two nearby places. The two cut ends are rejoined by normal DNA repair enzymes, and when this happens, the DNA that was previously between the cuts is lost. Now if you want to make a change in the DNA rather than a deletion, you can, instead, insert new DNA, or "donor DNA," between the two cuts. The stuff that's inserted either fixes the gene that you're trying to do therapy on or provides some new desired function.

Fahy: How do you tell CRISPR where you want it to edit the genome?

Church: Almost all the previous gene editing mechanisms require protein to find the genetic target of interest which has been the needle in the haystack. But CRISPR is a little like a programmable computer, in which you can program the genetic location of interest by making and providing what is called guide RNA. Since RNA and DNA are so similar to one another, and tend to stick to one another if their base sequences match, you can make an RNA molecule that will bind to a predetermined segment of DNA. The guide RNA binds to both the DNA target area and to CRISPR, and then CRISPR acts on the DNA it is attached to thanks to the guide RNA. The guide RNA does **95%** of the genetic targeting work, and making guide RNA is really easy. Ultimately, the editing depends on four things working together: the genome, CRISPR, the guide RNA, and the donor DNA.

Fahy: Can you do more subtle things than delete or add DNA using CRISPR?

Church: Yes, a more interesting approach, in many ways, is to get rid of the DNA cutting activity of the CRISPR and attach to it an "activation domain" that activates any gene that's really close to it.

Fahy: You mean you can turn on a desired gene even without any signals from the cell that the gene should be on?

Church: Yes. The CRISPR/activation domain does all the heavy lifting, finding the needle in the haystack, the one place in 6 billion base pairs where you want it to bind, and once it binds, instead of cutting, it activates. That's it. Even if the gene is as off as can be, even if you have a cell that really has absolutely no intention of wanting that gene to be turned on (speaking anthropomorphically), you can still turn it on. In fact, the more off it is, the more impressive the induction ratio (ratio of the amount of gene activity after activation to the amount before activation) we get. We've seen induction ratios of up to **20,000 fold**. This is amazing but it's fairly predictable.

Fahy: Can you use the same approach to turn a gene off or to reduce its expression?

Church: Yes. You can reduce its expression by putting in repressive domains. Of course, if you really want to reduce the expression, you can delete it. That'll get it down to zero but there's no finesse in it. There's no control. If you want to turn it up and down, if you want to be able to fully regulate it from very low to very high, then you don't want to make any irreversible changes to the gene, and so the repressor and activator domains are a good way of doing that.

Fahy: Tremendous. But how can you fine-tune the repressor or the activator to go from very low to very high gene expression?

Church: You can use activators or repressors that respond to inexpensive small molecules a bit like a rheostat, to turn gene expression up and down. There are lots of small molecules, which are totally safe and do nothing unless your target repressor or activator is around to respond to them. It doesn't even have to be a pharmaceutical, it just has to be something harmless that's not commonly part of your diet or your body, and you can make it into one of the world's most effective regulators. It can be something transient, where you eat it or inject it, it does its job, decays, and then nothing happens until the next injection. You can also regulate expression with light if you have a way of getting light into the tissue in question. Those are some of the ways that you can regulate it.

In an interview with the *Washington Post* at the beginning of December 2015,[1] Dr. Church said that his lab is already reversing aging in mice, and that human applications may only be a few years away. Dr. Church stated:

"One of our biggest economic disasters right now is our aging population."

"If all those gray hairs could go back to work and feel healthy and young, then we've averted one of the greatest economic disasters in history." [1]

He said he sees:

"A scenario [in which] everyone takes gene therapy, not just curing rare diseases like cystic fibrosis, but diseases that everyone has, like aging." [1]

Dr. Church also described his personal passion in reversing human aging when he stated:

"I'm willing to become younger. I try to reinvent myself every few years anyway." [1]

This new CRISPR technology may change the world, and our lives, as we know them.

CRISPR is a technology originally developed by nature to fight viruses by cutting their DNA. Fortunately, it has now been modified by scientists to enable them to make specific controlled changes in targeted places in DNA. Once physicians are able to regulate or "edit" the DNA medically, then they can begin to work on restoring a state of youthful health in aging individuals.

How serious is the promise of CRISPR? Consider the following:

- A newer version of CRISPR was recently inserted into a re-engineered virus delivery system and successfully used to correct the gene defect that causes Duchenne muscular dystrophy in a mouse model by either direct injection into a leg muscle or by infusion into the bloodstream, resulting in improvements in the muscles throughout the body and even in the heart.[2]

- A leading scientific journal, ***Science***, at the end of 2015, declared CRISPR to be the "breakthrough of the year," standing above all other scientific discoveries for 2015.[3]

- On January 7, 2016, Dr. Church's company, Editas Medicine, filed papers to launch a $100 million IPO, and the company is already being backed by Google Ventures and the Bill and Melinda Gates Foundation.[4]

In short, in my estimation, the CRISPR revolution is a game changer, with staggering implications. If it all works out, nothing is going to remain the same. The prospects are as transformative as—if not more transformative than—such revolutions as the advent of the electric light, telephones, personal automobiles, airplanes, personal computers, the internet, and cell phones. Only this time, it's not just about how you live, but whether you live, and how long you will live: your health, your longevity, and the effect that health and longevity will have on your enjoyment of life.

Will it really work? We will see. Opinions vary. Surely, there will be many tricks to learn and many twists and turns along the road ahead. And heavyweight scientist Craig Venter even says it will take 100 years to get it right. But George Church's lab is reversing aging in the laboratory today. So far, it's looking very promising, moving with incredible speed, and based on a very solid foundation of scientific observations about aging. My money is squarely on Church and others pursuing similar paths. The end of at least some critical aspects of aging may very well be near at hand.

And the **Life Extension Foundation** is participating in this innovative and visionary project. The Life Extension Foundation has assisted Dr. Church by providing him data from a human super-centenarian research project that it funded. As Dr. Church mentions in his interview, studying super-centenarians may offer new insights into how human aging can be scaled back, once we have the right genetic tools to take advantage of those insights.

Since the Life Extension Foundation is dedicated to improving healthy longevity, and since Dr. Church is working on pushing the ultimate limits of improving healthy longevity, with potentially open-ended possibilities ahead, this issue of *Life Extension*® magazine features an extensive interview with Dr. Church that was conducted in his office at Harvard Medical School to enable us to present Dr. Church's work and thoughts to you.

This interview is much more technical than many readers will be used to, and some may not be able to understand all of it, but we felt it was important to bring this important research breakthrough for the benefit of *Life Extension*® readers in the pursuit of healthy longevity.

We hope you will be able to appreciate the substantive nature of what we think is likely to be a coming revolution that may touch your life in important ways.

CONROLLING HUMAN AGING BY GENOME EDITING

An Interview with George Church, PhD

Attempting to delay aging is now old hat. The new goal is to reverse it, not only in animals, but in humans. And **age reversal** is essential, as significant age-related disruption has already occurred in most people due to changes in our **gene expression** profiles.

Gene expression patterns change with age. This influences the rate at which an individual ages, and also determines what senile disorders they are likely to contract. But innovative gene-editing methods based on a unique technology called **CRISPR** *(clustered regularly interspaced short palindromic repeats)* are now being successfully harnessed for use as an age-reversal therapy for humans.

In response to these breakthroughs, ***Life Extension***® magazine sent biogerontologist Dr. Gregory M. Fahy to **Harvard University** to interview **Dr. George Church**, who is a leading developer of cutting-edge CRISPR techniques. Here, Dr. Church explains remarkable opportunities for transforming human aging that may begin to unfold sooner than most have imagined.

This interview with Dr. Church begins with a discussion on reversing cell aging by restoring youthful gene expression.

Fahy: If aging is driven by changes in gene expression, then the ability to control gene expression using CRISPR technology could have profound implications for the future of human aging. Why do you think aging may be at least partly driven by changes in gene expression?

Church: We know that there are cells that deteriorate with age in the human

body and that we have the ability to turn those back into young cells again. This means we can effectively reset the clock to zero and keep those cells proliferating as long as we want. For example, we can take old skin cells, which have a limited lifetime, and turn them into stem cells (stem cells are cells that can turn into other kinds of cells) and then back into skin cells. This roundtrip results in the skin cells being like baby skin cells.[5] It's as if my 60-year-old cells become 1-year-old cells. There are a variety of markers that are associated with aging, and those all get reset to the younger age.

Fahy: That's fantastic. Does this mean that reversing skin cell aging in your face would allow you to rejuvenate your entire face?

Church: If you rejuvenate at a molecular level, it doesn't necessarily mean that everything else rejuvenates. So, for example, if my face has a scar on it, it's not going to necessarily reverse that (although theoretically it's not out of the question). But we can reverse the tendency of your cells (and therefore of your whole body) to deconstruct when you reach your life expectancy.

The Technology: How Genes and Their Expression Can Be Modified

Fahy: So CRISPR has allowed you to reverse aging in human cells. CRISPR is an exciting technology. The CRISPR molecular machine—consisting of a protein and some associated RNA—can now be made in the lab or in our own cells and can change genes and gene expression. It's extremely powerful. Please tell us more about it.

Church: CRISPR is the latest method for performing genome editing (editing of your whole set of genes). Its advantage is in part that a specific CRISPR tool can be created far more easily than other gene editing tools, and CRISPR is about **5 times** more precise than other tools. The combination of the ease of construction, improved efficiency, and great flexibility makes it the most powerful gene editing tool to date.

Fahy: Right now, with CRISPR, it is possible to modify, delete, insert, activate, and tone down or completely inactivate any gene, with considerable fine-tuning, either temporarily or permanently. *(See sidebar: Gene Editing with CRISPR)* Now let's talk about what this fantastic new ability could be good for.

SPECIFIC OPPORTUNITIES FOR REVERSING HUMAN AGING

TFAM: Staying Energetic Indefinitely

Fahy: There are several very exciting stories in aging intervention these days. In 2013, the Sinclair lab at Harvard came out with the revelation that the aging of mitochondria (which are the producers of usable energy within cells) is driven in significant part by reduced levels of one particular molecule in the cell nucleus: oxidized NAD (NAD+).[6]

The team showed that they could correct mitochondrial aging just by giving old mice nicotinamide mononucleotide (NMN), which is a vitamin-like substance that can be converted into NAD+, for one week. This resulted in phenomenal overall rejuvenation, including reversal of signs of muscle atrophy, inflammation, and insulin resistance. Now your lab showed that there is a very exciting gene engineering alternative involving TFAM (Transcription Factor A, Mitochondrial). Why is TFAM important, and what have you done with it?

Church: TFAM is a key regulatory protein that is in this pathway of NMN and NAD+. It allows cells to manufacture the NMN precursor on their own, so you don't have to manufacture it outside the cell and then try to get it into the cell from outside. Ideally, you don't want to have to take NMN for the rest of your life, you want to fix the body's ability to make its own NMN and buy yourself rejuvenation for at least a few decades before you have to worry about NMN again. In order to accomplish this on a single cell level, we've used CRISPR to activate a TFAM activator, and we made it semi-permanent. *(See sidebar: Gene Editing with CRISPR)*

Fahy: With this technique, you were able to increase TFAM levels in the cell by **47-fold.** This resulted in restored ATP levels, increased NAD+, and an increased NAD+/NADH ratio. It also increased total mitochondrial mass and reversed several other age-related changes.

Church: Yes. We have a number of ways to measure mitochondrial function and age-related losses of those functions. When we activated TFAM, these changes returned to what you would expect of a younger cell state. And we built this anti-aging ability into the cell, so it's self-renewing and eliminates the need to take pills or injections.

GDF11: Achieving Overall Rejuvenation

Fahy: Now, let's move on to GDF11 (growth differentiation factor 11), which is a protein and a type of youth factor that is present in the blood of young animals, but that declines with aging.[7]

Church: Yes, my lab is involved with the GDF11 story. We collaborate with Amy Wagers, a Harvard biologist famous for her work on heterochronic parabiosis, and her group, who are among the real pioneers for this.

Fahy: GDF11 has been reported to rejuvenate the heart,[8] muscles,[9] and brain.[10] It restores strength, muscle regeneration, memory, the formation of new brain cells, blood vessel formation in the brain, the ability to smell, and mitochondrial function. All of this is done by just one molecule. Infusing young plasma, which contains GDF11, into older animals also provides benefits in other tissues, such as the liver and spinal cord, and improves the ability of old brain cells to form connections with one another.

How would you use CRISPR to make sure that GDF11 blood levels never go down?

Church: The CRISPR-regulating GDF11 could be delivered late in life, which is exactly when such an increase would be welcome. If you really wanted to stay at a certain level, you might want to put in a GDF11 sensor to provide feedback so you could automatically control GDF11 production so as to lock in a specific GDF11 level. If necessary, you could recalibrate and fine-tune this maybe once every few decades with another dose of CRISPR. But yes, it's a great molecule, and we've got a handle on it.

