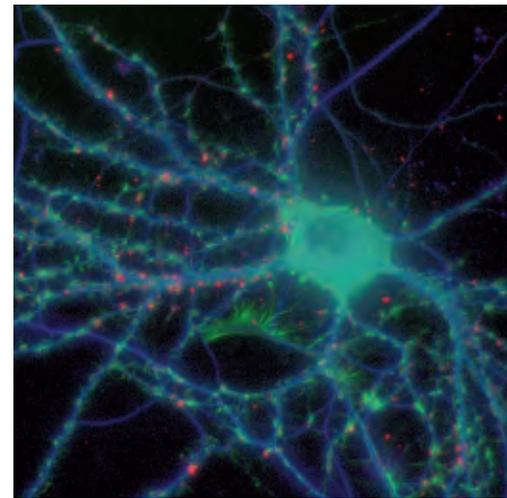


Empire State
Stem Cell Board
2008-09 Annual Report



The information contained in this report covers the activities of the Empire State Stem Cell Board (ESSCB) and the New York Stem Cell Science Program (NYSTEM) for the period April 1, 2008, through March 31, 2009. For more recent information regarding the ESSCB and the NYSTEM program, please visit the NYSTEM website at www.stemcell.ny.gov.

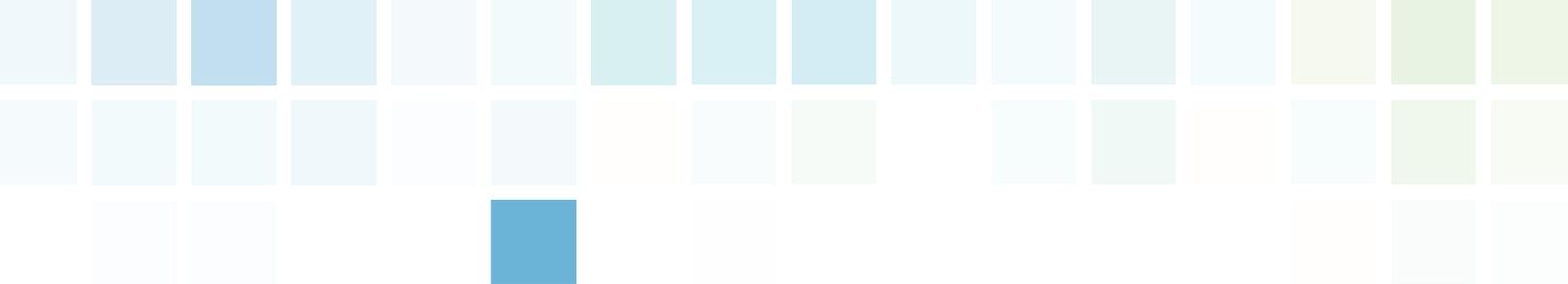


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Message from the New York State Commissioner of Health

The past year has been an exciting time for stem cell research in New York State, across the country and around the globe. Virtually every month significant research advances have emerged that demonstrate the hope that we hold for stem cells is well-founded.

Time magazine dubbed research that generated motor neurons from the stem cells of two patients with amyotrophic lateral sclerosis (ALS) as the single most important medical breakthrough of 2008. Progress was also seen in reprogramming adult cells and tissue engineering and in the U.S. Food and Drug Administration's approval of the first human clinical trial using an embryonic stem cell-based therapy to treat acute spinal cord injury. And in March of this year, President Barack H. Obama rescinded certain limitations on the embryonic stem cell lines that can be studied with federal funding, expanding opportunities for researchers to study new treatments and potentially find cures for debilitating and life-threatening conditions. Federal legislation, however, continues to prohibit support for the creation of new human embryonic stem cell lines, an important research objective that the Board supports.

Governor David A. Paterson's stem cell initiative has positioned New York State to take advantage of these developments and reinforces the State's position as a leader in biomedical research. During the 2008-09 fiscal year, more than \$104 million from the Empire State Stem Cell Trust Fund has been awarded to stem cell researchers and institutions. The Board's adoption of a Strategic Plan and use of an independent peer-review panel have ensured that the State's investment will support only the most promising research. This initiative is fostering a strong stem cell research community in New York State that will endure.

The historical developments in stem cell research over the past year have pointed to a new direction that holds not only the promise of cures for patients, but also remedies for some of our State's economic ills. Recognizing that these funds have the ability to stimulate New York's biomedical industry, a number of avenues are being pursued to identify the economic and other benefits of this program and explore means for ensuring that New York State residents reap the benefits of their investment.

I want to express my sincere appreciation to the members of the Empire State Stem Cell Board for their time, energy and extraordinary thoughtfulness that make this program a success. I also want to express my gratitude to the hundreds of individuals in the medical, scientific, educational, ethical and patient advocacy communities for their continued guidance and support. I look forward to learning what the next year will bring to this interesting, dynamic and important medical research field.



Richard F. Daines, M.D.

*Commissioner, New York State Department of Health
Chair, Empire State Stem Cell Board*



Message from the Executive Director of the New York Stem Cell Science (NYSTEM) Program

Much has been achieved toward fulfilling the Board's Strategic Plan in its second year of operation.

During the 2008-2009 fiscal year, the Board authorized 10 additional Requests for Applications (RFAs) that address all of the categories the Board identified as priorities in its Strategic Plan, resulting in an additional \$151 million committed to support: infrastructure; research; training; and ethical, legal and social implications and education. These commitments represent a substantial portion of the \$300 million made available for the first five years of the stem cell initiative.

Most gratifying this year was the tremendous response to an RFA for Investigator-Initiated Research Projects, and Innovative, Developmental or Exploratory Activities; 329 applications were received, with 78 being awarded a total of \$53.1 million. This level of response prompted the Board to recommend that this generic RFA be issued on a recurring basis. Proposals were also sought for Targeted Investigations of Induced Pluripotent Stem (iPS) Cells and Other Derivation Approaches that resulted in \$16.3 million being awarded to support 20 projects.

To extend this momentum into next year, the Board has approved the issuance on a continual basis of the generic research RFA and, to complement the funded iPS studies, the issuance of an RFA targeted to the Derivation, Characterization, Standardization and Optimization of Human Embryonic Stem Cell Lines.

Cognizant of current and future needs for a well-trained cadre of scientists to explore new avenues of research and transform today's discoveries into novel disease treatments, the Board also looked at strategies to enhance stem cell training and education. Two RFAs were issued to stimulate interest in stem cell science and related ethical, legal and social implications among undergraduates; one will support summer research experiences, while another will develop undergraduate course curricula or modules. Scientific training, one component of the first year's Institutional Development Awards, will also gain momentum with the Board's approval of new Fellow-to-Faculty Awards.

The sum of these accomplishments again positions New York State at the forefront of fostering stem cell research and all the promise the science embodies.



Lawrence S. Sturman, M.D., Ph.D.
Executive Director, NYSTEM

Members of the Empire State Stem Cell Board



Richard F. Daines, M.D., is the fourteenth New York State Health Commissioner. Prior to becoming Commissioner, Dr. Daines was the President and Chief Executive Officer (CEO) of St. Luke's-Roosevelt Hospital Center from January 1, 2002, until January 2007. Before joining the Hospital Center as Medical Director in 2000, he served as Senior Vice President for Professional Affairs of St. Barnabas Hospital in the Bronx, New York from 1994 and the Medical Director from 1987 to 1999. Dr. Daines received a Bachelor of History degree from Utah State University in 1974 and served as a missionary for the Church of Jesus Christ of Latter-day Saints in Bolivia, 1970-1972. He received his medical degree from Cornell University Medical College in 1978. He served a residency in internal medicine at New York Hospital and is Board Certified in Internal Medicine and Critical Care Medicine (1987-1997). Dr. Daines serves as Chair of the Empire State Stem Cell Board and its committees, the Funding and Ethics Committees. (F,E)



David C. Hohn, M.D., is President Emeritus and Executive Director of Health Policy at Roswell Park Cancer Institute (RPCI), where he served for 10 years as President and CEO. Dr. Hohn continues his national leadership role in health policy issues, especially as they relate to cancer research and treatment and training the next generation of cancer specialists. During his tenure as RPCI President, Dr. Hohn was widely credited with re-establishing the Institute as a leader in the national cancer community. He implemented the Institute's first strategic plan focused on making RPCI internationally and nationally competitive in cancer science; led the restructuring of RPCI as a public benefit corporation; stabilized funding and increased revenue; recruited over 160 senior leadership faculty, top-tier clinicians and scientists; completed a \$250-million renovation and rebuilding of the Institute campus; and implemented an innovative managed care strategy which opened regional access to RPCI. As Principal Investigator of the National Institutes of Health (NIH) National Cancer Institute Cancer Center Support Grant, Dr. Hohn led the successful renewal of Roswell Park's designation as a comprehensive cancer center – a designation the Institute has held continuously since 1974. Dr. Hohn came to RPCI from the University of Texas M.D. Anderson Cancer Center where, as Vice President for Patient Care from 1993 to 1997, his responsibilities included oversight of all clinical departments, clinical research programs and the protocol office. Dr. Hohn serves as Vice Chairman of the Empire State Stem Cell Board and its Committees. (F,E)

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(E) = Member of the Ethics Committee



Kenneth Adams, M.B.A., is President and CEO of The Business Council of New York State, which represents more than 3,000 member businesses, chambers of commerce and professional and trade associations. The Business Council's mission is to create an economic renaissance for New York State by shaping public policy to improve New York's economy. Prior to joining The Business Council in November, 2006, Mr. Adams was the President of the Brooklyn Chamber of Commerce. Under his leadership, the Brooklyn Chamber more than doubled its membership and significantly increased the impact of its marketing, advocacy and small business services. Mr. Adams substantially increased the Chamber's annual budget, launched 10 new economic development initiatives and improved the Chamber's relationships with government officials. Before joining the Brooklyn Chamber in 1995, he was the Director of the MetroTech Business Improvement District (BID) in Downtown Brooklyn. Under Mr. Adams' leadership, the BID augmented its services, improved community relations and received citywide recognition for its management and programs. He was the founding Executive Director of New York Cares, which he ran from 1988 to 1994, managing the organization's growth from 500 to 6,000 volunteers serving in citywide social service and community revitalization projects. He was also appointed by Governor Eliot Spitzer to serve on the Commission to Modernize the Regulation of Financial Services and the Children's Cabinet Advisory Group. (F)



Rev. Thomas Berg, Ph.D., is a Roman Catholic priest in the Archdiocese of New York and Executive Director of The Westchester Institute for Ethics and the Human Person. Rev. Berg received his M.A. in Liberal Studies from Wesleyan University in 1997 and his Ph.D. in Philosophy from Regina Apostolorum in 1999. He specializes in natural law theory, personhood theory and biomedical issues dealing with the beginning of life. For the past five years, he has dedicated most of his philosophical research to the question of the moral status of the human embryo. Working with members of the President's Council on Bioethics, he has organized an interdisciplinary group of scientists, philosophers and moral theologians to engage in an ongoing study of the moral and scientific feasibility of Altered Nuclear Transfer and other non-embryo-destructive sources of human pluripotent stem cells. He has recently co-edited a volume of essays by Catholic moral theologians entitled, *Human Embryo Adoption: Biotechnology, Marriage, and the Right to Life*. (E)

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Bradford C. Berk, M.D., Ph.D., is the Senior Vice President for Health Sciences at the University of Rochester and CEO of the Medical Center and Strong Health. Dr. Berk received his medical and doctoral degrees from the University of Rochester. He has served on the faculties of Harvard Medical School, Emory University and the University of Washington. He previously was Chair of Medicine (1999-2006) and Chief of the Cardiology Unit (1998-2003) at the University of Rochester. In addition, he was Director of the AB Cardiovascular Research Institute. Dr. Berk is a fellow of the American Heart Association and the American College of Cardiology, and a member of the Association of American Physicians. Dr. Berk is past-president of the North American Vascular Biology Organization (NAVBO). He is Consulting Editor for *Circulation* and *Circulation Research* and is on the editorial boards of *Arteriosclerosis, Thrombosis, and Vascular Biology (ATVB)* and the *Journal of Clinical Investigation*. He serves on the NIH National Heart, Lung and Blood Institute, Stem Cell Clinical Trial Network, and Gene and Cell-Based Therapies Data and Safety Monitoring Board. Dr. Berk has published more than 250 articles, chapters and books. His research interests include: molecular biology of the renin-angiotensin-aldosterone system; regulation of endothelial cell function, especially by shear stress; the role of oxidative stress in vascular injury biology; and the genetic mechanisms of vascular remodeling. (F)



Nancy Neveloff Dubler, LL.B., is Senior Associate at the Montefiore-Einstein Center for Bioethics, and Professor Emerita of Bioethics at the Albert Einstein College of Medicine. She received her B.A. from Barnard College and her LL.B. from the Harvard Law School. Ms. Dubler founded and directed the Bioethics Consultation Service at Montefiore Medical Center from 1978-2008 as a support for the analysis of difficult clinical cases presenting ethical issues in the health care setting. This service uses mediation as its process. She lectures extensively and is the author of numerous articles and books on termination of care, home care and long-term care, geriatrics, adolescent medicine, prison and jail health care and AIDS. She was Co-Director of the Certificate Program in Bioethics and the Medical Humanities, operated jointly by Montefiore Medical Center/ Albert Einstein College of Medicine with Cardozo Law School of Yeshiva University. Her most recent books are: *The Ethics and Regulation of Research with Human Subjects*, Coleman, Menikoff, Goldner and Dubler, LexisNexis, 2005; and *Bioethics Mediation: A Guide to Shaping Shared Solutions*, co-author, Carol Liebman, United Hospital Fund, New York, New York, 2004. She consults often with federal agencies, national working groups and bioethics centers. (E)

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Richard W. Dutton, Ph.D., was born in Great Britain, where he earned a Ph.D. in Biochemistry from London University, England, and a Masters of Arts and Bachelor of Arts degree in Biochemistry from Cambridge University, England. He spent many years as a Professor in the Department of Biology, at the University of San Diego, California, including service as Department Chair from 1986-1988, and is currently a member of the Trudeau Institute, Inc., in Saranac Lake, New York. He served as President of the American Association of Immunologists (AAI), and was awarded a Lifetime Achievement Award for his distinguished scientific accomplishment and extraordinary service to the AAI in April, 2004. In the past he has held memberships in various organizations and received many awards, such as the American Cancer Society Faculty Research Award. He has authored more than 200 publications to date, and was elected a Fellow of the American Association for the Advancement of Science in 2007. (F)



Robin Anthony Elliott, M.A., has been Executive Director of the Parkinson's Disease Foundation, Inc., since October 1996. He has been active in development, communications and not-for-profit management in New York City for more than 35 years, serving as Vice President for Development and External Affairs at Teachers College, Columbia University (1988-1995), and at Hunter College, The City University of New York (1982-1988); as Deputy to the Chancellor for University Relations at the City University of New York (1979-1982); and as Director of Information and Education for the Planned Parenthood Federation of America (1971-1979). Mr. Elliott grew up in southern England and received his B.A. from Magdalen College, Oxford University, and his M.A. in American Government and Politics from Columbia University. Avocationally, he is active in reproductive health and rights, including as Member of the Board of Directors of Advocates for Youth, a Washington-based organization he co-founded in 1980, and has served on the vestry of St. Michael's Church on West 99th Street in New York City, and the boards of directors of the St. Cecilia Chorus and Community Health Charities. Until recently, he was Chair of New Yorkers for the Advancement of Medical Research, a pro-stem cell research coalition of disease advocacy groups, scientists, universities and citizens' groups. (F)

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Brooke Ellison, M.A., has worked as an advocate for stem cell research for nearly a decade. In 1990, at the age of 11, she was in an accident that left her paralyzed from the neck down and dependent on a ventilator to breathe. However, Ms. Ellison never let her physical situation stand in the way of what she could achieve, and she graduated with honors from Harvard University in 2000 and from Harvard's Kennedy School of Government in 2004. In 2002, she published an autobiography, *Miracles Happen*, which was later made into a movie directed by Christopher Reeve. For more than a decade, she has worked across the country as a public speaker, delivering her message of hope, optimism and strength in the face of obstacles, using her own experiences as a vehicle to convey the message. Ms. Ellison was a candidate for New York State Senate in 2006, focusing on the need for New York to embrace funding for stem cell research. She has continued her work in the field of stem cell research and in July 2007 formed a non-profit organization, The Brooke Ellison Project, to educate and mobilize on behalf of the research. In addition, working with leading scientists and advocates in the field, she has produced a documentary to provide necessary information on stem cell research. (E)



Gerald D. Fischbach, M.D., is the Scientific Director of The Simons Foundation, where he oversees the Foundation's Autism Research Initiative. Formerly Dean of the Faculties of Health Sciences at Columbia University, and Director of the National Institute of Neurological Disorders and Stroke at the National Institutes of Health (NIH) from 1998-2001, he received his M.D. degree in 1965 from Cornell University Medical School and interned at the University of Washington Hospital in Seattle. He began his research career at the NIH, serving from 1966 to 1973. He subsequently served on the faculty of Harvard Medical School, first as Associate Professor of Pharmacology from 1973 to 1978, and then as Professor until 1981. He was then the Edison Professor of Neurobiology and Head of the Department of Anatomy and Neurobiology at Washington University School of Medicine. In 1990, he returned to Harvard where he was the Nathan Marsh Pusey Professor of Neurobiology, and Chair of the Neurobiology Departments of Harvard Medical School and Massachusetts General Hospital until 1998. Throughout his career, Dr. Fischbach has studied the formation and maintenance of synapses, the contacts between nerve cells and their targets, through which information is transferred in the nervous system. He is a member of the National Academy of Sciences, the American Academy of Arts and Science and the Institute of Medicine, a Fellow of the American Association for the Advancement of Science, a non-resident Fellow of the Salk Institute, and past-President of the Society of Neuroscience. (F)

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Samuel Gorovitz, Ph.D., former Dean of Arts and Sciences at Syracuse University, led in the development of the field of medical ethics and has published extensively on other topics in philosophy and public policy. He has given more than 200 invited lectures in dozens of countries on five continents, and in 1989 led a National Institutes of Health regional workshop on research with human subjects. His publications include more than 120 articles, reviews and editorials in philosophical journals, medical journals, public policy journals and newspapers. He is a co-author of the book, *Philosophical Analysis*, and an editor of several anthologies. His two most recent books are, *Doctors' Dilemmas: Moral Conflict and Medical Care*; and *Drawing the Line: Life, Death, and Ethical Choices in an American Hospital*. In fall 1996, he served as the Baker-Hostetler Professor of Law at Cleveland Marshall College of Law, and in fall 1998 was Visiting Scholar in the Department of Science and Technology Studies at Cornell University. Since 1988 he has served, by gubernatorial appointment, on the New York State Task Force on Life and the Law. He was Dearing-Daly Professor of Bioethics and Humanities at the State University of New York (SUNY) Upstate Medical University from 2001-2004, and during 2004-2005 was Visiting Professor of Philosophy and Bioethicist in Residence at Yale. He is Founding Director of the Renée Crown University Honors Program and Professor of Philosophy at Syracuse University. (E)



Bruce Holm, Ph.D., is Executive Director of the New York State Center of Excellence in Bioinformatics and Life Sciences, as well as Senior Vice Provost and Professor in the Departments of Pediatrics, Obstetrics and Gynecology, and Pharmacology and Toxicology at SUNY Buffalo. Dr. Holm's research centers on the development of therapeutics for treatment of critical care patients, and he has co-founded two biotechnology companies that have developed and received U.S. Food and Drug Administration approval for life-saving drugs used in both newborns and adults. He holds several patents for lung surfactant replacement drugs currently on the market. He received a Research Career Award from the NIH Heart, Lung and Blood Institute in 1991, and has been principal investigator on a variety of NIH, Howard Hughes Medical Institute, U.S. Department of Defense, National Aeronautics and Space Administration (NASA) and Markey Trust-funded projects totaling more than \$50 million in current active federal grant support. Dr. Holm has published more than 250 papers, book chapters and abstracts on such topics as the biology of lung development, the use of surfactant therapy and molecular therapeutics in acute diseases. (F)

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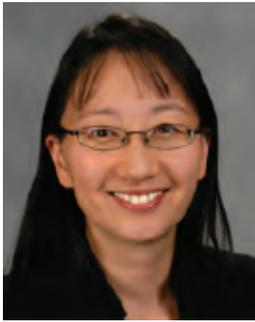


Hilda Hutcherson, M.D., F.A.C.O.G., is Associate Dean in the Office of Diversity, and a Clinical Professor of Obstetrics and Gynecology at Columbia University College of Physicians and Surgeons. Dr. Hutcherson is a fellow in the American College of Obstetricians and Gynecologists, and a member of the National Association of Medical Minority Educators, National Medical Association, North American Menopause Society and the American Medical Women's Association. She is the former director of the Pediatric and Adolescent Gynecology Program, and Co-Director of the Center for Women's Health at Columbia University Medical Center. Dr. Hutcherson serves on the Advisory Boards of the Columbia University Summer Research Fellowship Program, the Doris Duke Clinical Research Fellowship Program, the Associated Medical Schools Diversity and Community Affairs Program and the New York City Health Literacy Fellowship. She has received numerous awards for her teaching and patient advocacy contributions. Dr. Hutcherson has maintained a clinical practice in Obstetrics and Gynecology since 1985. (F)



Robert Klitzman, M.D., is an Associate Professor of Clinical Psychiatry (in Socio-medical Sciences) in the College of Physicians and Surgeons, and the Joseph Mailman School of Public Health at Columbia University. He co-founded and for five years co-directed the Columbia University Center for Bioethics, and is currently the Director of the Ethics, Policy and Human Rights Core of the HIV Center, and a member of the Division of Psychiatry, Law and Ethics at Columbia. Dr. Klitzman has written numerous articles and book chapters, as well as six books, examining ethical, social, psychological and policy issues related to stem cells, research ethics, genetic testing, reproductive decision-making, privacy of genetic and other health information, Institutional Review Board decision-making, professional education and other areas. His most recent book, *Mortal Secrets: Truth and Lies in the Age of AIDS*, examines views of medical privacy and ethical decision-making related to HIV and other realms, and their implications for public policy. He has also engaged in public education in medical ethics, writing about these issues for the *New York Times* and other publications. Dr. Klitzman has received several honors and awards for his work, including fellowships from the Aaron Diamond Foundation, the American Psychiatric Association, the Russell Sage Foundation, the Commonwealth Fund and the Rockefeller Foundation. (E)

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Vivian S. Lee, M.D., Ph.D., M.B.A., is Vice Dean for Science, Senior Vice President and Chief Scientific Officer of the New York University (NYU) Medical Center. She also is Professor and Vice Chair for Research in the Department of Radiology, and Professor of Physiology and Neuroscience. A practicing magnetic resonance imaging (MRI) radiologist, Dr. Lee is the principal investigator of three NIH research grants and serves as a charter member of the Medical Imaging NIH Study Section. She is also a Fellow and President-Elect of the International Society for Magnetic Resonance in Medicine. Dr. Lee has authored more than 100 peer-reviewed publications and a recent textbook, *Cardiovascular MRI: Physical Principles to Practical Protocols*. Her research focuses on development of quantitative functional MRI for the improved understanding of physiology and disease. Dr. Lee was awarded a Rhodes scholarship to study at Oxford University, where she received a doctorate in medical engineering. She earned her M.D. at Harvard Medical School, completed her residency in Diagnostic Radiology at Duke, and was a fellow in Body and Cardiovascular MRI and Thoracic Imaging at NYU. Dr. Lee completed an M.B.A. at NYU's Stern School of Business in 2006. (E)

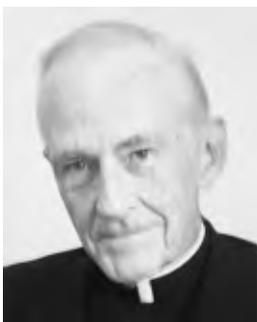


H. Hugh Maynard-Reid, D.Min., B.C.C., C.A.S.A.C., is Director of the Pastoral Care Department in the North Brooklyn Health Network, Health and Hospitals Corporation of New York City. He is a Board Certified Chaplain and a Credentialed Addiction and Substance Abuse Counselor by the State of New York. He also is certified in Human and Medical Bioethics. Previously, Rev. Dr. Maynard-Reid served as a minister for 15 years in New York City. He was also the Associate Professor of Old Testament and Biblical Studies at Northern Caribbean University (formerly West Indies College), and Adjunct Professor at Andrews University. He is a member of the New York State Task Force on Life and the Law and the Association of Professional Chaplains. He is an Advisory Member of Catholic Health Services of Long Island Pastoral Education and Chaplaincy Services. He served at North Brooklyn Network as a member of the Institutional Review Board and human research committee and is a member of the Ethics Committee. As a member of the Brooklyn Ecumenical Advisory, his community services work centers on community leaders' health education. (E)

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Samuel Packer, M.D., is Chair Emeritus of the Department of Ophthalmology at North Shore-Long Island Jewish Health System. He holds the endowed Arthur and Arlene Levine Professorship, and is a Professor of Clinical Ophthalmology, NYU School of Medicine. Dr. Packer began his ophthalmology practice in 1972. He has served as Chair of the Department of Ophthalmology at North Shore University Hospital (1984-2004) and Chair of the Department of Ophthalmology at the North Shore-Long Island Jewish Health System (2005-2007). As a board-certified ophthalmologist, he divides his time between his clinical practice and his interest in medical ethics, education and research. Dr. Packer began as a research collaborator at Brookhaven National Laboratory (1971-1993) and rose to the rank of Scientist. His major contribution was to pioneer the use of low-energy radioactive sources to treat melanoma of the eye. Dr. Packer received his medical degree from SUNY Downstate Medical Center, and completed a medical internship at Kings County Medical Center and an ophthalmology residency at Yale-New Haven Hospital. He has served as President of the New York State Ophthalmological Society, the Nassau County Medical Society and the Nassau Academy of Medicine. Dr. Packer has also been a member of the New York State Task Force on Life and the Law since 1992, served as Chair of the American Academy of Ophthalmology Ethics Committee and is the Executive Chair of the Lions Eye Bank for Long Island, as well as Chair of the Ethics Committee at North Shore Long-Island Jewish Health System. (E)



Rev. Monsignor William Smith, S.T.D., (*Deceased*), was a Professor of Moral Theology at St. Joseph's Seminary, Dunwoodie, Yonkers, New York, and a Roman Catholic priest ordained in 1966 for the Archdiocese of New York. Monsignor Smith received his B.A. in philosophy in 1961 from St. Joseph's Seminary and College. He received his M.Div. in 1965 and his M.A. in theology in 1966 from St. Joseph's Seminary. He received his S.T.D., a doctorate in moral theology, in 1971 from The Catholic University of America, Washington, D.C. From 1971 until the time of his death in January 2009, Monsignor Smith had been the Professor of Moral Theology at St. Joseph's Seminary. He was also Dean of the Faculty at St. Joseph's, teaching fundamental moral theology and medical ethics from 1977 through 1988, and again from 2000 through 2005. Monsignor Smith held the Margaret Leibman Berger Chair in Medical Ethics and was a member of the Ethics Committee at St. Vincent's Hospital in Manhattan and Calvary Hospital in the Bronx. (E)

