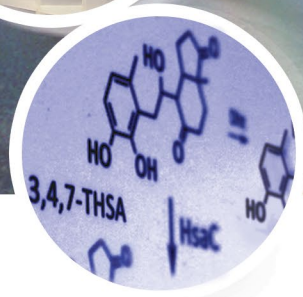
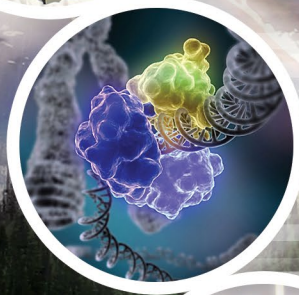
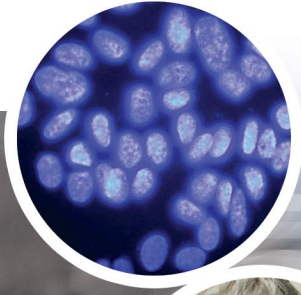


sens research foundation

reimagine aging



annual report

april 2013

contents

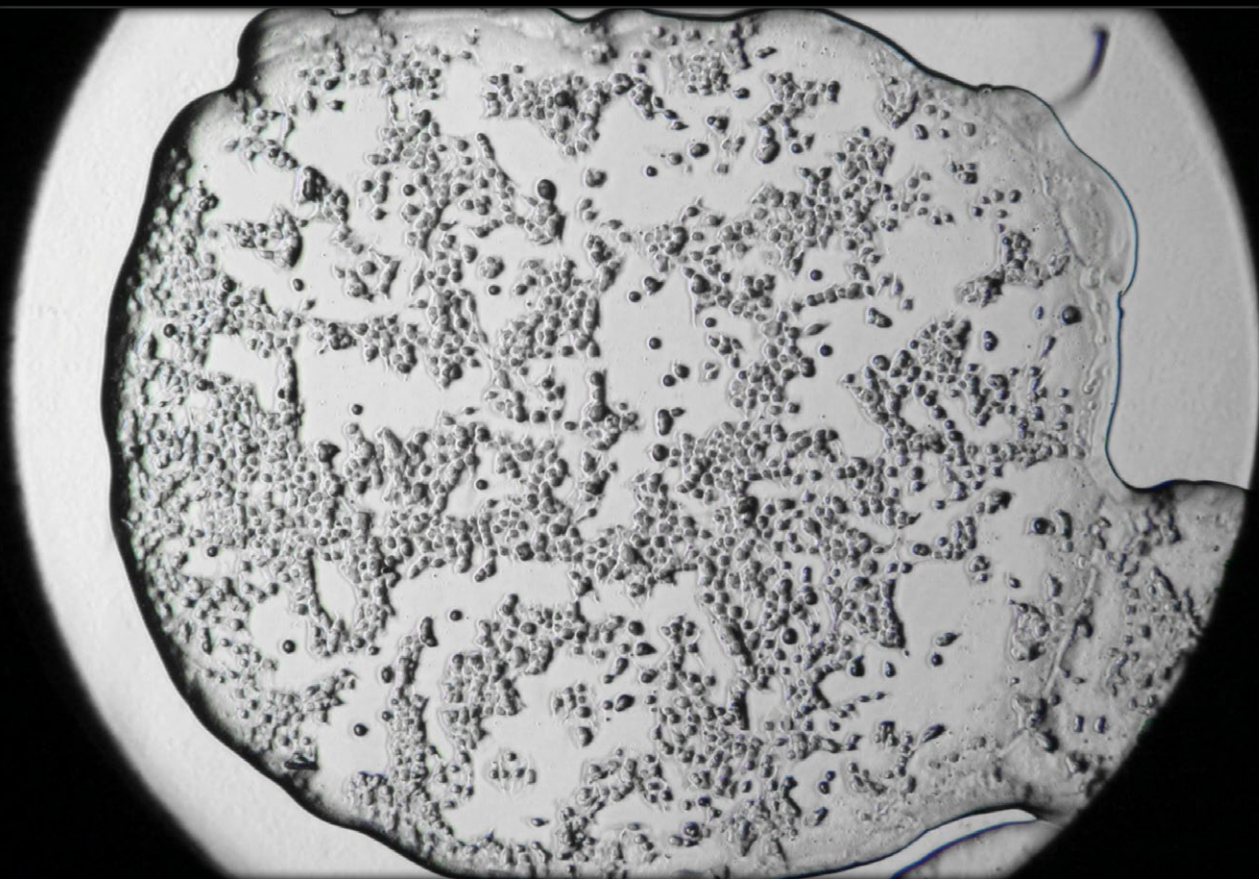
Introduction 2

Research Summary 3-10

Outreach 11-14

Education 15-16

Finances 17-18



sens research foundation - 110 Pioneer Way, Suite J - Mountain View, CA 94041 - USA
phone: 650-336-1780 - fax: 650-336-1781 - www.sens.org

Chief Executive Officer
Mike Kope

Chief Science Officer
Aubrey de Grey

Chief Operating Officer
Tanya Jones

Board of Directors
Jonathan Cain
Kevin Dewalt
Bill Liao
Barbara Logan
James O'Neill
Kevin Perrott
Mike Kope

© 2013, SENS Research Foundation

All rights reserved.

No part of this material may be reproduced without specific permission from SENS Research Foundation.

SENS Research Foundation's federal employer ID number is 94-3473864. Because SENS Research Foundation is a 501(c)(3) non-profit, your donation may be tax deductible.

reimagine

A world free of age-related disease

“The biggest driver of our long-term debt is the rising cost of healthcare for an aging population.”

– President Barack Obama’s 2013 State of the Union address¹

The United States will spend more than one trillion dollars on healthcare for seniors this year.² Heart disease, the greatest of the US’s health problems, has recently become the developing world’s biggest killer as well.³ The economic crisis noted in the President’s decisive comment is not ours alone: it is everyone’s. Meanwhile, the worldwide suffering caused by the diseases of aging remains too high to measure by any standard.

Of course the problem is not unnoticed. There is an immense amount of research being poured into the development of treatments for age-related disease. Gerontological research foundations and institutions are increasingly focusing on translational research, and the word ‘healthspan’, once a bit eccentric, is now in wide use.



Aubrey de Grey - CSO

Mike Kope - President, CEO

This is all good news, in itself, and we ourselves have been a member of the Healthspan Campaign since its inception.⁴ But an expressed focus on healthspan does little to define a biomedical organization’s work – enhancing human health is, after all, the fundamental purpose of medicine itself. To really do something about aging, we need to refocus at least some of this growing energy into attacking not only the pathologies of aging, but their underlying causes.

There is only one charity in the world doing the work – scientific, educational, and outreach-based – to address those causes.

Please, take a moment and reimagine aging with us.

Start by imagining a cure for cardiovascular disease.⁵ Bypass surgery is obsolete, and heart attacks and stroke no longer occur. It may not be easy to find such a cure, but it is possible, and that is why SENS Research Foundation exists. Treatments that could actually, truly, effectively repair the damage behind heart disease -- not just treat symptoms or stave off the inevitable -- could absolutely emerge, given the right research and development. It is simply that this particular branch of biomedical R&D is critically under-funded. We’re changing that.⁶

Now try to imagine a cure for *any* age-related disease: Alzheimer’s, diabetes, macular degeneration, arthritis, perhaps even cancer. It isn’t impossible. But the work required to bring about these cures is, again, critically under-funded.

With a little help, and a little imagination, we can change that, too.