We are also doing a number of other projects with Amy now, dealing with a range of muscle diseases such as muscle wasting. We're working on possible treatments involving proteins such as myostatin and follistatin.

Keeping Strong Muscles and Bones

Fahy: Speaking of myostatin, the lack of which causes super-development of

muscles, you mentioned in your 2014 SENS talk that you are interested in the possibility of enabling better muscle strength and less breakable bones. Is this another good treatment path for aging?

Church: Muscle wasting and osteoporosis are symptoms of aging. The key to dealing with them is to get at the core causes, even if they're complicated. There are genes known to be involved in muscle wasting and genes that can overcome that. We're interested in these very powerful things, like growth hormone, myostatin, and the target for some of the new osteoporosis drugs, RANKL (Receptor activator of nuclear factor kappa-B ligand).

Fahy: What about going beyond just correcting aging and actually super-protecting people by making them augmented with stronger bones or muscles than what they would normally have?

Church: Rather than waiting until the muscles are wasting and then trying to correct the problem, or waiting until someone breaks a bone and putting a cast on, the idea is to make the muscles and bones stronger to begin with. Think of it as preventive medicine. You have to be careful, but there are people naturally walking around with much denser bones and much stronger muscles that have no particularly bad consequences, so we know such things are possible.

Fahy: Can osteoporosis be reversed?

Church: I would say osteoporosis definitely could be reversed. The process of bone building and bone breaking down is a regulated process that responds to conditions such as the good stress of standing or running. So yes, it's an example of something that's reversible.

IKKβ: Reversing a Possible Whole-Body Aging Program

Fahy: Let's move on to another aging process of potentially tremendous significance. According to a paper published in Nature,[11] body weight, bodywide aging, and longevity are all controlled to a significant extent by the overexpression of one particular protein, IKKβ, in one highly specific place, the microglial cells in the medial basal hypothalamus in the brain. When this overexpression is prevented in mice, median and maximum life spans go up by 20% and 23%, cognition improves, exercise ability improves, and skin thickness and bone density also improves. In addition, collagen cross-linking is reduced and gonadotropin output goes up. If these improvements could be combined with the improvements caused by the other interventions we have discussed, the implications could be staggering.

Church: Yes. What you're referring to is something that a certain school of thought thinks is aging programmed by the neuroendocrine system, by the brain, and the reason why mice start dying at two and a half years and bowhead whales start dying after 160 years.

Fahy: Yes. And it's a particularly interesting problem because not only is it important in its own right, but it introduces the practical issue of fixing aging changes that arise in the brain. This part of the brain is protected from most things put into the bloodstream by the blood-brain barrier. Is it possible to get CRISPR technology through the blood-brain barrier and possibly address that particular pathway or other pathways in the brain?

Church: The blood-brain barrier is greatly overstated in that there are many, many things that cross it, such as various drugs, viruses, and even whole cells. So, the answer is yes, we can deliver CRISPR across the blood-brain barrier.

Telomerase: Heading Off Brain Aging and Cancer?

Fahy: Telomerase is widely recognized as an enzyme that may prevent aging on the cellular level. But the lack of telomerase may also drive brain aging[12] and cancer.[13] Could CRISPR be used to replenish telomeres?

Church: Yes, that certainly is feasible.

The State of Gene Expression Is a Measure of Aging in Humans

Fahy: Would you please explain epigenetics, and comment on evidence that there is an epigenetic clock of aging?

Church: Epigenetics is essentially everything that controls gene expression. One component of epigenetics is DNA methylation, which consists of the addition of chemical entities called methyl groups to DNA at specific places. DNA methylation is important in part because it is a particularly easy component of the epigenome (the set of all epigenetic states) to measure. It turns out that DNA methylation changes with aging.[14] In fact, the state of DNA methylation can predict the age of a person to within about three years.[15]

In principle, if you could change the biological age of a cell or of an organism to a younger state, and if those methylation sites (the sum total of which is referred to as the "methylome") are really reflective of age itself, then the methylome should change to the pattern you would expect at an earlier age. In other words, if aging itself changes, then this biomarker of aging should change in the same way. We use these methylation sites as a measure of how well we're doing in some of our studies where we're trying to get aging reversal, and it works extremely well.

DNA methylation is very good for estimating the age of a person, and it can also be changed. Even though it's always linked to chronological age in normal life, in the world of aging reversal and epigenetic tinkering, you can change it, and the change is meaningful.

Fahy: Not all 50 year olds are biologically 50. Some are biologically older and some are biologically younger. People age at different rates. Fascinatingly, these differences can be detected by the state of the methylome. If the methylome indicates a different age than your chronological age, you are really older or younger than your chronological age, and this was validated by a variety of other measures.[14,16]

Church: Yes, that is correct. The people who discovered the epigenetic clock of aging studied their outliers and found interesting correlations with them. There are multiple measurements for molecular level aging events, and they tend to reinforce one another. We don't know enough about connecting the dots between measures such as the methylome and aging factors such as GDF11, IKKβ, and TFAM, but if you're doing anything to reverse age, then the methylome should also reverse along with the reversal of aging.

Fahy: Apparently, the DNA methylation state gets more chaotic as we age. For example, the methylation patterns of identical twins begin to diverge over time, more aberrant patterns being associated with greater pathology. This is consistent with a recent theory that attributes the lack of aging in some species ("negligible senescence") to a relatively stable pattern of gene expression over time, and normal

aging to unstable and increasingly chaotic patterns of gene expression over time.[17] But if you change gene expression back to what it should be, all of that variability should be reversible, right?

Church: That's right. The variation in different parameters in any biological system increases when you get further away from the physiologically normal state. You can think of the methylation variance as another risk factor for aging and disease.

How to Quickly Discover and Begin to Correct Currently Unknown Causes of Aging on the Gene Level

Fahy: If aging is driven by changes in gene expression and those changes in gene expression can be reversed, then we need to be able to find all of the important age-related changes in gene expression as quickly as possible. How can this be done?

Church: Gene expression results in each cell having specific RNAs and proteins, and these can be surveyed. You don't necessarily have to define every single RNA in a particular cell to understand that cell, but you can, and we have in fact developed a new method to do this that allows us to see all of the tens of thousands of RNAs in a single cell at one time, and to see the RNAs in neighboring cells as well. So now we can see how different cells relate to one another in context. This new method, called fluorescent in situ sequencing, or FISSEQ,[18] allows us to count all the RNAs in a cell while simultaneously counting all of the RNAs in all of the cells it touches. Plus, we get the 3D coordinates for every RNA molecule in every cell.

Fahy: That's unbelievable. How can you use this method to search for changes that are related to aging?

Church: Suppose there are two different kinds of cell, and we want to know what gene expression states make them different from one another. We can first compare the two cells using FISSEQ in order to determine the differences in gene expression between them. Next, we can pick specific differences we think cause the cells to be different cell types, and change the expression of those particular genes in either or both cells using, for example, CRISPR, and see if we can change one kind of cell into the other. Even if we don't get it right the first time, we can take many guesses as to what the important RNAs are and just how much to tweak them until we do get it right.

The same principle can be applied to any pair of cells. By comparing old cells to young cells, we can find out what makes an old cell an old cell, and how to turn an old cell into a young one.

Fahy: Fantastic.

Church: One of the problems with studying development and aging is that it takes a long time. But if we know the epigenetic state of all these different cells, no matter how many years apart they are, it only takes a few days to reprogram a cell and duplicate the effects of decades of slow change in the body, or reverse those effects. So in principle we could turn a young cell into an old one or an old cell into a young one because the only difference between them is epigenetics, or gene expression.

Fahy: What other ways are there to identify powerful gene targets for intervention into human aging?

Church: There are basically four good ways to find key gene targets.

First, we can look at genes that underlie person-to-person variability in such things as low risk for viral infections, diabetes, osteoporosis, and so forth. The most extreme example here would be to compare normal people to super-centenarians, those who live to the age of 110 or older. They might have genes that are protective enough to find even with a small number of individuals, or even with a single individual.

There are hundreds of genes that have small effects, but then way out on the end of the bell curve is something like the myostatin double null mutant or human growth hormone over/under production. Genes that have gigantic effects and completely dominate the effects of small environmental and small genetic influences are the right kind of gene to look for.

The second way to find the best gene targets is to pick from discoveries made from basic studies like the GDF11 and TFAM that we talked about earlier.

A third way is to use a specialized highly genomic strategy, such as mutating thousands of genes one by one to see if any of these mutations block aging, or using the FISSEQ method we discussed earlier.

The fourth way to identify powerful gene targets is to compare closely related animals, one of which ages much more slowly than the other (like naked mole rats vs. rats).

No matter where you get your lead, you don't have to worry about having too many hypotheses. Just use CRISPR to activate or inhibit that candidate gene and look for the biomarkers of aging reversal we discussed earlier. The idea is to see whether your change has an impact or not, and whether it acts synergistically with the other things that have been shown in the past to have an impact.

Fahy: So if we saw something unusual or provocative in super-centenarians, we could create the same change in, for example, a normal human cell line and observe whether the right longevity pattern emerged.

Church: Yes.

Fahy: I've been told by James Clement, who is being funded by the Life Extension Foundation to do collaborative work with you on the genetics of super-centenarians *(See sidebar: Life Extension Foundation Funding of CRISPR Research)*, that you might even be able to take super-centenarian gene expression patterns and put them into mice and see if the mice age more slowly.

Church: Right. Our protocol will likely be to collect leads from the four different sources and try them out first on human cells. By going straight to human cells, we won't get into the trap of spending years working on mice, which is rather expensive, only to find out that it doesn't work in humans. We can actually do a cheaper and more relevant study in human cells, confirm them in mice, then test them in larger animals, and then in humans. I think that going from human cells to mice and back to humans is likely to save us time and money. Many human cellular testing systems are getting better and better, such as "organs on a chip" or organoids, which are getting to be more and more representative of in vivo biology.

Eliminating the Tradeoffs of Intervening in Aging

Fahy: Could the ability to target some genes and not others using CRISPR also make it possible to eliminate the side effects of some anti-aging interventions? For example, I'm working to show that it's possible to regenerate the thymus in humans and restore naïve T cell production using growth hormone. Although growth

hormone does not cause cancer in adult animals or people, it slows down DNA repair in animals, which is an effect that is unrelated to the beneficial effects of growth hormone and to regenerating the thymus.

Church: So you'd like to get rid of that effect on DNA repair while keeping the good effects.

Fahy: Yes. If you can use CRISPR to go right to the genes of interest and not act through the usual pathways, which also lead to places you don't want to go, the unwanted effects should be avoidable, right?

Church: Exactly. You could make a list of all the growth hormone targets and either pick the growth hormone targets you like and activate them selectively, or pick the growth hormone targets you don't like and block them so you could use growth hormone normally without inhibiting DNA repair.

The Feasibility of Applying CRISPR Technology to the Whole Body

Fahy: To reverse human aging, CRISPR technology will ultimately have to be applied in the whole body, and not just to cells in a test tube. How feasible is it to apply CRISPR technology in the intact body?

Church: Gene therapy can be based on either ex vivo manipulations, in which cells are removed from the body, genetically modified, and then put back into the body, or on in vivo (within the body) methods, in which, for example, a modified virus might be used to carry a gene package into many different cells in the body. Each of these methods has pros and cons.

There are viral and non-viral delivery systems that could be used to deliver CRISPR constructs and that will leave the blood vessels and go into the tissues. The delivery system could contain the CRISPR plus guide RNA plus the donor DNA, or it could just comprise the CRISPR, guide RNA, and protein activator, and so on. But whether it's a viral delivery or a non-viral delivery method, the total mass of gene editing devices that has to be delivered will have to be considerable. But there is no rush, you can deliver them slowly.

Fortunately, there are ways to manufacture biologicals that are dirt cheap. Things like wood and even food and fuel are all roughly in the dollar-per-kilogram range. If we could similarly make a kilogram of a viral delivery system and load it up with CRISPR, then it could become inexpensive enough to apply to the whole body.

Fahy: Yes, a kilogram would be plenty! So, the viral delivery system contains a gene for CRISPR, a separate gene for the guide RNA, etc. When it delivers these genes to the cell, the cell makes the resulting proteins and nucleic acids, and all of the components simply assemble all by themselves in the cell, is that right?

Church: Yes.

Fahy: Which is the best CRISPR delivery system?

Church: Adeno-associated viruses (AAV) are one of the favorite delivery systems right now because they can be nudged into going to tissues other than the liver (where many other delivery systems end up) more readily. This is an active field of discovery. It's moving quickly, and the CRISPR revolution just made it an even more desirable field to study.

Safety

Fahy: How selective can a virus be engineered to be for delivering CRISPR to just one cell class and not another in the body?

