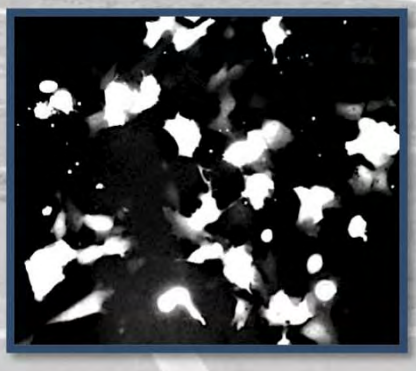
challenge accepted



annual report

2011

sens foundation

advancing rejuvenation biotechnologies

inside this report

"We choose to go to the moon in this decade, and do the other things, not because they are easy, but because they are hard, because that goal will serve to organize and measure the best of our energies and skills, because that challenge is one that we are willing to accept, one we are unwilling to postpone, and one which we intend to win, and the others, too."

- President John F. Kennedy

September, 1962

"We meet in an hour of change and challenge..."

- President John F. Kennedy,
Moon Speech, given at Rice University, September, 1962

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SENS Foundation works to develop, promote, and ensure widespread access to rejuvenation biotechnologies which comprehensively address the disabilities and diseases of aging. Our vision is a world in which all people have the opportunity to live their lives free from age-related illness and debilitation.

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

President Kennedy delivered his famous and inspirational "We choose to go to the moon ..." speech in 1962. I hope you will forgive our playfulness, or perhaps our temerity, in highlighting quotes from that speech throughout this Annual Report, but we thought it only appropriate.

It is, after all, the fiftieth anniversary of that speech; and we aspire to an 'Apollo program' of our own, one which will create the rejuvenation biotechnology industry necessary to develop damage repair interventions to age-related disease. All the efforts of SENS Foundation are designed to lay the groundwork for the rise of that industry.

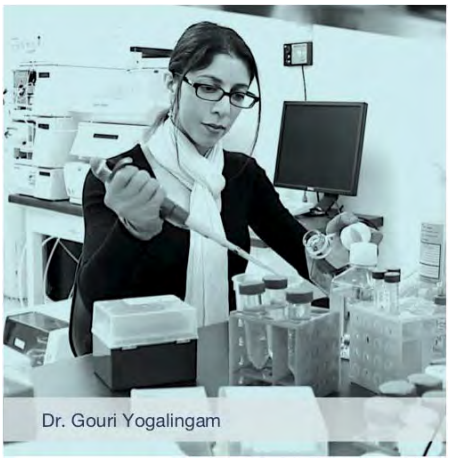
And today, just as in 1962, we do, indeed, meet "in an hour of change and challenge."

One such change is the focus of our dialogue with our stakeholders, our collaborators, and the public. You might say that the past three years have been SENS Foundation's 'Mercury project' – our proof-of-concept phase – during which we've worked to establish the feasibility of our line of inquiry through our research, education, and outreach programs. And in this we have been successful. The Thiel Foundation's substantial and continued funding has been met both with broader-based support and more key individual backers. Edward James Olmos has volunteered to lend his voice to our message. Jason Hope's philanthropic gift has launched our glucosepane research program at Cambridge and Yale Universities. We've worked hard to build new collaborations and outreach opportunities, and 2012 will show a significant research project in every major category of damage in the SENS technological proposal.

These successes are reflected in this report. We've expanded the internal research capabilities at the Foundation's Research Center, and the extramural collaborations you will see in the following pages involve the top tiers of regenerative medicine and aging research institutions. We've added new educational and grant programs, and the quality of the research presented at *SENS5: Rejuvenation Biotechnology* demonstrated a leap in the attention given to this emerging field. As SENS Foundation grows and matures, the conversations we are having at every level are shifting from *why* this should be done, to *how*.

Still, the challenge ahead is no small one. If we wish to claim the launch of our own Apollo program, we must be able to claim the launch of an entire rejuvenation biotechnology industry. To do that, we need to pave the way for burgeoning industry resources, political support, and wide-ranging investment. We need to be able to affect how the NIH defines what it means to be old, and how the FDA defines what it means to be sick. For all that, we need your continued support and attention, which remain vital to our success.