1: Transcript at http://articles.washingtonpost.com/2013-02-12/politics/37059380_1_applause-task-free-enterprise

2: Deloitte’s full report at http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us_dchs_2012_hidden_costs112712.pdf

3: From the WHO at <http://www.who.int/mediacentre/factsheets/fs317/en/index.html> -- full report available at http://www.who.int/nmh/publications/ncd_report_full_en.pdf

4: <http://www.healthspancampaign.org/media-center/press-release/new-healthspan-campaign/>

5: SRF’s animation at <http://sens.org/research>

6: Information on SRF’s research at <http://sens.org/research>

Research Summary

intramural projects

Lysosomal Aggregates

SENS Research Foundation Research Center,
Mountain View CA

Researchers: Gouri Yogalingam, Ghezal Beliakoff, Maximus Peto

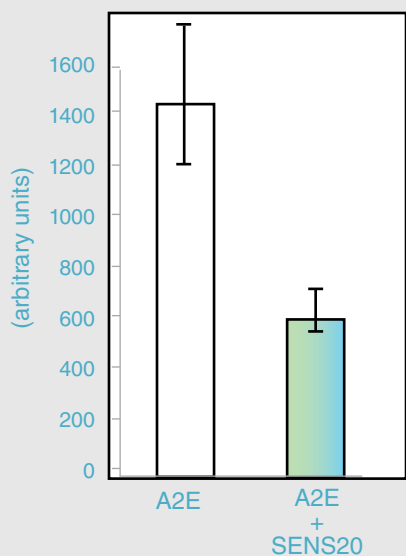
Cells are equipped with “incinerators” called lysosomes, where they send damaged or unwanted material for destruction. But some cellular wastes are so chemically snarled that even the lysosome is unable to shred them. With no way to eliminate these compounds, the cellular garbage simply builds up over time, progressively interfering with cell function.

The disabling of specific cell types by their characteristic waste products drives numerous age-related diseases. For instance, age-related macular degeneration (AMD) — a major cause of blindness — is believed to be primarily caused by the accumulation of the waste A2E in the retinal pigment epithelial (RPE) cells of the eye.

Identifying enzymes in other life forms that can degrade such wastes, and modifying these enzymes so they can be delivered to — and function in — our own lysosomes, would restore cellular function and prevent or reverse these diseases.

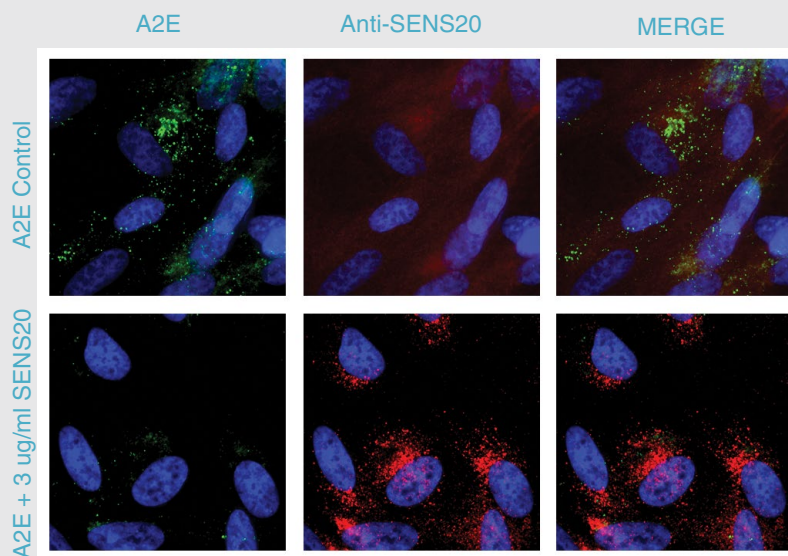
At the SENS Research Foundation Research Center (SRF-RC), our Lysosomal Aggregates team is working to efficiently deliver promising A2E-degrading enzymes identified in our earlier research into the lysosome of cells. One in particular (SENS20) has demonstrated tremendous efficacy in degrading A2E not only *in vitro* but in A2E-loaded RPE cells.

In 2013, the team will put a recombinant form of SENS20 to the test, assessing its ability to degrade A2E *in vitro* and in RPE cells, and verifying that it is not toxic to the cell.



Efficacy of SENS20 enzyme
in degrading A2E *in vitro*

Synthesis and purification of A2E → Uptake into RPE cells → Lysosomal uptake analysis after two days of recovery



Efficacy of SENS20 enzyme
in degrading A2E *in vivo*



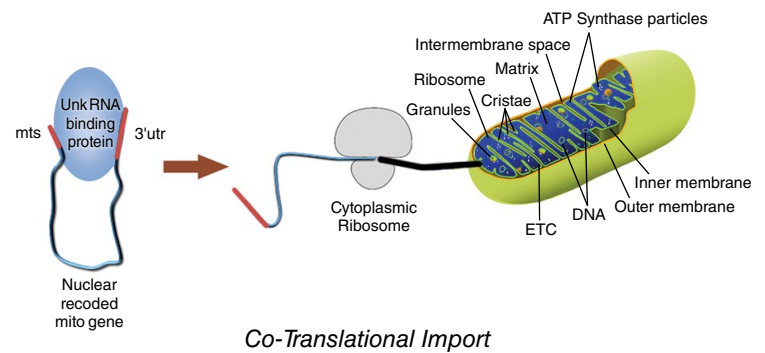
Mitochondrial Mutations

**SENS Research Foundation Research Center,
Mountain View CA**

*Researchers: Matthew O'Connor, Amutha Boominathan,
Jayanthi Vengalam*

Our cells' energy-producing mitochondria are at constant risk of major mutations in their internal genes, because they are housed close to where the mitochondria produce both cellular energy and the toxic byproducts of its generation. The Research Center's Mitochondrial Mutations team is working to engineer "backup copies" of vulnerable mitochondrial genes, located in the safer location of the cell's nucleus. This would let mitochondria keep producing energy normally, even after mitochondrial mutations have occurred.

SRF-RC scientists are now working to master and refine a superior method for accomplishing this goal. Our team has taken four cell lines from patients suffering from severe diseases caused by inherited mitochondrial mutations and made stable lines that express their improved mitochondrial gene constructs. They have begun collecting data confirming the targeting of gene transcripts and proteins to their mitochondrial locations, and the functional activity of the mitochondrial energy system, in such re-engineered cells.



Cancerous Cells

**SENS Research Foundation Research Center,
Mountain View CA**

Researchers: Haroldo Silva, David Halvorsen, Kelsey Moody

Cancer is a disease of unlimited cellular division. Healthy cells have a built-in limit on the number of times they can divide: with each division a stretch of DNA called the telomere progressively shortens, until it becomes so short that it prevents the cell from dividing or kills it outright. To bypass this limit, would-be cancer cells must exploit one of two escape systems. The most common method is to activate the gene for an enzyme called telomerase, which re-lengthens shortened telomeres. The other, less common approach is to activate a poorly-understood system known as alternative lengthening of telomeres (ALT). The goal of the SRF-RC's Cancerous Cells project is to identify the mechanisms of the latter and to use this knowledge

to disrupt the system, opening up the power to strongly suppress cancer.

Our team is screening several cancer cell lines, looking for cells that display ALT behavior, in order to test whether they are exploiting specific candidate ALT genes. The most effective way to identify such cells is by the extrachromosomal C-rich circular telomeric DNA (C-circles) that they generate.

Our researchers have recently developed an innovative version of the standard, radioisotope C-circle assay that instead uses a non-radioactive digoxigenin (DIG)-labeled probe, and are also working to establish new protocols for ALT-associated PML nuclear bodies, another key marker of ALT activity. Establishing these two assays is a critical step towards deciphering the molecular mechanisms behind ALT, developing novel diagnostics, and finding ways to shut ALT cancers down.