Church: For every thousand cells of a particular type that you target, you might deliver your payload to one other cell of a different type that was not targeted. That should be good enough. Also, if you've got something that is required for cells in general, then it should be delivered to all cells. Even if you have something that is cell specific, it doesn't necessarily matter to which cells it is delivered. But in cases where it does matter, you can get the delivery right about 999 times out of 1,000 right now.

Fahy: Could there be safety issues of having a one in 1,000 misdelivery rate? That would still come out to a lot of misdeliveries in a whole body.

Church: It helps to remember that most drugs actually go to all the cells in your body. It would be a double standard to say that CRISPR has to be more specific than any previous drug.

Safety also depends on what brand of "explosives" you're dealing with. It's like nitroglycerin versus TNT. If you make safety one of your top priorities, you're not going to be using something that can go awry, until you can make cell specificity very high.

Fahy: Another point of importance for the safety of using CRISPR in the whole body is not just which cell it goes into, but whether it edits the right gene or not. How accurately can CRISPR be targeted within the genome?

Church: In practice, when we introduced our first CRISPR in 2013,[19] it was about 5% off target. In other words, CRISPR would edit five treated cells out of 100 in the wrong place in the genome. Now, we can get down to about one error per 6 trillion cells.

Fahy: This must mean that the chance of a serious error is now low enough that it is very hard to measure, and far less than the spontaneous mutation rate.

Church: Yes. And beyond this, there are ways to use small molecules as conditional activators to ensure that intended effects happen only in the correct cells. The combination of a totally safe small molecule activator and programmable targeting is unprecedented.

Other checks can be put in as well for even greater safety. For example, once a viral payload gets inside the cell, it can make further decisions. It can essentially ask, "Am I in the right place?" before it acts. There's a whole field of molecular logic circuits that could be applied in order to avoid errors.

Affordability

Fahy: Is it going to be affordable for a human to reverse his or her aging process using this kind of approach?

Church: If you look at the current price, it looks very unaffordable. There are about 2,000 gene therapies that are in clinical trials, but the only gene therapy that's approved for human use costs over $1 million per dose. You only need one dose, but at that cost it's obviously unattainable for most people. It's the most expensive drug in history, as far as I know.

Fahy: What is that drug?

Church: It's called Glybera®. It treats pancreatitis, a rare genetic disease. But sequencing the human genome used to cost $3 billion per person, and now has come down to just $1,000 per person, so I think getting from over $1 million down to the thousands shouldn't be that hard.

Fahy: Another cost saver for aging intervention would arise if we could roll back aging significantly just by modifying five to 10 genes. That might get the overall cost down to something attractive.

Church: Right. The combination of having to hit, say, a trillion cells in the whole body and 10,000 genes would be daunting. But if you can do a subset of cells and a subset of genes, then it becomes more feasible to make it affordable.

Fahy: You have said that CRISPR therapy might have the potential to replace conventional drugs. Why is that?

Church: A big advantage of CRISPR is that it offers better opportunities than conventional treatments for "putting knobs in" where there aren't any control knobs now. Right now, you have to be very lucky to have a potent drug that will do what you want it to do and nothing else. With CRISPR, we can be far more precise.

How Many Aging Corrections Can Be Made at One Time?

Fahy: If we know what to do and we can afford to do it, how quickly can we proceed to correct aging? What about simultaneous modification of, say, 10 different cell types in the body that were causing most aging changes? Could they all be modified at the same time?

Church: "All" is a big word, but I think that many could be modified at once. This could be done by what we call multiplexing, using a mixture of viruses or delivery vehicles to enable many things to be done at one time. But you can also go slowly, starting with the highest priority tissues first and then going on to lower priority areas. Determining which tissues are the highest priority could vary with the patient's heredity, which might cause a particular tissue to be at higher risk for aging faster.

Getting It to the Clinic: How Long Will It Take?

Fahy: Using your most favorable pathway for intervention, how long will it take before a human trial might be possible?

Church: I think it can happen very quickly. It may take years to get full approval, but it could take as little as a year to get approval for phase one trials. Trials of GDF11, myostatin, and others are already underway in animals, as are a large number of CRISPR trials. I think we'll be seeing the first human trials in a year or two.

Fahy: Can you say what those trials might be?

Church: I helped start a company called Editas that is aimed at CRISPR-based genome editing therapies in general.[20] Some of those will be aimed at rare childhood diseases and others hopefully will be aimed at diseases of aging. We also have a company focused specifically on aging reversal that will be testing these therapies in animal and human models.

Aging Intervention, the FDA, and the Dietary Supplement Model

Fahy: Is the fact that the FDA does not recognize aging as a disease a problem?

Church: The FDA is willing to regulate many symptoms of aging, such as osteoporosis, muscle decay, heart disease, mental agility, and so forth. It tends to be harder to prove a preventative than it is to prove a drug that cures an immediately and hugely harmful disease. And actually, since the FDA doesn't want you making unjustified health claims of any kind, they would have to take responsibility for regulating any health-related condition that one might want to make claims about. It doesn't have to actually be a disease.

Fahy: It has been proposed that the FDA should just evaluate safety and not efficacy. How do you feel about that?

Church: I really like that. The Internet will probably weed out the non-efficacious. The nutritional supplement market is a perfect example of safety being all that is needed for approval. You can get a nutritional supplement on the market just based on safety, but you can't get a prescription drug on the market just based on safety. It really should be the same rule.

Fahy: The freedom to innovate and to create dietary supplements is what the Life Extension Foundation is all about. They fund all of my research in cryobiology, and they base their supplements on scientific literature. There are good effects of freedom and freedom to operate.

Church: That's true. I'm just saying that there is a double standard for the FDA. The standards for supplements are different from the standards for new prescription drugs.

Fahy: Perhaps if that were altered in favor of the standards for supplements, we'd have many more drugs and would all be a lot better off.

Church: Yes. Focusing on safety is probably the right model.

Fahy: Thank you, Dr. Church, for an amazing glimpse of the near future! ■

Dr. Bobby Dhadwar and Dr. Margo Monroe on Reversing Human Cellular Aging Right Now

After interviewing Dr. Church, Dr. Fahy had a chance to briefly interview two new postdoctoral fellows in the Church lab who have done the cellular aging reversal studies referred to in the Church interview. Here is the result of that interview.

Fahy: Please introduce yourselves and tell me how long you have both been in George's lab.

Dhadwar: I'm Bobby Dhadwar, and I've been here about a year and a half. I did my PhD at McMaster University, and then I came here to do my postdoc.

Monroe: I'm Margo Monroe, and I've been here a little short of a year and a half. I am from Florida, and then I went to Boston University to do my PhD in biomedical engineering, and then I came here for my postdoc, which concluded in November 2014. I am currently working in intellectual property at a law firm in Boston.

Fahy: Please tell me what you're excited about.

Monroe: What's exciting is: aging studies have been around forever, but this is different, we're figuring out how we can reverse aging.

Dhadwar: Agreed. We've shifted from trying to make a young animal live longer to rejuvenating an old animal to a younger state. This is a complete shift in perspective. When people originally thought about aging, they assumed it had a lot to do with accumulation of mutations, but that doesn't seem to be the case. Genetically, your genome is intact. There are no mutations that are causing the aging process. What's going on when you age is that you get this drift in the regulation of these gene networks so that you have a cell that's supposed to be, say, a skin cell, but then it starts expressing genes that it's not supposed to be expressing.

Fahy: So you're working on not only a different technology, but also a different concept.

Dhadwar: Right. A lot of times, when we talk to people about living a lot longer, they say, "No. I don't want to live into the hundreds. I don't want to be decrepit. I don't want to be in a state where I can't take care of myself for that many more years." But when we talk about living longer, we think of living a healthy, active lifestyle so that you're rejuvenated and you're really enjoying your life.

Fahy: You're actually biologically younger.

Monroe: Right.

Fahy: If you're biologically younger, all of these problems go away.

Monroe: It's like the slogan, "Oh, 50 is the new 30." It would just be a little bit more extreme in that regard.

Fahy: Yes. Exactly. One hundred is the new 30.

Monroe: Correct.

Dhadwar: There's been some really interesting studies just from the last year which makes it very interesting to look at epigenetics. You can actually tell the age of a person with a three- to four-year accuracy just by looking at the methylation status of a particular tissue in their body. We can actually use that as a tool now.

Monroe: To see if what we're doing works.

Fahy: So you don't have to develop a drug for human aging and then have to wait 50 years to see if it works.

Dhadwar: Exactly. We want to have a metric so we can ask, if we give someone this therapeutic, "Are they younger or older than before they took it?" We want to actually measure if we're reversing the aging process, and that's something we can actually push to the clinic.

Monroe: Right. It will be nice if, within a week, you can tell if a certain intervention is going to have success or not.

Dhadwar: Correct. We don't want to have to wait weeks, months or even years to actually see if an intervention has an effect, and then have to repeat the experiment, and then, in the end, find that it doesn't necessarily apply to humans. Our focus has been to develop a strategy that we can actually take to the clinic. Our endpoints will not include the age of death, because we're not interested in that.

Fahy: Obviously you're interested in signs of rejuvenation instead. Is it working?

Monroe: *In-vitro*, we're able to make a 94-year-old fibroblast look metabolically like a 22-year-old fibroblast. With just one gene. It is transcription factor A from mitochondria, a nuclear-encoded gene that transcribes the mitochondrial genome.

Fahy: TFAM?

Monroe: Yes, and it's so easy to do, too. It's amazing. We're so surprised.

Dhadwar: It's such a wonderful effect on just one simple target. Now, we're interested in combining that with other targets to actually complete the reversal process. TFAM might restore some of the age-related phenomena.

Monroe: The metabolic effects.

Dhadwar: Right. When you age, the number of mitochondria decline and the amount of energy your cells have declines. We can restore that, but that doesn't restore everything in the cell. So now we're targeting other pathways that will complement TFAM so we can have this cocktail that can actually reverse all the symptoms of aging.

Fahy: Spectacular. How many other things are you looking at for your cocktail right now?

Dhadwar: Right now, we're going after some of the major pathways known in aging. But we don't believe those might be all-encompassing, so that's where we're putting together a screening methodology where we can actually take a look at targeting multiple different genes and pathways and see which ones are implicated, because I think a lot of the studies that have been done before have been done in animals, and that's not always translatable to humans. So, we focus on the human system and take a look at targets that we can pull out that are relevant for humans.

Fahy: How are you finding these targets? With FISSEQ? *(See main Church interview for an explanation of FISSEQ.)*

Monroe: Yes. FISSEQ will be the downstream final readout.

Dhadwar: We're designing our system so we can target all these different genes at the same time. If we see there's change in our aging metrics then we know we've done something, and say, "Okay, that seemed to reverse this phenotype of aging."

Fahy: You can take a 94-year-old skin cell and make it into an induced pluripotent stem cell (iPS) as well. That has a biological age of 0, and requires only about three to four interventions.

Monroe: Right.

Dhadwar: But that takes a number of weeks to actually reprogram a cell. We're not interested in that. We want something that you can apply right away, one or two days at most, and see if you can actually reverse these aging phenotypes, to actually reverse the aging process without changing the identity of the cell. If you can do that, then you can develop a cocktail that you can apply to the whole body and rejuvenate a number of different tissue types, and it wouldn't be tissue-specific.

Fahy: Yes, for something like your TFAM, that would make sense, because mitochondrial aging will be universal for all cells.

Monroe: Right. Mitochondria are involved in a lot of different disease processes too, so when you think of cancer or neurological disorders, a lot of it arises because the mitochondria aren't working properly.

Fahy: Thank you both for a very exciting look at how rapidly solutions to aging may really be developed.

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THE CINEMATIC CRYONICIST: FOUR DOCUMENTARY VIDEOS, EARLY AND LATER

By R. Michael Perry

Summary: Documentary movies about cryonics have long been part of promotional efforts within the movement, as well as being of general interest to the public. A small portion of this interesting story is surveyed here, two videos from the Cryonics Society of New York, vintage 1971 or earlier; a commercially produced documentary from 1978; and an Alcor promotional movie from 2005.

Early on it was recognized that publicity is important for cryonics, and efforts focused on how to get the message out. Books were written, whole organizations were created, newsletters were started, conferences were held. Movies were also made, swelling over time to a floodtide of documentaries. Some originated in the cryonics movement itself, with the usual promotional and educational intent, others with news services or other commercial interests, for undoubtedly cryonics was an interesting theme to the public, even if few were ready to sign up. To do full justice to this effort would be far out of reach here, but we make a start by considering four videos, three from earlier times, prior to 1980, the fourth more recent. (Fictional productions having a cryonics theme have another long, variegated history which we must bypass here.)

One of the earliest organizations to do actual human cryopreservations was the Cryonics Society of New York (CSNY); they also contributed two short feature films which we review here. Understandably, these very low-budget, amateur efforts lack the refinements of some of the later productions, yet they have their own fascination for the glimpses and insights they offer into a fledgling movement. I've devoted extra space to these two productions, which have an interesting back-story—even finding them in the first place makes an interesting story.

