

sens **foundation**

advancing
rejuvenation
biotechnologies



end of year report
2010

“ In 2009 we launched SENS Foundation.

We did it to drive biomedical research towards a functional and cost-effective approach to extending individual health. We did it to raise awareness for an alternative to an increasingly complex and problematic pathology chase in medicine; to redefine regenerative medicine as applied to aging; to enable doctors to think about fixing patients before they were sick.

We did it to transform the way you think about medicine.

We knew it was a big agenda when we set out, and we were fully conscious of how small a public charity we were. We recognized that our first successful steps would depend upon our demonstration of fundamental credibility to the medical science community.

That is why I am especially pleased to present this 2010 end of year report. As you will read, we have created a mature organization and delivered the networks and collaborations needed to build the rejuvenation biotechnology field. We've expanded our own research programs and have used that expansion to develop collaborations with leading universities and research institutions in regenerative medicine, around the nation and the world.

We have found our voice with a substantial and mainstream scientific community.

We have, in short, found our voice with a substantial and mainstream scientific community. Rejuvenation biotechnology, as a research field, is emerging, and SENS Foundation has led that charge. For that, our thanks go to all of you, our researchers, supporters, and stakeholders.

We intend to use the voice we have earned. Regenerative medicine and stem cell research now bring in immense state, federal, and international funding. That kind of funding has put spectacular advances in organ replacement and tissue repair, for example, on the horizon. However, rejuvenation research - the application of those same regenerative concepts to the damage and diseases of aging - still receives all too little attention.

It is amazing that you might someday be able to receive a newly made heart, kidney, or liver. But in theory, there are damage repair interventions that could be simpler, cheaper, and made more widely available than that, and many of them remain completely unexplored. We need to fix that, and for that we need your continued support.

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michael kope
co-founder, ceo
sens foundation





SENS Foundation's research strategy is to support a mix of intramural work at our Research Center and extramural projects at university laboratories elsewhere. I am delighted with both our research progress and the expansion of its scope in 2010.

At the Research Center we have hired five additional full-time and one part-time staff, including Tanya Jones, our Director of Research Operations. We now boast two vibrant projects, within our LysoSENS and MitoSENS strands.

Our three-strong LysoSENS team is pursuing enzymatic solutions to the problem of eliminating two of the most notable components of age-related "molecular aggregates" – A2E and 7-ketocholesterol (7KC). A2E is a major cause of dysfunction of retinal epithelial cells, producing age-related macular degeneration (AMD), the leading cause of blindness in the elderly. 7KC, an oxidized derivative of cholesterol, is believed to be a major cause of the degeneration of macrophages into foam cells, which is the first step in atherosclerosis, one of the most lethal age-related diseases worldwide.

I am delighted with our research progress and expansion in 2010.

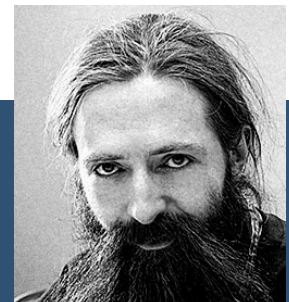
Our team has developed an in-house process for A2E synthesis, a critical step in our screening and evaluation programs for A2E-degrading enzymes. One such

candidate has been dramatically enhanced by fusion with a second enzyme, accelerating the rate of degradation of A2E up to 100-fold. On the 7KC side, we have identified a number of 7KC-metabolising enzymes, and have successfully subcloned them into a species of yeast which will allow us to determine whether the activity of a particular enzyme will be preserved if expressed in humans. We are developing methods for transfecting these enzymes into macrophages, to determine whether their expression can reverse the foam cell phenotype.