Research Summary

extramural projects

Extracellular Matrix Stiffening

Yale University, New Haven CT, and SENS Research Foundation Laboratory, Institute of Biotechnology, University of Cambridge, Cambridge UK

Researchers: David Spiegel (Yale); Chris Lowe, William Bains, Rhian Grainger, Graziella El Khoury (SENS Research Foundation/ Cambridge)

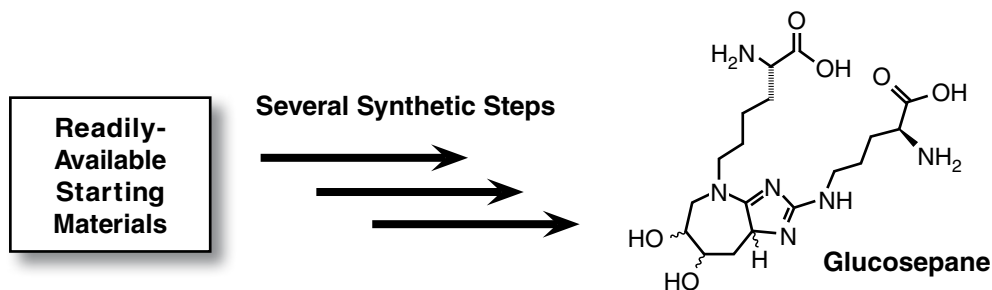
Our arteries slowly stiffen with age, in substantial part because of chemical crosslinking of their structural proteins by sugar and other fuels that circulate in the blood. This stiffening makes arteries progressively less effective at cushioning organs like the kidneys and the brain from the relentless pounding of the pulse and also leads to an insidious rise in systolic blood pressure with age. Put together, these effects contribute to the age-related erosion of the kidneys' ability to filter toxins out of the blood and drive the rising risk of disabling stroke and dementia.

Late in 2012, we announced the establishment of our new SENS Research Foundation Laboratory in partnership with the University of Cambridge Institute of Biotechnology. In collaboration with Dr. Spiegel's lab, the SRF Cambridge

center will initiate work on new agents to cleave apart crosslinked proteins, restoring youthful elasticity and buffering capacity to arteries. The specific molecular target will be glucosepane, the main crosslink that accumulates in aging human arteries and other tissues.

Dr. Spiegel has already developed a way to synthesize glucosepane in the lab; this artificially-produced glucosepane can now be used to develop reagents that can rapidly and specifically detect proteins that have been crosslinked by it.

The Cambridge group has been working on methods of extracting crosslinked proteins intact from the tissues of dogs and marmoset monkeys and to measure glucosepane cleavage in the test tube and in animal and human tissues. It is clear from this research that none of the commercially-available monoclonal antibodies against related crosslink molecules are able to cleave glucosepane to any significant degree, and many are useless. All of these findings further emphasize the importance of this project in developing novel crosslink-breaking therapies.



Making Glucosepane. *The Spiegel group's approach to making glucosepane. Two low-cost, common laboratory chemicals are combined in several steps to give the precursor to glucosepane, which can easily be used to make glucosepane itself or peptides.*



Lysosomal Aggregates

Rice University, Houston TX

Researchers: Pedro Alvarez, Jacques Mathieu, Jason Gaspar

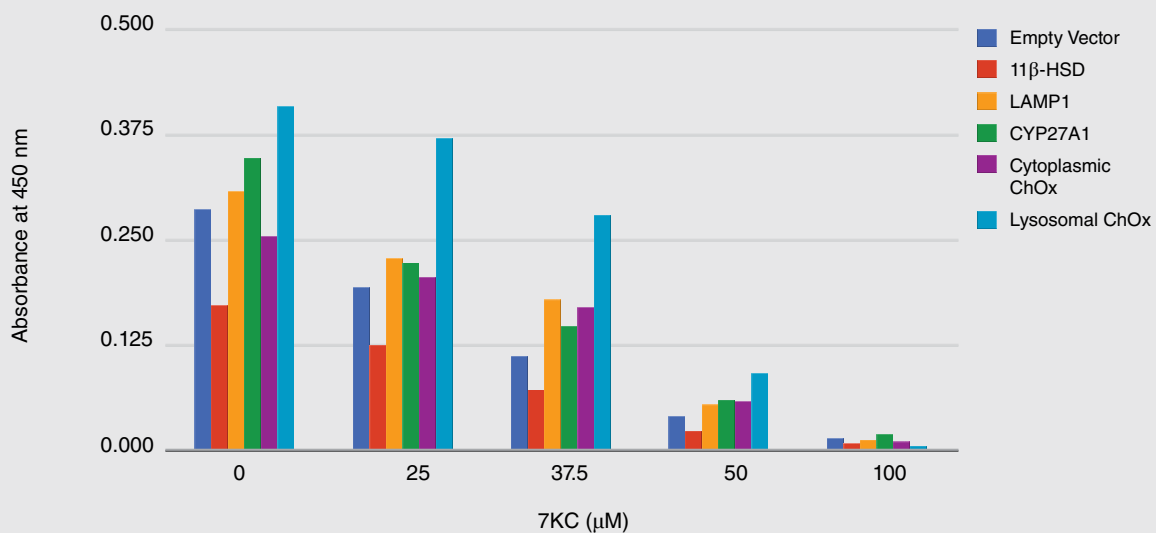
Atherosclerosis, like macular degeneration, is ultimately a disease of accumulating waste inside the lysosome. In this case, the crippling waste is composed of damaged products of cholesterol lipoproteins, such as 7-ketocholesterol (7KC). These products impair the lysosomes of the very immune cells (macrophages) that are recruited to the arterial wall to protect against them. Dysfunctional and dying macrophages go on to become the “foam cells” that are the basis of atherosclerotic plaques.

Our team at Rice University is working to develop novel enzymes to clear 7KC and other oxidized cholesterol products out of the lysosomes of macrophages and foam cells, restoring them to normal function and beginning the reversal of the atherosclerotic process. In 2012, Dr. Mathieu’s group showed, for the first time, that a novel cholesterol-metabolizing enzyme

could protect human cells against 7KC toxicity. Called DS1, this enzyme was almost unique in its ability to degrade both cholesterol and 7KC in preliminary testing *in vitro*. To test its ability to detoxify 7KC in human cells, the Rice team modified DS1 to hitch a ride on the shuttling vesicles that carry cargo to the lysosomes.

Dr. Mathieu *et al* showed that their lysosomally-targeted DS1 is very effective at protecting human fibroblast cells from the toxic effects of 7KC – substantially more powerful than either alternative cholesterol-metabolizing enzymes or DS1 targeted to the main cellular compartment instead of to the lysosome specifically.

In ongoing work, Dr. Mathieu *et al* are performing studies that involve altering the structure of many existing cholesterol-degrading enzymes to increase their activity towards 7KC. They are also testing the effects of novel enzymes that would remain active in the lysosome even if it had lost its normal acidity due to poisoning by 7KC.



Lysosomally-Targeted DS1 Cholesterol Oxidase Protects Against 7-Ketocholesterol Cytotoxicity in Human Fibroblasts. Higher absorbance at 450 nm indicates greater numbers of viable cells. Redrawn by SENS Research Foundation volunteer Alex Foster.

Research Summary

extramural projects, continued

Cancerous Cells

**Albert Einstein College of Medicine (AECOM),
Bronx NY**

Researchers: Jan Vijg, Silvia Gravina

Over time, cells suffer permanent damage (mutations) to the DNA code, and also damage (epimutations) to the “scaffolding” of DNA, which helps the cell to control which genes are turned on or off. While it is certain that mutations and epimutations play a major role in cancer, it remains controversial whether they also contribute to other age-related diseases and tissue dysfunction.

Answering these questions requires reliable ways to quantify the rate of accumulation of epimutations in single cells. Single-cell assays are necessary because many cells in a tissue will “intentionally” change their epigenetic state at once in response to a changing environment, whereas truly

random changes in the epigenetic state of cells will occur in each cell independently of its neighbors.

Dr. Gravina and coworkers in Vijg’s group have now successfully adapted the existing “bisulfite sequencing” method for evaluating a particular kind of epigenetic modification (DNA methylation), either at specific loci (such as the promoter regions of defined genes), or at thousands of methylation sites across the entire genome. The new assay will allow researchers for the first time to come to reliable answers about the role of epimutations in aging.

The AECOM group will now begin studies that apply their assays in the mouse brain. The technique could also become the basis of sophisticated new diagnostic technologies for the “epityping” of cancers (and potentially other diseased tissues). A patent and a publication are currently pending for this development.