A few years after these films were made CSNY had ceased its operations, stymied by costs and other roadblocks,[1] and Trans Time in the Bay Area, California, had become the leading organization offering cryopreservation services. A 1978 documentary, commercially produced as part of a series, *In Search Of* … and hosted by Leonard Nimoy (Star Trek's inimitable "Mr. Spock"), gave coverage to Trans Time and its operations, and is also covered here. Finally, in 2005 Alcor Foundation produced the impressive promotional video that rounds out our survey of cryonics documentaries.

THE FIRST CSNY FILM[2]

The first CSNY film (color, with sound), which was untitled (a proper title might be, *The Cryonics Alternative*), was the creation of Karl Werner. Werner was one of the five founding members, and the one who named the Cryonics Society of New York, Inc. (CSNY), in July 1965.[3] He has the distinction of having coined the word "cryonics" which, though it started as a company name, is now in general use. He studied at the Pratt Institute in Brooklyn, noted as a school for art and architecture, where he met Glenda Allen. Glenda joined him in his work with CSNY, becoming the organization's treasurer in December, 1967, and among other things, helping with the film. According to the CSNY newsletter *Cryonics Reports* the film was finished by January 1968 and was shown at the "First Annual Cryonics Conference" which was held the following March at the New York Academy of Sciences, NYC.[4]

Karl Werner, rendering by the author (composite) (KW2, KW3).

Glenda Allen, 1961 college yearbook photo (GA, KW1).

This "first" conference was not really the first public gathering devoted to the cryonics idea since several conferences before this event were staged by Ev Cooper and his Life Extension Society (LES). Another Cooper conference was scheduled October 1967, but was cancelled on very short notice due to circumstances detailed elsewhere.[5] The March 1968 conference was however the first to carry the new label "Cryonics" and signaled a shift in leadership in the movement from the promotion-only, discussion-oriented LES to groups like CSNY which had either cryopreserved people already or had near-

term plans and capability to do so. (CSNY would do their first cryopreservation, that of Steven Mandell, the following July.[6])

The film begins with a wintry, cemetery scene accompanied by the opening bars of Wagner's *Tannhaüser* overture. The camera pans here and there in the headstone-studded bleakness; then a female voice (Glenda Allen's[7]) announces: "Cryonics offers an alternative." The scene shifts to the archway entrance of the New York Academy of Sciences building and the narrator adds: "Welcome to the First Annual Cryonics Conference."

"New Year's Day, 1966," the narrator continues, "the Life Extension Society displayed, for the first time in public, a cryonic suspension unit." (This was at the Third Annual Freeze-Wait-Reanimate Conference, held in Washington, D.C., described by LES founder Evan Cooper as "wild, disorganized, but fruitful."[8]) A horizontal cryogenic capsule with one end opened is shown, Mussorgsky's *Pictures at an Exposition* starts in, and the narrator adds: "Robert Ettinger and other cryonics pioneers were interviewed by the press and TV news commentators." Ettinger is shown speaking; then the scene shifts to show others including Ed Hope, Curtis Henderson, and Saul Kent, as the narrator clarifies: "At that time no one had been frozen, and no group yet had the equipment and personnel to freeze a human being." But that was two years ago. "Since that time, several people have been placed in cryonic suspension." (James Bedford and Marie Phelps-Sweet in particular, both by the Cryonics Society of California.[9]) "The purpose of this film is to simulate a procedure that might be used to freeze someone today."

The scene shifts to a ringing telephone, and a male voice (Karl Werner's?) answers, "Hello, Cryonics Society." A search through paperwork is shown, a form is pulled up, and the narration continues: "When death is imminent, the freezing team must be mobilized immediately." Street scenes whiz by, a tray of surgical instruments is shown, and we are inside a facility of some sort where tables and apparatus can be seen. (Actual location: the St. James Funeral Home embalming room, Long Island, where the film was mainly produced.[10]) The narrator then notes: "As soon as the patient is pronounced dead, an external cardiac compressor is used to maintain oxygenated blood flow. It is imperative at this point to lower the body temperature as rapidly as possible in order to prevent brain damage." The patient is shown on a gurney in the laboratory-like setting. A cardiac compressor is running and alternately pushes down on the chest and relaxes, simulating heartbeat, also illustrating how tissue would be oxygenated by this process (by introducing oxygen into the lungs as the chest alternately is compressed and relaxes). Technicians scurry about (identifiable as Curtis Henderson, Saul Kent, and Fred Horn, the funeral director who would be in charge of perfusions for the CSNY cases.) "The body is perfused with a cryoprotective solution to minimize freezing damage. An incision is made in the carotid artery. To facilitate perfusion, blood clots must be removed. Heparin is then injected to prevent further clotting. The perfusate is circulated at a controlled pressure by means of a surgical pump." A roller pump is shown in operation, and solution filling a reservoir. "After a temperature slightly above zero degrees centigrade has been reached, and perfusion has been completed, the equipment is dismantled."

A sack of rock salt is shown. "Packing in salt and ice for twenty four hours induces the slow formation of extracellular crystals." This phase is completed quickly via time-lapse, and the body is wrapped in aluminum foil (see reference below, for second film) and put in a large rectangular box. "After the cooldown stage, the body is placed in a temporary container with dry ice until permanent storage is feasible." Blocks of dry ice are placed around the foil-wrapped body, and finally, the box is closed with a thick, insulating lid.

The dry ice box then is wheeled to a desired location, again allowing for time-lapse until, as noted before, "longterm storage becomes feasible." Then: "The final stage is begun with transference to the cryonic suspension unit, previously cooled with liquid nitrogen. This permanent unit consists of an inner cylinder suspended in a high vacuum for insulation, and enclosed in a steel outer cylinder." A horizontal capsule is shown with one end open, and the patient is lifted inside by two technicians (Saul Kent, Curtis Henderson). An endplate is put in position to close the inner cylinder and one of the technicians (Curtis Henderson) attaches rivets all around while music from

Scenes from the Werner film. Left to right, top to bottom, (1) Opening, cemetery scene. "Cryonics offers an alternative." (2) Entrance to New York Academy of Sciences, where the March 1968 "First Annual Cryonics Conference" would be held and the film shown. (3) Robert Ettinger at Third Annual LES Conference, Jan. 1, 1966. (4) Hearse used for patient transport. (5) Instruments used in patient preparation. (6) Fred Horn demonstrates removal of clots and injection of heparin. (7) After cryoprotective perfusion, dry ice blocks are placed around foil-wrapped patient to initiate freezing. (8) Patient is inserted into (horizontal) capsule. (9) Saul Kent (left) prepares to draw vacuum on now-closed capsule, assisted by Curtis Henderson.

Paul Dukas' *The Sorcerer's Apprentice* throbs in accompaniment. The inner container, it turns out, is suspended by thin steel rods within the outer container, with the annular space between them filled by foil (aluminized mylar) insulation.[11] A large plug wrapped in or consisting of aluminized mylar is shown, evidently intended to close the insulation the gap at the end between the inner and outer cylinders. It is put in place by the two technicians, and the heavy outer endcap of the capsule is put in place and attached, again with rivets (again Curtis Henderson doing the honors).

The narrator reports the conclusion to the venture: "A vacuum is drawn after the capsule has been completely sealed." This operation is carried out and the closed-up capsule is shown briefly as if in use. A voice is heard. It is Dylan Thomas intoning the closing lines of his famous poem, *And Death Shall Have No Dominion*, as the scene shifts back to the cemetery at the opening:

> Where blew a flower may a flower no more,
> Lift its head to the blows of the rain;
> Though they be mad and dead as nails,
> Heads of the characters hammer through daisies;
> Break in the sun till the sun breaks down,
> And death shall have no dominion.[12]

At the March conference Fred Horn, who operated the St. James Funeral Home in Long Island, gave a talk, "Perfusing and Freezing a Patient,"[13] just after the Werner film had been shown. Horn in his opening remarks commented: "This is the first time I've seen that film, even though it was made at my funeral home. You saw my lovely pink embalming room there. With that background music though, I think I'll be a little afraid to go there tonight." One expects there was a ripple of laughter from the audience at this point, though not recorded in the conference proceedings. Here in any case is the next, introductory section of Horn's interesting talk, which later recapitulates the movie's procedures in more detail:

CRYONICS & THE FUNERAL PROFESSION

At this time, the funeral director must be an integral part of the cryonic suspension team, because he is licensed by the State Department of Health throughout the United States to remove, embalm, hold, transport, and inter bodies declared legally dead. For purposes of cryonics, therefore, it is a great asset to have a funeral director who will cooperate.

I understand the Society in New York sent letters to many funeral directors in the New York area last year, in order to explain the cryonics field and enlist their aid. But the response was negligible. Either they were too busy with their type of interment, or they felt that you fellows were not much of a threat to them.

They didn't seem to realize the implications of this movement, or the effect it's going to have upon them in the future.

Fortunately, or unfortunately, I broke my leg skiing last year, and so had time to investigate the idea. When I first heard about it I thought of the threat to my business. What am I going to do if these fellows step in and take over? But you know when you really stop and think of it, if this thing can be pulled off, I would dig ditches for the rest of my life if it would contribute to the movement. This is the greatest idea ever conceived.

This is the way I feel about it – as far as the other funeral directors, I've spoken to them and there is minor interest, not too much, because basically they are too busy. They haven't the time to absorb the concept.

For a little subsequent history: in May 1968 Karl and Glenda were wed "by a minister from the Founding Church of Scientology," the June *Cryonics Reports* proclaiming it a "cryonics marriage." Karl was then Vice President and Glenda Treasurer of the organization.[14] In July 1968 CSNY did its first cryonics case, Steven Mandell, as noted. The following month, however, the Werners left cryonics in favor of Scientology because they felt the two movements had "opposing goals."[15] Horn, for all the brave words above, and an involvement in cryonics lasting several years, seems to have quietly reverted back to a "garden variety" funeral director when CSNY's freezings came to an end in the mid-1970s.[16]

Fred Horn, about 1968 (CR5).

Horn with patient (model, Diane Henderson) (CS1).

THE SECOND CSNY FILM[17]

CSNY (through Cryo-Span) would freeze several others over the next year and a half, including Ann Deblasio in January 1969 and Paul Hurst in March 1969. The Washington Memorial Park Cemetery in Coram had a small garage they generously allowed CSNY to use for its patient storage, though there was some uneasiness about this. Both patients were initially stored in dry ice, as had been Steven Mandell, who now was in a horizontal capsule of design similar (not identical) to the one shown in the Werner film. When Ann Deblasio was frozen her husband Nick commissioned construction of an upright capsule, a superior product made by Minnesota Valley Engineering

(MVE), the capsule taking several months to build. In August it was ready and Ann was placed inside. (The family was Catholic and a priest consecrated the capsule in a memorable ceremony.) The capsule was large enough to hold two occupants, but Nick reportedly did not want another man "sleeping with his wife"—instead saying he wanted to be in the capsule himself someday. So Hurst Sr. remained in dry ice for a few more months until another capsule could be finished by MVE, and he was placed in it. Around this time complaints of the cemetery management reached the point that CSNY was forced to move some of its patients to a new location, a little industrial bay at 171C Eads Street, West Babylon, also on Long Island. The two upright capsules with their occupants went there, while Mandell stayed behind for a while.[18]

In May 1970 Herman Greenberg was a 42-year-old accountant living in Atlantic City, New Jersey with an alternate residence in Philadelphia. Beverly, his very bright, 17-year-old daughter, was interested in films and photography and had already worked as a camera girl in the movie *The Beguiled*, which starred the young Clint Eastwood. Beverly had seen Bob Ettinger on TV and was interested in cryonics but hadn't considered it enough of an urgency to be actively involved. Suddenly Mr. Greenberg suffered a fatal heart attack, and was buried in a cemetery near Philadelphia. The devastated Beverly reported later: "I simply could not go on with my own normal existence thinking of my father decomposing in the ground." So, with a fierce determination not to let matters rest, she contacted Ettinger who put her in touch with CSNY. Others' objections and other difficulties were worked around. Greenberg's embalmed body after two weeks of burial was retrieved from the ground with a backhoe, frozen, and stored on dry ice at the West Babylon facility.[19]

The storage extended until about April the following year. The Greenberg mother and daughter, deprived as they were of their principal breadwinner, did not want the extra expense of building still another capusule. So Hurst Jr. generously agreed to let Beverly's father be placed back-to-back with his own father, and Beverly, with her film-making and dramatic instincts, sensed an opportunity. The feature film she made had the picturesque if ungrammatical working title, *The Icemen Cometh*. It showed her father's encapsulation against the backdrop of a wall mural with a giant image of a half-moon surrounded by blazing (simulated) stars against the black backdrop of outer space. She had paid about $150 (about $880 in 2016) for this item to transform the little den into something, well, of more cosmic significance, befitting the occasion. As she said later, "The reason it's here it that the capsule that holds the frozen bodies (one of them happens to be my father, and he's in there with another man) stands upright, vertical, and sort of gives the impression of being something about the space program." The film apparently was completed (color, with soundtrack like the Werner film) and was shown to a number of cryonics and media people. Possibly it even survives somewhere, but the only version I know of is missing a soundtrack and other features (including reportedly a cameo appearance by Beverly herself) and we must make do with that.[20]

Beverly Greenberg, aka Gillian Cummings (CS2).