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Michael A. Stocker, M.D., M.P.H., is Chairman of the Board of the New York City Health and Hospitals Corporation. Previously, he was CEO of Empire Blue Cross-Blue Shield from 1994 until 2005, when Empire was acquired by WellPoint, a company comprised of 14 Blue Cross-Blue Shield plans throughout the country. Dr. Stocker retired from WellPoint in April 2007. Prior to joining Empire, Dr. Stocker was President of CIGNA Health Plans. He also served as Executive Vice President and General Manager of U.S. Healthcare for the New York market. He was Medical Director at ANCHOR, a staff model health maintenance organization at Rush Presbyterian-St. Luke's Medical Center in Chicago for five years. He was also Associate Chairman and Program Director of the Department of Family Practice at Cook County Hospital in Chicago and practiced medicine in Chicago for 12 years. Dr. Stocker earned his undergraduate degree from the University of Notre Dame and his medical degree from the Medical College of Wisconsin. He received his residency training at the Mayo Clinic and at the University of California and is Board Certified in Internal Medicine and Family Practice. He also received a Master of Public Health from the University of Michigan. Dr. Stocker is a member of several boards and organizations, including the New York Stem Cell Foundation and the Arthur Ashe Institute for Urban Health. (F)

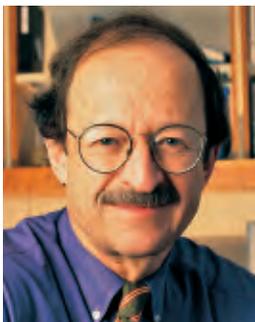


Daniel P. Sulmasy, O.F.M., M.D., Ph.D., a Franciscan Friar, held the Sisters of Charity Chair in Ethics at St. Vincent's Hospital, Manhattan, and served as Professor of Medicine and Director of the Bioethics Institute at New York Medical College, Valhalla, New York. He received his B.A. and M.D. degrees from Cornell University and completed his residency, chief residency and post-doctoral fellowship in General Internal Medicine at the Johns Hopkins Hospital. He received his Ph.D. in philosophy from Georgetown University in 1995. From 1991 to 1998, he served on the faculty at Georgetown, where he was Director of the Center for Clinical Bioethics and Senior Research Scholar of the Kennedy Institute of Ethics. He was appointed by Governor George Pataki to the New York State Task Force on Life and the Law in 2005. His research interests include the ethics of end-of-life decision-making, ethics education and spirituality in medicine. He is the author of four books, *The Healer's Calling*, *Methods in Medical Ethics*, *The Rebirth of the Clinic* and *A Balm for Gilead*. He serves as editor-in-chief of the journal *Theoretical Medicine and Bioethics*. His numerous articles have appeared in medical, philosophical and theological journals, and he has lectured widely both in the U.S. and abroad. (E)

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Robert N. Swidler, M.A., J.D., is General Counsel to Northeast Health, a not-for-profit health care system in New York's Capital Region that includes hospitals, nursing homes, home care, senior residences and other affiliates. He is also a member of the faculty of both Albany Medical Center's Alden March Bioethics Institute and the Union College/Mt. Sinai School of Medicine Bioethics Program. Previously, Mr. Swidler was a partner at Hiscock & Barclay, Deputy Commissioner and Counsel to the NYS Office of Mental Health, and Assistant Counsel to Governor Mario Cuomo. From 1985-1990, Mr. Swidler served as staff counsel to the New York State Task Force on Life and the Law, where he helped develop the Task Force's proposals on brain death, do-not-resuscitate orders, health care proxies and organ transplantation. Mr. Swidler has written numerous articles on health law topics, and co-authored chapters in the *Legal Manual for New York Physicians* on informed consent and life-sustaining treatment decisions. He was Chair of the New York State Bar Association Health Law Section during 1999-2000, and is currently editor of the Association's Health Law Journal. Mr. Swidler is a graduate of Columbia Law School (1982) and SUNY at Binghamton (B.A. '77, M.A. '78). (E)



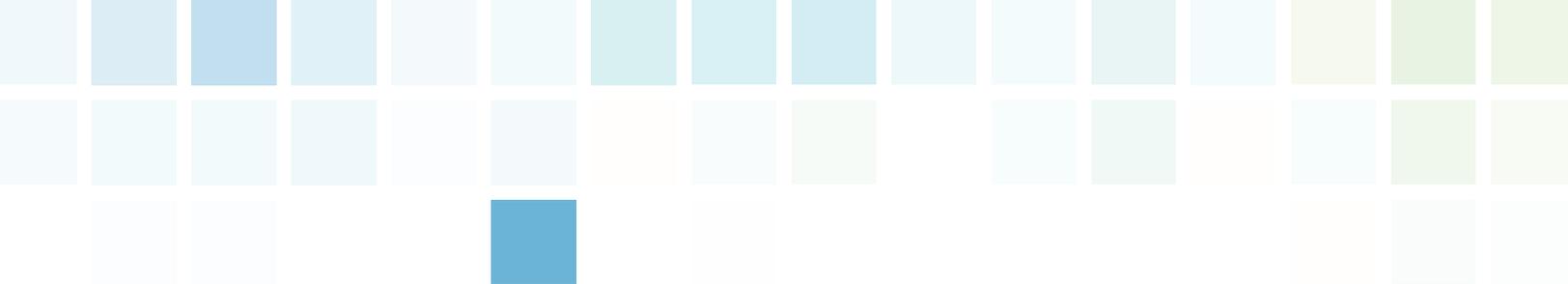
Harold Varmus, M.D., former Director of the NIH and co-recipient of the 1989 Nobel Prize in Physiology or Medicine, has served as the President and CEO of Memorial Sloan-Kettering Cancer Center in New York City since January 2000. Dr. Varmus received the Nobel Prize (jointly with Michael Bishop) for elucidating the molecular and genetic mechanisms that underlie the transformation of a normal cell to a cancerous one. He is a member of the National Academy of Sciences and the Institute of Medicine, and has received the National Medal of Science, the Vannevar Bush Award and several honorary degrees. In addition to authoring more than 300 scientific papers and four books, Dr. Varmus has been an advisor to the federal government, pharmaceutical and biotechnology firms and many academic institutions. He served on the World Health Organization's Commission on Macroeconomics and Health from 2000 to 2002; is a co-founder and Chairman of the Board of Directors of the Public Library of Science; chairs the Scientific Board of the Grand Challenges in Global Health project at the Bill and Melinda Gates Foundation; and is involved in initiatives to promote science in developing countries, including the Global Science Corps. His research at the Sloan-Kettering Institute mainly addresses molecular mechanisms of oncogenesis, using mouse models of human cancer. Dr. Varmus resigned from the Empire State Stem Cell Board in December 2008 upon his appointment as Co-Chair of the President's Council of Advisors on Science and Technology. (F)

(F) = Member of the Funding Committee
(E) = Member of the Ethics Committee



Madelyn Wils is Executive Vice President of the Planning, Development and Maritime Division of the New York City Economic Development Corporation (NYCEDC). She is responsible for most of the City's area-wide revitalization plans throughout the five boroughs. Prior to joining NYCEDC, Ms. Wils served as President of the Tribeca Film Institute. She managed the expansion of the organization, from programming a 10-day film festival into a diverse institution offering year-round cultural and educational events. From 2000 to 2005, she served as Chair of Community Board One in Lower Manhattan, where she played an integral role in the rebuilding of Lower Manhattan. Ms. Wils led the development of the Master Concept Plan for the East River Waterfront, and was awarded The Visionary Award from the New York League of Conservation Voters for her efforts. She negotiated significant capital projects for her community, including new schools and parks, community facilities, Little League fields and a library in Battery Park City. Ms. Wils was a founding board member of the Lower Manhattan Development Corporation and The Hudson River Park Trust. She has also served on other boards, including the Alliance for Downtown New York, the Battery Conservancy and the Lower Manhattan Cultural Council. (F)

(F) = Member of the Funding Committee
(E) = Member of the Ethics Committee



Activities of the Empire State Stem Cell Board

Introduction

In its first year of operation, the Empire State Stem Cell Board (Board or ESSCB) laid a solid foundation for operating effectively, efficiently and equitably through the development and adoption of by-laws, independent scientific peer-review policies, standards for New York State Stem Cell Science (NYSTEM) awardees and Requests for Applications (RFAs). From its inception, the Board and its committees, the Funding and Ethics Committees, also devoted significant time at each meeting to consideration of the Board's goals and priorities and the strategies for achieving those goals. This work culminated in the adoption of the Board's Strategic Plan at a meeting of the full Board on June 27, 2008. The Board's Strategic Plan established the mission of the Board as:

...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.

The plan also identified five key areas that required funding during the Board's first five years of operation to fulfill this mission: research, scientific training, infrastructure development, ethical, legal, social issues and education and administration. The Strategic Plan also committed the Board to performing an annual assessment of its progress towards these goals, examining potential intellectual property and fiscal policies to maximize the benefits of the NYSTEM program to New York State researchers and residents, and evaluating the economic and other benefits derived from the State's investment in stem cell research at regular intervals. In the 2008-2009 fiscal year, the Board relied upon its Strategic Plan and other important work performed in its inaugural year to advance the mission of the Board.

Economic Assessment and Intellectual Property Issues

The statute creating the ESSCB requires that all grants be subject to intellectual property agreements that identify the scope, if any, of the State's financial or other interests in the commercialization of the results, products, inventions and discoveries emanating from State-funded research. In keeping with this mandate, the Board's Funding Committee has imposed several requirements applicable to intellectual property rights. Principal among these are standards ensuring public access to the published results of State-funded research, sharing of research-developed products and methodologies within the research community and the right of the State to protect or commercialize State-funded discoveries that may be patentable and marketable whenever a grantee fails to do so.

In addition, the full Board has recognized the potential need for additional intellectual property requirements to ensure that the State and its residents benefit from publicly funded research. The Board has studied options employed in other state funding programs, such as California's, and included a commitment in its Strategic Plan to explore alternatives that may be less burdensome and do not create disincentives for public/private collaboration. To further this objective, the Board has established a workgroup composed of both Funding and Ethics Committee members, as well as other interested parties, to examine these issues. Under the direction of its Chair, Kenneth Adams, and with the assistance of NYSTEM staff, the workgroup convened a series of interviews with experts to help inform the Board about business development, intellectual property, technology transfer and patent protection issues. This workgroup will present its initial findings to the full Board at its June 11, 2009, meeting.

The Board has also recognized that the influx of NYSTEM funds into the State's research institutions will create jobs and help recruit and retain world-class investigators, who in turn will help these institutions secure additional research funding from the federal government and the private sector. Moreover, the resulting enhancement of stem cell research throughout the State will serve as a stimulus for private-sector investment in the biomedical, biotechnological and pharmaceutical industries, accruing broad economic benefits to our communities. Recognizing this potential, the ESSCB included a commitment in its Strategic Plan to assess these benefits at regular intervals and issued a Request for Proposals (RFP) that would engage a contractor to assess the economic and other benefits of the NYSTEM program.

Annual Meeting of Scientists

The Institutional Development Grants awarded in January 2008 require funded scientists to attend a NYSTEM-sponsored symposium or similar event and present their research findings. This requirement facilitates the goal of making the results of State-funded research openly available to maximize their potential benefit to New York residents and society as a whole. The first meeting of funded scientists was held on June 12, 2009, in Albany. A Program Committee of leading stem cell scientists from throughout the State was convened to develop the agenda for this meeting, consisting of speakers, presentations, break-out sessions, a panel discussion and a poster session to offer funded scientists ample opportunity to discuss their findings and interact with other stem cell scientists throughout New York State.

Education Initiatives

Board members have expressed a strong interest in educating the public about stem cell research. In addition to approving two RFAs that were issued in the Spring of 2009 to support undergraduate curriculum development and summer internships for undergraduate students, the Board has considered providing support for both formal and informal education programs. In June 2008, the Board heard a presentation from Dr. Samuel Silverstein of Columbia University about potential secondary education initiatives, and in January 2009, the Ethics Committee heard a presentation on museum and other informal educational programs from Dr. Alan Friedman, former Director and CEO of the New York Hall of Science. Over the next year, the Board expects to identify target audiences and consider one or more proposals to support programs and activities that will engage and educate the public about stem cell research. Additional information is found in the Training and Education section of this report.

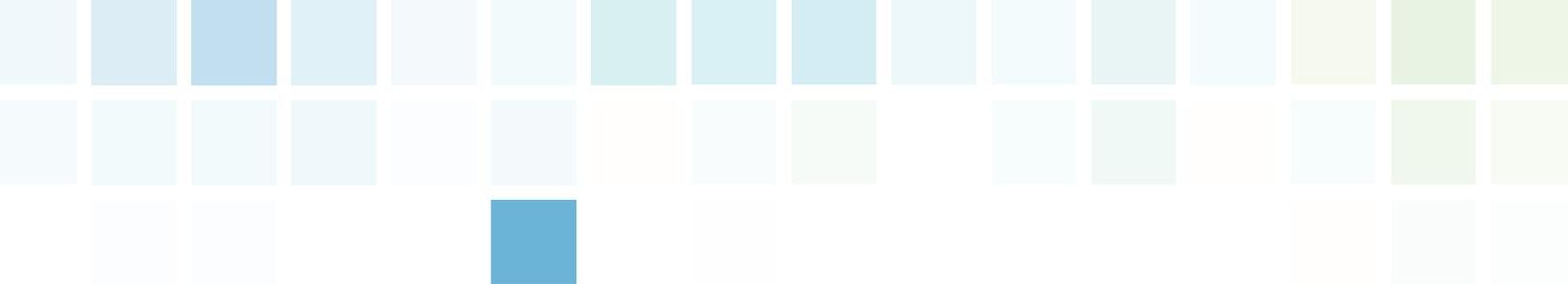
*ESSCB Board Meetings and Locations
for April 1, 2008 through March 31, 2009*

Date	Location	Committee(s)
April 1, 2008	New York City	Ethics Committee
May 13, 2008	Albany	Full ESSCB Board
June 27, 2008	New York City	Full ESSCB Board
September 4, 2008	New York City	Ethics Committee
September 19, 2008	New York City	Funding Committee
October 16, 2008	New York City	Ethics Committee
November 6, 2008	New York City	Funding Committee
December 18, 2008	New York City	Funding Committee
January 26, 2009	New York City	Ethics Committee
February 12, 2009	New York City	Funding Committee
March 16, 2009	New York City	Ethics Committee

The minutes for all Committee and Board meetings are available online at:
<http://www.stemcell.ny.gov/events.html>



May 13, 2008, Board meeting at the Empire State Plaza in Albany



Funding Committee Meetings and Activities

The activities of the Funding Committee in 2008-2009 fell into two primary categories: the review of applications and recommendation of awards, and the development of new funding proposals consistent with the Board's Strategic Plan.

Review and Recommendation of Award Applications

From May through July 2008, the NYSTEM program received 413 applications submitted in response to the four RFAs approved by the Committee earlier in 2008. These proposals were evaluated by independent scientific peer-review panels during August through October and were considered at Funding Committee meetings in September, November and December 2008.

In keeping with a key objective of the Board's Strategic Plan, the first awards considered by the Funding Committee in the fall of 2008 were designed to encourage collaborations among new and established stem cell investigators within and among New York State institutions, and in partnership with non-New York State investigators and institutions. The Funding Committee recommended awards to 18 New York State institutions totaling \$2.0 million to support New York State stem cell investigators engaged in consortium planning efforts with other stem cell researchers from across the State, the country and the world.

In November 2008, the Funding Committee recommended awards to nine institutions totaling \$32.4 million to support the development of shared core facilities and specialized equipment. As the location of many world-class biomedical research organizations, New York is well-positioned to be a leader in the field of stem cell research and policy. However, in its Strategic Plan the Board recognized that it needed to strengthen New York State's infrastructure to establish a solid foundation specifically for stem cell scientists that would foster the development of a robust stem cell community and encourage collaborations among researchers. These shared-use facilities and instruments will help researchers isolate, derive and characterize stem cell lines, including disease-specific cell lines; develop animal models; provide high-throughput analyses of cells; and maintain quality control and laboratory supplies needed for stem cell experiments.

Consistent with the Board's Strategic Plan, the remaining funding awarded in the 2008-2009 Fiscal Year supported investigator-initiated research in two categories: investigator-initiated research projects, including basic translational or pre-clinical stem cell studies or innovative higher-risk research proposals; and targeted research proposals directed at stimulating investigations of induced pluripotent stem (iPS) cells and other approaches for deriving stem cells.

In December, the Funding Committee considered the applications submitted in response to the Investigator-Initiated Research Projects (IIRP) and Innovative Developmental or Exploratory Activities (IDEA) in Stem Cell Research awards. An impressive 329 applications were received in response to this highly competitive RFA, and funding was approved for 78 researchers,

or about 25 percent of the applicants. It is noteworthy that the majority of applications were scored highly by the independent scientific peer-review panels and that only those applications scoring 1.9 or better (on a one-to-five scale, with one as the best possible score) were recommended for funding. These awards, totaling \$53.1 million, will facilitate scientific investigations of stem cell biology that will lead to a better understanding of the unique properties of stem cells and allow their use to understand and treat disease.

At its December meeting, the Funding Committee also awarded 19 investigators (20 awards) a total of \$16.3 million to support cutting-edge research on iPS cells and other derivation approaches. These 20 awards will stimulate and support investigations to devise improved methods for deriving pluripotent stem cell lines; defining cell reprogramming mechanisms; and comparing the utility of iPS with embryonic and other pluripotent stem cells for use in disease models and potential therapeutic applications.

Development of New Funding Proposals

After issuing the initial set of RFAs, the Funding Committee turned its attention to the development of other potential funding mechanisms consistent with the goals and priorities set forth in its Strategic Plan.

Based upon the strong response to the Board's initial RFA to support investigator-initiated stem cell research proposals, the Funding Committee agreed to issue the Investigator-Initiated Research Proposal RFA at regular intervals. This approach will not only advance the Board's goal of allocating most of the available funds to support stem cell research, but is also expected to encourage researchers to engage in stem cell research knowing that a committed stream of potential funding will be available to support their activities. The Funding Committee authorized the issuance of the next RFA for approximately \$15 million to fund additional investigator-initiated research proposals in the spring of 2009.

One of the goals set forth in the Board's Strategic Plan is

...to ensure a robust, interactive stem cell research community by providing training opportunities to support the entry of new and established investigators into stem cell research.

Although NYSTEM's initial RFA included funds to support training opportunities, few awarded institutions took advantage of training funds. Moreover, none of the funds made available in the second round of funding were specifically targeted for training and support of new or early-stage investigators. Consequently, the Funding Committee devoted considerable time to discussing potential options to support young investigators in the early stages of their careers, and an RFA with this goal was approved at the February 2009 Funding Committee meeting. Additional information on training and education is found in a later section of this report.

Recognizing the strong response to the RFA for shared facilities and a continuing need to provide support for the development of infrastructure early in the NYSTEM program due to the time needed for the design and construction of facilities, the Funding Committee also authorized the issuance of another RFA to provide \$15 million in funding for shared facilities.

Finally, the Funding Committee noted that few of the applications submitted in response to earlier RFAs involved the derivation of new human embryonic stem cell (hESC) lines. Acknowledging that researchers have been discouraged from this work by long-standing federal policies, and the limitations

of the cell lines approved for use in research funded by the National Institutes of Health (NIH), the Funding Committee decided at its February 2009 meeting to issue an RFA to support research on the derivation of new hESC lines.

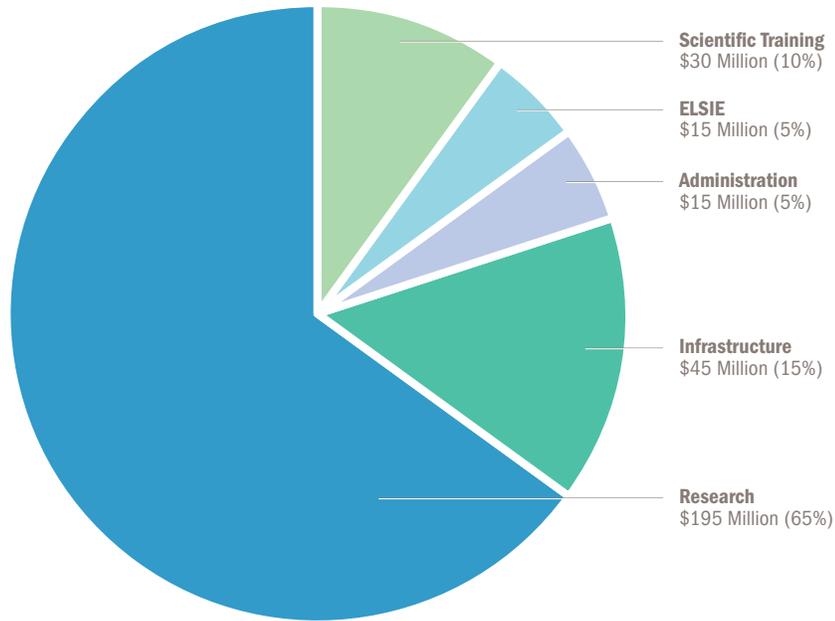
The tables and charts on the following pages show the funding commitments made as of March 31, 2009, in each category identified in the Board's Strategic Plan. The charts also compare those allocations to the expenditures for each area projected in the Strategic Plan. In preparation for publication of this Annual Report, the Funding Committee examined these data and considered potential changes to the Board's Strategic Plan. The Funding Committee concluded that the Strategic Plan has served the Board well during the past year, and should continue in effect over the next year without modification. The Committee also plans to use the attached charts to direct its commitments over the next year.



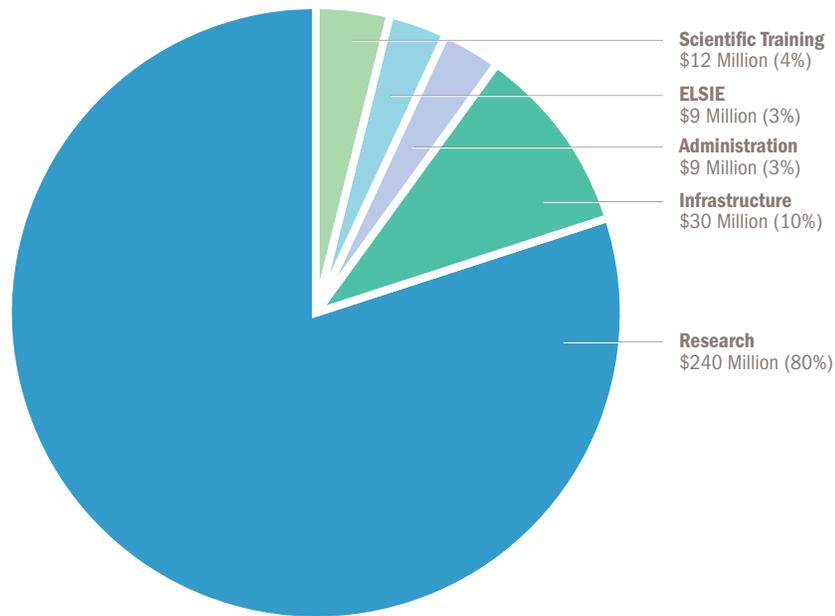
Funding Committee members Michael Stocker, M.D., M.P.H., and Madelyn Wils

*NYSTEM Funding Commitments as of April 2009
Compared to 2008 Strategic Plan Target Ranges*

**NYSTEM Projections for First Five Years
(Minimum Percent Research Target)
\$300 Million**

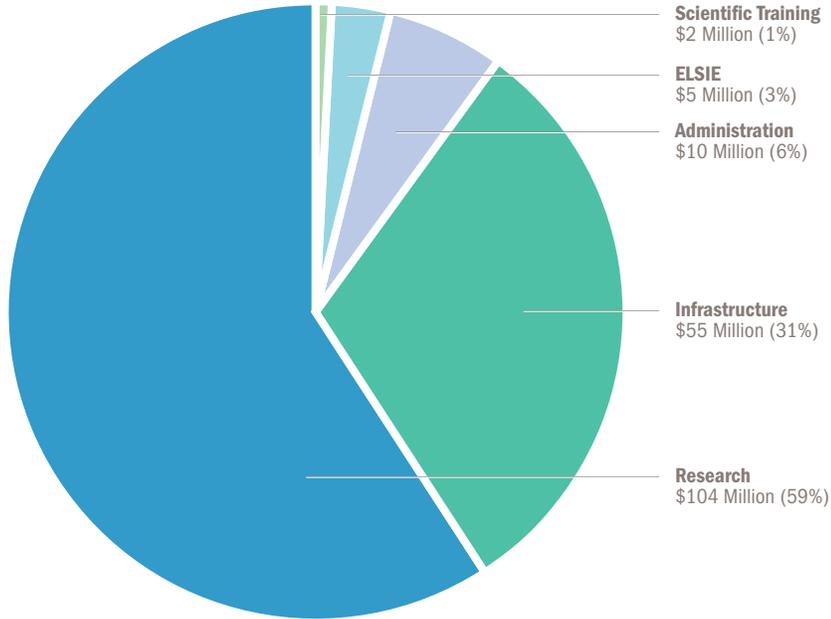


**NYSTEM Projections for First Five Years
(Maximum Percent Research Target)
\$300 Million**

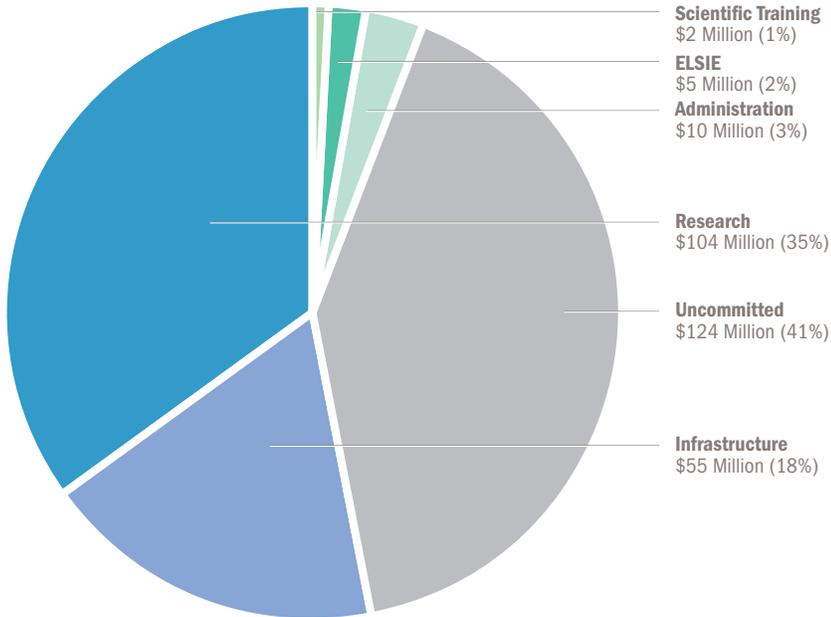


All dollar amounts are rounded to the nearest million.