To call again on President Kennedy's words, we are not doing this because it is easy. It is absolutely an hour of change. Help us accept the challenge.


Dr. Gouri Yogalingam


Dr. Gayathri Swaminathan (l), Dr. Oki O'Connor (r)


Researcher Max Peto

intramural projects

SENSF-RC: MitoSENS

Thirteen proteins critical to the respiratory chain are encoded only in mitochondrial DNA. However, nuclear DNA is much less susceptible to damage and is more easily repaired. The goal of this project is to test whether these thirteen genes, when encoded in the nucleus, can successfully be expressed and integrated into the mitochondria.

In 2011, in-house researchers Dr. Matthew "Oki" O'Connor and Dr. Gayathri Swaminathan successfully established multiple stable cell lines for each of the five modified mitochondrial genes with which they are working.

They also built and optimized protocols for isolating mitochondrial fractions, extracting mitochondrial inner membrane proteins, and analyzing components of the oxidative phosphorylation pathway. Additionally, they have standardized assays to assess the activity of Complexes I and V of the respiratory chain, and optimized conditions for immunocapture of the complexes. Heading into 2012, the team is beginning rigorous testing of the nuclear expression they observed in their five targeted mitochondrial genes.

Following that, they will analyze the complexes of the respiratory chain, which should demonstrate and confirm that the proteins encoded by these five genes have been integrated properly into the complexes. If protein integration is confirmed, the team will move on to testing ways to functionally rejuvenate aged or otherwise damaged respiratory chain complexes. If successful, this approach could ultimately lead to novel ways of treating mitochondrial dysfunction -- which has positive implications both for age-related disease and other mitochondrial disorders that can occur at any point in life.

SENSF-RC/Stanford : LysoSENS

Lysosomes are the cell's last and best resort for degrading damaged or unwanted material. However, materials that the lysosome cannot degrade can form lipofuscin, filling the lysosome and causing it to lose its function.

The purpose of this project is to identify enzymes that can degrade A2E, a component of lipofuscin in retinal pigment epithelial (RPE) cells, and to successfully target those enzymes to the lysosomes of RPE cells.

The Research Center's LysoSENS team, under the oversight of Dr. Gouri Yogalingam (jointly affiliated with SENS Foundation and Stanford University), has optimized protocols for the large-scale and rapid production and purification of A2E. Our new processes have led to verification of successful A2E degradation in vitro using two candidate enzymes, laccase and manganese peroxidase (MnP). We have also determined that recombinant MnP has the potential to be taken up by RPE cells effectively, thanks to its extensive mannosylation.

In the coming year, the team will test delivery of MnP to the lysosomes of A2E-loaded RPE cells by receptor-mediated endocytosis, a realistic therapeutic delivery mechanism. They will continue to express and purify other A2E-degrading enzymes, and to scale up enzyme pro-duction, as they have throughout the last year.

SENS Foundation has, with the hiring of Dr. Yogalingam, also established a formal collaboration with the Mochly-Rosen lab at Stanford University. In exchange for Dr. Yogalingam's time and Stanford's own laboratory resources, SENS Foundation has awarded a small grant to Stanford in support of Dr. Yogalingam's ongoing research on A2E-degrading enzymes.

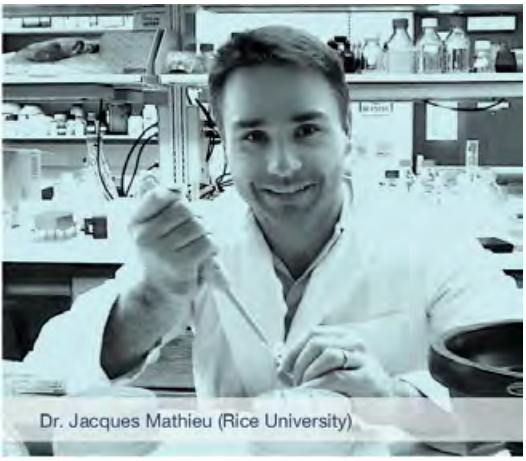
extramural projects

Rice University: LysoSENS

When macrophages in the walls of blood vessels accumulate 7-ketocholesterol (7KC), another compound that lysosomes frequently fail to degrade, they can stop functioning and become "foam cells", ultimately contributing to the formation of atherosclerotic plaque and potentially exacerbating conditions like Alzheimer's. The goal of this project is to find enzymes that can degrade 7KC and to target them to the lysosomes of macrophages.

