The New York State Stem Cell Science (NYSTEM) Program
A Report On Progress
And a Vision for the Future
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*Items not printed can be found at [http://stemcell.ny.gov](http://stemcell.ny.gov)

**ON THE COVER:** Stem cell photos by Anna Yoney, Gist Croft, and Ali Brivanlou, The Rockefeller University (left) and Devin Chandler-Militello and Steven Goldman, University of Rochester (bottom)
Message From the Chair of the Strategic Planning Coordinating Committee

LAST SUMMER, I was invited by NYSTEM to chair the development of an updated strategic plan for stem cell research in New York. In my new position as Vice President for Regenerative Medicine at the New York Stem Cell Research Foundation Institute, I had only recently joined the community of stem cell scientists in New York. What I found here was inspiring—an exceptional group of researchers who are dedicated to advancing our knowledge of stem cell biology and therapy, state-of-the-art laboratory facilities that expedite discoveries in the field, and an environment that recognizes and supports the promise of stem cell research through the publicly funded NYSTEM program.

Although New York’s reputation as a center for leading-edge stem cell research was—and remains—well-deserved, the stem cell research field and the NYSTEM program itself were facing a new challenge. Since NYSTEM was first established more than 8 years ago, stem cell research has evolved rapidly. Scientific advances have brought many concepts for stem cell-based therapies closer to the point of clinical testing in human patients—a process that requires significant, long-term investment. At the same time, stem cell scientists must cope with a substantially reduced federal budget for biomedical research and development, making it more difficult for them to obtain federal research grants and restricting their abilities to test innovative ideas, train the next generation of researchers, equip their laboratories, and conduct clinical trials. In light of these changes, the Empire State Stem Cell Board decided to revisit its 2008 Strategic Plan in order to update its mission and goals in ways that would foster all of the stages of research, development, and commercialization that are needed to bring successful new stem cell therapies to patients.

Reflecting the collaborative nature of the New York stem cell research community, a strategic planning process was devised that made full use of the wide-ranging expertise in stem cell science, ethics, business, and therapy development that is available in the State. A strategic planning coordinating committee and a strategic plan ethics workgroup were assembled, both of which included members of the Board, as well as external experts. In addition, a Scientific Advisory Panel comprising the directors or other leaders of New York stem cell centers was formed. The Scientific Advisory Panel

MAHENDRA RAO, M.D., Ph.D.
Chair, Strategic Planning Coordinating Committee
provided up-to-date information on the state of the field in general and in New York specifically, advised the strategic planning coordinating committee on successes and challenges its members encountered in the NYSTEM program, and contributed detailed examples of scientific progress made with the support of NYSTEM funds.

As an adjunct to the strategic planning process, the Board solicited an external review of the NYSTEM program. An External Review Panel (ERP) of four prominent stem cell experts from outside New York was convened. The ERP was asked to undertake an independent assessment of NYSTEM activities, achievements, and challenges and to make recommendations for future improvements or changes to the program. The ERP made salient points about the need for improvements, but overall it shared my enthusiasm for the New York State program.

The resulting plan builds on clear successes of the NYSTEM program to date in fostering stem cell research, training, infrastructure development, and ethics leadership across the State. Moreover, the plan lays out the Board’s vision for the future of stem cell science in New York—a future that brings the promise of stem cells into a new reality of cell-based cures for many diseases and conditions that affect New Yorkers and others around the world.

As evidenced in this Strategic Plan, the Board is optimistic about the state of stem cell science in New York, and so am I. This is an exciting time for the biomedical research community as we stand poised on the verge of a new era of stem cell-based medicine. I believe that this updated Strategic Plan will ensure that the mission and goals of the NYSTEM program are closely aligned with the evolving needs and opportunities of stem cell science in New York for the benefit of the State and its citizens. I thank all who participated in this strategic planning process (see Appendix 2 and Acknowledgements) for sharing their insights and knowledge, as well as for their unwavering, enthusiastic commitment to New York’s stem cell research enterprise.

July 2015
Investing in New York Through Stem Cell Science and Regenerative Medicine

A report of the Empire State Stem Cell Board 2015

Devin Chandler-Militello, Steven Goldman, University of Rochester

Freyja McClanahan, Holly Colognato, Stony Brook University
Executive Summary

Since its creation in 2007, the New York State Stem Cell Science Program (NYSTEM) has advanced the understanding and translation of stem cell science in New York by supporting research, training, infrastructure, ethics analysis and guideline development, and general education.

This second strategic plan has two components. First, it reports on NYSTEM progress to date and describes highlights of the many research and programmatic accomplishments of New York’s extraordinary investigators. Second, it sketches a roadmap for the state’s future support of stem cell research, guided by a new program mission: to enable New York to deliver on the vital promise of stem cells and reap the rewards of an already substantial investment.

Clinical trials, treatments, and cures are on their way, here and around the world. New York State has played a leading role in reaching this critical midpoint. Now that the scientific community is poised to bring new therapies to patients in need, New York State must retain its leadership role.

Our accomplishments are impressive, but more funding is needed to develop and deliver cures and to sustain the vibrant research community that NYSTEM has helped to establish. NYSTEM must prevent the exodus of top researchers to states offering greater opportunities and attract fresh ideas and innovative minds to New York. Continued funding is essential to expand the economic benefits of stem cell discoveries for the state’s hospitals, universities and research institutions, and individual taxpayers. Finally, we must increase our ability to attract and promote the establishment of successful pharmaceutical and biotech industries.

The Empire State Stem Cell Board proposes a plan for the future that continues its original goals with two new areas of particular emphasis: first, bridging the gulf between fundamental discoveries and the development of cures; and second, expanding commercial opportunities for scientists and industry. NYSTEM is ready to guide the stem cell community to the next phase. It will not happen in New York, however, without a renewed commitment of resources.
The Promise of Stem Cells

What are they? Where will they take us?
Experts believe that stem cells hold the key to the future of medicine. Stem cells will be used to replace cells damaged by neurodegenerative diseases like Alzheimer’s and Parkinson’s disease. They will replace heart cells damaged by cardiac arrest. They will conquer cancer.

**Between Concept and Cure**

Whatever the source of stem cell used, the critical transitional stage from research discovery to proven therapy is the most underfunded. Often referred to as the “Valley of Death,” this part of the process occurs after “proof of concept” has been established—when discoveries have proved successful in animal models or in vitro—but before they are ready to be tested for safety and efficacy in humans. Biotechnology companies are reluctant to take on projects at this stage because the return on investment is too distant, while most federal funding goes to more basic research. This leaves investigators in a quandary as they prepare to conduct critical experiments needed to take basic discoveries to the point where commercial entities will support continued development.

Bridging the “Valley of Death” is a top priority of the Empire State Stem Cell Board (ESSCB) in this Strategic Plan. The New York State Stem Cell Science Program (NYSTEM) has begun this work with the recent decision to support six Consortia—each targeting a different unmet medical need. But these six projects are only the beginning. The teams will need more support before the enormous costs of getting their products ready for consumers will be assumed by private investors. And there are so many more promising projects waiting in the wings.

NYSTEM stands ready to pilot the state’s exceptional scientists and research institutions across the gulf between concept and cure. With continued funding and hard work, New York will deliver on the commitment made to the public when NYSTEM was created. New York’s patients, and patients around the world, are waiting.
The State of the Science in Stem Cell Research

Since the ESSCB released its first strategic plan for NYSTEM in 2008, understanding of stem cell biology has evolved considerably. Major research advances have moved the field closer to clinical translation for some diseases, and policy changes at the federal level have made stem cell research, specifically with human ES cells, more accessible for academic researchers. However, declining federal budgets for biomedical research overall are significantly impeding research progress at a crucial time in the translation of scientific discoveries to new clinical therapies.

Advances in Stem Cell Research

Important progress in stem cell research, conducted within and outside of New York, has propelled the field in new directions since the ESSCB’s first strategic plan was formulated in 2008. In particular, at the time of NYSTEM’s founding, scientists in Japan had only recently announced the discovery of mouse and human “induced pluripotent stem (iPS) cells.” iPS cells are derived from adult cells, such as skin or blood cells, that have been reprogrammed with four specific genes. This causes the cells to revert to a pluripotent state, meaning they are capable of forming nearly every cell type in the body. Like embryonic stem cells, iPS cells are pluripotent, but because they can be derived from cells acquired from human patients with genetic diseases, they are extremely amenable to disease modeling. Over the last several years, the stem cell research field has seen an explosion in the number of new iPS cell lines created with specific genetic mutations and pathologies associated with a variety of rare and common diseases. NYSTEM-supported researchers have been at the forefront of this effort, generating iPS cell lines from patients with Huntington’s disease, genetic heart conditions, Parkinson’s disease, LEOPARD syndrome, and numerous other diseases (see the Progress Report Addendum for more information on NYSTEM-funded advances in iPS cell line creation).

By combining stem cells with state-of-the-art technologies, scientists are making important advances in regenerative medicine faster than ever. For example, 3-dimensional printing technology is being combined with stem cells to generate human tissues and organs for in vitro disease modeling, drug discovery, and cell-based transplants. Significant progress was made on the development of new models for toxicology research using stem cells in recent years. Other researchers are combining gene therapy with stem cells of the immune system to generate an immune response capable of eradicating cancer cells. Finally, genome editing technologies can be used to turn on or off, or edit, almost any gene in the body; this could have many applications in hematopoietic stem cell-based therapies, such as thalassemia or sickle cell disease. Cross-disciplinary opportunities to capitalize on advances in other fields will continue to expand as the understanding of basic stem cell biology matures.

Another critical advance in the stem cell field has been the initiation of new clinical trials for cell-based therapies. In 2010, Geron began the first clinical trial testing an hES cell-based therapy to treat spinal cord injuries.7 Also in 2010, Advanced Cell Technology, now Ocata Therapeutics, started two clinical trials testing the use of hES cell-derived cells to treat Stargardt’s macular dystrophy and dry age-related macular degeneration.

7 In 2013, Geron’s stem cell assets were acquired by BioTime, Inc., which formed Asterias to continue these trials.

Finally, in 2014, ViaCyte launched a trial of hES cell-derived pancreatic beta cells for the treatment of diabetes. Although definitive results from these trials have not yet been published, they indicate the beginning of a new phase for clinical translation of hES cell research. Furthermore, many trials using other types of stem cells, such as those derived from bone marrow, are in progress. In its 2014 annual report, the Alliance for Regenerative Medicine (ARM) identified just over 100 phase I, II, and III clinical trials of stem and progenitor cell-based therapies for such diverse diseases and conditions as ulcerative colitis, ischemic stroke, hematological malignancies, and chronic kidney disease, among others. More recently, Japan’s regulatory authority gave the green light for the first-in-human clinical trial of a therapy derived from iPS cells. In September 2014, a Japanese team at RIKEN Center for Developmental Biology implanted retinal tissue derived from iPS cells into a person with age-related macular degeneration. Researchers around the world are watching closely.

Finally, efforts are underway to create new products and to commercialize critical discoveries arising from stem cell research or in support of cell-based therapies. In 2014, ARM estimated that more than 700 companies worldwide focus on regenerative medicine, including at least 268 in North America. The majority of those companies, 56%, are associated with the development of therapeutics and devices, and the rest are developing tools, banks, and services for the regenerative medicine field, such as stem cells for drug discovery and toxicity testing, bioprocessing tools, manufacturing, and engineering and quality control, among others. ARM estimates the overall regenerative medicine field to be valued at $4.74 billion from venture capital and private equity, grants, public offerings, and other sources of financing, of which $1.872 billion is related to stem cell and progenitor cell therapy. As part of its annual report, ARM interviewed 16 pharmaceutical and large-cap biotech companies regarding their strategic perspectives on regenerative medicine. It noted that, A recurring message that echoed throughout each interview is that pharma does not want to miss this opportunity; they are monitoring the space diligently and methodically assessing the key questions to commercialize and bring these products to market. Lastly, not one company representative stated that they were not interested in this burgeoning field.

Federal Funding for Stem Cell Research

NYSTEM, like other state-sponsored stem cell research programs, was initially launched in response to policies enacted by then-President George W. Bush, which severely restricted the use of federal funding for research on hES cells. Many people, in New York and elsewhere, believed that these policies were slowing the pace of advancement and cutting off promising areas of stem cell research. On March 9, 2009, President Barack Obama issued Executive Order 13505 “Removing Barriers to Responsible Scientific Research Involving Human Stem Cells.” In response, the National Institutes of Health (NIH) issued new guidelines for federal funding of stem cell research, permitting funding of research on hES cell lines derived under specific criteria, including proper informed consent. As of February 2015, approximately 300 hES cell lines listed on the NIH Human Embryonic Stem Cell Registry are eligible for use in NIH-funded research. Importantly, however, among other restrictions, federal funds remain limited to use on extant hES cell lines only; to this day, federal funds cannot be used for the derivation of new hES cell lines. NYSTEM is one of the very few sources providing funds for these activities.

The enabling changes in the federal policy for stem cell research funding have been offset by a dramatic decrease in overall funding for biomedical research at the NIH. Today’s scientists face an extremely competitive environment to secure funding to conduct research, especially the early career scientists who have not reached their full potential. According to analyses conducted by the Federation of American Societies for Experimental Biology (FASEB), the NIH budget appropriation has

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8 Alliance for Regenerative Medicine: Regenerative Medicine Annual Industry Report 2014
been essentially flat for the past decade, with the Fiscal Year (FY) 2013 budget at its lowest level in 13 years. However, after adjusting for inflation, the NIH budget for FY 2013 was $5 billion (22.4%) less than in FY 2003. In addition, the number of research project grant awards decreased by 20.3% from 10,393 in FY 2003 to 8,283 in FY 2013, and the number of R01-equivalent grants for investigator-initiated research dropped by 34% over the decade. The average scientist is now 42 years old before obtaining his or her first R01 award compared to 36 years old in the 1980s. Moreover, data from the NIH Data Book published by the NIH Office of Extramural Research show that the success rate of all new grant applications in FY 2014 was 15%, down from 26% in FY 2003; likewise, the success rate of new R01-equivalent applications was only 15% in FY 2014 compared to 24% in FY 2003.9

The recent federal budget limitations have severely impacted the ability of U.S. biomedical scientists, including those in New York, to maintain their laboratory operations, train the next generation of scientists, and purchase state-of-the-art equipment for research. In January 2015, Francis S. Collins, M.D., Ph.D., NIH Director, stated:

_The effect that unprecedented budget pressures are having on biomedical research cannot be ignored. Due to inflation, the NIH budget has lost almost 25% of its purchasing power over the last decade...The decline has had important consequences; the NIH once funded 1 in 3 research proposals, but now only has enough resources to support 1 in 6. As a result, a great deal of excellent science is being left unfunded... These challenging fiscal times are also impeding the ability of the NIH and NIH-funded institutions to recruit and retain the brightest minds in science._10

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The Rationale for New York’s Continued Investment in Stem Cell Science

Despite the rapid pace of advancement, scientific research is a long-term process. The development of stem cell-based therapies for human diseases requires much discovery research to better understand the basic biology of different types of stem cells, as well as the molecular and cellular bases of disease. In addition, extensive preclinical safety and toxicity testing are needed before human clinical trials of stem cell-based therapies can be initiated. Clinical trials themselves are remarkably costly. Continued, reliable funding is critical throughout the process from discovery to therapy, particularly through early phase clinical trials that establish therapeutic safety.

By establishing NYSTEM in 2007, New York made a decision to invest in the promise of stem cell science. That investment has already realized substantial returns. The NYSTEM community is now poised to take its work to the next phase. This young field needs time to mature before robust stem cell therapies will be safe and efficacious to treat diseases. Continued support is needed before our scientists can translate the fruits of their research into clinical trials, proven therapies, and cures.

Equally important, continuing the NYSTEM program will reap lasting benefits for New York, including the greater expansion of its thriving research community and the further growth of the state’s economy. NYSTEM dollars will continue to retain our best stem cell scientists in New York and bring additional research support personnel to the state, leverage additional investments from other funders, and foster the commercialization of stem cell discoveries through new patents, licensing, and start-up development in New York. Without sustained, strategic investment in stem cell research, however, the State risks ceding the ultimate rewards of scientific progress made here to other states that take a long-term view of stem cell investment. Those states will welcome our investigators, their discoveries, and both the immediate and long-term economic benefits.
The ESSCB is revisiting NYSTEM goals for several reasons. First, the Board intended the original strategic plan to guide the NYSTEM program for five years, after which it would reevaluate its agenda in light of advances in the field. Next, NYSTEM-funded research is at a critical stage, with the funding of six multi-investigator Consortia, which are moving stem cell-based therapies from laboratory research towards early phase clinical trials for multiple sclerosis, Parkinson's disease, age-related macular degeneration, sickle cell disease, ovarian cancer, and blood cancers and genetic disorders of blood cells. Also, the entry of iPS cells into the picture has vastly expanded the breadth of NYSTEM-supported research from what was originally contemplated. In addition, the ESSCB recognized the need to establish a strong rationale for the strategic use of remaining NYSTEM funds to ensure appropriate stewardship of the public trust. Finally, the ESSCB lays out its vision for the future: extension and expansion of the NYSTEM program to cement New York’s standing as a leader in the discovery, development, and testing of stem cell-based cures and as a hub for up-and-coming pharmaceutical/biotech companies that are investing in stem cell research and regenerative medicine.
NYSTEM Progress:
Scientific, Medical, and Economic Impact of NYSTEM-Supported Activities, 2007-2015
Assessing Achievement of the Original Goals

IN ITS 2008 STRATEGIC PLAN, the ESSCB articulated a mission statement for the NYSTEM program:

To foster a strong stem cell research community in New York State and to accelerate the growth of scientific knowledge about stem cell biology and the development of therapies and diagnostic methods under the highest ethical, scientific, and medical standards for the purpose of alleviating disease and improving human health.

