We are building a future free of age-related disease
Message from the CEO

LISA FABINY-KISER
CEO

What does it take to change the world?

A vision. - A passion. - A team. - A community.

If the COVID-19 pandemic taught us anything at all, it is that our world is indelibly connected. What affects one of us, affects all of us. To combat serious issues, to make real lasting change, we must work together, pooling all of our resources.

"Together, we will build this new world, one brick at a time."

Like so much in our modern world, curing the diseases of aging is a collaborative effort.

In 2021, SRF found itself at the center of a brand new way to fundraise. The ingenuity and generosity of Richard Heart, and the willingness to envision a life free from age-related disease from a forward-thinking global community, provided SRF with unprecedented resources. We gained not only in dollars, but also in number of supporters. Our vision struck a chord that reverberated across a broader group of people than ever before. Our mission inspired so many to put their trust and resources behind us, and we could not be more grateful or more determined to honor their support through the acceleration and expansion of our vital research.

At the same time, we had a changing of the guard at SRF. Undergoing internal investigations in the public eye, under intense scrutiny. Saying goodbye to our visionary founder, to a full half of our Board of Directors, and to our long-time Director of Education.

Within the last year, SRF has seen more upheaval, more incredible support, and more intense criticism, than in the entirety of the previous decade.

And yet we remain, passionately in pursuit of the mission that drove our founding. Our dedication to making the ‘Strategies for Engineered Negligible Senescence’ a life-saving reality is rock-solid, as we hope this Annual Report will make clear.

Our mission is vital; one hundred thousand people die every day of age-related disease. Millions more suffer due to age-related decline and disability. Our mission cannot be side-tracked, cannot be delayed, and must take precedence over all other concerns.

Last year was difficult, but also empowering. Our leadership may change, but our founding vision is powerful and keeps us focused on the path ahead. Our mission is our defining priority.

Together, we will build this new world, one brick at a time.

Sincerely,

LISA
Leadership

MARIA ENTRAIGUES ABRAMSON
Director of Outreach

DR. EMILY LILLIAN FISHMAN
Director of Academic Affairs

KELLY BOEMMEL
Director of Operations

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The Team | 2022

Research Group Leads

DR. AMUTHA BOOMINATHAN
Research Group Lead, MitoSENS

DR. ABDELLHADI REBBAA
Research Group Lead, RepleniSENS

DR. AMIT SHARMA
Research Group Lead, ApoptoSENS

The SRF team is composed of mission-driven individuals who are the building blocks of our future. They work tirelessly toward our goal of ending age-related disease.

DR. MARCELA ATZORI
Research Associate

JESSICA BLAIR
Outreach Coordinator

KATRINA BOEMMEL
Accounts Payable Clerk

ANNE CORWIN
Facilities Manager
Cancer and heart disease kill 80% of us. Curing either only gets us 3 extra years of life, because the next thing kills us. We can do better than curing either by focusing on repairing the damage early! Every year billions of dollars go into research that, at the very best, maxes out at 3 years of value — while research that could get us more than 3 years of healthy life goes unfunded!

We have a chance for outsized returns because while other research has billions put into it, rejuvenation research doesn’t yet — your dollars can have more impact.

- Richard Heart

HIGHLIGHT:

NIH National Institute on Aging

SENS Research Foundation & Cyclarity Therapeutics awarded a $252,000 Grant by the National Institute on Aging.
INCOME

Corporate Donations: $76,412
Other: $469,930
Foundation Grants: $1,486,500
Individual Donations: $5,685,487
Crypto: $22,370,396
Total: $30,088,725

EXPENSES

Education: $718,336
Outreach: $1,039,636
Admin: $1,128,002
Research: $2,665,840
Total: $5,551,814
Support our combined
LONGEVITY

Donate via:

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BITCOIN, ETHEREUM, and other digital currencies
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AMAZON SMILE
EBAY FOR CHARITY
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Mountain View, CA 94041

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LinkedIn: /company/sens-foundation
In addition to conducting research, SENS Research Foundation invests in the future of regenerative medicine by providing funding and support to promising biotechnology startups.

