CRYONICS

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Alcor in Estes Park

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Bredo Morstøl becomes an Alcor patient after 33 years of frozen storage.

CRYONICS

Editors
R. Michael Perry, Ph.D (RMP; author of unattributed articles).; Sarah Kelly; Marji Klima

Contributing Writers
Marji Klima
John Cullen
James Arrowood
Rebecca Lively
Blake Honiotes
Diane Cremeens
R. Michael Perry, Ph.D.
Reason
George Church, Ph.D.

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Letters to the Editors welcome:
info@alcor.org

Advertising inquiries:
480.905.1906 x113
advertise@alcor.org ISSN: 1054-4305

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Cover shows view from the Ice House at the Stanley Hotel, late August, 2023. Bredo Morstøl, now an Alcor patient, is in the capsule draped with Norwegian flag, undergoing cooldown from dry ice to liquid nitrogen temperature. To the right is an Alcor "Bigfoot" dewar, of a type now in use, which has been cut away to show interior and permit visitors to (temporarily!) occupy. (This particular dewar had some hard-to-address performance issues and thus instead was "recruited" for the service it now performs.) Both items (with Bredo's container in a bullet-resistant, clear housing) are now part of an exhibit in the Ice House that forms the International Cryonics Museum, a world first.

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Stanley Hotel in Estes Park, Colorado, around sunset.

Credit: Carol M. Highsmith, Library of Congress

New Horizons: Alcor in Estes Park!

No, we haven't moved our headquarters! We're still (mainly!) in Scottsdale, Arizona and plan to stay that way for the foreseeable future. But an unusual circumstance (putting it mildly) came up, and we are now in custody of a cryonics patient in Estes Park, Colorado, and are maintaining him in a dewar there, on the grounds of the Stanley Hotel, with the help of the hotel staff.

The gentleman in question, Bredo Morstøl, officially became a patient of Alcor in late August, after many years of private maintenance in frozen storage. Coincidentally, Alcor held its Annual Strategic Meeting on the Stanley Hotel grounds and combined this with a conference, offering presentations on current developments and future goals, which are introduced here, with more detailed coverage planned for a later issue. We also have some other interesting articles, going back to our conference in 2022. So – read, ponder, and enjoy!

The Pavilion, Stanley Hotel grounds, at the start of the Alcor Board Meeting and Conference, Aug. 26, 2023. The small body of water in back is the Ice Pond where ice was harvested in winter in the days before refrigeration and stored in the Ice House for use in warmer months. (The same Ice House fittingly now stores Alcor's cryopatient, Bredo Morstøl.)

Getting Started

The day was sunny and warm, the scenery was spectacular, and the talks were interesting and informative. First came the Alcor public board meeting, then the conference. The conference opened with a long, introductory presentation involving several people: Marji Klima, John Cullen, James Arrowood, Rebecca Lively, Blake Honiotes, Diane Cremeens; as here reported. (Transcriptions, here and elsewhere, are lightly edited and/or abridged for clarity and conciseness – RMP.)

Opener and Introductions for the Alcor Conference in Estes Park, Colorado, Aug. 26, 2023

Marji Klima. Good morning, everyone. Welcome to the Stanley Resort. I'm sure that it's been very interesting for everybody that's been here. It's just such a beautiful setting and obviously with this as a backdrop for our annual meeting, we are all very pleased. So, I want to thank you all for making the trip out here just to enjoy this incredible place. And you know, I hope you take the time to take tours, really go around, investigate the grounds and see all the wonderful things. I also want to firstly thank John Cullen, our host, the owner of the Stanley Hotel. He's helped us out tremendously to make this happen, to bring everything out here. As you can imagine, with the small staff we have, it's been quite the effort to get all of this done on so short notice. So, I also want to thank our staff because they are incredible. We have had an incredible year in terms of cases, in terms of deployments, in terms of everything that we do with new initiatives. We have a dedicated staff that really goes all out and tries to service our members, take care of our members, help one another. So, my congratulations to our staff because they also helped pull this off. Now, John Cullen is going to take over and give us a little talk about this incredible place we're in.

John Cullen. Good morning. Welcome to the Stanley Hotel. Stanley is a 28-year quest for me. I call it the gift that keeps on taking, say $70 million. And 28 years later I consider it maybe only half done. I have owned 51 hotels in 17 countries and every time I sold a hotel in New York or Chicago or Dubai or London or Doha, Qatar, the profits of that hotel got sucked up into this place like a dry sponge. And I wanted to really build this building that you're in right here. I said, gee I don't have the money and somebody walks into my London Hotel and offers me way too much money for it. And I go well, now I get my little quarter-million-dollar tour.

There's a spirit, if not an adventure, in the Stanley Hotel. I bought it 28 years ago on a fluke. What do I mean by that? I put in a joke bid into bankruptcy here 28 or 29 years ago. And I'm a bit of a nerd and I bid pi because it's as simple as pie to put in a bid. So I bid $3.141 million. Nerdiest thing I've ever done in my life. I placed third but still won. So how do you be a third-place winner in today's world? Well, maybe there's a larger spirit, the first bidder paid 10 million bucks. The Bailiff comes over to the judge, whispers in his ear, and arrests the guy on the spot on a felony arrest warrant and out he goes the other door. So, thank you contestant number one for playing, hope you're happy wherever you are. Second guy bids $5.7 million and he has a disqualification because he has a financing contingency and I'm actually in the room to get my $100,000 non-refundable back because I had just bought a hotel in San Francisco between the bid and all that. So I just want my 100 K back. They opened up the third envelope, 3.14 …. Oh, crap. I won.

So I go up to the Stanley Hotel 28 years ago and there's no paved roads, no sprinkler system, no fire alarm system. Eleven of the fourteen buildings do not have a civil set of windows. Three buildings don't have a roof and I stand and, looking at this, my head of operation goes, "JC, this is like indoor camping." And here we are today. That first year, revenue was $1.4 million the entire year. We did 1.4 million last week. And so, we've grown this into a destination that is an extraordinary achievement, not only in terms of the sense of just the growth and all that, but during some very difficult times of wars and floods and global pandemics, we've maintained the independency of this hotel. We didn't sacrifice to become a Marriott Hilton, Sheridan Hyatt Western, whatever. We made sure of that through a spirit of inclusion, constant reinvention, readapting to a different guest. The guest today is obviously different than they were 28 years ago.

I thank God that the internet happened to be "invented" the same year I bought the hotel, so I could use it to tell the story. Believe it or not, in 1964 this was actually a Sheraton. Disastrous! As an independent storytelling place it now brings 9, 10 different subsets of people together. I'm very proud to say that each one of them thinks it's their hotel, not mine

F. O. Stanley was one of the great inventors of all time. In 1904, at the age of 31, he held 31 patents. He was a most prolific inventor. Yes, there was this Stanley Steamer which he's obviously known for. But what he really made his money on was that he actually invented silver nitrate photography. He wanted to have this hotel because he went to the Mount Washington Hotel in New Hampshire, and he had tuberculosis at the time, and he felt better. Well, you know that it's basically clean air more than anything else. But he said, well, gee if I feel good at 2,400 ft elevation, I'll go to 7,500 ft. And in one of his Stanley Steamers he crossed the country, went as high as he could up here to Estes Park, and put up his hotel.

He needed the money to build the hotel here. So he sold his patent on silver nitrate photography to this guy named George Eastman, who then merged with Kodak and became Kodak Eastman. So, he is arguably the founder of all motion picture film technology. You never know where inventions take you, never on a straight path. He came up here and he was given four or five years to live. He built this white and red castle, Georgian style architecture, much like the New Hampshire Hotel he was in, and he lived 28 more years, much to his wife's chagrin. You never know where technology takes you. He enjoyed the

Stanley Hotel as his real home, and he had an extra 24 years of life up here and that made all the difference. Yeah, maybe more due to clean air, not really a science, but he got an extra quarter century of life, and this was his real home. On that, there's much more to the story, much more invention, much more to talk about. But I'm gonna turn it over to James. I will say that this hotel is probably my greatest achievement. Yes, I have done hotels in 17 countries. But this one's never failed me, and I hope to share that with you guys for a very, very long time. James.

James Arrowood: Good morning, everybody. It's hard to follow John, but the good news is that one of the things I wanted to achieve when I started with Alcor was to offer more to our members. So today I'm going to tell you some things we haven't disclosed yet, one of which is about John, Alcor, and the Stanley.

We are entering into a long-term relationship that involves the movement of a famous local character, Bredo Morstøl, and his body from the mountains to the Stanley property in Estes Park, where he is in Alcor's first remote, cryonic suspension here on the property. And the reason for that is part of growing Alcor and achieving where I think we ought to be, and where we're headed. It is to show that when you have a good business model or you have a good model of anything, it ought to be replicatable. You ought to be able to do it other places. That's important, to show that we can do that as an organization.

So, you are witnessing for the first time, like I said, a remote cryopreservation, that you as members who did us the honor of traveling this far out will get an opportunity to see for the first time this afternoon, after this meeting. Bredo's body is in the Ice House here on the property. Our DART (Deployment and Recovery) team, which is one of our new initiatives as well, and they're here today, will be introduced to you properly and formally in a few hours, I think.

Our DART team completed the removal of Bredo's body, stored on dry ice at a site in the mountains near Nederland, at 4:30 in the morning yesterday. They successfully placed it in a container to be cooled to liquid nitrogen temperature. The cooldown is ongoing, thanks to our staff people, mainly Jacob Graber and Mike Perry.

Look at this, this is amazing, right? This is for our membership. This is where we ought to be, folks. The world-class Stanley hotel, our host, has also been unbelievable. And one of the knocks we get at Alcor is, gosh, why are you spending members' money on stuff like this, James?

Well number one, it's valid because guess what, if you're going to be the best in the world, act like it. If you're going to be the Harvard at what you do, start acting like it. But also guess what? John through his generosity has helped fund all this. All right?

Some of our members have donated money specifically for marketing for the purposes of this sort of event for all of you. It is not coming out of your dollars that we have for research. And that's how we need to operate moving forward.

Now, there are several things I want to talk about.

For those of you who don't know, when I started at Alcor, I started with some personal beliefs from my career in law practice. One of these is, it's extremely important that when you start somewhere new, to go to the scene. You go and you meet people. You break bread.

I went to Texas, went to California, and then to 13 other states, two on the East Coast. I met with members in person, shook hands, said, hey, what can Alcor do better for you?

And the number one thing I heard was, James, I want to make sure Alcor can come get me when it's my time.

Okay?

And we had used contractors, and we still have them, but I said, well, Alcor needs to come up with a robust in-house capability to make sure our members feel secure that we can come get them in a timely manner with professionally trained individuals. And I said, who are the best in the world at doing that? I want those people. Let's go get them. And so we did.

And today, that will be explained to you further, the DART team, but they're here and they'll be introduced to you in an hour or two. And I'm very proud of that as an organization. Our staff helped put that together.

So that's one thing that's going on.

Next: media. Another thing I heard from members is, hey, James, a lot of people think we're kind of strange. We're that group that cuts people's heads off. We've heard that before, right? And I said, well, that's messaging. Let's reorient people and let's help them understand what we're really about. Because in talking to members, I said, why did you sign up with Alcor? What are you doing here?

And yeah, part of it is hey, the possibility, maybe remote, but in the future, something happens with our brains and there's some sort of revival technology. But they ultimately said, I want to contribute, and I want to be a part of the science, I want to be a part of this "Apollo moon landing" mission where we're working to preserve organs, preserve the brain, and ultimately have that be useful for ourselves and for society. And so, I said, you know, let's tell that story because that's a good story to tell.

That's where all of you as members are visionaries. You're the people who said, I can look outward, and I can say, hey, this is the direction I want to head in. This is the organization I want to be a part of to help me get there. So that's the story we're telling now.

And fortunately, one of the things I did when I went to California was to contact a member, Charlie Matthau. You might recognize the last name. His father was Walter Matthau, the actor. Again, our strength is in our membership. We have some world class people who are members of Alcor, people who have changed the world. Seriously. They're confidential members, a lot of them. But I went out and I met with them face to face and I said, what in our membership can we use as an asset to propel

the mission forward in the way it ought to be going forward? Well, you know what Charlie Matthau is good at? He's good at media. Born and raised in Hollywood. He knows everybody there. Just ask him. He'll tell you.

Matthau in 2012

I went to Charlie, broke bread, and said, Charlie, Alcor has a problem. We need to reorient the message, tell people about the hard science and the things we're trying to achieve. We're essentially crowdfunding history, crowdfunding our "Apollo moon landing" in biology. And Charlie said hey I can help with that. I'm going to get you all the media you need and I'll take charge of that. And so, we took him up on that. And now we have Hollywood quality broadcast people roaming around and filming what we're doing, and we can trust the message because Charlie's an OG, "Original Gangster "or Old Guy with Alcor, a 30-plus year member, and quite open about it. He's one of our first 200 members and he's on our team.

Now, for all of you members out there, I asked Diane, our Membership Coordinator, and she gave me a list: We have extremely highly educated, extremely smart people, people from all walks of life, and I've met them. People in government, in science, in all kinds of fields. Our members are our greatest strength, I mean that. Membership contributions from people like Charlie and others are going to help us get where we need to be.

You know, if we're going to be the Harvard at this, the Stanford at this, the best in the world at this, which I think we are, and the science is very, very good, then we need to act like it and we as a group need to chip in to help us all get there.

So, in media we're making great strides. It is not costing Alcor anything, just my time.

So that's the good news. We have recovery teams. We have great media. We have a partnership with the Stanley Hotel now, which is phenomenal. Why? Because as members, moving forward over the length of that partnership, you're going to have discounts on hotel rooms. We're giving back to the membership. You can enjoy this beautiful property at a discount. The tour where Bredo's body is remotely located in the Ice House here, that will be free to all Alcor members. If you come up to this property, whether you stay here or not, you show your Alcor membership card, and you will be able to see the science in action. This is the First International, we're calling it, Cryonics Museum. So you as members who traveled here today, afterwards, I will host you on a tour. We're still curating it, but you're going to see the installation and you're going to see firsthand the science.

Because what are we about, folks? What we're really about is biology, chemistry, physics, mechanical engineering, computer science. And all of those components will be on display for the public for over 200,000 visitors a year. We have the very first remote, cutaway dewar where you can step inside and take a selfie. Isn't that cool? And you'll all get a chance to do that today.

And guess what? You know what that does for Alcor? 250,000 people? Hey! It's an option! So more than 250,000 people a year come through on that tour. You know how many selfies on social media we're going to get all over the world? And do you know what is the cost to Alcor? Zero dollars. So that message is going out to the world, folks, at no cost to you as members. And that's what we're doing. All right?

Now, that's the good news.

There are some things that still need work. And I say this because on the Internet or in my email box, I'm sure the comments will be blazing. But when you're running an organization, in order to establish credibility, you need to acknowledge where things can be done better. And then you need to step into it and start making those changes.

So that's what I'm here to do with our group, with Marji, and with our staff. Some of those changes:

We know the website needs work. I'm in the process of raising the funds because that I can't get for free at the professional level. We're making progress. We know also that the sign-up process needs to be easier, cleaner, faster. We know that members want to see, again, some better media.

We hear, oh, there's the insurance, the sign-up, the financing, the funding. We understand, folks. That's an imperfect model right now. We have some folks I know working on that and who have helped move the model along. But it can be better.

We understand where we're doing the math, the actuarial math. This is difficult. And this is a story that hasn't been well told to our membership. We have not done a great job of educating our membership about how this is funded and how it's spent. It's very important we educate you. So I'm going to take a minute to do that really quickly.

But one of the greatest critiques I hear in media, and by the way, when I went out on these tours, it wasn't always fun or easy. I would sit down and I would get hammered by questions of, why aren't you guys doing this or that any better? Hey, I've been here a few months. Give me a break. Give me some time here. But the point is, on the finance model for those who don't know, over half of the cost of this, right off the top, doesn't come to operations. Marji and I can't buy a paper clip with it. Okay? We are a 501(c)(3) nonprofit. That's extremely important. We are a scientific research and educational institution. I want everybody to remember that. What that means is, right off the top, over 50% of the cost of cryopreservation goes into the patient care trust, long term care. That's what makes us special. That's what makes us great. Why?

Because you as members can see the financials on the website, I think, but we have an extremely large pot of money, the Patient Care Trust Fund, to take care of what's called the Patient Care Bay, that is to say, our patients. And if you come in for a tour, you'll see that. That's where you see all the dewars and where the bodies are located.

As a whole, our operation is not-for-profit, and that's extremely important. Why? Because the for-profit models in the past have

failed, and when they failed, people thawed out. That's really bad. And our Patient Care Trust is a separate entity from Alcor, with a separate amount of money. The majority of the cost goes to that. Why? Because very smart computer scientists, people I see in the room, have extrapolated and done math that I could never do. And they've calculated the cost of liquid nitrogen per cubic foot, square footage of floor space, and so on, for the next 100 or 200 years.

All right. I can't even imagine what that's like, but there's a bleed-off rate and what have you. They figured out that cost. It is now safe. It's protected money.

Well, that means Marji and I have, I don't know, 45% of the cost to actually conduct this operation, to do what we do. Anywhere in the world? The coast of Africa recently? Meet Sarah, our Director of Development and Readiness Coordinator. God bless her, she went out to the coast of Africa for weeks. Our DART team was in Hawaii. We had multiple simultaneous deployments at once, the first time in history at Alcor. So, our staff was recovering our members all over the world simultaneously.