It then set forth six strategic goals and a target budget for the major components of the NYSTEM program: advancing the science of stem cell biology in New York; training stem cell researchers; developing infrastructure for stem cell research; ethical, legal, and social issues and education (ELSIE) in stem cell research; administration of the NYSTEM program; and benefits of promoting stem cell research in New York, evaluation, and public accountability (Figure 2.1. Funds were not targeted specifically for the last category).

Since 2007, NYSTEM has successfully created a diverse, wide-ranging, and productive stem cell research portfolio in New York through implementation of the programmatic framework laid out in the first strategic plan (Figure 2.2, Appendix 4). The program has issued 22 Requests for Applications (RFAs) and five Requests for Proposals (RFPs), awarded 321 contracts to New York investigators and four contracts for administrative support in the form of peer review services and scientific oversight. It has committed approximately $372 million for stem cell research, infrastructure, training, and education in New York for state FYs 2007–2017. NYSTEM funding has had wide geographic impact in New York, with 35 institutions receiving funding across the state as of July 2014 (Figure 2.3).

NYSTEM funding has enabled important scientific advances in stem cell biology and the development of stem cell-based therapies for rare and common diseases that affect patients in New York and worldwide. Training programs for stem cell researchers have attracted new talent and innovative thinking to the field. NYSTEM-funded multi-institutional, shared infrastructure for stem cell research has supported the science and, as importantly, facilitated the growth of a robust, collaborative, statewide stem cell research community across New York institutions.

While it is not feasible to describe every research advance or newly created facility in a report of this nature, this chapter provides an overview of the progress and achievements made by NYSTEM-supported researchers to date with respect to each goal set out in the 2008 Strategic Plan. Illustrative examples are provided in sidebars to highlight successes in each category. More examples of significant achievements are included in the Progress Report Addendum.
Figure 2.1: **2008 Strategic Plan: Categories and Target Distribution of Funding for FY 2007/2008—2011/2012**

<table>
<thead>
<tr>
<th>STRATEGIC GOAL</th>
<th>TARGET PERCENT</th>
<th>TARGET EXPENDITURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advancing the Science of Stem Cell Biology</td>
<td>65%-80%</td>
<td>$195–240 million</td>
</tr>
<tr>
<td>Training Stem Cell Researchers</td>
<td>4%-10%</td>
<td>$12–30 million</td>
</tr>
<tr>
<td>Developing Infrastructure for Stem Cell Research</td>
<td>10%-15%</td>
<td>$30–45 million</td>
</tr>
<tr>
<td>Ethical, Legal, and Social Issues and Education</td>
<td>3%-5%</td>
<td>$9–15 million</td>
</tr>
<tr>
<td>Administration of the NYSTEM Program</td>
<td>3%-5%</td>
<td>$9–15 million</td>
</tr>
</tbody>
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Figure 2.2: **NYSTEM-Supported Research by the Numbers**

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Number of Requests for Applications released</td>
<td>22</td>
</tr>
<tr>
<td>Number of Requests for Proposals released</td>
<td>5</td>
</tr>
<tr>
<td>Number of contracts awarded to New York grantees</td>
<td>321</td>
</tr>
<tr>
<td>Number of contracts issued for administrative support</td>
<td>4</td>
</tr>
<tr>
<td>Total funding awarded</td>
<td>$372 million</td>
</tr>
<tr>
<td>Number of New York institutions supported***</td>
<td>35</td>
</tr>
<tr>
<td>Additional external funding obtained*</td>
<td>&gt;$152 million</td>
</tr>
<tr>
<td>Additional external donations obtained**</td>
<td>&gt;$142 million</td>
</tr>
<tr>
<td>Jobs supported in New York*</td>
<td>&gt;750</td>
</tr>
<tr>
<td>Invention reports, patent applications, and patents**</td>
<td>93</td>
</tr>
<tr>
<td>New start-up companies established***</td>
<td>7</td>
</tr>
<tr>
<td>Technology licensing agreements signed**</td>
<td>4</td>
</tr>
</tbody>
</table>

* As of January 2015. ** As of 2011; based on a survey of funded investigators conducted in 2012. *** As of July 2014.
Figure 2.3 **Locations of NYSTEM Funded Institutions — all Mechanisms**
2008 Strategic Plan Goal I: Advancing the Science of Stem Cell Biology in New York

**Mission:** Support innovative basic, translational, and clinical research that builds on the potential of stem cells to detect, treat, and cure human diseases.

The ESSCB primarily fulfills its goals by issuing funding mechanisms designed to address the needs of the developing field and soliciting research proposals from scientists at New York institutions. All applications for awards are peer-reviewed by independent panels according to criteria set by the Board, and decisions are based on scientific merit, availability of funds, and programmatic balance. NYSTEM has issued nine RFAs for stem cell research, resulting to date in 247 awards with a total commitment of $235.31 million (Figure Add.1 in the Progress Report Addendum).

These RFAs have provided three major classes of research awards to stem cell researchers in New York:

- **Investigator-Initiated Research Projects (IIRP) and Innovative, Developmental and Exploratory Activities (IDEA) awards** are intended to stimulate and support scientific investigations on any aspect of stem cell biology that will lead to a better understanding of the unique properties of stem cells and allow their utilization to treat disease.

- **Targeted research awards** solicit proposals for specific, predefined areas of research that have been designated as particularly high priorities for the NYSTEM portfolio. To date, one targeted RFA has been released for research on iPSC cell technologies and one on derivation of new hES cell lines.

- **Consortia awards** are designed to accelerate translational research through clinical applications of stem cell research for prevention and/or treatment of disease.

NYSTEM-Funded Advances in Stem Cell Research

**Consortia**

A major highlight of the NYSTEM program is its portfolio of Consortia, which are funded to translate important findings from the laboratory bench into new stem cell-based therapeutic approaches for human diseases. These Consortia, which represent a significant investment of human and financial resources, position

![Figure 2.4: NYSTEM Funding Areas by $ (millions)](image-url)
New York at the cutting-edge of stem cell research and regenerative medicine. The six Consortia selected for funding to date are:

- **SUNY-Upstate Medical University, partnering with University of Rochester and University at Buffalo**, to test the potential of oligodendrocyte progenitor cell delivery for restoration of function in multiple sclerosis, $12.1 million;
- **Sloan Kettering Institute for Cancer Research**, to develop an ES cell-derived dopamine neuron source for cell therapy in Parkinson’s disease, $14.9 million;
- **Regenerative Research Foundation**, to develop the retinal pigment epithelial stem cell as a cell replacement therapy for age-related macular degeneration, $10.8 million;
- **Weill Cornell Medical College**, for the development of a cure for sickle cell disease by enabling the genetic modification of a patient’s own blood stem cells, $15.7 million;
- **Roswell Park Cancer Institute**, to re-engineer adult stem cells derived from blood to target ovarian cancer, $11.9 million;
- **Icahn School of Medicine at Mount Sinai**, for continued development of a process to increase the number of stem cells in cord blood collections for transplant in patients with blood cancers and genetic disorders of blood cells, $8.8 million.

**Research progress**

In addition to the Consortia, NYSTEM-funded researchers across the state have generated important and exciting findings in basic stem cell biology, as well as stem cell research related to understanding and curing a variety of human diseases. Examples of research progress made as a direct result of NYSTEM can be found in the Progress Report Addendum.

**Disease areas**

Stem cell science covers a diverse range of scientific topics, and mirroring that diversity, NYSTEM supports research ranging from basic to disease-oriented science (Figures 2.4 and 2.5 – note these charts do not include research supported through either the Institutional Development or Consortia Planning awards). A large bulk of NYSTEM-supported science, 22% ($51.3 million), would be described as basic research, but the majority is focused on disorders and diseases, with significant portions going to study the bases of and potential therapies for neurological disorders (20% or $48.5 million), hematological disorders excluding cancer (17% or $41 million), and cancer (15% or $35.9 million). Other targets of NYSTEM-funded research include cardiovascular diseases, eye diseases, disorders and injuries of the musculoskeletal system, psychiatric disorders, liver diseases, diabetes, plus many others.

![Figure 2.5: NYSTEM Funding Areas by Number of Awards](image)
Parkinson’s disease (PD) is a crippling neurodegenerative condition affecting 1 million patients in the United States and more than 5 million worldwide. The hallmark of PD is the loss of a specific type of nerve cell in the patient’s brain—the so-called dopamine nerve cells. Today’s most effective drug therapy was discovered nearly 50 years ago and is plagued by decreased effectiveness over time. Deep brain stimulation (DBS) is a powerful, yet costly, surgical treatment option for PD patients. However, DBS can trigger psychiatric side effects, including depression, and represents a costly procedure involving constant surgical follow-ups.

Furthermore, neither drug therapy nor DBS can bring back the dopamine nerve cells lost to the disease.

Cell replacement therapy is a novel option with the potential to permanently restore lost dopamine brain function in PD patients. However, the development of a cell therapy for PD has been slowed down by the lack of suitable cells. Only very recently, it has become possible to produce the precise nerve cell type lost in PD in the laboratory. The use of lab-grown cells presents an exciting new therapeutic option for PD patients that may overcome some of the current limitations of drug therapies or DBS.
NYSTEM has been absolutely essential for our ability to push forward towards a first human trial using lab-grown dopamine cells in PD. Financial support from NYSTEM was a key ingredient on the initial road of discovery, to identify the “recipe” of molecules needed to coax human stem cells into dopamine neurons. This was a challenging task that has taken nearly 10 years to complete. Support through NIH has generally been limited for this effort, and private support has been important but short-lasting and insufficient. Only the sustained financial support through NYSTEM enabled us to follow our vision and to allocate the resources needed to finally crack this challenge. In 2011, we were able to demonstrate that lab-grown cells can cure mice, rats, and monkeys with experimental PD. Even more important, we obtained NYSTEM support to enable the transition towards human studies. When academic science fails to generate a cure, the process is often called the “valley of death,” and funding agencies rarely step in to help in this transition. Providing support to bridge this valley is one of the most important contributions of NYSTEM for the field of regenerative medicine. The NYSTEM contract has enabled the creation of a multidisciplinary Consortium with the overarching goal of developing an optimized, clinical-grade source of human dopamine neurons for cell therapy in PD by 2017.

In addition to direct financial support, support for building the infrastructure needed to develop stem cell-based products in New York State has been similarly essential. For example, our NYSTEM-supported stem cell core facility enabled us to quickly disseminate our knowledge to other groups within New York State and beyond working on PD or other human disorders that may benefit from stem cell-based products. The in-house clinical grade cell production facility could be equipped specifically for the needs of our Parkinson’s project. The resources developed through this contract will benefit not only our own project but also pave the way for other New York State investigators ready to translate their work.

An important component of developing a first in human therapeutic stem cell product is the multidisciplinary nature of the effort. Our project involves basic scientists, engineers, manufacturing specialists, neurologists, surgeons, ethicists, trial experts, and patient advocates who are dedicated to the achievement of this goal. The involvement of patient advocates is particularly important both to get input from the patient community but also as an effective means to spread information on the trial back into the community. Nearly every day we are contacted by PD patients or their relatives who are desperate and willing to try any promising new experimental approaches. While such interest from the patient community illustrates the need for novel and better therapies in PD, it is important to gauge expectations and to explain the nature and goals of early stage clinical trials. Based on our technology, there are currently three major efforts across the world to implement lab-grown dopamine cells as a therapy for PD. In addition to our New York State Consortium, there are efforts in Europe and in Japan that work on slight variations of our technology for their own human trials. Thanks to NYSTEM, our group is in an excellent position to be a world-leader in this effort and to bring the potential benefits to the local PD patient population, as well as exploring the potential economic advantages in what is a multibillion dollar market in PD pharmaceutics.

Stefan Irion, Mark Tomishima, Lorenz Studer and Viviane Tabar
**2008 Strategic Plan Goal II:**
Training Stem Cell Researchers

**Mission:** Ensure a robust, interactive stem cell research community in New York State by providing training opportunities to support the entry of new and established investigators into stem cell research.

NYSTEM fosters training of stem cell researchers at all levels of the research career path. Four RFAs have been issued for support of new stem cell research faculty, cross-disciplinary training and collaboration of new or established faculty in stem cell science, and institutional funding for the training of multiple graduate students and postdoctoral fellows working in stem cell laboratories (Figure Add.2 in the Progress Report Addendum). Twelve awards have been made in these combined categories for a total of $18 million. Institutional training programs for students and fellows have been funded at research institutions across the state. Unlike NIH training awards, NYSTEM-funded training programs can be used to support foreign predoctoral students and postdoctoral fellows, allowing New York stem cell investigators to recruit the most talented candidates from anywhere in the world to enhance New York’s research enterprise.

To date, through the four extant Institutional Training programs, NYSTEM has supported 20 Ph.D. students and 29 postdoctoral fellows.

In addition to its training programs, NYSTEM seeks to foster a robust, collaborative stem cell research community in New York through its Annual Meetings, convened every year since 2009. The most recent NYSTEM Annual Meeting was held May 14–15, 2015, at The Rockefeller University in New York City. The meeting attracted approximately 200 attendees from across the state, including principal investigators, postdoctoral fellows, graduate students, and administrators, as well as experts from outside New York. Along with plenary and poster sessions showcasing the breadth of stem cell research progress being made across the state, the meeting included a special session on the three most recently awarded Consortia. Importantly, the meeting was highly interactive, with ample opportunities for attendees to establish communication and collaboration with their peers around the state.

**Impact of NYSTEM Training Programs for Stem Cell Researchers**

Key to the success of any scientific field is providing substantial funding for the next generation of researchers, as well as for the recruitment and support of established researchers. For this reason, a cornerstone of the NYSTEM program is its grant support for students, fellows, new investigators, and established investigators with critical expertise. Examples of the impact made by NYSTEM-funded fellows and researchers in NYSTEM training programs can be found in the sidebars and in the Progress Report Addendum.
I have spent my entire academic career focused on stem cell research. I feel as if I hold a personal stake in the subject, as stem cell research shows tremendous promise in alleviating our most devastating diseases and malignancies, many of which have wrought tragedy in my own family and community. When it was time to choose where to do my graduate training, the [NYSTEM-sponsored] Stem Cell Biology training program at the New York University (NYU) School of Medicine was my number one choice. It has and continues to foster a rich environment where I can develop and expand my scientific, critical thinking, and creative abilities.

I was very fortunate to have the opportunity to choose among Ph.D. programs at other top schools... but I strategically chose to attend NYU specifically for their Stem Cell Biology program. With dozens of faculty spanning the gamut of model organisms and tissues systems, I am constantly afforded an enormous degree of flexibility to choose in which stem cell area I want to specialize. Academic training and laboratory rotations are rigorous and backed by thorough oversight and mentorship; this ensures that I not only become an exceptionally well-trained scientist, but that I also stay on-track and exceed—not just meet—requirements in the process. I have forged lifelong relationships with mentors, professors, and peers, which opens the door for fruitful, multidisciplinary collaborations, as well as access to science and career guidance.

I would not be able to achieve my ambitions without the backing and support of the exquisite training I receive through the Stem Cell Biology program. Funding is the lifeblood of stem cell research, and I am proud to be a part of an institution that is one of the first to invest in the training of future leaders in this promising, robust, and ever-evolving field. As scientific paradigms shift to those with immediate human impact, stem cell research will most certainly be at the nexus of this change. Training programs like the Stem Cell Biology program at NYU will guarantee next-generation researchers are on the frontlines propelling groundbreaking work into the future.
2008 Strategic Plan Goal III:
Developing Infrastructure for Stem Cell Research

Mission: Expand stem cell research capacity in New York State by establishing and ensuring access to appropriate infrastructure and resources.

NYSTEM recognizes that widely available, state-of-the-art infrastructure and instrumentation are critical to achieving its mandate to create a world-class environment for stem cell research across New York. To date, four RFAs have been issued to fund shared core facilities and instrumentation, resulting in 48 awards for a total of $94.18 million (Figure Add.3 in the Progress Report Addendum). These facilities foster communication and the open exchange of ideas and resources among stem researchers within and across institutional boundaries. Many of these shared facilities enable collaboration not only among New York researchers but also with those across the country and internationally. These facilities support the preeminence of New York as an environment in which to conduct innovative research at the forefront of stem cell science.