**Repair**

By safely breaking down excess cholesterol, we believe that CDP can repair the failure of reverse cholesterol transport that is at the heart of atherogenesis. Rather than accumulating to make macrophages dysfunctional, excess cholesterol will instead be catabolized.

**Ichor**

Ichor is a diversified longevity therapeutics company founded by SRF alumnus Kelsey Moody. Their lead LYSOCLEAR is a LysoSENS therapy for age-related macular degeneration, founded on technology transfers from SRF.

**Revel**

Spun out from Yale to turn SRF-funded fundamental research on the AGE crosslink glucosepane into working GlycoSENS rejuvenation biotechnology to reverse the stiffening of the arteries by aging.

**Oisín**

Seed funding from SRF and the Methuselah Foundation launched Oisín Biotech, a longevity therapeutics startup that uses licensed liposome technology and a patent-pending DNA construct to deliver “suicide genes” that trigger the self-destruction of senescent cells.

**Cyclarity**

A promising small-molecule approach to removing 7-ketocholesterol from foam cells, the drivers of atherosclerosis, to prevent and reverse humanity’s number one killer.

**Covalent**

SRF funded successful research to engineer candidate AmyloSENS therapies to precisely bind and cleave wild-type transthyretin amyloidosis, a major driver of heart failure in people at the extremes of current lifespans.
Our first virtual Donors Appreciation Event was held via the exVO VR platform in January 2022. Nearly 300 attendees joined our full staff, Board members, and co-founders to share perspectives, network, and celebrate in gratitude to our generous donors.

“Since our founding days, we’ve seen a dramatic shift in the mindset of the public regarding longevity science.

Outreach, as an ongoing, dynamic dialogue between SRF and the rest of the world, has been a critical factor in this shift.”
Some of the events we’ve been a part of...

WebMD
- February 18th, 2021

Ask Me Anything Webinar
- April 23rd, 2021

Canadian Undergraduate Technology Conference (CUTC)
- July 24-25th, 2021

Maximon-Longevity Investors Conference
- September 27, 2021

RAADfest
- Oct 1-3, 2021

Future Summit #TransVision 2021: Madrid, España
- October 7th, 2021

Gerontological Society of America 2021 Annual Scientific Meeting
- November 10-14, 2-21

35th Annual Conference of Aging Interventions – Society for Neurochemistry India
- December 2-4, 2021

The Darwin International Conference
- December 2-5, 2021
SRF was founded to operate at the forefront of innovation in medical research—a core philosophy that has guided our every move since 2009. We exist to pursue the critical work that nobody else is doing yet because it either falls outside the quick profit-securing model private industry relies on, or beyond the threshold of what more traditional institutions consider a “safe bet”.

As such, it seems appropriate that our most successful fundraiser to date ($26,546,283) emerged out of the cryptocurrency space, an exciting new frontier in its own right.

In July 2021, HEX founder Richard Heart—a long-time SRF supporter—created a new currency, Pulse. Via the Pulse Chain Airdrop, participants made a “sacrifice” (donation) to SENS Research Foundation in exchange for a chance to earn Pulse.

Donors were able to make their tax-deductible contribution in any currency, including crypto, credit, stock, and fiat; SRF then liquidated gifts for their USD values and sent those values to Richard so he would be able to determine how much Pulse people had earned.

It was a new way of doing things that meant we had to absorb a lot of information in a very short period of time, but as all our supporters would surely agree, time is of the essence when you’re fighting aging!

We cannot thank Richard (and everyone involved in making the ensuing campaign possible) enough. We are honored beyond words that our organization was selected to receive this incredible windfall.

We take seriously the responsibility to make sure the gift is used to directly enable more research in more crucial areas necessary to accelerate the pursuit of effective health-sustaining, life-extending medical breakthroughs.

…it gives me great pleasure knowing that we were able to support an organization committed to extending human life. We hope our cryptocurrency donation will spur other digital coins to step up their support for life-changing research.