Extracellular Aggregates

**University of Texas, Houston TX, and Brigham and
Women’s Hospital, Harvard University, Boston MA**

Researchers: Sudhir Paul, Yasuhiro Nishiyama, Stephanie Planque (University of Texas); Brian O’Nuallain (Brigham and Women’s Hospital, Harvard Medical School)

As part of the degenerative aging process, proteins that normally remain dissolved in bodily fluids become damaged and adopt an abnormally clumped form called amyloid. Amyloid clumps are toxic and hard for the body to break down, and they accumulate in deposits that build up in various organs with age, disrupting organ structure and impairing function. Amyloid composed of the transporter protein transthyretin (TTR) deposits in the heart and other organs with age. TTR amyloid begins to impair heart function in 20-25% of individuals over the age of 80 and is increasingly

prevalent at later ages. The teams at Texas and Harvard are working to develop diagnostic and therapeutic antibodies that would recognize and remove and/or degrade TTR amyloid deposits from tissues, preventing or reversing its contribution to age-related heart dysfunction and failure.

To generate potential therapeutic TTR-targeting antibodies, Dr. O’Nuallain immunized three different strains of mice using either TTR amyloids made from the normal, non-mutant form of TTR or mutant TTR that was not in its amyloid state, or both. After production on a larger scale in hybrid cells, the candidate antibodies were turned over to Dr. Paul, who tested their ability to cleave “synthetic” TTR amyloid suspensions. One (TB5B11) looks especially promising, being apparently effective in degrading TTR amyloids without attacking physiological TTR.

Cancerous Cells/Cell Loss and Atrophy

Wake Forest Institute for Regenerative Medicine (WFIRM),
Winston-Salem NC

Researchers: Graça Almeida-Porada, Christopher Porada

At Wake Forest, SENS Research Foundation is funding Dr. Graça Almeida-Porada's group in a project to restore intestinal structure and function. Dr. Almeida-Porada's central goal in this project is the development of a regenerative medicine approach to treating inflammatory bowel disease (IBD), an autoimmune disorder that devastates the cells lining the intestine.

The WFIRM team is developing a combination cell therapy using two kinds of stem cells: engineered marrow stromal cells (MSC) and endothelial progenitor cells (EPC). With

a safer minicircle method now being used to deliver an enhancing gene for the MSC, and with ongoing work on a higher-expression construct to improve the utility of the MSC, the researchers will begin testing the engineered cells' ability to reset the inflammation and restore the blood vasculature cells in the intestinal walls. They will do this using a highly reproducible and established mouse model of IBD.

Though IBD is not itself a disease of old age, SENS Research Foundation is supporting this work because therapies that repopulate the cells of the gut are critical to the development of the dramatically superior cancer therapies that we are pursuing. These therapies would deplete the stem cell reserves of several tissues, meaning that clinicians will need a way to rebuild those stores with fresh stem cells.

Cell Loss and Atrophy

Wake Forest Institute for Regenerative Medicine,
Winston-Salem NC

Researchers: John Jackson, Shay Soker, James Yoo

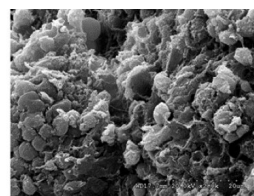
The thymus is a gland located at the top of the breastbone, where a class of immune cells called T-cells mature. As part of the degenerative aging process, the thymus shrinks in size; and the structure and function of the remaining tissue decays, progressively weakening the body's ability to fight off never-before-encountered infections. Thymic atrophy is one of the reasons why we become increasingly vulnerable to influenza, pneumonia, and other infectious diseases as we age. Engineering healthy, youthful thymic tissue would help to restore the vigorous immune response of youth.

The Jackson lab is now extending an exciting tissue engineering platform to the thymus: the decellularized scaffold technique. In this method, donor organs are purified of their original cells and DNA, leaving behind an amazingly complex non-living protein structure which can be repopulated with cells taken from the recipient of the engineered neo-organ.

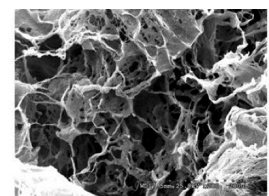
Already, the WFIRM team has produced thymus scaffolds

from mice and pigs. Epithelial cells have been seeded onto these scaffolds, leading to stromal cell proliferation and partial coverage of the scaffolding, which the researchers are now characterizing. To complete the reseeding procedure, bone marrow stem cells depleted of T-cells will be added to the epithelial-cell-seeded scaffold, and the production of new T-cells will be observed.

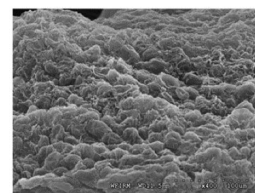
Once the initial characterization of the scaffolds has been performed, the engineered thymus will be transplanted into mice lacking one of their own, and researchers will evaluate their T-cell production capacity and the functional properties of the resulting cells.



Normal Thymus



Decellularized Thymus



Recellularized Thymus

Research Summary

extramural projects, continued

Death-Resistant Cells

Buck Institute for Research on Aging, Novato CA

Researchers: Judith Campisi, Kevin Perrott, Sam Curran, Nick Schaum

Cellular senescence is an abnormal metabolic state that cells sometimes enter in response to stressors that put the cell in danger of cancerous and other forms of excessive growth, and is first and foremost a state in which cells irreversibly stop dividing. However, senescence also affords these cells resistance to signals for apoptosis and induces the adoption of the senescence-associated secretory phenotype (SASP), in which they secrete numerous inflammatory signaling molecules and protein-degrading enzymes into their local environment.

SASP is thought to play a role in the chronic inflammation that is widespread in aging tissues and promotes the progression and propagation of not only the many diseases of aging, but the more generalized rise in frailty that limits mobility and independence with age.

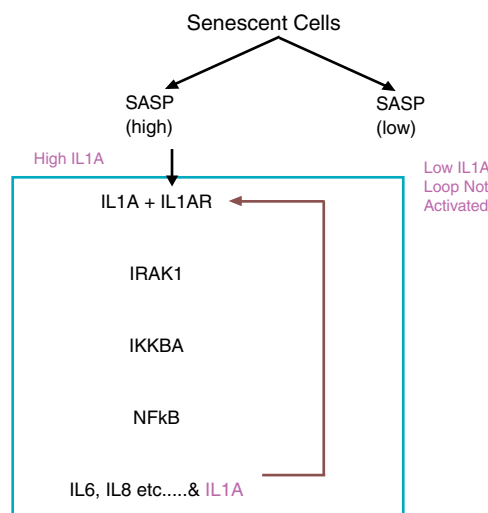
With funding from SENS Research Foundation, scientists at the Buck Institute have been screening small molecules for their effects on fibroblasts (a kind of skin cell) that have been rendered senescent by ionizing radiation in vitro. Their aim is to identify agents that could interrupt the SASP

and its downstream effects, or selectively kill senescent cells. Such agents could potentially ameliorate diseases and disabilities of aging that are driven by the SASP.

In 2011, the team identified the natural phenolic compound apigenin as an effective SASP inhibitor in these cells. Last year, they performed several studies characterizing the mechanisms underlying apigenin's effect. They discovered that apigenin downregulates expression of the genes for the various SASP factors (rather than, say, making the factors less stable) and generated evidence that it does so via the stress-inducible protein p38. This protein in turn reduces the activity of the transcription factor nuclear factor kappa-B (NFκB), which induces many components of the SASP.

Additionally, apigenin interrupts a vicious circle in which a component of the SASP can feed back to further increase SASP secretion. Its effects so far do not seem to involve modulation of the DNA damage response.

Separately, the resolution of some intellectual property issues will now allow Buck researchers to resume screening a library of natural compounds for their effects on SASP. They have also begun investigating the causes of senescence in mesenchymal stem cells.