SENS Foundation launched its second major in-house project in the MitoSENS strand, hiring Dr. Matthew O'Connor as research leader in September 2010, and more recently adding Dr. Gayathri Swaminathan to the team. Allotopic expression – the addition of mitochondrially-encoded genes to the nucleus, protecting them from oxidative damage – is expected to relieve many aging-related pathologies, including sarcopenia (loss of muscle with age). Allotopic expression has been demonstrated for three of the thirteen genes required to complete the process in humans: our former collaborators – the group of Dr. Marisol Corral-Debrinski – were responsible for much of this progress. The goal of the new project is to demonstrate allotopic expression of the remaining ten genes, individually and in combination.



dr aubrey de grey
co-founder, chief science officer
sens foundation



“ In addition to these major projects, a team at the Research Center developed a prototype “scrubber” – a device able to selectively deplete “anergic” (proliferation-resistant) T cells (a type of white blood cell) from the bloodstream of mice. This depletion was demonstrated to result in a long-term return to a more youthful T cell profile, and led to an academic publication and patent. The prototype has since been loaned to our extramural collaborator Dr. Janko Nikolich-Zugich, to conduct further studies.

In extramural research, progress has been similarly heartening.

In the lab of Dr. Janko Nikolich-Zugich at Arizona University, we have funded work by Dr. Megan Smithey exploring the relationship between persistent viral infections and immunosenescence, the reduced capacity of the aged immune system to respond to infections. This project has made several exciting discoveries. Most notable is a dramatic improvement in immune response when T cells from young adult mice are transferred into older mice partially depleted of their own T cells, strongly indicating that the decline in function of T cells in aged individuals is due to an intrinsic defect of these cells. The continuation of this work in 2011 is expected to provide sufficient data to allow clinical testing to begin.

In the fall, we initiated two projects: one on removing senescent cells (Kevin Perrott in the lab of Dr. Judith Campisi at the Buck Institute), and one designed in collaboration with the Supercentenarian Research Foundation’s Stan Primmer, involving Drs. Sudhir Paul of the University of Texas and Brian O’Nuallain of Harvard University. This latter project targets senile systemic amyloidosis and isolated atrial amyloidosis. Both are caused by the aggregation of proteins to form damaging amyloids, leading to significant age-related disorders of heart function. The goal is to develop antibodies able to detect and destroy these aggregates.

We continue to fund extramural LysoSENS work by Jacques Mathieu and Rob O’Callahan in the laboratory of Prof. Pedro Alvarez at Rice University. This team has recently produced two enzymes with activity against 7KC, currently being taken forward into cell-based assays. They have also begun development of a selection-based assay for mutagenesis libraries – a key step in high-throughput “directed evolution” of the enzymes already discovered.

Also in 2010, SENS Foundation began a multi-project collaboration with the world-leading Wake Forest Institute for Regenerative Medicine. Projects in the areas of immunosenescence, extracellular matrix cross-linking, and intracellular aggregates will start in 2011, conditional on sufficient funding.



dr aubrey de grey
co-founder, chief science officer
sens foundation

“ Finally, our credibility within the broader academic community has been confirmed by the addition to our Research Advisory Board (RAB) of Dr. Ana Maria Cuervo, a world-renowned specialist in the role of lysosomes and autophagy in aging-related disease, and Dr. Daniel Kraft, an international expert in stem cell biology and therapeutics. The RAB now consists of seventeen highly prestigious scientists with expertise spanning the full range of rejuvenation biotechnologies: their endorsement of our approach and research can be found on the SENS Foundation website. ”

Research Focus: Role of Epimutations in Organismal Aging

In 1959, Leo Szilard published a paper proposing that random mutations of the genome, accumulating throughout life, would lead inevitably to a derangement of metabolism throughout the body, resulting in aging and death. More recently, a second type of DNA damage – epimutation – has been recognized.

Both mutations and epimutations accumulate with age, and both are instrumental in cancer. The threat from cancer-causing DNA damage is radically greater than from other types, since a single cancerous cell can kill. There is a theory that organisms susceptible to cancer will evolve such powerful genome maintenance mechanisms that non-cancerous DNA damage will be kept well below a critical level in a currently normal lifetime. Thus, we do not expect the capability to repair mutations or epimutations to be required in a comprehensive rejuvenation biotechnology platform, as long as that platform includes a cast iron defence against cancer. It is important, therefore, that we confirm the theory is correct, such that we can safely avoid the need to develop robust DNA repair so long as we can thoroughly prevent cancer (which is another SENS strand).