- Richard Heart, in EIN Newswire
Richard Heart’s support for the SENS paradigm goes all the way back to 2006, and he is a longtime proponent of longevity medicine in general. In addition to being an integral part of SRF’s community, his many successful roles include entrepreneur, author, YouTuber, keynote speaker, and philanthropist.

Heart is also widely known in the crypto industry for his astute advice, particularly when it comes to scam avoidance. He is also the founder of HEX, the world’s first Blockchain Certificate of Deposit, which has enabled many to receive incredible return on their investments via HEX. This has, in turn, opened up a whole new avenue for charitable giving.

Cryptocurrency offers people alternatives to the traditional financial system; within this context, HEX replaces savings accounts that charge people high levels of interest. Put simply, investors “stake” or hold their coins for a fixed time period, and once their stake expires, HEX pays the investors the interest they are owed. As the ‘lock down’ period increases, so does the return on investment.

More recently, Heart founded the PulseChain Airdrop network, which as many of our supporters know, raised an astounding $27 million for SENS Research Foundation in summer 2021. His decision to direct his followers (often called Hexicans) to donate to SRF through the Airdrop not only drew in a new, enthusiastic support base, but acted as a megaphone to spread the word about the critical importance of regenerative medicine to a wider audience than ever before.

PulseChain was created by copying the Ethereum network, allowing for faster, easier, and more environmentally friendly transactions. Anyone who owned coins on the Ethereum network – including all currencies and NFTs – would see their coins inflated by at least x10,000.

Heart also gave free HEX coins to Bitcoin holders, which required them to stake or hold their coins. People who claimed HEX as Bitcoiners received 20% extra bitcoin value on their net worth.

This combination of financial incentive and philanthropic generosity came together and delivered for SRF on an absolutely unprecedented level, and we are beyond grateful to Richard for his initiative and hard work on this front.

...there’s nothing more important than healing the people. People are so important, that we actually generated the concept of importance. And the concept of importance dies with us.

- Richard Heart, via YouTube
Research Integrated Science Education
During 2021, SRF launched a new RISE teaching module, “How does cellular senescence affect health?” This module explores the phenomenon of cellular senescence and its proposed role in aging and disease. Interactive activities and discussion slides help guide students in evaluating published senescence-related research. The module features videos presenting both senescence-specific concepts (such as induction and biomarkers) and essential laboratory protocols, i.e., Quantitative Polymerase Chain Reaction Protocol and Immunofluorescent Staining Protocol.

Dominican Master of Biological Sciences
In 2021, Dr. Amit Sharma welcomed his first graduate student into his lab, Ashley Brauning. Her thesis will investigate the accumulation of age-related senescent cells and senescence-related biomarkers.

Postbaccalaureate Fellowship Program
Six recent college graduates served fellowships at the Buck Institute for Research on Aging, Harvard Medical School, the Sanford Consortium for Regenerative Medicine, Underdog Pharmaceuticals, and the SRF Research Center. Postbaccalaureate research projects sought to contribute to the development of therapies for Alzheimer’s Disease, atherosclerosis, brain cancer, age-related senescence, and lung inflammation in older COVID-19 patients.

Summer Scholars
During 2021, a total of thirteen students interned at the Buck Institute for Research on Aging, Harvard Medical School, Rubedo Life Sciences, the Sanford Consortium for Regenerative Medicine, Stanford University, Underdog Pharmaceuticals, and of course the SRF Research Center. Research topics included Alzheimer’s Disease, atherosclerosis, brain cancer, cellular senescence, computational analysis of aging biomarkers, fibrosis, mitochondrial dysfunction, and pulmonary disease.
Summer Scholars