NYSTEM Funding Commitments to Date
\$176 Million



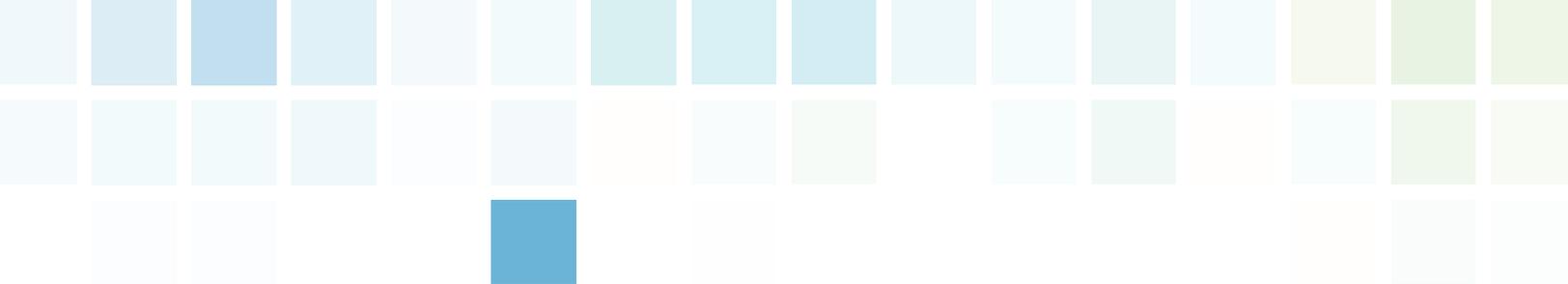
NYSTEM Funding Commitments to Date as a Percentage of First Five Years Projected Funding (Showing Uncommitted Funds)
\$300 Million



All dollar amounts are rounded to the nearest million.

*NYSTEM Funding Commitments
as of April 2009*

	INFRASTRUCTURE Shared Facilities/ Resources and Equipment	RESEARCH Grants	SCIENTIFIC TRAINING Training/ Conferences/ Workshops	ELSIE Ethical, Legal, Societal Issues and Education	ADMINISTRATION Board Functions, Grant Admin, Peer Review	TOTAL
25 Institutional Development Grants	\$ 7,423,547	\$ 5,973,965	\$1,115,038			\$ 14,512,550
18 Planning Grants for Consortia		\$ 2,031,397				\$ 2,031,397
9 Shared Facilities/ Large Equipment Grants	\$32,411,791					\$ 32,411,791
20 Targeted iPS Grants		\$ 16,312,580				\$ 16,312,580
78 Generic Grants		\$ 53,159,750				\$ 53,159,750
Curriculum RFA – Issued 3/18/09				\$2,520,000		\$ 2,520,000
Summer Internships RFA – Issued 4/08/09				\$2,700,000		\$ 2,700,000
Shared Facilities RFA	\$15,000,000					\$ 15,000,000
Targeted hESC RFA		\$ 6,500,000				\$ 6,500,000
Recurring Generic RFA		\$ 15,000,000				\$ 15,000,000
Fellow to Faculty RFA		\$ 4,312,500	\$1,080,000			\$ 5,392,500
Peer Review Contract					\$ 8,600,000	\$ 8,600,000
Board/Grant Admin					\$ 1,600,000	\$ 1,600,000
Total – All Contracts and Approved RFAs/RFPs	\$54,835,338	\$103,290,192	\$2,195,038	\$5,220,000	\$10,200,000	\$175,740,568



Ethics Committee Meetings and Activities

Standards for Research

During the course of the year, the Board's Ethics Committee engaged in robust public discussions about the ethical, legal and social implications of stem cell research. The Committee considered a wide range of issues, including standards for informed consent of donors of biological materials, payments to oocyte donors providing oocytes solely for research purposes and appropriate measures to show respect for the human embryo while conducting research.

The Committee's discussions throughout the year were informed by numerous sources, including guidelines drafted by widely recognized consensus bodies, such as the National Academy of Sciences (NAS), the International Society for Stem Cell Research (ISSCR) and the Institute of Medicine (IOM); laws and regulations of other states and countries; and peer-reviewed literature from respected publications. The Committee also heard presentations from experts in a variety of fields, including:

- Dr. Catherine Racowsky, Director of the Assisted Reproductive Technology Laboratory at Brigham and Women's Hospital in Boston, and Associate Professor of Reproductive Biology at Harvard Medical School, who advised the Committee about health risks involved in ovarian stimulation, including ovarian hyperstimulation syndrome and other potential physical and psychological complications. (June 27, 2008)
- Carl Coleman, J.D., Director of Health Law and Policy at Seton Hall University and former Executive Director of the New York State Task Force on Life and the Law, who presented various models for compensating oocyte donors, as well as information on donor payment policies of other states and countries. (September 4, 2008)
- Dr. Jennifer Schneider, practicing physician board-certified in Internal Medicine, Addiction Medicine and Pain Management, who addressed the short- and long-term health risks to women of donating oocytes, and advocated for the creation of a registry of oocyte donors. (October 16, 2008)
- Dr. Kevin Eggan, Assistant Professor of Molecular and Cellular Biology at Harvard University, faculty member of the Harvard Stem Cell Institute and 2006 recipient of a MacArthur Foundation Genius Award, who spoke about the indispensability of human embryonic stem cell (hESC) research, despite developments in the reprogramming of differentiated cells. Dr. Eggan also addressed the need for fresh oocyte donations for somatic cell nuclear transfer research, which he characterized as the "most promising" area of stem cell research. (October 16, 2008)
- Dr. Alan J. Friedman, a museum consultant and former director of the New York Hall of Science, who supplied extensive information about developing museum and other types of educational exhibits to present stem cell science and its potential to the public. (January 26, 2009)

Respect for the Embryo

The Ethics Committee held discursive and collegial public discussions on the important issues related to using human embryos in stem cell research. The Committee explored various cultural and religious viewpoints about the embryo, but recognized that consensus on the moral status of the embryo would not likely be reached. The Committee agreed, however, that human embryos, as defined in the Strategic Plan, deserve respect. The Committee also expressed support for the Strategic Plan's statement that:

Some individuals believe that human embryos possess a moral status that would preclude their use in any kind of medical research. Others do not accept that premise and, given the extraordinary promise of stem cell therapeutics, believe it could be considered unethical to block or even retard progress in this area of research in any of its forms. Many believe that embryos deserve special protection, and have distinct and special characteristics more than those held by other types of human cells, but that if these issues are carefully considered, and if the intent of the research is to yield benefits for many patients suffering from disease, research involving human embryonic cells is ethically permissible.

The Committee then turned its attention to analyzing ways in which researchers could demonstrate respect for an embryo that may be destroyed in the course of stem cell research. In particular, the Committee agreed that embryos should be used in research only where the research has scientific merit, and the protocol has been reviewed and approved by a peer-review committee. The Committee also recommended that embryos should not be used if they have developed for more than 14 days or after formation of the primitive streak. Finally, members proposed encouraging science that may ultimately lead to use of non-embryonic stem cell sources.



Ethics Committee member Vivian S. Lee, M.D., Ph.D., M.B.A.

Informed Consent

During the year, the Committee revisited its initial interim recommendations regarding informed consent. The Committee began with the premise that securing fully informed consent from donors is among the most significant determinants of ethical research. Therefore, the Committee developed specific recommendations for informed consent standards to be included in all NYSTEM contracts.

In formulating its recommendations, the Committee carefully considered the prior work of the NAS and ISSCR, reflected in these bodies' guidelines for the conduct of human stem cell research. Generally, Committee members continued to recommend compliance with either set of guidelines. However, in certain instances the Committee recommended that NYSTEM contracts require adherence to unique provisions found in one set of guidelines or specific modifications to the guidelines to ensure New York State-funded research adhered to the highest ethical standards.

Recognizing a universal concern that the informed consent process is frequently focused singularly on the informed consent form, the Committee asserted that consent should result from a dynamic process, in which the essential information is conveyed to the donor through an interactive conversation, in language understandable to the donor. Consequently, the Committee recommended compliance with ISSCR provisions that emphasize the importance of providing potential donors with both the opportunity to ask questions about the research and the time to fully consider the issue of donating.

With respect to donors of oocytes, the Committee emphasized that such donors should be treated like research subjects. Thus, the Committee stressed that researchers must take special care in apprising oocyte donors of both short- and long-term risks associated with donating. In order to ensure that the risks and benefits of donating are conveyed in an unbiased manner, the Committee cautioned that individuals responsible for obtaining consent should have no vested interest in the research and must disclose whether they have any financial interest in either the research or in obtaining the consent. The Committee also recommended that, in addition to communicating the risks and benefits of donating and the purpose of the research project, the responsible individuals must inform the donor that he or she will not receive any financial benefit from the results of the research, even if such results have commercial potential.

Acknowledging that it would be difficult for researchers in other states to be aware of and adhere to the specific standards recommended by the Ethics Committee, the Committee agreed that funded researchers should be able to use hESC lines created out-of-state, or not derived using NYSTEM funds, provided these lines were created in compliance with NAS or ISSCR guidelines. The Committee also recommended that researchers should be able to use, in NYSTEM-funded research, the stem cell lines approved by the NIH in 2001 for use in federally funded research.

The recommendations of the Ethics Committee regarding informed consent were transmitted to and unanimously adopted by the Funding Committee in April 2009.

Finally, the Committee agreed that it would be beneficial to develop model informed consent forms for NYSTEM-funded researchers in acquiring informed consent. The Committee has begun to design the forms based on those offered by ISSCR.

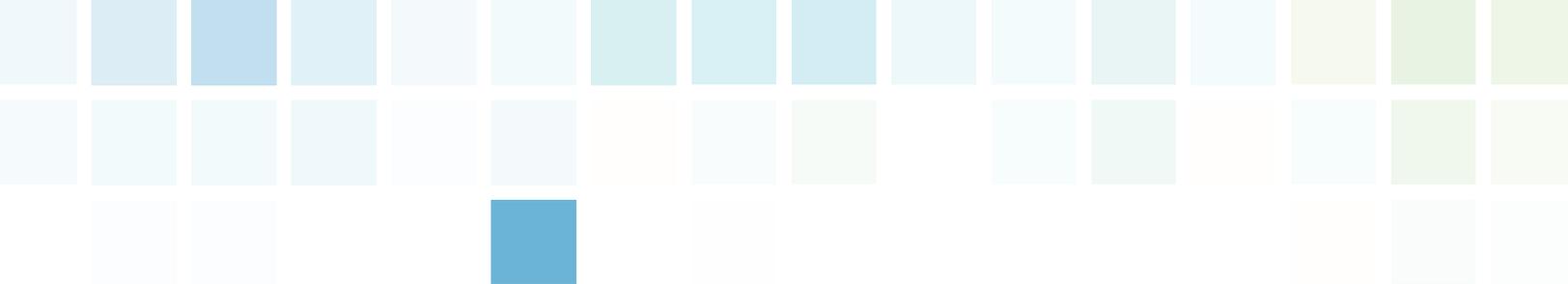
Donor Payment

The issue of providing payments to women for donation of oocytes directly and solely for research is complex, entailing legal, ethical and practical aspects. The Committee reviewed the medical literature and heard presentations addressing the scientific need for fresh donations of oocytes, state and international policies on donor payment and payment policies in the clinical context (such as *in vitro* fertilization). The Committee identified and analyzed a variety of ethical issues related to donor payment, including: the potential for undue inducement to donate; equitable compensation for women donating solely for research purposes who accept the same risks and burdens of undergoing hormonal and ovarian stimulation as women donating for *in vitro* fertilization (IVF) purposes; and parity consistent with other areas of research participation. The Committee also deliberated on practical implications, such as the impact on the number of donations for research garnered by other states that do not allow payment beyond reimbursement of direct expenses, and the implications for interstate and international collaborations should New York State adopt a unique policy for donor payment.

The Ethics Committee preliminarily endorsed the concept that reimbursements to donors for direct expenses, as defined by NAS and ISSCR, was ethically acceptable and preferable to offering no reimbursements whatsoever. The Committee expects to prepare recommendations concerning donor payments and NYSTEM-funded research in the near future.



*Commissioner Richard F. Daines, M.D., Chairman of the Board,
and Judy Doesschate, J.D., Executive Secretary of the Board*

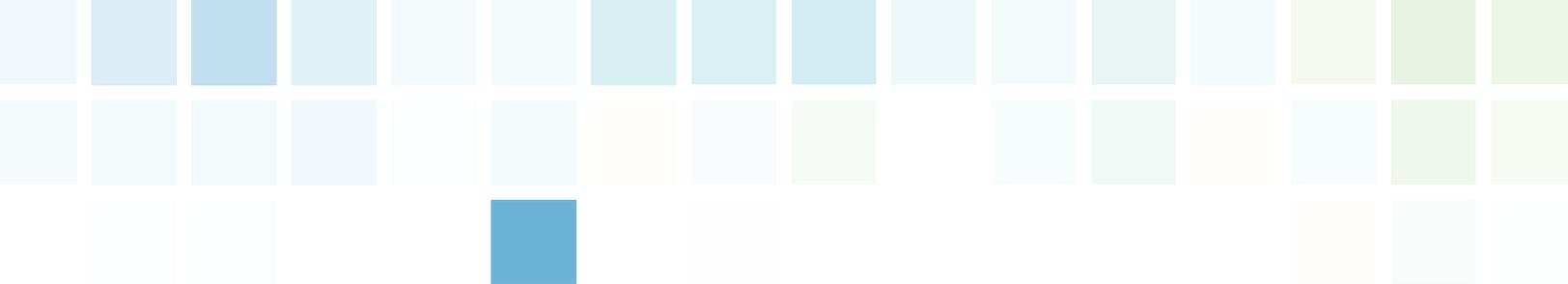


Administrative Expenses

As stated in its Strategic Plan, “the Board is committed to ensuring public access to information regarding its activities and programs and to the outcomes of NYSTEM-funded research, training and development.” That plan targets three to five percent of available funding to support administrative activities, including, but not limited to, the administration of an independent scientific merit peer-review process; program development and evaluation; contract monitoring; website development; outreach; and coordination of scientific meetings. Administrative expenditures during the 2008-2009 State Fiscal Year totaled approximately \$1.5 million and constituted three percent of the \$50 million appropriated. It is expected that out-year administrative expenditures will more closely approximate five percent, based on full program implementation.

Specific administrative expenditures include:

- Personal services costs – \$546,000: *Salaries for program staff*
- Supplies – \$17,000: *General office supplies and computer software for program and Board operations*
- Equipment – \$10,500: *Computers, printers and other small office equipment*
- Board meeting expenses – \$63,500: *Travel reimbursement, speaker honoraria, and webcasting costs, for 11 Board and Committee meetings, primarily convened in the Department of Health offices*
- Peer review services – \$802,000: *Coordination of 14 independent peer-review panels to evaluate 413 applications received in response to four RFAs*
- Contractual services – \$32,000: *Office support and consultant services to assist in the development of a strategic plan*



Empire State Stem Cell Board Grants in Progress

Building the Stem Cell Research Community

Scientific progress depends on both the inspiration and hard work of individuals and an active community of scientists and institutions that provides essential resources and serves as a sounding board. Science thrives best when new findings and ideas are evaluated through different perspectives, so that they can be challenged, tested and refined. Because stem cell science is a rapidly expanding new field, the Board recognized that community building and infrastructure development were crucial first steps to accelerating the pace of stem cell research and development in New York State.

I. INSTITUTIONAL DEVELOPMENT GRANTS

To jump-start community building and infrastructure development, one of the Board's first acts was to award Institutional Development Grants to 25 institutions. These awards provided research project support in the form of supplements to current funding or bridge funding for investigators between grants. Such supplemental funding enabled investigators to extend their research in a variety of ways, including studies of human embryonic stem cells. The awards also funded shared facilities and equipment, expanding access to important new technologies. Through these awards, the Board supported large equipment purchases and the establishment and operation of core facilities. Finally, a significant impediment to scientists entering the stem cell research field is the time and effort required to develop necessary skills. Therefore, the awards also supplied some support for training of researchers in experimental techniques required for the maintenance and use of human and mouse embryonic stem cells.

The support provided by the Institutional Development awards in the first year has already contributed to significant scientific progress in the form of important publications and even a patent application (see Appendix II for details). However, another measure of the program's success, one perhaps even more pertinent to NYSTEM's long-term goals, was the enhancement of interactions among stem cell researchers. For example, these awards inspired seminars and meetings within institutions to bring together stem cell scientists seeking opportunities for collaboration so that they could share their latest findings. The Institutional Development awards will culminate in an intensive scientific symposium, hosting representatives from each of the funded institutions to share their results and accomplishments and serve as a venue to establish and strengthen inter-institutional links.

“Catalysis” is an over-worked word outside of chemistry, but the NYSTEM grants for infrastructure awarded on January 7, 2008, not only will enable Columbia University to build core facilities for our scientists pursuing stem cell research, but catalyze a series of meetings and interactions that will make a true and productive community of our multitude of stem cell researchers.

–David Hirsch, Executive Vice President for Research, Columbia University

II. PLANNING GRANTS FOR EMERGING OPPORTUNITIES AND CONSORTIA DEVELOPMENT

In another effort to foster multi-institutional collaborations and establish a comprehensive, stable infrastructure for the stem cell research community, the Board issued 18 awards for consortia planning, to support the design of shared facilities and development of stem cell training and education programs. The diverse planning groups brought together with these awards worked to lay the foundations for future consortia intended to target the big questions in stem cell science and translation of research findings. These questions require the cooperation of scientists with diverse but complementary expertise, and lie beyond the scope of individual research laboratories.

III. SHARED FACILITIES/RESOURCES AND EQUIPMENT/ INSTRUMENTATION FOR STEM CELL RESEARCH

To bolster the stem cell community further and ensure that investigators have access to state-of-the-art technology beyond the capacity of individual laboratories or institutions, the Board allocated funds for core facilities through an additional mechanism. The Shared Facilities and Equipment awards supported the purchase of instrumentation and expansion and operation of facilities and specialized resources, all for multiple users. These awards required that, for each proposal, at least three primary users be identified and at least 50 percent of their use be stem cell-related. This mechanism funded specialized laboratories to: isolate, derive and characterize stem cell lines, including disease-specific cell lines; develop animal models; implement high-throughput analyses of cells; and provide routine material support for stem cell experiments. Nine institutions received these awards, and the projects are detailed in Appendix II. The resulting facilities and instrumentation are critical for meeting the needs of researchers, advancing stem cell research and further nurturing the stem cell community in New York State.

Advancing Stem Cell Science in New York State

In its Strategic Plan, the Board committed the majority of its resources to advancing the science of stem cell biology in New York State by supporting innovative basic, translational and clinical research that builds on the potential of stem cells to detect, treat and cure human diseases. Consistent with that goal, the Board approved for funding a total of 98 applications submitted in response to two RFAs. One RFA solicited proposals for investigations of induced pluripotent stem (iPS) cells and other derivation approaches, and the second sought investigator-initiated projects on any important topic in stem cell research. Both RFAs provided for three years of research funding through a standard mechanism, the “Investigator-Initiated Research Project” (IIRP); and 60 of the 98 recommended awards were for IIRPs. In addition, both RFAs apply a second mechanism, the “Innovative, Developmental or Exploratory Activities Award” (IDEA) to offer two years of support for preliminary testing of novel or high-risk hypotheses. With this mechanism, the Board sought to fund research projects with a high likelihood that results obtained would yield the opportunity to apply for future funding and encourage talented investigators from related fields to enter stem cell science. The types of research programs funded by these two RFAs are summarized below, and all are listed in Appendix III under Awards Approved.

I. TARGETED INVESTIGATION OF INDUCED PLURIPOTENT STEM (IPS) CELLS AND OTHER DERIVATION APPROACHES

Because of the remarkable promise of iPS cells (see the Recent Highlights section for more details), the Board wanted to stimulate and support investigations aimed at developing improved methods for deriving pluripotent stem cell lines, understanding the mechanisms of “reprogramming” mature cells, and comparing iPS cell lines to embryonic and other pluripotent cell lines for use in disease models and potential therapeutic applications. The 20 applications funded in response to this RFA are supporting investigations on the nature of pluripotency and the potential applications of iPS and other pluripotent cell lines to understanding and treating ailments, such as the blood diseases thalassemia and porphyria, and neurological diseases, including Parkinson’s, amyotrophic lateral sclerosis (ALS) and multiple sclerosis.

II. INVESTIGATOR-INITIATED RESEARCH PROJECTS (IIRP) AND INNOVATIVE, DEVELOPMENTAL OR EXPLORATION ACTIVITIES (IDEA) IN STEM CELL RESEARCH

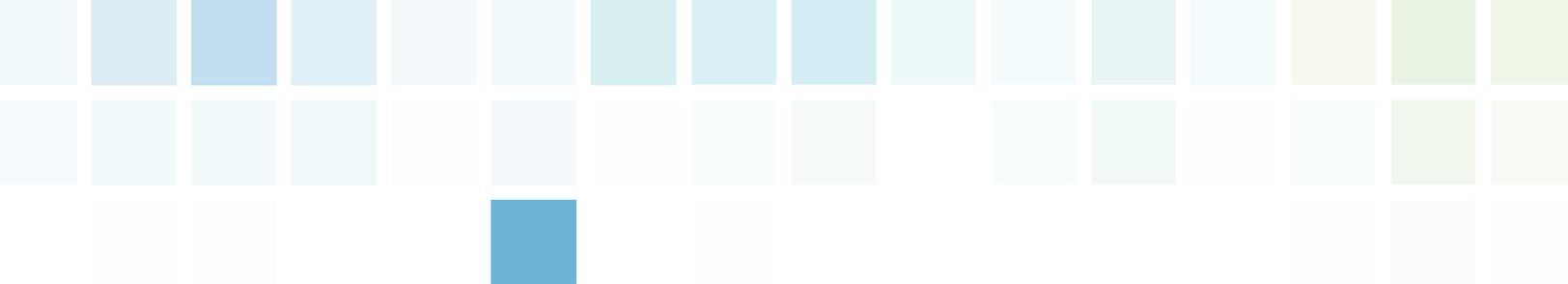
The Board recognized that despite great progress in recent years, stem cell science is still at an early stage in the medical application of stem cells to human disease problems. Therefore, the Board sought to stimulate and support scientific investigations on aspects of stem cell biology that will lead to a better understanding of the unique properties of stem cells and allow their utilization in treating disease through a broad-based approach, by encouraging innovative applications from any area with promise to accelerate development of new therapies. Based on the results of peer review, the Board recommended funding for 78 of the 329 applications received in response to this RFA.

The projects undertaken use an array of approaches to target many important disease problems and conditions, including those of heart, cancer, diabetes, nerve, kidney and liver; and to tackle the important basic questions of stem cell science. Significantly, a number of the funded projects were translational in nature, intended to move findings toward clinical application.



“The NYSTEM award supported cornerstone technologies critical for the advancement of stem cell research that allow scientists to better understand how stem cells live and function in the body – and whether such information can be translated into new approaches to treat human diseases, such as diabetes, cancer, blindness and Alzheimer’s.”

– Dr. Gladys Teitelman
SUNY – Downstate Medical Center
(Shown with graduate student Jennifer Winkler)



Training and Education

As previously noted, the mission of the ESSCB is to:

...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.

With this in mind, the Funding Committee discussed potential options for supporting young investigators in the early stages of their careers. At the Funding Committee's February 2009 meeting, an RFA was approved to support highly promising stem cell researchers in their transition from fellows to faculty members. It is hoped that this funding will encourage promising young researchers to move to, or stay in, New York State and help invigorate New York's stem cell research community. Another RFA to create summer opportunities for undergraduates to conduct research in the field of stem cell biology was also previously approved by the Funding Committee and was released in April 2009.

One of the goals set forth in the ESSCB's Strategic Plan is to

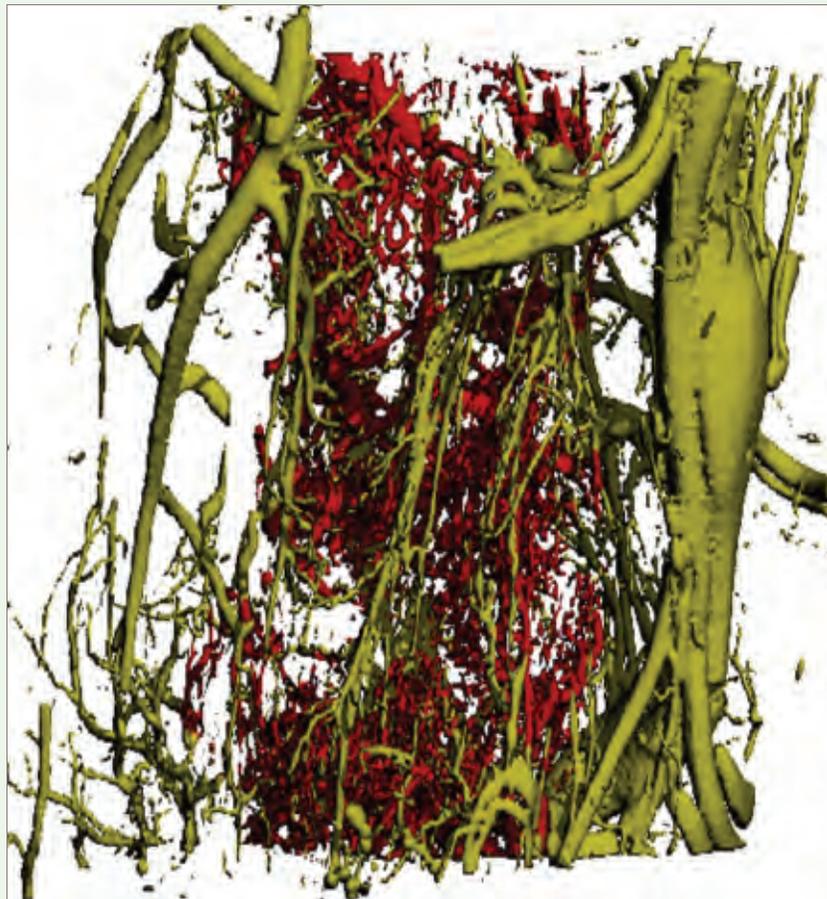
...ensure that stem cell research in New York State adheres to the highest standards of medical ethics and that the ethical, legal, social and psychological implications of advances in stem cell research are appropriately addressed by engaging diverse communities in research, scholarship and education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

In furtherance of this objective, the Ethics Committee proposed an RFA to support the development of an undergraduate-level course, or modules within a course, on stem cell science and its ethical, legal and social implications. This RFA was approved by the Funding Committee and was issued in March 2009.

The Board has also discussed other education and outreach activities, including museum programs, secondary education initiatives, media seminars and website development options. In June 2008, Dr. Samuel Silverstein of Columbia University presented the Board with information regarding the effectiveness of his work in providing hands-on laboratory opportunities to high school teachers; and in January 2009, Dr. Alan Friedman, former Director of the New York Hall of Science, outlined options for a stem cell museum exhibit for the Ethics Committee.