At Albert Einstein College of Medicine in New York, SENS Foundation has been funding Dr. Silvia Gravina in the lab of Dr. Jan Vijg, to evaluate whether random changes in DNA methylation (a major type of epimutation) are sufficiently widespread to have a significant impact on the aging process.

The standard protocol for studying these changes involves conditions which typically lead to extensive DNA degradation. This is a particularly serious issue for single-cell analysis, which our work requires in order to detect *bona fide* adventitious changes, rather than ones made “on purpose” by the cell in response to other types of damage. Dr. Gravina’s first success was in optimizing conditions to minimize such degradation. She was then able to demonstrate that her optimized protocol was effective in single cells of several types – hepatocytes, fibroblasts, and neurons.

A far more reliable assessment of damage can be derived through comprehensive, gene-specific measurements, and Dr. Gravina is now developing this approach using so-called “next-generation” sequencing. Preliminary results are very promising.

An additional requirement for this project is a new method for isolating the target DNA: existing techniques are not effective for neurons, due to their complex and fragile structure. To meet this requirement Dr. Gravina has developed a protocol to enrich single neuronal nuclei.

Drawing together all of these preliminary achievements, Dr. Gravina is now working directly on our project’s ultimate aim – quantifying genome-wide levels of epimutation in the nuclei of single neurons from aged mice – with key results expected in 2011. The interim results are currently being prepared for academic publication in a leading peer-reviewed journal.

dr aubrey de grey
co-founder, chief science officer
sens foundation

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2010 saw the Foundation take major steps in clarifying and delivering its message. In November our CEO, Mike Kope, delivered a speech as part of *Breakthrough Philanthropy*, which was the clearest statement to date of our mission: a video is available at sens.org.

In Los Angeles we began to hold regular meetings, bringing together supporters, donors, scientists, industry experts and Foundation staff. Those meetings were used as a ‘test bed’ for a wider, global outreach program. Their organizer, Maria Entraigues, has now joined our team as Global Meeting Coordinator.

In 2010 we organized sessions at three major international conferences, including the Genetic Policy Institute’s *World Stem Cell Summit*, in Detroit, MI. Our focus is now on the fifth SENS Conference which will be held in Cambridge, England in autumn 2011.

On-line, we upgraded our website, and began a greater level of integration with social networking sites such as Facebook and Twitter. Work is currently underway for a further iteration of the site, to increase the general accessibility of information about the Foundation, and better serve the needs of our donors and supporters.

Our Academic Initiative continued to support the next generation of researchers in rejuvenation biotechnologies. Tyler James joined us as Coordinator for the program, undertaking a great deal of behind-the-scenes work to restructure and streamline the Initiative, prior to our planned roll-out of new, for-credit university courses in rejuvenation biotechnology.

Looking ahead, we are reframing some of our thoughts in terms of the biotech industry. Healthcare costs continue to escalate, without concomitant rises in healthspan, a trend which will create individual, economic, and societal consequences. We believe the time has come to talk about the potential for change which rejuvenation biotechnology can bring to the way we address these issues, and to healthcare efficiencies in age-related disease.

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Staff Focus: Maria Entraigues

Maria Entraigues is SENS Foundation's Global Meeting Coordinator (and also our Volunteer Coordinator).

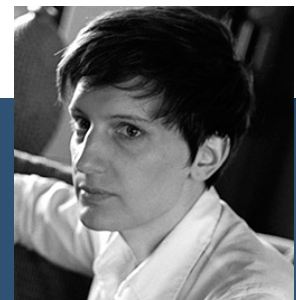
Maria was born in Buenos Aires, Argentina and is now an American citizen. She moved to America in 1992 to study under a scholarship at Berklee College of Music, Boston before establishing herself in Los Angeles as a singer. She's written songs and performed as a soloist singer and actress for several feature films, commercials, musicals, and TV shows.