Enabling Technology: Maximally Modifiable Mouse

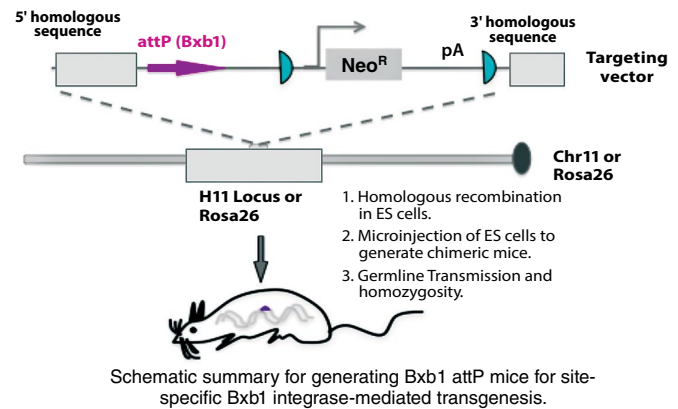
Applied StemCell, Inc, Menlo Park CA

Researchers: Ruby Yanru Chen-Tsai, Jiabin Qiu, Qi Zheng, Ivy Zhang

In many cases, it will be convenient to perform initial testing of rejuvenation biotechnologies by engineering the genes for therapeutic proteins into mouse models. Regrettably, projects involving germline genetic modification of mice are by their nature lengthy efforts, and the delay is even greater when the modification needs to be tested for its ability to rejuvenate aging mice. This is because the mice must first be engineered with the transgenes as embryos, and then be born, weaned, and raised into adulthood for two or more years before any testing can be attempted.

If a mouse could be engineered to readily take up significant genetic modification at any point during its life, it would substantially contract the timeline needed to gather critical data regarding the effectiveness of applied interventions. A promising alternative to conventional mammalian-virus-based somatic gene therapy is the use of phage integrases from viruses that infect bacteria, to

catalyze precisely-targeted, one-way insertion of genes into the host genome. The phage integrase from the mycobacteriophage Bxb1 is extremely precise and has already been demonstrated to be a highly effective tool for somatic gene therapy in fruit flies. Unfortunately, mammals lack the sites in their genomes that this integrase targets. The Maximally Modifiable Mouse project aims to generate a new line of transgenic mice with the needed site engineered into their genomes. The Bxb1 integrase system could then be used at any time during the mice's lifespan to insert therapeutic genes of any size into their genomes, with no risk of mutational disruption of their own genes and with rapid testing turnaround times.



Rejuvenation of the Aging T-Cell Pool

University of Arizona College of Medicine and Arizona Center on Aging, Tucson, AZ

Researchers: Janko Nikolich-Zugich, Megan Smithey

As part of the degenerative aging process, the immune system becomes progressively weaker over time, and we become terribly vulnerable to infectious disease. One key suspect is the expanding pool of old T-cells that will only target a long-fought foe, and that gradually “crowd out” T-cells that are specialized in fighting other pathogens. Another is the gradual shrinkage and decay of the thymus gland, whose job it is to help generate new T-cells. This study was a rough pilot of several potential approaches to redressing those deficits.

Mice in the experimental groups were first infected with one

of two persistent viral infections that are known to add to the development of anergic T-cell clones: herpes simplex virus or murine cytomegalovirus.

Groups then received different treatments, including the depletion of their old T-cell populations and the infusion of young, naïve T-cells at different time points. Each mouse was then vaccinated against West Nile Virus (WNV), an infection that is very deadly in old mice, and finally subjected to real infection with live WNV.

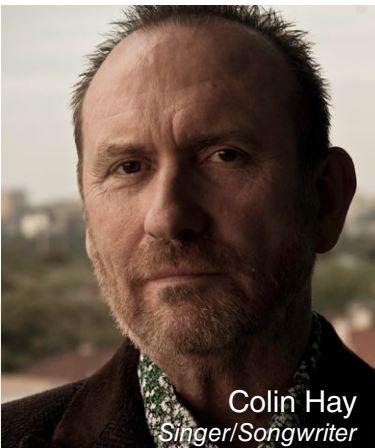
No intervention seemed to give test animals a better T-cell immunological response to WNV vaccination as compared with old, untreated animals. However, the results leave open the possibility that future therapies delivered to aging humans could prove effective at rejuvenating the immune system.

Outreach

“Reimagine Aging” Campaign

In 2012, we kicked off the Reimagine Aging campaign, our largest-ever outreach initiative. A host of celebrities have already joined the effort by offering their own thoughts on aging, and what it means to them. Some of their takes are positive, others negative; some are humorous, and all contain real insight. That insight is exactly what we’re after -- what better way is there to help people reimagine aging than to offer them a fresh perspective on the issue?

This campaign will provide SRF with an unprecedented fundraising tool that can at once broadcast the Foundation to a wider audience and encourage new donors to lend their support. We will continue to build upon these celebrities’ contributions, and are in the process of bringing the campaign more prominently to the web. We hope to unveil new participants and quotes in the near future.



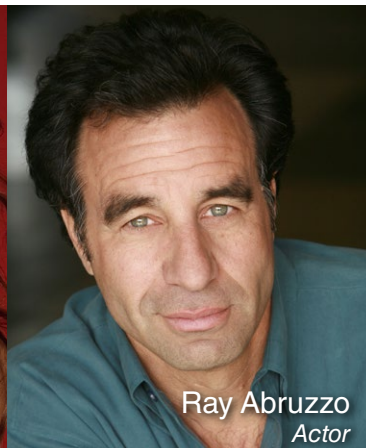
Colin Hay
Singer/Songwriter

“Aging to me is knowing when to throw away the leather pants.”



Cecilia Noël
Singer/Songwriter

“To me, aging means having to exercise my sense of humor, while my body cries in pain.”



Ray Abruzzo
Actor

“To me aging means realizing the first word I utter as I get out of bed is ‘OY.’”

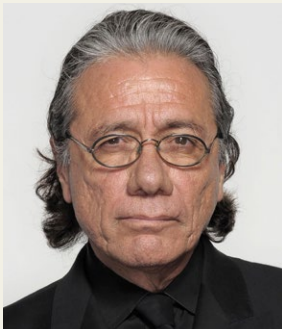


Ambassador Jorge T. Lapsenson

“Aging to me is the darkness that slowly but steadily absorbs the light from the fire of life.”

Visit sens.org/outreach to see what these and other celebrities have to say:

Edward James Olmos
Actor/Director



Alfonso Arau
Filmmaker



Richard Wurman
Creator of the TED Conference



Larry Wilcox
Actor



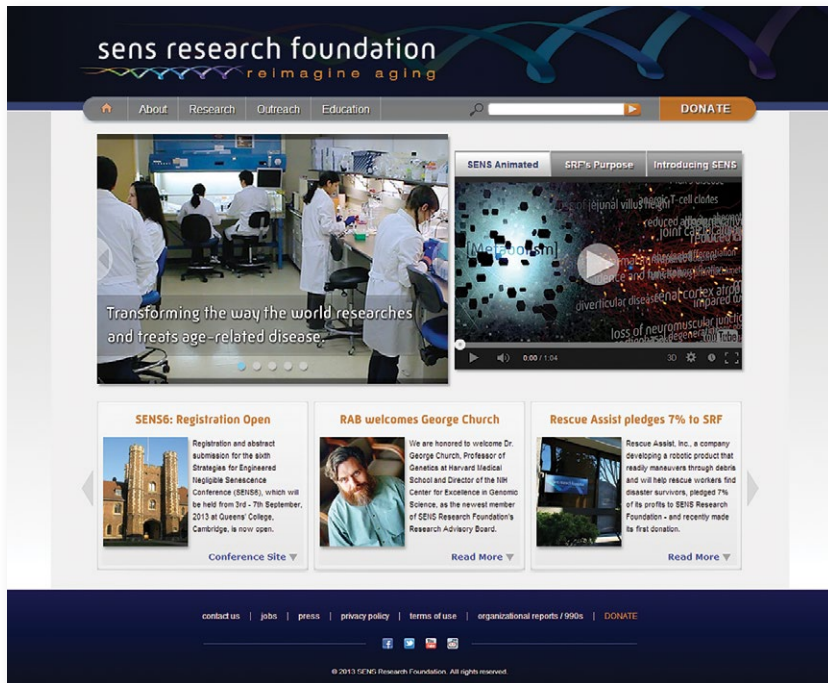
Herbie Hancock
Music Icon



PHOTO BY DOUGLAS KIRKLAND



Web Presence, Branding Updates



Our outreach efforts in 2012 culminated in the launch of our all-new website, pictured at left. This redesigned site features top-notch computer animations describing SRF's strategy for treating heart disease and the fundamentals of the SENS approach, as well as new video content and the latest SENS-related news. The website also includes in-depth summaries of each research project that SRF is conducting or funding, as well as information on our outreach and educational efforts.