Last year, our team at Rice University successfully isolated a microbial enzyme that rapidly degrades 7KC. They reengineered the enzyme, enabling it to be targeted to the lysoome, and then applied it to human fibroblasts. This experiment revealed that the enzyme was effective in the short-term at preventing 7KC from damaging these cells. Work continues on this enzyme at Rice, and a manuscript regarding this work is being prepared for publication.

"Man, in his quest for knowledge and progress, is determined and cannot be deterred." - JFK



Dr. Jacques Mathieu (Rice University)

Researcher Kevin Perrott (Buck Institute)

Dr. Silvia Gravina (Albert Einstein College of Medicine)

Albert Einstein College of Medicine: OncoSENS

Though the role of DNA mutations in cancer has long been apparent, the role of epimutations is less well characterized. The purpose of this project is to determine how important DNA epimutations might be to the pathogenesis of cancer.

SENS Foundation-funded work at the Albert Einstein College of Medicine has led to the development of a novel bisulfite sequencing method that can detect methylation patterns within the promoter regions of a single cell's DNA. A manuscript is in preparation for submission to a major journal, and the group is pursuing a patent. They are also beginning to test a genome-wide DNA methylation assay.

Buck Institute for Research on Aging: ApoptoSENS

Senescence is a genetic program that normal dividing cells invoke to prevent excessive cellular proliferation. At times, senescent cells fail to apoptose when they are intended to. The purpose of this project is to find molecules that counter some of these cells' harmful secretions, and possibly clear the death-resistant cells.

Kevin Perrott, in his SENS Foundation-funded research in Dr. Judith Campisi's lab at the Buck Institute, has found multiple compounds that reduce senescent cells' secretion of interleukin-6 (IL-6), an important component of senescent cells' cancer-promoting signalling. He has found one of these compounds, apigenin, to have particular promise. Apigenin is now being tested further, in order to determine its mechanism of action.

Cambridge University, Yale University: GlycoSENS

Chemical reactions in the body between carbohydrates and proteins can lead to protein "cross-links" that prevent two proteins from being able to slide past each other properly. This eventually causes the loss of elasticity of the arterial wall, loss of flexibility in the lens of the eye, and loss of tensile strength in the ligaments. Glucosepane is by far the most common of the known cross-links.

SENS Foundation has established a new laboratory at Cambridge University for the study of glucosepane, in addition to other targets of rejuvenation research. We have recruited Dr. William Bains to lead the lab, and hired a postdoctoral researcher to assist him. The lab's first task is to develop reagents that can detect glucosepane cross-links, an advance that would benefit research efforts on glucosepane's structure, abundance, and potential to be degraded.

A new collaboration between this lab and Yale University will enable the testing of agents that may be able to cleave the cross-link.

University of Texas, Harvard University: AmyloSENS

Extracellular protein aggregates, also frequently known as amyloids, can impair the function of cells and tissues. Their presence is a hallmark not only of Alzheimer's and diabetes, but of cardiac disease. This project seeks to use catalytic antibodies to clear transthyretin (TTR) amyloids in order to treat such disorders as senile systemic amyloidosis.

SENS Foundation-funded researchers at the University of Texas and Harvard University optimized methods for creating TTR fibrils and cross-linked TTR. They are presently vaccinating mice with these TTR immunogens to generate antibodies that might be used in the diagnosis of systemic amyloidosis and related diseases.

Their immunogen samples will be used to test the activity of TTR-degrading catalytic antibodies, which could have significant therapeutic potential. They have already discovered and begun to characterize naturally-occurring human catalytic antibodies specific for fibrillar TTR.