2021 Postbaccalaureate Fellows
Madeline Howarth
Mohit Aspal
Ashley Brauning
Annalise Bracher
Jenny Ng

2021 Masters
Longsha Liu

2021 Summer Scholars
Alexandra Steinberg
Analise Betts
Caroline He
Chloe Lindberg
Emily Wallace
Jay-Miguel Fonticella
Julia Kooser
Julianna Quinn
Kevin Li
Laura Schmidt-Hong
Natalia Mendonca
Noa Petler
Sophia Epstein
ApoptoSENS: Building Better Ways to Destroy Senescent Cells

Senescent cells are damaged cells that accumulate in our tissues with age and undermine our health. Drugs that selectively trigger cellular suicide in these rogue cells have been developed, and shown to have sweeping rejuvenating effects in laboratory animals. When you treat mouse models of diseases of aging with senolytics, the onset of disease is pushed back — and in some cases, existing disease is reversed. Aging mice that are given these “senolytics” act and look like younger animals. Biotech startups have launched around the technology, and several senolytic drugs are already being tested in human clinical trials.

Two teams at SENS Research Foundation are working to improve on these early efforts, to fully reap the promise these studies inspire for the benefit of aging humans.

One ApoptoSENS team led by Dr. Amit Sharma is focusing on ways to harness the power of the immune system to help our bodies defend against senescent cells. We are born with cells in our immune system designed to detect and destroy senescent cells — but some senescent cells evade detection, and more and more of them are left behind as we age and our immunological sentries lose their edge. Dr. Sharma and his team are working on ways to revitalize these aging cells, and also to back them up with a SWAT team of souped-up, far deadlier (to senescent cells) engineered cells.

This first ApoptoSENS group is currently closing in on a short list of five proteins presented selectively on the surface of senescent cells. They will engineer immune cells to seek and destroy senescent cells that display the protein most indicative of a cell’s senescent state, and then test the engineered cells’ ability periodically to wipe the senescent cells out.

Additionally, Dr. Sharma’s team recently identified a small subset of immune T-cells that may be even more effective than the current best-in-class cells at targeting senescent cells. Dr. Sharma and his colleagues are working intensely to figure out how these cells do it, and how best to mobilize them to shield our health.

Meanwhile, Forever Healthy Fellow Dr. Tesfahun Admasu is focused on a recently-discovered subset of senescent cells that have turned out to be resistant to existing senolytic drugs, and finding new ways to take them down. A key way that senescent cells damage and destabilize the cells around them is by secreting a complex mixture of signaling molecules known as the SASP. One of the ways the SASP harms us is by acting as a medium for the transmission of senescence from existing (primary) senescent cells to the once-healthy cells around them. Like the bite of a zombie, the SASP turns once-healthy cells into “secondary” senescent cells, spreading a destructive legion across the aging body.

With help from other SRF ApoptoSENS researchers, Dr. Admasu has discovered that secondary senescent cells stubbornly resist bombardment by several of the best-known senolytics. But probing their metabolism, he discovered...
that these cells exhibit a little-known vulnerability – one that could be used to target primary cells. As proof-of-concept, the SRF researchers showed that an existing molecule that activates this pathway destroys both primary and senescent cells, while leaving healthy cells alone. While this molecule is not suited for human clinical use, SRF ApoptoSENS scientists are now testing other compounds that target the same pathway. They are confident that their discovery can be turned into a new class of senolytic drugs capable of taking out the hardest-to-target of all senescent cells in the aging body. The rejuvenation benefits of this achievement could well exceed anything thus far hinted at by animal studies of senolytics.

GlycoSENS: Repairing Damage to the Foundation of Cells

The extracellular matrix (ECM) consists of structural proteins that support cells and organs and carry out functions of their own. Damage to the ECM, and not just to cells themselves, is part of what drives the aging process. The most directly lethal site of ECM damage is the large artery responsible for cushioning organs like the brain and the kidneys from the incessant pounding of blood coming out of the heart.

One form of ECM damage is advanced glycation endproduct (AGE) crosslinks, which occur when neighboring proteins that are meant to move independently react with sugars and get linked together. This constrains the proteins’ range of motion, preventing them from carrying out their normal function.