The upgraded site is part of a broader update to our branding and online presence that also includes our new name, logo, tagline, and social media pages. Taken together, these are a key part of our ever-growing efforts to encourage researchers, government officials, and the public at large to reimagine aging.

CSO Dr. Aubrey de Grey: Making SENS Across the Globe

SENS Research Foundation continues to work to change the way *the world* researches and treats age-related disease. Toward this end, our Chief Science Officer Dr. Aubrey de Grey has attended a wide variety of conferences and speaking engagements over the past year, interfacing with fellow scientists, businesspeople, policymakers, and members of the international public alike.

His travels brought him to Techfest 2012 in Mumbai, India; the Eleventh World Congress of Bioethics in Rotterdam, The Netherlands; the Ciudad de las Ideas in Puebla, Mexico; and the 8th Annual World Stem Cell Summit in Palm Beach, Florida. At that conference -- the world's largest devoted to stem cells -- Dr. de Grey moderated a panel on the use of regenerative medicine to extend healthy human lifespan, alongside panelists from the Wake Forest Institute for Regenerative Medicine, the Buck Institute for Research on Aging, and the Harvard Stem Cell Institute.

Dr. de Grey's efforts in this area will of course continue throughout 2013 and beyond, as a critical component of SENS Research Foundation's outreach strategy. A world without age-related disease is possible -- but only if we effectively communicate the importance of repairing the cellular and molecular damage that underlies the pathology to the international community.



Outreach

Research Advisory Board



Our Research Advisory Board is made up of 25 field-leading scientists who help guide our research strategy, assisting us in our mission to transform the way the world researches and treats the diseases of aging.



We would like to welcome the newest member of our Research Advisory Board, Dr. George Church. Dr. Church is Professor of Genetics at Harvard Medical School, and is a luminary in the field of genomics.

Our distinguished members:

Pedro Alvarez, PhD

Chair, Department of Civil and Environmental Engineering, Rice University

Anthony Atala, MD

Director, Wake Forest Institute for Regenerative Medicine

Maria A. Blasco, PhD

Director, Molecular Oncology Programme, Spanish National Cancer Research Centre (CNIO)

Judith Campisi, PhD

Professor, Buck Institute for Research on Aging; Senior Scientist, Lawrence Berkeley National Laboratory

George Church, PhD

Professor, Department of Genetics, Harvard Medical School

Irina Conboy, PhD

Assistant Professor, Department of Bioengineering, UC Berkeley, and Berkeley Stem Cell Center

Marisol Corral-Debrinski

Research Director, Fondation Voir et Entendre, Institut de la Vision, Université Pierre et Marie Curie

Leonid Gavrilov, PhD

Senior Research Scientist, Center on the Demography and Economics of Aging, NORC and the University of Chicago

S. Mitchell Harman, PhD

Director and President of Kronos Longevity Research Institute

William Haseltine, PhD

Chair, Haseltine Global Health

Daniel Kraft, MD

Executive Director, FutureMed, Singularity University

Chris Mason, PhD

Chair of Regenerative Medicine Bioprocessing, University College London

Stephen Minger, PhD

Global Director of R&D, Cell Technologies, GE Healthcare

Janko Nikolich-Zugich, MD, PhD

Chair, Department of Immunobiology and Co-Director, Center on Aging, University of Arizona

Graham Pawelec, PhD

Professor of Experimental Immunology, Tübingen University

Bruce Rittmann, PhD

Director, Swette Center for Environmental Biotechnology, Biodesign Institute, Arizona State University

Nadia Rosenthal, PhD

Director, Australian Regenerative Medicine Institute

Jerry Shay, PhD

Chair in Geriatrics, Department of Cell Biology, University of Texas Southwestern Medical Center

Vladimir Skulachev, ScD

Director, A.N. Belozersky Research Institute of Physico-Chemical Biology, Moscow State University

David Spiegel, PhD

Associate Professor of Chemistry, Yale University

Alexandra Stolzing, PhD

Group Leader, Stem Cell Biology and Regeneration, Fraunhofer Institute

Rudolph Tanzi, PhD

Joseph P. and Rose F. Kennedy Professor of Child Neurology and Mental Retardation, Harvard University

Fyodor Urnov, PhD

Head, Advanced Genomics Technologies, Sangamo Biosciences; Associate Adjunct Professor, UC Berkeley

Jan Vijg, PhD

Chair, Department of Genetics, Albert Einstein College of Medicine

Michael West, PhD

CEO, Biotime Inc.

SENS6 Conference: September 3-7, 2013

Queens' College, Cambridge, UK

Over the past decade, SENS Conferences have showcased the latest cutting-edge advances in regenerative medicine and biotechnology at the University of Cambridge, a historic haven of excellence in technology and science. Past speakers have included Nobel Laureate Mario Capecchi, Geron founder Michael West, medical pioneer William Haseltine, the NIH National Institute of Neurological Disorders and Stroke's Roscoe Brady, leading bioethicists John Harris and Arthur Caplan, and media mogul Moses Znaimer.



This year, SENS6 will extend the superlative quality of the SENS Conferences with a keynote address from world-renowned Harvard geneticist George Church. The conference will also feature presentations by the Gerontological Society of America's James Appleby, the Mayo Clinic's Jan van Deursen, the McGowan Institute's Eric Lagasse, MIT's Todd Rider, Carnegie Mellon's Alan Russell, Cambridge's own Robin Franklin, and many others.

We invite you to join us this September as we connect with leading scientists and change-makers in the regenerative medicine movement. To register, please visit us online at sens.org/sens6.

SRF and CASMI: New Models for Medical Innovation

SENS Research Foundation is delighted to announce a new collaboration with the Centre for the Advancement of Sustainable Medical Innovation (CASMI). CASMI is a joint venture between the University of Oxford and University College London that is led by Dr. Richard Barker, Sir John Tooke, and Sir John Bell. The Centre's remit is to develop new models for medical innovation to address current failures in the translation of basic bioscience into affordable and widely adopted new treatments.

SENS Research Foundation is supporting CASMI's first two doctoral students, Natasha Davie and David Brindley. Ms. Davie is investigating T-cell therapies for diseases of aging, while Mr. Brindley is working on novel approaches to the risk-benefit evaluation of healthcare innovations. Both of their projects promise to help accelerate the translation of regenerative medicine research into patient benefits, a key goal for SRF.

SRF and University of Denver: Exploring Healthspan Demographics

SENS Research Foundation has teamed up with researchers at the University of Denver in a pioneering study to push the boundaries of prior aging-oriented demographic analyses. This work will extend the International Futures (IF) forecasting system to provide tools for the analysis of healthspan demographics.

Initially, this project will look at aging issues globally and across the century, then follow with a look at a range of possible human futures across several dimensions of uncertainty. The new IF system will assist in constructing strong and closely integrated models in many issue areas, including health, education, the economy, physical resources (food and energy), and environmental factors.

Education

SRF Education Offers Student Internships, New Online Coursework

SENS Research Foundation is committed to educating students and the public about rejuvenation biotechnologies. To that end we created the Academic Initiative, now known as SRF Education. SRF Education established two exciting new programs last year: student internships and online coursework.

In June of 2012, we launched our summer internship program by inviting eight students from across the United States to the SRF-RC and the Buck Institute for Research on Aging.

Each student conducted his or her own laboratory research project for three months on topics such as the characterization of stem cells and small molecule screening.



Jennie Sims, 2012 summer intern

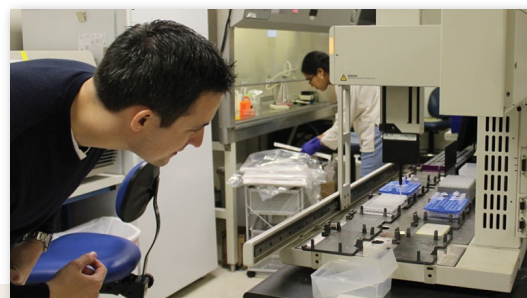


Intern project posters on display, SRF-RC, 2012

In 2013, we are placing interns at the SRF Research Center, the Buck Institute, the Wake Forest Institute for Regenerative Medicine, and SUNY Upstate Medical University.