NYSTEM-funded shared resources include:

NEW YORK UNIVERSITY, Developing an integrated platform for siRNA and shRNA-based genome-scale screens in eukaryotic stem cells

REGENERATIVE RESEARCH FOUNDATION, NeuraCell

RENSSELAER POLYTECHNIC INSTITUTE, an Upstate New York Shared Facility for Basic Stem Cell Research

RESEARCH FOUNDATION FOR MENTAL HYGIENE, Imaging Stem Cells in the Brain for Studying Neuropsychiatric Disorders

THE ROCKEFELLER UNIVERSITY, Shared Facilities and Resources for Stem Cell Research

SLOAN KETTERING INSTITUTE, the SKI Stem Cell Research Facilities

STONY BROOK UNIVERSITY, Shared Facilities for the Stony Brook Stem Cell Center

UNIVERSITY AT BUFFALO, Western New York Stem Cell Culture and Analysis Center

UNIVERSITY OF ROCHESTER, Upstate Stem Cell cGMP Facility

WEILL CORNELL MEDICAL COLLEGE, a Shared Facility for the Derivation, Validation, and Distribution of Stem Cells for Disease Modeling.

Examples of infrastructure and shared resources supported by NYSTEM funding and their contributions to New York’s status as a location for world-class stem cell research are found in the Progress Report Addendum.
Attracting New Scientific Talent to the New York Stem Cell Research Community

A primary goal established by the Empire State Stem Cell Board in its first strategic plan was to foster the recruitment of promising new stem cell investigators to New York. According to data obtained from a survey of institutional administrators, New York institutions recruited more than 500 new stem cell scientists at varying career stages from 2007–2011 alone (see Appendix 5a). Three principal investigators who established new research laboratories in New York within the past 7 years share their stories:

**Ulrich G. Steidl, M.D., Ph.D.**
Associate Professor of Cell Biology and Medicine and the Diane and Arthur B. Belfer Faculty Scholar in Cancer Research, Albert Einstein College of Medicine

Dr. Ulrich Steidl credits the creation of NYSTEM as a trigger for his recruitment to Albert Einstein College of Medicine in 2008 from Harvard Medical School. Since that time, Dr. Steidl has competed successfully to obtain four NYSTEM grants (two IDEA and two IIRP awards) on the transcriptional control of cancer stem cells in acute myeloid leukemia and on epigenomic determinants regulating hematopoietic (blood) stem cells. NYSTEM funding allowed him to discover key genes involved in the regulation of normal and leukemia stem cells, which have led to three patent applications, industry collaborations, and four ongoing clinical trials. The IDEA awards led his group to develop critical new methodologies for epigenetic studies of blood stem cells. Importantly, results generated with the support of his NYSTEM awards played a pivotal role in helping him to obtain funding from the federal government (R01 grant from the National Cancer Institute), private foundations (e.g., Leukemia and Lymphoma Society), and companies (e.g., GlaxoSmithKline) that bring more research funds and jobs to New York.

**Matthias Stadtfeld, Ph.D.**
Assistant Professor of Cell Biology, Skirball Institute of Biomolecular Medicine, New York University School of Medicine

In 2012, Dr. Matthias Stadtfeld moved to New York from Boston where he had been a postdoctoral fellow at Massachusetts General Hospital and the Harvard Stem Cell Institute. He started his own lab at the New York University School of Medicine (NYUSOM) with the goals of understanding the process of reprogramming adult cells into iPS cells and using those cells to create specific blood cell types. NYSTEM resources have been instrumental in helping Dr. Stadtfeld launch a successful research program. He was awarded a NYSTEM IDEA grant in 2013 to support his work on blood cell reprogramming.

(continued)
differentiation. The results of that research will make his lab competitive for larger, longer-term grants from NYSTEM, NIH, and other sources. Dr. Stadtfeld also cites the importance of NYSTEM training programs that support both a graduate student and postdoctoral fellow in his lab. These training grants to NYUSOM, he states, “allow me to have two more people than I would have normally, based on my funding. And that allows me to do research that I couldn’t do without NYSTEM.” Finally, his research includes a collaboration with an NYUSOM RNAi screening facility that was created with NYSTEM funding for infrastructure development. Overall, Dr. Stadtfeld is pleased with his decision to establish his lab at NYUSOM. “I think New York is in an excellent position right now,” he explains, “I’m happy with how the stem cell field has developed in the city and in the state in the last couple of years. It’s quite a good place to be.”

Nicole Dubois, Ph.D.
Assistant Professor of Developmental and Regenerative Biology, Icahn School of Medicine at Mount Sinai

When Dr. Nicole Dubois was looking for an institution at which to launch her own lab in 2013, she had several choices. After completing her postdoctoral fellowship at the McEwen Center for Regenerative Medicine in Toronto, she could have stayed in Canada or, being a native of Switzerland, she considered returning to her roots in Europe. Ultimately, Dr. Dubois chose the Icahn School of Medicine at Mount Sinai as the best location for her lab. She recalls, “comparing the different places, it was extremely clear to me that in terms of the scientific community, as well as the opportunities for stem cell research, New York was truly outstanding in many ways…I’ve found that confirmed now that I’ve moved here.” Dr. Dubois was able to quickly secure a NYSTEM IDEA grant to support her research on iPS and hES cells as model systems to study heart development and disease. Moreover, a NYSTEM-funded shared resource facility at Mount Sinai provided technical support that helped her get experiments up and running in a short time and also allowed her to be immediately embedded within the stem cell community. As a result, Dr. Dubois has already established multiple collaborations based on her NYSTEM-funded project.

Dr. Dubois appreciates NYSTEM’s impact on stem cell research in New York. “I believe that the fact that New York has such a diverse, extensive, and very collaborative stem cell community is strongly linked to the fact that there are additional support systems in place, such as NYSTEM, that significantly support this type of research,” she notes, “This works like a positive feed-forward loop: the stem cell community can grow and do good research with the additional funding, which consequently attracts more stem cell scientists to the community. There are not many places in the United States that can offer such opportunities.”
2008 Strategic Plan Goal IV: Ethical, Legal, and Social Issues and Education in Stem Cell Research

Mission: Ensure that stem cell research in New York State adheres to the highest standards of medical ethics and that the ethical, legal, social, and psychological implications of advances in stem cell research are appropriately addressed by engaging diverse communities in research, scholarship, and education on these issues.

Activities of the ESSCB and its Ethics Committee

In keeping with its charge to adhere to the highest standards of medical ethics and to monitor and respond to the ethical, legal, social, and psychological implications of stem cell research, the ESSCB and its standing Ethics Committee engage in ongoing efforts to establish standards for all NYSTEM-funded research and related activities. The ESSCB has also designed initiatives to provide informal education to diverse groups within the general public, with the purpose of promoting awareness and interest in the world of stem cells. A list of achievements can be found in the Progress Report Addendum. Two significant accomplishments are the development of a policy on oocyte donation and the creation of model consent forms.

- In June 2009, the ESSCB issued a policy allowing NYSTEM investigators to compensate women who donate their oocytes directly and solely to stem cell research for the expense, time, burden, and discomfort associated with the donation process. The policy allows the use of NYSTEM funds to compensate donors of oocytes for research in amounts equal to those allowed by the State for donors of oocytes for in vitro fertilization. It prohibits compensation based on the number or quality of oocytes donated.

  To date, NYSTEM is the only funding agency to take this position on compensation of oocyte donors for research. In its 2013 review of the California Institute of Regenerative Medicine (CIRM), the Institute of Medicine (IOM) noted that New York’s policy allowed it to support research like Dieger Egli’s SCNT work, “which would be unlikely to be undertaken by a CIRM-funded scientist given CIRM’s rules against compensating egg donors and the difficulties scientists have experienced in recruiting uncompensated donors.”

- In November 2011, the Ethics Committee created and the Funding Committee approved model consent forms for tissue donation, including eggs provided directly and solely for stem cell research; eggs collected during the course of fertility treatments and in excess of clinical need; sperm provided directly and solely for stem cell research and sperm in excess of clinical need; embryos created for fertility purposes and in excess of clinical need; and somatic cell donation for human embryonic stem cell research. NYSTEM is the only stem cell research funder to issue model consent forms for tissue donation for stem cell research.

NYSTEM Support for ELSIE Activities Related to Stem Cell Research

In addition to the activities of the ESSCB Ethics Committee as described above, NYSTEM actively supports education programs for the general public. To date, five RFAs have been issued, resulting in 14 awards for $4.42 million (Figure Add.4 in Progress Report Addendum). Stem cell education programs supported by NYSTEM and staff-led activities reach a wide array of audiences, including undergraduate students with both biology and non-biology majors, precollege students, and the general public.

A cornerstone of the education awards portfolio was the development of undergraduate curricula for stem cell research and related issues. Five awards were made to New York institutions:

- Columbia University, Stem Cells: Biology, Applications, and Ethics
- The New School, Interdisciplinary Stem Cell Curriculum for Non-Majors
- Binghamton University, the Business and Biology of Stem Cells in Cell Therapy
- Syracuse University, Interdisciplinary Portable Course on Stem Cells
- University of Rochester, the Science and Ethics of Stem Cells: a Case Study-Based Course for Undergraduates.

Examples of other educational opportunities made possible by NYSTEM can be found in the Progress Report Addendum.
2008 Strategic Plan Goal V: Administration of the NYSTEM Program

Mission: Administer the Empire State Stem Cell Trust Fund under the highest standards of accountability and integrity on behalf of the people of New York State.

Accountability and Protection of New York’s Investment in Stem Cell Science

The State of New York has made a significant commitment to stem cell science with the hope and expectation that its investment will pay off in the form of new therapies to treat and cure many devastating diseases that affect New Yorkers and others worldwide. As steward of the public’s investment, NYSTEM is committed to administering the program according to the highest standards of integrity, accountability, and transparency.

To this end, four contracts have been awarded in response to Requests for Proposals (RFPs) for peer-review and oversight services (Figure Add.5 in Progress Report Addendum). NYSTEM has contracted with an independent organization, the American Institute of Biological Sciences (AIBS), to manage the peer review of grant applications. NYSTEM further fulfills its goal of administering the program through the establishment of standard protocols for grant review, award, and contracting.

Applications submitted in response to RFAs are forwarded to AIBS for peer review. Once applications receive a peer review score from the expert panel, the ESSCB Funding Committee considers each application according to criteria it has determined and makes award recommendations to the New York State Commissioner of Health, who has authority to approve the final funding plan.

In addition, through separate contracts, AIBS facilitates ongoing, independent review and oversight of the six NYSTEM-funded Consortia for the acceleration of new therapeutic applications of stem cells. These Oversight Panels, comprised of top international experts, make recommendations to NYSTEM based upon their continuing evaluation of the respective Consortia.

Public Access to Information

The NYSTEM website (http://stemcell.ny.gov) provides public access to information on advances in stem cell research, biographies of many New York stem cell scientists, agendas of NYSTEM Annual Meetings that include research abstracts, and press releases about new program funding and other programmatic events. Information about the ESSCB, including membership rosters and scheduled events, is announced on the NYSTEM website.

As of April 2015, the full ESSCB has met 15 times and the Funding and Ethics Committees have convened in separate meetings a combined 27 times to conduct NYSTEM business. ESSCB and Committee meetings are open to the public in accordance with the requirements of Article 7 (Open Meetings Law) of the Public Officers Law, except when otherwise provided by law, such as during the discussion of grant applications and the work of applicants. In order to facilitate public access, all ESSCB meetings are broadcast live on the Internet through the New York State Department of Health website (www.health.ny.gov/events/webcasts/). Meeting minutes are posted on the NYSTEM website.
**2008 Strategic Plan Goal VI:**

*Mission:* Ensure New York State preeminence in the application of knowledge derived from stem cell research for the greater public good and the generation of long-term support for stem cell research.

**NYSTEM Has Enhanced the New York Research Enterprise and Economy**

Investing in stem cell science, as for all biomedical research fields, is a long-term process. Stem cell science is an evolving field, with much to be learned about basic stem cell biology and the potential of different types of stem cells to repair or replace diseased tissue. Nonetheless, significant progress has been made toward potential clinical applications in some disease areas, and investigators have developed innovative tools, reagents, and products that facilitate research in the field. NYSTEM scientists have leveraged the funding provided by the state to create a highly interactive and productive research community that has increased the value of the NYSTEM investment to enhance the New York research enterprise and economy.

NYSTEM-funded researchers and institutions have successfully attracted funding from other sources to augment the stem cell research environment in New York (see also Appendix 5.c). As of 2011, at least $142 million was donated from private philanthropic sources for the support of stem cell research and/or the creation or maintenance of stem cell research centers or institutes at New York institutions. Another $152 million was obtained by stem cell investigators from research funding organizations, including the NIH, foundations, industry, or other sources. These numbers, which are derived from 2012 and 2014 surveys of funded investigators plus other sources, likely underestimate the full value of new resources that the NYSTEM investment has attracted to New York since 2007.

New York researchers have also created value through patenting and commercialization of their NYSTEM-supported research findings (see also Appendix 5.d). To date, at least seven start-up companies have been launched by NYSTEM-funded stem cell investigators (Figure 2.6). These companies focus on developing therapies for a variety of diseases, as well as creating diagnostic tools and reagents to facilitate stem cell research. Importantly, the creation of new industry in New York brings new jobs and investment to the state and highlights the real impact that NYSTEM investment has on the New York economy. In the future, the ESSCB envisions a new role for NYSTEM in fostering interactions between funded investigators and the pharmaceutical and biotechnology industries to accelerate commercialization of NYSTEM-funded discoveries, as described in Chapter 3.
Figure 2.6: **Start-Up Companies in New York Based on Stem Cell Technology**

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<thead>
<tr>
<th>START-UP COMPANY</th>
<th>PRINCIPAL INVESTIGATOR, INSTITUTION</th>
<th>BUSINESS FOCUS</th>
</tr>
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<tbody>
<tr>
<td>Angiocrine Biosciences</td>
<td>Shahin Rafii, Weill Cornell Medical College</td>
<td>Therapies for leukemias and blood disorders</td>
</tr>
<tr>
<td>Blood Cell Technologies</td>
<td>Wadie Bahou, Stony Brook University</td>
<td>Blood product diagnostics and therapeutics</td>
</tr>
<tr>
<td>Epibone</td>
<td>Gordana Vunjak-Novakovic, Columbia University</td>
<td>Anatomically shaped living bone grafts</td>
</tr>
<tr>
<td>Marrow Source</td>
<td>Yupo Ma, Stony Brook University</td>
<td>Ex vivo expansion of stem cells</td>
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<tr>
<td>RegeneRx</td>
<td>Jeremy Mao, Columbia University</td>
<td>Bio-Pulp</td>
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<tr>
<td>StemCulture LLC</td>
<td>Christopher Fasano, Jeffrey Stern, and Sally Temple, Regenerative Research Foundation</td>
<td>Stem cell culture supplies</td>
</tr>
<tr>
<td>Tara Biosystems</td>
<td>Gordana Vunjak-Novakovic, Columbia University</td>
<td>“Organ-on-a-chip” platform to provide physiologically-relevant human tissue models for both toxicology and drug discovery applications</td>
</tr>
</tbody>
</table>
As Co-Founder, Principal Investigator, and Scientific Director of the Neural Stem Cell Institute (NSCI) in Rensselaer, Sally Temple, Ph.D., has dedicated her research program to developing neural stem cell-based therapies for eye, brain, and spinal cord disorders, trauma, and neurodegenerative diseases. NYSTEM has supported her promising research through a variety of mechanisms, including an IIRP grant for work on cortical development, a targeted grant to study stem cell applications in Parkinson’s disease, and a shared facility award to create NeuraCell, a centralized collection of different types of neural stem cells and knowledge to aid the field. In addition, Dr. Temple and her colleagues were awarded a $10.8 million NYSTEM Consortium grant in 2011 to accelerate the development of stem cell therapy for age-related macular degeneration, the leading cause of blindness in the elderly. Dr. Temple credits NYSTEM funding for helping her and her colleagues grow NSCI, by supporting a critical mass of scientists and a productive research environment. This also contributed to the launch of a start-up company, StemCulture, LLC, that serves the entire human stem cell research field.

According to Dr. Temple, “One tends to think of translating discoveries toward therapeutics, and that is certainly our primary motive—in our particular case, we want to contribute to combating neurodegenerative diseases—however, along the way, there is a lot of value in the other things that we find.” The lightbulb moment came when Dr. Temple’s lab switched from using mouse stem cells exclusively to incorporating studies with human pluripotent stem cells into the research program. Human stem cells are notoriously finicky in culture, and they must be fed every day, including holidays, or they
lose pluripotency and differentiate into specialized cell types. Thus, maintaining human stem cell cultures is a labor-intensive, time-consuming, and expensive process. To overcome this problem, Dr. Temple encapsulated cell growth factors in tiny beads that provide sustained release of the factors into stem cell cultures over time, much like a slow-release aspirin pill gradually releases medication into the body. By putting the beads into the culture fluid, human stem cells only need to be fed two or three times per week. Not only does this technology make the cell culturing process more manageable for scientists, it also improves the health of the stem cells because they are bathed in a more stable culture environment.

As Dr. Temple reported on her sustained-release growth factor beads to the research community, other stem cell scientists quickly began to request some beads for use in their own labs. Making and distributing the beads was not in the purview of the nonprofit NSCI, so Dr. Temple co-founded StemCulture to commercialize the sustained-release technology. The company is currently housed in a building constructed by the University at Albany Foundation that provides incubator space for both nonprofit and for-profit ventures. Keeping StemCulture in Rensselaer allows Dr. Temple and her co-founders to maintain close oversight of the company lab and contributes to the New York’s standing as a leading center of stem cell research. The company now has a global reach, selling stem cell culture reagents to labs across the United States, as well as in Europe, Japan, and soon, China. The company’s product line continues to grow as researchers propose additional growth factors that could be enhanced with sustained-release technology.