Dr. Jonathan Clark’s GlycoSENS group at the Babraham Institute is diving deep into the effects of aging on the ECM. The resulting picture is complex, with an increase in irreversible crosslinks in the tendon with age, but also a progressive loss of reversible crosslinks that allow the tendon to adapt to and absorb force. Also unexpected are the effects of sugars that bind to the ECM without forming crosslinks.

Given that complexity, it’s unsurprising that the changes in the functional properties of aging ECM are also more complex than is generally appreciated, with different mechanical properties changing in different ways. Sorting all of this out will be essential to developing rejuvenation biotechnologies targeting the most impactful aspects of ECM damage with novel rejuvenation biotechnologies.
LysoSENS: Targeting Tau Inside Brain Cells

Alzheimer’s, other neurodegenerative diseases of aging, and “normal” age-related cognitive decline are associated with accumulation of a protein called tau in the neurons of the aging brain. Researchers have developed antibodies targeting abnormal tau in an effort to forestall, arrest, or reverse these conditions, but clinical trials have so far yielded disappointing results.

One reason for these failures is that they’ve used tau-targeting antibodies that bind to aggregates in the spaces outside of brain cells, failing to reach the aggregates within neurons where they inflict most of their harm. Another is that such binding antibodies only capture one tau aggregate at a time, and then must drag it back through the brain’s blood vessels in order to dispose of it. This is both inefficient and potentially harmful, as the antibody-aggregate complex interacts with the vessel wall during the removal process.

SRF’s aberrant tau LysoSENS team is developing next-generation biotechnology to overstep these limitations. Instead of conventional antibodies, they are using catabodies: catalytic antibodies that chop up their targets instead of merely binding to them. Whereas one binding antibody can only remove one tau aggregate, catabodies can cleave one aggregate and then move quickly on to the next. Since the target aggregate is broken down into harmless cellular debris, there’s no need to make the perilous journey outside of the brain.

Additionally, the team is using a new system to target the catabodies inside brain cells, where clearing tau aggregates has the greatest benefit.

LysoSENS: Molecular Wrenches to Dismantle Lipofuscin

Long-lived cells like heart and brain cells accumulate stubborn waste products as we age. Lipofuscin is the best-known of these wastes, and yet in many ways the least understood. While many other kinds of junk inside our cells are mangled versions of a single, defined protein, lipofuscin is a complex mixture of different materials from inside the cell, and has other properties that make it hard to study.

To finally get some real insight, SRF is funding Dr. Tilman Grune at the German research institute DIfE to isolate, characterize, and develop candidate rejuvenation biotechnologies against authentic lipofuscin derived from human hearts. He has developed a novel way to isolate this paradoxically precious waste without altering its chemical makeup, and is now applying multiple technologies to characterize it.

Meanwhile, Dr. Grune and colleagues have extracted microorganisms from different environmental sources, and given them nothing but lipofuscin as an energy source, so that only microbes with enzymes that allow them to digest lipofuscin will survive. From these experiments, his group has now isolated twelve strains of bacteria. They are now further investigating these strains and will isolate their specific enzymes. So far, it appears that the enzymes target sufficiently convoluted kinds of bonds that they are extremely unlikely to harm functional parts of the cell. After additional study, the most promising enzymes will be modified to target and work within the human lysosome, creating new rejuvenation biotechnologies to clear our cells of this stubborn waste.
RepleniSENS: New Neurons to Preserve the Brain

All our organs lose cells as we age, but nowhere is that loss as costly as in the brain’s neocortex. It’s the physical basis of our memories, emotions, and identities — and yet perversely, it’s not among the few regions of the brain that produce and receive new neurons. This challenge is exacerbated by the brain’s large surface area, the high risk of local injections to the brain, and the intrinsic properties of neurons as a cell type.