Herman Greenberg, rendering by author (CH, BG).

The film as we have it follows roughly the latter part of the procedure in the Werner movie, after the cryoprotective perfusion (not done in this case) and freezing to dry ice temperature are complete. The immediate task at this point would be maintaining the patient on dry ice, and whatever preparation would be needed to begin the transfer to liquid nitrogen storage (encapsulation). We first see Curtis Henderson with a hammer and a wood chisel or some similar implement, chipping and splitting large blocks of the white, snowy frozen CO_2 and putting the pieces into a coffinlike container that, it appears, already holds the patient. A cover of what appears to be a thin sheet of plastic is placed on the box, and dry ice is put on top of it (rather than a thick lid as in the Werner film. Was this because removal of the patient from dry ice storage was about to occur?) There is an article in the Spring 1971 CSNY newsletter, *Immortality* (formerly *Cryonics Reports*), that, without naming Greenberg, describes the procedures that would have been used for maintaining him on dry ice, since the others were already in capsules. A sequence of illustrations has a starting scene with Fred Horn placing aluminum foil on the face of the patient in a dry ice box, with the comment that it is to "protect against the accumulation of frost on the skin coming from water moisture in the air." "The rest of the body," it says, "was wrapped in foil prior to placement in the box."[21]

The next three scenes with minor adjustments could serve, after some introductory remarks, as narration for the early part of the movie. First, "Cryo-Span Corp. Curtis Henderson [is here shown] in the process of slicing 50-lb. blocks of dry ice into smaller segments prior to insertion into the temporary storage box." "Dry ice," we then are told, "is purchased from a local distributor (Jolly Tim) in Farmingdale, L.I." After this—and it is shown in the movie (or appears to be—allowing for the fuzzy details)—"Henderson places evenly sliced segments of dry ice adjacent to the patient's head. Care is taken never to rest even a single piece of dry ice on any portion of the body. Approximately 150 pounds of dry ice is used for each refilling of the box." When this operation is complete, "[the p]atient is now assured of dry ice preservation for about 4 or 5 days. He awaits the transfer to indefinite preservation in liquid nitrogen at -196°C. If it is impossible to make a rapid transfer, the patient can remain in dry ice storage for an extended period."

The movie continues with brief shots of the patient in the dry ice box, body wrapped in aluminum foil but face unwrapped and

Filling the Hurst/Greenberg capsule with liquid nitrogen, lunar wall mural as backdrop (CS2).

defrosted (accomplished by rubbing with isopropyl alcohol[22], *not* by warming!) The transfer involves attaching a rope harness, with straps around the body in two places and using an overhead hoist. We see the normally upright capsule cradled on its side, presumably with much or all of its usual interior liquid nitrogen briefly removed. The two straps are removed one after the other as the patient slides further and further into the topmost slot of the sideways capsule, aluminum foil is replaced around the head by Curtis, and the split lid in two parts is put on. Then the capsule itself is hoisted upright and steadied by Saul Kent and someone else, maybe Curtis. For the final stage of the operation, the lid components are again removed, a fill tube is hooked over the edge, and the capsule is filled with liquid nitrogen.

The drama in this case doesn't quite end there. There are some closing shots of the upright capsule in a scaffold-like truss with a platform partway up that allowed access to the lid for topping off with liquid nitrogen and other purposes. (Unlike the horizontal capsule this thermos-style container with easily removable lid could be opened without difficulty to expose the inner compartment where patients were stored. This proved convenient for adding more patients as well as inspections and other purposes. The general design is still in use today.) In the background the half-moon image looms large. The West Babylon facility where the movie was made consisted of an office and the adjoining room where the upright capsule with the patients was kept;[23] this in turn could be entered and exited through an overhead garage door.[24]

As the movie is ending you see a brief credits page (absent in the Werner film), which hints at what we don't see or hear in the incomplete copy we possess ("Gillian Cummings" is a stage name Beverly used):

CURTIS HENDERSON

GILLIAN CUMMINGS

Portions of "Prospects of Immortality" by Professor Robert C. W. Ettinger, Courtesy of Professor Ettinger and Doubleday, Inc.

Print by MOVIELAB

Copyright MCMLXXI Gillian Cummings

Evidently the film quoted portions of Ettinger's famous book (slightly wrongly cited here; actual title is *The Prospect of Immortality*). Movielab, where copies of the film were or were to be run off, was a famous motion picture processing facility that occupied a 10-story office building in New York City.[25] Did she actually have a few copies of her finished feature film made ("printed") here, or was this a fantasy?

The Icemen Cometh: *(1) The foil-wrapped patient at dry ice temperature, prior to encapsulation, face briefly exposed for photography. (2) Diane Henderson. (3) Curtis Henderson. (4) Patient is placed in capsule, feet first. (5) Capsule is hoisted and pushed upright, Saul Kent and another assisting. (6) Curtis Henderson, another face shot. (7) Capsule is filled with LN2, Henderson supervising. (8) Film credits. (9) All done, "THE BEGINNING."*

Movielab ad from 1956 (ML1).

Movielab building (portion), Nov. 2015, now with new owners (SG, ML2).

Presently this is an unsolved mystery along with the more important question of whether a copy of the film, along with other photography work Beverly did, survives somewhere, maybe with relatives.

In any case the drama in the film was intriguingly mirrored in the facial gestures of the "star" performer who did most of the work, Curtis Henderson, something I've never seen in the many other documentaries on cryonics that have by now been made, often by professionals with substantial budgets. Appropriately, the film concludes not with "The End" but "The Beginning."

Tragically, Beverly herself did not survive long, as has been reported elsewhere.[26] With all her brilliance and talents, she

had trouble finding employment and frequently spent nights in her car in the facility, having nowhere else to stay. (Curtis Henderson could have provided quarters, as he had done before, but was having marital difficulties which he didn't want to aggravate by having this young woman he worked with spending nights in his home.) When it got cold she was said to have run the motor of her car briefly to warm up. When, in November 1973, she was found dead in her car in the facility, with the keys in the ignition and the gas tank empty, the car was pointed toward the lunar wall mural. Mike Darwin thinks maybe that was the last thing she saw.[27] (Following this, despite her interest in cryonics and commitment to preserving her father, she was cremated and her father reburied.[28])

BEHIND THE SCENES

The two films as I found them were at the beginning of a reel of old cryonics clips. Jerry Searcy found this item in the video collection of a non-cryonics friend in Las Vegas some years ago. How it got where he found it, apparently unique in a hoard of quite other-type material, is another mystery. The friend didn't want it and gave it to Jerry. The other clips on the reel are of more recent vintage such as a Phil Donahue show that pitted Alcor officials against a recognized cryobiologist in a debate about cryonics. The first clip is the Greenberg film, the second the Werner film. Both films have no interior titles and no direct information as to when and by whom they were made. (Curtis Henderson also had a copy of the Greenberg film similar to the one Jerry found, and other copies of this and the other film may survive. Other CSNY films, unknown to me, may even exist.[29]) Close study, comparison with newsletter reports, and recollections of people who remembered the early days, made the original provenance clear.

In this I was fortunate in being able to contact Karl Werner for background on the film he made (though he could not remember making it) and Mike Darwin for background on Beverly Greenberg and the film she made. These two deserve special thanks.

Evidently the movies were copied from celluloid originals, both I would guess by Curtis Henderson. The video portion is only low-grade as I've noted, and the sound track in the Werner film is not stellar but is at least intelligible. The videos run at 30 frames per second. The Werner film when I first played it had what sounded like a little girl's high-pitched voice-over describing all the cryonics procedures briskly with rather more technical savvy than your average fourth-grader. Werner said it wasn't anybody he could recognize, unless just maybe it was his girlfriend Glenda, only with the sound speeded up. *Sound speeded up?* Somewhere I remembered reading that old film movies ran at 24 frames/sec. not 30. I tried slowing the Werner movie down to 80% its original rate, using some editing tools, and it did the trick, a more deliberate, mature woman's voice emerging, and Werner confirming that it indeed was Glenda. (I also slowed the Greenberg film down by the same amount for the online version.)

As for the Greenberg film, in addition to the missing sound track which could not be remedied, there was the matter of the credits page reprinted above, which came out very overexposed and fuzzy in the copy and required some work at decipherment. Plus Mike Darwin had important background information, as noted.

Decipherment. Top: video copy frame of film credits, showing fuzziness and image doubling. Bottom: reconstruction based on frames such as preceding and other information (used in online version).

THE 1978 DOCUMENTARY[30]

Three of the four videos we consider here were made by cryonics organizations. The one reviewed now was instead part of a TV series, *In Search of* …, which aired from 1977 to 1982. "Cryogenics: The Real Truth" was Episode 3 no. 6 (54th in the overall series) and aired Oct. 19, 1978. As the (unidentified) announcer says at the beginning, "This series presents information based in part on theory and conjecture. The producer's purpose is to suggest some possible explanations, but not necessarily the only ones, to the mysteries we will examine." The rest of the narration is done by Leonard Nimoy who, it appears, gained popularity for the whole series through being recognizable as "Mr. Spock" in the original *Star Trek* episodes.[31]

Early on we see a microscope view of the freezing of an early-stage mouse embryo consisting of a few cells: "Frozen alive to one hundred degrees below zero, a three-day-old embryo is held in suspended animation. As temperatures approach absolute zero, all chemical and biological activity ceases. In this state, frozen life might be preserved forever." After this are scenes and commentary establishing that "Since the dawn of man, cold has been our cruelest enemy. … When flesh freezes, cells are usually disrupted beyond repair." MIT scientists are studying how freezing damage occurs. "Red blood cells are relatively easy to freeze safely. With the aid of protective chemicals, and moderate cooling speeds, most cells survive. If they're chilled at the correct rate, even human tissue cells sometimes survive freezing." Some arctic insects "freeze in winter and thaw without ill effect in summer." "Is it conceivable," Nimoy asks in person, "that larger animals, even people, could survive freezing? To answer this provocative question, we must first examine the state of the art of freezing the separate elements of life."

Sperm, blood and early-stage embryos have been frozen and successfully warmed and restored to function. "Blood cells and embryos have survived cooling to within a few degrees of absolute zero. As the temperature drops toward its theoretical limit, molecular motion virtually ceases. Processes of growth and deterioration stop. In this state the essence of life could be preserved forever. There are those who would like to imagine that freezing could make man immortal."

Freezing advocates clearly have an uphill battle. "The balance of temperature within the human body is incredibly delicate. A drop of only five degrees in body temperature brings on the potentially lethal

state called hypothermia." *Potentially* lethal doesn't necessarily mean lethal however. The scene shifts to a laboratory showing a white-clad researcher with dark, long hair—Dr. Paul Segall—who is conducting a hypothermic experiment. A rat has been chilled down to zero Celsius (the ice point) and its heart and breathing stopped. Segall narrates as an assistant uses a desk lamp to warm the animal while giving artificial respiration with a rubber bulb pump:

"Usually, between fifteen and eighteen degrees we reestablish heartbeat, sometimes before. So in the next couple of minutes, since the temperature is rising rapidly, we should begin to see a heartbeat. That's it! We got a beat! That is a heartbeat! There's another one. Yeah. Keep going, Judy. Beautiful! Beautiful! All right. Heartbeat established at thirteen point five degrees centigrade."

Hibernation, which nature has perfected, suggests "another approach to suspended animation." Along with hibernation there is the freezing of the remains of creatures in arctic regions for thousands of years, mammoth meat, for example, "so fresh it can be eaten." Some think that "freezing and reviving whole animals might be possible." We see a large van with "Trans Time, Inc." on the side and are told that in California, "Art Quaife operates a cryonic suspension facility." Quaife himself explains about cryonics:

"It's placing patients into low-temperature suspension after they've been pronounced legally dead, in hope that at some future date medical science may be able to cure whatever they died of, repair any damage caused by the freezing procedure, and restore them to life." A small patient storage capsule is shown and Quaife continues: "In this capsule we have the head of a seventy-nine-year-old man, who is a retired Army colonel. He died about two years ago of respiratory ailments, and was placed in suspension by a team in Los Angeles." A larger capsule is shown. "This capsule contains two whole-body patients. One is a sixty-five-year-old Maryland man, the other is a seventy-five-year-old midwestern woman. Both of them died four years ago of cerebral strokes. It also contains the brain of a fifteen-year-old girl who was murdered in Berkeley in 1976."