At present, NYSTEM does not have mechanisms or resources in place to assist researchers, like Dr. Temple, who have opportunities to capitalize on discoveries in stem cell science and to commercialize their research findings, whether therapeutic or technological. While Dr. Temple was fortunate to have access to resources provided by the Regenerative Research Foundation, she suggests that many institutions struggle with technology transfer. In her view, NYSTEM support has already been “transformative” by creating leadership within the state, retaining key people, and building new programs that are advancing science and discovery at a great pace. Now, NYSTEM could carve out an important role by assisting researchers and institutions to generate intellectual property and secure patents, identify commercial opportunities, and even invest at the venture capital level in promising start-ups based on its funded research. “There is a whole new world of opportunities in the biotech and biomed space, and so many new discoveries have been generated from stem cell research that one hopes there will be further investment in this area,” she states. “It takes a long time to get a program to that productive point, and I feel that we are now at the nexus of taking off. I am very hopeful that this will be recognized and invested in over the next 10 years.”
NYSTEM Is a Model for State Funding of Stem Cell Research

NYSTEM is one of several state-specific programs for stem cell science and regenerative medicine, including the California Institute of Regenerative Medicine (CIRM), the Connecticut Stem Cell Research Grants-in-Aid Program, and the Maryland Stem Cell Research Fund, that were created in response to the restrictions imposed by President Bush. Other initiatives—the New Jersey Commission on Science and Technology Stem Cell Research Program and the Illinois Regenerative Medicine Institute—were each launched in 2005 but are no longer functioning. In terms of financial commitments, NYSTEM is second only to CIRM, which has a budget authorization of $3 billion over at least 10 years. The Connecticut program provides $100 million over 10 years, and Maryland has funded approximately $91 million in stem cell research since 2006, with commitments varying each year according to state appropriations. Programs in New Jersey and Illinois each provided approximately $15 million for stem cell research grants before shutting their doors. A final, related program is the $3 billion Cancer Prevention Research Institute of Texas, created in 2007 in part in response to CIRM, NYSTEM, and the other state-funded programs.

In addition to these state programs, other countries are following suit and creating programs specifically aimed at building regenerative medicine as key pillars of their biotechnology and health care economies. These include Canada’s Centre for Commercialization of Regenerative Medicine, the United Kingdom’s Catapult, which aims to grow a UK cell therapy industry, Japan’s Center for iPS Cell Research and Application, and Korean as well as European Union initiatives. Most of these programs focus specifically on commercialization of stem cell research, indicating clearly that these other governments see the potential for both improved health and economic wellbeing of their citizens.

An analysis published in February 2015 looked at the effect of state stem cell funding programs on publication trends in the stem cell research field. The analysis showed that California and Connecticut researchers increased their share of hES cell-related research publications after the establishment of their respective state programs. In contrast, New York and Maryland maintained their percentages. The authors suggested that this outcome in New York and Maryland may indicate how well those states maintained their share of hES cell-related research stemming the potential brain drain created by other states’ investment in the field. However, another likely explanation in New York is the success of the ESSCB intentionally allowing for and supporting a broad definition of stem cell research: rather than focusing primarily or exclusively on hES cells, NYSTEM and the ESSCB recognized that critical scientific discovery and viable cures might come from a variety of embryonic, adult, or induced pluripotent stem cell sources. A further sign in support of this is the move by CIRM in more recent years to fund research on a broad array of stem cell types, not just hES cells.
External Review of the NYSTEM Program

To evaluate its effectiveness in a transparent and unbiased manner and provide public accountability, NYSTEM commissioned an independent, external review of the program and its accomplishments, strengths, and weaknesses. Four internationally renowned experts in stem cell science from institutions outside New York agreed to serve as an External Review Panel (ERP) for this purpose:

SEAN MORRISON, PH.D., ERP Chair, Mary McDermott Cook Chair in Pediatric Genetics and Director of the Children’s Medical Center Research Institute at the University of Texas Southwestern Medical Center, Howard Hughes Medical Institute investigator, and President of the International Society for Stem Cell Research (ISSCR). Dr. Morrison studies stem cells and cancer cells in the nervous and hematopoietic systems.

JOHN KESSLER, M.D., Ken and Ruth Davee Professor of Stem Cell Biology, Benjamin Boshes Professor and Chair, Department of Neurology, Professor, Department of Pharmacology, and former Director, Stem Cell Institute at Northwestern University. Dr. Kessler’s research focuses on stem cell biology and approaches to regeneration of the damaged or diseased nervous system.

STORY LANDIS, PH.D., until October 2014 the Director of the National Institute of Neurological Disorders and Stroke, NIH. In 2007, Dr. Landis was appointed Chair of the NIH Stem Cell Task Force. Dr. Landis’ research has focused on nervous system development.

DAVID SCADDEN, M.D., Gerald and Darlene Jordan Professor of Medicine at Harvard University, Chief of the Center for Regenerative Medicine at the Massachusetts General Hospital, Co-director of the Harvard Stem Cell Institute, and Co-chair and Professor, Harvard University Department of Stem Cell and Regenerative Biology. Dr. Scadden investigates the regulation of the hematopoietic stem cells by the microenvironment or niche.

The ERP was charged with evaluating the NYSTEM program according to a number of criteria, including its impact on stem cell research in New York and its effect on advancing the field overall toward clinical translation. The panel also considered NYSTEM’s broader impact on navigating ethical issues and public education. Finally, the panel evaluated NYSTEM administrative processes, such as budgeting, governance, peer review, contracting, oversight, and the development of grant programs.

The ERP began its work in October 2014 and issued its final report, NYSTEM: Capitalizing on opportunities and confronting challenges. A Report by the NYSTEM External Review Panel, on March 22, 2015. Appendix 3, http://stemcell.ny.gov/node/981. Overall, the ERP was highly complimentary regarding the direction and achievements of the NYSTEM program and its funded scientists; however, the panel also identified several challenges that the program must address in order to improve efficiency and productivity. The ESSCB has carefully reviewed the ERP report and incorporated many of its recommendations into the updated Strategic Plan for 2015–2019 and its vision for NYSTEM’s future (Chapter 3).
III. The Future

Charting a Path to the Future
The overarching intent of this updated strategic plan is to facilitate NYSTEM support for the next, critical phase of stem cell science and translational clinical development, while continuing support for discovery research and a robust, collaborative stem cell community in New York. A fundamental principle driving the development of updated strategic goals is the protection and enhancement of New York’s already significant investment.

TO ASSIST NEW YORK State to maintain its leadership role in the field, the ESSCB proposes the following overarching goals for the next phase of stem cell research support:

• Achieving renewal of stem cell research support with long-term, stable funding and additional resources for the development and clinical testing of promising cures.
• Bridging the Valley of Death in stem cell therapy development. Supporting translational and clinical research, with an emphasis on increasing the number of multi-investigator Consortia for therapeutic development, with sufficient time and resources to bring new therapies to the point at which industry is willing to support late-stage trials, development and dissemination to patients; in addition, continuing abundant support for basic research.
• Retaining and recruiting highly qualified research professionals at all career stages, within the context of broader efforts to build and nurture the biomedical research enterprise in New York, with a target increase of 20% over current levels within five years.
• Creating and/or expanding specialized infrastructure in New York for the development of cell-based therapies and screening of small molecules with stem cells for drug development.
• Exploring strategies to maximize the economic potential of the NYSTEM program and its research advances by creating new jobs, building alliances between stem cell investigators and the pharmaceutical/biotechnology industry, and attracting new stem cell-related industry to the state. Bringing biotech into the treatment development process earlier in order to minimize the gap between concept and cure. Currently, there are fewer than 30 stem cell-related biotechnology companies based in New York. NYSTEM’s five-year target is to increase this number to 50, including at least 10 based on NYSTEM-supported research.

Updated Strategic Goals for NYSTEM Funding

As set forth in Figure 3.1, the Board recommends that future funding initiatives increase actual expenditures for research and training, while modestly de-emphasizing infrastructure spending. Further, based on the low priority given to these programs by the ERP, the Board recommends that future expenditures for ELSIE programs be deferred, at least until program resources, including staff levels, are increased.

Based on the experience and track record of the first phase of funding, the ESSCB wishes to adhere to its original goal structure, while redirecting some aims in each goal category, and emphasizing the importance of cures and commercialization.
Goal #1: Provide Ongoing Support for New York Stem Cell Science, Scientists, and Entrepreneurs

- **Advance stem cell science.** The ESSCB recommends that the majority of NYSTEM resources continue to be used to support basic, translational, and clinical research in stem cell science and regenerative medicine with the overarching goal of understanding and treating human diseases. The Board remains committed to funding the highest quality, investigator-initiated research as determined by peer review, without bias toward particular cell sources, models, or disease targets.

- **Support translational research.** The ESSCB wants to emphasize new translational and clinical research through Consortia and other mechanisms to accelerate the delivery of stem cell-based therapies to human patients. This is the time to transition into the next phase of stem cell support, namely, helping funded investigators navigate the difficult path to the clinic. Researchers need additional resources, support in learning how to deal with regulators, and training in regulatory matters.

- **Target the Valley of Death.** The Valley of Death is not a gap in scientific development. It is a gap in financial support for scientific development. It is a place where brilliant concepts and discoveries often reach the end of the road. Why? Not because they do not deserve funding, but because sources of funding for this stage of development barely exist. Federal funding takes investigators to the near side of the gulf. Private investors remain at a distance. While biotech and pharmaceutical companies are increasingly interested in stem cell therapies, they will rarely invest substantial funds in a product when the marketing phase is more than three to five years in the future.

  This simple economic fact provides two opportunities for NYSTEM. First, NYSTEM must provide more gap funding for this critical, underfunded stage of development. Second, it must assume a role in facilitating interactions between investigators and the pharmaceutical/biotechnology industry in order to attract late-stage funding from industry or venture capital sources. Government cannot provide the tremendous amount of money needed to support these projects through clinical testing and on to development and commercialization. NYSTEM must explore and support expert...
The Future

A report of the Empire State Stem Cell Board, 2015

research into viable business models to entice industry into the field at an earlier stage.

- **Create opportunities to assist investigators with commercialization of research findings.** NYSTEM-funded research has already resulted in numerous patent applications and patents and has begun to be commercialized. As the stem cell field continues to mature toward the development and testing of new treatments and cures, those numbers will grow. The ESSCB recommends that NYSTEM, through a commissioned study or other means, identify mechanisms for how best to foster commercialization and create new jobs and businesses in New York. Moreover, NYSTEM and the ESSCB have an opportunity to leverage programmatic resources to help attract more pharmaceutical/biotechnology industry—both start-up and established companies—to the state and to the field.

- **Train stem cell investigators.** New York has become a leader in the stem cell research field, but the next generation of stem cell researchers is at risk, threatened by decreased NIH resources for training and research. More training programs are essential to maintain New York’s competitive position.

- **Develop stem cell research infrastructure.** The ESSCB acknowledges the critical role of NYSTEM funding in developing infrastructure and shared resources for stem cell research in New York to date. With many state-of-the-art facilities and equipment in place across the State, the Board reaffirms its original target allocation but recommends that actual expenditures for infrastructure be monitored to more closely come within the allocation.

Consistent with this Goal, the ESSCB has approved three initiatives that are under development for release as RFAs in 2016:

- **Innovative Partnerships for Commercialization of Stem Cell Research Discoveries:** To promote New York State research institutions partnering with business entities to facilitate development and commercialization of products, technology, tools, and therapies related to stem cells. This will be the first of a series of projects designed to partner NYSTEM investigators with industry. NYSTEM also plans to conduct sessions where researchers can present exploitable ideas to representatives and investors from the private sector and to facilitate transfer or handoff of exploitable concepts for development.

- **Empire State Stem Cell Distinguished Professor Awards:** To recruit top level stem cell scientists and their established research programs to New York State research institutions, thereby furthering NYSTEM’s mission to accelerate the understanding of stem cell biology in New York and the development of therapies and diagnostic methods. Part of the thinking here is that young, developing researchers will follow top faculty to work under these experts, further enriching the New York stem cell environment.

- **Translational RFA:** Consistent with the ESSCB goal to help New York researchers to bridge the Valley of Death, the Board is working on various models to provide opportunities to prepare scientific discoveries for development, translation, and ultimately, clinical trials.

Another pending initiative for NYSTEM is to explore collaborations with New York State agencies charged with economic development, to help focus efforts to create new jobs and businesses in the biotechnology sector.

Two related RFAs supporting research and training are ready for release in the next fiscal year as well:

- **Investigator Initiated Research Projects (IIRP) and Innovative, Developmental or Exploratory Activities (IDEA) in Stem Cell Research, Cycle V:** To stimulate and support basic, applied (mechanistic, technological), translational, preclinical, and clinical scientific investigations on any aspect of stem cell biology that will lead to a better understanding of the unique properties of stem cells and allow their utilization to treat disease.

- **Empire State Institutional Training Programs in Stem Cell Research for Predoctoral and Postdoctoral Fellows, Cycle III:** To provide funding for institution-based training programs that will enable New York State to attract and retain the most promising and exceptionally talented predoctoral and postdoctoral fellows and to support the continued training of researchers with extraordinary potential for making significant contributions to the fields of stem cell-related research.
Goal #2: Provide Ongoing Leadership on Ethical, Legal, and Social Issues and Education Related to Stem Cell Science

- **Develop ethics guidelines and policies for stem cell research.** As stem cell research in New York advances towards clinical trials, the ESSCB affirms its commitment to ensuring that all stem cell research and stem cell-based clinical trials in New York be conducted according to the highest ethical, medical, and scientific standards. Ongoing issues for possible discussion include, but are not limited to: guidance for stem cell-based clinical trials, including issues related to long-term follow-up of human subjects; model consent forms for participants in stem cell-based clinical trials; new technologies that can affect the germline; guidelines for regulatory oversight of clinics that offer stem cell therapies in New York or to New Yorkers; and global issues related to stem cell “tourism.” The Board expects to continue its engagement of scientific and ethics experts to develop clear and rational guidelines for the conduct of NYSTEM-funded stem cell research in New York and to respond to new issues that arise as the stem cell field continues to advance.

- **Resume the Board’s Role in Providing General Education to Teach the Public about Stem Cell Science and to Attract Young People to the Field.** Consistent with its conviction that stem cells hold the key to the future of medicine, the ESSCB believes it is imperative to educate the public and teach pre-college students about stem cell biology. While recommending a temporary hiatus in this category of funding, the ESSCB has not abandoned this commitment and recommends it be resumed as soon as higher levels of funding and staffing are restored.

Goal #3: Enhance the Administration of the NYSTEM Program

- **Promote NYSTEM leadership and collaboration in the broader stem cell community:** The ESSCB expects that NYSTEM, representing New York and the State’s stem cell community as a whole, will continue to collaborate in national and international initiatives related to stem cell research. For example, NYSTEM should encourage and support investigator participation in stem cell line repository and/or registry initiatives to ensure that novel and important hES and iPS cell lines developed in New York laboratories and elsewhere are made available to the field. NYSTEM should explore the potential for participation in ongoing efforts to create regional, national, and/or international biobanks for pluripotent stem cell lines for the purpose of gathering HLA-matched lines for cell-based therapies. NYSTEM should also participate in national and international cooperative efforts to standardize and harmonize stem cell research, such as standards for translational/clinical work that are being developed by the Food and Drug Administration (FDA) and the National Institute of Standards and Technology.

- **Improve the peer review process.** Consistent with the enabling legislation¹, NYSTEM needs greater involvement in and control over its peer review process. Specifically, NYSTEM staff should oversee and participate more in the recruitment and selection of panel members. The ESSCB clarifies, for the benefit of staff and the peer review contractor, that NYSTEM’s involvement in this manner, so long as it does not interfere with the review of applications, would not compromise the independence of the peer review process. In addition, revision of the peer reviewer recruitment strategy and consideration of the development of at least partial standing panel membership or sharing panels with other funders are needed to ensure continuity and consistency of reviewer credentials.

¹ PHL §265-b(2)(a) requires that the Funding Committee “provide for an independent scientific peer review committee composed of individuals with expertise in the field of biomedical research who shall review grant applications based on the criteria requirements and standards adopted by the funding committee, and make recommendations to the funding committee for the award of grants.”
The ESSCB Endorses the ERP’s Recommendations for the Enhancement of Stem Cell Funding in New York

As noted in Chapter 2, NYSTEM solicited an external review by a panel of distinguished scholars in the field who are also experienced managers of research institutes and funding organizations. See NYSTEM: Capitalizing on opportunities and confronting challenges. A Report by the NYSTEM External Review Panel, Appendix 3 and stemcell.ny.gov/node/981.