Sam Curran (presenting), 2012 summer intern



Reto Hoehener, 2012 summer intern

New Staff Spotlight



Dr. Gregory Chin
Director, SRF Education

Greg earned his B.S. in Genetics from the University of California, Davis in 1996 and his Ph.D. in Developmental Biology from Stanford University in 2002. His research focused on DNA damage repair and DNA damage checkpoints. He has taught at such institutions as the University of California, Los Angeles and Cold Spring Harbor Laboratory. As the new Director of SRF Education, Greg will be leading SRF's effort to inspire the next generation of biomedical students.

centration was measured and then
lowest mRNA concentration (to
cy in mRNA extraction and initial cell
formed on the samples using the
uplicate.
values were normalized to the
ne
TCCCAAGCGGTTTGC



SRF Education is developing coursework on regenerative medicine and its applicability to the diseases of aging, a topic that is not being covered anywhere else.

In 2012, we filmed ten lectures by top regenerative medicine researchers (several of whom are shown on this page) at universities across the United States and beyond.

Coursework videos will be freely available on our website in 2013.

Dr. William Bains
University of Cambridge
Instructor: *Cross-linking of the Extracellular Matrix*



Dr. Judith Campisi
Buck Institute for Research on Aging
Instructor: *Senescent Cells, Cancer, and Aging*

Dr. Daniel Kraft
Stanford University
Instructor: *Stem Cell Biology and Therapy*



Dr. Claudia Gravekamp
Albert Einstein College of Medicine
Instructor: *Cancer and Vaccination*



2013 and Beyond

As we look forward, SRF Education will continue to build upon the Academic Initiative's earlier work. Specifically, we will continue to grow our internship program and online course offerings. We expect to increase both the number of summer internship positions we fund and the number of participating research institutions each year.

We also plan to delve into more detail on the topics covered by our introductory regenerative medicine online course by expanding each lecture into a full course of its own. Widening the scope of our internship program and online coursework offerings will enable SRF to make a greater impact on future scientists and doctors, while educating the public in general.

If you'd like to learn more about these or our other SRF Education programs, please visit our website at sens.org/education.

Finances

We are pleased to report that, in 2012, SENS Research Foundation was able to support expenses that were double those from the previous year. This was made possible through not only the continued support of our generous donors, but also through the receipt of a new, multi-year restricted grant from SENS Foundation EU (SENSF-EU) resulting from the settlement of the de Grey family trust. The total SENSF-EU grant was for \$13 million, of which \$2.5 million has been received by SRF. The remainder of the grant has been recorded as a receivable.

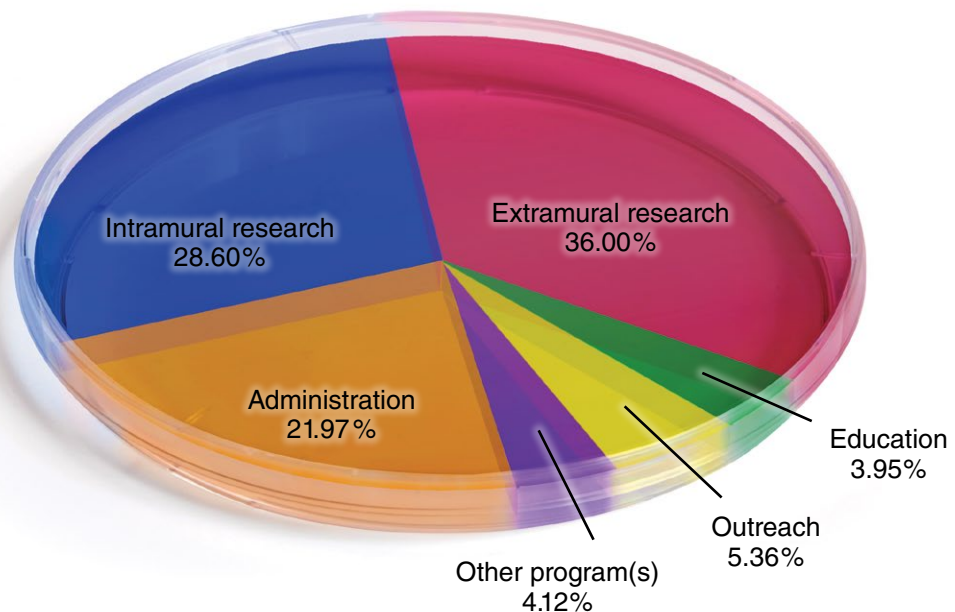
As a research-based outreach organization, the scientific work that we fund plays a critical role in our mission. For this reason, we have focused our growth on our extramural research program, tripling its size by adding more than \$750,000 of funding. This aggressive expansion has led to the addition of nine new projects, including two at the Wake Forest Institute for Regenerative Medicine, bringing our total funded to seventeen. Meanwhile, we were able to add \$300,000 to our intramural research budget, bringing

a third major project, more staff, and new equipment to our Research Center in Mountain View, California. Simultaneously, we built SRF Education into a larger and more robust educational program, creating our first online course and a successful summer internship program that involved both our Research Center and the Buck Institute for Research on Aging. This has set the stage for further growth in 2013, which will include the development of more coursework and the addition of new internship campuses.

Overall, our expenses in 2013 should increase by an amount equal to 2012's increase. Given our secure base of funding sources, we expect to sustain this higher level of operation indefinitely.

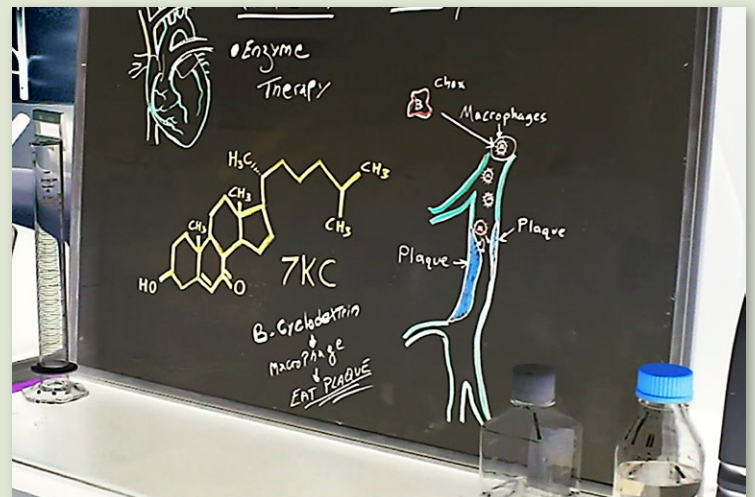
We are deeply appreciative of the individuals and foundations that enable us to pursue our mission through their support. We would like to thank Peter Thiel, Jason Hope, SENSF-EU and the de Grey family trust, the Methuselah Foundation, and the many other donors who make all of our efforts possible.