In 2004, her interest in science, particularly the aging process, led her to volunteer to help Dr. Aubrey de Grey and the SENS program.

Among her many interests and activities she is also a pilot, flight school owner and Cultural Attaché of the Argentine Consulate in LA.



dr sarah marr
co-founder, executive vice president
sens foundation





Over the past year, the infrastructure of SENS Foundation's Research Center has expanded significantly. We recently relocated to a new facility, more than tripling our available space. Extensive renovations converted the space from an empty shell into a fully operational lab environment, greatly extending the capabilities of our previous incubator space. A successful 'lab warming' event at the end of renovations generated donations and the loan of several items of required equipment.

Since the beginning of 2010, our Research Center has expanded to a staff of seven, and the new facility allows for the addition of several more researchers. This growth has allowed us to accelerate research on the LysoSENS project and to expand our work to include MitoSENS.



tanya jones
director of research operations
sens foundation



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Obtaining new lab space has also proven critical to our ability to perform research, removing diverse problems and providing an independent, clean and high quality environment.

This has been a year about infrastructure for the Research Center: establishing a professionally managed laboratory to serve as the foundation on which we can build our research program.

We are particularly delighted to have recruited two scientists who each have over four years of post-doctoral experience in top universities. Dr. Gayathri Swaminathan will shortly be joining Dr. Matthew O'Connor on our MitoSENS team. From one hundred excellent applicants, we were fortunate to have our top candidate accept a position with the Foundation.

Dr. Swaminathan is an expert cell biologist, and we look forward to her joining us at the Research Center at the beginning of March.

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Researcher Focus: Matthew O'Connor

Matthew "Oki" O'Connor joined us in September. He is a research scientist, specializing in the cellular basis of the aging process.

Dr. O'Connor first became interested in the biology of aging when reading about telomeres in *Scientific American* when he was sixteen years old. He won an early entrance to college and received his B.S. from Shimer College and M.S. in Molecular Biology from Northwestern Medical School, where he studied learning and memory. At Baylor College of Medicine he earned his Ph.D. in Biochemistry for his work characterizing the proteins which protect and regulate telomeres.

In 2006 Dr. O'Connor decided to follow the so-called 'California Gold Rush' in stem cell research to do postdoctoral research in the Bioengineering Department of UC Berkeley, studying muscle stem cells. He presented some of his results at the third SENS conference in Cambridge, England.

Now at the SENS Research Center in Mountain View, California to head our MitoSENS project, Dr. O'Connor is excited to be working on mitochondrial rejuvenation: "MitoSENS has the potential to transform the way we think about the accumulation of cellular damage caused by free radicals."



tanya jones
director of research operations
sens foundation

2010 finances

SENS Foundation received \$1,356,000 of donations in 2010. In addition to expressing our gratitude for all the donations which we received, we would like to thank Peter Thiel, Jason Hope and Dan Stoicescu for their generous support of the Foundation.

Our total expenditure was \$1,119,000.

68% of our expenditure went on intra- and extramural research, including grants to external facilities, direct payment of external researchers, our CSO and his support team, and costs of the SENS Foundation Research Center (including staffing costs, facilities and operational costs, and relocation costs).

In total, 73% of expenditure was attributable to charitable purposes, including research, and outreach through the Academic Initiative and Foundation events.

administration

legal and accounting costs	\$ 26,000
staff	<u>\$205,000</u>
	\$231,000

sens foundation events	\$14,000
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general