The ESSCB recognizes that implementation of some of the ERP’s recommendations exceeds its direct authority, but it nevertheless reaffirms and endorses many of them. These include:

- Renew funding for stem cell research in New York.
- Stabilize the annual NYSTEM appropriation.
- Increase the NYSTEM staff.
- Support development opportunities for staff and scientists.
- Streamline administrative processes for RFAs.
- Speed up time from RFA release to contract execution.
- Create an alternative contract approval process for NYSTEM; streamline the bureaucratic approval process for awards.
- Improve dissemination of NYSTEM accomplishments to keep the public informed and support funded investigators and institutions; empower NYSTEM staff to communicate program accomplishments.

The Urgency of Supporting Stem Cell Science in New York

The stem cell research field is on the verge of delivering curative therapies for the most devastating human conditions. The Board considers it a burning imperative that New York take a leadership role in this future, building on the basic and translational research advances supported by NYSTEM to date and investing in new avenues of stem cell research to maintain a robust pipeline of new discoveries and therapies. The benefits to New York of continuing NYSTEM funding beyond the current appropriation are manifold, while abandoning the program after the originally allocated funds have been expended presents dire risks.

NYSTEM fills an important gap in funding innovative stem cell research that is not supported adequately by the federal government or biopharmaceutical companies. Federal funding for biomedical research has been reduced. Industry is reluctant to fund research in the so-called Valley of Death. As noted by the ERP, the NIH rarely provides support for this essential stage of development, without which potential cures cannot be realized.

NYSTEM has created a cohesive and collaborative scientific community of stem cell scientists in New York through its Annual Meetings, multi-institutional shared resources, and Consortia for translational research, among other awards and activities. These efforts give New York a competitive edge by establishing an attractive, supportive environment for recruitment of talented researchers who further enhance the stem cell research community. With diminishing federal funds for research, however, a significant, reliable funding stream for stem cell research is needed in order to retain the scientific talent that has been created and nurtured by NYSTEM in New York.

In 2005, in response to California’s approval of the $3 billion CIRM program, a New York Times article warned of the potential for a scientific “brain drain” to that state. The article stated, “the lure of California is real.” New York State created NYSTEM within one year of CIRM’s first awards, and there is little evidence that the potential brain drain materialized at the time. Indeed, a significant achievement of NYSTEM funding over the past several years has been to prevent that predicted loss of scientific talent.

CIRM, however, has launched a new campaign, seeking $5 billion – almost double its original funding – for its second phase. If NYSTEM funding is not extended as well, particularly with federal funding severely reduced, a growing number of promising researchers will leave New York for opportunities in California and elsewhere. Only a long-term commitment by the State can ensure that New York retains its position as a preeminent stem cell research community.

Retaining Stem Cell Research Talent in New York: Shahin Rafii, M.D.

In 2004, when California approved state funding for stem cell research and before New York had established its own funding program, many scientists in New York and elsewhere considered relocating, drawn by California’s investment. Shahin Rafii, M.D., a world-leading expert on the use of stem cells for organ and tissue regeneration, weighed the option of moving his lab to the West Coast but ultimately decided to continue building his research program at Weill Cornell Medical College. Now, more than 10 years later, Dr. Rafii, the Arthur B. Belfer Professor in Genetic Medicine and Director of the Ansary Stem Cell Institute at Weill Cornell, is happy with his decision to remain in New York. “There’s no question in my mind that it was a risk not to go to California and have free money at the time,” he says, “but by staying, we were able to achieve many milestones for translating our findings on the vascular niche for stem cell expansion into the clinical setting.”

Over the past decade, Dr. Rafii and his team made significant breakthroughs in stem cell science and published high-impact publications in prestigious journals like Nature and Cell. His research findings culminated most recently in a NYSTEM Consortium award of $15.7 million for the development of a stem cell-based therapy for sickle cell disease. Dr. Rafii acknowledges the importance of NYSTEM support for his research program and for the New York stem cell research community in general, especially in light of the low levels of funding that are currently available from NIH. “The impact of NYSTEM on progressing translational science and basic science has been tremendous. It has allowed many scientists who are working with human embryonic stem cells or other types of stem cells that are high-risk/high-yield and would not otherwise have been funded by NIH or any other agency to be able to secure grants by NYSTEM and move their projects forward,” he maintains. Moreover, “the Consortium grant that we got has rejuvenated my program. [The institution] was proud and energized by the fact that we got this grant to go to the next step. How could you get nearly $16 million from any other entity right now to do high-risk/high-impact translational medicine? Without NYSTEM funding, my lab would have been much less productive, much less innovative, much less transformative.”

In addition to his academic research program, in 2012, Dr. Rafii co-founded a start-up company, Angiocrine Biosciences, based on stem cell technology developed in his lab. The company provides a platform for using endothelial cells from blood vessels to expand stem cell populations. NYSTEM does not currently provide specific resources for commercialization of stem cell research findings, and Dr. Rafii credits the visionary leadership at Weill Cornell and the Ansary Stem Cell Institute for providing incubator space within the
university’s facilities that allowed him to launch the company in New York. He suggests that in order to exploit the potential of stem cell discoveries and intellectual property within the State, it is essential that New York generate affordable, high-quality incubator space for companies within New York City and the vicinity, along with tax breaks to create jobs and foster innovation. As Dr. Rafii points out, one successful therapy for heart disease, brain disorders, or any number of other diseases could pump billions of dollars into the State economy.

Based on his experiences, Dr. Rafii contends that reliable funding is one of the keys to retaining the best and brightest stem cell researchers in New York: “I think that to maintain brilliant, innovative, creative scientists in New York State, we need to generate a niche for them where they can flourish. And the more they stay here, the more jobs are created, the more intellectual property is created, and the more money comes to New York State.” Through ongoing support of NYSTEM, the State has an opportunity to make it appealing for scientists who have made discoveries and generated intellectual property within New York institutions to stay here, bringing scientific, medical, and economic benefits to the public.
Why Haven’t You Cured Anything Yet?

Michel Sadelain and Beta Thalassemia: the Long Road from Concept to Cure

Basic Research to Proof-of-Concept
Michel Sadelain, M.D., Ph.D., is Director of the Center for Cell Engineering and the Stephen and Barbara Friedman Chair at Memorial Sloan Kettering Cancer Center (MSKCC). In 1989, he began a two-decade long program to find a cure for beta thalassemia. His experience illustrates the long-term commitment and resources needed to bring a promising idea from concept to a first-in-humans clinical trial.

Beta thalassemia patients have a mutation in the gene for the beta chain of hemoglobin, a protein in red blood cells that carries oxygen from the lungs to all tissues in the body. Without enough hemoglobin, patients develop potentially life-threatening anemia, and in its most severe form, beta thalassemia can be fatal by age 4–5 years. While the disease can be managed with frequent, lifelong blood transfusions, this treatment is expensive and time-consuming and has significant side
effects. Dr. Sadelain reasoned that a cure for beta thalassemia could be achieved by adding a functional gene or repairing the mutated beta hemoglobin gene in the patient’s own hematopoietic (blood-forming) stem cells of the bone marrow that produce red blood cells. For the next 10 years, Dr. Sadelain’s team, along with others in the field, studied the biology of the beta-globin gene, hematopoietic stem cells, and gene transfer strategies to provide functional, therapeutic genes.

Proof-of-Concept to First-in-Human Trials

In a landmark Nature paper in 2000, Dr. Sadelain’s group reported that they had cured beta thalassemia in a mouse model that mimics the human disease. Yet, despite the clear success of his proof-of-concept therapy in animals, it would be another decade before Dr. Sadelain could launch a clinical trial to test the most important question: would the strategy work in human beta thalassemia?

Bringing Dr. Sadelain’s vision to reality required seven additional years of basic research, ongoing dialogue with the FDA as together they charted a new path through the regulatory process, a separate clinical trial on collecting hematopoietic stem cells from thalassemia patients, construction of a GMP (good manufacturing practice) facility at MSKCC, plus near constant writing of grant applications on other potential cell-based therapeutic avenues to help justify and fund MSKCC’s investment in the GMP facility. These efforts required financial support from multiple sources, including the NIH, the New York-based Cooley Anemia Foundation, several private foundations in Italy, as well as private philanthropy to MSKCC. Finally, in 2012, the FDA granted approval for the first-of-its-kind human phase 1 safety trial on Dr. Sadelain’s therapy. Results are expected within the next few years.

In addition to his beta thalassemia trial, Dr. Sadelain is collaborating with investigators at Weill Cornell Medical College on the development of a stem cell-based therapy for sickle cell anemia, another hereditary blood disorder. The team, led by principal investigator Shahin Rafii, M.D., is supported by a NYSTEM-funded $15.7 million Consortium Award to Weill Cornell together with MSKCC.

According to Dr. Sadelain, NYSTEM’s investment in the clinical research Consortia is a major strength of the agency and of New York. As he says, “Having an agency that understands what it takes to bring a beautiful idea to a first-in-human therapeutic application is a critical advantage in the state of New York. Many other agencies, including the NIH, stall at exactly that point. NYSTEM brings a lot to this realm and fills a clearly underserved, undersupported aspect of research.”
New York Without NYSTEM

Although NYSTEM research is positioned for rapid progress on clinical translation of stem cell research into new therapies, the value of New York’s investment to date and the future development of scientific findings could be lost if the program does not continue. Only a sustained commitment to support stem cell research in New York will ensure that the returns on that investment are realized here. If NYSTEM funding is not renewed, infrastructure will be abandoned or underutilized, jobs will be lost, and opportunities for economic growth will be left unrealized. Without renewed funding for stem cell research and regenerative medicine, the state may lose its leadership role in the future of medicine.

Gordana Vunjak-Novakovic, Columbia University
Conclusion

EIGHT YEARS AFTER its formation, this is the perfect moment for the ESSCB to report on successes and challenges, update its strategic plan for NYSTEM activities, and chart a path to the future. New York’s exceptional scientists have made substantial progress in the years since NYSTEM was launched. Because of their work, there are more opportunities than ever to transform exciting discoveries into long-awaited treatments for conditions that are still incurable today. The ESSCB envisions a future in which New York capitalizes on its outstanding research community, universities, and hospitals to lead the way to stem cell-based cures and effective regenerative medicine. With an ongoing commitment to the NYSTEM program, New York will solidify its role as a world leader at the cutting edge of medical research, treatment, and biotechnology.

Lorenz Studer, Zehra Dincer, Memorial Sloan Kettering Cancer Center
The Empire State Stem Cell Board thanks the many individuals who contributed to the development of this strategic plan, including NYSTEM scientists who offered their scientific expertise, as well as knowledge of the stem cell field and the impact of NYSTEM funding on the New York research enterprise, the distinguished scientists of the External Review Panel who provided a considered and thorough review of the program, and NYSTEM staff and consultants for ongoing advice and support.

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Highlights of NYSTEM-supported research accomplishments include:

- **Stem cell niche:** The molecular mechanisms controlling stem cell self-renewal and niche competition hold great potential for advances in treating growth deficiencies, in cancer biology, and in regenerative medicine. However, the microenvironment that comprises the stem cells’ niche in vivo and the relationships between stem cells in their niche are poorly understood. Dr. Erika Bach, New York University School of Medicine, is using NYSTEM funding to identify the molecular pathways that allow stem cells to self-renew and occupy their niche using the *Drosophila* testis as a model system. She has uncovered a pattern of competitive behavior among the stem cells that might be relevant to the early steps of oncogenesis, such as in the development of carcinoma, glioma, and leukemia.

- **Mitochondrial diseases:** With NYSTEM support, a novel scientific technique to help prevent inherited mitochondrial diseases was developed in New York. To prevent passing on mutant mitochondrial DNA from mother to child through the cytoplasm of an affected egg, Dr. Dieter Egli and Dr. Daniel Paull, of the New York Stem Cell Foundation, and Dr. Michio Hirano and Dr. Mark Sauer, at the Columbia University Medical Center, developed a new technique to transfer the mother’s nuclear DNA to an enucleated and mitochondrial disease-free egg cell. They found that the transfer caused no detectable adverse effects on the egg cell or in stem cell lines derived following the exchange. Their findings demonstrated that nuclear genome transfer could offer an effective solution to preventing the transmission of defective mitochondria in humans.

- **Ovarian cancer:** With NYSTEM funding, Dr. Alexander Nikitin, Cornell University, identified a previously unrecognized stem cell niche at the junction of different types of epithelial cells in the ovary. Importantly, the stem cells in this region appear to be susceptible to transformation into cancerous cells. Further study of this stem cell niche may help investigators better understand the pathogenesis of ovarian cancer and, ultimately, develop targeted therapies for this devastating disease, which represents the fifth leading cause of cancer deaths among women in the United States.

- **Rare diseases:** A NYSTEM grant to Dr. Richard Gronostajski, University at Buffalo, provided key insights into the role of a protein known as “Nfix” in the biology of adult neural stem cells (NSCs). Some patients with Sotos syndrome or Marshall-Smith syndrome, both rare genetic diseases, have mutations in the Nfix gene. Nfix has also been implicated in medulloblastoma, a type of brain cancer. Thus, with NYSTEM support, Dr. Gronostajski’s research on NSCs has the potential to improve our understanding of multiple human diseases.

- **Tumor stem cells:** With NYSTEM funding, Dr. Elaine Fuchs, the Rockefeller University, has studied long-lived tumor stem cells that may contribute to recurrence of tumors after anti-cancer treatment. Using squamous cell carcinoma (SCC) as a model, she identified molecular pathways by which the growth factor TGF-β induces heterogeneity among SCC-associated stem cells. That heterogeneity allows some of those stem cells to become resistant to anti-cancer therapy, thereby promoting metastasis and recurrence. This research might point to new strategies to combat drug-resistance in cancer treatments.

- **Cancer:** Dr. Mark Noble, University of Rochester, is using NYSTEM funding to discover novel weaknesses of glioblastoma cells and basal-like breast cancer cells, two cancers that have been enormously difficult to treat. In the case of glioblastomas, among the most malignant of all human tumors, funding from NYSTEM has enabled the discovery of multiple drugs that can be used to treat these tumors. Many of these drugs are already FDA-approved for other uses, so this work may lead rapidly to clinical trials in patients with glioblastomas. Another NYSTEM grant to Dr. Jianwen Que, also at the University of Rochester, supports analysis of esophageal stem cells that are thought to be the critical cell population that gives rise to esophageal cancers.
NYSTEM: REPORT ON PROGRESS AND VISION FOR THE FUTURE

**Tissue engineering:** Dr. Gordana Vunjak-Novakovic and her research team at Columbia University have grown bone grafts that can match a patient’s original jaw bone for facial reconstruction surgery to repair injuries, disease, or birth defects. With NYSTEM funding, they have also engineered thick, vascularized, and electromechanically functional cardiac tissue by culturing stem cells on a scaffold perfused with culture medium to mimic blood flow and by stimulating the cells with electrical signals. This research has led to a heart patch that could be laid over injured heart tissue to restore normal function in someone who has suffered a heart attack. Among the innovations coming from her lab is a cell micropatterning technology to study the initiation of developmental asymmetry and diagnose disease. One of her NYSTEM-supported research projects investigates the influence of electrical stimulation and conditioning on the function, development, and phenotypic maturation of hES cell- and iPS cell-derived cardiomyocytes.

**Psychiatric disorders:** Numerous recent lines of evidence point to interneuron dysfunction as an underlying cause of affective psychiatric disorders, including autism spectrum disorders, schizophrenia, and attention deficit hyperactivity disorder. Dr. Gordon Fishell, New York University School of Medicine, used his NYSTEM grant to study interneurons and to learn how to direct embryonic stem cells to produce interneurons in the laboratory. The cells can then be used for high-throughput screening to identify drugs that might have potential to treat interneuron-associated disorders.

**Sarcoma:** Dr. Stuart Aaronson, the Icahn School of Medicine at Mount Sinai, is using NYSTEM funding to characterize human mesenchymal stem cells and their relationship to different types of sarcomas. His team has found that a molecular pathway known as Wnt signaling is active in many human sarcomas and that blocking this pathway can inhibit sarcoma cell growth. On the basis of this work, Dr. Aaronson has initiated a collaborative grant competitively funded by the Pfizer Centers for Therapeutic Innovation in New York City to devise a novel Wnt-based intervention for sarcoma treatment.

**Porphyria:** NYSTEM-funded research in the laboratory of Dr. David Bishop, the Icahn School of Medicine at Mount Sinai, is providing proof-of-principle for...
autologous stem cell therapy for congenital erythropoietic porphyria (CEP), a rare metabolic disorder.

**Liver disease:** Dr. Sanjeev Gupta, Albert Einstein College of Medicine, used NYSTEM funding to develop new ways to differentiate stem cells into hepatocytes (liver cells). He then used the hepatocytes to reverse acute liver failure in animal models. Dr. Gupta also developed a new imaging method for diagnosing Wilson disease, and a method for correcting the disease with cell therapy in animal models. He filed invention disclosures for both lines of research. Also at Einstein, Dr. Charles Rogler identified pathways that regulate the differentiation of liver stem cells and discovered that by blocking these pathways in mouse livers, he could stop the production of cells associated with liver fibrosis. Dr. Rogler has applied for a patent to use these inhibitors to block fibrosis in human patients.