NYSTEM staff have also undertaken educational activities to further the Board's mission through the use of the NYSTEM web site and public outreach. The NYSTEM web site was updated in October 2008 to include a directory of stem cell scientists in New York State. The directory contains profiles of 184 scientists, including those listed in *Stem Cell Research in New York State: A Snapshot*, as well as other investigators identified since that report's initial publication. More scientists will be added to the web site as they are identified and provide information. The database is searchable by full text, by key word(s)

and/or by institution, or may be browsed in its entirety or by alphabetic subset. In addition, “Frequently Asked Questions” about the NYSTEM program and stem cell science are new on the site as of spring 2009, along with an updated glossary. Also, NYSTEM staff are working with a regional technology-focused high school to develop a model stem cell science program for students; once completed and tested, the model will be posted on the NYSTEM web site for use by others throughout New York State and elsewhere. NYSTEM staff also attended meetings of the Interstate Alliance for Stem Cell Research at the National Academy of Sciences in Washington, D.C. in April 2008 and in Baltimore, Maryland in October 2008, and the International Stem Cell Science meeting in Philadelphia, Pennsylvania in June 2008.

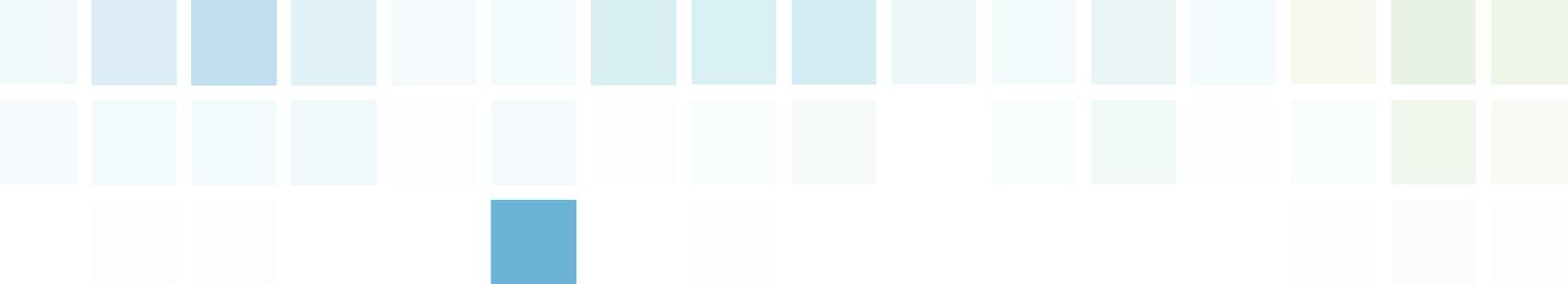


VASCULAR NETWORK

A micro-CT based method is applied to quantitatively evaluate vascular network during bone graft healing. The vessel network in new bone callus is shown as red whereas the vessel network in soft tissue as yellow.

Image Source: Dr. Xinping Zhang, University of Rochester

Project Title: Gli2 Activated MSCs for Bone Regeneration and Reconstruction



Recent Highlights in the Field of Stem Cell Research

Introduction

Stem cell research is moving at a remarkable pace. This past year, several research milestones advanced the understanding of how science might reverse degenerative diseases or replace damaged human tissue. Stem cell biologists have formed strong alliances with engineers, mathematicians and clinicians to break down the walls between these diverse disciplines and overcome the challenges of translating bench science into effective medical treatments. Recent advances in the reprogramming of adult cells to a stem cell-like state are exciting researchers. The induced pluripotent stem (iPS) cell approach allows scientists to generate stem cell lines from patients suffering from hard-to-study and incurable diseases, such as Parkinson's disease, amyotrophic lateral sclerosis (ALS) and diabetes. Scientists now can monitor disease progression at the cellular level in a laboratory dish and identify new treatments, diagnostics and early prevention methods.

In the area of cell-based therapy, investigators are applying a tissue engineering approach. Research that combines stem cells and biomaterials with cytokines, a category of signaling molecules, is offering a new paradigm to regenerate damaged tissue or organs. In December 2008, physicians in Spain performed a tracheal transplant, using the patient's own adult stem cells harvested from her bone marrow, and gave the patient a newly reconstructed airway for breathing. A significant milestone came on January 23, 2009, when the U.S. Food and Drug Administration (FDA) granted clearance for the world's first human clinical trial of embryonic stem (ES) cell-based therapy to treat acute spinal cord injury. Emerging approaches from fundamental biology to biomedical engineering are advancing stem cell research discoveries toward practical applications to improve human health. With the Empire State Stem Cell Trust Fund, New York State is now being recognized as a growing force in this effort. The following section provides an overview of recent research highlights in stem cell and regenerative medicine fields.

FEBRUARY 2008: BEATING HEART CREATED IN LABORATORY – MINNESOTA

Scientists at the University of Minnesota have, for the first time, produced a bioartificial beating heart. Researchers in Dr. Doris Taylor's laboratory "decellularized" rat and pig hearts by perfusion with detergents, removing all the cells while preserving the underlying three-dimensional scaffold of extracellular matrix that constitutes the organ's physical framework. The decellularized heart was then injected with multiple cell types (cardiomyocytes, fibrocytes, endothelial cells, smooth muscle cells, etc.). After incubation in a "bioreactor," macroscopic contraction and pump function were observed. About 3,000 individuals in the U.S. are awaiting a heart donor and 22 million individuals worldwide are living with heart failure. This study is a seminal

step toward the goal of supplying transplant patients with “bioartificial” hearts, or replacing part of a diseased heart with a working component grown in the laboratory.

“Perfusion-decellularized matrix: Using nature’s platform to engineer a bioartificial heart.” Ott HC, Matthiesen TS, Goh SK, Black LD, Kren SM, Netoff TI, Taylor DA. *Nature Medicine*. 2008; 14(2):213-21.

APRIL 2008: A STEP CLOSER TO TREATING PARKINSON’S DISEASE – NEW YORK AND JAPAN

Drs. Viviane Tabar and Lorenz Studer from the Sloan-Kettering Institute, together with researchers from Weill Cornell Medical College in New York City and The Riken Institute in Japan, have, for the first time, established the feasibility of using cells from a mouse to treat Parkinson’s disease in the same mouse. Therapeutic cloning, also known as somatic cell nuclear transfer (SCNT), is a technique that replaces the nucleus of an egg with the nucleus from a somatic cell, in this case skin cells from mice tails. The embryonic stem (ES) cells generated via SCNT are genetically matched with the donor somatic cells. The ES cell lines from Parkinsonian mice underwent differentiation into dopaminergic neurons and were transplanted back into matched host mice. These mice showed significant neurological improvement without adverse immunological response. Even though much more work will be needed to move this breakthrough from mice to humans, it demonstrated the potential for therapeutic cloning in the treatment of Parkinson’s disease.

“Therapeutic cloning in individual Parkinsonian mice.” Tabar V, Tomishima M, Panagiotakos G, Wakayama S, Menon J, Chan B, Mizutani E, Al-Shamy G, Ohta H, Wakayama T, Studer L. *Nature Medicine*. 2008; 14(4):379-81.

JUNE 2008: HUMAN STEM CELLS CAN TREAT FATAL MYELIN DEFICIENCY – NEW YORK

For the first time, human glial progenitor cells were shown to be an effective treatment to cure fatal myelin deficiency in “shiverer” mice. Neuroscientists, led by Dr. Steven Goldman at the University of Rochester Medical Center, have used human cells to help myelin-deficient mice regrow myelin around their nerve fibers and thereby prevent an otherwise inevitable early death and poor quality of life. The myelin sheath that surrounds long fiber-like sections



“The NYSTEM grant has significantly accelerated the pace of research. These funds will have a major impact on the stem cell community and diseases, including Parkinson’s, radiation injury and blood disorders.”

– Dr. Lorenz Studer
Memorial Sloan-Kettering Cancer Center

(axons) of nerve cells in the brain and spinal cord acts like insulation around electrical wires – it stops leakage of electrical impulses that control vital body functions, including movement. Insufficient or defective myelin causes a number of diseases, including a rare and fatal congenital disorder, called pediatric leukodystrophy, that affects thousands of children. The researchers at the University of Rochester Medical Center injected the glial progenitor cells into 26 newborn mice that had been genetically programmed with the condition. Most of the mice died at the early age typical for the disease, but six lived much longer, and four appeared to be completely cured, a feat never before achieved with shiverer mice. This research finding is a promising first step that perhaps one day will lead to treatments for similar neurological conditions in humans, especially children.

“Neonatal chimerization with human glial progenitor cells can both remyelinate and rescue the otherwise lethally hypomyelinated shiverer mouse.” Windrem MS, Schanz SJ, Guo M, Tian GF, Washco V, Stanwood N, Rasband M, Roy NS, Nedergaard M, Havton LA, Wang S, Goldman SA. *Cell Stem Cell*. 2008; 2(6):553-65.

AUGUST 2008: FIRST MOTOR NEURONS CREATED FROM ALS PATIENTS – MASSACHUSETTS AND NEW YORK

A collaboration between Dr. Kevin Eggan at the Harvard Stem Cell Institute, Massachusetts, and Drs. Hynek Wichterle and Christopher Henderson at Columbia University, New York City, has demonstrated the successful conversion of skin cells from an 82-year-old woman with amyotrophic lateral sclerosis (ALS) into iPS cells by genetic reprogramming. These iPS cells, genetically matched to the patient, were successfully differentiated into motor neurons, the cell type destroyed in ALS. This breakthrough makes it possible to study the progression of a patient’s specific disease in the laboratory, and to develop drug screening or other laboratory assays for discovery of safe and effective new treatments for ALS patients.

“Induced pluripotent stem cells generated from patients with ALS can be differentiated into motor neurons.” Dimos JT, Rodolfa KT, Niakan KK, Weisenthal LM, Mitumoto H, Chung W, Croft GF, Saphier G, Leibel R, Goland R, Wichterle H, Henderson CE, Eggan K. *Science*. 2008; 321(5893):1218-21.

SEPTEMBER 2008: SCIENTISTS CREATE DISEASE-SPECIFIC STEM CELL LINES – MASSACHUSETTS AND WASHINGTON

Dr. George Daley from Harvard Medical School, together with scientists from Massachusetts General Hospital and the University of Washington, have found a way to produce 20 immortal cell lines from diseased patients by converting their somatic cells into pluripotent stem cells with the same genetic errors. Such disease-specific stem cell lines will enable scientists to investigate multiple different genetic disorders, such as Parkinson’s disease, Huntington disease, muscular dystrophy, Down syndrome and type 1 diabetes, in the laboratory rather than in the patient, a major step toward improved therapies. The new iPS lines developed from the cells of patients ranging in age from one month to 57 years will be deposited in a new cell bank being established at Massachusetts General Hospital.

“Disease-specific induced pluripotent stem cells.” Park IH, Arora N, Huo H, Maherali N, Ahfeldt T, Shimamura A, Lensch MW, Cowan C, Hochedlinger K, Daley GQ. *Cell*. 2008; 134(5):877-86.

OCTOBER 2008: TRANSFORMATION OF LIVING PANCREATIC CELLS INTO INSULIN-PRODUCING β -CELLS - MASSACHUSETTS

Cells of adult organisms arise from sequential differentiation steps that are generally thought to be irreversible. This research serves as an example of direct cell reprogramming to convert adult cells into other cell types for tissue repair and regeneration. A research team led by Dr. Douglas Melton from the Harvard Stem Cell Institute has discovered a new strategy to re-express a specific combination of key developmental regulators *in vivo* that transform mature exocrine cells in adult mice into cells that closely resemble β -cells, the endocrine cells that produce insulin. Aside from their structural similarity to β -cells, the induced cells express the same essential genes and resume the ability to secrete insulin lost in diabetes. This study moves the cell reprogramming strategy one step closer to a therapeutic application for a widespread disease.

“*In vivo reprogramming of adult pancreatic exocrine cells to beta-cells.*” Zhou Q, Brown J, Kanarek A, Rajagopal J, Melton DA. *Nature*. 2008; 455(7213):627-32.

NOVEMBER 2008: FINDING SAFER WAYS TO GENERATE INDUCED PLURIPOTENT STEM CELLS - WISCONSIN, MASSACHUSETTS, JAPAN, CANADA AND UNITED KINGDOM

In 2006, Dr. Shinya Yamanaka at Kyoto University in Japan was the first to discover that, by inserting four genes into mouse skin cells, they would revert to an early stage very similar to an ES cell, with the potential to become nearly any type of cell in the body. These new ES-like cells were named iPS cells. A year later, Dr. Yamanaka and, independently, Dr. James Thomson of the University of Wisconsin at Madison, used the same method to produce the first human iPS cells. Human iPS cells have many potential applications, such as production of disease-specific cells that can be used to study how genes trigger diseases like cancer and neurodegeneration, and to discover drugs to prevent genetic diseases or regenerate damaged tissue.

A major limitation of the iPS technology is its use of potentially harmful viruses that integrate their DNA into the host cell's chromosomes and can therefore trigger cancer. Dr. Konrad Hochedlinger and Harvard Stem Cell Institute colleagues at Massachusetts General Hospital and Joslin Diabetes Center found that adenoviruses can deliver the four genes (*Oct4*, *Sox2*, *c-Myc* and *Klf4*) needed to convert an adult cell to an iPS cell. According to their report in the journal *Science*, the iPS lines have no residual trace of the adenovirus since these viruses do not integrate into and disrupt the DNA of the host.

In the same issue of *Science*, the Japanese team led by Dr. Shinya Yamanaka also reported an alternative method for generating iPS cells, by repetitive transfection of two expression plasmids (non-viral carrier DNA) containing the essential genes to produce iPS cells. Although low efficiency is a drawback of this approach, the production of virus-free iPS cells addresses a critical safety concern for the potential use of iPS cells in regenerative medicine.

The latest development in iPS technology comes from Canada and the United Kingdom, where researchers have developed another way to create iPS cells efficiently without using viruses. The researchers introduced the four genes that reprogram the cells and then removed the genes by using a specific enzyme. Researchers worldwide are now exploring the use of chemicals instead of viruses or plasmids to introduce the genes needed to convert differentiated cells into iPS cells. This novel iPS technology has stimulated scientists to re-think the traditional mechanism of the “biological clock” and may lead to possible cures for a range of degenerative diseases.

“Induced pluripotent stem cells generated without viral integration.” Stadtfeld M, Nagaya M, Utikal J, Weir G, Hochedlinger K. *Science*. 2008; 322(5903):945-9.

“Generation of mouse-induced pluripotent stem cells without viral vectors.” Okita K, Nakagawa M, Hyenjong H, Ichisaka T, Yamanaka S. *Science*. 2008; 322(5903):949-53.

“PiggyBac transposition reprograms fibroblasts to induced pluripotent stem cells.” Woltjen K, Michael I, Mohseni P, Desai R, Mileikovsky M, Hämmäläinen R, Cowling R, Wang W, Liu P, Gertsenstein M, Kaji K, Sung HK, Nagy A. *Nature*. 2009; 458(7239):766-70.

NOVEMBER 2008: AIRWAY RECONSTRUCTION: TISSUE-ENGINEERED STEM CELL TRACHEA – SPAIN, UNITED KINGDOM AND ITALY

A 30-year-old woman in Spain whose trachea was damaged from tuberculosis is the first person to receive a new tissue-engineered airway segment grown from her own stem cells. A significant potential benefit of using autologous stem cells is that the patient may be able to avoid having to take immune suppressant drugs for the remainder of her life. Specialists from four European institutions came together to carry out the operation: the Hospital Clínic of Barcelona at the University of Barcelona, Spain; the University of Bristol in the United Kingdom; the Politecnico di Milano in Italy; and the University of Padua, also in Italy. A segment of trachea from a donor cadaver was decellularized and seeded with the patient’s own epithelial cells and mesenchymal stem cell-derived chondrocytes. The graft was maintained in a bioreactor prior to transplantation. This innovative procedure shows it is possible to create a cell-based, tissue-engineered airway that not only works properly, but is also free of the risk of rejection, opening the way for treating other serious diseases by using biomaterials combined with a patient’s own stem cells.

“Clinical transplantation of a tissue-engineered airway.” Macchiarini P, Jungebluth P, Go T, Asnaghi MA, Rees LE, Cogan TA, Dodson A, Martorell J, Bellini S, Parnigotto PP, Dickinson SC, Hollander AP, Mantero S, Conconi MT, Birchall MA. *Lancet*. 2008; 372(9655):2023-30.

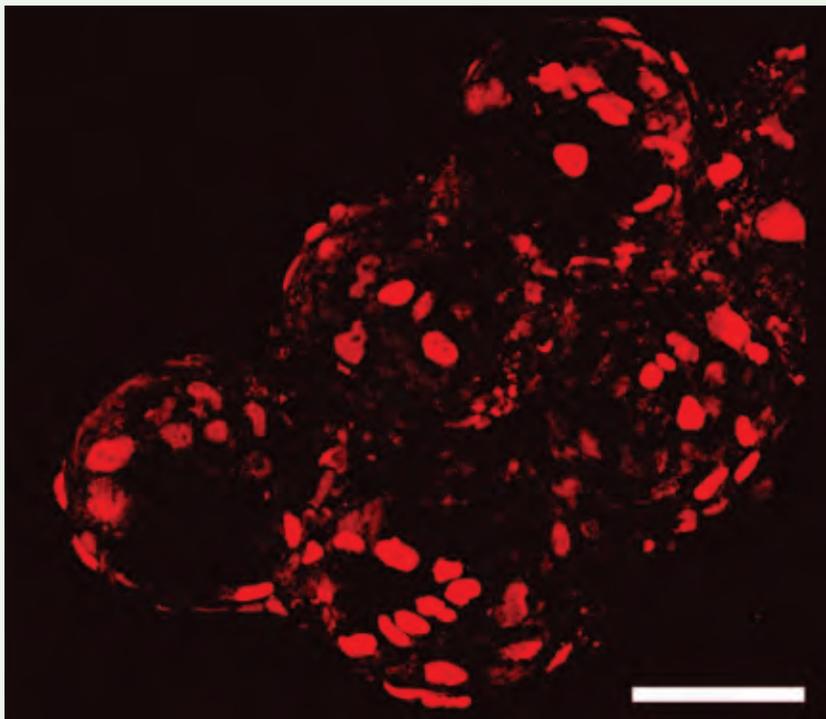
DECEMBER 2008: PATIENT-DERIVED INDUCED PLURIPOTENT STEM CELLS RETAIN DISEASE TRAITS – WISCONSIN

Spinal muscular atrophy (SMA) is one of the most common inherited forms of neurological disease leading to infant mortality. Patients experience selective loss of lower motor neurons, resulting in muscle weakness, paralysis and often death. Scientists led by Dr. James Thomson and Dr. Clive Svendsen from the University of Wisconsin at Madison have generated iPS stem cells from skin fibroblasts from a child with SMA. These cells carried the disease genotype and, upon differentiation into motor neurons, showed selective deficits compared to cells derived from the child’s unaffected mother. This is the first study to show that human iPS cells can be used to model a specific pathology seen in a genetically inherited disease, and allow scientists to observe the course of a disease unfold in cells in a laboratory dish.

“Induced pluripotent stem cells from a spinal muscular atrophy patient.” Ebert AD, Yu J, Rose FF Jr, Mattis VB, Lorson CL, Thomson JA, Svendsen CN. *Nature*. 2009; 457(7227):277-80.

JANUARY 2009: FDA APPROVES FIRST CLINICAL TRIAL OF A HUMAN EMBRYONIC STEM CELL TREATMENT - CALIFORNIA

A significant milestone was attained for stem cell-based therapies this year when the U.S. Food and Drug Administration (FDA) approved a clinical trial involving human embryonic stem cell hESC derivatives, in this case, to treat patients paralyzed by spinal cord injury. The FDA cleared the way for Geron Corporation of Menlo Park, California, to give eight to 10 patients with spinal cord injury a single injection of neural cells produced from ES cells. The major concern surrounding ES cell-based therapy is the risk of growing tumors after surgery. The Geron cells were derived from one of the stem cell lines approved for federal funding under the President Bush Administration policy. This phase I trial is designed to examine the safety of the treatment using GRNOPC1 cells. Geron's press release can be found at: <http://www.geron.com/media/pressview.aspx?id=1148>

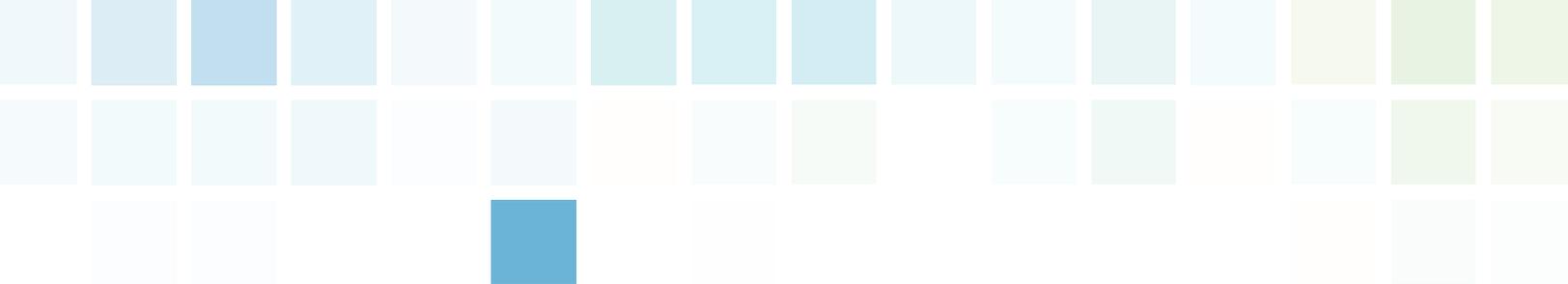


MICROCARRIER BEADS

Differentiation of human embryonic stem (hES) cells into definitive endoderm lineage by using microcarrier beads for scale up expansion. (Bar: 100 micrometers)

Image Source: Dr. Emmanouhl S. Tzanakakis, State University of New York, Buffalo

Project Title: Scalable Expansion and Directed Differentiation of Human Embryonic Stem Cells to Pancreatic Progeny



Recent Highlights in New York State Stem Cell Research

Overviews of Disease Areas

In pursuit of improved human health and quality of life, stem cell research offers great potential to fill the gaps in understanding disease mechanisms and facilitating discovery of new therapeutic treatments. New York State is well-positioned to be a leader in the field of stem cell research because of its wealth of world-class research institutions and teaching hospitals. The following scientific overview focuses on the representative disease areas New York researchers are now tackling with stem cell-based strategies. The location of institutions performing stem cell research in New York State appears in **Appendix III**. The institutions listed on the map (p. 74) have all been funded by NYSTEM.

CENTRAL NERVOUS SYSTEM

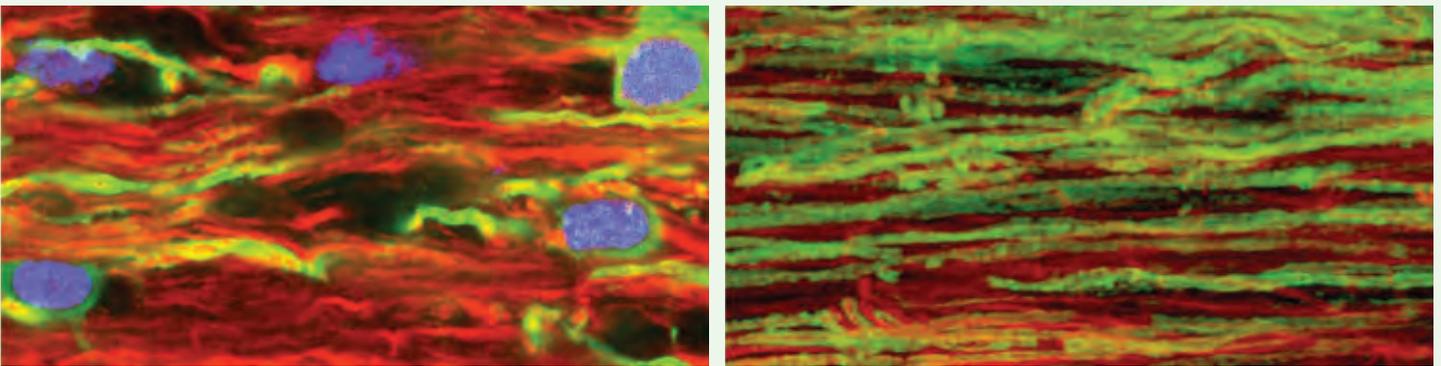
The human central nervous system is composed of many different subtypes of neurons and glial cells that are critical to maintaining normal brain function. Through its functional circuitries, the nervous system controls body movement, memory and breathing. Most neurodegenerative disorders involve multiple genes, multiple cell types and possible environmental factors. It is impossible in most cases to model a neuronal disease without using the affected diseased cells. However, creating disease-specific neurons from induced pluripotent stem (iPS) cells offers a template to perform drug screening, a potentially powerful approach to elucidate disease mechanisms and identify new treatments. The establishment of effective and accurate differentiation methodology can guide human embryonic stem cells (hESC) or neural stem cells toward a specific neural lineage, and contribute to therapies for neurodegenerative diseases and injuries. New York scientists are wielding much creativity in navigating the complex neurological maze.

Motor Neuron Disorder Spinal motor neurons are one of the best-characterized cell types in the human nervous system and one of few cell types successfully generated from hESC in culture. Recent advances in direct reprogramming of human skin cells into an ES cell-like state enable scientists to derive patient-specific iPS cells that can be used to investigate currently untreatable human diseases. One important goal of stem cell research is to model human disease and develop new treatments. Towards that end, **Dr. Hynek Wichterle** and **Dr. Christopher Henderson** at **Columbia University** have derived iPS cells from patients with amyotrophic lateral sclerosis (ALS), a devastating motor neuron disease. The research is underway to determine whether defects observed in mouse models of this disease can be reproduced in human iPS cells. At **Columbia University Medical Center**, work in **Dr. Tomas Jessell's** laboratory explores how neurons acquire identities that direct the assembly of neural circuits and how the organization of these circuits controls

specific behaviors. An important question still to be addressed is whether ES cells can be converted to highly specialized classes of motor neurons, capable of enervating appropriate muscle targets in the animal. Dr. Jessell's research aims to devise efficient drug screens to define chemicals that promote the survival of human ES cell-derived motor neurons carrying relevant disease genes, and to help evaluate the potential of cell replacement therapies in motor neuron disease.

Parkinson's Disease While neurodegenerative diseases share many important commonalities, the specific attributes of each disease create diverse challenges for stem cell intervention. Although the cause of Parkinson's disease is still unknown, its pathology is due to the progressive degeneration of dopaminergic neurons. **Dr. Lorenz Studer** and **Dr. Viviane Tabar**, stem cell scientists in the Stem Cell and Tumor Biology Laboratory at the **Memorial Sloan-Kettering Cancer Center**, are differentiating iPS cells into specific neurons and evaluating the ability of these neurons to integrate into a rat brain that had undergone a lesion that mimics Parkinson's disease. The opportunity to observe the impact of this process on rat behavior while monitoring for tumor formation will yield invaluable information for determining the potential of iPS cells for cell replacement therapy.