University of Arizona: ApoptoSENS

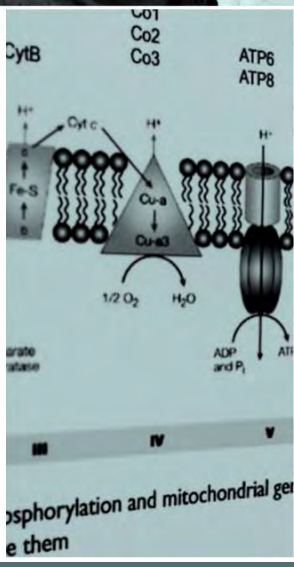
The immune system declines with age because of loss of cells in the thymus and accumulation of inactive cells in the periphery. Both phenomena lead to decline in numbers of active cells, especially a subset called naive cytotoxic T cells. In this project we seek to reverse both processes.

Thus far, mice infected with two persistent viruses known to exacerbate inactive cell accumulation have been treated with permutations of treatments for each problem: growth factors and adoptive cell transfer to restore cell numbers, and antibodies and antivirals to eliminate inactive cells. In 2012 we will discover the extent to which these mice are restored in resistance to a novel infection.

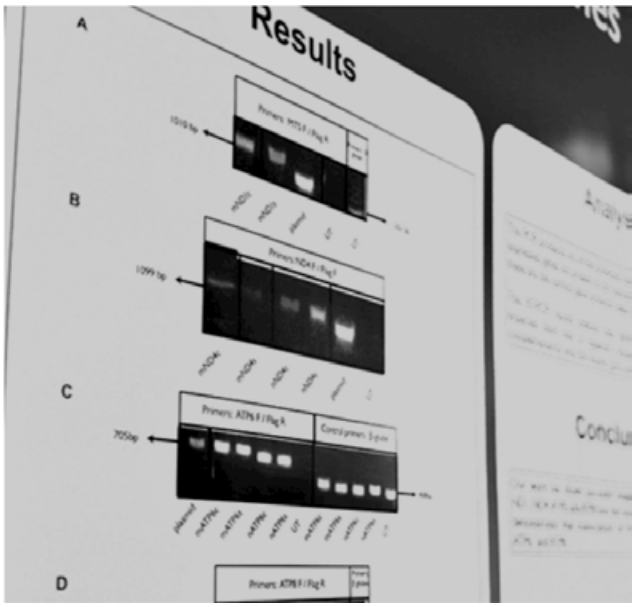
"it is one of the great adventures of all time..."

- JFK

"do all this,



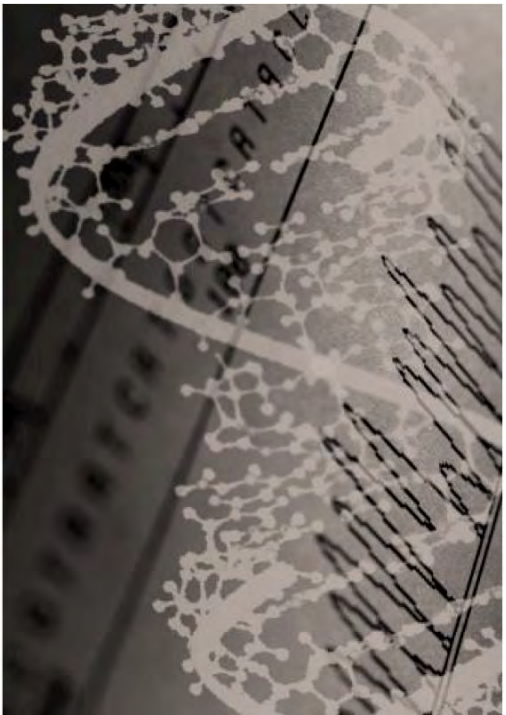
do it right,



...and do it first." -JFK

"To solve these mysteries, to solve them for the good of all men."

- JFK



sens five: rejuvenation biotechnology conference

From August 31st to September 4th, 2011, SENS Foundation held its fifth biennial conference, *SENS5: Rejuvenation Biotechnology*, at Cambridge University. As the largest-ever gathering of scientists, academics, authors, and thinkers focusing on rejuvenation biotechnologies, *SENS5: RB* continued to raise the standard to which these conferences are held.