A flasback action sequence is shown, voiced over by Nimoy. "One of the patients arrives already frozen to dry ice temperature. His body is placed in a plastic bag. It is wrapped in alternating layers of foil and fiberglass. The insulation will reduce the risk of thawing in case the liquid nitrogen in his capsule boils away. Carefully the patient is eased into the steel capsule where he will remain until someone tries to revive him. After encapsulation, liquid nitrogen was added. It has been replenished ever since."

A young woman has questions for Quaife:

"Has any person or animal ever been brought back, revived after having been frozen for such a long time?"

Quaife: "No human has ever been revived from the temperature of liquid nitrogen. We wouldn't know how to do that today. But there have been many successes with lower forms of life and less complicated organisms."

"If I were interested in cryonic suspension what would it cost me to enroll in your program?"

Quaife: "First you would become a suspension member of the Bay Area Cryonics Society, and that would cost you a thousand dollars. Beyond that you'd have to provide funding for your suspension. We recommend a minimum of fifty thousand dollars' worth of funding."

"If I were to decide to sign up for the program, what assurance do I have that you'd keep the temperature, even that you would keep me in suspension, that you would bring me back? It's basically an act of faith."

Quaife: "Well, the procedure isn't perfected so no, we can't give any guarantees. The only guarantee we can give you is that if you are put in a grave you have virtually no chance of coming back. If you're frozen you have some chance."

Some hostile cryobiologists express doubts about the likely success of cryonics, and the narrator notes that "in the world today there are about twenty frozen bodies waiting with a bare wisp of hope for the future." Most of these "believe that medical science will eventually find a way to reverse the process of aging and extend our lives indefinitely." However the frozen embryo offers a "more realistic chance of immortality," being already in use for mice and cattle, where frozen embryos thawed and implanted in surrogate mothers produce healthy offspring. "The process will surely work for humans as well."

Nimoy in person concludes: "The use of cold storage to preserve human sperm, embryos, and even whole people, raises many ethical and social questions.

"Cryogenics: The Real Truth" from In Search Of…*: (1) Leonard "Mr. Spock" Nimoy wonders if people could survive freezing. (2) "If human embryos could be frozen successfully, we could send our children on journeys into the distant future." (3) Freezing an early-stage mouse embryo. (4) Calf produced by bovine uterine implantation of a previously frozen embryo, the first such success in the U.S. (5) Dr. Paul Segall explains his work with resuscitation of rats chilled to the ice point. (6) Art Quaife of Trans Time explains about the services his cryonics company offers. (7) A patient at Trans Time is prepared for encapsulation. (8) Quaife answers questions about cryonics from a young inquirer. (9) A "voyage into the future."*

Whose sperm and embryos should be saved? Could everyone afford to be frozen, or only the rich? The research in cryobiology will surely lead to lifesaving medical advances. But even if we achieve suspended animation, we may not be able to deal with the unknown consequences of frozen immortality."

(But wouldn't it be great to be able to try?)

THE ALCOR VIDEO[32]

In 2005 Alcor commissioned an inspiring video on cryonics (if you're at all sympathetic to cryonics) which, though it's really a promotional piece for the company, is mostly "generic" in its presentation. WalshCOMM produced *The Limitless Future*; the narrator is Steve Wood. Actually, there are two versions, about 28 minutes and 10 minutes, respectively; the shorter one is reviewed here.

"From the beginning of time," begins the narration, accompanied by soft background music, "this has been mankind's dream: to explore the wonders of nature in all its magnificence; to experience the treasure of life with all its possibilities; to unravel the mysteries of time, with all its promise." A major limiting factor in this quest is that *life is too short*. Is there any possible remedy?

"In 1964, physics teacher Robert Ettinger published *The Prospect of Immortality*, detailing the prospect of freezing a human until medical science advanced enough to restore the person to good health. Man's dream of suspending life was on the verge of reality, and it was called cryonics."

Well, it was *soon* called cryonics, thanks to Karl Werner (see above). People, of course, were not then lined up to take advantage of the new prospect of cryopreservation, but a landmark event of this sort did soon occur, the freezing of James Bedford in January 1967. The Bedford freezing actually involved two steps. First was the initial freezing, carried out January 12, 1967 by the Cryonics Society of California, under the direction of Dante Brunol. (Robert Nelson was president of the organization and coordinated the effort.) A few days later Bedford, now chilled ("prefrozen") to dry ice temperature, arrived in a shipping container at Cryo-Care Equipment Corporation in Phoenix, Arizona. There he was placed in a horizontal, long-term storage capsule and cooled to liquid nitrogen temperature—for the second step of his cryopreservation.[33]

No one was on hand from the initial freezing, but engineer and MIT graduate Ted Kraver, who worked at Cryo-Care, offers his comment on the encapsulation: "He was brought in, oh, I think about late afternoon, and we had the capsule ready. And we started the procedure, and we had, uh—it took until about three in the morning, three or four in the morning, before we could finally get Dr. Bedford, who had been prefrozen, into the capsule, all the instrumentation hooked up ...." (In the longer version of the movie Kraver further confirms that liquid nitrogen was then added to the capsule for maintenance at cryogenic temperature.)

There is a brief excursion at this point to note that "cryonics not only captured the imagination of scientific men like Ted Kraver, but of Hollywood as well." Scenes from the movie *Forever Young* are shown, then a flashback to a city street some decades back, accompanied by the delicate piano tones of Scott Joplin's *Maple Leaf Rag*: "Even before Ettinger's vision in the 1960s, science and technology were already extending our lifespans. Since Henry Ford introduced his first Model T, the average American lifespan has increased by fifty percent. In the early 1900s, no one dreamed of a cure for polio, let alone life-extending heart transplants, life-giving in-vitro fertilization, or life-changing stem cell research."

"And," the narration continues, "with each new scientific and medical advancement, we understand more about the true nature of our biology." Today we use CPR and defibrillators to revive people formerly given up for dead. "So if death is not simply the moment when our heart stops, then when does it occur?"

Dr. Steve Harris offers an answer: "Well, people are beginning to reassess what they mean by death, and this has been long overdue, because we know that metabolism, the machinery of life, doesn't have to be active for life to be there in some kind of form. We should be thinking about the fact that life is—is the information, and that it is potentially as permanent as you'd like it to be."

The narrator comments that cryonics "is the next logical step for significantly extending life." Joe Waynick, then CEO of Alcor, adds: "Death is not an event, it is a process, and at the moment of legal pronouncement, you're still very much biologically alive. And if we can access your body at the time of pronouncement, and put you into biostasis immediately, then we have essentially stopped your biological clock and we're able to preserve you in that biologically viable state, for an indefinite period of time."

We see tall, shiny dewars rising in Alcor's Patient Care Bay, and the narration resumes with a rare promotional comment: "This is the world's leader in cryonics, and cryonics research and technology: the Alcor Life Extension Foundation in Scottsdale, Arizona." Alcor's operating room is shown; here "the work of cryonics is routinely performed."

"There are three basic steps. First, the stabilization. Under ideal circumstances it starts within an instant of a physician pronouncing legal death." Steve Harris explains: "In the first part of the procedure, when the person, just after their heart has stopped, um, the main problem is trying to get them cold as fast as possible and the idea is to remove as much of the heat as you can, and cool them as rapidly as possible, because of the damage that happens as a function of temperature."

For the next step, special solutions called cryoprotectants "are carefully infused." Tanya Jones tells us that this cryoprotection "is the step of the procedure that is probably the most critical. It is the one that prepares the tissues for the lower temperatures, and reduces the damage that occurs when you freeze tissue."

After this is the third, final and longest step, "a carefully controlled and monitored cooldown." In this way the temperature of -196° Celsius is reached, and the patient is transferred to a longterm storage dewar, an upright capsule similar to a giant thermos bottle, which has now been in use for decades. The narrator comments that "nearly seventy patients are maintained this way at Alcor's Patient Care Bay" (the total now is more than double that).

The scene shifts outdoors: from the dewars of Alcor to a laboratory facility on a sunny day. The narrator comments: "In southern California, Twenty-first Century Medicine is breaking new ground in the world of cryobiology. Here their work focuses on the full circle of preserving organs in deep cold, and then, recovering them, with minimal damage. The implications of this work are far-reaching. Each year, more than sixteen thousand people die, because they need an organ transplant, and there is none available."

Employee Dr. Brian Wowk adds: "Well right now, as everyone knows, we're based in the United States, with a rapidly aging population that is going to have tremendous medical needs in coming decades. And a lot of those needs can be addressed by transplantation and tissue replacement, especially bioengineered tissues."

The narrator continues: "As research gets closer and closer to perfecting cryoprotectants, the odds of successfully reversing the process get better. Until that time, what about damage that results from imperfect methods, especially for those who were cryopreserved before the advent of today's new cryoprotectants?"

Enter encryption expert Dr. Ralph Merkle: "In the future, with nanotechnology, we'll have medical tools and medical instruments that are molecular in their size and in their precision, and these tools will be able to deal directly with the fundamental causes of damage and ill health. We'll be able to cure and heal in cases that today would be considered hopeless."

More comment follows from the narrator and Joe Waynick to the effect that advancing sciences are not going to stop merely because, as can be expected, it will make some people uncomfortable. The narrator continues: "It is in our nature to explore, to seek, to question, both scientifically and philosophically. And we will continue to question, to challenge the thresholds of science, to dream of tomorrow."

Finally, nearing the end, we hear from Cheryl Walsh of WalshCOMM that produced the movie: "…I lost my mother when I was twenty and she was forty-nine., and I have to tell you that there's so many parts of my life that she didn't get to experience. I want to experience all those times with my children, and my grandchildren, and my great grandchildren. And, I don't know what's going to happen to me. You never know. My mother was a healthy person, and then one day she was sick, and then she was gone, and that could happen to me. I would love the opportunity to suspend my life, to not suffer through illness and pain, and then to be reanimated at a time when I can be a healthy person again, and live a healthy life."

BRIEF AFTERTHOUGHTS

Old movies bring the past to life and sometimes are the best sources we have. But, we might ask, what of it? We've looked at movies spanning nearly four decades, starting in the 1960s. We see, for instance, that even in the 1960s procedures appeared to be quite sophisticated. Have things improved very much in more recent times? One improvement, vitrification in place of more damaging procedures that allowed partial freezing, was achieved by 2000 at Alcor (though mainly for neuro cases until 2005)[34]. But this is a subtlety largely lost on the public today (and also not emphasized in the movie; only the longer version covers it briefly). The bottom line still, just as in the earliest days, is that human beings or other large organisms cannot be restored to a functioning state from cryopreservation. We may be making good progress toward such a possibility, but the evidence is insufficient in the minds of very many, including many reputable scientists. So cryonics still seems like a very long shot to the public at large, and an "act of faith" they don't particularly feel like indulging in. We have to live with that.

Yet for those of us who are involved, cryonics still seems worthwhile. For me the main reasons for confidence are the Merkle-type arguments that (1) cryopreservation techniques may be imperfect but do preserve brain structure down to the molecular level, and (2) future technology including nanotechnology will make repairs or replacements possible so damaged tissue can be restored to functioning. At minimum, it seems highly likely that cryonics patients will be restored to a healthy, conscious state. The worst deficit is likely to be some, possibly severe or total, amnesia. This however in turn should be at least partly remediable using surviving sources such as records, photos, diaries and the like, and recollections of others including fellow cryonicists. We may hope that advances in artificial or augmented intelligence and just our general state of knowledge will make it feasible to use such sources to reconstruct likely memories and implant these appropriately in the otherwise amnesiac patient. The more extensive these sources are, the better the reconstruction should be. (On this basis it is worthwhile to preserve identity-relevant information in durable form, a topic of longstanding interest.)