Glial Disorders Formation of the insulating myelin sheath surrounding nerves is crucial for maintaining normal neuronal circuits that are able to transmit signals within the body. Myelination is dependent upon the coordination of glial cells for support and protection. Demyelinating disorders, such as multiple sclerosis, result from the absence of glial cells. Several strategies have been developed for cell-based repair of demyelinated lesions of the brain and spinal cord. In particular, glial progenitor cells capable of oligodendrocytic maturation and myelination have been derived from human brain tissue, as well as from hESC cells, and have proved effective in myelinating both congenitally hypomyelinated and adult demyelinated brain and spinal cord. At the **University of Rochester**, **Dr. Steven Goldman's** research team has devised techniques for identification, isolation, transplantation and assessment of human glial



MYELINATION

Confocal microscopy sections of oligodendrocytes transplanted shiverer mouse brain at 20 (left) and 35 (right) weeks.

Image Source: Dr. Steven A. Goldman, University of Rochester

Project Title: iPS Cell Therapy for Diseases of Adult Acquired Demyelination

progenitor cells and has achieved widespread myelination of congenitally demyelinated brain. The investigators are developing the means to generate myelinogenic glial progenitor cells from human iPS cells, and to establish their myelination capacity and safety *in vivo*, after transplantation into the brains of neonatal, myelin-deficient shiverer mice. This approach may prove to be an attractive strategy for restoring lost myelin in diseases such as multiple sclerosis, transverse myelitis, optic neuritis and subcortical stroke, in which no genetic abnormalities prevent the use of a patient's own cells as an iPS source.

Cerebral Cortex The cerebral cortex is a major region of the brain that is concerned with movement, sensation and thought. The nervous system and vascular cells in the cerebral cortex are damaged in diseases such as stroke, Alzheimer's disease and during brain tumor formation. **Dr. Sally Temple** of **The Regenerative Research Foundation** is conducting experiments to determine how gene expression changes during normal brain development. Neural stem cells produce many different subtypes of cells, and each subtype arises on a precise time schedule during development. Dr. Temple has designed a culture system and identified different classes of neural progenitor cells in the embryonic cerebral cortex. These studies will supply a database of genes important for making each major cortical neuron type, as well as the developing vasculature, at specific times during development. The target genes can be investigated in future studies, identifying their roles in the stem cell niche and in nervous system diseases.

Cortical Interneurons Derived from Embryonic Stem Cells Neurons in "the brain can be broadly grouped into two classes: excitatory cells that increase electrical activity and inhibitory cells that act as brakes by reducing electrical activity. Both are vital for the brain to function properly. Excessive excitation leads to giant waves of electrical activity that can result in epileptic seizures that affect one in every 250 adults. A treatment option showing considerable potential is a transplant of sufficient numbers of inhibitory interneurons into specific regions of the brain of a patient with epilepsy. These inhibitory interneurons act as brakes to prevent seizures from occurring. **Dr. Gordon Fishell** at **New York University** is investigating the most effective methods for generating inhibitory interneurons from ES cells by controlling cell culture micro-environmental factors or manipulating the internal cell signaling pathways. Initial testing in animal models will yield important information for moving stem cell research from bench to bedside.

CANCER

Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. According to the American Cancer Society, cancer accounted for one-quarter of deaths in the United States in 2008, exceeded only by heart disease. Gold standard cancer therapies often involve surgery, radiation and chemotherapy to physically reduce or remove the tumor mass. Even after a series of invasive treatments, however, in most cases the cancer returns. This reoccurrence of disease, as well as other evidence, supports the existence of cancer stem cells. New York State research scientists are working to develop novel approaches to target the cancer stem cells that appear to be responsible for tumor progression.

Targeting Different Types of Cancer Despite advances in surgical, radio- and chemotherapies during the past decades, breast cancer remains one of the most lethal cancers. At **Albany Medical College**, **Dr. Jihe Zhao** is proposing a new concept to distinguish breast cancer metastatic stem cells from primary

cancer stem cells. If the metastatic stem cells are indeed different from primary cancer stem cells, this study would open a new avenue for designing more effective anti-cancer therapies specifically targeting the cancer cells responsible for metastasis. Prostate cancer is the most common cancer and the second leading cause of cancer death in American men. **Dr. Wendy Huss** of **Roswell Park Cancer Institute** is studying prostate cancer as a model of solid tumors. Researchers in Dr. Huss' laboratory are isolating potential prostate cancer stem cells from specimens obtained from prostate cancer patients. Therapy against cancer stem cells would decrease the risk of recurrent prostate cancer and reduce morbidity and mortality due to this disease.

Head and neck cancer is an aggressive disease for which survival rates have improved only marginally in the last 30 years. **Dr. Julio Aguirre-Ghiso** at **Mount Sinai School of Medicine** has discovered that cancer stem cells from head and neck tumors can adopt a quiescent state. In this state, they become resistant to current therapies, and, in time, become active and aggressive. Identifying cancer stem cells and studying how they reprogram into a dormant state may provide insight into this process. To address cancer metastasis, cancer researchers are developing more effective drugs and new drug combinations. Often this approach has not improved overall survival, but has increased toxicity to normal tissue and contributed to debilitating illness in patients. At the **Roswell Park Cancer Institute**, **Dr. Bonnie Hylander** is attempting to identify a new generation of drugs that specifically target cancer stem cells with reduced side effects in pancreatic cancer patients. Dr. Hylander has devised a model for scientists to establish an ongoing, renewable source of cancer stem cells by growing cells from patients' tumors in immune-deficient mice. These cancer stem cells can be tested for sensitivity to many different therapeutic approaches and may, in fact, provide answers that can benefit other cancer patients in the future.

Targeting Melanoma Melanoma development has classically been perceived as a stepwise process in which mature melanocytes in the epidermis progressively acquire genetic mutations in oncogenes or tumor-suppressor genes, ultimately leading to metastatic melanoma. Although the apparent target of transformation is differentiated melanocytes, melanomas may also be derived from transformed melanocytic stem cells that may be responsible for the highly infiltrative and metastatic behavior of these tumors. At **New York University**, **Dr. Eva Hernando** is characterizing a melanoma stem cell population from a mouse melanoma model. Another research group at the **University of Rochester** led by **Dr. Lei Xu** aims to establish a new paradigm to find cancer stem cell markers and contribute to the eradication of cancer cells in malignant melanomas. Using microarray analyses, several genes relevant to human malignant melanoma have been identified. These results provide important insights and research tools for understanding cancer stem cells in malignant melanoma, and may lead to more effective treatment strategies for this deadly disease.

Using Mesenchymal Stem Cells to Treat Cancer Mesenchymal stem cells can migrate to and participate in many inflammatory processes, including tumor initiation and tumor growth. **Dr. Igor Matushansky** at **Columbia University** is using the tumor-homing properties of mesenchymal stem cells to deliver drugs capable of targeting tumor bulk and cancer stem cells. This approach is designed to use the mesenchymal stem cells as a "Trojan horse" to maximize drug concentrations at tumor sites via tumor site-specific delivery of chemotherapy. Elimination of tumor bulk would render cancer stem cells more accessible to stem cell differentiation agents delivered via a similarly targeted mechanism and would prevent cancer recurrence.

HEART

Heart disease is the leading cause of death in the United States and is a major cause of disability. According to the National Center for Health Statistics in 2005, almost 652,000 people die of heart disease in the U.S. each year, accounting for nearly 27 percent of all U.S. deaths. Research scientists and cardiovascular clinicians in New York State are working together to design more effective treatments for heart disease. The engagement of stem cells in cardiac tissue repair and replacement may provide new weapons in the long-standing battle against heart disease.

Cardiac Conduction System During a normal lifespan, the heart beats more than two billion times. The ability of hearts to beat in an exceedingly reliable and regulated manner depends on a specialized network of cardiac cells that possess unique electrical properties. Abnormalities in heart rhythm represent an important public health problem. Implantable electronic devices such as pacemakers and defibrillators are effective, but these approaches involve surgical intervention, ongoing medical management including battery changes and risk of device failure. **Dr. Glenn Fishman** of **New York University** is developing an ES cell-derived conduction system to study the network of cells within the heart that regulates heart rhythm. Scientists will be able to use these ES cell-derived conduction system cells as a platform for the discovery of novel targets for treatment of rhythm disturbances, particularly life-threatening cardiac arrhythmias, and identify potential new medications to prevent heart rhythm disorders. Utilizing another approach, **Dr. Michael Rosen** at **Columbia University** applies mathematical modeling in mammalian cell lines to identify ion channel constructs whose anti-arrhythmic mechanism of action is novel and does not cause arrhythmias. In the initial proof-of-concept studies, co-culture of mesenchymal stem cells expressing these ion channels with muscle cells showed significant reduction of arrhythmias in a canine heart attack model whose arrhythmias mimic the human condition. Dr. Rosen's group is now developing a new method to deliver these ion channel genes to cardiac muscle cells via human mesenchymal stem cells. The stem cell-based delivery of novel ion channel constructs to normalize cardiac conduction holds significant therapeutic potential.

Ischemic Heart Failure and Cardiovascular Patch Heart failure from narrowed coronary arteries continues to be the most common cause of death and disability in the United States (U.S.). Early clinical trials have demonstrated the safety, feasibility and efficacy of a variety of bone marrow-derived stem cell therapies in humans with ischemic heart disease. Nevertheless, chronic effects on function are controversial, and a mechanistic understanding of bone marrow components injected into the coronary arteries or myocardium is lacking. **Dr. Gen Suzuki** at the **State University of New York at Buffalo** is using a large animal model, the pig, resembling human ischemic cardiomyopathy, and cardiosphere-derived stem cells, to gain a better understanding of the cellular mechanisms of heart and vascular regeneration *in vivo* and to extend this regenerative therapy to therapeutic applications in human ischemic heart failure.

Heart disease and stroke are the principal components of cardiovascular disease. Upon myocardial infarction, scar tissue reduces the contractile function of the heart and leads to wall thinning and dilation, heart remodeling and, ultimately, heart failure. The research interest in **Dr. Gordana Vunjak-Novakovic's** laboratory at **Columbia University** is to apply interdisciplinary approaches to reconstruct a cardiovascular patch for heart repair. The human

cardiac progenitor cells are derived from hESCs by mimicking the culture environment during normal heart development. Researchers subsequently use biomaterials coated with human cardiac progenitors to test the function of contractile cardiac patches in animal models with heart infarction. The combination of stem cell biology with a tissue engineering approach offers a promising strategy for cell-based therapies.

BLOOD

Clinically, blood stem cell transplantation is the most common and successful procedure for replacing damaged or lost blood cells. Blood stem cells are accessible from the umbilical cord, peripheral blood and bone marrow.

Red Blood Cells Ten percent of individuals in the U.S. suffer from anemia, and 38,000 units of blood are transfused every day to treat people with these disorders. At present, all that blood must originate from blood donors. The ability to grow a large quantity of human red blood cells from stem cells offers the possibility of producing universal donor red blood cells to treat anemic children and adults. **Dr. James Palis** at the **University of Rochester** has discovered a red blood precursor cell in the mouse embryo with the ability to divide every day to form two identical daughter cells – a process termed self-renewal. Most importantly, these red blood precursor cells, which are found in the mouse embryo but not in the adult mouse, can be cultured for months and yet are still able to become normal mature red blood cells. Dr. Palis' team is working to determine whether similar red blood precursor cells can be derived from hESCs. Another research group led by **Dr. Margaret Baron** at **Mount Sinai School of Medicine** is using ES cells and iPS cells as model systems, in conjunction with the embryoid bodies' technique, to define optimal conditions for directed differentiation of pluripotent stem cells along the red blood cell lineage.

Targeting Leukemia Stem Cells Despite the emergence of new drugs effectively reducing the tumor mass with multiple rounds of chemotherapies, relapse continues to be the most common cause of death in acute myeloid leukemia. Recent scientific evidence suggests a novel model for acute myeloid leukemia in which rare leukemia stem cells give rise to functionally heterogeneous bulk tumor cells with a limited lifespan. Leukemia stem cells, in fact, do not respond well to common therapeutic agents and result in treatment failure. **Dr. Ulrich Steidl's** laboratory at the **Albert Einstein College of Medicine** is working on identifying surface markers for leukemia stem cells in different subtypes of acute myeloid leukemia. The prospect of isolating leukemia stem cells carries important implications for future applications in research as well as the clinic setting. Research in **Dr. Craig Jordan's** laboratory at the **University of Rochester** focuses on defining the key molecular features that control survival of acute myeloid leukemia stem cells, and applying this knowledge to develop more efficacious drugs to treat acute myeloid leukemia. By using large-scale gene expression profiling techniques to monitor leukemia stem cells undergoing cell death, scientists can identify candidate genes to target for screening a large collection of drugs approved by the U.S. Food and Drug Administration. Dr. Jordan's group has successfully identified one such drug that will soon be entering clinical trials.

Antiviral Resistance Plasmacytoid dendritic cells represent a blood-cell type specialized in virus recognition and rapid antiviral immune responses. ES cells and iPS cells hold the potential to give rise to all cell types of the adult body, raising the hope of stem cell-based cell replacement therapies. **Dr. Boris Reizis'** research group at **Columbia University** focuses on generating plasmacytoid

dendritic cells from ES cells and iPS cells, to examine their proper function in immune responses against viruses. In the long term, development of functional plasmacytoid dendritic cells for transplantation offers a desirable therapeutic option for increasing antiviral resistance in immunocompromised individuals such as the elderly, organ transplant recipients and AIDS patients.

OTHER DISEASES – LIVER, DIABETES, KIDNEY, MUSCLE

Liver Hepatitis C is a liver disease caused by the hepatitis C virus and transmitted through direct contact with blood. No vaccine is available for this disease, and only a low percentage of patients respond to the combined therapy of interferon alpha and ribavirin. The majority of infected individuals go on to develop chronic liver disease and typically require a liver transplant for survival. At **Albert Einstein College of Medicine**, **Dr. Mukesh Kumar** is evaluating various genetic sequences that could interfere with hepatitis C viral replication/infection in a liver cell line. The use of stem cells or fetal tissue-derived liver cells to express these genetic sequences and replace diseased liver cells with healthy cells capable of resisting virus infection offers another possibility for an effective treatment for this chronic liver disease.

MicroRNAs (miRNA) are a newly described set of small genetic elements that are highly conserved through evolution. Genetic studies have shown that miRNAs regulate cell fate decisions in specialized stem cells. However, the role of miRNAs in liver stem cell differentiation remains unknown. Researchers in **Dr. Charles Rogler's** laboratory at **Albert Einstein College of Medicine** are working towards identifying miRNAs playing critical roles in liver stem cell differentiation. Understanding the cell signaling pathways regulated by miRNAs will expand current understanding of stem cell differentiation at the molecular level and may lead to practical applications in the area of liver stem cell transplantation.

Given the worldwide shortage of donor organs for transplantation, cell-based therapies are under development for treatment of acute liver failure and inherited liver disorders. Hepatocyte transplantation and construction of bio-artificial liver devices could become potential alternatives to liver transplantation for some of these diseases. **Dr. Jayanta Roy-Chowdhury** at the **Albert Einstein College of Medicine** is studying the generation of functional hepatocytes from hESCs. These hESC-derived hepatocytes are being carefully compared with adult hepatocytes in terms of protein synthesis, metabolism of ammonia and detoxification of drugs. Dr. Roy-Chowdhury's studies are an essential step to refine methods for generating an unlimited supply of functional human hepatocytes for development of cell-based therapies for treatment of liver diseases.

Diabetes Type 1 and type 2 diabetes are chronic metabolic disorders characterized by hyperglycemia due to the failure to maintain physiological regulation of glucose levels by insulin. Frequent insulin administration is essential for survival of type 1 and about 30 percent of type 2 diabetes patients. Cell therapy to replenish pancreatic islet cells and restore glucose homeostasis offers a very promising approach. Human ES cells may serve as a renewable source of islets and yield functional cells. However, studies on stem cell proliferation and differentiation to various cell types have been performed only in small-volume cultures. The development of bioreactor systems suitable for culturing stem cells and their specialized progeny in large quantities will enhance stem cell-based therapies. **Dr. Emmanouhl Tzanakakis** at the **State University of New York at Buffalo** is optimizing the conditions and

parameters for establishing a microcarrier-stirred suspension bioreactor with a high surface-to-volume ratio, allowing scaled-up production of cells. Bioreactor technology that leads to production of large numbers of pancreatic islet-like cells secreting insulin could ultimately be valuable in stem cell-based therapeutics for diabetes.

Adrenal Gland The outer portion of the adrenal gland, the adrenal cortex, is an endocrine organ that produces steroid hormones. These hormones are required throughout life to regulate kidney function and help the body respond to stress. Inappropriate function of the adrenal cortex is a significant risk factor for hypertension, and some genetic diseases of the cortex become lethal without hormone replacement therapy. ES cells have the potential to supply an unlimited source of adrenal cells that could be used both for studying adrenal gland function and in cell replacement therapies. However, no well-defined procedures are available at present for generating adrenal cells from ES cells. **Dr. Edward Laufer** at **Columbia University** is pursuing this goal by recapitulating the normal steps that occur during adrenal gland development in the embryo. Understanding the molecular mechanism of endocrine regulation in adrenocortical cells will aid scientists in gaining insight for eventual cell replacement therapies in patients with malfunctioning adrenal glands.

Muscle Loss of skeletal muscle may occur as a consequence of a developmental anomaly or as a result of traumatic injury or surgery to remove a tumor. Structural defects that affect striated tissues range from functionally benign to profoundly debilitating. For example, structural defects to the musculature of the face may have a negligible impact on the ability of a patient to survive. However, even minor cosmetic defects in the muscles of the face can have profound psychological implications. Defects in the structure of muscle in the arms or legs can limit mobility and severely compromise the quality of life. The long-term objective in **Dr. Louis Terracio's** laboratory at **New York University** is to engineer a biological implant, constructed from patients' own skeletal muscle stem cells, that can be used to restore the structure and function of compromised skeletal muscle. The current research focus is to develop a skeletal muscle prosthesis in a pig model to obtain the basic parameters for stem cell isolation, purification and expansion methodology prior to refinement, using human biopsy material. These muscle studies will establish the initial framework for skeletal muscle repair needed for application to human cells.

Understanding Pluripotency and Cell Reprogramming

An important objective of the New York State Stem Cell program is to support fundamental research for further development of iPS cell technologies and to characterize the resulting stem cells in relation to hESCs. Pluripotency is the fundamental property of ES and iPS cells. Understanding how this property is controlled is a necessary step to manipulate cells for therapeutic purposes.

Analyses of Pluripotency hESC research holds great potential to revolutionize medicine by providing cell populations for future transplantation therapies, as well as for developing models to unravel the mechanisms of complex diseases. Recent efforts have shown that human skin cells can be reprogrammed directly to a pluripotent ES cell-like state using defined molecules. The exact similarity between these human iPS cells and bona fide hESCs is still unclear. **Dr. Ihor Lemischka** at **Mount Sinai School of Medicine** is attempting to understand the molecular and cellular nature of pluripotent stem cell states and how such states are altered during a change in cell fate. The functional, molecular and biochemical properties of hESC and iPS cells are compared rigorously in Dr. Lemischka's laboratory to uncover how pluripotency is

established and maintained. Large-scale gene expression and protein content analysis, short-hairpin RNA technology, synthetic biology techniques and sophisticated bioinformatic and computational tools are employed for global comparison in different pluripotent stem cell lines.

Signaling Cascades in Cell Reprogramming Induced expression of certain genes can reprogram adult skin cells into pluripotent stem cells. As demonstrated by gene expression profiling, reprogramming is a multi-step process. However, the intracellular signaling cascades that are downstream targets of reprogramming factors at various stages have yet to be determined. **Dr. Asa Abeliovich** at the **Columbia University Medical Center** is working on dissecting the mechanisms and kinetics of iPS cell generation, pivotal to development of new reprogramming strategies with enhanced efficiency and safety. Rapid kinetics via phosphorylation and other protein modifications, switch-like regulation and the availability of well-established chemical inhibitors make signaling cascades an exciting target. Dr. Abeliovich seeks to illuminate intracellular signaling molecules that might become valuable drug targets to achieve better reprogramming. Another researcher at the **Mount Sinai School of Medicine**, **Dr. Saghi Ghaffari**, is interested in elucidating the regulation of signal pathways and transcriptional programs that control stem cells. The Ghaffari laboratory recently identified a nuclear factor that may increase both the efficiency and safety of current methods for generating iPS cells. The function of this particular nuclear factor can be substituted by chemical compounds, with the potential to eliminate the need for viral gene or plasmid DNA transfer techniques. This research is likely to make a significant impact on understanding the molecular mechanism of pluripotency, as well as providing a potentially safer means to produce iPS cells.

Stem Cell Immunology

The major sources of potential stem cell treatments are autologous (from the same individual) and allogeneic (from a different individual). Utilization of a patient's own stem cells to treat disorders or injuries is the superior approach, since it eliminates the concern of immune rejection. However, autologous transplantation is unlikely in most cases, especially if the patient cannot provide healthy stem cells due to disease. The alternative allogeneic bone marrow and cord blood stem cell transplantations represent important therapies for many diseases at present. Directed differentiation of hESCs into various tissue-specific cell types offers another potential approach for cellular transplantation. Before stem cell research can be translated into new therapies, scientists and physicians need to gain more insight into patient immune response to allogeneic stem cell-based therapy.

Stem Cell Transplantation The use of stem cells to restore damaged tissue function or treat degenerative diseases becomes more and more appealing. A clear understanding of immunological responses to different classes of stem cells is important for the development of therapeutic strategies using allogeneic stem cells. **Dr. Soosan Ghazizadeh** at the **State University of New York at Stony Brook** is using a well-characterized skin regeneration model to analyze stem cell engraftment. Two immunophenotypically distinct populations of stem cells are transplanted and the engraftments are tracked in live animals by monitoring surface fluorescence. Another strategy, genetically engineering stem cells to express negative immunoregulatory factors so as to reduce immune rejection, is also under development. Engineering a stem cell with universal donor capability that can evade host immune responses will have a significant impact on adoption of stem cell-based therapies for diseases or injuries.

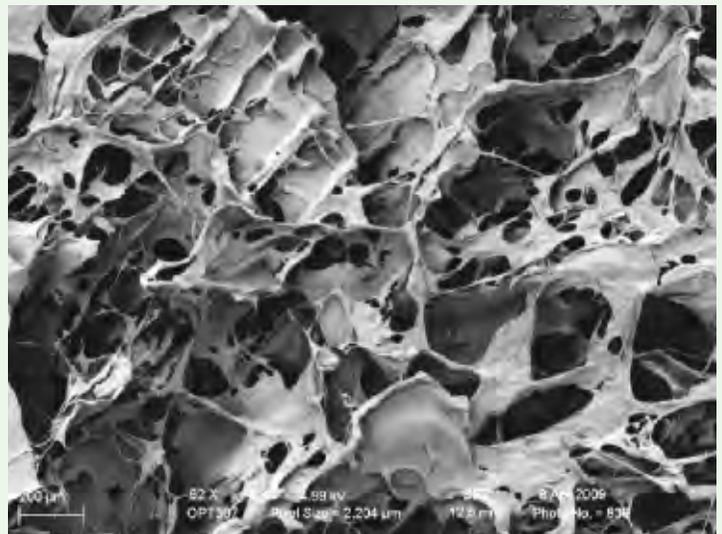
Gut Immune System The gut is not only involved in the digestion and absorption of food; it is also an important immune organ. In healthy subjects, the intestinal wall separates food and bacteria from thousands of immune cells that can produce antibodies to fight bacteria, fungi and viruses. In newborns suffering from severe immunodeficiency due to the lack of an immune system, or in patients who undergo chemotherapy and radiation for cancers, the majority of the immune cells in the gut are absent. It is unclear whether gut immune cells are replaced when patients are transplanted with either bone marrow or cord blood stem cells. After transplantation, some patients experience chronic gut infections and food intolerance. At the **Wadsworth Center**, **Dr. Maria Lopez's** laboratory is working with an immunodeficient mouse model that received a cord blood transplant to study whether immune cells can establish lymphocytes (B and T cells) in the gut as efficiently as in the spleen and other lymphoid organs after engraftment. This model could also be used to investigate ways to accelerate development of gut immunity, and ascertain whether protein critical for neutralizing pathogens is secreted into the gut lumen. This research serves as a unique model to understand the development of gut immunity.

Tissue Engineering and Biomaterials

The primary focus of New York's stem cell research funding program is to support innovative research that will advance the understanding of stem cell biology and apply basic research discoveries to new therapies and diagnostic methods for human diseases. Tissue engineering is an interdisciplinary field that applies the principles of engineering and the life sciences to the development of biological substitutes that restore, maintain or improve tissue or organ functions. The combination of stem cells, biomaterials, growth factors and the biomimetic environment provides a wide spectrum of potential therapeutic applications for clinical uses.

Bone and Cartilage About 70 million people in the U.S. suffer from arthritis and related disorders, with 4.7 million arthritis patients in New York State alone. The U.S. spends more than \$75 billion per year on treating arthritis and related conditions. Osteoarthritis is a chronic, degenerative disease. Currently, total joint prosthesis with metal and plastic joints (total knee and hip) is the primary surgical treatment choice for individuals with late-stage arthritis. A critical shortcoming of current total joint prostheses is that they last about 10 years on average, during which wear debris accumulates. A biologically based joint replacement therapy should circumvent the limitations of metal and plastic joints. **Dr. Jeremy Mao's** group in collaboration with other researchers at **Columbia University** has made substantial progress in repairing joints with stem cells and biomaterial scaffolds. Their findings in a preclinical rabbit model implanted with biological joints demonstrate very promising outcomes. A biological joint replacement that can integrate and remodel with the host tissue could become the long-term solution for patients suffering from arthritis at any age. Another research group focusing on cartilage regeneration led by **Dr. Hani Awad** at the **University of Rochester** has devised a process known as harvesting articular cartilage tissue from deceased organ and tissue donors. The donor cartilage is minced, decellularized, dissolved and then re-formed as a porous sponge-like construct to repair cartilage injuries. The porous cartilage constructs can be coated with the patient's own bone marrow-derived mesenchymal stem cells and implanted into the injured site to promote articular cartilage regeneration.

Blood Vessels In cardiovascular therapies, demand is growing for small-diameter blood vessels as replacement grafts. Although venous grafts are at present the gold standard, their 10-year failure rate is approaching 35 percent. Bioengineered vascular grafts are capable of remodeling in response to host signals and offer a clear alternative to existing technologies. However, obtaining cells from the patient's vessels requires invasive surgery and may injure the donor site. **Dr. Stelios Andreadis** at the **State University of New York at Buffalo** is exploring a new avenue of using hair follicles as a source of vascular cells. It is known that hair follicle stem cells contribute to hair and skin regeneration; however, they may also provide a rich and easily accessible source of autologous vascular cells that can be used to engineer small-diameter, biological vascular grafts. Hair follicle stem cells may also serve as an important cell source for regeneration of other cardiac tissue, such as heart valves and cardiac patches, and may further increase their potential clinical impact on cardiovascular therapy.