The logistics of that are that, within hours of getting notice, we have to be on a plane anywhere in the world. And it's really hard to do. Not only that, but we have to have kits. And those kits contain the other great expense of cryopreservation. It's called M22, or liquid gold, as I like to call it. That chemical, that perfusate that goes into you, at the time of legal death, is extraordinarily expensive. You can't go to Home Depot and buy it or whip it up at home like a batch of mayonnaise.

So long story short, of that 45% of the original funds, we are often left with $10,000 to $20,000 operationally to recover people. That means supporting a team of highly trained individuals, airfare, hotel, anywhere in the world. The economics of this, folks, are tough. And we need to do a better job of educating people about that.

All right?

We need to do a better job of figuring out funding for people and how that works, whether it's through insurance or through other modules. But I want you to know we're working on it.

Okay?

So we're taking care of the immediate issues and we're working on the things that we know you want us to work on. And I think that's all you can ask of us.

We're a small crew. I think we're now about 13 core employees, and then our DART team, five more, 18 in all.

So, folks, I'm going to end on that, but I want to invite all of you when this ends today. I'll be available.

Does anybody have any questions?

Somebody asked about the DART team. Well, you'll see the burly looking guys over here. They're going to be introduced to you later by name. One of the points I made earlier is we are the best in the world. By the way, congratulations. You're members of an organization that is the best in the world at what it does. But I want to be better than that. I want to be the best at every aspect of what we do. And the best in the world at what we need to come get us are the first responders. Firemen, people with advanced training, senior level, and military. I'll let the people with special training tell their own story. But military veterans who are trained for medical evacuations. They'll give youy some idea of the success they've had. So we went out and got them, put together a team. On average, in the past, movement of patients was 20 or 30 minutes. That would be from vehicle to location; it's very difficult to move a body like that. Our teams have been averaging, in difficult locations, under seven minutes.

There was a question about government funding. Is there a prospect for that in the future? Answer: absolutely! In fact, one of the things I did when I started here, was to contact Sarah Kelly, a hardworking member of our staff, and say, "go get us some grants." Alcor has not traditionally done a good job at pursuing government grants. We need to do better. So we are already in the process and Sarah has learned how to apply for some of those grants. We also have some outside help that I'm looking to secure because that's a whole process in terms of grants. We've been in contact with the experts in that area and we're working on it. Sarah wants to add something. She says that we've already acquired some ad grants. So, we're also looking for some of the science grants and things like that. So there has been some success on the grant front. Credit to Sarah.

We have a question about the magazine. And I have heard from a lot of members. We have members of all ages. And one of the things when I came in at Alcor, was that we sat down, Margie and I, and we looked at the kind of budget we have and how money was being spent. Now mind you, we don't have a marketing budget. There's the deal with John – thank God for that. But it didn't cost us anything.

Well, the magazine will, and it needs to be educational, but we have two groups. We have people who want it to be kind of informational and social and tell about all of our membership and talk about those sorts of things. But we have another group that wants it to be pure science, which is more like a journal. So that's been a challenge for us because it came at great expense to Alcor. Publishing a magazine can be extremely expensive. So Margie and I are still in the process of analyzing what we think the best spend is. And certainly, a printed magazine will probably not be the case moving forward. There might be kind of an annual year-in review on the scientific journal side that may be a printed edition, but just costwise, we want to be good stewards of your membership dues and your money. And part of that is doing analysis. We think that there's probably some sort of digital combination that we're going to put together.

We do have a very generous benefactor that has offered some donations to us, that might, when we get them, be used for things like the magazine. And I would like to start hiring professionals because we do have a lot of volunteers and we appreciate that, but we have a small staff and it's really hard to do it that way.

So when we get a little bit of spend for this, which I'm working on, then I think we're going to be able to apply that to maybe a digital kind of newsletter or something that's really nicely done, but doesn't detract from our staff time. Because our time needs to be focused on the research and on members and getting our members. So, I'd like to bring in some outside help, but we need funds for that. Working on it.

Now, there's a question about transitions. There is work on that, not just the DART team, which you'll hear more about. That's incredibly important, the first step. But also, you know, I always joke, all politics is local. So we have to start close and then kind of expand as we go.

But one of the things I did on my East Coast trip was I met in person with funeral home directors. So, for instance, the people on the East Coast could start forming relationships, contact them, let them know, hey, I'm an Alcor member. Now we know there's a specific spot they can go to and a person they can talk to to get the transport permits. There are a lot of permit issues and transport issues as to where your body goes at the time of death if you're in a hospital and it goes there.

What happens? I don't want to say too much. I don't like to talk about things until they're inked, until the documents are signed. But we are in the process of hosting, for the first time, a training of funeral home directors and operators throughout the country that will come to Alcor. A lot of them have only heard about what they hear in the media and think it's a strange organization. They don't want anything to do with it. Well, we want to normalize what we do by bringing them to Alcor and showing them our processes and saying, hey, this is a legitimate component of afterlife care.

Okay?

So the answer is yes, we're working on it. I don't want to give you final details, but my plan is to look at the concentrations of Alcor members and make sure that we have local capacity there for people where we can give you a name and you can contact them and you can feel secure about that. That's the goal and we're working on it.

[New board members were elected this morning before the present gathering started: Rebecca Lively and Blake Honiotes, who now give brief introductions.]

Rebecca Lively: Hi, I'm Rebecca. I know a lot of y'all. I know the board now, so that's cool. I know a handful of folks in the room. I know a handful of folks online. What I would say is, hi, I'm Rebecca Lively. I've been signed up for cryonics since I was 24 or 25, so a little while now. I signed up shortly after I met my now husband and he told me what it was, and I said that's for rich people. He said, actually, no. It's affordable and he gave me lots more information and I was like, well, then why doesn't everyone do it? That's actually the question I've continued to ask ever since and just continued to have very surprising conversations with people who are not in this room. When I'm like, hey, did you know that this exists? Hey, did you know that it's affordable? They're like, that's cool. I'd rather just die. It's really sad to me. Anyway, that's my background, how I got involved in cryonics.

I've written a couple of articles for Alcor or for *Cryonics* magazine. I think there's a profile in one of the old editions on me and my family. I have three kids, a whole range of ages. I am an attorney by trade and by school and by having a law license. Those things all make me an attorney. I practiced law for about 13 years and then about three years ago made the transition to software development work. So, I have that sort of mix of the legal side, which I think is really important as a board member, although if you look down the list of board members, there's JD next to a lot of our names.

I have now at least a touch of computer science, which I also think is something that is helpful and good to have on our board. So I was humbled and excited to be asked to join the board. I am really, really, really excited to have a way to give back to our community that I care a whole lot about. So I'm glad to be here. Thank you for asking me to introduce myself. I'm really looking forward to digging in, learning more and helping us grow and be better as an organization.

There is a question: where am I located and what state is the law license from? And the answer is the same, Texas. So thank you.

[Blake Honiotes next addresses the group.]

Blake Honiotes: Hey, everybody. It's great to be back. For those of you who don't know me, I am a former Medical Response Director for Alcor. I left the organization roughly a year ago for a variety of reasons. I'm a nurse by background. My bedside career was pretty much exclusively in trauma critical care. I am definitely a convert, if you will. When I joined the organization, I really didn't know much about cryonics. I actually worked for Steve Graber's wife. And she said, hey, this company that my husband works for is looking for this Medical Response Director.

And I had 10 billion questions. So I was able to join as a staff member first and obviously serve membership in that capacity. And then for a variety of reasons, I'm back in a mainstream hospital setting in leadership. Actually, at a pediatric hospital. And I just felt like I was really missing the cryonics community in a lot of ways and my ability to serve and give in a meaningful way. And so when I was approached to join the board, I jumped at that opportunity just because, as Rebecca pointed out, there's a lot of JDs, but there's not a lot of medical people on the board, namely none, outside of me. So, I felt like it was something that I could really contribute to and really give back.

I'm thrilled to be here in this capacity. I am located just outside of Phoenix. I am around and happy to help and provide any sort of guidance I can give to Shelby, who's doing an incredible job – but she's my successor – and be able to provide any sort of feedback I can on case work and process improvements and such from the medical perspective.

So I'm thrilled, honored and humbled to be here and in such a beautiful location. When I left it was about 96 degrees. So my wife is pretty jealous that I'm here and not in 96 degrees right

now. I appreciate all of you and if there's ever anything I can do for any of you, you just let me know. Thank you.

James Arrowood: Okay, and Rebecca, you raised a great point kind of how you thought this was strange and this is only for rich people. Thank you for raising that point because I do want to touch on that a little bit. You're reminding me of something in my travels and from the media in particular: I have heard that refrain over and over again. And I think in our analysis of membership, you know, we get some demographic information and the vast majority of Alcor's members are not rich people. They're very smart people, but they're not necessarily rich. And so, I want you to know, for people online and elsewhere, to understand, that the financing model through life insurance, if you do it right, is actually a very affordable option for you, however you view any of it. But by participating in this, remember we're here to advance the science. And the advancement of the science is the brain, but it's also cryonics. There are a lot of other applications I don't want to get into today, but I do want you to know that your money and your membership are going to explore things that are advancing the science and may have other applications. Those applications may be incredibly valuable for Alcor and for the public. You know, we're talking about DNA, about organ banking, about a lot of things that the Alcor science is very, very good at. And if it can be organized and applied properly, we can change the world collectively.

You're a member of that, you're contributing to that. And so, we're looking bigger now, guys, in the sense of we're looking further out. We're looking how to expand our reach and how to help not just our members, but the public in a variety of ways with our research.

So, do we have any more questions online? Anybody in the room? John.

John Cullen: So now that the cat's out of the bag about what's up over at the ice house, this is the Ice Pond. This is where F. O. Stanley harvested ice 120 years ago and would cut ice in blocks and put it in the Ice House where Bredo now resides. And there's a solemnness in that building that you're going to feel and experience there, where it is a resting place. It is a temple, it is its own unique spirit of building.

I need to do a shout out here for the efforts and the story of what is now Bredo's place. Number one, this was not just about Bredo being in the house. Bredo was at risk. This was a rescue mission in all forms and shapes. It is a well-known person, a lot of media attention was on this person. And the source of money for the dry ice was there sometimes and sometimes it was not, the patient was at risk. A shout out to the professionalism here and the thoroughness of the entire Alcor team.

Yes, the DART team really knocked my socks off by getting in and out of Nederland in seven minutes and 20 seconds. I mean, that is just an amazing story. Behind that, there was James and Margie and the team. If there were 900 emails to Norway, I'm probably rounding down. We stuck through this. The Alcor team stuck through this because at the end of the day, this really was a rescue mission of brand, a rescue mission of story and a rescue mission of a patient that has needed to be where he is for a very long time.

I want to read to you the email that I got unsolicited from Brad Wickham, the last ice man, the person that put the ice there for Bredo for the last decade or so. This is midnight last night.

Brad Wickham, read by John Cullen: Dear John, personal note of thanks. It's important I share with you some thoughts and regards. It has been a privilege to serve Trig[ve Bauge, the grandson of Bredo], but afterthought says that it's been emotional and traumatizing at times. Realizing that I'm now extricated from responsibility, but also the toxicity that has occurred over these times, maybe even taken advantage of at times, et cetera, et cetera, let's just say you've become for lack of better term, my savior.

I'm grateful. I've lost sleep worrying about how this would turn out for over a decade. When I say I feel relieved, I say that regard as a very, very large relief on behalf of me and my family. My wife and I will be home for a month in October. We would love to take your offer up to see Bredo in the house. Until then, I will shudder by then. I have some free time and dedicate that to whatever you need. Respectfully and at your service, the old caretaker.

John Cullen: Guys, this was a rescue mission. I feel good about protecting the brand, the story, and the patient here, and I commend the entire team. I've had two trips to Oslo, one to Scottsdale. I am a bit of a nerd. I had to see it for myself a couple different ways and I feel really good about the team that we are dealing with, the professionalism we are dealing with, and the future going forward. Thank you. James.

James Arrowood: Just a quick note here. When I first started, I want to give Diane Cremeens and Mike Perry a lot of credit, for what's going on today. I got the phone call regarding Bredo and I thought, this is crazy. I want nothing to do with this as an organization. And I can remember those conversations at Margie's point, I said, we're not touching this.

And, credit to John, credit to my mentor who always taught me to go to the scene. I met with John in person, thanks to Diane,

who would not leave me alone. Every day I walked in the office, she said, "you have to go see this." I have a lot of respect for Diane in her opinion. She's been one of the longest serving employees at Alcor. And I said, you know what, Diane, because you said so, I will get on a plane. And I'll meet with John, and I did. And this is a culmination of that to the benefit of our members. So Diane, thank you, thank you very much.

Diane Cremeens: Hello everyone. My announcement has to do with contracts. As most of you know, being you are Alcor members, we have to sign updated agreements. The bulk of the

contracts can be done online. You can sign electronically. I brought the last will and testament to donate your remains and the consent for cryopreservation that we are required to sign in person here. Ashley's a notary. And we have lots of witnesses. So I would like to get everybody who hasn't done that yet, completed today. And then you can go back online to our website, sign up now. I will email you all the logistics as far as how to sign up. You're basically reapplying. And I will email you the updated agreements, click, click, click, you electronically sign them and then you are done.

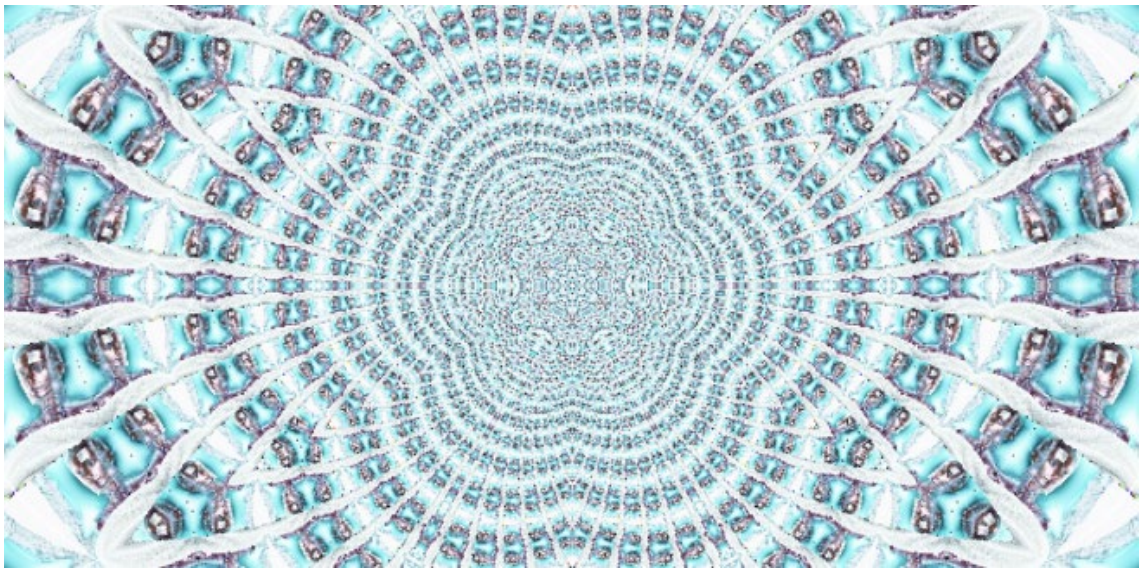
I have 24 different versions of Alcor Agreements in force right now. I would like to get that down to one. So, after or during lunch, come see me, Ashley and me, and we'll get your contracts signed and taken care of. My job is to get everybody to sign up, and I would love to have all the agreements before the end of the year. If you don't get them updated, your membership dues will probably change, because we changed over to an age-based dues, your age times $15. All of our current members, who were smart enough to sign up with Alcor before then, we want you to sign updated agreements and lock in your current member dues that you have right now. So that's some of the reason we want to get these done.

All right. There's a question about Bredo, how did I get into that? Well, Trygve Bauge, Mike Perry and I have been trying to get the board of directors to kind of help them out to come rescue him. And then Trig gave me a call. He talked to John and then we got on the phone talking together. And then I was like, you know, I've got to bring in James and Margie for this. So we did a conference call and that's how we got everyone together to take care of Bredo.

I'm just so excited. I've been with you for years. How did I come to Colorado? I came out here for a family wedding. And when we were talking to Trig, I thought, well, just my family would come up here for a visit and then we got in contact with John so we can do a tour. So I was out here just on a family visit. My nephew got married down in Loveland. That's how I came out here. And then after I saw everything, I was like, yeah, this is going to work. Because John I think said, like 8 million people come through Estes Park in a year, and over 500,000 come here. So, yeah, we have a lot of people and that's so much potential.