**Radiation injury:** Radiation therapy is an important form of treatment for some cancers, but it can have potentially serious side-effects. In NYSTEM-funded research, Dr. Viviane Tabar, Memorial Sloan Kettering Cancer Center, injected human pluripotent stem cell-derived oligodendrocytes, a type of brain cell, into the brains of mice treated with radiation therapy. The injected cells facilitated regeneration of the myelin sheath, the protective coating around neurons in the animals’ brains, and the treatment improved the behavioral and cognitive function of the animals. This research suggests a potential clinical application for stem cells in reversal of brain injury following radiation therapy in human cancer patients.

**Age-related cognitive impairment:** With NYSTEM funding, Dr. Grigori Enikolopov, Cold Spring Harbor Laboratory, is exploring why the number of new neurons in the hippocampus region of the brain declines with age. His research indicates that the neural stem cell pool in the hippocampus is depleted over time because the stem cells convert into astrocytes after one cycle of neuron production, thereby losing their capacity for future neuron differentiation. This “disposable stem cell model” represents a new paradigm of stem cell behavior compared to the conventional self-renewing model in which stem cells revert to a quiescent, renewable state after generating differentiated cells and retain their potential to generate additional cells in the future.

**Stem cell biology:** NYSTEM-funded research by Dr. Urs Rutishauser, Memorial Sloan Kettering Cancer Center, showed that enhancing the expression of a chemical (polysialic acid) on the surface of embryonic stem cells could improve the survival, migration, and integration of these cells when grafted into adult host tissue. This line of research has important implications for the viability of future stem-cell based cell replacement therapies and is a component of Dr. Lorenz Studer’s Consortium.

**Stem cell differentiation:** With NYSTEM-funding, Dr. Ming-Ming Zhou, the Icahn School of Medicine at Mount Sinai, developed small molecule compounds that are capable of inducing stem cell differentiation. Such chemical ligands can be used as powerful research tools, as well as developed into potential therapeutic agents for anti-cancer therapy.

**New iPS and hES cell lines:** With the help of NYSTEM funding, researchers across the state have successfully derived many new iPS and ES cell lines, including patient-specific iPS cell lines. Characterizing these new stem cell lines and differentiating them into tissue-specific cells in the lab allow researchers to uncover molecular pathways underlying disease and to develop new targeted therapies. The lines include, but are not limited to:

- **Dr. Daesung Shin** in the Hunter James Kelly Research Institute of the University at Buffalo is creating iPS cells from skin cells of Krabbe disease patients in order to create brain cells from them and determine how to keep those cells alive and disease-free. This research will lead to new and better treatments of a whole class of newborn diseases like Krabbe disease.

- **Dr. Dieter Egli**, New York Stem Cell Foundation, derived 16 new hES cell lines with the help of NYSTEM funding and gained new insights into the state of the X-chromosomes in stem cell lines derived from females. He also pioneered technologies used in somatic cell nuclear transfer (SCNT) for the generation of SCNT-derived ES cells. Dr. Egli, along with Dr. Scott Noggle and other colleagues, used SCNT to generate pluripotent stem cells from skin cells of patients with type 1 diabetes. This advance was named by Time magazine as the “#1 Medical Breakthrough of 2011.”

- **Dr. Janet Paluh**, University of Albany SUNY, derived and characterized new iPS cell lines from individuals of ethnic and minority descent, including Hispanic, Dutch, Polish, Italian, and other origins.

- **Dr. Angela Christiano**, Columbia University, derived iPS cells from individuals with the rare but devastating skin disease epidermolysis bullosa (EB) with revertant mosaicism, using cells that had
spontaneously corrected the genetic defect that causes EB. She showed that the iPS cells could be differentiated into functional keratinocytes, cells that form the outer layer of skin. Moreover, these cells formed 3-dimensional skin equivalents in vitro and reconstituted normal skin in a mouse model. This research suggests that iPS cell-derived keratinocytes might be useful for providing a source of genetically matched, but EB-free, skin cells for patients with EB.

- Dr. Scott Noggle, New York Stem Cell Foundation, developed more than 50 new iPS cell lines, as well as new embryonic stem cells lines with mutations in genes that cause Huntington’s disease and Spinal Muscular Atrophy. This research led to two patent applications for improved methods to generate stem cell lines.

- Dr. Charles Antzelevitch, Masonic Medical Research Laboratory, developed iPS cell lines from patients with early repolarization syndrome (ERS), a condition that can result in the development of life-threatening arrhythmias and sudden cardiac death.

- Several iPS cell lines have been derived from skin cells of patients with long QT syndrome by Dr. Robert Kass, Columbia University. Long QT syndrome is a heart rhythm disorder that can cause fast, irregular heartbeats, leading in some cases to fainting, seizure, or sudden death. Dr. Kass' work is providing proof of concept that iPSC-derived muscle cells can be used to study the pharmacology of this inherited arrhythmia with the goal of identifying more specific therapies in patients harboring the mutations.

- Dr. Jian Feng, University at Buffalo, derived new iPS cell lines from Parkinson’s disease patients who carry a mutation in the parkin gene. He then developed an improved method for differentiating the iPS cells into neurons in the midbrain that are implicated in the disease. On the basis of this research, Dr. Feng has filed a patent application for using his iPS cell-derived neurons to identify disease-modifying drugs for Parkinson’s disease.

- Dr. Bruce Gelb, the Icahn School of Medicine at Mount Sinai, and his collaborator Dr. Ihor Lemischka, derived 15 iPS cell lines from patients with a group of rare developmental diseases caused by mutations in genes that are part of the “Ras” molecular pathway. They have characterized cardiomyocytes (heart muscle cells) derived from human iPS cells from individuals with LEOPARD syndrome, as well as perturbed myeloid hematopoietic differentiation from human iPS cells derived from patients with Noonan syndrome with juvenile myelomonocytic leukemia.

- Dr. Michel Sadelain, Memorial Sloan Kettering Cancer Center, derived and characterized multiple iPS cell lines from patients with hematopoietic diseases, including beta-thalassemia and sickle cell anemia, and identified “safe harbors” where gene insertions for reprogramming or therapy would not otherwise affect the genome.

- Dr. Sally Temple, Regenerative Research Foundation, created several retinal pigment epithelial stem cell lines. These novel stem cells have enabled drug screening for promising drug candidates to treat common retinal disease, such as age-related macular degeneration, and serve as a potential therapeutic basis for her Consortium.

- At Columbia University, Dr. Hynek Wichterle derived iPS cell lines from cells of patients with amyotrophic lateral sclerosis (ALS or “Lou Gehrig’s disease”). He characterized the pluripotent potential of these cells lines and assessed their ability to differentiate into spinal motor neurons—the cells that are lost in ALS.
NYSTEM Programs for Training Stem Cell Researchers

**Highlights from NYSTEM-sponsored training initiatives include:**

- A graduate student in the laboratory of Dr. Mark Noble was supported by a NYSTEM training grant at the University of Rochester to study Krabbe disease, a rare, genetic nervous system disorder. The research conducted by this graduate student was so promising that another student who joined this effort had such compelling data within one year that she was able to obtain her own NIH Predoctoral Fellowship to work on this problem. The results obtained by these two students enabled the laboratory to attract funding from the Legacy of Angels, an international foundation focused on Krabbe disease. Moreover, their promising findings supported a NYSTEM grant application for new funding in 2014 to evaluate the potential protective drugs for Krabbe disease identified in their research.

- At the New York University School of Medicine, graduate student Simon Vidal Villanueva, working in the laboratory of Dr. Matthias Stadtfeld, was supported by a NYSTEM institutional training award to study reprogramming. He found that a combination of three small molecules could increase the efficiency of reprogramming mouse skin cells to pluripotent stem cells by over 50%. Moreover, these small molecules shortened the time required for generation of iPSCs to less than 5 days. He discovered a number of new genes that were upregulated and had not yet been associated with reprogramming. In ongoing research he is testing whether these genes, in addition to the usual four genes used for reprogramming, can improve the efficiency of reprogramming without the need for the three molecule combination.

- NYSTEM funding supported the work of a postdoctoral fellow, Dr. Dilek Colak, in Dr. Samie Jaffrey’s laboratory at Weill Cornell Medical College. Her research fundamentally altered the understanding of the molecular pathways that lead to the most prevalent genetic form of mental retardation, fragile X syndrome (FXS), which is a type of “trinucleotide repeat disease.” Other groups built upon her work and showed that a similar mechanism operates in a related disease, Friedreich’s ataxia. These studies point to a novel mechanism that may have a general role in numerous trinucleotide repeat diseases. Her work provided critical data needed for a successful NIH grant application to further understand the cause of FXS and to develop new treatments.

- Dr. Elsa Vera, a postdoctoral fellow in the laboratory of Dr. Lorenz Studer at the Sloan Kettering Institute for Cancer Research, has made progress on using telomere shortening as a strategy to induce age-related features in iPSC cell-derived neural cells. The overall idea of “inducing age” in iPSC cell-derived lineages is an exciting approach for modeling late-onset diseases, such as Alzheimer’s disease or Parkinson’s disease. With support from a NYSTEM institutional training award, Dr. Vera has successfully shown iPSC cell telomere shortening upon pharmacological manipulation of telomerase activity in vivo. This allowed her to obtain neural cells with differential telomere lengths and to correlate telomere shortening with the identification of potential age-related phenotypes in dopamine neurons.

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**Figure Add.2: Initiatives to Support Training Stem Cell Researchers**

<table>
<thead>
<tr>
<th>INITIATIVE</th>
<th>AWARD DATE*</th>
<th>NUMBER OF AWARDS</th>
<th>TOTAL FUNDING**</th>
</tr>
</thead>
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<tr>
<td>Empire State Institutional Training Programs in Stem Cell Research for Predoctoral and Postdoctoral Fellows (2014)</td>
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<tr>
<td>Institutional Awards for Short Term Faculty Training and Collaborative Opportunities (2011)</td>
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<td>Empire State Institutional Training Programs in Stem Cell Research for Predoctoral and Postdoctoral Fellows (2010)</td>
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<tr>
<td>Empire State Stem Cell Scholars: Fellow-to-Faculty Awards in Stem Cell Research (2009)</td>
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<td>3</td>
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</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>12</td>
<td>$18.00 million</td>
</tr>
</tbody>
</table>

*Indicates the date funding awards were approved by the ESSCB.  **Indicates total funding committed; actual expenditures may be less.
Highlights of NYSTEM-supported shared resources and facilities, and their contributions, include:

- The Western New York Stem Cell Culture and Training Facility (WNYSSTEM), funded through a NYSTEM Shared Facility Award, has trained more than 40 faculty, students, and staff from the University of Buffalo and Roswell Park Cancer Institute in culturing hES cells and has contributed to dozens of grant applications and peer-reviewed publications. The facility has allowed investigators who wanted to do stem cell research but were held back by a lack of experience in pluripotent stem cell culture techniques to initiate stem cell studies. In addition, WNYSSTEM contributes to a consortium of Stem Cell Core facilities named “Stem Cell COREdinates” composed of 18 stem cell shared facilities in the United States, including seven from New York. This consortium includes some of the premier stem cell facilities in the United States, and WNYSYSTEM participation enhances the visibility of New York in the national stem cell research community.

- The New York University RNAi Core, funded by a NYSTEM Shared Facility Award, supports stem cell-related screening projects from a number of New York City institutions, including Rockefeller University, Columbia University, Mount Sinai Hospital, Memorial Sloan Kettering Cancer Center, and Albert Einstein College of Medicine. The award allows NYU to offer state-of-the-art screening capabilities to any stem cell researcher in New York and provides support for staff development/training. The staff expertise supported by the Award includes assay optimization, development, data visualization/analysis, and pathway analysis.

- NYSTEM funding to the University of Rochester established an upstate cGMP (current Good Manufacturing Practices—a requirement for use of products in human patients) facility for growing clinical grade cells for transplantation. This important, state-of-the-art facility has enabled two NYSTEM-funded Consortia, targeting multiple sclerosis and age-related macular degeneration, to proceed on the path to clinical trials, something that would not be possible without cGMP-produced cells to comply with FDA requirements. The Rochester facility has become a model for the region and its Director, Michael Fiske, is lecturing throughout the nation and providing guidance to similar projects.

- With NYSTEM support, Weill Cornell Medical College is creating a shared facility for the derivation, validation, and distribution of human and mouse ES cell lines for disease modeling. Under the leadership of Dr. Todd Evans, this core facility supports a consortium of investigators and staff that have unmatched access to cell lines and a strong track record of expertise in these areas. Collaborating across three major biomedical campuses in New York City, the core creates, banks, and provides new disease-associated lines and other tools for disease modeling that can be used by investigators across the State to better understand human diseases and to develop novel therapeutics.

- A NYSTEM Shared Facility Award supports a pluripotent stem cell core at Albert Einstein College of Medicine that has trained and supported more than 25 investigators.

NYSTEM Investment in Infrastructure and Shared Resources

<table>
<thead>
<tr>
<th>INITIATIVE</th>
<th>AWARD DATE*</th>
<th>NUMBER OF AWARDS</th>
<th>TOTAL FUNDING**</th>
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<tbody>
<tr>
<td>Shared Facilities for Stem Cell Research (2013)</td>
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<tr>
<td>Shared Facilities for Stem Cell Research (2009)</td>
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<td>Research (2008)</td>
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<td>25</td>
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</tr>
<tr>
<td>TOTAL</td>
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<td>48</td>
<td>$94.18 million</td>
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</table>

*Indicates the date funding awards were approved by the ESSCB. **Indicates total funding committed; actual expenditures may be less.
An example of the success of this core facility is the work of Dr. Jayanta Roy-Chowdhury, who has generated iPS cell lines from subjects with three inherited liver diseases (Crigler-Najjar syndrome type 1, alpha-1-antitrypsin deficiency, and primary hyperoxaluria type 1). His work was then further supported by NYSTEM to improve the methods for differentiation of the iPS cells to hepatocyte (liver)-like cells. These cells have been characterized extensively and used for disease modeling and functional testing by transplantation into the livers of animal models of human diseases. Separately, Dr. Eric Bouhassira, director of the pluripotent stem cell core, developed GenPlay, an application helping investigators to analyze stem cell genomic data. The GenPlay website has been viewed over 300,000 times and has about 300 registered users worldwide. Recently, a highly innovative core for genomic and epigenomic analyses of single stem cells was created at Einstein and is available to other New York State institutions to continue discovery efforts toward bringing the newly developed therapeutic strategies to the clinic.

- NeuraCell is a shared research facility that provides neural stem cell (NSC)-related products, services, and training to the research community. The shared facility provides NSCs and specialized NSC culture media that were developed in house. In addition, it offers specialized molecular tools, such as custom lentiviral shRNA and over-expression vectors optimized for NSCs, and some NSC-relevant antibodies. Created by Dr. Sally Temple, NeuraCell has become a valuable resource for building a regional stem cell community, assisting researchers to achieve short-term goals of efficient, high-quality data generation for projects and grant applications, and progressing toward longer-term goals aimed at generating stem cell-based therapies.

- Finally, using stem cells and their derivatives, scientists can model in culture the abnormal processes that lead to disease in humans. In “high-throughput screening” (HTS), chemical compounds can be tested for their ability to ameliorate the defects. The High-Throughput Screening and Chemistry Shared Facility at the Columbia University Medical Center has been a tremendous success, demonstrating the ability of such facilities to become self-sufficient with time. Dr. Chris Henderson, who oversaw the creation of the facility, told the NYSTEM External Review Panel that it had “taken off beyond their hopes,” fostering work in both the stem cell and cancer arenas.
Activities of the ESSCB and Its Ethics Committee

• In November 2007 and March 2008, the Board issued and revised standards for the first round of research funding by NYSTEM. The initial standards were predominantly based on the extensive prior work of national and international experts who had participated in the development of ES cell research guidelines for the National Academy of Sciences and the International Society for Stem Cell Research. Revised recommendations expanded on those guidelines for composition of Embryonic Stem Cell Research Oversight (ESCRO) committees, as well as specific requirements for written documentation of ESCRO committee policies and procedures and conflict of interest issues. In addition, the revised guidelines subject research involving human pluripotent stem cells to ESCRO (now “SCRO”) committee oversight.

• In 2009, the NIH issued Draft Guidelines to implement President Obama’s Executive Order 13505 removing certain restrictions on federal funding of hES cell research. In May 2009, the ESSCB submitted official comments on the Draft Guidelines, including recommendations to allow funding for stem cell lines derived from embryos created for research purposes; to align with Common Rule principles related to informed consent; to endorse the use of ESCRO committees; and to allow the use of cell lines created prior to the effective date of the guidelines as long as they were acceptably derived.

• In FY 2009–2010, the ESSCB revised the NYSTEM contract to conform to new NIH guidelines for ES cell research released in July 2009, making it easier for researchers to comply with both standards. Collectively, the revisions imposed stringent informed consent standards for donors that exceed the legal requirements for participation in human subjects research.

• In November 2011, the ESSCB issued guidelines for chimera research, the combination of certain types of human cells with animals, their cells, or embryos. The guidelines recommend that NYSTEM investigators adhere to the standards established by the National Academy of Sciences or the International Society for Stem Cell Research when conducting research involving human pluripotent stem cells, while highlighting key ethical issues for researchers and institutional bodies to consider when reviewing research protocols involving chimeras.