An interesting question arises. How much is enough? What degree of preservation do we really need for confidence that what comes back is really the "same" person or "close enough"? This is a deep philosophical as well as technical issue, something else to address in another place. ■

The Limitless Future:*(1) Title illustration, (2) Encapsulation of James Bedford at Cryo-Care, 1967, from* Life *magazine article. (3) Dr. Steve Harris explains the first step of cryopreservation, "trying to get them cold as fast as possible." (4) Early stages of cooling the patient. (5) Cryoprotection is now carried out, using automated equipment to infuse (perfuse) cryoprotectant into the patient. (6). Tanya Jones explains that cryoprotection is probably the most critical step of the operation. (7) The laboratory at Twenty First Century Medicine, which is working toward successful cryopreservation and recovery of organs. (8) Dr. Ralph Merkle explains that future nanotechnology should be useful for recovery of cryonics patients which are unrecoverable today. (9) Cheryl Walsh relates her personal experiences and desire to see the more distant future.*

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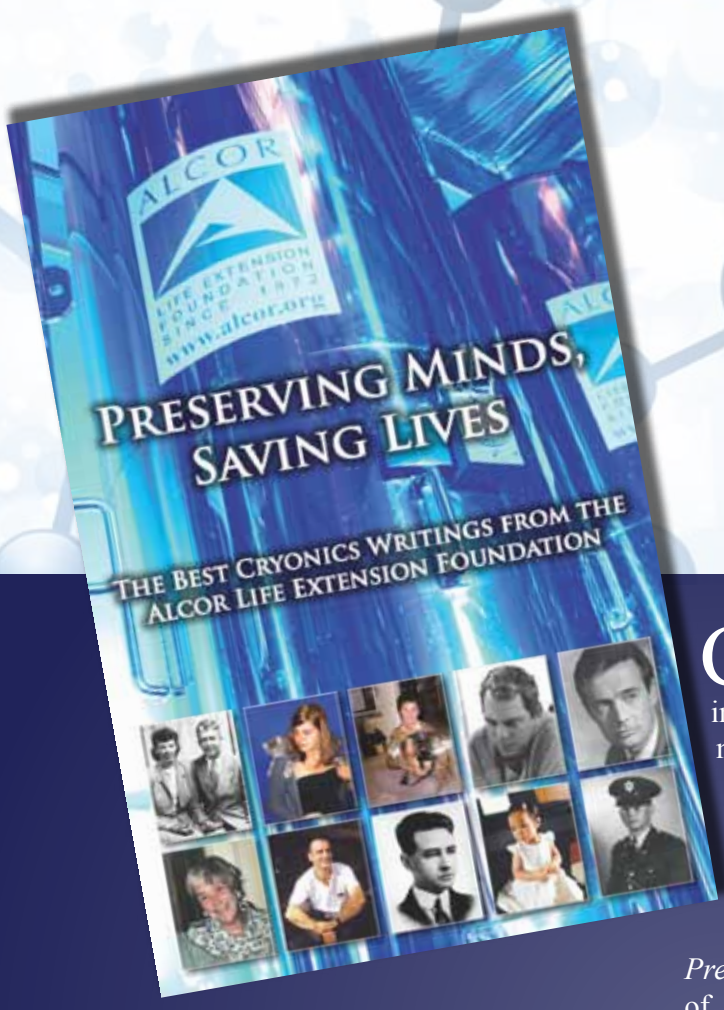

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Cryonics is an experimental medical procedure that uses ultra-low temperatures to put critically ill people into a state of metabolic arrest to give them access to medical advances of the future. Since its inception in the early 1960s, the practice of cryonics has moved from a theoretical concept to an evidence-based practice that uses emergency medical procedures and modern vitrification technologies to eliminate ice formation.

Preserving Minds, Saving Lives offers an ambitious collection of articles about cryonics and the Alcor Life Extension Foundation. From its humble beginnings in 1972, and its first human cryonics patient in 1976, Alcor has grown to a professional organization with more than 1,000 members, more than 140 human patients, and more than 50 pets, all awaiting a chance to be restored to good health and continue their lives.

This book presents some of the best cryonics writings from *Cryonics* magazine from 1981 to 2012. There are clear expositions of the rationale behind cryonics, its scientific validation, and the evolution of Alcor procedures. Also covered are repair and resuscitation scenarios, philosophical issues associated with cryonics, and debates within the cryonics community itself.

Soft Cover Edition: $20 – Hard Cover Edition: $35
To order your copy, go to: www.alcor.org/book
or call 1-877-GO ALCOR (462-5267)

Table of Contents

"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."

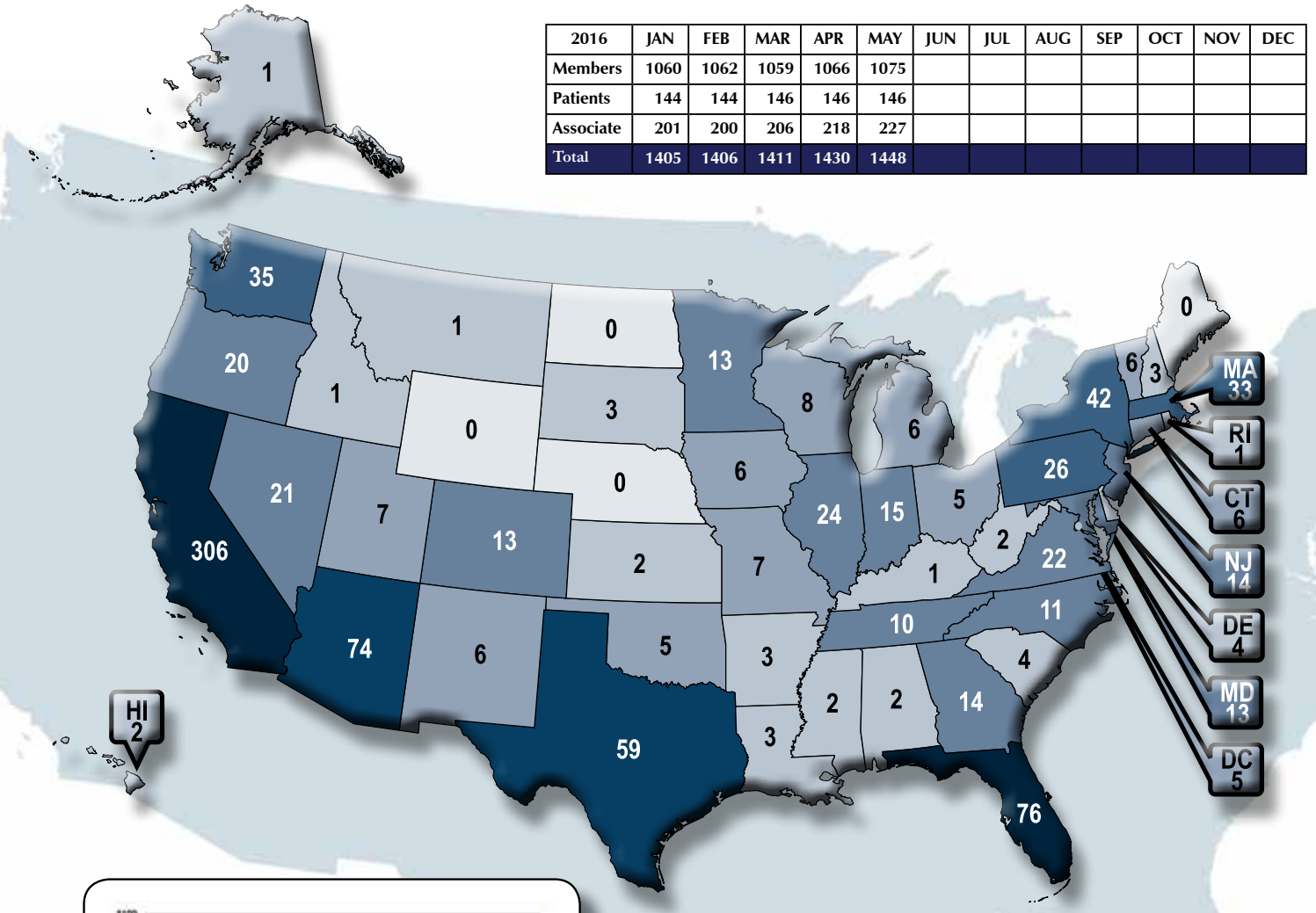
– Aubrey de Grey, Ph.D.
Biomedical Gerontologist and Chief Science Officer of the SENS Research Foundation

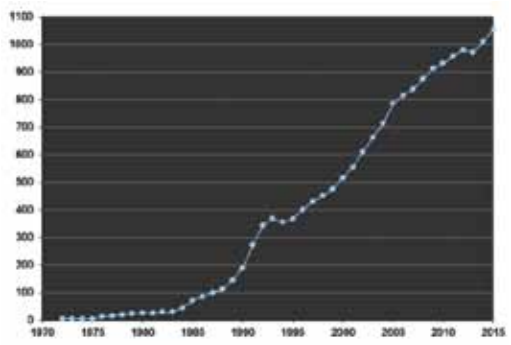
"Alcor appears to be the leading organization in the application of cryonics in medicine. I'm proud to be a part of this effort."

– Michael D. West, Ph.D.
Stem Cell Scientist and Chief Executive Officer of BioTime, Inc.

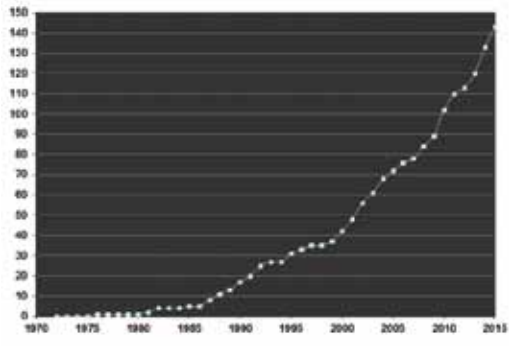
Membership Statistics

2016	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Members	1060	1062	1059	1066	1075							
Patients	144	144	146	146	146							
Associate	201	200	206	218	227							
Total	1405	1406	1411	1430	1448							





Number of Alcor members



Number of Alcor patients

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

International

Country	Members	Patients
Australia	13	3
Canada	50	2
Chile	1	0
China	0	1
Germany	10	0
Hong Kong	1	0
Israel	1	1
Italy	3	0
Japan	4	0
Mexico	4	0
Monaco	1	0
Netherlands	1	0
New Zealand	1	0
Norway	1	0
Portugal	4	0
Singapore	1	0
Spain	3	1
Thailand	4	1
United Arab Emirates	1	0
United Kingdom	28	3
TOTAL	**130**	**12**

Making Micromotors Biocompatible

In the 1966 film Fantastic Voyage, Czech scientist and defector Jan Benes discovers a way to miniaturize matter, enabling his colleagues to navigate a pint-size submarine through his blood vessels and into his own brain to destroy a lethal blood clot. Today, this sci-fi gem is edging closer to reality. With the help of microfabrication, researchers are beginning to learn how to deploy tiny, cellular-scale machines into biological systems. Micromotors of all shapes and sizes are being developed to sense environmental toxins in air or water, deliver drugs to target tissues, and perform surgical procedures at the single-cell level. What complicates their use in living organisms or cell-culture systems, however, is that their tiny size leaves them struggling against fluid forces. Blood or viscous cell-culture fluids make it difficult for small motors to control their movements. To counter the viscosity, many efforts begin with propulsion systems that prove toxic to living cells. Here, *The Scientist* explores four strategies for making micromotors biocompatible and getting them in shape for real-life voyages.

Jyoti Madhusoodanan / The Scientist
1 Jun. 2016
http://www.the-scientist.com/?articles.view/articleNo/46186/title/Making-Micromotors-Biocompatible/

Stem Cells Shown Safe, Beneficial for Chronic Stroke Patients

People disabled by a stroke demonstrated substantial recovery long after the event when modified adult stem cells were injected into their brains. Injecting modified, human, adult stem cells directly into the brains of chronic stroke patients proved not only safe but effective in restoring motor function, according to the findings of a small clinical trial led by Stanford University School of Medicine investigators. The patients, all of whom had suffered their first and only stroke between six months and three years before receiving the injections, remained conscious under light anesthesia throughout the procedure, which involved drilling a small hole through their skulls; the next day they all went home. Although more than three-quarters of them suffered from transient headaches afterward — probably due to the surgical procedure and the physical constraints employed to ensure its precision — there were no side effects attributable to the stem cells themselves, and no life-threatening adverse effects linked to the procedure used to administer them.

Stanford Medicine / Bruce Goldman
2 Jun. 2016
http://med.stanford.edu/news/all-news/2016/06/stem-cells-shown-safe-beneficial-for-chronic-stroke-patients.html

UW Completes Trials of Wearable Artificial Kidney

Researchers at the University of Washington have completed their first clinical trial of the wearable artificial kidney. It could mean more freedom for those who now require dialysis. Jonathan Himmelfarb Director of the Kidney Research Institute at the University of Washington points out the various parts of the first successful portable artificial kidney. "This is the dialysiser, these cartridges right here are the sorbents, this is a major pump." His team has just completed the first clinical trial with kidney patients from around the Pacific Northwest. "The goal of this is to provide patients of the future with new opportunities to lead a different kind of life with kidney dialysis," Dr. Himmelfarb says. More than 26 million American adults have kidney disease. They routinely spend three days a week, four hours each time, having toxins filtered from their blood by a large dialysis machine at an outpatient clinic. Now Dr. Himmelfarb and team will begin planning and design of the next prototype that will overcome device related technical problems.