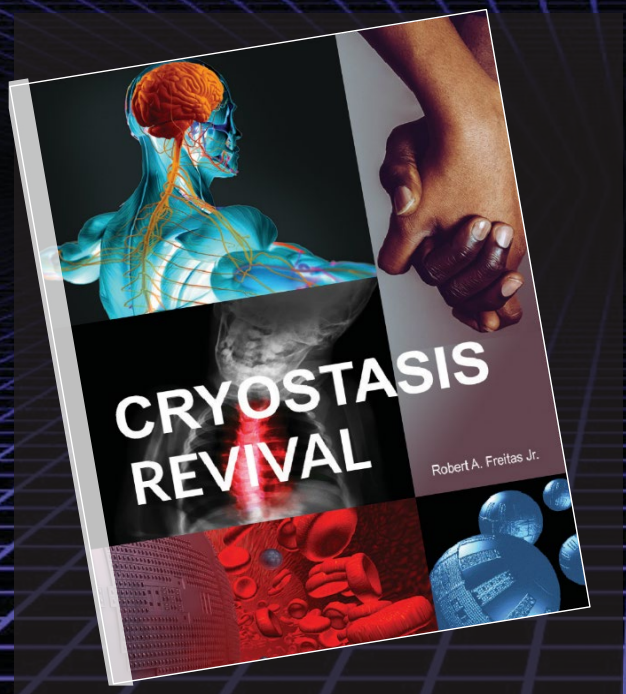
James Arrowood: On that note, let's end, thanks, Diane. There's a longer story, of course, about Bredo, but go online, look up the Frozen Dead Guy Festival. That'll give you the long history. [Also see "More on Bredo Morstøl," this issue.] Trig, his grandson, dutifully, respectfully and reverently kept him on dry ice, and I will tell you his condition was good. We are a research organization, so we took a look at his body and his stasis, and he looked really good. We were actually pleasantly surprised and pleased with how well he had been preserved over the years.

Photo credits: John Cullen: https://grandheritage.com/about-us/feature-owner-stanley-john-cullen/, cropping; Charles Matthau: https://en.wikipedia.org/wiki/Charles_Matthau#/media/File:Charles_Matthau_2012_Shankbone.JPG, cropping; Brad Wickham: https://www.5280.com/meet-the-man-who-looks-after-nederlands-frozen-dead-guy/, photo by Chet Strange, cropping. Others Alcor archives.



New Book by Robert A. Freitas Jr.

Cryostasis Revival: The Recovery of Cryonics Patients through Nanomedicine



Cryostasis is an emergency medical procedure in which a human patient is placed in biological stasis at cryogenic temperatures.
A cryopreserved patient can be maintained in this condition indefinitely without suffering additional degradation, but cannot yet be revived using currently available technology.
This book presents the first comprehensive conceptual protocol for revival from human cryopreservation, using medical nanorobots.
The revival methods presented in this book involve three stages: (1) collecting information from preserved structure, (2) computing how to fix damaged structure, and (3) implementing the repair procedure using nanorobots manufactured in a nanofactory – a system for atomically precise manufacturing that is now visible on the technological horizon.

"Robert Freitas is an extraordinary thinker and author whose previous works have been transformational for our ability to visualize the extraordinary capabilities of future medical technology. In Cryostasis Revival, he now puts his prodigious previous knowledge of nanomedicine to the task of envisioning methods for healing those whose injuries challenge even the ultimate limits of future medicine. His illuminating results and new insights will greatly inform debate over, and may even help to resolve, controversies that have persisted for decades." — ***Gregory M. Fahy, Ph.D., Fellow, Society for Cryobiology & Executive Director, 21st Century Medicine, Inc.***

"Future repair and revival of damaged cryopreserved tissue has been the subject of speculation for decades. This book by a nanomedicine expert examines the problem in detail far beyond anything ever written before. With more than 3000 references, it's both wide-ranging and intensely specific about diverse technical aspects of the problem. It will surely stimulate much discussion, and be an invaluable resource for thinkers about nanomedical cell repair for years to come." — ***Brian Wowk, Ph.D., complex systems cryobiologist, Chief Technology Officer, 21st Century Medicine, Inc.***

"We now have considerable evidence that cryopreserved patients retain the physical structures encoding memory and personality. For most people, the difficulty lies in understanding how it could ever be possible to repair and revive patients. Leading nanomedicine expert Robert Freitas fills in that gap with admirable and remarkable depth. Cryostasis Revival provides an unparalleled clarification of pathways for researchers to explore in the quest to make human cryopreservation reversible." — ***Max More, Ph.D., former president, Alcor Life Extension Foundation***

"Cryostasis Revival is the most magnificent tour de force on cryonics ever done with the signature flair, comprehensive coverage and authoritative style of Robert A. Freitas Jr. It describes all the issues involved in reviving cryopreserved patients: from the philosophical (what is "information theoretic death") to the practical (what damage actually takes place during a cryopreservation) to the technological (how to apply nanotechnology to restore a cryopreserved patient) and more. Nothing else even approaches such a complete and incisive treatment of this life-saving subject. Cryostasis Revival is the book to give anyone who's thinking about cryonics but "isn't sure about the science." — ***Ralph C. Merkle, Ph.D., Senior Research Fellow, Institute for Molecular Manufacturing.***

Free electronic book and hardback copies for sale at:
https://www.alcor.org/cryostasis-revival or Amazon.com

Membership Statistics

2022-23	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov
Cryo Members	1403	1411	1412	1417	1415	1415	1417	1424	1419	1422	1423	1418
Basic Members	32	32	33	36	34	35	35	35	35	36	38	39
Patients	203	203	204	205	206	208	212	212	217	218	222	224
Assoc./Apps	232	218	221	218	223	217	218	219	228	238	245	249
Total	**1870**	**1864**	**1870**	**1876**	**1878**	**1875**	**1882**	**1890**	**1899**	**1914**	**1928**	**1930**

Back of Ice House, Stanley Hotel, showing LN_2 tank attached to Bredo's capsule inside, late Aug. 2023.

More on Bredo Morstøl

Bredo Morstøl in youthful maturity, about 1935, composite based on several images.

Alcor has dealt with some unusual cryonics cases in its fifty-plus-year history. But in some important ways, the case of Bredo Morstøl (pronounced "bread-oh more-stul") is surely the most unusual of all. By taking on this case as we have, Alcor has transformed itself into a different organization. The ramifications of it will, by appearances, take years to play themselves out, with what we think, with due caution, will be good consequences, both for Alcor and cryonics more generally.

A native of Norway, born in 1900, Bredo Ragnvald Morstøl was a landscape architect who, at his retirement in 1967, was head of the Parks Department in Bærum county and had about 100 people working under him. When he arrested in November 1989 at age 89, he was frozen by his grandson, Trygve Bauge, also a Norwegian national. Transported to the U.S. on dry ice, Morstøl was stored at Trans Time's facility in Oakland, California until December 1993. But Trygve, who was then living in Boulder, Colorado and had a background in architecture, had ambitions of setting up his own cryonics facility nearby.

The Rocky Mountain Life Extension Center never did really come to fruition as planned, but the upshot was that Mr. Morstøl ended up in a shed near the little town of Nederland, 17 miles into the mountains from Boulder. There he rested for nearly 30 years, packed in dry ice which was replenished about once a month. Due to an expired visa, Trygve himself was deported back to Norway in December 1993, just after his grandfather was moved to Nederland, but was able to continue maintaining him on dry ice through proxies.

At first resistant and nervous, the town of Nederland gradually came to accept the frozen man in their midst, and he was "grandfathered" in. Finally, in 2002, they decided to capitalize on the situation by inaugurating the Frozen Dead Guy Days, a festival extending over a weekend in March which, after a fashion, honored the icy resident. Films, tours, dinners, merchandise for sale, contests, snow sculpting—were among the attractions offered at the FDGD, and people swarmed in.

More recently, a decision was made to relocate the festival and Bredo himself to the Stanley Hotel grounds in Estes Park, some 45 miles from Nederland. The FDGD was held in Estes Park in March 2023, with plans to continue annually, and Bredo himself arrived in August. Concurrently, arrangements were made for Bredo to become a patient of Alcor, contracts were signed, and finally, the frozen patient was transferred to an Alcor-supplied dewar in the Stanley Hotel's Ice House, and cooled from dry ice to liquid nitrogen temperature. Safe in his dewar he now rests, with an attached LN_2 tank in back of the Ice House for periodic refills. The tank itself is refilled periodically, and Bredo in his dewar is checked remotely, daily, at Alcor HQ in Scottsdale, Arizona. Staff is also available at the Stanley Hotel, to handle any immediate contingencies.

Bredo's new residence, the Ice House at the Stanley Hotel in Estes Park, also houses the first International Cryonics Museum, courtesy of Alcor.

Credits: Alcor archives; private communications from Trygve Bauge (emails); author (RMP)'s personal knowledge; R. Michael Perry, "Controversial Cryonaut," *Physical Immortality*. 3(2) (2Q 2005), 4.

Start preparing your

MEMORY BOX ...now!

Start your own time-capsule!

Create a Memory Box with items to augment your memories when you are resuscitated.

No one knows better than you what you will want to have with you.

Alcor makes available to every member and patient, without charge, one acid free Memory Box about the size of a standard banker's box (H10" x W12" x L15") for memorabilia to be stored underground at a commercial storage site called Underground Vaults and Storage (UV&S) in Kansas. Additional Boxes are a one-time charge of $250 each for perpetual storage.

Some of the most popular items that have been placed into storage are such things as letters, cards, photographs, diaries, journals, notebooks, books, clippings, army records, directories, recipes, video tapes, cassettes, medical records, flash drives, and external drives.

If you would like to begin working on your own Memory Box, or perhaps contribute items to a Box for an Alcor Member already in stasis, or if you have any questions, please contact **Ashley Bettini at** ashley.bettini@alcr.org.

Asset Preservation Trusts for Alcor Members

Would you like to have access to your assets when you are revived?

Would you like to talk to someone who understands cryonics as well as trusts and estate planning?

There are two unique revival trusts that have been developed to help accomplish those goals. The Asset Preservation Trust is an individual trust for Members who can place a minimum of $500,000 into it, and the pooled Multi-Investor Future Income Trust (MIFIT), which requires a minimum investment of $25,000.

Want to learn more? Contact Linda Chamberlain at linda.chamberlain@alcor.org

Engineering and Delivery of Desirable Genetic Traits

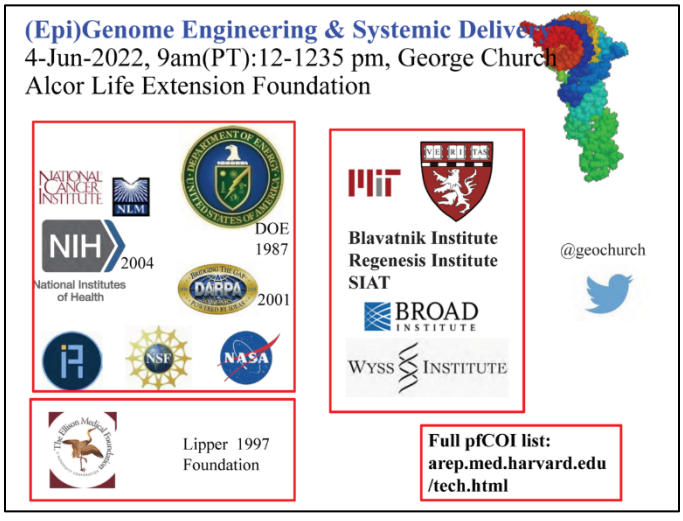
George Church

Talk presented at Alcor's 2022 conference, transcribed (with AI help) and lightly edited by R. M. Perry. Introduction is adapted from Alcor's webpage: https://www.alcor.org/2022-conference/. I am indebted to Dr. Church for supplying the slides used in his talk for this text version – RMP..

George Church is an American geneticist, molecular engineer, and chemist. Church is the Robert Winthrop Professor of Genetics at Harvard Medical School, Professor of Health Sciences and Technology at Harvard and MIT, and a founding member of the Wyss Institute for Biologically Inspired Engineering. He is known for his professional contributions in the sequencing of genomes and interpreting such data, in synthetic biology and genome engineering, and in an emerging area of neuroscience that proposes to map brain activity and establish a "functional connectome." Among these, Church is known for pioneering the specialized fields of personal genomics and synthetic biology. He has co-founded commercial concerns spanning these areas, and others from green and natural products chemistry to infectious agent testing and fuel production, including Knome, LS9, and Joule Unlimited (respectively, human genomics, green chemistry, and solar fuel companies). Here we welcome George Church!

Thank you. And I'm looking forward to the Q and A at the end of this. So, this is my potential financial conflict of interest, on this webpage on the lower right. [Slide 1].

I'll be talking about genome engineering, epigenome engineering and systemic delivery of desirable traits. [Slide 2]. So, to start with some examples from nature of resilience and particular adaptations of the freezing and then how we deliver this via enhanced organs, and cell therapies, here, we have a need for freezing of large organs. And then on our way to preserving entire organisms, not just organs, we want to delay death as much as possible, so the technology will get better. We want to prevent and reverse aging and cell death, and I'll give some examples of how we've been approaching that and progress we've made. And then I'll just give like a one slide snippet on the kind of multi factorial way we can deal with a very complicated problem with a very simple solution, which is applied to resistance to all viruses, including ones we've never seen before. And then finally, I just want to show how some of the things



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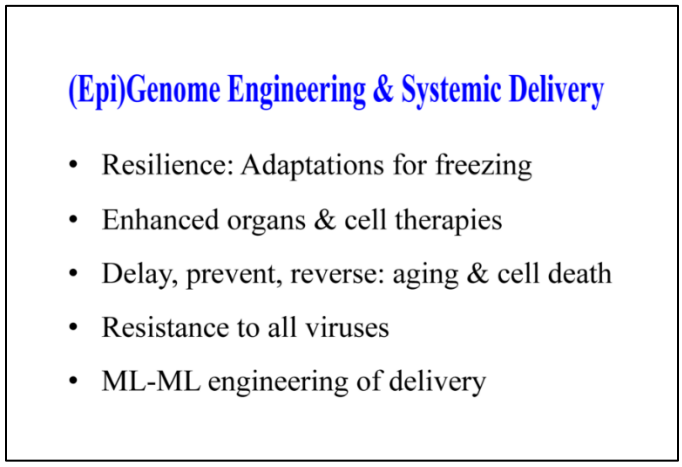

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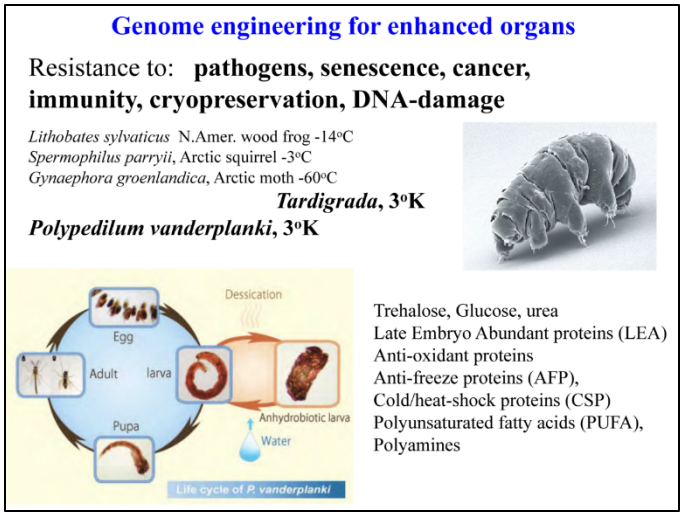
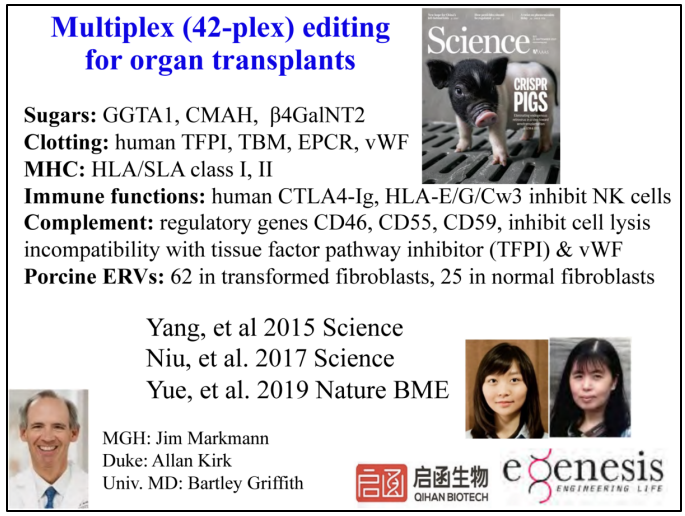




Slide 3

that were developed in the previous bullet points can be engineered with machine learning and mega-libraries such as the delivery of these things.

So, here's the one slide on natural resilience or resistance. [Slide 3]. And I'm going to give examples of almost all these various pathogen systems, senescence resistance, cancer, immunity resistance, immune rejection, cryopreservation, DNA damage. The last two are somewhat coupled and also coupled with desiccation. You have a number of animals that are closer to humans but don't survive complete freezing and thawing. Tardigrade and polypedilium do survive complete freezing and thawing, at least at particular stages of development. And they and others have this long list of molecules that are typically induced in preparation for being resilient to drying or freezing. Trehalose is a key one that has been found in a number of organisms including the tardigrade.

We'd like to be able to deliver these internally, not all of them get in from the blood system efficiently. We would like to give them time to be expressed and equilibrate. So that's where we are with our ability to deliver either through organs, cells or gene therapies.

One of our most complicated animal engineering projects which is successful now is producing organs that are being transplanted into both nonhuman primate preclinical trials as well as a handful of humans. As for the nonhuman primate clinical trials, some of them have 500 days survival, going on two years and, these 42 gene edits have been accumulated since the sixties. In the 1960s, a chimpanzee kidney survived for nine months in a human. But it was the only one out of 13 recipients that had a good outcome. So it's clearly not acceptable for clinical use.

Over the years since 1963 these genes have accumulated in the field. We took everybody's wish list and did them all at once.

There are three different sugars that differ between the animals and humans. Clotting complement cascades are incompatible. We have major incompatibility with other immune functions that keep the transplant from having a super resistance

Slide 4

to immune rejection. And finally, in knowledge of retroviruses, the FDA was not jazzed about it that every organ in the pig is releasing viruses and all humans seem to replicate these viruses. So an immune suppressed patient would not be a good place to evolve zoonotc diseases.