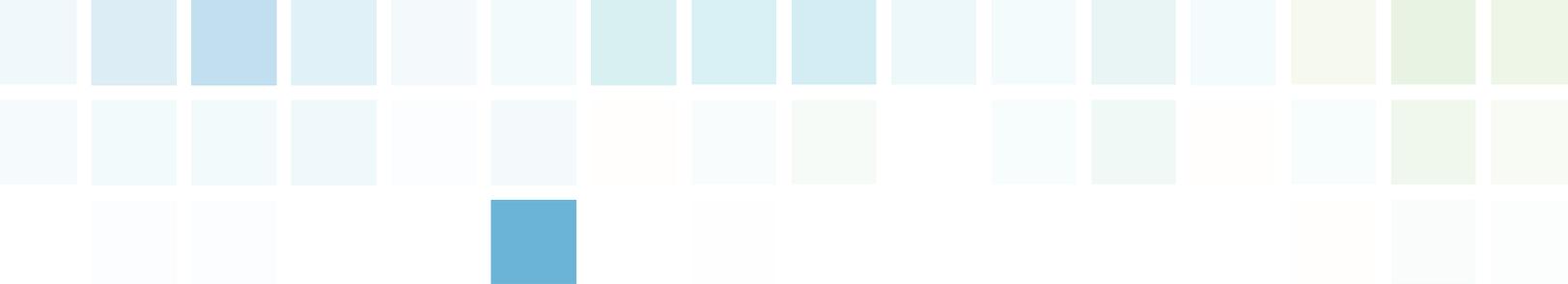


CARTILAGE SCAFFOLD

Lyophilized cartilage morsels are processed to yield porous sponge-like scaffolds for cartilage regeneration. Scanning electron microscopy (SEM) imaging of articular cartilage (left) and the porous cartilage-derived scaffold (right) revealed the porous structure of the scaffolds compared to native tissue.

Image Source: Dr. Hani A. Awad, University of Rochester

Project Title: Modulating Stem Cell Differentiation Using Novel Allograft Scaffolds for Cartilage Repair



NYSTEM Awards: Appendix I Abstracts of Institutional Development Awards

ALBERT EINSTEIN COLLEGE OF MEDICINE

Principal Investigator: Harry Shamoon

Cell Production Core, Epigenetics and Reprogramming Core, Cell Transplantation Core

Three core functions developed through the NYSTEM award support stem cell research in diverse diseases, including hemophilia, anemia, heart disease, liver diseases and brain disorders. Research funded by the award also impacted the science of developmental biology, cancer and aging research. A Cell Production Core was created within the Einstein Center for Human Embryonic Stem Cell Research. Large-scale production of stem cells (100 million to one billion cells) is necessary for advancing research in these areas. Sixteen investigators have worked in the core with ES cells, induced pluripotent stem (iPS) cells, differentiation of ES and iPS cells, analyses of cell populations or for training. An Epigenetics and Reprogramming Core facilitates implementation of new genetic technologies for stem cell research. The core supports high-throughput technologies to characterize genetic changes in stem cells, including stem cells derived from reprogramming of mature cells, or iPS cells; and of differentiated cells generated from stem cells with which more can be learned about cancer and inherited diseases. Data from the core have already led to a publication. A Cell Transplantation Core provides animal models for studying stem cells. To verify that stem cells can differentiate into multiple lineages, native or modified cells are being transplanted into animals, followed by analyses at various intervals to confirm that stem cells can indeed generate desired types of mature cells. Furthermore, these models will establish whether stem cells can repopulate organs and restore deficient functions. Several mouse models now housed in the core are being bred in preparation for xenotransplantation experiments. Data generated by the core's staff resulted in a publication of methods for tracking transplanted human stem cells in immunodeficient mice and studies of the function of transplanted cells with imaging methods. This facility succeeded in establishing a Stem Cell Research Institute that is creating cross-cutting opportunities in stem cell research and regenerative medicine. Additional NYSTEM funds will ensure that all three stem cell cores can be maintained during the next four years.

CITY COLLEGE OF NEW YORK

Principal Investigator: John Tarbell

Stem Cell Research Institutional Development: Training and Core Equipment

A group of faculty members at the City College of New York (CCNY) is actively working in several areas of stem cell research. Projects are under way using either mouse ES cells or adult human mesenchymal stem cells from bone marrow. The specific aims of the award were: (1) to set up a core facility for flow cytometry in the Biomedical Engineering (BME) Department at CCNY for stem cell research; and (2) to provide stem cell training funds for the participating faculty and their graduate students. NYSTEM funds supplied a four-color fluorescence-activated cell sorting (FACS) instrument for the BME Department, home of four faculty members participating in this proposal. Isolation and characterization of stem cells are the first critical steps in most stem cell research projects, and a FACS system is essential equipment for high-purity stem cell characterization and isolation. Although faculty members are currently conducting research related to stem cells, comprehensive training in core methods for individuals who perform stem cell research serves as the foundation for development of long-term research capabilities using human embryonic stem cells (hESC) at CCNY. In November 2008, Dr. Robert Majeska, a research scientist in the BME Department, attended FACS training by BD Biosciences in Massachusetts. Since then, two participating principal investigators, Drs. Sihong Wang and Lane Gilchrist, have been working with the FACS in their stem cell-related experiments. The instrument is expected to be continuously used by all BME faculty and other City College faculty conducting stem cell research. NYSTEM funding also allowed several others to attend stem cell training/conferences. Overall, stem cell research at CCNY is in its infancy, and this award furnished critical funds for training and core equipment that will move stem cell research at CCNY to the next level.

COLD SPRING HARBOR LABORATORY

Principal Investigator: David Spector

Supplements for Studies of the Molecular Mechanisms Regulating Stem Cells in Development, Neurogenesis and Cancer

The Cold Spring Harbor Laboratory (CSHL) stem cell research program takes a multi-pronged approach with a common goal: to determine the molecular mechanisms regulating stem cell activity. Understanding these mechanisms is important for the future development of stem-cell related therapies and will ensure their safety and effectiveness. Using animal, plant and human cell lines, CSHL investigators study how stem cells are controlled in cancer, the brain and during plant development. CSHL neuroscientists examined the targets of deep-brain stimulation, revealed the mechanisms of action of electroconvulsive shock and investigated the consequences of action of fluoxetine, an anti-depressant, on neurogenesis in the developing brain. These studies will impact understanding of the antidepressant action, and highlight differences in their action in adults as compared to their effects during pregnancy, in children and in adolescents. With plants as a model system, scientists here discovered that the chromatin-remodeling protein, HIRA, plays dual roles in regulating stem cell activity; HIRA is required to generate stem cells, as well as to repress stem cell activity upon differentiation – roles likely to be conserved in mammals. Finally, in relation to cancer, the investigators found that Rnd3/RhoE and DOCK7 proteins, both of which regulate activities of the Ras oncogene,

are novel regulators of granule cell progenitor (GCP) proliferation and differentiation. GCPs can produce brain tumors in children, and this ability appears to be linked to the switch from differentiation to proliferation. Further studies of the intricate and complex signaling networks in GCPs will contribute to better understanding of how medulloblastomas arise. This knowledge ultimately could aid the treatment and management of these childhood brain cancers. Stem cell-directed therapy has the potential to become a powerful tool against many diseases. CSHL's program is committed to understanding the basic mechanisms regulating stem cells, facilitating progress in developing these therapies. This is an emerging area at CSHL, and NYSTEM funding provided the initial resources to enable its success.

COLUMBIA UNIVERSITY MEDICAL CENTER

Principal Investigator: James Goldman

FACS Core, Ultradeep Sequencing Core and Ultrasound-Guided Microinjection Core Facilities for Stem Cell Research

Columbia University Medical Center's stem cell research community ranges from investigators probing the basic mechanisms of stem cells to clinicians dealing directly with such devastating diseases as diabetes, amyotrophic lateral sclerosis (ALS), cancer and others, for which the potential of stem cell therapy is being explored. NYSTEM funding may accelerate the impact of fundamental discoveries on practical therapy. Ultimately, the goal is to use stem cells as a proxy to model and study human diseases and as an unlimited source of cells for cell-based drug discovery and cell replacement therapy. To this end, NYSTEM Institutional Development Award funds allowed creation of three core facilities: a Fluorescence-Activated Cell Sorting (FACS) Core, an Ultradeep Sequencing Core and an Ultrasound-Guided Microinjection Core Facility. Additional funds from the National Institutes of Health and the Howard Hughes Medical Institute underwrote the purchase of two deep sequencers, and, with combined funding from all three sources, equipment was purchased and staff recruited to support the operation of both facilities. Full use of the sequencers is anticipated after both become completely operational. The FACS facility is already having great impact on stem cell research, is already well utilized and provides far more flexibility and far higher output than the existing FACS Core. The Ultrasound-Guided Microinjection System is in use by researchers to transplant cells or genes of interest into rodent embryos. The facilities established with NYSTEM funds will enable tangible extension of stem cell research efforts by more than 60 investigators institution-wide.

COLUMBIA UNIVERSITY - MORNINGSIDE

Principal Investigator: Gordana Vunjak-Novakovic

Functional Imaging Core for Stem Cell Research

Columbia University – Morningside has a rapidly growing critical mass of stem cell investigators conducting synergistic activities. The opportunity afforded by NYSTEM funds fostered new engineering methods, and removed some of the barriers to rapid expansion of basic and translational knowledge in stem cell biology. Realizing that cross-disciplinary interactions among engineers and basic scientists are crucial for full utilization of the immense potential of stem cells, a state-of-the-art Functional Imaging Core for Stem Cell Research was established, while simultaneously enhancing the Comparative Proteomics Center. These world-class resources help meet some of the key needs of stem cell investigators, facilitate advanced training and promote interdisciplinary

collaborations at Columbia and in the State of New York. The Stem Cell Imaging Core was established with NYSTEM funds, supplemented by a cost-match of \$412,000 from Columbia, that were used to purchase five pieces of equipment: (1) a two-photon/confocal microscopy system; (2) an *in vivo* imaging system; (3) a microplate reader; (4) an automated histology facility; and (5) a high-resolution mass spectrometer, located within the Department of Biomedical Engineering (items 1-4) and the neighboring Department of Biology (item 5). The cost-match has facilitated equipment purchases, maintenance contracts and the necessary renovations of laboratory space. Together, these systems enable functional dynamic imaging and proteomic analysis of stem cells and engineered tissues, and offer new insights into molecular and physical phenomena that drive stem cell self-renewal and differentiation. Twenty-six principal investigators from six departments are benefiting from the capabilities of this facility. To further facilitate the utilization of the Core, a new course was developed, “Advanced Microscopy: Fundamentals and Applications,” and offered in the spring of 2009. The impact of the Core will be to nurture an entirely new kind of stem cell science emerging from the integrated use of proteomics and imaging technologies.

CORNELL UNIVERSITY

Principal Investigator: Alexander Yu. Nikitin

Accelerating Development of Cornell Stem Cell Research: Supplements, Equipment and Training

NYSTEM funding provided critical support for further enhancement of the Cornell Stem Cell Program. The program held its first Annual Stem Cell Research Symposium, distributed stem cell research-related travel and training awards, hosted invited stem cell speakers and funded stem cell research-related training at the Fluorescence-Activated Cell Sorting core facility. The success of the program is evident from its securing NYSTEM awards for development of a consortium on stem cells, microenvironment and cancer, and for establishment of the Cornell mammalian cell reprogramming core. Taken together, the Institutional Development Award significantly invigorated stem cell research at Cornell University and fostered a fertile background for further growth of the Cornell stem cell research community. Three main areas of stem cell-related research interest saw marked progress: (1) deriving, maintaining and selectively



“Our NYSTEM Institutional Development grant significantly invigorated stem cell research at Cornell University and provided the most fertile background for further growth of the Cornell stem cell research community.”

*– Dr. Alexander Nikitin
Cornell University*

differentiating embryonic and adult stem cells and reprogrammed pluripotent cells; (2) recreating the temporal and spatial environment encountered in developing and adult tissues; and (3) understanding the relevance of fundamental processes governing the control of stem cells in diseases such as cancer. These areas were supported by four mechanisms: (1) bridge funding; (2) supplemental funding; (3) stem cell research training; and (4) shared equipment/core facilities. Investigators supported by bridge funding were successful in collecting preliminary results essential for successful future funding applications in the areas of stem cells and retinoic acid and new mouse infertility genes on the X chromosome. Investigators supported by supplemental funding have attained progress in: developing tissue-engineered neural stem cell niches; defining subpopulations of mesenchymal progenitor cells in adult bone marrow; elucidating the functions of micro RNAs in regulation of normal adult stem cells; pursuing spermatogonial stem cell transplantation; and identifying a new marker of skin stem cells. Training in stem cell research facilitated research projects aimed at directed differentiation of hESCs in rats and preparation of stem cells for a genome-wide analysis of nascent transcription complexes.

HUNTER COLLEGE – CITY UNIVERSITY OF NEW YORK

Principal Investigator: Ann Henderson

Stem Cell Research Institutional Development: Research and Training

With this award, Hunter College has solidified the incorporation of embryonic stem (ES) cell research into its research program. The effort involves two projects. In the first project, carried out in the laboratory of Ben Ortiz, rare and challenging technology has now been refined to direct ES cell differentiation towards lymphocyte lineages. This technology will enable more rapid and less expensive assessment of the activity of gene regulatory elements during T-cell development, as well as participation in translational research projects with clinical implications. The Ortiz laboratory is now one of the few in the world with the ability to use this technology, which will be shared with other laboratories at City University of New York (CUNY). In the second project, conducted in the laboratory of Paul Feinstein, equally challenging technology is being developed with which neuronal cells can be re-programmed to adopt an ES cell-like state using alternatives to iPS cell technology. With the aid of NYSTEM funding, each project has shown significant progress in mastering



“The NYSTEM Institutional Development Award was wonderful. It got us going in stem cell research.”

*– Dr. Ann Henderson
CUNY – Hunter*

these technical challenges. Analysis of how ES cells are able to reprogram somatic cells into pluripotent cells will eventually lead to generation of designer stem cells for each individual. The combined efforts of both laboratories are aimed at stem cell engineering and customizing ES cells for gene transfer, tissue transplantation and therapeutic intervention.

SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH

Principal Investigator: Lorenz Studer

Accelerating MSKCC Stem Cell Research: Supplements, Equipment and Training

Memorial Sloan-Kettering Cancer Center has accrued a strong tradition in stem cell research using multiple stem cell types. The NYSTEM award was designed to build on these strengths and focus on three specific areas to enhance further stem cell research at the institution: (1) supplementing funding for seven ongoing stem cell projects to accelerate the pace of research; (2) purchasing shared equipment to improve capacity for stem cell researchers; and (3) enhancing ongoing training efforts in stem cell research. Considerable progress was achieved in all seven research projects that received NYSTEM funding. Among the highlights from these studies are: (1) publication of a novel technique to convert hESCs and iPS cells into neural cells; (2) development of ES cells with a photo-convertible fluorescent signal that allows more effective tracking of stem cells in culture and *in vivo*; and (3) gaining new insights into the role of nucleopore composition on differentiation of neural stem cells in the developing embryo. New equipment for both molecular biology and microscopy studies was purchased and greatly contributed to improved capacity for stem cell researchers at the institution. A training course was developed on genetic modification and differentiation of stem cells, and more than 20 researchers were trained. This course complements ongoing training in basic techniques of handling human stem cells. The NYSTEM award significantly accelerated the pace of research through supplemental funds, new equipment and design of improved training courses. A core strength of these studies is the close interaction of researchers studying basic biology and translation. The findings enabled by these funds will have a major impact on the stem cell research community by yielding novel differentiation techniques, genetic tools and basic biological insights. Areas to be impacted by these studies include Parkinson's disease, radiation injury in the central nervous system and blood disorders amenable to cell transplantation.

MONTEFIORE MEDICAL CENTER

Principal Investigator: Brian Currie

Core Equipment for a Cellular Therapeutics Facility

Montefiore Medical Center (MMC) is committed to support stem cell and cellular therapeutics research. In collaboration with the Albert Einstein College of Medicine, MMC is dedicated to bring basic research advances into clinical practice. To that end, a new Cellular Therapeutics Facility is being constructed to meet current good manufacturing practices, requirements of the U.S. Food and Drug Administration (FDA). This facility will support development of clinical research projects that make use of various human adult stem cells, umbilical cord blood-derived stem cells and human fetal liver cells. It will be overseen by Dr. Ljiljana V. Vasovic, who has extensive experience in this arena and who will bridge the Cellular Therapeutics Facility and the MMC Hematopoietic Progenitor Cell (HPC) Processing Laboratory, part of the long-standing Bone Marrow Transplant Program at MMC. The Cellular

Therapeutics Facility represents the next stage in developing the capacity to translate stem cell research. During the funding period, the Hematopoietic Progenitor Cell Processing Laboratory maintained licensure from New York State and served institutional needs through standard operating procedures and a quality assurance program, in accordance with guidelines of the American Association of Blood Banks, the FDA and New York State. NYSTEM funds allowed purchase of specific equipment for this facility. Moreover, original research was performed in the laboratory under a project entitled, “Bioengineering of a Stem Cell-Coated Vascular Graft Derived From Placental Vessels,” directed by Dr. Vasovic.

MOUNT SINAI SCHOOL OF MEDICINE

Principal Investigator: Ihor Lemischka

Institutional Development Support of Stem Cell Research and Core Facilities

The Black Family Stem Cell Institute at the Mount Sinai School of Medicine (MSSM) has set the goal of bringing the newest discoveries in the field of stem cell science into the arena of clinical medicine. MSSM has committed significant resources to facilitate this goal, including complete renovation of 10,000 square feet of space designated to house five to six newly recruited stem cell faculty members. A central mission is to build interactions with the numerous outstanding clinical and translational research projects already in place at MSSM. A major vehicle for instituting such interaction is the existing hESC core facility. The differentiation of hESCs in culture into multiple lineages offers unprecedented opportunities to understand the earliest stages of human development; to generate differentiated cell types for future cell replacement therapies; and to open avenues to understanding the causes of complex diseases. This research also provides the foundation for design of innovative cell-based therapies and novel drugs. A major vehicle for establishing intra-institutional interactions is the hESC Core Facility, recently converted to an MSSM Shared Resource Facility with NYSTEM support. This facility will make a number of hESC lines available to scientists at a discount. In addition, the hESC SRF actively participated in assisting MSSM principal investigators with pilot projects, such as generation of several iPS cells as disease models. Last, but not least, the hESC shared resource facility continued to educate the scientific community in hESC technology. NYSTEM funding also allowed bridging Dr. Lemischka’s research grant. Towards this end, evaluation began of an inducible lentiviral vector system for use in hESCs. Researchers generated 26 stable hESC sublines targeting 15 genes with shRNA. Knockdown of three of these genes resulted in morphological changes resembling a differentiated cell phenotype that is being analyzed further. Several other screens to study hESCs were also initiated to examine differentiation and enhance hESC culture conditions.

NEW YORK MEDICAL COLLEGE

Principal Investigator: Thomas Hintze

Stem Cell Research Institutional Development: Supplementing Research and Training

Two areas for application of NYSTEM funding were identified at New York Medical College (NYMC). The first was supplemental funding to continue and enhance investigations on identification of adult cardiac and coronary vascular stem cells in the human heart. A vascular progenitor cell and a cardiac

progenitor cell were identified (in the heart), and these appear to integrate into adult mammalian cardiac muscle, resulting in formation of both new blood vessels and new heart muscle cells. The vascular progenitor cells, when injected into the coronary artery, organize into blood vessels, and preliminary data suggest that these new vessels deliver blood flow to the ischemic heart tissue. These cells are being grown and will be made available to the scientific community. Coronary vascular stem cells also are used to create a biological bypass in a canine heart, in an effort to reduce reliance on stents for treatment of atherosclerotic plaque. Another application of NYSTEM funding was establishment of a Translational Cardiac Stem Cell Core to facilitate the growth of stem cell biology and potential therapeutics at this institution. To this end, two associate professors were recruited, Drs. Carol and Leonard Eisenberg from the Medical University of South Carolina, with credentials in stem cell and developmental biology. The Eisenbergs relocated in June 2008, organized a large laboratory and recruited three postdoctoral fellows to work in the laboratory. They also developed a support facility to help faculty at NYMC expand their studies into stem cells. For instance, the Eisenbergs have trained Dr. Caroline Ojaimi to grow adult vascular stem cells for use in Dr. Hintze's studies of myocardial ischemia. Through a partnership between NYMC and Westchester Medical Center, large pieces of equipment were purchased, including cell culture hoods and a Zeiss confocal microscope.

NEW YORK STATE PSYCHIATRIC INSTITUTE

Principal Investigator: René Hen

Contribution of Hippocampal Neurogenesis to the Action of Antidepressant Medications: From Mice to Men

Most antidepressants display a delayed onset of therapeutic efficacy. Specifically, selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) often require several weeks of administration to reach full clinical efficacy. This delay has led to the neurotrophic hypothesis that, downstream of increases in monoamines elicited by antidepressants, growth-related events such as dendritic remodeling and neurogenesis are taking place in various limbic areas. Neurogenesis is the process by which stem cells located in certain parts of the adult brain continuously give rise to neurons. The laboratory showed, using two neurogenesis ablation strategies (a radiologic and a genetic



“NYSTEM was successful in bringing together groups that would not normally have collaborated.”

*– Dr. René Hen
New York State Psychiatric Institute*

one), that mice lacking neurogenesis specifically in the hippocampus no longer respond to the SSRI fluoxetine and the tricyclic desipramine in two chronic models of antidepressant response: the novelty-suppressed feeding test and the chronic unpredictable stress paradigm. These results suggest that hippocampal neurogenesis is required for the full efficacy of antidepressants, at least in these two animal models. The goal of this proposal was to further dissect this phenomenon in rodents and to extend the findings to humans. To conduct this research, NYSTEM funds supported purchase of a confocal imaging system and software suite that has allowed visualization of neurogenesis and differentiation in mouse hippocampal sections. Furthermore, the laboratory succeeded in conducting preliminary immunofluorescent studies using human brain tissue, a technologically difficult task, to examine the effects of antidepressants on human neurogenesis.

NEW YORK UNIVERSITY

Principal Investigator: Daniel Stein

A High-Throughput Sequencing Core for Stem Cell Research

The great potential of stem cells for regeneration therapy rests on their unique ability to produce many or all of the other types of cells present in an organism. Thus, one major question is which genes (and other properties) make stem cells function differently from other cells? Previous technologies have relied on miniature “probes” to test for the presence of an active gene. However, this approach limits sensitivity and can miss certain genes. The greater sensitivity of the new high-throughput sequencing technology enables indiscriminate sampling of the contents of cells, allowing detection of the unique aspects of stem cells that might have evaded probes. New York University (NYU) used NYSTEM funding to acquire powerful new high-throughput sequencing technology (SOLiD v. 3, Applied Biosystems) in order to advance research into the properties that differentiate stem cells from other cells. NYU researchers will use high-throughput sequencing to analyze stem cells on many levels, including active genes, small regulatory RNAs and chromatin states of DNA. Researchers at NYU’s Center for Genomics and Systems Biology work on a variety of models to study the basic science of stem cells, while those at the College of Dentistry conduct proof-of-principle studies to investigate their applications for regenerative medicine. NYU researchers are now well positioned to capitalize on high-throughput sequencing technology through procurement of additional funding from federal and other sources.

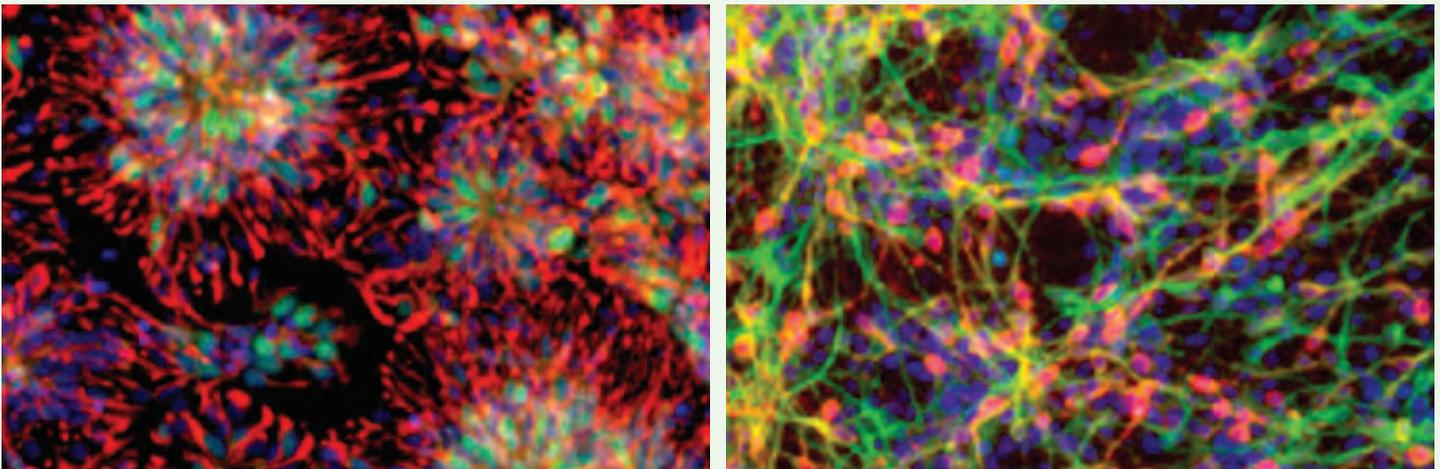
NEW YORK UNIVERSITY SCHOOL OF MEDICINE

Principal Investigator: Ruth Lehman

Stem Cell Research Supplements, Training and Core Equipment

The New York University School of Medicine the NYSTEM Award to supplement funding for nine projects already underway at the Kimmel Center for Stem Cell Biology, as well as to acquire state-of-the-art equipment and create training programs to attract more researchers to the stem cell field. The major overarching goal of these projects is to identify and characterize stem cells in various tissues and experimental systems. Four investigators focused on the identification of stem cell populations, such as: mesenchymal stem cells from bone marrow; trophoblast stem cells, which give rise to the placenta; bladder stem cells; and prostate stem cells. In each system, the investigators developed tissue- or stem cell-specific markers that allow identification and characterization

of stem cell groups. One investigator differentiated mouse ES cell cultures into specific subtypes of neurons. Finally, four laboratories are using genetic analysis in model organisms (mouse, zebrafish, flies and worms) to better understand the signals required for specification of progenitor populations and maintenance of stem cell populations in the adult. Both the identification of tissue-specific stem cell populations and characterization of the signals that control stem cells to prevent or stimulate differentiation into specific cell types are fundamental in the quest to develop strategies for regenerative medicine, and to devise probes that identify cancer stem cells. In addition to these specific research accomplishments, funds from NYSTEM allowed purchase of an additional cell sorter that is in heavy use by the institution's stem cell researchers to identify and separate specific cell populations. As part of the group's educational programs, a stem cell course was organized for graduate students, postdoctoral fellows and medical trainees that was taught first in spring of 2008 and offered again in spring of 2009. Travel grants were awarded to graduate students and postdoctoral fellows to attend stem cell meetings and courses. A symposium on inflammation was held November 21, 2008, and covered topics on cell type selection of hematopoietic stem cells.