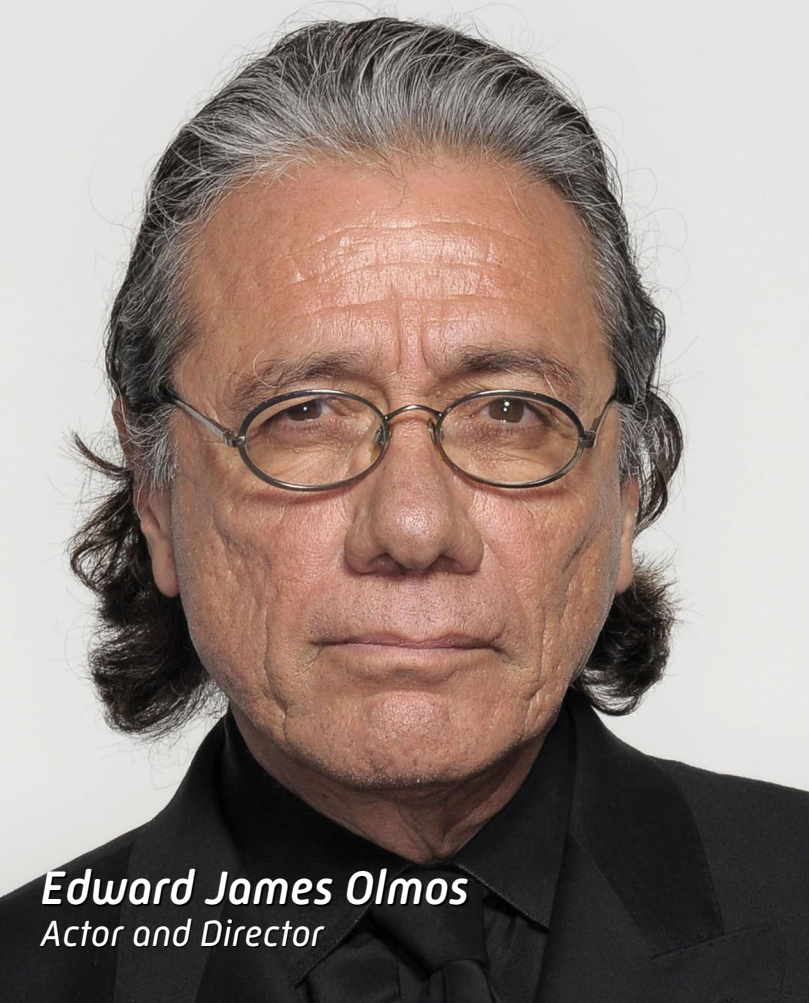
2012 - Expenses by Percentage



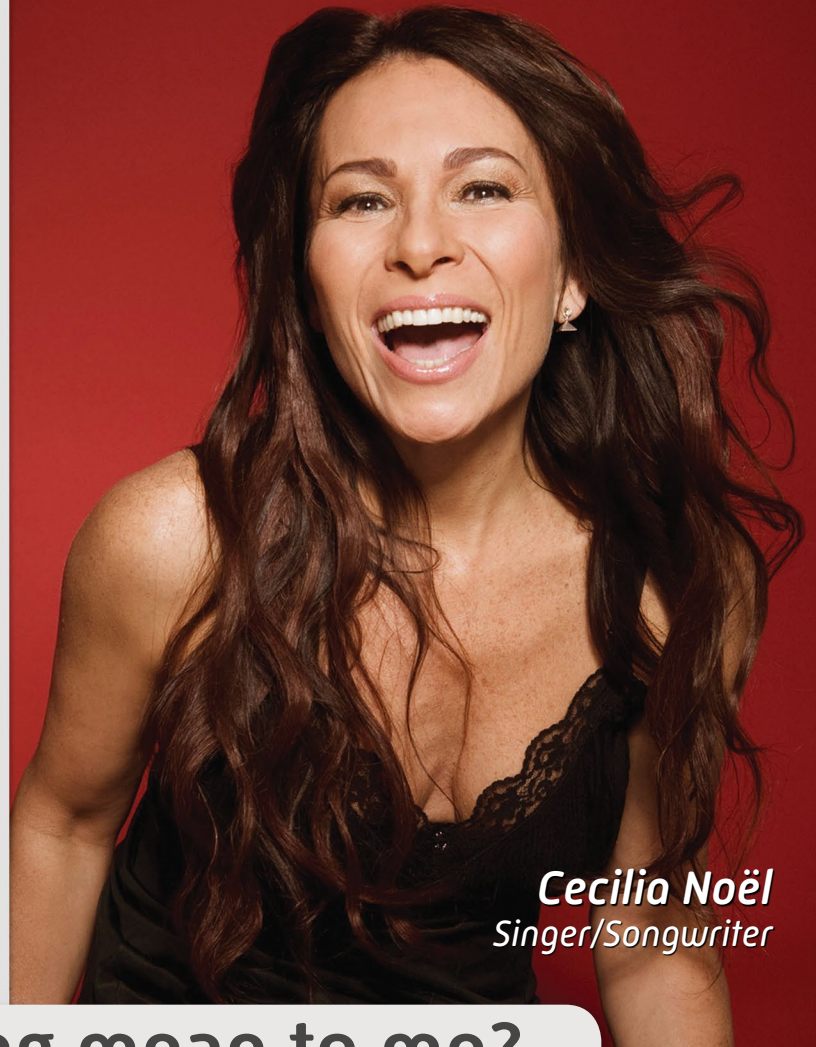
2012 Financial Data

Income	
Unrestricted donations	\$107,000
Restricted grants	\$520,000
Foundation grants	\$807,000
Restricted bequests	\$13,130,000
Other income	\$20,000
TOTAL	\$14,584,000
Expenses	
Intramural research	\$854,000
Extramural research	\$1,075,000
Education	\$118,000
Outreach	\$160,000
Other program(s)	\$123,000
Administration	\$656,000
TOTAL	\$2,986,000





Edward James Olmos
Actor and Director

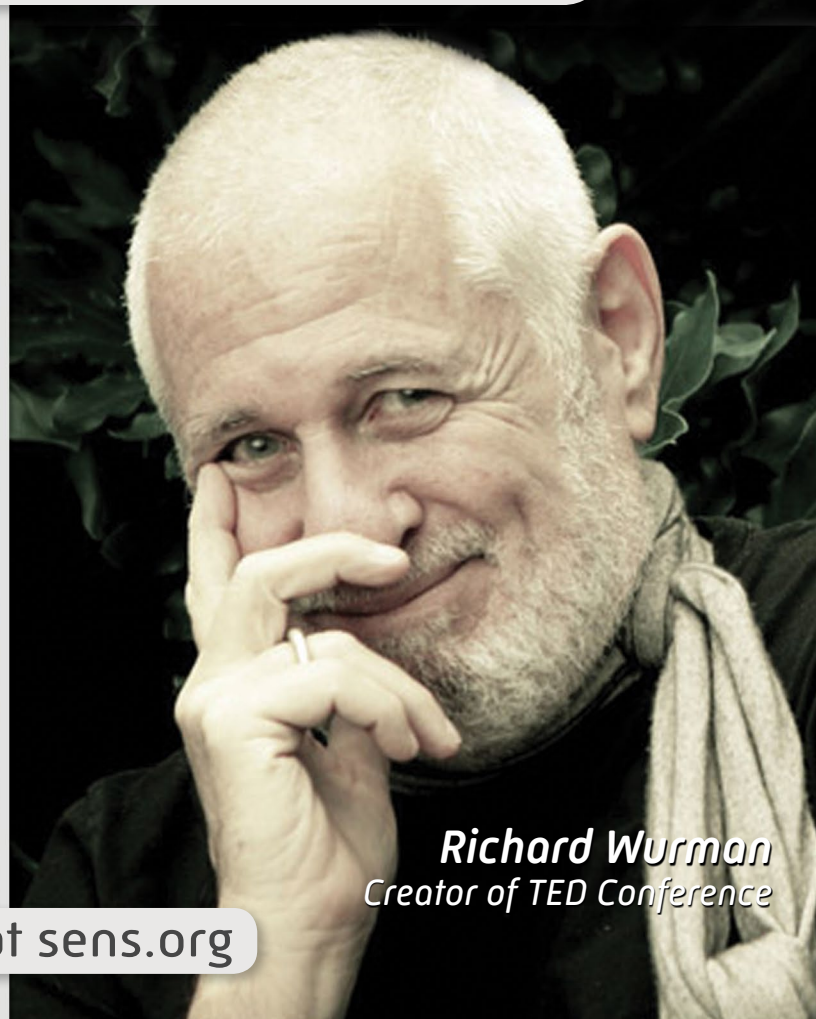


Cecilia Noël
Singer/Songwriter

What does aging mean to me?



Herbie Hancock
Music Icon



Richard Wurman
Creator of TED Conference

Find out at sens.org

PHOTO BY DOUGLAS KIRKLAND