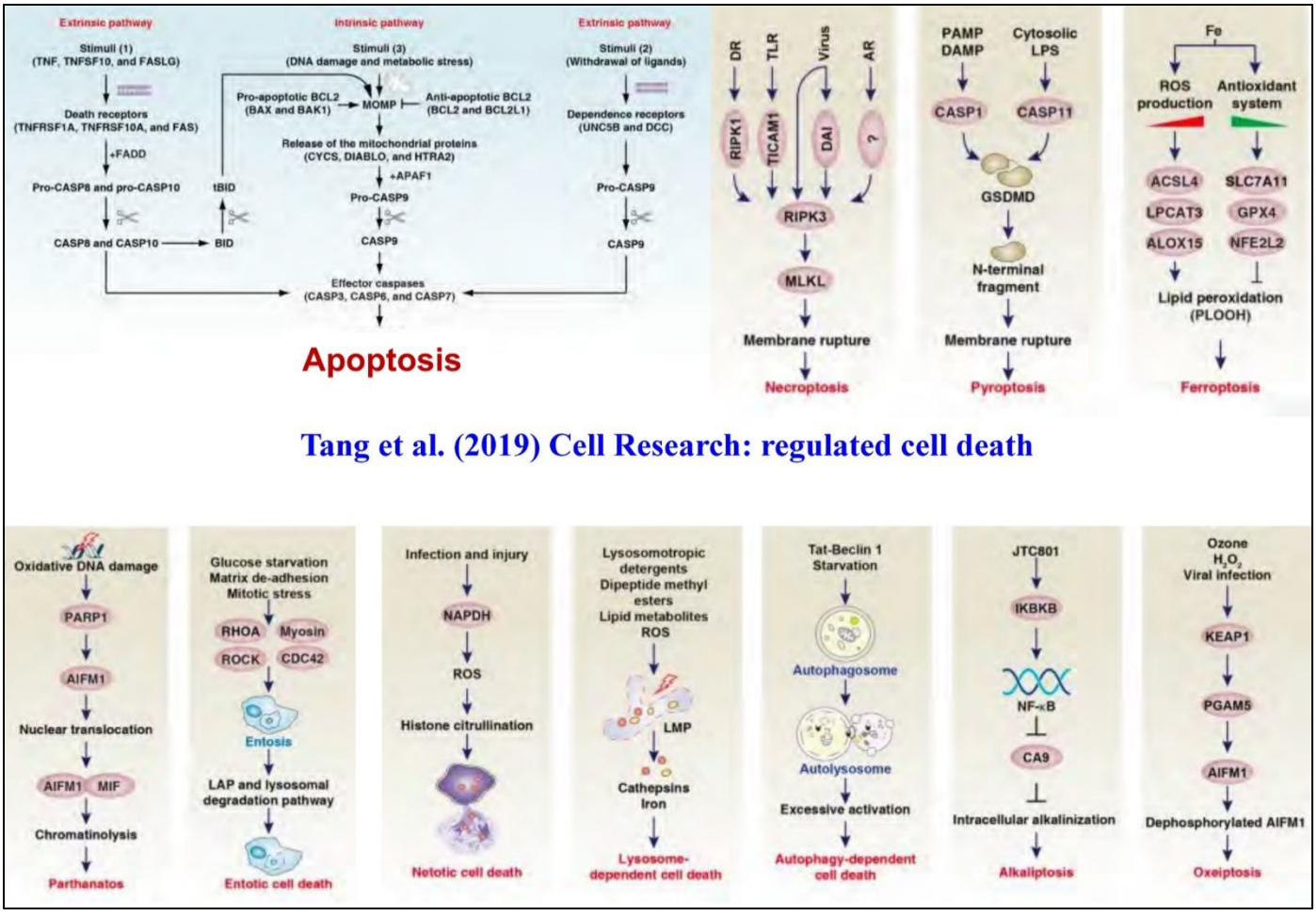
So we knocked out all these body retroviruses and showed that they were completely gone, that there were none produced in these cases. And we got into multiple pig strains. It's very robust, all of these things are robust. [Slide 4].

There's a series of papers on this. Luhan Yang, one of the authors, was a graduate student, postdoc in my lab and co-founded these two companies in China and Cambridge, Massachusetts. Jim Markmann, another, is one of several surgical heads in different hospitals that are trying out our organs and some organs from other groups in hospitals right now.

Now, the point of this is not just to deal with the crisis of missing organs, it's to make enhanced organs, and that was what the point of the slide [Slide 3] was, to make them so that they do not succumb to anything that came from this list after they're transplanted. So, one of the things that we had to deal with immediately is to make out of these, this 42 edits in the pig genome, is this regulated cell death. [Slide 5]. And there's a lot of these terms that end in the word -tosis, apoptosis, the earliest and most well known. And there's necroptosis and pyroptosis and all of these, and the pathways are fairly well understood, and we've leveraged that in order to make multiple edits at once. [Slide 6].

So here we're making somewhere between 25 and 80 edits at once and, without any protection against these regulated cell deaths, we get no multiplex editing and we don't get any of the multiple edits that we want. But with these two factors, basic growth factor and a P 53 inhibitor, almost everything is completely edited at all the sites.

Now, where are we going with this? First, one thing is we're using our ability to make multiple edits to not just knock out endogenous retrovirus as we did in the case, but to prevent exogenous viruses from coming in. And like all these are the sort



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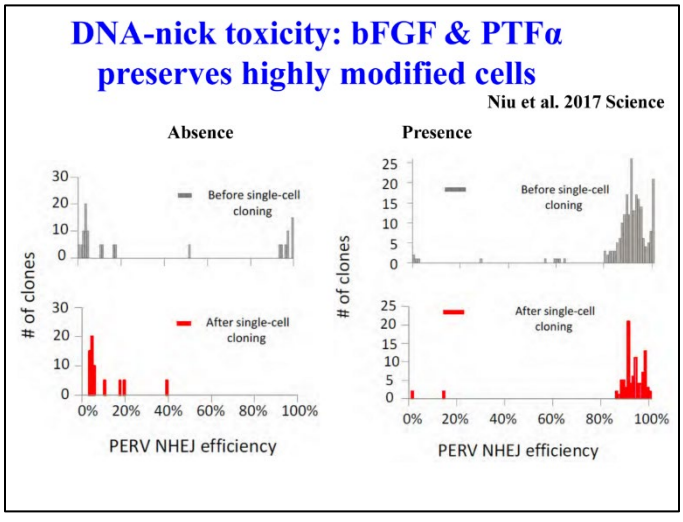

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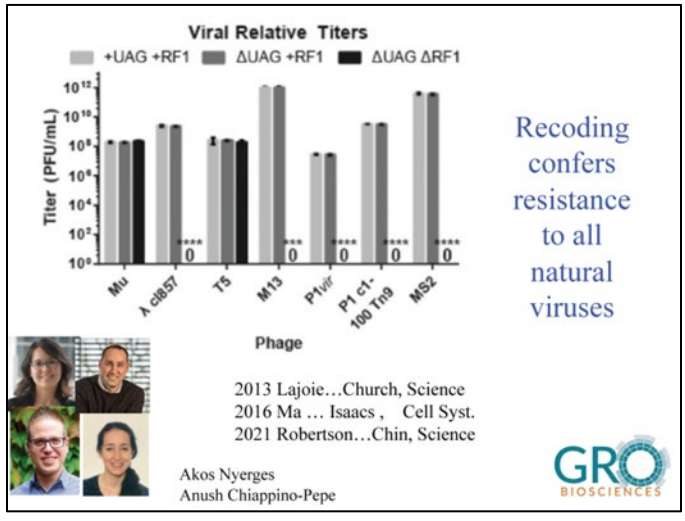
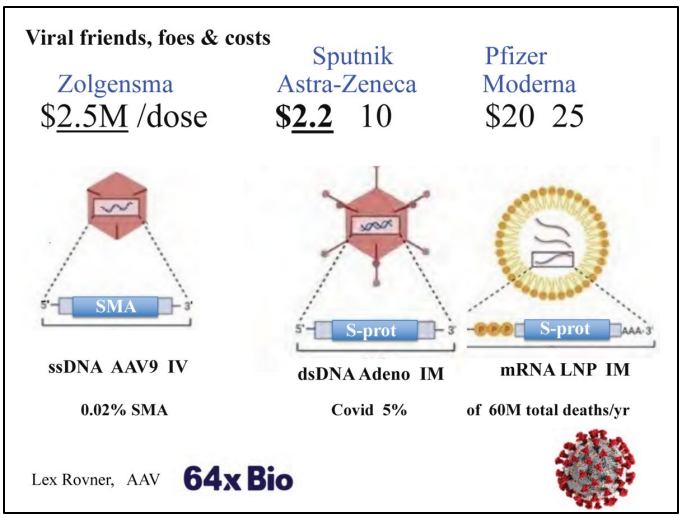


Slide 7

in the organs you're transplanting, et cetera. And in fact, in some of the most highly publicized work, not from our lab, but from another group, they did a human transplant of a pig heart. The person died within two months, probably due to porcine cytomegalovirus.

So, this whole business about viruses is very important for transplants and many other medical reasons. We now have demonstrations of this. This is an old slide of unpublished data showing how we think we have resistance to all viruses and, in one organism. [Slide 7]. Pretty far from human, it's an industrial microorganism, E. Coli, but the method we use is recruiting –



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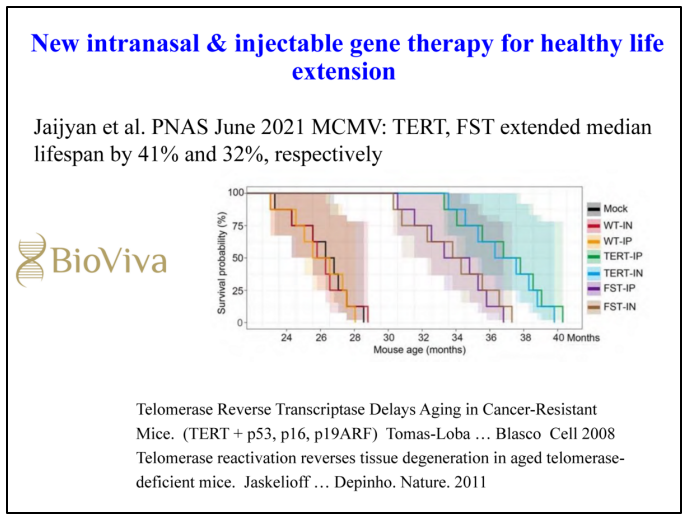


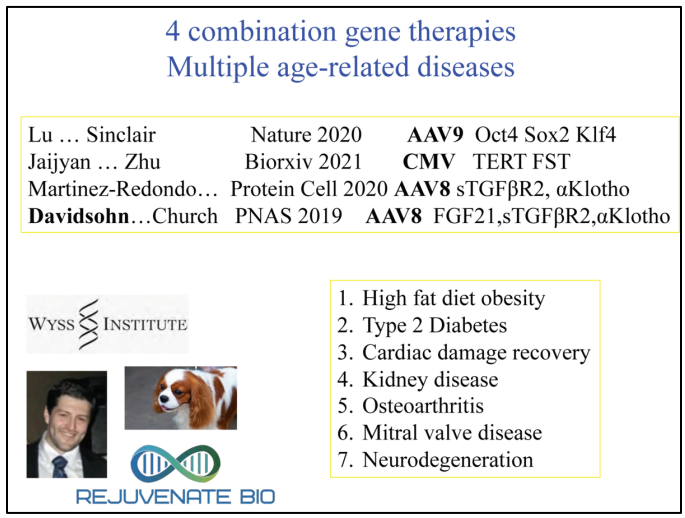
Slide 9

we don't really have time to go into it, but we can talk about it in the Q and A if you want. We made it resistant to viruses, even random viruses, we took thousands of random viruses from farm excrement, for example, and tested and really found that it's completely resistant. This sort of thing has been done now in three different laboratories. And one company is using some of these engineers for work in its products for clinical trials.

Now, viruses can be our friends as well as our foes. I showed two examples where we wanted to knock them out. But the other way we can use the viral process is for delivering either rare drugs like Zolgensma, one of the first approved gene therapies for SMA (spinal muscular atrophy), or common ailments like the pandemic COVID-19. [Slide 8]. The Zolgensma was AAV, adeno-associated virus, while the Astra-Zeneca and Sputnik were adenovirus. So this doesn't require ultravirus (filterable virus). And it's more immunogenic, it's appropriate for use in the vaccine. This one, the Zolgensma, was over $2 million, while the Astra-Zeneca was just over $2 a dose. So you can see that the size of the market makes a big difference in the price. And, and my group has always been looking for ways to reduce the cost of both diagnostics and therapeutics.

We brought down diagnostics sequencing by about 20 million-fold, and now this looks hopeful for anything of high importance, and the two things that come to mind are pandemics and aging. 64X Bio is one of the manufacturers of epiviral capsules for this sort of thing.

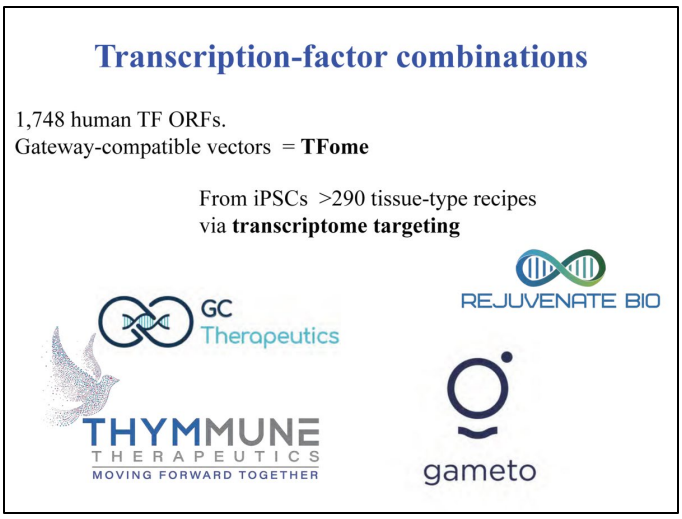
Here I give two slides of examples of how we're using viral delivery of usually one or up to four different payloads for aging reversal or in this case, longevity. [Slides 9, 10]. In most cases of the end point it is important to get FDA approval, because the aging reversal is much faster; demonstration is especially prolonged for long lived organisms like humans. But here we show mouse normal survival plots, and then the extended survival one gets with either telomerase addition or folistatin addition, published in PNAS recently, delivered either injectively or intranasally. [Slide 9]. And then I also refer to earlier literature on this telomerase, either in short line or later in life.



Slide 10

Now, this is a part of a context of four different publications and applications. [Slide 10]. All these are combinations just like we have combination therapies for HIV and cancer, antibiotics and so forth. I think this is going to be important to nine major pathways as you all know. I think we have to get them all and we have to get them all very efficiently made youthful. I mention the cytomegalovirus which has a very large usage as a package for gene delivery. But most of our work was in AAV and in fact, all three papers using AAV as a delivery were with Noah Davidson, postdoctoral fellow in my lab and now CSO at Rejuvenate Bio, also cofounder.

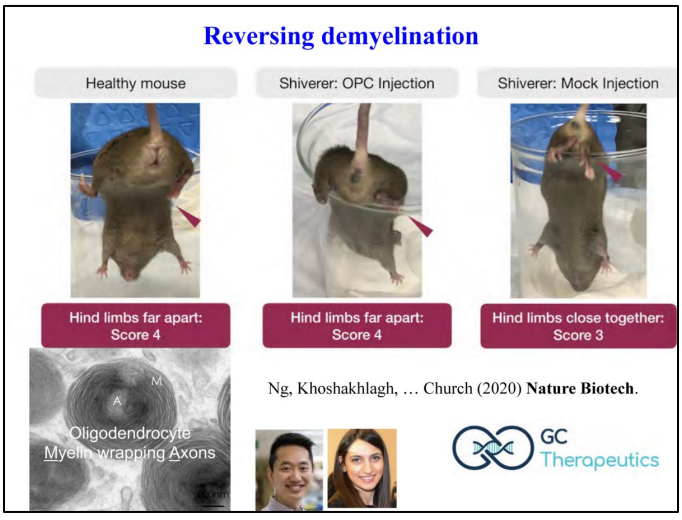
These are various things like the famous Yamanaka factors, three of them, Oct4, Sox2, Klf4. And then silo versus TCF beta receptor, alpha klotho and Growth Factor 21 have been delivered and initially, we looked at four different diseases of aging. We're following bio marketing, but we also want to be able to get multiple diseases of aging because that's what will make it more convincing for approval and/or market.



Slide 11

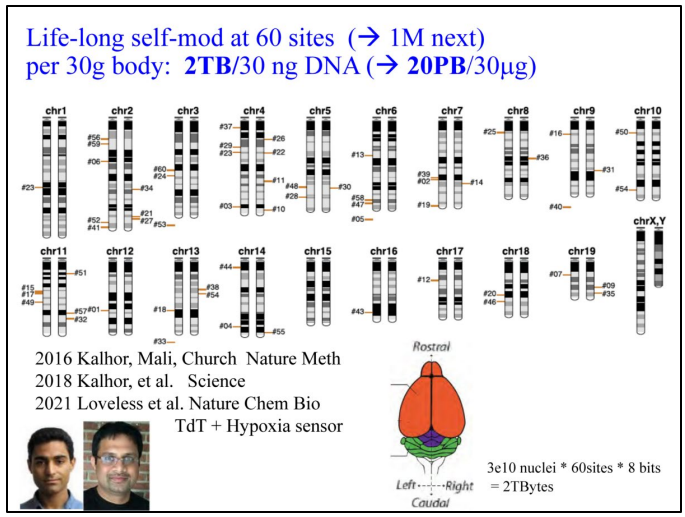
This initial market is dogs. The veterinary market gets quicker approval and quicker return on investment so that we can then move on to human clinical trials very soon. We want to do this very cautiously to make sure that this works, is very robust. It's now been extended to seven different diseases.