• In addition to issuing guidelines and standards, the Ethics Committee, along with the full ESSCB, held an ongoing discussion regarding respect for the embryo. After extended debate, the Committee recommended that NYSTEM-funded research utilize the fewest number of embryos necessary and that such use have sufficient scientific justification. Further, the ESSCB requires that experiments with human embryos halt before or at 14 days of development, before formation of the primitive streak, the first stage of development at which the three germ layers are discernible.

• The ESSCB regularly invites experts to make presentations on a variety of relevant subjects, including ESCRO committee issues and oversight; embryos, ethics, and altered nuclear transfer; oocyte donation risks; research uses of donated eggs; the law and ethics of gene patenting; and issues related to beginning clinical trials with pluripotent stem cells, among other topics.
Outcomes of NYSTEM-Funded ELSIE Activities include:

- Dr. Daniel Kalderon, Columbia University, developed a stem cell course for undergraduate students with biology-related majors. The course has three notable features: it is the only course for biology majors with a significant nonbiology component (i.e., ethics); four faculty members collaborate as instructors; and the course includes invited public seminar speakers and a lab visit. In Dr. Kalderon's experience, students taking this course displayed a thirst for mixing pure biology with practical applications and ethics. The students also valued the direct contact with experts who are actively engaged in cutting-edge research and ethics scholarship in the stem cell field.

- With a focus on disability rights, feminist studies, and responsive justice policy perspectives, Dr. Katayoun Chamany at The New School created “Stem Cells Across the Curriculum,” a collection of educational modules that address stem cell research and its ethical, social, and legal dimensions. Four educational modules that have teaching notes, assignments, rubrics, and case studies, alongside visual resources and animated Power Point slide shows, were created. These materials were used in three semester-length courses and in shorter format in Gender Studies and the Higher Education Opportunity Program at The New School. Beyond The New School, four educators at the high school, undergraduate, and graduate school levels have featured the case studies in their courses on reproductive bioethics, law, and science, including Vassar College, University of California Davis, and San Francisco State University.

- Dr. Robert Van Buskirk, Binghamton University, created a course focused on the science, ethics, federal rules, intellectual property, commercial perspective, and religious issues that relate to the use of human stem cells. According to Dr. Van Buskirk the impact of this course on the students has been unexpectedly high due to two distinctive features. First, discussions with a guest bioethicist, who is also a college professor and Catholic priest, provided a unique opportunity for students to explore their own religious perspectives on the use of hES cells. Second, the course included lab modules that took place in a start-up biotechnology company focused on stem cell-related products. Feedback from students indicated that this was the first upper level science course that interconnects government, religion, science, biotechnology, and medicine and that it was one of the best and most diversified courses in the sciences that many of them had taken.

- An interdisciplinary team led by Dr. John Russell from Syracuse University partnered with the SUNY-Upstate Medical University to develop a highly interdisciplinary course entitled “Stem Cells and Society” that was offered during the spring semesters of 2011 and 2012. A total of 76 students have completed the course during these two semesters. The course was structured around three modules: “Science and Metaphysics of the Beginnings of Life,” “Stem Cell Sources and Normative Ethics of Stem Cells,” and “The Future of Stem Cells.” Each module presented...
the relevant science, ethics, law, and religion issues and discussed the role of the media in forming public opinions. These interdisciplinary aspects were further emphasized in a series of case studies.

- In a collaboration between the University of Rochester and Monroe Community College, Dr. Dina Markowitz designed an undergraduate stem cell course for non-majors (“The Science and Ethics of Stem Cells”) that provided students with an overview of stem cell science and an opportunity to explore related ethical, legal, and social implications (ELSI) of the field. The course instructors used a case-study method of instruction, in which students were presented with real-life scenarios that cover scientific concepts, as well as ELSI issues of stem cell science. The multidisciplinary team included biology curriculum experts, a philosopher with expertise in ELSI and medical/research ethics, and a stem cell researcher.

- Dr. Alice Heicklen, Columbia University, directed summer undergraduate fellowships in stem cell science. In each year, the program had a cohort of eight students, who performed exceptionally well with six articles published or in review after the first 2 years. In addition, at least seven students presented their research at conferences, and several others worked with high school teachers to develop teaching modules in the greater New York area.

- Dr. Lisa Fortier created a training program at Cornell University to provide rigorous training for veterinary students in stem cell laboratory science, as well as an understanding of legal, ethical, and clinical application issues surrounding stem cells. One veterinary student scientist who completed the program, Ms. Hannah Holmes, studied the use of in situ tissue engineering methods to recruit a body’s own stem cells to the site of an injury. Such an approach has therapeutic potential as it avoids the risks and costs of direct stem cell delivery from an external source.

- Dr. Soosan Ghazizadeh at Stony Brook University established a training program to recruit highly talented and motivated dental students to engage in cutting-edge research in stem cell biology and regenerative medicine as it relates to dentistry. Ms. Sihana Rugova is working on a research project related to the interaction of dental stem cells in the periodontium with various materials used in implants using both ex vivo and in vivo approaches. She is mentored by two dental school faculty members, Marcus Abboud, DDS, PhD, who is an oral surgeon with expertise in dental material/implant and digital technologies, and Marcia Simon, PhD, a professor of oral biology with expertise in stem cell biology and tissue regeneration.

- NYSTEM-funded scientists are deeply engaged in the presentation of stem cell science to the public, through talks at churches, synagogues, retirement centers, Rotary clubs, and other public forum, and also through talks at the Science Teachers Association for New York State. Most recently, NYSTEM awarded $250,000 to the American Museum of Natural History for programs that build stem cell literacy among diverse adult audiences through on-site and online learning experiences. This initiative capitalizes on the Museum’s experience providing successful adult education programs, as well as its partnership with Khan Academy, to provide online educational content in addition to live sessions in the Museum. Scientific expertise in stem cell biology will be provided by the New York Stem Cell Foundation.

### Figure Add.5: Requests for Proposals for Administrative Support

<table>
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<tr>
<th>INITIATIVE</th>
<th>AWARD DATE*</th>
<th>NUMBER OF AWARDS</th>
<th>TOTAL FUNDING**</th>
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</thead>
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<td><strong>TOTAL</strong></td>
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*Indicates the start date of the contract. **Indicates total funding committed; actual expenditures may be less.
Appendix 1:  
Roster of the Empire State Stem Cell Board

Current ESSCB Members

Howard A. Zucker, M.D., J.D., Chair*‡  
Commissioner  
New York State Department of Health  
ESSCB Term: 2014–present

Allen M. Spiegel, M.D.,  
Vice Chair*‡  
Marilyn and Stanley M. Katz Dean  
Albert Einstein College of Medicine  
ESSCB Term: 2009–2015

Jean M. Baric-Parker, M.S., M.A.‡  
Adjunct Lecturer  
St. Bernard’s School of Theology and Ministry  
ESSCB Term: 2014–present

Bradford C. Berk, M.D., Ph.D.*  
Senior Vice President for Health Sciences  
Professor of Medicine, Cardiology and Pharmacology  
University of Rochester Medical Center  
ESSCB Term: 2007–present

Richard Dees, Ph.D.‡  
Associate Professor of Philosophy and Bioethics  
University of Rochester  
ESSCB Term: 2014–present

Nancy Neveloff Dubler, LL.B.‡  
Professor Emerita of Bioethics  
Albert Einstein College of Medicine  
ESSCB Term: 2007–present

Robin Elliott, M.A.*  
Executive Director  
Parkinson’s Disease Foundation  
ESSCB Term: 2007–present

Samuel Gorovitz, Ph.D.‡  
Professor of Philosophy  
Former Dean, Arts and Sciences  
Syracuse University  
ESSCB Term: 2007–present

David C. Hohn, M.D.,  
Former Vice Chair*‡  
President Emeritus and Executive Director of Health Policy  
Roswell Park Cancer Institute  
ESSCB Term: 2007–present

Robert Klitzman, M.D.‡  
Professor of Clinical Psychiatry  
Columbia University College of Physicians and Surgeons  
ESSCB Term: 2007–present

Gary Koretzky, M.D., Ph.D.*  
Dean, Weill Cornell Graduate School of Medical Sciences  
Vice Dean for Research  
Professor, Department of Medicine  
Weill Cornell Medical College  
ESSCB Term: 2015–present

Fonda Dawn Kubiak, Esq.*  
Assistant Federal Public Defender  
Western District of New York  
ESSCB Term: 2014–present

Rev. H. Hugh Maynard-Reid, D.Min., BCC, CASAC‡  
Director of Pastoral Care Services  
North Brooklyn Health Network  
Woodhull Medical Center  
ESSCB Term: 2007–present

Norma Jean Nowak, Ph.D.*  
Professor of Biochemistry  
Executive Director  
New York State Center for Excellence in Bioinformatics and Life Sciences  
University at Buffalo  
ESSCB Term: 2014–present

David P. Speach, M.D.*  
Associate Professor, Departments of Orthopaedics and Rehabilitation and Physical Medicine and Rehabilitation  
University of Rochester School of Medicine and Dentistry  
ESSCB Term: 2015–present

Melissa Wasserstein, M.D.*  
Associate Professor of Genetics and Genomic Sciences and Pediatrics  
Icahn School of Medicine at Mount Sinai  
Director, Program for Inherited Metabolic Diseases  
Mount Sinai Hospital  
ESSCB Term: 2013–present

Camille P. Wicher, Ph.D., J.D., RN, MSN‡  
Vice President of Clinical Operations, Corporate Ethics and Research Subject Protection  
Roswell Park Cancer Institute  
ESSCB Term: 2013–present

Madelyn Wils*  
President and Chief Executive Officer  
Hudson River Park Trust  
ESSCB Term: 2007–present

*Member of the Funding Committee  
‡Member of the Ethics Committee
Former ESSCB Members

Richard F. Daines, M.D., Chair*‡
Commissioner
New York State Department of Health
ESSCB Term: 2007–2010 (deceased)

Nirav Shah, M.D., M.P.H., Chair*‡
Commissioner
New York State Department of Health
ESSCB Term: 2011–2014

Kenneth Adams, M.B.A.*
President and CEO
Empire State Development Corporation
ESSCB Term: 2007–2011

Jann K. Armantrout†
Diocesan Life Issues Coordinator
Roman Catholic Diocese of Rochester, New York
ESSCB Term: 2010–2014

Fr. Thomas Vincent Berg, LC, Ph.D.†
Executive Director
The Westchester Institute
ESSCB Term: 2007-2012

Inmaculada de Melo-Martin, Ph.D.†
Associate Professor, Division of Medical Ethics
Department of Public Health
Weill Cornell Medical College
ESSCB Term: 2012–2014

Richard Dutton, Ph.D.*
Member
Trudeau Institute
ESSCB Term: 2007–2010

Brooke Mackenzie Ellison, Ph.D., MPP.†
Research Assistant Professor
Stony Brook University
Founder and President
Brooke Ellison Project
ESSCB Term: 2007–2014

Gerald Fischbach, M.D.*
Scientific Director, Simons Foundation Autism Research Initiative
Executive Vice President Emeritus
Health and Biomedical Sciences
Columbia University
ESSCB Term: 2007–2011

Richard Gronostajski, Ph.D.*
Professor of Biochemistry
Founder and Head, Developmental Genomics Group
Director, Western New York Stem Cell Culture and Analysis Center
University at Buffalo
ESSCB Term: 2011–2013

Bruce A. Holm, Ph.D.*
Senior Vice Provost
University at Buffalo
Executive Director
NYS Center of Excellence in Bioinformatics and Life Sciences
ESSCB Term: 2007–2011 (deceased)

Hilda Y. Hutcherson, M.D., FACOG*
Clinical Professor
Department of Obstetrics and Gynecology
Columbia University
ESSCB Term: 2007–2012

Donald Landry, M.D., Ph.D.**†
Samuel Bard Professor and Chair, Department of Medicine
Physician-in-Chief of the Medical Service
New York-Presbyterian Hospital/Columbia University Medical Center

Vivian S. Lee, M.D., Ph.D., M.B.A.‡
Professor and Vice Chair for Research
Department of Radiology
Vice Dean for Science, Senior Vice President and Chief Scientific Officer
New York University Medical Center
ESSCB Term: 2007–2011

Mario G. Loomis, M.D., F.A.C.S.*
Vice Chairman of Surgery
Orange Regional Medical Center
ESSCB Term: 2010–2014

Samuel Packer, M.D.*‡
Chair Emeritus, Department of Ophthalmology
North Shore-Long Island Jewish Health System
Arthur and Arlene Levine Professorship and Professor of Clinical Ophthalmology
NYU School of Medicine
ESSCB Term: 2007–2014

Rev. Msgr. William B. Smith, S.T.D.†
Faculty Member
St. Joseph’s Seminary
ESSCB Term: 2007 (deceased)

Michael Stocker, M.D., M.P.H.*
Chairman of the Board
New York City Health and Hospitals Corporation (HHC)
Retired CEO, Empire Blue Cross/Blue Shield
ESSCB Term: 2007–2012

Daniel Sulmasy, O.F.M., M.D., Ph.D.†
Professor of Medicine
Director of the Bioethics Institute
New York Medical College
Sisters of Charity Chair in Ethics
Saint Vincent’s Hospital Manhattan
ESSCB Term: 2007–2009

Robert N. Swidler, M.A., J.D.‡
General Counsel
Northeast Health
ESSCB Term: 2007–2010

Harold Varmus, M.D.*
President
Memorial Sloan Kettering Cancer Center

*Member of the Funding Committee
†Member of the Ethics Committee
The second Empire State Stem Cell Board Strategic Plan, for 2015–2019, was developed through a planning process that involved members of both ESSCB committees, scientific advisors from stem cell institutes across New York, outside stem cell research experts, and NYSTEM staff. A strategic plan coordinating committee was led by Mahendra Rao, M.D., Ph.D., Vice President of Regenerative Medicine at the New York Stem Cell Foundation, who is an internationally respected stem cell researcher with experience in government, academic, and business sectors. Dr. Rao is the former Director of the NIH Center for Regenerative Medicine, former vice president of Regenerative Medicine at Life Technologies, Inc. (now Thermo Fisher Scientific), and co-founder of Q Therapeutics, a neural stem cell company.

The Coordinating Committee solicited the advice of a Scientific Advisory Panel comprising the directors and other leaders of 11 stem cell institutes located in academic institutions across the State of New York, as well as an executive from one New York-based pharmaceutical company. The Scientific Advisory Panel provided feedback on the impact of NYSTEM grant programs and other activities, the current state of the science in stem cell research and its movement towards clinical applications, the environment for stem cell research in New York, and high priorities for future NYSTEM funding and programmatic development. NYSTEM staff provided data on completed and in progress funding programs, accomplishments of the program as assessed by surveys of NYSTEM-funded investigators and institutions in 2012, future funding availability, and program successes and challenges. Finally, a Strategic Plan Ethics Workgroup was assembled to evaluate and update the strategic goals related to ethical, legal, and social issues and education in stem cell research.

The Coordinating Committee, alone or with the Scientific Advisory Panel, met by teleconference and in person three times from July 2014 to month 2015. The Ethics Workgroup met twice from September 2014 to month 2015. The ESSCB reviewed progress and provided input on the developing strategic plan at meetings of the full Board in October 2014, April 2015, and June 2015.

**Strategic Planning Coordinating Committee**

*Mahendra Rao, M.D., Ph.D.*, Chair  
Vice President, Regenerative Medicine  
New York Stem Cell Foundation

*Bradford C. Berk, M.D., Ph.D.*  
University of Rochester Medical Center  
ESSCB, Funding Committee

*Melissa Wasserstein, M.D.*  
Mount Sinai Hospital  
ESSCB, Funding Committee

**Dennis Whalen**  
President  
Health Care Association of New York State

**Camille P. Wicher, Ph.D., Esq., RN, MSN**  
Roswell Park Cancer Institute  
ESSCB, Ethics Committee
Strategic Plan Ethics Workgroup

Audrey R. Chapman, PhD, M.Div., S.T.M.
UCHC Auxiliary/Joseph M. Healey, Jr. Chair in Medical Humanities and Bioethics
University of Connecticut Health Center

Inmaculada de Melo-Martin, Ph.D.
Weill Cornell Medical College
ESSCB, Ethics Committee

Robert Klitzman, M.D.
Columbia University
ESSCB, Ethics Committee

Camille P. Wicher, Ph.D., Esq., RN, MSN
Roswell Park Cancer Institute
ESSCB, Ethics Committee

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Wadie F. Bahou, M.D.
Director, Stony Brook Stem Cell Facility Center
Stony Brook University School of Medicine

Stephen Chang, Ph.D.
Vice President, Research and Development
New York Stem Cell Foundation

Paul S. Frenette, M.D.
Chair and Director, The Ruth L. and David S. Gottesman Institute for Stem Cell and Regenerative Medicine Research
Albert Einstein College of Medicine

Richard Gronostajski, Ph.D.
Director, Western New York Stem Cell Culture and Analysis Center
University at Buffalo

Christopher E. Henderson, Ph.D.
Director, Columbia Stem Cell Initiative
Co-Director, Motor Neuron Center
Columbia University

Ruth Lehmann, Ph.D.
Director, The Helen L. and Martin S. Kimmel Center for Stem Cell Biology
New York University

Ihor R. Lemischka, Ph.D.
Director, The Black Family Stem Cell Institute
Mount Sinai Hospital

Alex Nikitin, M.D., Ph.D.
Leader, Cornell Stem Cell Program
Director, Stem Cell Pathology Unit
Cornell University

Mark D. Noble, Ph.D.
Director, UR Stem Cell and Regenerative Medicine Institute
University of Rochester

Shahin Rafii, M.D.
Director, Ansary Stem Cell Institute
Weill Cornell Medical College

Neil Stahl, Ph.D.
Senior Vice President, Research and Development Sciences
Regeneron Pharmaceuticals, Inc.