The event's diverse group of presenters covered a wide array of topics and disciplines, ranging (to list just a few) from keynote speaker Dr. Caleb Finch's demographic analysis, to Dr. Ben Bahr's success in restoring cognitive function in an Alzheimer's mouse model by enhancing lysosome function, to Dr. John Jackson's initial work at Wake Forest Institute for Regenerative Medicine (WFIRM) on thymic tissue regeneration, to intestinal repair techniques developed by Dr. Graça Almeida-Porada (also of WFIRM), to Albert Einstein College of Medicine's Dr. Jean Hébert's approach to restore the loss of cells and degraded circuitry of the aging neocortex. *SENS5: RB* was also especially notable in that a higher percentage of presentations than in previous SENS conferences presented technologies that are already working in living animals or even in humans, rather than just in cell culture.

twenty twelve and beyond

There are always a host of presentations, seminars and panels from SENS Foundation, which can be found on our events calendar at *sens.org*. Now, we are building on the success of our 2011 conference, and our research accomplishments and developing collaborations over the past year, and taking our dialogue beyond the academic community. SENS Foundation's 2012 events are being designed to better integrate the latest academic achievements with the pharmaceutical, biotechnology, non-profit and governmental constituencies that can help us promote the concept of a rejuvenation biotechnology industry.

From left: Aubrey de Grey, Geoffrey Ginsburg, Alan Russell, Alison Murdoch at the "Regenerative Medicine & Healthy Aging" conference in Kazakhstan

from the cso

I was working in my office at the SENS Foundation Research Center a matter of weeks ago when this delightful little piece of writing (excerpted at right) crossed my desk. I must say, Ms. Banerjee is entirely correct. I do rather dislike her headline.

As SENS Foundation's Chief Science Officer, I deal extensively with the media. I also give a great number of talks, and speak with many people about SENS Foundation's mission. Recently, a number of people have told me that my message has changed -- that they are surprised that I might object to a headline discussing thousand-year lifespans. They believe that I have toned down my approach to discussing SENS Foundation's work and its implications. I can see why people think this; it is true that the things that I am now saying are different than the things I have been saying in the past. But it isn't my message that is different (or SENS Foundation's, for that matter), but rather the topics that we are discussing.

What has changed is the fact that we now have specific research, details, and ongoing proof-of-concept work to discuss. SENS Foundation has matured as an organization. We have moved well beyond the point of needing to defend the SENS platform as worth testing out in the laboratory; we have won that battle. Instead, we are discussing how SENS Foundation can best go about its work of building an industry and creating a comprehensive, practical suite of rejuvenation biotechnologies. And so, I no longer discuss and emphasize what the future might hold. Rather, I discuss and emphasize what is going on right now at the SENS Foundation Research Center in Mountain View, California, and in Foundation-funded laboratories across the world.

Allow me to return briefly to Ms. Banerjee's article. As I stated, I do not like her headline. I would prefer one like this: "Foundation Sets Sights on Aging Diseases, Disabilities." We aren't just talking about aging any more. We are beginning to do something about it. In my eyes, that simple fact is infinitely more sensational than any speculation about the future, however bold and controversial that speculation may be.

In all honesty, I am grateful to Ms. Banerjee for writing the article she did; it no doubt brought more attention to our cause. I enjoyed my time in India, and of course my travels throughout 2011 to other nations (including China, Kazakhstan, Russia, Germany, and Spain) on behalf of SENS Foundation. Our mission is to fulfill what we see as a profound obligation to do our best to help medicine keep older people healthy, just as it now does for the young, by advancing rejuvenation biotechnologies. That is what SENS Foundation is about, and yes, you can write that down.