That's gene therapy. But we also have cell therapies where we want to be able to generate any cell type we want, whether it's B cells, T cells, macular cells, endothelial cells, gametes, gameto, thymus cells. [Slide 11]. GC therapeutics has really looked toward pioneering this, I'll show you in just a second. We have over 1,700 open reading frame transcription bankers where we think we can take almost any cell at any point in development backwards and forwards in developmental time. We typically use iPSCs (induced pluripotent stem cells), but we can use other cell types and we have about 300 different tissue type recipes that come from transcriptome targeting, look at the transcriptome of the target, and use that.



Slide 12

And here's an example from GC therapeutics [Slide 12]. Alex and Parastoo published a Nature Biotech paper where they're producing most of those 290 recipes, including oligodendrocytes and neurons and you could wrap them as happens in the white matter of the brain and the spinal column and that could rescue a demyelinating disease in mice. This is moving towards clinical trials as well.

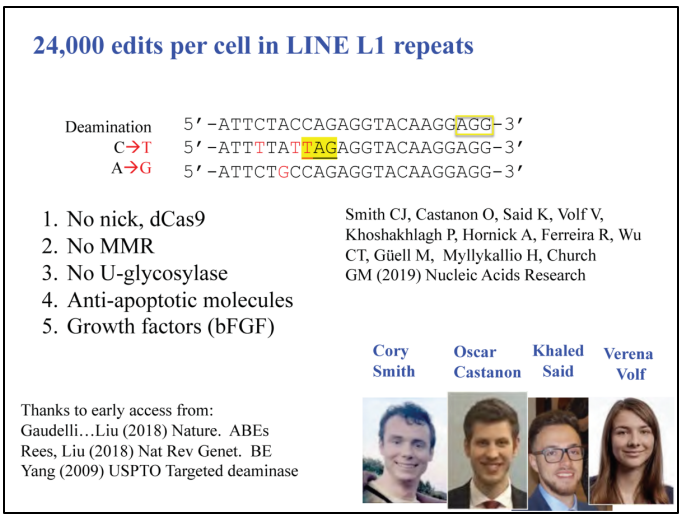


Slide 13

Now I've been talking about pretty high levels of multiplex editing, but really let's explore what the highest level is because for complex diseases we like to at least have the option of making lots of edits. And I'm not going to explain the full background of why we're doing this experiment. But it has to do with recording information, like a flight recorder or ticker tape, but putting in DNA in the living organism. Our first demonstration was about two terabytes of information storing 1 billionth the mass of the of the animal. [Slide 13]. This is just reporting from 60 random sites, trapped the genome, they're constantly randomly changing throughout the lifetime from egg to adult. And then we can selectively query parts of it. So, we didn't read the whole two terabytes, but certainly recorded it for no cost other than just growing up the animals.

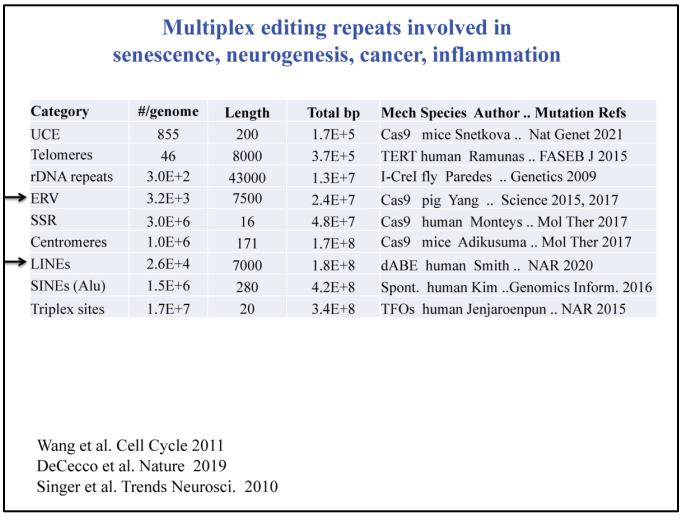
This is a series of papers here, I should point out that Loveless et al is is not from my labs, that UC Irvine did a beautiful job of extending this to include terminal transferase for more bits of information per site, and a physiological sensor for hypoxia. But this was initiated by Reza Kalhor, now Professor at Johns Hopkins and Prashant Mali, who has helped us with the initial work on CRISPR and came back to work with us on this recording device.

But anyway, we want to move from two terabytes to 20 petabytes. And we want to do that by harnessing the parts of the genomes that are repetitive and not essential. We don't know what parts we can interfere with until we start mutating them. And so we've started with what we suspect is a loss of territory here, in the 40% of the genome that's repetitive, it will be possible to mutate. We started with Line 1 elements in human stem cells. [Slide 14]. And we found empirically that adenine deamination, A to G, was way better. Native CRISPR CAS-9 cleavage is lethal. At this point, we have 24,000 targets in the typical human genome, and even 100 is lethal, but 24,000 is very lethal.



Slide 14

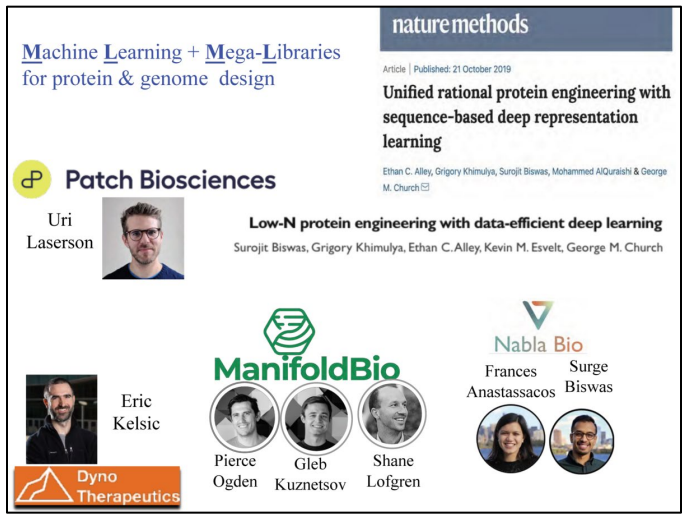
So anyway, we had to do everything we could to avoid any kind of double string break, any kind of nick that would be amplified to apoptosis. And the C deamination caused some toxicity. It also caused a lot of off target A, as our preferred benefit, A to G and we had to do all these things, including the tricks that I mentioned earlier. This is work from Corey and Oscar, Khaled and Verena, and I also thank David Liu who gave us a lot of enzymes prior to publication. This is published in Nucleic Acids Research, but we want to go beyond this.



Category	#/genome	Length	Total bp	Mech Species Author .. Mutation Refs
UCE	855	200	1.7E+5	Cas9 mice Snetkova .. Nat Genet 2021
Telomeres	46	8000	3.7E+5	TERT human Ramunas .. FASEB J 2015
rDNA repeats	3.0E+2	43000	1.3E+7	I-CreI fly Paredes .. Genetics 2009
→ ERV	3.2E+3	7500	2.4E+7	Cas9 pig Yang .. Science 2015, 2017
SSR	3.0E+6	16	4.8E+7	Cas9 human Monteys .. Mol Ther 2017
Centromeres	1.0E+6	171	1.7E+8	Cas9 mice Adikusuma .. Mol Ther 2017
→ LINEs	2.6E+4	7000	1.8E+8	dABE human Smith .. NAR 2020
SINEs (Alu)	1.5E+6	280	4.2E+8	Spont. human Kim ..Genomics Inform. 2016
Triplex sites	1.7E+7	20	3.4E+8	TFOs human Jenjaroenpun .. NAR 2015

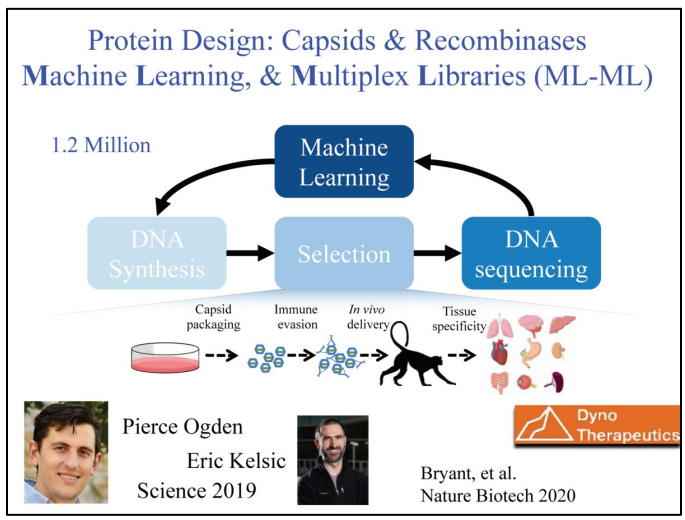
Slide 15

So, it went from like 42 edits in pigs including endogenous retroviruses. These line elements which make reverse transcriptase to be used for even more frequent outer level elements, and all of these repetitive elements, are involved in various physiological processes. [Slide 15]. They're not just junk DNA but they can be involved in senescence, neurogenesis, cancer, inflammation, according to literature outside of my line. So, we've done endogenous retroviruses to completion and, not yet published, we've done line elements of humans to completion. Now we're moving on to centromeres, simple sequence repeats and outer elements which add up into the tens to hundreds of millions of base pairs in the genome that we have available for this kind of mutagenesis. So, we've done ERVs and LINEs to saturation.



Slide 16

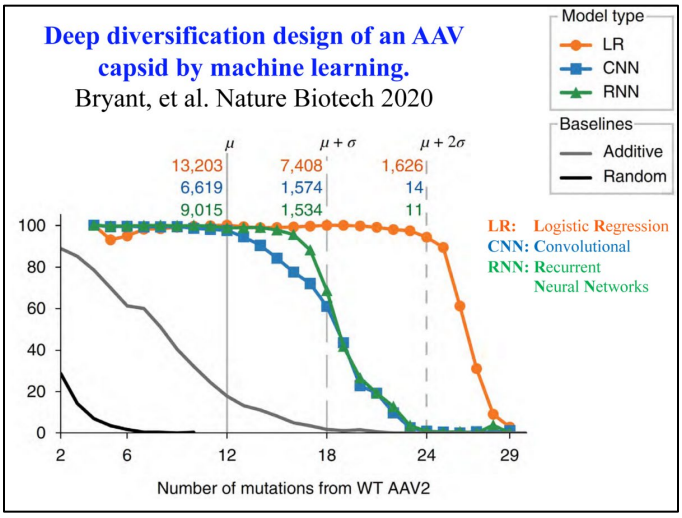
Now, I just want to end on how we can extend this sort of delivery. Any other new protein or enzyme pathway, we can engineer using machine learning and mega-libraries. [Slide 16]. They're very powerful separately but together they're extremely powerful. Mega-libraries can be reached on billions to people who do millions, when we do mammalian experiments in vivo. And we published seven papers on using machine learning and established four companies, Nabla, Manifold, Dyno, and Patch, doing four different things ranging from antibodies to A to capsids to systematic mutagenesis.



Slide 17

Here's just one quick example of that, that we have using this machine learning multiple libraries, which is called ML-ML. [Slide 17]. We don't make random mutagenesis, but we make design mutagenesis at first systematically throughout the entire target, making every possible codon shape protein, millions of these designed viruses at once. And then we learn from how they evade the immune system, how they get to all the tissues that we want them to get to, ideally for say aging reversal or

cryopreservation, we want to do it for every cell type. But we can study that tissue type and compare it to the wild type parental virus. This is work from Pierce and Eric who cofounded Dyno Therapeutics and published these two papers in Science and Nature Biotech describing this library method.



Slide 18

And here's an example of how it is where the X axis is the number of mutations out of 28 amino acids we can change, and the Y axis is the percent of viability of those. [Slide 18]. And if you just use a naive model or random mutation, it's very hard to get more than 4 to 6 mutations before you kill the protein of the virus delivery system completely. But if we use logistic refreshing, then it's really pretty easy to get to 24 out of 28 amino acids changed. And there's still a noticeable yield of 28 out of 28, essentially all amino acids changed to something. Again, this is in the nature of the different approaches. So, we're applying this to a number of different proteins and nucleic acids and cellular systems.

I went through that quickly, so there's plenty of time for Q and A where I can go back to the slide as necessary, or we can talk about the inspiration of naturally occurring adaptations of freezing. We can talk about how we can not only deal with the organ crisis, but these enhanced organs are resistant to pathogens, to senescence, to freezing, to immune response. And so, we put this under the general category of resilience. We want to delay, prevent, and reverse aging, and cell death is kind of aging in a microcosm which has very real consequences for instructions where we're making lots of edits at once. We have found a way to fight at least some of that cell death, and of course, reverse some aging. We have, of course, reversed aging in the stem cell formation, which will also be used quite routinely where you can take an 80-year-old cell and basically turn it into an embryonic cell, and pretty much in between. I stated without much evidence – so I apologize – that we think we can now get virus resistance in any organ or cell. And then finally, we have this machine learning megalibrary for engineering, not just for delivery but a variety of other purposes. Period. Full stop. Thank you.

Questions:

Q. I'm curious since you talked about resistance to all viruses: do you have any idea of a time frame for, say, a universal vaccine for everything in the COVID family? Or in the flu family or even broader than that? Would you be willing to get at a time frame for that kind of development?

A. The resistance to all viruses requires recoding, and it only applies to cells that have been recoded. While a vaccine is, in a way, less powerful, it's hard to do all viruses. It's more powerful and it distributes systemically to most of your body through the immune system. Even though you've only applied it to a small number, say, of cells by intramuscular injection. There are efforts to make more comprehensive vaccines. For example, I'm on the board of David Baker's Institute for Protein Design and they're aiming for key conserved features of the influenza virus. I think this is quite challenging, and it requires a great deal of knowledge about the virus and the virus family that it's in, while the method that we use of recoding preemptively eliminates all viruses because they all depend on the genetic code. You can make the host as a synonymous code where you move around the codons. We are also interested in vaccines that work. We have an active project on that. But we give news from the front on a more general, powerful method.

Q. How soon before you expect to be able to use gene therapy on yourself? What criteria will you require?

A. Well, almost all the experiments I described are being done on my cells, mainly for bioethics, rather than coercing my colleagues to be guinea pigs. But they're done, either with my cells in culture or in animals. So that, for the mouse rescue experiment, we're using oligodendrocytes reprogrammed from my skin cells, to save the mouse. So we need to go through the animal clinical trials, so that the point of the question is when. I think we're getting close to the end of the animal clinical trials for many of the different experiments I described. And so they will all be going into human clinical trials. I've been a guinea pig almost my entire life, both my parents experimented on me, you know, [laughter], very scientifically on this. So I may volunteer for some of this. I've been a volunteer in the personal genome project and through that the stem cells in manipulated forms are available. But I think everybody should be very cautious and make sure that the clinical trials are done correctly with, ideally, a double blind placebo control or some other control standard, whatever the best practice at the time is. So yeah, we'll be doing this very cautiously.

Q: What have you and your colleagues done specifically about freezing resistance and aging reversal so far?

A. With aging reversal, very little on freezing resistance. We wanted to develop the tools where we can make multiple changes and get both high-level resistance to freezing but also tolerance of the mechanisms that cause high-level resistance. I mean, it's possible there's going to be simpler methods than what we're doing, but we figured we would plan the worst-case scenario, and hope for the best. And some of those cases were manipulated multiple genes at once for an aging reversal. I gave four examples, including the citable version of the growth factor receptors, thyroid's growth factor, alpha klotho, and the

Yamanaka factors. All of these are aging reversal in the sense that they cause rapid recovery, sort of youthful recovery from a variety of organ insults, or reverse age-related diseases, of seven different categories. But probably the first veterinary product will be for mitral valve disease. It doesn't mean that it only does mitral valve disease. We're trying to avoid things that are just dealing with a specific symptom. But you just get approval from the FDA for one disease and then you can at your leisure, check out all the other consequences. But this particular spaniel has a very early onset but age-related disease in the mitral valves. And that's looking very good in the preclinical trials. A lot of the tests are done on pets and the pet owners spoke at some of the meetings that I won't hear [chuckles lightly].

Q.. What do you make of professor Evan Ashley's idea of a superhero vaccine? What does that mean actually?

A. Unfortunately, I'm not sufficiently familiar with that, but I can say that, if you use the term vaccine broadly as meaning a preventative or something that you do in advance, there's kind of growing tendency to use gene therapy-like methods for vaccines. I showed four examples in that slide on the intersection of gene therapies and vaccines including getting down to a $2 per dose number, which I find quite attractive. [Slide 8]. Then, it could include almost any component of your body that you would like to add in higher amounts. It could be either components that are dropping during aging or components that normally stop early but don't need to. There's all kinds of economies that developed evolutionarily in our ancestors that didn't have the total resources we have today, didn't have as much food as we have today, for example. There's all these economies that we program. So if you call those vaccines, almost all the gene therapies would be included. You know, I maintain a website of all the examples of mutations that either occur naturally in human populations to give them some superpowers – some people call it that – or, or even nonnatural, synthetic biology, things that we've done, typically in mice. And the list is quite, quite, long. It's over 40 pretty well established genes that could be made into gene therapies.