Dr. Jean Hébert of the Albert Einstein College of Medicine (AECOM) is making progress on a revolutionary strategy to fulfill this desperate need. He starts with microglia, a type of cell that helps maintain brain neurons. His team will engineer microglia to unwind their developmental state and begin life anew as neurons when given the right chemical signal. He will then administer a drug that makes room for transplanted, engineered microglia by killing off a significant number of the microglia already resident in the brain. This allows the therapeutic engineered microglia to quickly spread across the neocortex, turn into new neurons, integrate into local circuits, and strengthen the integrity of the brain.

His RepleniSENS lab has already achieved aspects of this in mice, and the group is now working with microglia derived from reprogrammed human cells. In the pilot studies, they used mice genetically engineered with a “suicide switch” that allowed the team to destroy the resident microglia at will. They are now developing a novel method that would do the same in nonengineered mice (and eventually humans), leaving the transplanted microglia unharmed and free to repopulate the opened spaces. Upcoming mouse studies will test the ability of engineered microglia to release the neuronal survival molecule BDNF, first in an animal model of Alzheimer’s disease and later in otherwise-healthy aging mice.

MitoSENS: Rehabilitating the Cellular Power Plants

Mitochondria are the power plants of our cells, producing the energy that fuels them. Unlike most other parts of the cell, mitochondria have their own independent DNA, which they use to produce necessary to their function. With age, increasing numbers of cells become dysfunctional as they are overtaken by mitochondria bearing large deletions in their mitochondrial genomes.

The MitoSENS group at SENS Research Foundation is pursuing two ways to overcome this problem. One is allotopic expression (AE): placing “backup copies” of the 13 protein-encoding mitochondrial genes into the safe haven of the nucleus. The cell’s backup AE copies could then provide the proteins needed for their mitochondria to keep running in spite of any mutations.

After a highly successful AE of the mitochondrial gene ATP8 to the nucleus in cells, and some progress with ND4 and ATP6, the MitoSENS team have now achieved a remarkable first: AE in the cells of a living, breathing mouse. The gene is properly expressed in the cells of multiple tissues, and the protein enters the mitochondria and slots into the cell’s energy-generating machinery. This is a critical step in the process of turning AE into a working rejuvenation biotechnology for humans.

The MitoSENS team is also working on a system that will allow them to transplant whole mitochondria with specially-engineered genomes into cells. These enhanced mitochondria will be able to seek out and destroy any mutant mitochondria already present in the cell, thus replacing them with healthy dominant mitochondria and restoring normal function to the cell.
Degenerative aging is caused by the accumulation of multiple kinds of cellular and molecular damage in our tissues over time. So securing lives of indefinite youthful health will require the removal, replacement, and repair of many kinds of damage, not just one. And yet to date, nearly all experimental studies of rejuvenation biotechnologies test just one therapy in isolation.

Cases in point: on the one hand, our bodies lose cells with age — both the cells that directly carry out functions in our organs, and the stem cells that renew some (though not all) of our aging tissues. On the other hand, we accumulate damaged cells that actively undermine our health, such as senescent cells. Irony aside, this juxtaposition of insults is ruinous to our health.

Senolytics (ApoptoSENS) and stem cell transplantation (repleniSENS) are two of the most well-established rejuvenation biotechnologies in mouse models, and are also a complementary match: out with the old, and in with the new! The StenoStem team at SENS Research Foundation will use highly selective senolytics to destroy senescent cells in aging mice, and follow this up with transplantation of young mesenchymal stem cells (MSCs), which both replace some functional cells in the body and restore a healthy signaling environment. Each of these treatments is known to have rejuvenating effects in mice; for the first time, our SenoStem scientists led by Dr. Hadi Rebbaa will demonstrate their combination, and reveal their potential for synergistic rejuvenating effects.

2021 Publications:


For an extensive description of our research, please read our 2022 Research Report.
SRF RESEARCH ADVISORY BOARD

DISTINGUISHED SPECIALISTS AND WORLD-RENOWNED EXPERTS GUIDE OUR RESEARCH BUDGET AND ENSURE FOCUS ON PROJECTS WITH THE GREATEST POTENTIAL TO MAKE MAJOR BREAKTHROUGHS IN AGE-REVERSING BIOMEDICINE.