operating costs	\$14,000
travel and attendance	<u>\$54,000</u>
	\$68,000

academic initiative	\$41,000
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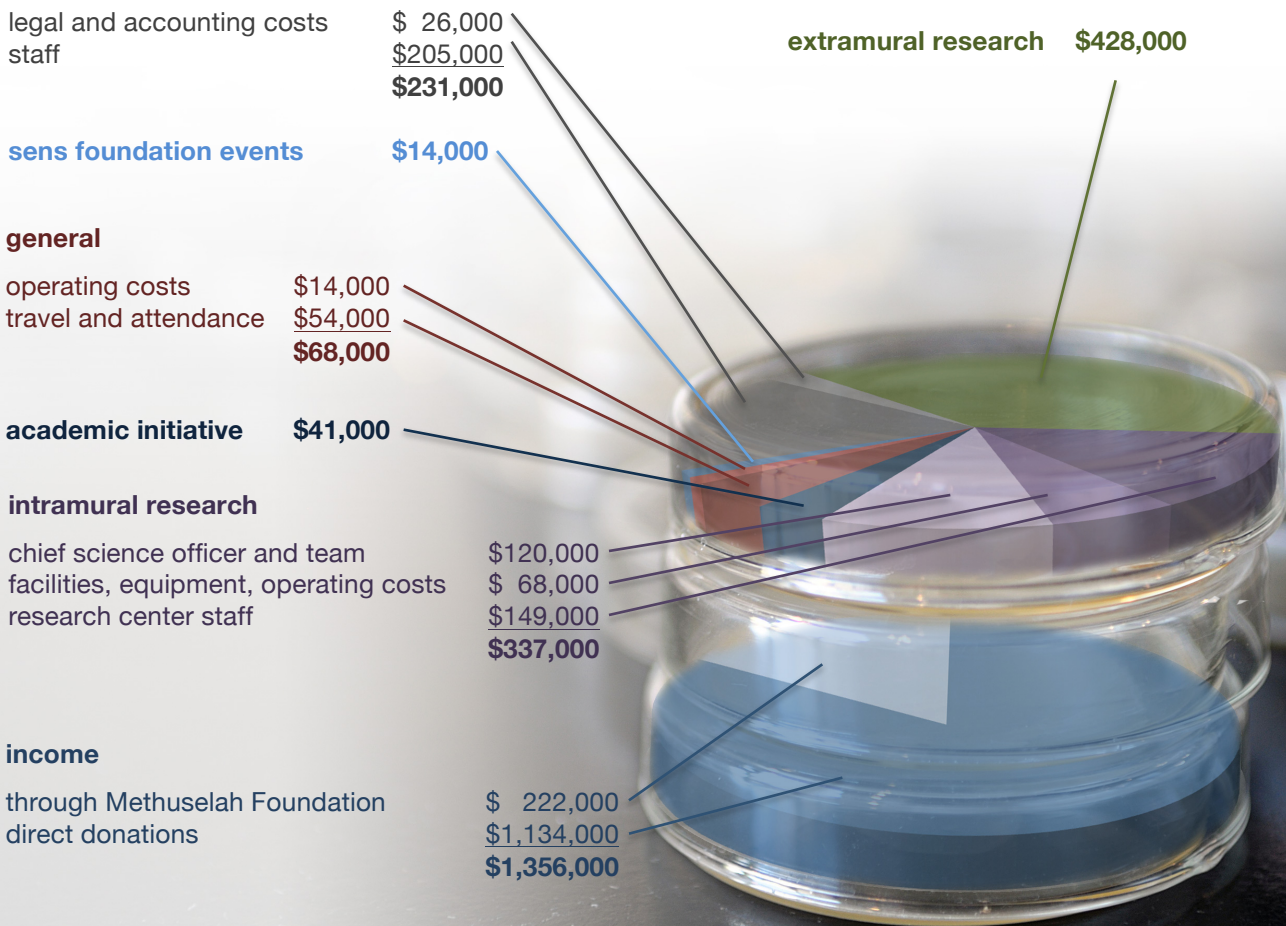
intramural research

chief science officer and team	\$120,000
facilities, equipment, operating costs	\$ 68,000
research center staff	<u>\$149,000</u>
	\$337,000

income

through Methuselah Foundation	\$ 222,000
direct donations	<u>\$1,134,000</u>
	\$1,356,000

extramural research \$428,000



sens foundation
year end report 2010
www.sens.org

* figures are given to nearest \$1,000

* calculations based on cash and accruals positions for 2010

sens foundation is a 501(c)(3) public charity