Q. What is your opinion on what is good from the side effects, the delivery system, the additives of the actual DNA being changed?. And who do you trust in the clinical trials?

A. As for the original side effects, you're talking about 20 years ago, more than 20 years ago, for gene therapy, were due to one or two things, either the retro viral vector, integrated near an oncogene causing the disease or an immune reaction to the viral capsid for adenovirus, which is quite immunogenic even today. So both of those strategies were abandoned 20 years ago and we have much better methods now. If you put in way too much virus, then you will get a complement cascade clogging things up. But there are hundreds of gene therapies in clinical trials now, several that have been approved by the FDA. So, I think I trust the groups that have done that, that have gotten FDA approval so far. And I think it's a pretty well-established pattern that other groups could follow as well. I don't trust people that are doing it on too small a scale, and not having controls or not using double blind. But other than that, I think it's straightforward enough that any normal clinical trial unit could pull it off. It's not cheap. You know, developing the COVID vaccine in a gene therapy format was not cheap, but it did only take a year. That was good. It ended up being inexpensive to the end user. But that's only because the market was so large.

Q. Just one more question. Are you signed up for cryopreservation? If so when and if not, why not?

A. I would say not yet. It's not that I'm opposed to it in any way. It's that I am concerned that the exponential rate of improvement in my field, at least, if not in all fields of human experience, is so fast that if I went to sleep for a few months, much less a few years, I would be completely out of touch. So that's my concern; I want to stay awake. But I probably will get around to it once we've got sentient beings, you know, animals, being restored. Then I will sign up

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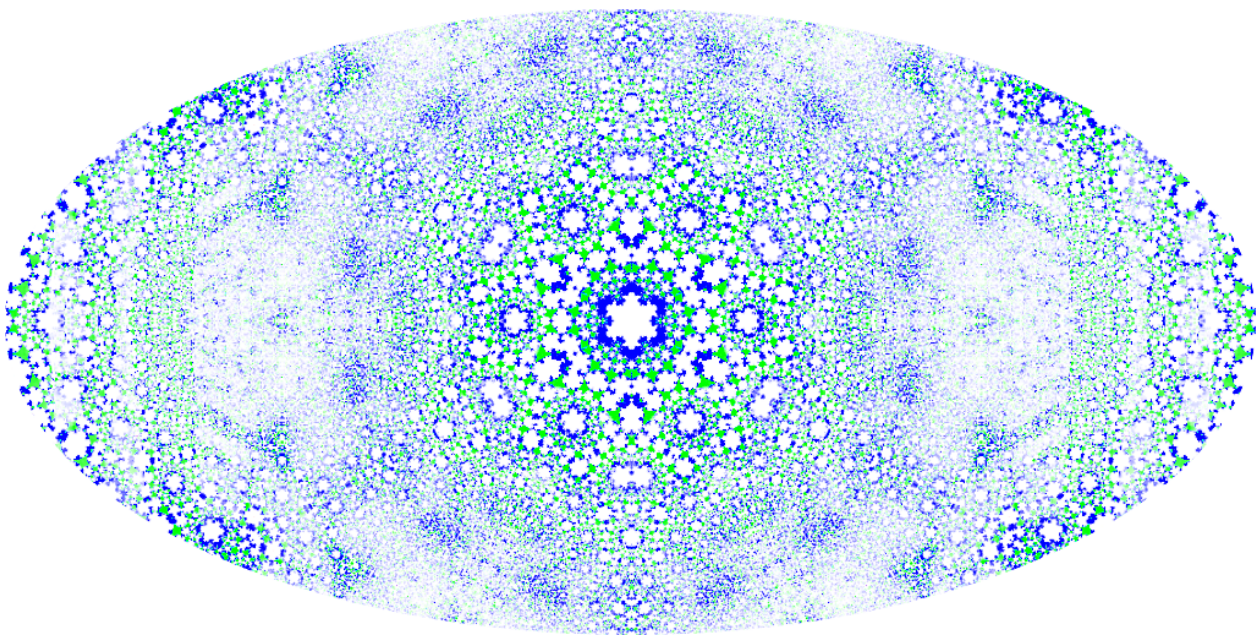


Growing Cryonics to the Mainstream:

A Few Thoughts, in the course of which I'll Probably offend someone in the Room

by Reason,

presented at the Alcor 50th Anniversary Conference, June 5, 2022

Reason is well-known for his Fight Aging! website, and is also co-founder and CEO of Repair Biotechnologies, aiming to reverse the progression of atherosclerosis. He's been an angel investor and has also done nonprofit fundraising. Here he starts with an imaginary "better world" where cryonics was accepted long ago, and goes on to consider our world and how we might make it more like that one.

In a Better World...

It was self-evident to everyone that cryopreservation was a great idea sometime quite soon after it became a practical possibility, sometime in the 1930s.

After 80-90 years of growth, the funerary industry is now largely the cryonics industry.

Major inroads have been made towards revival technologies, thanks to materials science, computing, and biotechnology.

In Reality...

Cryonics has been a tiny, fragile concern since its late inception in the 1960s.

It isn't self-evidently a good idea to everyone!

Cryonics has remained a community characterized by few people, little funding, mainly non-profit ventures, extremely slow growth, little resilience.

50 years is a really long time to continue having the same discussions about how to grow the community!

As you all know, in the 1930s, it became possible to produce liquid nitrogen at industrial scales. So, in a better world than the one we are in, people said, oh, wait, look at what we can do with this. And then a bunch of other people said this was a great idea, let's go with this. And the better part of a century later, the entire funerary industry was, in fact, the cryonics industry and we're starting to think about revival.

Unfortunately, we don't live in that world, we live in a world in which actually not many people think this is a self-evidently good idea. And as a result, we've been on the fringe for 50 years and we continue to have discussions about how do we stop this happening. I think this is really important. I think all you think this is really important, which is why we keep having these conversations about how do we not be on the fringe anymore? How do we actually grow this into a real and interesting industry? So I'm gonna be opinionated for a short period of time here and talk about, firstly, sales and marketing as the approach to getting this whole thing bigger. And secondly, making things more technologically capable as a path to making things bigger. And it's no great secret to anybody who knows me that I'm kind of biased towards one of those.

So, could we make cryonics a success if we could just figure out the magic formula to make the entire world think that cryonics is a great idea right now? I mean, why would we do this? The fundamental reason for doing this is that growth is funded by customers. At the high level, any industry has the amount of funding to do research and development, scaling up by the number of customers it has. And cryonics just does not have many

customers, which is why it's moving very slowly, and it doesn't really matter where that funding comes from.

For most industries, it comes from outside investment when you get a certain trajectory of customers. But if you want to bootstrap and just take customer money and use it for R & D to make the next best product to get more customers, that works. Except cryonics is struggling with this because, chicken and egg, there are not enough customers.

Now, is this actually a sales or marketing problem? And I'm well aware that certain European folk are in fact running a test of this proposition right now. I feel that this is a popular topic and always has been because it's very much a patient advocacy community at root, the cryonics community. It's a pretty short step from hey, persuade a person that this is a really good idea to hey, persuade this person to be a customer. A short jump, it feels like, but really it's not, as any sales guy will tell you. But also historically, the cryonics organizations have been really, really bad at sales and marketing, and by really, really bad, I mean, not really in their DNA, not interested in it, it's not what they're about. And so that's kind of why we are where we are today.

But it's important to realize that when we say sales and marketing, what we really mean is, what is the product? And we might all think, well, the product is, don't die. That's okay, but in this case it's via this rather convoluted technological approach that involves liquid nitrogen and other fun stuff. And demonstrably, it's not what the man on the street is willing to pay for.

It may be that for example, what is actually being sold here is insurance and cryonics organizations haven't figured that out yet and haven't decided to try to sell insurance in this particular flavor. Whether that's correct or not, we see the trouble with sales is that it doesn't really matter what you're trying to sell and fail at. You can always look out there in the world and say, wow, that totally useless item is doing really, really well. How are they doing this? So, any sales person can come to you, any product guy, any marketing guy can come to your failure and say you're just not doing it right. That's not an unreasonable argument, but it doesn't mean that we actually know what does "doing it right" look like. That's part of the challenge of okay, if it is really sales and marketing and product, what do we do about that?

And I don't think anybody really knows other than, let's keep trying things. But "let's keep trying things" is not really a plan that has a good, defined set of progression and likely costs. So maybe there is a way in which cryonics in its present iteration, its present state of technological growth can be sold to the world on that. And we just haven't found it yet for some definition of "we." I shouldn't say that I'm trying to do that, but my opinion is that the market has spoken over the last 50 years or so and said no, just no at its present state, this is not something I wish to participate in. Maybe that's a lesson that we need to take away and think about it a little bit.

This gets to the second point, which is look, if you want people to like your mouse trap, you need the damn mouse trap. It needs to exist, it needs to have the right color, it needs to be out there in front of people. So fundamentally, people are not willing to make leaps of faith.

There's the old story about how if you're demoing new technology to your CEO as a lowly engineer, and the end product is going to be blue, your prototype had better be blue. People don't want to take risks. They're very leery of it. And to a first approximation, the man in the street only sees what exists and is very unwilling to devote attention or belief to something that does not yet exist.

So, in the case of cryonics, we have this issue that, really, most people are only going to jump in after cryonics actually exists completely – after we can reverse vitrification for a human. And obviously, anybody who says that and insists on this kind of capability, this state of the art before they will join us, is not going to be of any help whatsoever in our getting there. It's the eternal challenge. So the core issue as I see it is that very, very little of cryonics is proven from the point of view of the man in the street. This is a bit distressing.

What it means by "proven" is, the man in the street doesn't care about technology demonstrations, papers, single studies, doesn't care that mouse and rabbit organs have been vitrified and reversed. They probably wouldn't care if a single human being was vitrified and reversed but only if it was widely used. So, we can ask why do people even understand this business about cold and preservation? It's because everybody has a freezer. Literally, it's so widespread that you can't avoid understanding that cold preserves. And therefore, this is a logical argument. So in order for something to exist to the man in the street and for him to think that it's worth participating in, it has to not just exist as a technological capacity, it also has to be very widely used to the point where it's, well, unavoidable.

So, in that sense, how useful is a new technological capacity to convince people that yes, cryonics is a real thing? It's something like how relevant is it to cryonics multiplied by how widely deployed and used is it. So, as I mentioned, if you just go do some reversible vitrification in the lab, nobody cares to a first approximation in the population of people who might give a few hundred dollars a year to a cryonics organization. And we want, you know, tens of thousands or millions of such people out there to care enough to do that.

So concretely, I think there's some very critical accomplishments we will need. Obviously, one of them is, just do it! Just have reversible vitrification. Have little furry mammals dancing around after having been vitrified and restored and totally happy. At which point it will be an easy sell, comparatively speaking, organs are a much easier prospect. Next, a robust assay for quantification of brain vitrification is needed that we all agree on, where you can easily say, okay, this guy has a score. This is how well he did. At this point, you can optimize vitrification based upon that assay and some of these issues are closed and some of them are not.

Now, obviously the really hard path that eventually has to be embarked upon and which some people are already starting on is, let's do reversible vitrification of living organisms, mammals in particular, and getting it into the veterinary industry is probably a good approach. Though I think that industry will struggle with the whole motivation to actually revive any vitrified animals. I don't think that's gonna happen an awful lot. But if you do get to the point where you can get to the end of this list, and you're vitrifying and reviving a few humans, that's

about the best thing you could possibly do. And we all know this, that it's going to be very, very hard and very lengthy.

Now, the funny thing about the man in the street is that he doesn't care about quality. They have a very binary viewpoint, where a person is giving a little bit of attention to something. They think in binary fashion, it exists, it doesn't exist, they don't care about quality. People are not signing up or refusing to sign up for cryonics based on how good cryopreservation is. I can assure you of that.

It's absolutely necessary to robustly determine the quality of vitrification, this has to happen, it's a technological capability that everybody understands and is working towards and needs to be done. But it's going to do next to zero to the prospect of how you sell cryonics to the masses at large. They just do not care. It's an unfortunate consequence of life, but some technologies are necessary. But also, there's no motivation to develop them from the pure sales perspective. Now, my own personal vote for the best way forward that satisfies the relevance and widely used criteria is to push forward and get reversible vitrification of organs going. This will immediately be used by the organ transplant industry and vastly improve and revolutionize that industry in a very noisy fashion as soon as it's out there and approved by the powers that be, the regulators. And it's also very close to realization, there are groups that have maybe a year or two of funding away from getting something that is viable. At this point you can found a company and get going and push it into the pipeline with not an enormous amount of money. By "not an enormous amount of money," I should say maybe $20 million to get to the point at which you can pull in the necessary other hundreds of millions to get past the regulators. In fact, this conclusion could serve for most of my presentations.

So, my my personal take on this is sorry, sales folk. We need to do technological progress first, then get back to the sales. I think the market has repeatedly rejected cryonics. And by market, I mean, the broader group of the man in the street where we're gonna find the million people. We need to get a decent set of research funding going to be self-sustaining, which means that, you know, we need to improve the current state of technological capabilities in order to convince these folk. Yes, we can continue to experiment with marketing and should. But there's no guarantee. And if you went and spent $20 million on experimenting with marketing, I think the odds are that you wouldn't get very far or at least nowhere near as far as you would if you went and spent 20 million in a philanthropic way or indeed even a venture investment way on the reversible vitrification of organs. This would be to disrupt the organ donation industry in a very loud way that people would see and make it a much shorter leap to say, ok, if we can do this for hearts and livers and kidneys, then why do you think it's going to be impossible to do it for a whole person and to the man in the street? I think that will be a compelling enough argument to make a big difference to the way in which we can go out there and try to convince more people to become members of organizations such as Alcor and thereby magically increase the amount of funding going to ongoing research and development. It's a virtuous cycle. But I think we just need that, that impetus, of a few tens of millions of dollars at the outset to go to the best possible technological capabilities to make the arguments easy enough that we can get over this hump of bootstrapping and get on with it. And that is that.

Questions, Comments:

Rudi Hoffman: Bravo, thank you so much, Reason. Reason is an amazing guy. I wanted to ask of anyone, and Reason, if we knew the status of the Organ Preservation Alliance. There is a fellow cryonicist who was kind of quietly not out of the closet intentionally. And because he did not want organ preservation to be conflated with cryonics, basically, he was able to create two symposia that were attended by major pharma and got huge amounts of DARPA money, something like about $100 million in funding. And I wish we could have had him speak here because he actually helped create that Organ Preservation Alliance that pulled in really mainstream funding and defense money. But it feels like it's kind of fallen off the grid. And I don't know what the status on that is, very relevant to your point, which I absolutely agree with. Organ preservation is certainly the most direct path to getting cryonics mainstream. So, does anyone know what the status on that is? Do you happen to know, Reason?

Reason: I think that's a Dave Goodall question. He was very involved in the early efforts with the new organ approach, to manufacture organs. But yeah, it would be great to get some of those guys in the room and talking about that in the next conference. Perhaps. Any questions?

Unidentified: I've been a fundraiser my whole life, for causes I believe in, and I've certainly taken the 20-people-per-dollar approach of trying to get the common man to follow along. But one of the approaches that I've used, and I'm sure you guys probably do in the background, is to go after any high-network individuals and try to "cross" them, and that might involve business, it might involve charity. I've got a lot of guys that are wealthy and important, and you follow on with them. So, I'm wondering about those that are after the 100 million, the billion, the 50-million-dollar guys. And also, there's actually kinds of action out there like crypto, there's a lot of different whales that are kind of quiet. What made me involved is because this is stuff that is kind of a lot of their style of thinking. And so, for me early on, I like to go after crumbs off the table with a large bag and then I try to get the small bag, you know, for me.

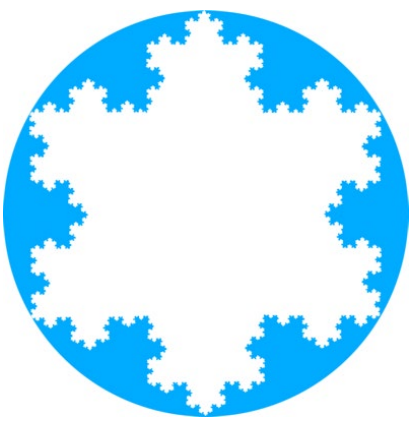
Reason: Oh, absolutely. This is where that 20 million would come from. The crypto guys are actually, if anything is to be taken as sort of representative, doing about 40% of biotech investment in the rejuvenation side of things. And I know that the recent large donation to the research fund that Alcor got came from the crypto space. So, these guys are out there, they have a lot of money, they're younger, which means they still have a lot of their fire and they're interested in changing the world. If anything, if I have enough time to advance my eternal thesis, it's that the reason the dotcom revolution produced so much change is that the people who got wealthy, they were younger than the traditional wealthy people who were very set in their ways. And then crypto is that, dialed up to ten. So now you have 20-somethings out there with $100 million wanting to change the world. And hey, talk to these guys. A lot of them are very into rejuvenation and getting into cryonics.