NEURAL DIFFERENTIATION

*Differentiation of human embryonic stem (hES) cells toward midbrain dopamine (DA) neurons.
Neural intermediate state (neural rosettes) (left) and terminal differentiation into DA neurons (right).*

Image Source: Dr. Viviane Tabar, Sloan Kettering Institute

Project Title: In Vivo Function of Human iPS Derived Neural Precursors

ORDWAY RESEARCH INSTITUTE

Principal Investigator: Stewart Sell

Bone Marrow Stem Cell Origin of Breast Cancer

The possibility that breast cancer may originate from bone marrow-derived stem cells (BMDSCs) is being examined by transplantation of BMDSCs from transgenic male mice bearing a strong mammary cancer oncogene under the control of a mammary gland-specific promoter into lethally irradiated female recipients of the same inbred strain. If BMDSCs migrate to the breast and, under the influence of the microenvironment of the breast tissue or by fusion with breast cells, express the mammary epithelial phenotype, the mammary-specific promoter will be activated, the transgene will be expressed in the mammary epithelial cells and cancer will develop. The NYSTEM award allowed Ordway to complete a preliminary experiment in which breast cancer cells containing Y chromosomes (male cells) were seen in one-eighth of irradiated female recipients of transgenic male bone marrow. This tumor was diploid, suggesting transdifferentiation of BMDSCs into breast epithelial cells. More recently, research showed that donor-derived BM mesenchymal stromal cells may indirectly induce development of cancers in both the epithelial and mesenchymal tissues of a recipient, as well as directly produce breast cancers by mesenchymal-to-epithelial transition. These studies indicate that both generation and growth of tumors are closely related to the type of tissue stroma. By further studying this effect, Ordway researchers expect to identify strategies for treating the stromal cells that may affect the development or growth of cancers. For example, preliminary data indicate that knocking out expression of *Bmi1* in tumor stroma cells inhibits tumor initiation and breast cancer upon transplantation. Thus, in the future it may be possible to treat cancers by treating the cancer stroma.

POLYTECHNIC INSTITUTE

Principal Investigator: Kalle Levon

Multifunctional Scaffolds for Stem Cell Growth Design and Control

The landmark transition from Polytechnic University to Polytechnic Institute of New York University, in conjunction with NYSTEM support, connects the research to a broader environment with an enormous expansion of opportunities, and had a very deep impact on education and research activity in a small institute like Polytechnic. NYSTEM funding supports an integrative program between Polymer Science and Engineering, Biomedical Engineering and Bioinformatics, which affords investigators the opportunity to participate in the interdisciplinary area of tissue engineering with expertise in polymer science. At Polytechnic, doctoral students are benefiting from improved research infrastructure and Master's in Science students are integrating into the tissue engineering research program. Mechanical support by scaffolding is needed for stem cells to grow in a coordinated manner *in vivo*. Such scaffolding can also be used to store and release growth factors and other chemicals for optimal cell differentiation and proliferation. Just as nanofibers for biosensing and nanogel particles for drug delivery applications were previously prepared, this expertise is now being combined for preparation of multifunctional three-dimensional nanofiber/nanogel scaffolds with the potential for dimensional control of the scaffold's electrostatic behavior. The NYSTEM award has provided for stem cell training in the laboratories of several collaborators as the most efficient method of jump-starting stem cell research at Polytechnic, and multiple intra-

institutional collaborations were initiated involving protein modification, stability and scaffold formation for better recreation of *in vivo* stem cell micro-environments. In one instance, Dr. Marcel van den Brink, at Memorial Sloan-Kettering Cancer Center, assisted in evaluating three-dimensional nanofibrous scaffolds as an experimental approach for regenerating the native structural and functional properties of living tissue. At present, these three-dimensional nanofiber systems are being used to model hematopoietic stem cell proliferation and differentiation along the T-lymphocyte lineage *in vitro*.

ROSWELL PARK CANCER INSTITUTE

Principal Investigator: Andrei Gudkov

Institutional Development of Stem Cell Research Capabilities

The NYSTEM funds awarded to Roswell Park Cancer Institute (RPCI) were directed to achieve three goals: (1) improvement of the research infrastructure critical for furthering stem cell research; (2) support of pilot projects focused on the role of stem cells in the biology of cancer and their clinical significance; and (3) recruitment/education of new investigators to stem cell research. Supported research projects were aimed at the innate biology of both normal adult stem cells and cancer stem cells, investigating both therapeutic targeting of cancer stem cells and protection of benign stem cells in organs sensitive to collateral damage by chemotherapy/radiotherapy. The goal of the award was to develop multi-pronged approaches to enhance therapeutic efficacy for destruction of cancer stem cells by identifying agents that target cancer stem cells, while protecting vulnerable benign stem cells in bone marrow and the gastrointestinal tract that, if damaged, limit therapeutic options due to side effects. A significant infrastructural need of the RPCI stem cell research community was increased access to instrumentation for FACS to facilitate isolation/enrichment of populations of benign adult stem cells and cancer stem cells. NYSTEM funds supported the acquisition of a new FACS instrument with multiple excitation sources, fluorescence detectors and sterile sorting options. The FACS is an essential resource for multiple pilot projects centered on isolation and characterization of benign adult stem cells and stem cells from prostate cancer, lung cancer, human tumor xenografts and cell-line models of human cancers, as well as isolation of benign adult stem cells from blood vessels, bone marrow and the intestines. Important new findings include: (1) the identification of differences in gene expression between human cancer stem cells and benign stem cells from multiple organs that could lead to new biomarkers for cancer detection and for the identification of more effective targeted therapies; (2) the development of new human tissue-based pre-clinical model systems that allow analysis of the interaction between the normal tissue microenvironment surrounding a cancer and cancer stem cells; (3) the demonstration of differential toxicity of cancer stem cells versus benign tissue cells in response to radiation and chemotherapeutic treatment regimens; and (4) the demonstration that benign stem cells of the bone marrow and intestine can be selectively protected from therapeutic doses of radiation by selective activation of survival pathways.

STATE UNIVERSITY OF NEW YORK – BUFFALO

Principal Investigator: Kenneth Trampusch

Institutional Development of Stem Cell Research With Supplements and a Multi-Photon Microscopy Core

The centerpiece of the stem cell program at the State University of New York (SUNY)'s University at Buffalo (UB) is the program's physical workspace at the New York State Center of Excellence in Bioinformatics and Life Sciences that positions a genomic research core and high-performance computing center directly adjacent to a planned stem cell core facility. This unique environment allows researchers, scientists and clinicians from many backgrounds and specialties to combine their expertise in exploration of stem cells and their potential as therapies. Through an understanding of the role and function of stem cells in normal development and disease, UB researchers seek to capture and direct the innate capabilities of stem cells to treat diabetes, stroke, cardiovascular disease and many other conditions. It is believed that this collaborative research environment will support the translation of basic research into clinical care and, when coupled with investment in commercialization, will strengthen the economy of New York State. NYSTEM funding supplemented four research projects and improved the ability to perform stem cell research at UB through a state-of-the-art Stem Cell Research Core Facility. Research findings obtained here include: (1) the discovery that the novel Integrative Nuclear FGF Receptor-1 Signaling (INFS) pathway enhances the latent potential of neural stem/progenitor cells (NS/PCs) to undergo neuronal differentiation, thus promoting neurogenesis in the adult brain; (2) development of a novel technology that allows monitoring of gene expression in a nondestructive manner by utilizing fluorescent reporter proteins under the control of a regulatory sequence; (3) modeling statins' effects on chronic myocardial ischemia and myocardial regeneration in pigs; and (4) generation of mesenchymal stem cells from humans and pigs that improve cardiac function when injected into cardiomyopathic hamsters, a result of their trophic activities. The capabilities of the core facility were expanded by upgrading the current Zeiss LSM510 confocal microscope system to a multiphoton system for use in stem cell research. The multiphoton confocal microscope is being used by a large cadre of stem cell researchers.

STATE UNIVERSITY OF NEW YORK – STONY BROOK

Principal Investigator: Peter Brink

Shared Equipment and Supplemental Funding for Stem Cell Research

Stem cell-based therapeutics is a new and exciting research avenue with great potential for clinical applicability. Stem cells represent an autologous or allogeneic delivery system able to, in principle, deliver small molecules focally or systemically. This general tenet has been the driving force in Stony Brook's stem cell initiative. Stony Brook's projects examine the use of stem cells to repair the heart and regenerate skin electrically. The team organizes seminar series and group research meetings to enhance integration among stem cell laboratories on campus. Stony Brook has established collaborations with researchers at Columbia University and Worcester Polytechnic Institute as part of a newly initiated project on mechanical repair of the heart. This institution's NYSTEM award has supported ongoing research in seven laboratories pursuing both adult stem cell and ES cell projects, and funded the purchase of a confocal

microscope to augment the research efforts of all investigators involved. In all the laboratories, either graduate, undergraduate or high school students are participating in various aspects of their respective stem cell projects, again made possible by support from this award. The funding enabled creation of a dedicated confocal microscopy center for use by the collaborating investigators and others now conducting stem cell-related research. Other investigators include Drs. Wadie Bahou and Uta Mol, both now funded by NYSTEM for specific stem cell-related research projects. NYSTEM funds also permitted expansion of an existing tissue culture facility by providing salary support. Incubators were purchased and set up for culturing stem cells within the Department of Physiology and Biophysics. Finally, a seminar series was established and hosted four speakers during the last year; a student journal club is in place as well.

STATE UNIVERSITY OF NEW YORK - DOWNSTATE MEDICAL CENTER

Principal Investigator: Gladys Teitelman

Core Facilities and Supplementary Funding for Stem Cell Research

The intent of this NYSTEM award was to enhance or add new functionality to research activities and equipment critical for stem cell research at SUNY-Downstate. Dr. Gladys Teitelman received supplemental funds in support of her groundbreaking work on pancreatic stem cells and diabetes, and three facilities were augmented to support the research of many laboratories performing stem cell-related work pertaining to cancer, immunology, eye development and Alzheimer's disease. The FACScan flow cytometer was repaired and has provided indispensable service to multiple users, most notably to Drs. Stacy Blain and Chris Roman, whose research enterprises on cancer and autoimmune disease/immunology would be severely hampered without this instrument. Data gathered with this refurbished equipment were essential in three breakthrough publications from the Blain laboratory and two from the Roman group. The FACScan also was indispensable in producing new data for manuscripts in preparation by many members of the Downstate stem cell research community. The transgenic facility continued to offer expertise in the design of genetically modified animals by technical support staff funded by this award. Equipment will be purchased with the remaining funds for preservation of mouse embryos to increase functionality of the facility. The service contract for the confocal microscope enabled its maintenance in excellent working condition and provided essential services to the many laboratories requiring the instrument. The contract not only made available routine service, but also replacement parts, which would have been very expensive if purchased separately. The purchase of the fluorescent microscope was substituted for that of a dissecting microscope with camera. This microscope allows reaching very fine pancreatic ducts with perfusion solution, improving the yield of endocrine precursor cells required for the experiments. Supplemental funds were also used to purchase a state-of-the-art polymerase chain reaction (PCR) thermocycler. This machine is heavily used by members of several participating groups. An extremely valuable resource, it generated data for several publications in preparation.

STATE UNIVERSITY OF NEW YORK – UPSTATE MEDICAL UNIVERSITY

Principal Investigator: Gerold Feuer

Whole-Mouse Imaging Core for Stem Cell Research

The Center for Humanized Severe Combined Immunodeficient (HU-SCID) Mouse Models at the State University of New York (SUNY) Upstate Medical University is a unique facility and research unit created to foster interdisciplinary scholarship and research focused on developing and utilizing HU-SCID mice. These mice support development and maturation of a human immune system following inoculation with human stem cells. This is a novel animal model with the potential to become a broad platform for investigations in stem cell biology, as well as the study of human viral infections and cancer stem cells. The focus of this highly specialized Center is to better understand disease pathogenesis and devise preclinical models to test novel antivirals, vaccines and chemotherapeutic drugs. SUNY-Upstate has used the NYSTEM Institutional Development Award to purchase an IVIS 200 whole-mouse imaging system. The IVIS is instrumental for quantifying the maturation and development of human cancer cells and stem cells in SCID mice. More recent data from the IVIS system have enabled monitoring the reduction of tumor burden in mice engrafted with adult T-cell leukemia (ATL) cells and treated with an oncolytic virus specifically designed to target and destroy ATL cells *in vivo*. The IVIS is equipped with a special camera to detect signals from either bioluminescent and fluorescent light emitted from tumor or stem cells implanted in SCID mice. To take full advantage of the sensitive detection capabilities of the IVIS, vectors were updated to express more sensitive fluorescent proteins. Thus, implementation of the system has already had an impact on these studies. An expanding robust demand has emerged from the academic and biotech/pharmaceutical science sectors for animal models to investigate stem cell applications and therapeutics *in vivo*, and laboratories here are making considerable progress in developing suitable animal models to evaluate human hematopoietic and ES cell development. It is anticipated that major advances in the understanding of human stem cell biology will arise from using the IVIS system to accelerate these investigations.



“This NYSTEM program has been instrumental in allowing biomedical research to continue to be performed at SUNY Upstate, and it has been a real boon in particular for the upstate region in terms of jobs and the economy.”

– Dr. Gerold Feuer
SUNY – Upstate Medical University

THE ROCKEFELLER UNIVERSITY

Principal Investigator: Michael Young

FACS Sorting and Multi-Photon Microscopy Facilities for Stem Cell Research

The Rockefeller University requested funds to support the purchase, installation and operation of a FACS machine and to expand FACS capacity within the institution. FACS is one of the most critical technologies for the stem cell field, since it identifies and sorts cells within a population, allowing researchers to collect and characterize stem cells and their differentiated descendents.

The Rockefeller University has successfully installed and commissioned a FACS and began offering full service on the unit through its Flow Cytometry Resource Center on September 15, 2008. The University installed a Becton Dickinson FACS Aria-II, chosen primarily for its broad range of lasers and detectors, and for the University's prior experience and satisfaction with other Becton Dickinson cytometry instrumentation. The unit installed is equipped with five lasers (355, 405, 488, 561, 640 nm), with capacity for an additional two lasers, and 17 detectors, and offers improved aerosol containment over earlier models. Such containment is recommended for work with human cells and other potentially infectious materials. In March 2009, the University relocated the instrument into newly renovated space, designed specifically to support biosafety level- 2 (BSL-2) projects. Since the FACS Aria-II became operational in mid-September, many Rockefeller researchers have run sorts on the new instrument, including: Elaine Fuchs, Ralph Steinman, Emil Gotschlich, Shai Shaham, Bruce McEwen, Nathaniel Heintz, Jeffrey Friedman, Christian Munz, Charles Rice, Hermann Steller and Alexander Tarakhovskiy. More Rockefeller stem cell researchers are expected to begin using the new cell sorter in the coming months.

TRUDEAU INSTITUTE

Principal Investigator: Troy Randall

Supplemental Funding of Stem Cell-Related Research

Investigators at the Trudeau Institute study stem cells associated with the immune system and its response to infectious diseases. The NYSTEM award supplemented funding for two research projects. The first project examines the impact of aging on T-cell and T-cell progenitor function. Immunological memory is the basis for protection from infection following vaccination. Importantly, vaccine efficacy declines with increasing age, leaving older individuals more susceptible to infections that are normally preventable. Thus, understanding how aging impacts the function of memory helper T-cells is critical for designing effective vaccines. This laboratory's studies have shown that immunological memory generated during youth functions well into old age, while that generated later in life functions poorly. With NYSTEM support, it was found that aging defects are not dictated by the bone marrow stromal cell population, but rather are intrinsic to the naïve CD4 T-cell populations. Using a transgenic mouse model, it was also determined that the age of the host environment does not have a negative impact on the function of newly produced CD4 T-cells. The second project examines the interaction between hematopoietic cells and mesenchymal stem cells to understand how they form organized lymphoid tissues in response to inflammation. Inflammation induces mesenchymal stem cells to differentiate into stromal cells through several parallel mechanisms. A new mechanism was identified whereby lymphoid tissue

inducer cells in the lung promote differentiation of mesenchymal stem cells into stromal cells. The Trudeau Institute has a long history of studying and treating tuberculosis, and these new results show that infection with tuberculosis-causing mycobacteria leads to accumulation of progenitor cells in the lung, which can then generate new lymphoid tissue.

UNIVERSITY OF ROCHESTER

Principal Investigator: David Guzik

Research Supplements and High-Throughput Screening Instrumentation for Stem Cell Research

The University of Rochester (UR) Stem Cell and Regenerative Medicine Institute was founded in 2008 to integrate the thriving stem cell research community at UR. More than 40 faculty from 15 different departments are engaged in stem cell research, along with more than 35 research-track faculty and senior research fellows and more than 200 other staff. The range of existing stem cell research at UR enabled use of NYSTEM support to target efforts for achieving quantum jumps in the problems under study. To enrich stem cell research as broadly as possible, the funding was applied to analysis of multiple stem and progenitor cell populations and addressed a wide range of questions. NYSTEM support also made possible the establishment of a high-throughput screening facility to facilitate small molecule drug discovery. NYSTEM funds were highly successful in accelerating qualitative advances in understanding stem cell biology and stem cell medicine. Examples of these discoveries include: (1) research in the central nervous system, on mesenchymal stem cells (MSCs) and on stem cells of the *Drosophila* gut revealed shared mechanisms that integrate cell division, differentiation, oxidative stress and pathways by which signaling molecules normally modulate precursor cell function. This work brings researchers closer to an understanding of the most fundamental rules that govern precursor cell function in health and disease; (2) molecular research on neurogenesis in the songbird brain has revealed common principles that appear to regulate normal stem cell function and also play important roles in the biology of brain tumors; (3) work on drug discovery is revealing new compounds and regulatory mechanisms that enable selective targeting of leukemia stem cells and has identified a drug already in clinical use with the novel property of enhancing MSC function. The former findings are being tested as a new strategy for treating cancer, and the latter are being pursued as a means of enhancing fracture repair; and (4) researchers developed a technique of noninvasively imaging transplanted stem cells of such sensitivity that now as few as 500 labeled stem cells may be tracked using clinically relevant magnetic resonance imaging (MRI) systems. NYSTEM funding also led directly to multiple new collaborations, several successful grant applications and a diverse range of manuscripts currently in preparation.

WEILL CORNELL MEDICAL COLLEGE

Principal Investigator: Harry Lander

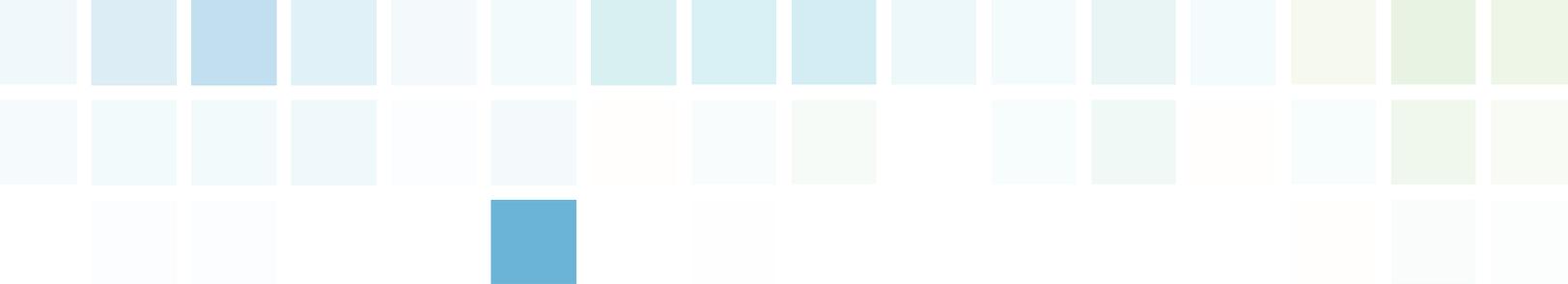
Echocardiography and Stem Cell Physiology Core Facilities, Specialized Training Programs and Supplemental Funding for Stem Cell Research

The NYSTEM award funded nine supplemental projects, one training award and two shared equipment/core facility programs at Weill Cornell Medical College. The supplemental projects comprised studies on cancer, lung disease caused by smoking, brain disorders such as Alzheimer's disease and cardio-

vascular disease. NYSTEM funding allowed substantial progress to be attained by these research groups. For example, as a result of NYSTEM supplemental funding, a National Institutes of Health (NIH)-funded study comparing smokers versus nonsmokers for expression of a major signaling pathway was extended to include a comparison of smokers with chronic occlusive pulmonary disease (COPD) versus healthy smokers. Results from these studies will likely shed light on the disease processes by which COPD arises and may help identify strategies to treat the condition. Funding of the shared equipment core for small animal echocardiography was critical for fully assessing the effects of stem cell manipulation in animal models of disease. High-resolution ultrasound technology offers a strategy to characterize changes in structure over time in the living organism and to define the physiologic consequences of experimental genetic engineering in a high-throughput fashion, as well as providing an interrogation technique that is rapid and efficient. In the cardiovascular and neurologic systems, ultrasound can generate information about the structure and function of the heart, brain and associated and peripheral blood vessels. Access to this core is critical to the study of cardiovascular and neuronal diseases. The training aspect of the award allowed Dr. Elizabeth Ross to acquire capabilities leading to translation of previous findings and experience with mouse ES cells into hESC studies, directly resulting in an NIH grant application. Clearly, the NYSTEM award was of enormous benefit to stem cell research at Weill Cornell Medical College specifically, and New York State in general. The faculty at Weill Cornell is appreciative of the opportunities presented by the award and expects to leverage the funds to yield a multi-year return on the investment.



Vice Chair David Hohn, M.D.



NYSTEM Awards: Appendix II Publications and Patents

Publications Resulting From NYSTEM Institutional Development Awards

In January 2008, the first NYSTEM awards were made to 25 New York State institutions to increase their capacity to engage in stem cell research. Of those 25 awards, 17 provided funding for research activities totaling \$6.1 million. In an environment where four or more years of research may be required to produce a single publication, NYSTEM support has already contributed to 13 papers published or in press as of March 31, 2009 (1-13), representing research from 10 supported investigators at five institutions. Highlights include work from Dr. Lorenz Studer's group at Sloan-Kettering Institute published in *Nature Biotechnology* that greatly improved the efficiency of converting hESCs and human iPS cells into neural cells (1); and results of a collaboration between Drs. Andrew Yen and Michael Kotlikoff at Cornell University, published in *Proceedings of the National Academy of Sciences*, identifying cardiovascular precursor cells in the neonatal heart. (2)

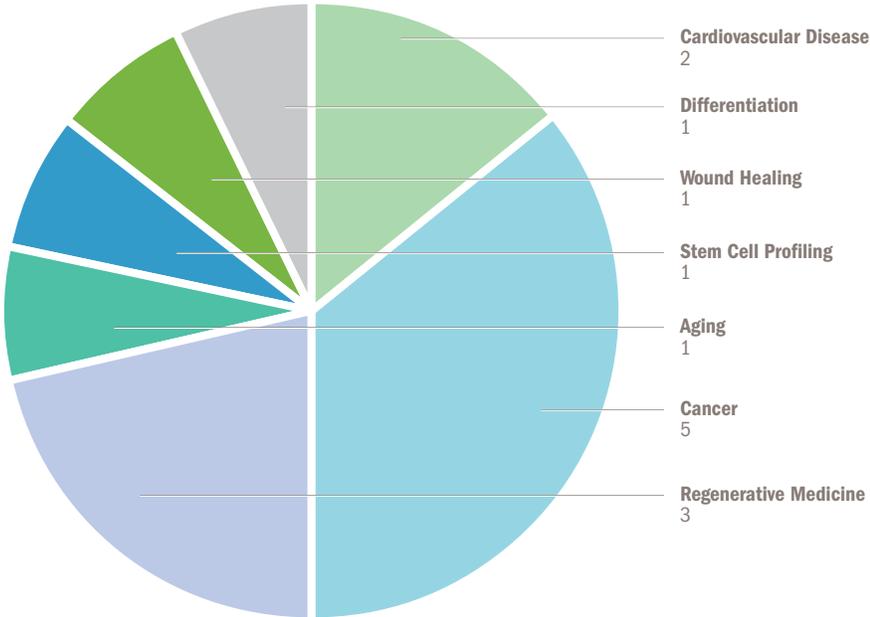
Other NYSTEM-supported findings include:

- The first successful spermatogonial stem cell transplantation for generation of transgenic dogs, an important model for human disease (Dr. Andrew Travis, Cornell University) (3)
- Pravastatin induces cell division of resting heart muscle cells, thereby improving heart function (Drs. John Canty and Thomas Cimato, SUNY at Buffalo) (4)
- Damage to skin cells produces a homing signal for a stem cell population involved in wound healing (Dr. Ira Cohen, SUNY at Stony Brook) (5)
- Comparing ES with mesenchymal stem cells shows that loss of pluripotency correlates with expression of fewer Wnt-signaling molecules (Dr. Hsien-Yu Wang, SUNY at Stony Brook) (6)
- Retinoic acid, a chemotherapeutic agent, works in conjunction with a B vitamin to induce differentiation of certain cancer cells (Dr. Andrew Yen, Cornell University) (7)
- Aging does not reduce the ability of bone marrow stem cells to generate functional immune cells (Drs. Laura Haynes and Susan Swain, Trudeau Institute) (8)
- Primitive endoderm formation is the result of cell movement, adhesion and selective apoptosis in the inner cell mass (Dr. Hadjantonakis, Sloan-Kettering Institute) (9)

Bibliography

1. Chambers, S. M., C. A. Fasano, E. P. Papapetrou, M. Tomishima, M. Sadelain, and **L. Studer**. 2009. Highly efficient neural conversion of human ES and iPS cells by dual inhibition of SMAD signaling. *Nat Biotechnol* **27**:275-80.
2. Eaton, S. M., A. C. Maue, **S. L. Swain**, and **L. Haynes**. 2008. Bone marrow precursor cells from aged mice generate CD4 T cells that function well in primary and memory responses. *J Immunol* **181**:4825-31.
3. Kauss, M. A., G. Reiterer, R. P. Bunaciu, and **A. Yen**. 2008. Human myeloblastic leukemia cells (HL-60) express a membrane receptor for estrogen that signals and modulates retinoic acid-induced cell differentiation. *Exp Cell Res* **314**:2999-3006.
4. Kim, Y., D. Turner, J. Nelson, I. Dobrinski, M. McEntee, and **A. J. Travis**. 2008. Production of donor-derived sperm after spermatogonial stem cell transplantation in the dog. *Reproduction* **136**:823-31.
5. Okoye, U. C., C. C. Malbon, and **H. Y. Wang**. 2008. Wnt and frizzled RNA expression in human mesenchymal and embryonic (H7) stem cells. *J Mol Signal* **3**:16.
6. Plusa, B., A. Piliszek, S. Frankenberg, J. Artus, and **A. K. Hadjantonakis**. 2008. Distinct sequential cell behaviours direct primitive endoderm formation in the mouse blastocyst. *Development* **135**:3081-91.
7. Potapova, I. A., **I. S. Cohen**, and S. V. Doronin. 2009. Apoptotic endothelial cells demonstrate increased adhesiveness for human mesenchymal stem cells. *J Cell Physiol* **219**:23-30.
8. Reiterer, G., R. P. Bunaciu, J. L. Smith, and **A. Yen**. 2008. Inhibiting the platelet-derived growth factor receptor increases signs of retinoic acid syndrome in myeloid-differentiated HL-60 cells. *FEBS Lett* **582**:2508-14.
9. Shen, M., and **A. Yen**. 2008. c-Cbl interacts with CD38 and promotes retinoic acid-induced differentiation and G0 arrest of human myeloblastic leukemia cells. *Cancer Res* **68**:8761-9.
10. Shen, M., and **A. Yen**. 2009. Nicotinamide cooperates with retinoic acid and 1,25-dihydroxyvitamin D(3) to regulate cell differentiation and cell cycle arrest of human myeloblastic leukemia cells. *Oncology* **76**:91-100.
11. Smith, J., R. P. Bunaciu, G. Reiterer, D. Coder, T. George, M. Asaly, and **A. Yen**. 2009. Retinoic acid induces nuclear accumulation of Raf1 during differentiation of HL-60 cells. *Exp Cell Res* **315**: 2241-8.
12. Suzuki, G., V. Iyer, T. Cimato, and **J. M. Canty, Jr**. 2009. Pravastatin improves function in hibernating myocardium by mobilizing CD133+ and cKit+ bone marrow progenitor cells and promoting myocytes to re-enter the growth phase of the cardiac cell cycle. *Circ Res* **104**:255-64, 10p following 264.
13. Tallini, Y. N., K. S. Greene, M. Craven, A. Spealman, M. Breitbach, J. Smith, P. J. Fisher, M. Steffey, M. Hesse, R. M. Doran, A. Woods, B. Singh, **A. Yen**, B. K. Fleischmann, and **M. I. Kotlikoff**. 2009. c-kit expression identifies cardiovascular precursors in the neonatal heart. *Proc Natl Acad Sci U S A* **106**:1808-13.