Aubrey

THE TIMES OF INDIA
Mumbai

This man might live to 1,000

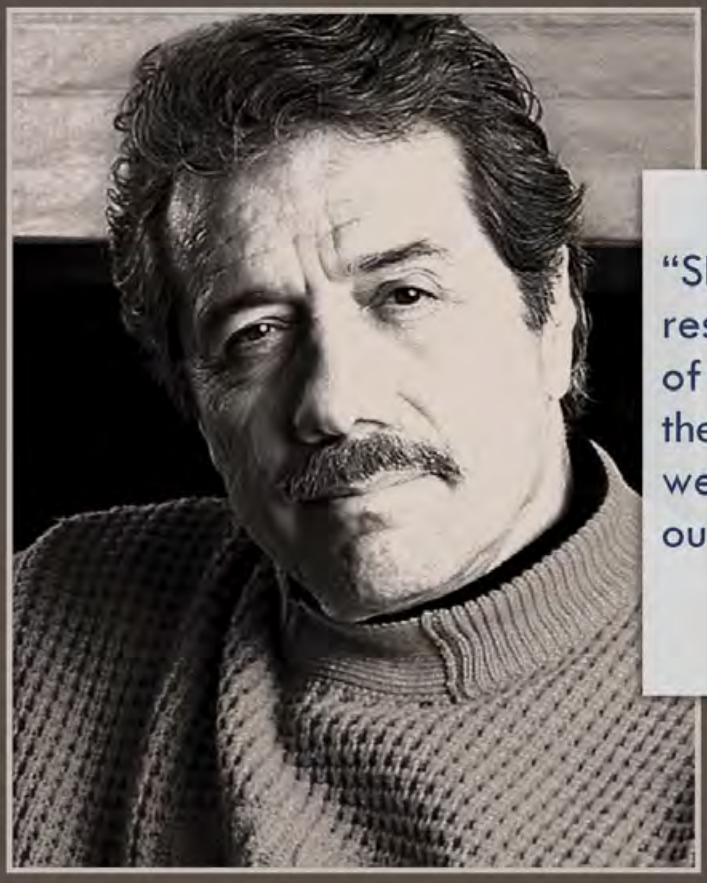
Agniva Banerjee, TNN Jan 9, 2012

MUMBAI: When he sees the PDF of this article, Aubrey de Grey will not like the headline. He will absolutely hate it, since he particularly instructed TOI not to give it. His suggestion, sorry, instruction was: Longevity, a side effect of regenerative medicine. "Here!" he shouted above the din of the bar a few metres from the IIT's main gate, shoving the pen back into the correspondent's hand. "Write that down...Yes, go on! Write that down," he said...

Clearly, newspaper headlines are not the strong point of de Grey, a scientist whose research has underlined the need to stop the ageing process in humans, a need that many have questioned, saying what will then be the meaning of being human.

He dismisses such philosophical questions as irrational and unscientific. "Ageing kills more people every day than any other thing. Yet we do not consider it a disease," he says, his piercing eyes trying to drill the point in. "People don't know about the science. People don't want to think about it. Ageing causes suffering, diseases... Alzheimer's, cancer... We intend to fix them."

"Our obligations to ourselves as well as others require us to make this effort." - JFK



"SENS Foundation delivers pioneering research into treatments for the diseases of aging. Please join me in supporting them in this critical mission, and together we will change the concept of aging, for ourselves and future generations."

- Edward James Olmos

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Rice University

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Wake Forest Institute for Regenerative Medicine

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Spanish National Cancer Research Centre (CNIO)

Judith Campisi, PhD
Buck Institute for Research on Aging

Irina Conboy, PhD
UC Berkeley, and Berkeley Stem Cell Center

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academic initiative

The SENS Foundation Academic Initiative has made considerable progress in 2011. Student membership has risen steadily, an Initiative outreach program has been put in place, and an all-new SENSFAI website has been launched at sens.org/ai. There you can find the Academic Initiative's new mission and vision statements along with a great deal of additional information and content.

Most importantly, the Academic Initiative has significantly expanded its budget, which is enabling the program to give more grants and scholarly awards than it has at any time in the past. That has also allowed us to announce our new summer internship program, and to begin development of our first online course, which is expected to be completed in late 2012.