Natasha Vita-More: I have a couple of points. Your last statement, on crypto, I just won a competition with my new project, the H+ DAO, and one of *its* first projects is going to be working with an AI blockchain and cryonics, dealing with neurons. That ties into my former research working with vitrifying neurons. It also ties into a larger research program with others who are working with synapses and neurons. This is the second part. So that's in the process. And I think it was a great comment the gentleman made over there and your mention of it in that community of lots of people with a lot of money and looking for a culture to join. I think tapping into that would be great through any decentralized autonomous organization. The second point is about a mammal. There is, on the drawing board, a project that is going to be working with a mammal following my previous research. I'm not asking for funding for that. I'm asking for lab space for it, but I think that is in the works and I agree with the mammal approach, the organs, we have Greg Fahy working on that. So, I think that your talk was excellent. Thank you very much. But I think those three projects are on the drawing board and I think they have to happen sooner rather than later. So, I agree with you 100%. Thank you.

Reason: You're welcome. Do we still have a couple of questions – shall we, like, run out here with a microphone? Why not?

Unidentified (2nd): It was mentioned that you did angel investing and such. And I was just thinking, as you were talking, thinking about this whole thing as like a startup business, right? Usually on a startup business you start out with the problem and consider what competitors are doing to solve the problem versus what you're planning. Well, the problem we're trying to solve here is the problem of death, right? Like we don't want to die, we want to find a way to get around that. And we're thinking about who are our competitors right now, that are solving that. And I feel like the only other people that are really trying to solve this are well, the ones that would give you heaven, right? These religions claim you can get around the problem their way, versus what we're doing, a scientific approach. I think we have a better solution to the problem of death, potentially, than these other competitors. But I guess my question would be, what other competitive advantages do we have? Or what could we learn from other companies or organizations that are also trying to solve that problem?

Reason: Well, let's offend somebody in the room and say that, what we learn from religion is that lying works. It's really good. It's pretty amazing. So actually, the other thing we can learn is that a literal solution to the problem of death personally is to die. Um, because we don't hear any complaints, right? And certainly, if we believe the whole going to oblivion thing, then, after you're dead you're not really concerned about that. So that seems like a bad way to approach the world because at the end of the day you end up with, let's get rid of everybody. That would solve everything, and that way, it's a great solution. Technically, yes. But I think we'd prefer to do things the staying alive and having fun way. And unfortunately, none of the competitors are really as yet offering a viable solution to that problem. There is no competitor in that sense. So, there will be the rejuvenation industry which will largely solve the problem to the point of being a valid competitor, but you still have falling pianos, and equivalent future things that do as much damage. There will always be the need for emergency medicine where this person needs to be vitrified right now. Even in a world in which aging is defeated. So as of now, I think cryonics being plan A remains an entirely viable point of view. We just need to persuade a few more people that that is true. And hopefully without going the path of founding a cult and aggressively misrepresenting the state of the world and the universe and fundamental truth and all the rest of it. I think we can do it without doing that. And while retaining the scientific method. It might be a little slower, but the results will be better.



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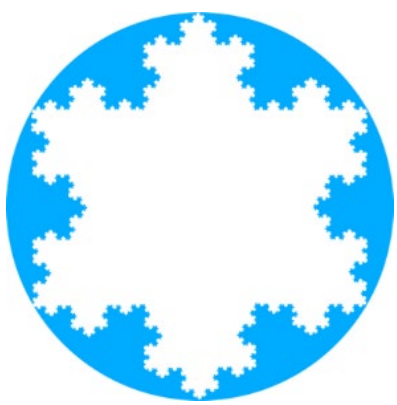


DNA methylation networks underlying mammalian traits

Amin Haghani, Caesar, Z. Li, Todd R. Robeck, Joshua Zhang, Ake T. Lu, Julia Ablaeva, Victoria A. Acosta-Rodríguez, Danielle M. Adams, Abdulaziz N. Alagaili, **[...]**, and Steve Horvath **+180 authors**

Science,11 Aug 2023, Vol 381, Issue 6658, DOI: 10.1126/science.abq5693

Editor's summary: DNA methylation installs a methyl group to cytosine, placing an epigenetic mark that regulates gene expression. Comparative epigenomics combines epigenetic signatures with phylogenetic relationships to understand species characteristics. Haghani *et al*. evaluated methylation levels in highly conserved DNA sequences, profiling ~15,000 samples across 348 mammalian species (see the Perspective by de Mendoza). Phylogenetic trees suggest that the divergence of DNA methylation profiles closely mirrors genetic evolution. Species with longer maximum life spans have developed tidier methylation patterns within the genome, characterized by unique peaks and troughs of methylation. Methylation patterns associated with maximum life spans generally differ from those connected to age or interventions that affect mortality risk in mice. These data provide a rich resource of information for fields including evolutionary biology and longevity research. —Di Jiang

Universal DNA methylation age across mammalian tissues

Lu, A.T., Fei, Z., Haghani, A. *et al.* Universal DNA methylation age across mammalian tissues. *Nat. Aging* **3**, 10 1144–1166 (10 Aug. 2023). https://doi.org/10.1038/s43587-023-00462-6.

Author Correction to this article was published on 06 September 2023

Abstract: Aging, often considered a result of random cellular damage, can be accurately estimated using DNA methylation profiles, the foundation of pan-tissue epigenetic clocks. Here, we demonstrate the development of universal pan-mammalian clocks, using 11,754 methylation arrays from our Mammalian Methylation Consortium, which encompass 59 tissue types across 185 mammalian species. These predictive models estimate mammalian tissue age with high accuracy ($r > 0.96$). Age deviations correlate with human mortality risk, mouse somatotropic axis mutations and caloric restriction. We identified specific cytosines with methylation levels that change with age across numerous species. These sites, highly enriched in polycomb repressive complex 2-binding locations, are near genes implicated in mammalian development, cancer, obesity and longevity. Our findings offer new evidence suggesting that aging is evolutionarily conserved and intertwined with developmental processes across all mammals.

From: Decoding Lifespan: New DNA Research Unveils Secrets of Aging

University of California - Los Angeles Health Sciences August 12, 2023, https://scitechdaily.com/decoding-lifespan-new-dna-research-unveils-secrets-of-aging/, accessed 12 Aug. 2023.

Researchers from the UCLA David Geffen School of Medicine and UCLA Health led an international research team that published two articles detailing changes in DNA – changes that researchers found are shared by humans and other mammals throughout history and are associated with life span and numerous other traits.

"We've discovered that the life spans of mammals are closely associated with chemical modifications of the DNA molecule, specifically known as epigenetics, or more accurately, methylation. In essence, mammals with longer life spans exhibit more pronounced DNA methylation landscapes, whereas those of shorter-lived species have more subdued, flatter methylation patterns," said the senior author of both articles, Steve Horvath, Ph.D., ScD, an expert on the aging process and a professor in human genetics and biostatistics at UCLA at the time the studies were conducted.

Jason Ernst, a professor of biological chemistry, computer science, and computational medicine at UCLA, said, "The technology we designed to measure DNA methylation levels across mammals along with the tissue sample contributions from a large consortium of researchers led to the production of a highly unique data set, which, when analyzed with advanced computational and statistical tools, unveiled a deeper understanding of the relationship between DNA methylation, life span, aging, and other biological processes across mammals."

The studies, one published in *Science* and the other in *Nature Aging,* focus on DNA methylation, or cytosine methylation, a chemical modification of cytosine, one of the four building blocks of the DNA molecule.

High-speed TIRF and 2D super-resolution structured illumination microscopy with a large field of view based on fiber optic components

Henning Ortkrass, Jasmin Schürstedt, Gerd Wiebusch, Karolina Szafranska, Peter McCourt, and Thomas Huser

Optics Express Vol. 31, Issue 18, pp. 29156-29165, 16 Aug. 2023.

Abstract: Super-resolved structured illumination microscopy (SR-SIM) is among the most flexible, fast, and least perturbing fluorescence microscopy techniques capable of surpassing the optical diffraction limit. Current custom-built instruments are easily able to deliver two-fold resolution enhancement at video-rate frame rates, but the cost of the instruments is still relatively high, and the physical size of the instruments based on the implementation of their optics is still rather large. Here, we present our latest results towards realizing a new generation of compact, cost-efficient, and high-speed SR-SIM instruments. Tight integration of the fiber-based structured illumination microscope capable of multi-color 2D- and TIRF-SIM imaging, allows us to demonstrate SR-SIM with a field of view of up to 150×150 μm^2 and imaging rates of up to 44 Hz while maintaining highest spatiotemporal resolution of less than 100 nm. We discuss the overall integration of optics, electronics, and software that allowed us to achieve this, and then present the fiberSIM imaging capabilities by visualizing the intracellular structure of rat liver sinusoidal endothelial cells, in particular by resolving the structure of their trans-cellular nanopores called fenestrations.

From: Researchers achieve high-speed super-resolution imaging with a large field of view

by Optica, https://phys.org/news/2023-08-high-speed-super-resolution-imaging-large-field.html, accessed 18 Aug. 2023.

Researchers have developed a fluorescence microscope that uses structured illumination for fast super-resolution imaging over a wide field of view. The new microscope was designed to image multiple living cells simultaneously with a very high resolution to study the effects of various drugs and mixtures of drugs on the body.

"Polypharmacy—the effect of the many combinations of drugs typically prescribed to the chronically sick or elderly—can lead to dangerous interactions and is becoming a major issue," said Henning Ortkrass from Bielefeld University in Germany. "We developed this microscope as part of the EIC Pathfinder Open-Project DeLIVERy, which aims to develop a platform that can investigate polypharmacy in individual patients."

In the journal *Optics Express*, the researchers describe their new microscope, which uses optical fiber delivery of excitation light to enable very high image quality over a very large field of view with multicolor and high-speed capability. They show that the instrument can be used to image liver cells, achieving a field of view up to 150 x 150 μm^2 and imaging rates up to 44 Hz while maintaining a spatiotemporal resolution of less than 100 nm.

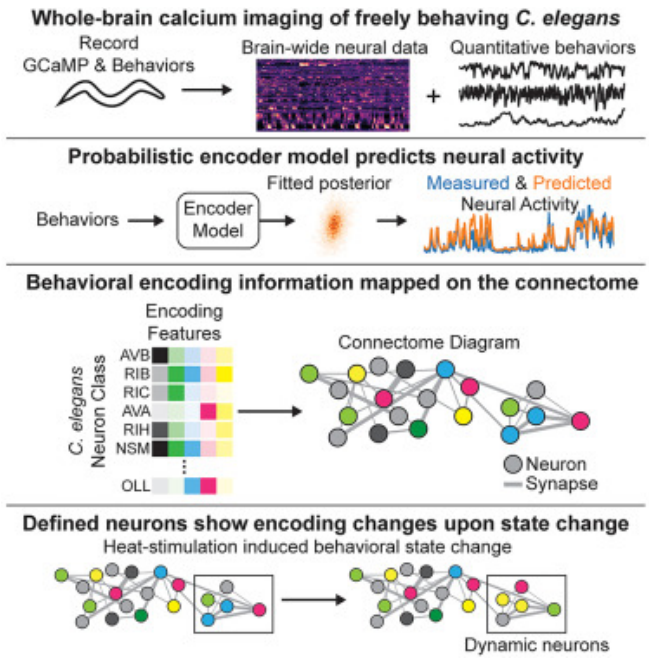
"With this new microscope, individual drug combinations can be tested on isolated cells and then imaged with super-resolution to observe dynamics of cell membrane features or organelles," said Ortkrass.

Brain-wide representations of behavior spanning multiple timescales and states in *C. elegans*

Atanas et al., 2023, Cell 186, 4134–4151 September 14, 2023, https://doi.org/10.1016/j.cell.2023.07.035

Summary: Changes in an animal's behavior and internal state are accompanied by widespread changes in activity across its brain. However, how neurons across the brain encode behavior and how this is impacted by state is poorly understood. We recorded brain-wide activity and the diverse motor programs of freely moving C. elegans and built probabilistic models that explain how each neuron encodes quantitative behavioral features. By determining the identities of the recorded neurons, we created an atlas of how the defined neuron classes in the C. elegans connectome encode behavior. Many neuron classes have conjunctive representations of multiple behaviors. Moreover, although many neurons encode current motor actions, others integrate recent actions. Changes in behavioral state are accompanied by widespread changes in how neurons encode behavior, and we identify these flexible nodes in the connectome. Our results provide a global map of how the cell types across an animal's brain encode its behavior.

Graphical Abstract:



From: Mapping the mind: worm's brain activity fully decoded

Neuroscience News 21 Aug 2023, https://neurosciencenews.com/brain-mapping-worm-behavior-23787/ accessed 21 Aug. 2023

Summary: Researchers successfully mapped the neural activity

of the C. elegans worm, correlating it to its behaviors such as movement and feeding. Using novel technologies and methodologies, they developed a comprehensive atlas that showcases how most of the worm's neurons encode its various actions.

This study provides an intricate look into how an animal's nervous system controls behavior. The team's findings, data, and models are available on the "WormWideWeb."

Key Facts:

1. The study employed a new microscope and software system that tracked almost all behaviors of the worm and the activity of every neuron in its head.
2. The research revealed neurons encode both current and past behaviors, allowing the worm to understand how its past actions impact its present situation.
3. A significant discovery was that 30% of the neurons that encode behavior can remap their behavior encoding, adapting their functions based on changing circumstances.

Ageing-associated changes in transcriptional elongation influence longevity

Debès, C., Papadakis, A., Grönke, S. *et al.* Ageing-associated changes in transcriptional elongation influence longevity. *Nature* **616**, 814–821 (2023), https://doi.org/10.1038/s41586-023-05922-y, 12 Apr. 2023.

Abstract: Physiological homeostasis becomes compromised during ageing, as a result of impairment of cellular processes, including transcription and RNA splicing1·2·3·4. However, the molecular mechanisms leading to the loss of transcriptional fidelity are so far elusive, as are ways of preventing it. Here we profiled and analysed genome-wide, ageing-related changes in transcriptional processes across different organisms: nematodes, fruitflies, mice, rats and humans. The average transcriptional elongation speed (RNA polymerase II speed) increased with age in all five species. Along with these changes in elongation speed, we observed changes in splicing, including a reduction of unspliced transcripts and the formation of more circular RNAs. Two lifespan-extending interventions, dietary restriction and lowered insulin–IGF signalling, both reversed most of these ageing-related changes. Genetic variants in RNA polymerase II that reduced its speed in worms5 and flies6 increased their lifespan. Similarly, reducing the speed of RNA polymerase II by overexpressing histone components, to counter age-associated changes in nucleosome positioning, also extended lifespan in flies and the division potential of human cells. Our findings uncover fundamental molecular mechanisms underlying animal ageing and lifespan-extending interventions, and point to possible preventive measures.

From: German scientists make a 'major discovery' that could slow down the ageing process

Camille Bello, EuroNews Next, 26 Aug. 2023, https://www.euronews.com/next/2023/08/26/german-scientists-make-a-major-discovery-that-could-slow-down-the-ageing-process, accessed 28 Aug. 2023

Despite centuries of research and progress in medicine, there are still many mysteries that remain unresolved, chief among them being an understanding of what causes ageing and how can we slow it down or reverse it.

But a new study by a team of scientists in Germany, published in the scientific journal Nature, may finally have found the answers to these questions.

Researchers from the University of Cologne in Germany have not only discovered that gene transcription – the process in which a cell makes an RNA copy of a strand of DNA – becomes faster with age but less precise and more error-prone; they also found that certain processes could help us reverse this decline.

"This is, so far, the only eureka moment in my life. I mean, this is a type of discovery that you don't make every other day," said Dr Andreas Beyer, the lead researcher, calling the findings "a major discovery."

Before Beyer and his team started their investigative project 10 years ago, the typical ageing study would "just look at differential gene expression," says Beyer.

Previous studies, he explains, were asking questions like "When you age, which genes are getting turned on and which genes are getting turned off?" and "How does that change the regulation or the metabolism in the cell?"

But nobody was asking how the transcription process itself changes as we age, a line of inquiry that could yield insights to ultimately help us reverse, or stop, decline.

Transcription is fundamental to Beyer's research as it is the process in which a cell makes an RNA copy of a piece of DNA.

This copy is important because it carries the genetic information needed to make new proteins in a cell. Proteins determine the health and function of the cells, and cells then structure all living things.

Because genes give cells their purpose, their transcription needs to be flawless.

A split and inducible adenine base editor for precise in vivo base editing

Zeng, H., Yuan, Q., Peng, F. *et al.* A split and inducible adenine base editor for precise in vivo base editing. *Nat Commun* **14**, 5573 (2023). https://doi.org/10.1038/s41467-023-41331-5

Abstract: DNA base editors use deaminases fused to a programmable DNA-binding protein for targeted nucleotide conversion. However, the most widely used TadA deaminases lack post-translational control in living cells. Here, we present a split adenine base editor (sABE) that utilizes chemically induced dimerization (CID) to control the catalytic activity of the deoxyadenosine deaminase TadA-8e. sABE shows high on-target editing activity comparable to the original ABE with TadA-8e (ABE8e) upon rapamycin induction while maintaining low background activity without induction. Importantly, sABE exhibits a narrower activity window on DNA and higher precision than ABE8e, with an improved single-to-double ratio of adenine editing and reduced genomic and transcriptomic off-target effects. sABE can achieve gene knockout through multiplex splice donor disruption in human cells. Furthermore, when

delivered via dual adeno-associated virus vectors, sABE can efficiently convert a single A•T base pair to a G•C base pair on the *PCSK9* gene in mouse liver, demonstrating in vivo CID-controlled DNA base editing. Thus, sABE enables precise control of base editing, which will have broad implications for basic research and in vivo therapeutic applications.