Lori Matsukawa / KING
2 Jun. 2016
http://www.king5.com/news/health/uw-completes-trials-of-wearable-artificial-kidney/229276922

Tiny Diamonds Could Enable Huge Advances in Nanotechnology

Nanomaterials have the potential to improve many next-generation technologies. They promise to speed up computer chips, increase the resolution of medical imaging devices and make electronics more energy efficient. But imbuing nanomaterials with the right properties can be time consuming and costly. A new, quick and inexpensive method for constructing diamond-based hybrid nanomaterials in bulk could launch the field from research to applications. University of Maryland researchers developed a method to build diamond-based hybrid nanoparticles in large quantities from the ground up, thereby circumventing many of the problems with current methods. The technique is described in the June 8 issue of the journal *Nature Communications*. The process begins with tiny, nanoscale diamonds that contain a specific type of impurity: a single nitrogen atom where a carbon atom should be, with an empty space right next to it, resulting from a second missing carbon atom. This "nitrogen vacancy" impurity gives each diamond special optical and electromagnetic properties.

UMD Right Now
8 Jun. 2016
http://umdrightnow.umd.edu/news/tiny-diamonds-could-enable-huge-advances-nanotechnology

Creating a DNA Record with CRISPR

Utilizing the bacterial CRISPR/Cas adaptive immune system, researchers at Harvard have developed a method for permanently recording molecular events in living cells, according to a report published in Science today (June 9). The system integrates specific synthetic DNA elements into the bacterial genomes in temporally-ordered arrays, which, once sequenced, can provide a readout of the bacteria's timeline of DNA events. "The importance of the work is in providing a proof of principle: that a fascinating bacterial immune system may be utilized as a tool harboring an impressive recording capacity," said microbiologist Udi Qimron of Tel Aviv University who was not involved in the work. The CRISPR/Cas system works by snipping short DNA elements from the genomes of infecting viruses, integrating those elements into the bacterium's genome (at the CRISPR locus), and using the RNAs produced from the integrated elements to direct destruction of the corresponding virus. In essence, the bacterium keeps a DNA account of its viral foes, and uses it against them.

Ruth Williams / The Scientist
9 Jun. 2016
http://www.the-scientist.com/?articles.view/articleNo/46279/title/Creating-a-DNA-Record-with-CRISPR/

White House Invests $160M in Artificial Tissue Biofabrication Technology

The White House has launched an initiative to reduce the amount of time patients have to wait for organ donations, by encouraging and facilitating living donation and by investing in new technology that could provide artificial alternatives to living tissue. Together with a group of universities and private sector companies, the Department of Defense (DOD) plans to invest $160 million in the Advanced Tissue Biofabrication Manufacturing Innovation Institute (ATB-MII). The U.S. Department of Health and Human Services estimates that there are 121,272 Americans on the donor waiting list, and though 30,000 organ transplants were performed last year, a new patient is added to the list every 10 minutes. President Obama prioritized improving patient access to organ transplantation in his latest State of the Union address, and this latest initiative builds on efforts implemented in recent years, according to a White House fact sheet.

Suzanne Hodsden / Med Device Online
16 Jun. 2016
http://www.meddeviceonline.com/doc/white-house-invests-m-in-artificial-tissue-biofabrication-technology-0001

Gene Editing Could Destroy Herpes Viruses Living inside You

Almost all of us carry one form or another of herpes virus, and the consequences can be far worse than the occasional cold sore. Herpes viruses also cause shingles and can be implicated in blindness, birth defects and even cancer – and as yet, we can't rid ourselves of them. One of our best ways to combat herpes viruses is by blocking the enzyme they need to copy their DNA so that they can replicate. But although this can keep the level of virus in your body down, it cannot wipe out the infection. Worse, it doesn't work on dormant herpes viruses that are waiting inside our cells for the right time to flare up again. But gene editing may allow us to destroy these latent viruses. Robert Jan Lebbink at the University Medical Center Utrecht, the Netherlands, and his colleagues are developing a therapy that might safely clear certain herpes viruses from the body by messing with their DNA. Lebbink's team have been experimenting with CRISPR, the gene-editing technique that can be used to cut DNA at precise points in a sequence. This means gene editing can help destroy dormant viruses. …

Colin Barras / New Scientist
30 Jun. 2016
https://www.newscientist.com/article/2095716-gene-editing-could-destroy-herpes-viruses-living-inside-you/

Just Gellin': How to Grow Strong Muscles-on-a-Chip

During normal embryonic development, skeletal muscles form when cells called myoblasts fuse to form muscle fibers, known as myotubes. In past experiments, mouse myotubes have detached or delaminated from protein-coated plastic scaffolds after approximately one week and failed to thrive. In this experiment, the researchers fabricated a gel scaffold from gelatin, a derivative of the naturally occurring muscle protein collagen, and achieved much better results. After three weeks, many of the mouse myotubes were still adhering to these gelatin chips, and they were longer, wider and more developed as a result. The researchers anticipate that human myotubes would thrive equally well on gelatin chips. These new and improved "muscles-on-a-chip" could then be used to study human muscle development and disease, as well as provide a relevant testing ground for new potential drugs.

USC News
1 Jul. 2016
http://news.usc.edu/103493/just-gellin-how-to-grow-strong-muscles-on-a-chip/

Cannabinoids Remove Plaque-Forming Alzheimer's Proteins from Brain Cells

Salk Institute scientists have found preliminary evidence that tetrahydrocannabinol (THC) and other compounds found in marijuana can promote the cellular removal of amyloid beta, a toxic protein associated with Alzheimer's disease. While these exploratory studies were conducted in neurons grown in the laboratory, they may offer insight into the role of inflammation in Alzheimer's disease and could provide clues to developing novel therapeutics for the disorder. "Although other studies have offered evidence that cannabinoids might be neuroprotective against the symptoms of Alzheimer's, we believe our study is the first to demonstrate that cannabinoids affect both inflammation and amyloid beta accumulation in nerve cells," says

Salk Professor David Schubert, the senior author of the paper. Alzheimer's disease is a progressive brain disorder that leads to memory loss and can seriously impair a person's ability to carry out daily tasks. It affects more than five million Americans according to the National Institutes of Health, and is a leading cause of death.

Salk Institute, La Jolla, Calif.
27 Jun. 2016
https://www.salk.edu/news-release/cannabinoids-remove-plaque-forming-alzheimers-proteins-from-brain-cells/

Rebuilding the Brain Using AI, Electrodes, and Machine Learning

Like a computer, the brain requires huge numbers of connections to work, allowing messages to be passed from one part of the brain to another, or from the brain to the body. If any of those connections are blocked or broken, the messages can't get through. The Center for Sensorimotor Neural Engineering (CSNE), based in the US and funded by the country's National Science Foundation, is developing a mixture of homegrown machine learning software and off-the-shelf hardware that could, in the future, be used to restore limb function to those with brain or spinal cord injury. Often in the past, researchers focused on trying to tackle the problem of limb paralysis by creating robotic hands or other prostheses that a patient could control using the electrical signals made by their brain. The CSNE is instead hoping to use technology as a bridge between different parts of the nervous system that have become disconnected, enabling those parts that have lost function to become active once again. "…These are implantable devices …" Rajesh Rao, director of the CSNE, told ZDNet.

ZDNet
6 Jul. 2016
http://www.zdnet.com/article/rebuilding-the-brain-using-ai-electrodes-and-machine-learning-to-bridge-gaps-in-the-human-nervous/

A Roadmap to Resuscitation

Successful rejuvenation 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 list is a list of landmark papers and books that reflect ongoing progress towards the resuscitation 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(January 1994):16-31 (Part I) & *Cryonics* 15(April 1994):20-32 (Part II).

Ralph C. Merkle, **"Cryonics, Cryptography, and Maximum Likelihood Estimation,"** First Extropy Institute Conference, Sunnyvale CA, 1994.

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, pp. 685-805.

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

MEETINGS

ABOUT THE ALCOR FOUNDATION

The Alcor Life Extension Foundation is a nonprofit tax-exempt scientific and educational organization dedicated to advancing the science of cryopreservation and promoting cryonics as a rational option. Being an Alcor member means knowing that—should the worst happen—Alcor's Emergency Response Team is ready to respond for you, 24 hours a day, 365 days a year.

Alcor's Emergency Response capability includes specially trained technicians and customized equipment in Arizona, northern California, southern California, and south Florida, as well as many additional certified technicians on-call around the United States. Alcor's Arizona facility includes a full-time staff, and the Patient Care Bay is personally monitored 24 hours a day.

ARIZONA

FLAGSTAFF:

Arizona without the inferno. Cryonics group in beautiful, high-altitude Flagstaff. Two-hour drive to Alcor. Contact eric@flagstaffcryo.com for more information.

PHOENIX
VALLEY OF THE SUN:

This group meets monthly, usually in the third week of the month. Dates are determined by the activity or event planned. For more information or to RSVP, visit http://cryonics.meetup.com/45/ or email Lisa Shock at lisa@alcor.org.

AT ALCOR:

Alcor Board of Directors Meetings and Facility Tours—Alcor business meetings are generally held on the second Saturday of every month starting at 11:00 AM MST. Guests are welcome to attend the fully-public board meetings. Facility tours are held every Tuesday at 10:00 AM and Friday at 2:00 PM. For more information or to schedule a tour, call Marji Klima at (877) 462-5267 x101 or email marji@alcor.org.

CALIFORNIA
LOS ANGELES:

Alcor Southern California Meetings—For information, call Peter Voss at (310) 822-4533 or e-mail him at peter@optimal.org. Although monthly meetings are not held regularly, you can meet Los Angeles Alcor members by contacting Peter.

SAN FRANCISCO BAY:

Alcor Northern California Meetings are held quarterly in January, April, July, and October. A CryoFeast is held once a year. For information on Northern California meetings, call Mark Galeck at (650) 772-1251 or email Mark_galeck@pacbell.net.

FLORIDA

Central Florida Life Extension group meets once a month in the Tampa Bay area (Tampa and St. Petersburg) for discussion and socializing. The group has been active since 2007. Email arcturus12453@yahoo.com for more information.

NEW ENGLAND
CAMBRIDGE:

The New England regional group strives to meet monthly in Cambridge, MA—for information or to be added to the Alcor NE mailing list, please contact Bret Kulakovich at 617-824-8982, alcor@bonfireproductions.com, or on FACEBOOK via the Cryonics Special Interest Group.

PACIFIC NORTHWEST

A Yahoo mailing list is also maintained for cryonicists in the Pacific Northwest at http://tech.groups.yahoo.com/group/CryonicsNW/.

OREGON:

The contact person for meetings in the Portland area is Aschwin de Wolf: aschwin@alcor.org. See also: https://www.facebook.com/portland.life.extension

BRITISH COLUMBIA (CANADA):

CryoBC, a special interest group within the nonprofit Lifespan Society of BC (http://www.lifespanbc.ca/) holds meetings for cryonicists in the Vancouver area. To be notified of meetings join the CryoBC mailing list: https://groups.yahoo.com/neo/groups/cryobc/info

TEXAS
DALLAS:

North Texas Cryonauts, please sign up for our announcements list for meetings (http://groups.yahoo.com/group/cryonauts-announce) or contact David Wallace Croft at (214) 636-3790 for details of upcoming meetings.

AUSTIN/CENTRAL TEXAS:

A new group for the Austin area has been started for those interested in discussion and understanding of the relevant technologies and issues for cryopreservation, genomics, epigenetics and medical research for increased life/health span. Contact Tom Miller, 760-803-4107 or tom@blackmagicmissileworks.com.

JAPAN

Cryonics meetings are held monthly in Tokyo. Send queries to grand88@yahoo.com.

ALCOR PORTUGAL

Alcor Portugal is working to have good stabilization and transport capabilities. The group meets every Saturday for two hours. For information about meetings, contact Nuno Martins at n-martins@n-martins.com. The Alcor Portugal website is: www.alcorportugal.com.

UNITED KINGDOM

Alcor members in the UK can contact Garret Smyth at Alcor-UK@alcor.org for information about local meetings.

If you are interested in hosting regular meetings in your area, contact Alcor at 877-462-5267, ext. 113. Meetings are a great way to learn about cryonics, meet others with similar interests, and introduce your friends and family to Alcor members!

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.)

How do I enroll?

Signing up for a cryopreservation is easy!

Step 1: Fill out an application and submit it with your $90 application fee.
Step 2: You will then be sent a set of contracts to review and sign.
Step 3: Fund your cryopreservation. While most people use life insurance to fund their cryopreservation, other forms of prepayment are also accepted. Alcor's Membership Coordinator can provide you with a list of insurance agents familiar with satisfying Alcor's current funding requirements.
Finally: After enrolling, you will wear emergency alert tags or carry a special card in your wallet. This is your confirmation that Alcor will respond immediately to an emergency call on your behalf.

Not ready to make full arrangements for cryopreservation? Then **become an Associate Member** for $5/month (or $15/quarter or $60 annually). Associate Members will receive:

- *Cryonics* magazine by mail
- Discounts on Alcor conferences
- Access to post in the Alcor Member Forums
- A dollar-for-dollar credit toward full membership sign-up fees for any dues paid for Associate Membership

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

ALCOR
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