Taken together, these changes make the Academic Initiative by far the best way for students and other young scientists to become involved with SENS Foundation's work. If you are interested in doing your own research training project, interning at the SENS Foundation Research Center, working with a team on a literature review, or just spreading the word, you should visit the Academic Initiative's new website and get started with us today.

sens foundation
academic initiative

Student Profiles

stuart calimport

Stuart is one of the Initiative's most active and longest-established mentors. He recently began his PhD studies at the UK's Aston University. Throughout these new studies he continues to mentor new students, and is a significant contributor to and co-author of the Initiative's new DNA methylation review.

daniel wuttke

Daniel has a master's degree in biochemistry from Germany's Ruhr University Bochum, and is currently working toward his PhD at the University of Liverpool. He will be a co-author of an upcoming Academic Initiative review, *The Role of DNA Methylation in Aging, Rejuvenation, and Age-Related Disease*.

kristopher barnes

Kris, an undergraduate student at the State University of New York at Oswego, came to the Academic Initiative in 2011 to work on his own bench project on the effects of PQQ on the lifespan of C. elegans. Kris's project is funded by an Initiative materials grant.

"We mean to be a part of it -- we mean to lead it."

- JFK

summary

We are delighted that SENS Foundation was able to make expenditures of $1,518,000 in 2011. This was an increase of over $400,000 from 2010, overwhelmingly in support of direct research and conference projects.

Over 75% of our expenditures went to our core mission of research, outreach and education, including grants to extramural researchers, expansion of our intramural research program, our biennial Cambridge conference, and outreach through our Academic Initiative.

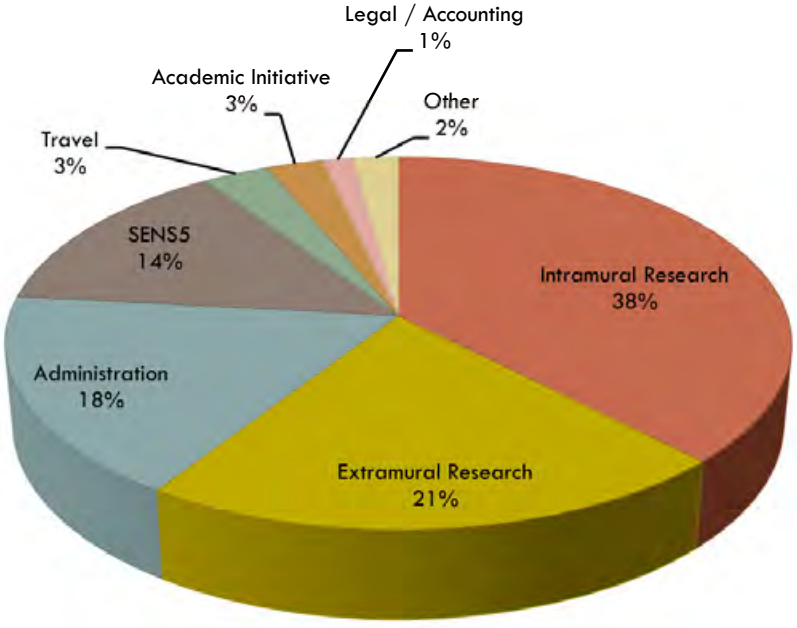
We doubled our investment in our internal research capabilities, expanding the facility itself, adding capital equipment available for performing research, and increasing staff. With the 2011 addition of four new collaborations, we also laid the groundwork for a similar expansion of our extramural research programs in 2012.

SENS Foundation had income of $1,507,000 in 2011. We greatly appreciate the support of the many individuals who contributed to our mission. We would like to thank Peter Thiel, Jason Hope, the Methuselah Foundation, and all of our contributors and volunteers for their on-going generosity. We expect a significant increase in both revenues and expenses for 2012, as we begin to see distributions from a de Grey family trust, under a grant from SENSF-UK. This support will be in addition to the contributions we receive from other sources.

"I don't think we ought to waste any money, but I think we ought to do the job."

- JFK

expenses by percentage



expenses

Intramural Research:	$572,423
Extramural Research:	$324,913
Academic Initiative:	$40,734
SENS5:	$211,192
Administration:	$266,558
Legal and Accounting:	$21,756
Travel:	$48,023
Other:	$32,401
TOTAL:	**$1,518,000**

income

Foundation grants:	$950,000
Non-Profit organization grants:	$227,352
Individual donations:	$160,100
Conference income:	$150,500
Other:	$19,408
TOTAL:	**$1,507,000**

*"We meet in an hour of **change** and **challenge**..."*

This is SENS FOUNDATION

ADVANCING REJUVENATION BIOTECHNOLOGIES

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