Lorenz Studer, M.D.
Director, Center for Stem Cell Biology
Memorial Sloan Kettering Cancer Center

Sally Temple, Ph.D.
Scientific Director, Neural Stem Cell Institute
Regenerative Research Foundation

Gordana Vunjak-Novakovic, Ph.D.
Director, Laboratory for Stem Cells and Tissue Engineering
Columbia University
As reported in Chapter 2 and the Progress Report Addendum, NYSTEM has realized many achievements. Research progress, including in the stem cell field, is reported most often in peer-reviewed scientific journal publications. To date, NYSTEM funding has resulted in more than 1,000 publications, including research articles, research protocols, review articles, and book chapters. Many of these have been in high impact journals, such as *Science*, *Nature*, and *Cell*, and have had major impacts on their fields.

In addition to research publications, NYSTEM has had a tangible impact on New York in other measurable ways. The following appendices provide information on additional metrics that illustrate the breadth of impact that New York’s investment in stem cell research has had on the State’s research community and its overall economy. These data are derived from the 2012 and/or 2014 surveys of investigators and institutions, unless otherwise indicated, and thereby underestimate the full effect of NYSTEM activities in New York.

**APPENDIX 5.A. Growth of the New York Stem Cell Research Community**

A primary goal for NYSTEM has been to create a robust intellectual and resource-rich environment for stem cell research. One means to achieve this goal is by attracting new stem cell researchers at all career stages, training new students and postdoctoral fellows, and providing support for laboratory personnel engaged in stem cell research. NYSTEM estimates that more than 500 new research jobs have been created in New York as a result of the program, as well as hundreds more in the community as additional services are needed to accommodate new personnel. The 2012 and 2014 surveys of institutional administrators provided self-reported data on the recruitment of new investigators to New York and the size of the stem cell research community overall.

**Attracting New Investigators**

Institutional administrators were asked to report the number of new stem cell researchers recruited to their institutions each year from outside New York. New investigators included those at the following career stages: non-tenure track (e.g., postdoctoral fellows), entry level tenure track (e.g., assistant professors), mid-career scientists (e.g., associate professors), and senior research leaders (e.g., tenured professors, center directors). Among the institutions that responded to the 2012 survey, at least 505 new researchers were recruited to 18 New York institutions in 2007–2011 (Figure App.5.a.1, updated with data from the 2014 survey).
### Figure App.5.a.1

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### Figure App.5.a.2 Growth of the New York Stem Cell Community

[Graph showing the growth of the New York Stem Cell Community with data points for Faculty and Staff from 2007 to 2014.]
Growing the Stem Cell Community Overall

In 2012 and 2014, institutional administrators were asked to report the total number of faculty members, as well as the total number of individuals working in stem cell research laboratories. The data indicate a steady growth in the New York stem cell community since the inception of the NYSTEM program (Figure App.5.a.2). The number of faculty members conducting stem cell research has increased from at least 256 in 2007 to 476 in 2014; the number of laboratory personnel has increased from 971 in 2007 to 2,191 in 2014.

In 2012, institutions were also asked to provide data on the numbers of undergraduate students, graduate students, and postdoctoral fellows pursuing stem cell-related training or careers. Of the institutions that responded to the survey, 17 reported one or more student or fellow engaged in stem cell research (Figure App.5.a.3). These data indicate that around 20%-25% of all trainees in New York stem cell laboratories have received support from NYSTEM, demonstrating the significant impact of NYSTEM funding.
APPENDIX 5.B. Increasing Research Capacity in New York

In addition to increasing the number of stem cell personnel, NYSTEM has enhanced biomedical research capacity in New York by establishing multiuser core facilities. These facilities foster collaborations within and across institutions in New York, and many provide services to colleagues in other national and international institutions, establishing New York as a premier location for state-of-the-art research in the stem cell field. All data from 2007–2011 were self-reported by institutional administrators in the 2012 survey of NYSTEM-funded institutions.

New shared facilities with intra-institutional users include 15 institutions with 35 facilities, 2007–2011:

- **Albert Einstein College of Medicine** (31 users): Cell Sorting/Flow Cytometry, Xenotransplant, Pluripotent Cell Core (including iPS), Genomic Core

- **Columbia University** (457 users): High-Throughput Screening Facility, Cell Production Facility, Ultrasound Guided Imaging Facility, CCT1 Flow Cytometry Facility, Chemical Probe Synthesis Facility, Stem Cell Imaging Core, Neurogenesis Laboratory, Herbert Irving Comprehensive Cancer Center Flow Cytometry Shared Resources, Quantitative Proteomics Center

- **Cornell University** (72 users): Mammalian Cell Reprogramming Core, Flow Cytometry Core

- **CUNY** (20 users): Proteomics Laboratory

- **Ichsan School of Medicine at Mount Sinai** (76 users): hESC/hiPSC Shared Resource Facility, High-Content Screening Facility

- **Masonic Medical Research Laboratory** (5 users): Stem Cell Center

- **Memorial Sloan Kettering Cancer Center** (56 users): Stem Cell Research Facility

- **New York Stem Cell Foundation** (70 users): NYSCF Laboratory

- **New York University** (601 users): Genome Technology Center, RNAi Facility, Microscopy, Flow Cytometry/Cell Sorting Center, High Performance Computer Center

- **Regenerative Research Foundation** (38 users): NeuraCell, Stem Culture

- **Stony Brook University** (6 users): Stony Brook Stem Cell Facility

- **University at Albany** (50 users): Tissue Culture Core, Microscopy Core

- **University at Buffalo** (4 users): Stem Cell Culture and Analysis Center

- **University of Rochester** (3 users): Upstate Stem Cell cGMP Facility

- **Weill Cornell Medical College** (45 users): Ansary Stem Cell Center, Tri-Institution Derivation Facility

Facilities with cross-institutional users, including colleagues at other institutions within and outside New York, 2007–2011:

- **Albert Einstein College of Medicine**: Genomic Core (users at NIH, University of Georgia)

- **Columbia University**: Cell Production Facility (Salk Institute), Neurogenesis Laboratory (New York State Psychiatry Institute), Herbert Irving Comprehensive Cancer Center Flow Cytometry Shared Resources (Hospital for Special Surgery, Mount Sinai, NAWI RX, PANPHARMA), Quantitative Proteomics Center (Albert Einstein College of Medicine, Cabrini College, CCNY, Louisiana State University, Metropolitan Museum of Art, New York University, Robert Wood Johnson Medical School, SUNY-Downstate, University of California San Diego, University of Illinois at Chicago, University of Medicine and Dentistry of New Jersey, Weill Cornell Medical College)

- **Cornell University**: Mammalian Cell Reprogramming Core (Duke University, Fox Chase Cancer Center, Harvard University, Masonic Medical Research Laboratory, Mount Sinai), Flow Cytometry Core (U.S. Department of Agriculture, Vybion)

- **Ichsan School of Medicine at Mount Sinai**: hESC/hiPSC Shared Resource Facility (Fred Hutchinson Cancer Center, Massachusetts General Hospital, Medical College of Wisconsin, Memorial Sloan Kettering Cancer Center, NIH, New York Stem Cell Foundation, New York University, Oregon Stem Cell Institute, Princeton University, Regenerative Research Foundation, Salk Institute, Stanford University, Stony Brook University, University of Illinois at Chicago, University of Pittsburgh, University of Rochester,
In 2013, seven multiuser facilities were created or re-funded by NYSTEM. As these facilities were not included in the 2012 survey of NYSTEM-supported institutions, accurate data are not available regarding the number of users or collaborating institutions:

- Albert Einstein College of Medicine: Einstein Shared Facilities for Stem Cell Research
- Columbia University: Large-Scale Biochemical Profiling for Stem Cell Research in New York
- Cornell University: Cornell Stem Cell Modeling and Phenotyping Core
- Regenerative Research Foundation: NeuraCell
- Research Foundation for Mental Hygiene-NYSPI: Imaging Stem Cells in the Brain for Studying Neuropsychiatric Disorders
- Sloan Kettering Institute for Cancer Research: the SKI Stem Cell Research Facilities
- Weill Cornell Medical College: A Shared Facility for the Derivation, Validation, and Distribution of Stem Cells for Disease Modeling

University of Washington, Weill Cornell Medical College)

- Masonic Medical Research Laboratory: Stem Cell Center (University of Cologne)
- Memorial Sloan Kettering Cancer Center: Stem Cell Research Facility (Albert Einstein College of Medicine, Columbia University, Institute for Basic Research in Developmental Disabilities, Mount Sinai, Museum National D’historie Nautalle, New York University, Rockefeller University, Rutgers University, University of Milan, Weill Cornell Medical College)
- New York Stem Cell Foundation: NYSCF Laboratory (Columbia University, Harvard University, Project ALS)
- New York University: Genome Technology Center (Columbia University, Mount Sinai, Prague, Stony Brook University, University of Zagreb School of Medicine, Weill Cornell Medical College), RNAi Facility (Albert Einstein College of Medicine), Microscopy (Columbia University, MBMR Biolabs, Weill Cornell Medical College), Flow Cytometry/Cell Sorting Center (Montefiore Medical Center, New York Blood Center, SUNY-Downstate)
- University at Albany: Microscopy Core (Rensselaer Polytechnic Institute)
- University at Buffalo: Stem Cell Culture and Analysis Center (Targacept, Inc.)
- University of Rochester: Upstate Stem Cell cGMP Facility (Regenerative Research Foundation)
- Weill Cornell Medical College: Ansary Stem Cell Center (Albert Einstein College of Medicine, Memorial Sloan Kettering Cancer Center, Rockefeller University), Tri-Institution Derivation Facility (Albert Einstein College of Medicine, Memorial Sloan Kettering Cancer Center, Rockefeller University)
APPENDIX 5.C. Leveraged Funding for New Institutional Funds, Donations, and Federal Grants

Metrics that can be used to assess the leveraging of NYSTEM money include philanthropic donations and new awards from non-NYSTEM sources based at least in part on NYSTEM-funded research.

Philanthropy

Institutions that received NYSTEM money were queried as to the amount of philanthropic support they received over the period of 2007–2011. Two questions were asked: first, whether they had a stem cell institute or center that was funded in whole or in part by through direct donations and, if so, the amount; second, the amount of donations earmarked for stem cell research not reported in the previous question.

Of the 23 institutions responding to the 2012 survey, nine reported having stem cell institutes or centers, all of which had received philanthropic donations ranging in value from $100 to $10.3 million. The total donations to these institutions was $91.4 million and, with the exception of 2008, the total donations increased annually, ranging from $11.1 million in 2008 to $26.6 million in 2011, the last year reported. While NYSTEM alone did not lead to these donations, its work to increase New York’s capacity for stem cell research correlates with an increase in philanthropic donations to New York’s institutional stem cell centers.

Seven of the 23 institutions also reported receiving donations earmarked for stem cell research. Only one of these, The Rockefeller University, did not report having a specific stem cell institute. Earmarked donations ranged in size from $10,984 to $10.3 million. These donations do not show the same upward trend as those to the stem cell centers, with an annual high of $14.1 million in 2007, at the height of the controversy over human embryonic stem cell research during the presidency of George W. Bush, and lows of $6.9 and $6.5 million in 2008 and 2009, respectively, the troughs of the economic recession. Combining the donations reported in response to both questions shows a nadir of philanthropy in 2008 with a climb to new heights in 2011.

Research Funding

In addition to querying institutional administrators, NYSTEM-funded investigators were asked to provide the value of additional research funds they had obtained as a result of NYSTEM awards. A total of 95 responses to this question were received from 181 investigators surveyed in 2012. Of those, 38 indicated that their NYSTEM funding had led to additional funding from other sources. All told, it is estimated that NYSTEM support has contributed to at least $152 million in additional funding from other sources. The bulk of this, $91.7 million, comes from the NIH, with an additional $44.1 million from foundations, $3.3 million from industry, and $12.6 million from other sources.

There are several caveats attached to these data. First and foremost, all of the data are self-reported, and just under three-quarters of the investigators who received funding responded. This approach also does not necessarily include additional funding obtained by co-principal investigators, as they were not surveyed directly. In some cases, it is unclear whether annual support or total grant value was reported. One final caveat, of the $302 million awarded at the time of the 2014 survey, only $277 million had been contracted and only $176.5 million had been spent as of July 1, 2014.
APPENDIX 5.D. Commercialization of NYSTEM-Funded Research

NYSTEM institutions self-reported intellectual property and technology transfer activities resulting in whole or in part from NYSTEM funding in surveys conducted in 2012 and 2014. These results too likely underestimate the commercial impact of NYSTEM funding. Reported outcomes include: 38 invention reports from 11 institutions; 49 patent applications from nine institutions; six new patents issued from four institutions; four new licensing agreements from four institutions; and seven new start-ups/business entities in New York based on stem cell technology from four institutions (Figure App.5.d.1).

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<td>Purified Protein Gbeta1Ggamma2 heterodimer; Purified Ric-8A; Purified Ric-8B full length; Purified Ric-8B (Delta Sign) 9</td>
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<td>Weill Cornell Medical College</td>
<td>Methods for optimizing human embryonic stem cell expansion and differentiation (D5302)</td>
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**NEW PATENT APPLICATIONS**

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<td>Ulrich Steidl</td>
<td>Identification of a novel diagnostic marker and therapeutic target of leukemia cells</td>
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<td>Ulrich Steidl</td>
<td>61/932,973 Epigenetic signature prognostic for survival in AML patients</td>
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<td>Sanjeev Gupta</td>
<td>A method for using soluble substances to generate hepatocytes in defined developmental stages from stem cells</td>
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<td>Columbia University</td>
<td>61/222,733 Primary cilia regulate mesenchymal stem cells</td>
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<td>61/399,519 Controlled scaffold design for tissue-to-tissue interface engineering</td>
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<td>61/434,190 Human induced neuronal cells</td>
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<td>61/505,407 Human induced neuronal cells</td>
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<td>61/519,491 Chondrogenic extracellular matrix hydrogel tissue scaffolds</td>
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<td>PCT/US2011/163328 Methods for producing tissue scaffold directing differentiation of seeded cells and tissue scaffolds produced thereby</td>
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<td>PCT/US2011/043687 Tissue scaffolds for controlled release of active agents</td>
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<td>Ichan School of Medicine at Mount Sinai</td>
<td>U.S. Provisional. 61/343272. Generation of anterior endoderm from pluripotent cells</td>
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<td>Japan. Generation of anterior foregut endoderm from pluripotent cells</td>
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<td>U.S. Provisional, 61/329,813 - Induced pluripotent stem cells and uses thereof</td>
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<td>Compositions and methods for diagnosing and treating melanoma; five associated applications</td>
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<td>David Levy</td>
<td>Role of mitochondrial STAT3 in disease and methods to detect and modulate its activity</td>
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<td>Ubiquitin-Regulated Chronic Myelogenous Leukemia initiation and progression</td>
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<td>University of Rochester</td>
<td>Archibald Perkins, Yan Zhang</td>
<td>61/666223 Methods in treating MDS1_EVI1 mediated cancer</td>
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<td>61/752,688 Direct Reprogramming of Human Endothelial Cells Into Functional Hematopoietic Multi-lineage Progenitors by Defined Factors</td>
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<td>Albert Einstein College of Medicine</td>
<td>Charles Rogler</td>
<td>8,729,046 B2 miR-27b: a novel target for treatment of liver fibrosis</td>
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<td>Gordana Vunjak-Novakovic</td>
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<td>StemCulture LLC/Rensselaer: Provider of stem cell culture supplies</td>
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APPENDIX 5.E. Clinical Translation

The mission of the ESSCB and NYSTEM includes support for clinical research. The ESSCB began its support of translational work with the approval of six major awards for Consortia that are attempting to bring stem cell-based therapies to clinical trials. See Chapter 2 at page 16.

In addition, Dr. Angela Christiano, at Columbia University, reported that her NYSTEM funding has contributed to a clinical trial in collaboration with Dr. Mitchell Cairo at the New York Medical College to use bone marrow stem cells for the treatment of Epidermolysis Bullosa. Dr. Ulrich Steidl, at Albert Einstein College of Medicine, is testing a chemotherapeutic drug in two types of cancer, acute myelogenous leukemia and myelodysplastic syndromes, based on his NYSTEM-funded research.
Appendix 6: Abbreviations

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<td>ARM</td>
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<td>hES</td>
<td>human embryonic stem cell</td>
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<td>IDEA</td>
<td>Innovative, Developmental or Exploratory Activities</td>
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<td>Investigator-Initiated Research Project</td>
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<td>iPS</td>
<td>induced pluripotent stem cell</td>
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<td>National Institutes of Health</td>
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