From: New gene-editing tool reduces unintended mutations by more than 70%

Paul McClure, New Atlas, 21 Sep 2023, https://newatlas.com/medical/new-gene-editing-tool-reduces-unintended-mutations-by-more-than-70-percent/, accessed 23 Sep 2023

Researchers have found that splitting the gene editor used in traditional CRISPR technology creates a more precise tool that can be switched on and off, with significantly less chance of causing unintended genome mutations. They say their novel tool can potentially correct around half of the mutations that cause disease.

CRISPR is one of those scientific terms that has made it into the everyday lexicon. Arguably one of the biggest discoveries of the 21st century, the gene-editing tool has revolutionized research and the treatment of genetic and non-genetic diseases. But the primary risk associated with CRISPR technology is 'off-target edits,' namely unexpected, unwanted, or even adverse alterations at locations in the genome other than the targeted site.

Now, researchers at Rice University have developed a new CRISPR-based gene-editing tool that's more precise and significantly reduces the likelihood of off-target edits occurring.

"Our team set out to create a much-improved version that can be turned on or off as needed, providing an unparalleled level of safety and accuracy," said Hongzhi Zeng, the study's lead author. "This tool has the potential to correct nearly half of the disease-causing point mutations in our genome. However, current adenine base editors are in a constant 'on' state, which could lead to unwanted genome changes alongside the desired correction in the host genome."

DNA consists of two linked strands that wind around each other, forming a double helix that resembles a twisted ladder. The 'rungs' of the ladder are made of base pairs, two complementary nucleotide bases held together by hydrogen bonds: adenine (A) pairs with thymine (T) and cytosine (C) with guanine (G).

Base pair mutations are also called 'point mutations' and are responsible for causing thousands of diseases. Traditional CRISPR uses either an adenine base editor (ABE) or cytosine base editor (CBE) to create point mutations at desired sites. Here, the researchers took an ABE and modified it.

They split the ABE into two separate proteins that remain inactive until a sirolimus molecule is added. Sirolimus, also known as rapamycin, is a drug with anti-tumor and immunosuppressant properties that's used to prevent rejection in organ transplantation and treat certain types of cancer.

"Upon introduction of this small molecule, the two separate inactive fragments of the adenine base editor are glued together and rendered active," said Zeng. "As the body metabolizes the rapamycin, the two fragments disjoin, deactivating the system."

Controlling piezoresistance in single molecules through the isomerisation of bullvalenes

Reimers, J.R., Li, T., Birvé, A.P. *et al. Nat Commun* **14**, 6089, 3 Oct 2023, https://doi.org/10.1038/s41467-023-41674-z

Abstract: Nanoscale electro-mechanical systems (NEMS) displaying piezoresistance offer unique measurement opportunities at the sub-cellular level, in detectors and sensors, and in emerging generations of integrated electronic devices. Here, we show a single-molecule NEMS piezoresistor that operates utilising constitutional and conformational isomerisation of individual diaryl-bullvalene molecules and can be switched at 850 Hz. Observations are made using scanning tunnelling microscopy break junction (STMBJ) techniques to characterise piezoresistance, combined with blinking (current-time) experiments that follow single-molecule reactions in real time. A kinetic Monte Carlo methodology (KMC) is developed to simulate isomerisation on the experimental timescale, parameterised using density-functional theory (DFT) combined with non-equilibrium Green's function (NEGF) calculations. Results indicate that piezoresistance is controlled by both constitutional and conformational isomerisation, occurring at rates that are either fast (equilibrium) or slow (non-equilibrium) compared to the experimental timescale. Two different types of STMBJ traces are observed, one typical of traditional experiments that are interpreted in terms of intramolecular isomerisation occurring on stable tipped-shaped metal-contact junctions, and another attributed to arise from junction–interface restructuring induced by bullvalene isomerisation.

From: Game changing microscopic sensor 500k times smaller than a human hair is the size of a single molecule

Christopher Plain, The Debrief, 3 Oct 2023, https://thedebrief.org/game-changing-microscopic-sensor-500k-times-smaller-than-a-human-hair-is-the-size-of-a-single-molecule/, accessed 14 Oct 2023

Researchers have developed a microscopic sensor the size of a single molecule that they are describing as a potential game changer with a range of potential technological applications. About 500,000 times smaller than the width of a single strand of human hair, the revolutionary sensor could radically impact the precision and performance of personal electronic devices, aviation systems, and even systems used in space travel.

When your cell phone magically counts your steps while you jog, or your car's airbag is able to deploy with split-second precision, it is tapping into the power of piezoresistors. In fact, engineers use this type of pint-sized sensor, which transforms pressure or force into an electronic signal, in applications ranging from aviation control systems to life support systems used in space travel.

Still, even wider use of these types of sensors is limited by their size, much like many electronic applications. Now, an international team of researchers says they have developed a highly accurate, high-performing piezoresistor that is as small as a single molecule. And based on the initial testing, their microscopic sensor has seemingly limitless applications across a number of

industries.

To design and build their new microscopic sensor, the researchers say they used a single bullvalene molecule. That's because when this type of molecule is mechanically strained, it reacts to form a whole new type of molecule. The newly formed molecule is a completely different shape from the original, which alters electrical flow by changing resistance.

"The different chemical forms are known as isomers, and this is the first time that reactions between them have been used to develop piezoresistors," said Dr. Thomas Fallon, a researcher from the University of Newcastle and one of the co-authors of the research describing the sensor's development.

Another co-author, Professor Jeffrey Reimers from the University of Technology Sydney, said building this type of single-molecule piezoresistor and detecting shapes from their electrical conductance "is a whole new concept of chemical sensing." In fact, their device is so reactive the researchers say it can detect the change in the shape of a reacting molecule back and forth about once every millisecond.

A highly integrated bionic hand with neural control and feedback for use in daily life

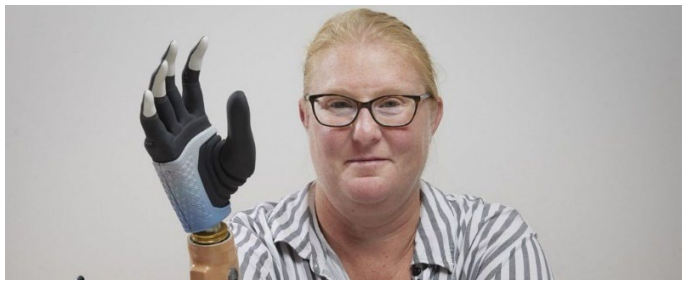
Max Ortiz-Catalan, Jan Zbinden, Jason Millenaar, Daniele D'Accolti, Marco Controzzi, Francesco Clemente, Leonardo Cappello, Eric J. Earley, Enzo Mastinu, [...], and Rickard Brånemark +5 aut,

Science Robotics 11 Oct 2023 Vol 8, Issue 83 DOI: 10.1126/scirobotics.adf7360

Abstract: Restoration of sensorimotor function after amputation has remained challenging because of the lack of human-machine interfaces that provide reliable control, feedback, and attachment. Here, we present the clinical implementation of a transradial neuromusculoskeletal prosthesis—a bionic hand connected directly to the user's nervous and skeletal systems. In one person with unilateral below-elbow amputation, titanium implants were placed intramedullary in the radius and ulna bones, and electromuscular constructs were created surgically by transferring the severed nerves to free muscle grafts. The native muscles, free muscle grafts, and ulnar nerve were implanted with electrodes. Percutaneous extensions from the titanium implants provided direct skeletal attachment and bidirectional communication between the implanted electrodes and a prosthetic hand. Operation of the bionic hand in daily life resulted in improved prosthetic function, reduced postamputation, and increased quality of life. Sensations elicited via direct neural stimulation were consistently perceived on the phantom hand throughout the study. To date, the patient continues using the prosthesis in daily life. The functionality of conventional artificial limbs is hindered by discomfort and limited and unreliable control. Neuromusculoskeletal interfaces can overcome these hurdles and provide the means for the everyday use of a prosthesis with reliable neural control fixated into the skeleton.

From: Revolutionary bionic hand fuses with woman's bones, muscles, and nerves

Carly Cassella, Health, 17 October 2023, https://www.sciencealert.com/revolutionary-bionic-hand-fuses-with-womans-bones-muscles-and-nerves, accessed 19 Oct 2023.



Karin with her prosthesis. (Bionics Institute)

A 50-year-old Swedish woman who lost her hand in a farming accident has been fitted with a cutting-edge prosthesis that has proved transformational. The bionic hand is based on revolutionary technology that connects directly to a user's bones, muscles, and nerves – creating a human-machine interface that allows AI to translate brain signals into precise yet simple movements. The woman who received the bionic hand, Karin (whose full name is undisclosed), now has a limited sense of touch and can move all five of her bionic fingers individually with a success rate of 95 percent. After two decades of living without a right hand, she can now carry out 80 percent of her usual daily activities, like preparing food, picking up objects, zipping and unzipping clothes or bags, and turning door knobs or screws. What's more, after receiving the prosthetic hand, Karin's excruciating phantom pain, which she said felt as though her hand was going through a meat grinder, decreased significantly.

"I have better control over my prosthesis, but above all, my pain has decreased,"says Karin. "Today, I need much less medication."

"The fact that [Karin] has been able to use her prosthesis comfortably and effectively in daily activities for years is a promising testament to the potential life-changing capabilities of this novel technology for individuals facing limb loss," says robotics engineer, Max Ortiz Catalán, who led the research at the Bionics Institute in Melbourne, Australia and the Center for Bionics and Pain Research in Sweden (which he helped found).

When Karin was initially fitted with the prosthesis, three years ago, researchers say the technology was one of a kind. No other hand prosthesis on the market contained embedded sensors. To this day, most models have sensory electrodes on the outside, just under the 'skin' of the robot.

This convention, however, dilutes the quality and quantity of sensory signals going to and from the robotic hand, limiting its control – a problem that has plagued prosthetic technology since it first arose roughly 60 years ago. Over the last decade, Catalán has been working on a better solution that relies on 'osseointegration'. Basically, that means when an implant is placed into a person's bone, the bone cells will grow tightly around it.

"This integration is so strong that we can actually attach the artificial limb directly to the skeleton,"explains Catalán.

A rhythmically pulsing leaf-spring DNA-origami nanoengine that drives a passive follower

Centola, M., Poppleton, E., Ray, S. *et al.* A rhythmically pulsing leaf-spring DNA-origami nanoengine that drives a passive follower. *Nat. Nanotechnol.* **19**, 226–236, 19 Oct 2023, https://doi.org/10.1038/s41565-023-01516-x

Abstract: Molecular engineering seeks to create functional entities for modular use in the bottom-up design of nanoassemblies that can perform complex tasks. Such systems require fuel-consuming nanomotors that can actively drive downstream passive followers. Most artificial molecular motors are driven by Brownian motion, in which, with few exceptions, the generated forces are non-directed and insufficient for efficient transfer to passive second-level components. Consequently, efficient chemical-fuel-driven nanoscale driver–follower systems have not yet been realized. Here we present a DNA nanomachine (70 nm × 70 nm × 12 nm) driven by the chemical energy of DNA-templated RNA-transcription-consuming nucleoside triphosphates as fuel to generate a rhythmic pulsating motion of two rigid DNA-origami arms. Furthermore, we demonstrate actuation control and the simple coupling of the active nanomachine with a passive follower, to which it then transmits its motion, forming a true driver–follower pair.

From: Molecular engineers successfully create a working DNA 'nanomachine'

Shubhangi Dua, Interesting Engineering, 20 Oct 2023, https://interestingengineering.com/innovation/molecular-engineers-working-dna-nanomachine, accessed 23 Oct 2023

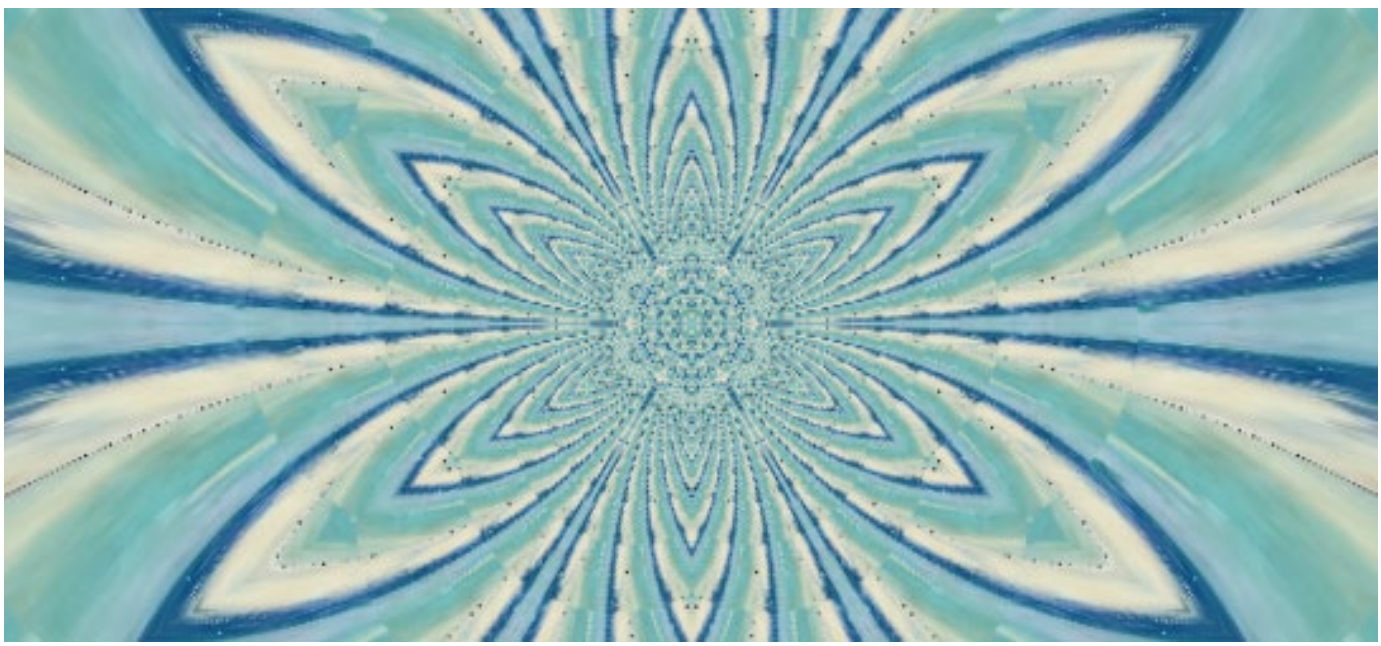
Molecular engineers have devised an unimaginably tiny machine at the nanometer (nm) scale similar to molecular robots, which can move and work together in a controlled manner. Petr Šulc, an professor at Arizona State University's School of Molecular Sciences, worked with Professor Michael Famulok from the assistant University of Bonn, Germany, and Professor Nils Walter from the University of Michigan on this project.

The team designed and developed nano assemblies at the molecular level. They devised a DNA nanomachine measuring 70 nm × 70 nm × 12 nm, driven by the chemical energy of DNA-templated RNA-transcription-consuming nucleoside triphosphates, according to the study.

This nanomachine uses chemical energy to generate controlled, rhythmic pulsating motion. This advancement illustrated the potential for creating precise, controllable nanoscale devices with applications in various fields such as nanotechnology, medicine, and materials science. The scientists reported that the structure is composed of almost 14,000 nucleotides, which form the basic structural units of DNA.

Šulc explained that being able to simulate motion in such a large nanostructure would be impossible without oxDNA, the computer model that their group uses for the design and design of DNA nanostructures.

"It is the first time that a chemically powered DNA nanotechnology motor has been successfully engineered. We are very excited that our research methods could help with studying it, and are looking forward to building even more complex nanodevices in the future."



After artwork by Jeffrey Thomas Riche

A Roadmap to Revival

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

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

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

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

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

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

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

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

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

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

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

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

Robert A. Freitas Jr., "**Cryostasis Revival: The Recovery of Cryonics Patients through Nanomedicine**," Alcor Life Extension Foundation, 2022 (https://www.alcor.org/cryostasis-revival/).

"Revival of Frozen patients in the future," *left* image Dall-E 2, Feb. 2023.

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).

Step 1: Find more information and create an account here: www.alcor.org

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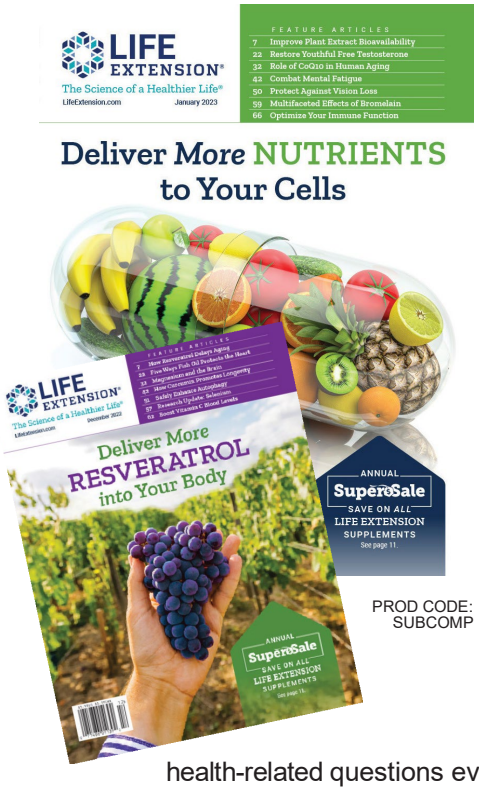

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