Distribution of Publications



NYSTEM Awards: Appendix III Awards Approved by the Funding Committee

Institutional Development Awards – RFA Issued in SFY 2007-2008*

CONTRACT TERM – APRIL 1, 2008 THROUGH MARCH 31, 2009

Contract Number	Contract Amount	Principal Investigator	Institution
C023041	\$ 150,899	Currie, Brian P.	Montefiore Medical Center
C023042	\$ 997,382	Lander, Harry M.	Weill Medical College of Cornell
C023043*	\$ 606,422	Tramosch, Kenneth M.	Research Foundation of SUNY – Buffalo
C023044*	\$ 380,933	Spector, David L.	Cold Spring Harbor Laboratory
C023045*	\$ 198,000	Josephson, Ira R.	Research Foundation of CUNY – City College
C023046*	\$ 768,426	Young, Michael W.	Rockefeller University
C023047	\$ 101,457	Randall, Troy D.	Trudeau Institute, Inc.
C023048	\$ 155,980	Henderson, Ann H.	Research Foundation of CUNY – Hunter
C023049	\$ 553,586	Stein, Daniel P.	New York University School of Medicine
C023050*	\$ 1,000,000	Nikitin, Alexander Yu.	Cornell University
C023051	\$ 999,933	Shamoon, Harry	Albert Einstein College of Medicine of Yeshiva University
C023052*	\$ 215,718	Hintze, Thomas H.	New York Medical College
C023053*	\$ 871,000	Brink, Peter R.	Research Foundation of SUNY – Stony Brook
C023054	\$ 504,809	Hen, René	Research Foundation for Mental Hygiene, Inc. – NYS Psychiatric Institute
C023055*	\$ 1,000,000	Goldman, James E.	The Trustees of Columbia University in the City of New York
C023056*	\$ 1,000,000	Guzick, David S.	University of Rochester School of Medicine
C023057	\$ 419,442	Gudkov, Andrei	Roswell Park Cancer Institute
C023058*	\$ 999,715	Lehmann, Ruth E.	New York University School of Medicine
C023059	\$ 196,581	Feuer, Gerold	Research Foundation of SUNY – Upstate Medical University
C023060	\$ 192,267	Teitelman, Gladys	Research Foundation of SUNY – Downstate Medical University
C023061	\$ 1,000,000	Vunjak-Novakovic, Gordana	The Trustees of Columbia University in the City of New York
C023062*	\$ 1,000,000	Lemischka, Ihor R.	Mount Sinai School of Medicine
C023063*	\$ 100,000	Sell, Stewart	Ordway Research Institute, Inc.
C023064	\$ 1,000,000	Studer, Lorenz	Sloan Kettering Institute for Cancer Research
C023065*	\$ 100,000	Levon, Kalle M.J.	Polytechnic University
	<u>\$14,512,550</u>		

*Indicates a request for a no cost extension to the contract term

*Planning Grants for Emerging Opportunities
and Consortia Development for Stem Cell Research*

CONTRACT TERM – NOVEMBER 1, 2008 THROUGH OCTOBER 31, 2009

Contract Number	Contract Amount	Principal Investigator	Project Title	Institution
C023888	\$ 120,000	Bouhassira, Eric	New York Blood Disease Consortium	Albert Einstein College of Medicine of Yeshiva University
C023889	\$ 76,800	Henn, Fritz A.	Planning Collaborative Research Between Cold Spring Harbor Laboratory, Stony Brook School of Medicine and Brookhaven National Laboratory	Brookhaven National Laboratory
C023890	\$ 118,920	Stewart, David J.	Cold Spring Harbor Stem Cell Training Program	Cold Spring Harbor Laboratory
C023891	\$ 119,960	Vunjak-Novakovic, Gordana	Molecular, Genetic and Biophysical Regulation of Human Stem Cells for Medical Impact	The Trustees of Columbia University in the City of New York
C023892	\$ 120,000	Goldman, James E.	Stem Cell Biology: Novel Insights into and Therapeutic Treatment of Human Disease	The Trustees of Columbia University Medical Center in the City of New York
C023893	\$ 120,000	Nikitin, Alexander Yu.	Stem Cells, Microenvironment and Cancer	Cornell University
C023894	\$ 118,180	Gupta, Sanjeev	Liver Cell Transplantation	Montefiore Medical Center
C023895	\$ 120,000	Lemischka, Ihor	System Biology and Stem Cells: An Integrated, Multidisciplinary Strategy	Mount Sinai School of Medicine
C023897	\$ 85,409	Sell, Stewart	Stem Cells and Aging Consortium	Ordway Research Institute
C023898	\$ 120,000	Temple, Sally	Retinal Stem Cell Consortium	Regenerative Research Foundation
C023896	\$ 119,705	Hintze, Thomas H.	Translational Cardiovascular Stem Cell Consortium	New York Medical College
C023899	\$ 120,000	Gudkov, Andrei	Pharmacological Targeting of Stem Cells	Health Research, Inc. – Roswell Park Cancer Institute
C023900	\$ 119,797	Solomon, Susan L.	Design of a New York Stem Cell Foundation Stem Cell Screening Lab	The New York Stem Cell Foundation
C023901	\$ 119,948	Fossett, James	New York Institute for Ethical Stem Cell Research	Research Foundation of SUNY – University at Albany
C023902	\$ 120,000	Batuman, Olcay	SUNY Downstate Vascular Stem Cell Genome Consortium	Research Foundation of SUNY – Downstate Medical Center
C023903	\$ 118,800	Cohen, Ira S.	Mechanical and Electrical Regeneration of Heart with Stem Cells	Research Foundation of SUNY – Stony Brook
C023904	\$ 76,751	Noble, Mark D.	Clinical Translation in Stem Cell Medicine: From Principles to Practice	University of Rochester
C023905	\$ 117,127	Beal, M. Flint	Development of a Safe and Effective Stem Cell-Based Therapy of Parkinson's Disease	Weill Medical College of Cornell University
	<u>\$2,031,397</u>			

Equipment/Instrumentation for Stem Cell Research

CONTRACT TERM - JANUARY 1, 2009 THROUGH DECEMBER 31, 2009

Contract Number	Contract Amount	Principal Investigator	Project Title	Institution
C024173	\$481,738 <u>\$481,738</u>	Spector, David	Confocal Microscope	Cold Spring Harbor Laboratory

Shared Facilities/Resources for Stem Cell Research

CONTRACT TERM - JANUARY 1, 2009 THROUGH DECEMBER 31, 2012

Contract Number	Contract Amount	Principal Investigator	Project Title	Institution
C024172	\$ 5,993,889	Bouhassira, Eric	Einstein Comprehensive Human Pluripotent Stem Cell Center	Albert Einstein College of Medicine of Yeshiva University
C024174	\$ 1,629,645	Schimenti, John	Cornell Mammalian Cell Reprogramming Core	Cornell University
C024175	\$ 2,707,911	Lorenz, Studer	The Sloan-Kettering Institute Stem Cell Research Facility	Memorial Sloan-Kettering Cancer Center
C024176	\$ 3,812,528	Lemischka, Ihor	NYSTEM Shared Facilities/Resources for Stem Cell Research Grant for the Human Embryonic Stem (hES) Cell Core at Mount Sinai School of Medicine (MSSM)	Mount Sinai School of Medicine
C024178	\$ 5,136,655	Feuer, Gerold	Development/Operation of Shared Facilities/Resources: Expansion of the Humanized SCID Mouse Center and Stem Cell Processing Lab	The Research Foundation of SUNY – Upstate Medical University
C024179	\$ 5,861,451	Noggle, Scott	Shared Facility for Derivation, Distribution and Translational Research with Human Pluripotent Stem Cells	New York Stem Cell Foundation
C024180	\$ 4,864,705	Brivanlou, Ali	Shared Facilities and Resources for Stem Cell Research at the Rockefeller University and Weill Cornell Medical College	Rockefeller University
	<u>\$31,930,053</u>			

*Investigator-Initiated Research Projects
(IIRP) in Stem Cell Research*

CONTRACT TERM – JANUARY 1, 2009 THROUGH DECEMBER 31, 2011

Contract Number	Contract Amount	Principal Investigator	Project Title	Institution
C024313	\$ 1,080,000	Aaronson, Stuart	Role of Wnt Signaling in Sarcomas Initiated from Human Mesenchymal Stem/Progenitor Cells	Mount Sinai School of Medicine
C024314	\$ 1,080,000	Aguirre-Ghiso, Julio	Plasticity of Head and Neck Cancer Initiating Cells	Mount Sinai School of Medicine
C024315	\$ 1,055,958	Andreadis, Stelios	High-Throughput, Real Time Dynamic Monitoring of Stem Cell Differentiation	Research Foundation of SUNY – Buffalo
C024316	\$ 1,010,490	Andreadis, Stelios	Hair Follicle Stem Cells for Cardiovascular Tissue Regeneration	Research Foundation of SUNY – Buffalo
C024317	\$ 1,080,000	Bahou, Wadie	Therapy of Hemophilia A Using Megakaryocyte-Targeted Stem Cell Delivery	Research Foundation of SUNY – Stony Brook
C024318	\$ 1,080,000	Baron, Margaret	Red Blood Cell Development in Differentiating Embryonic Stem (ES) and Induced Pluripotent Stem (iPS) Cells	Mount Sinai School of Medicine
C024319	\$ 1,050,872	Bohmann, Dirk	Nrf2 as a Regulator of Stem and Progenitor Cell Function	University of Rochester
C024320	\$ 1,001,308	Chen, Di	Canonical Wnt Signaling Controls Mesenchymal Stem Cell Differentiation	University of Rochester
C024321	\$ 1,080,000	Christiano, Angela M.	Stem Cell Therapy for Epidermolysis Bullosa	The Trustees of Columbia University in the City of New York
C024322	\$ 933,689	Dailey, Lisa	Functional Identification of Transcriptional Determinants of the ES Cell State and Early Lineage Commitment	New York University
C024323	\$ 1,079,996	Enikolopov, Grigori	Regulation of the Life Cycle of Adult Neural Stem Cells	Cold Spring Harbor Laboratory
C024324	\$ 1,080,000	Ferland, Russell	The Role of Filamins and Formins in Stem Cell Development	Rensselaer Polytechnic Institute
C024325	\$ 1,069,779	Feuer, Gerold	HTLV Infection of Human Hematopoietic Stem Cells: Induction of Novel Lymphoma in Humanized SCID Mice	Research Foundation of SUNY – Upstate Medical Center
C024326	\$ 900,000	Fishell, Gordon	The Directed Differentiation of Embryonic Stem Cells into Specific Cortical Interneuron Subtypes	New York University
C024327	\$ 1,080,000	Fishman, Glenn	Embryonic Stem Cell Derived Cardiac Conduction System Cells	New York University
C024328	\$ 591,420	Ghazizadeh, Soosan	Immune Responses to Allogeneic Stem Cell Transplantation	Research Foundation of SUNY – Stony Brook

*Investigator-Initiated Research Projects
(IIRP) in Stem Cell Research (Continued)*

CONTRACT TERM – JANUARY 1, 2009 THROUGH DECEMBER 31, 2011

Contract Number	Contract Amount	Principal Investigator	Project Title	Institution
C024329	\$ 1,002,632	Goff, Stephen	Characterization of the Retroviral Silencing Machinery in Embryonic Stem Cells	The Trustees of Columbia University in the City of New York
C024330	\$ 1,080,000	Hen, Rene	Contribution of Hipocampal Stem Cells to the Action of Antidepressants: From Mice to Men	Research Foundation for Mental Hygiene, Inc. – NYS Psychiatric Institute
C024331	\$ 1,049,875	Jacobs, Christopher Rae	Mechanosensitive Primary Cilia in Osteogenic Differentiation of Stem Cells Due to Loading	The Trustees of Columbia University in the City of New York
C024332	\$ 1,080,000	Jessell, Thomas	The Molecular Logic of Embryonic Stem Cell Derived Motor Neurons	The Trustees of Columbia University in the City of New York
C024333	\$ 1,007,280	Lacy, Elizabeth	Mechanisms by Which Nuclear Pore Composition Regulates Stem/Progenitor Differentiation	Memorial Sloan-Kettering Cancer Center
C024334	\$ 1,080,000	Linhardt, Robert	Stem Cell Glycomics in Microarray Format	Rensselaer Polytechnic Institute
C024335	\$ 719,890	Lu, Helen	Stem Cell-Mediated Integrative Rotator Cuff Repair	The Trustees of Columbia University in the City of New York
C024336	\$ 1,079,985	Mao, Jeremy	Functional Synovial Joint Replacement by Stem Cell Homing	The Trustees of Columbia University In the City of New York
C024337	\$ 1,040,161	Morse, Randall	Epigenetic Control of Murine Neural Stem Cell Self-Renewal and Differentiation Mediated by Bmi-1	Health Research, Inc. – Wadsworth Center
C024338	\$ 358,500	Calvi, Laura	Therapeutic Stimulation of the Hematopoietic Stem Cell Niche	University of Rochester
[C024339	\$ 820,841	Ovitt, Catherine]	<i>Award Declined</i>	<i>University of Rochester</i>
C024340	\$ 1,049,110	Palis, James	Erythroid Precursor Self-Renewal	University of Rochester
C024341	\$ 1,053,458	Perera, Tarique	The Role of Endogenous Hippocampal Stem Cells in Treating Non-Human Primate Models of Depression and Anxiety	The Trustees of Columbia University in the City of New York
C024342	\$ 1,080,000	Pessin, Jeffrey	Role of Adipocyte Progenitor Cells in Adipose Tissue Turnover and Obesity	Albert Einstein College of Medicine of Yeshiva University
C024343	\$ 1,069,157	Rogler, Charles	Roles of MicroRNAs in Hepatic Stem Cell Differentiation	Albert Einstein College of Medicine of Yeshiva University
C024344	\$ 1,023,800	Rosen, Michael	Stem Cell-Based Platform Therapy for Lethal Cardiac Arrhythmias	The Trustees of Columbia University in the City of New York
C024345	\$ 1,080,000	Ross, Margaret Elizabeth	Neuronal Specification, Expansion and Self-Renewal of hESC Derived Precursors	Weill Medical College of Cornell University

(Continued)

*Investigator-Initiated Research Projects
(IIRP) in Stem Cell Research (Continued)*

CONTRACT TERM – JANUARY 1, 2009 THROUGH DECEMBER 31, 2011

Contract Number	Contract Amount	Principal Investigator	Project Title	Institution
C024346	\$ 1,080,000	Roy-Chowdhury, Jayanta	Amelioration of Hepatic Metabolic Defects by Stem Cell-Derived Human Hepatocytes	Albert Einstein College of Medicine of Yeshiva University
C024347	\$ 1,070,964	Rutishauser, Urs	Use of Polysialic Acid to Improve Integration of ES-Derived Cells into the Brain	Memorial Sloan-Kettering Cancer Center
C024348	\$ 1,080,000	Schildkraut, Carl	Differential Regulation of DNA Replication During Neural Lineage Specification in Human ES Cells and Human iPS Cells of Yeshiva	Albert Einstein College of Medicine University
C024349	\$ 1,048,941	Snoeck, Hans-Willem	Generation of Thymic Epithelial Cells from Embryonic Stem Cells	Mount Sinai School of Medicine
C024350	\$ 961,499	Steidl, Ulrich	Transcriptional Control of Cancer Stem Cells in Acute Myeloid Leukemia	Albert Einstein College of Medicine of Yeshiva University
C024351	\$ 1,022,300	Suzuki, Gen	Modification of Resident Cardiac Stem Cells by Circulating Hematopoietic Stem Cells in Ischemic Cardiomyopathy	Research Foundation of SUNY – Buffalo
C024352	\$ 1,049,036	Temple, Sally	Changes in RNA Synthesis and Timing of Cortical Development	Regenerative Research Foundation
C024353	\$ 1,002,134	Terracio, Louis	Skeletal Muscle Derived Stem Cells	New York University
C024354	\$ 1,033,979	Tumbar, Tudorita	Control of Hair Follicle Stem Cell Proliferation and Epithelial Skin Tumorigenesis by Concerted RUNX1 and CDKN1a Action	Cornell University
C024355	\$ 589,686	Tzanakakis, Emmanouhl	Scalable Expansion and Directed Differentiation of Human Embryonic Stem Cells to Pancreatic Progeny	Research Foundation of SUNY – Buffalo
C024356	\$ 813,496	Wang, Hsien-yu	Novel Chimeric Frizzled as Tools to Program hESC Differentiation	Research Foundation of SUNY – Stony Brook
C024357	\$ 756,732	Zhang, Xinping	Gli2 Activated MSCs for Bone Regeneration and Reconstruction	University of Rochester
C024358	\$ 1,080,000	Zhou, Ming-Ming	Molecular Deciphering of Stem Cell Epigenetic Silencing	Mount Sinai School of Medicine
C024964	\$ 1,079,790	Jordan, Craig	Therapeutic Targeting of Leukemia Stem Cells	University of Rochester
	<u>\$45,775,917</u>			

*Innovative, Developmental and Exploratory Activities
(IDEA) in Stem Cell Research*

CONTRACT TERM - JANUARY 1, 2009 THROUGH DECEMBER 31, 2010

Contract Number	Contract Amount	Principal Investigator	Project Title	Institution
C024281	\$ 240,000	Anderson, Stewart	Deriving Forebrain Interneurons from ES Cells by Inducible Expression of Lhx6	Weill Medical College of Cornell University
C024282	\$ 240,000	Neelamegham, Sriram	Glycan Engineering of Stem Cells	Research Foundation of SUNY – Buffalo
C024283	\$ 240,000	Awad, Hani	Modulating Stem Cell Differentiation Using Novel Allograft Scaffolds for Cartilage Repair	University of Rochester
C024284	\$ 240,000	Bach, Erika	Elucidating the Role of the JAK/STAT Pathway in Stem Cell Self-Renewal	New York University
C024285	\$ 240,000	Bernstein, Emily	Investigation of Polycomb-Mediated Chromatin Alterations During Embryonic Stem Cell Differentiation	Mount Sinai School of Medicine
C024286	\$ 240,000	Brown, Anthony	Regulation of Mammary Stem Cells by Wnt Signaling	Weill Medical College of Cornell University
C024287	\$ 240,000	Doetsch, Fiona	Molecular Profiling and Differentiation Potential of Purified Adult Neural Stem Cell Lineages	The Trustees of Columbia University in the City of New York
C024288	\$ 240,000	Fraser, Stuart	Copper Transporter-1, Ctr1: A Critical Regulator of Embryonic Stem Cell Differentiation	Mount Sinai School of Medicine
C024289	\$ 240,000	Hadjantonakis, Anna-Katerina	Characterization of Extraembryonic Endoderm (XEN) Cells	Memorial Sloan-Kettering Cancer Center
C024290	\$ 240,000	Hazelrigg, Tulle	Maintenance of Adult Germ Stem Cells by Histone Modification	The Trustees of Columbia University in the City of New York
C024291	\$ 240,000	Hernando, Eva	Study of the Cell-of-Origin and Cancer Stem Cells in Melanoma	New York University
C024292	\$ 240,000	Huss, Wendy	High Transporter and Aldehyde Dehydrogenase Activity in Benign and Cancer Prostatic Stem Cells	Health Research, Inc. – Roswell Park Cancer Institute
C024293	\$ 239,787	Kottman, Andreas	Does Graded Expression of Shh by Dopaminergic Neurons of the Mesencephalon Influence the Maintenance and Differentiation of Neural Stem Cells of the Adult Subventricular Zone?	The Trustees of Columbia University in the City of New York
C024294	\$ 240,000	Kumar, Mukesh	Manipulation of Stem Cells for Treating Viral Hepatitis of Yeshiva	Albert Einstein College of Medicine University
C024295	\$ 240,000	Laufer, Edward	Differentiation of ES Cells into Adrenocortical Lineages	The Trustees of Columbia University in the City of New York

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*Innovative, Developmental and Exploratory Activities
(IDEA) in Stem Cell Research (Continued)*

CONTRACT TERM – JANUARY 1, 2009 THROUGH DECEMBER 31, 2010

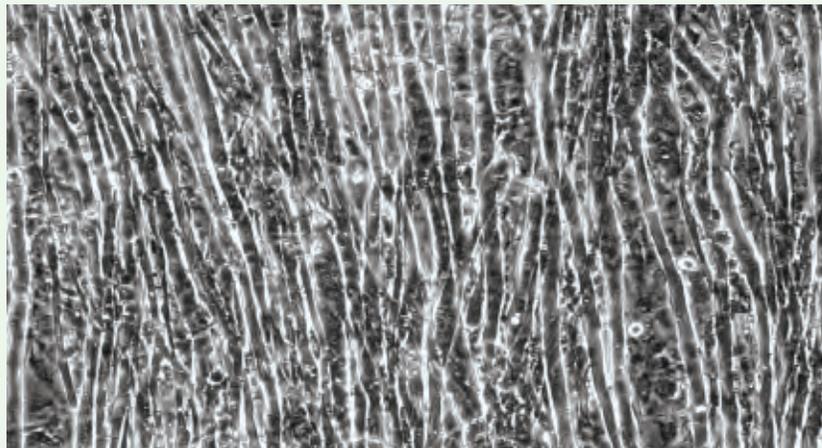
Contract Number	Contract Amount	Principal Investigator	Project Title	Institution
C024296	\$ 240,000	Levy, David	Derivation and Characterization of Dendritic Cell Lineages From Hematopoietic Stem Cells	New York University
C024297	\$ 240,000	Lopez, Maria	Hematopoiesis of the Gut Immune System and Gut Immunity in Immunodeficient Mice	Health Research, Inc. – Wadsworth Center
C024298	\$ 240,000	Lowry, Natalia Abramova	Novel Surface Markers for Neural Stem Cell Enrichment	Regenerative Research Foundation
C024299	\$ 240,000	Manley, James	Alternative Splicing of mRNA Precursor Links to Pluripotency of Human Embryonic Stem Cells	The Trustees of Columbia University in the City of New York
C024300	\$ 239,628	Matushansky, Igor	Using Mesenchymal Stem Cells to Deliver Tumor Environment Activated Quantum-Dot Drug Conjugates Targeting Cancer Bulk and Cancer Stem Cells	The Trustees of Columbia University in the City of New York
C024301	\$ 240,000	Nance, Jeremy	Establishing the <i>C. elegans</i> Germline Stem Cell Niche	New York University
C024302	\$ 224,103	Ortiz, Benjamin	TCR α Locus Control Region Activity During In Vitro Stem Cell Differentiation: Application Towards Improving Lentiviral Gene Therapy Vectors	Research Foundation of CUNY – Hunter College
C024303	\$ 240,000	Owens, David	Epithelial Progenitor Cells as Targets for Cutaneous Neoplasia	The Trustees of Columbia University in the City of New York
C024304	\$ 240,000	Raghavan, Srikala	Exploring the Function of MicroRNAs in Epidermal Stem Cells	The Trustees of Columbia University in the City of New York
C024305	\$ 240,000	Hylander, Bonnie	Role of Cancer Stem Cells in Resistance to Targeted Therapy and Tumor Recurrence	Health Research, Inc. – Roswell Park Cancer Institute
C024306	\$ 240,000	Steidl, Ulrich	Identifying Epigenomic Determinants of Hematopoietic Stem Cells Commitment	Albert Einstein College of Medicine of Yeshiva University
C024307	\$ 232,678	Tall, Gregory	Deciphering the Role of Mammalian Ric-8 Proteins in Stem Cell (Asymmetric) Division	University of Rochester
C024308	\$ 239,134	Timmermans, Marja	The Role of the Chromatin-Remodeling Factor HIRA in Recruitment of Polycomb Complexes and Regulation of Pluripotency	Cold Spring Harbor Laboratory
C024309	\$ 227,452	Wallenfang, Matthew	Transplantation of Adult Male Germline Stem Cells of <i>Drosophila Melanogaster</i>	Barnard College

(Continued)

*Innovative, Developmental and Exploratory Activities
(IDEA) in Stem Cell Research (Continued)*

CONTRACT TERM - JANUARY 1, 2009 THROUGH DECEMBER 31, 2010

Contract Number	Contract Amount	Principal Investigator	Project Title	Institution
C024310	\$ 240,000	Xu, Lei	Identifying the Stem Cells in Malignant Melanoma	University of Rochester
C024311	\$ 240,000	Yan, Jun	Identification and Characterization of Endothelial Niche Factor(s) That Stimulates Self-Renewal and Neurogenesis of Neural Stem Cells (NSCs)	Regenerative Research Foundation
C024312	\$ 240,000	Zhao, Jihe	Transcriptional Control of Stem Cell Metastasis of Breast Cancer	Albany Medical College
	<u>\$7,642,782</u>			



SKELETAL PROSTHESIS

Muscle stem cells are aligned in the direction of streaked collagen and begin to fuse into myotubes.

Image Source: Dr. Louis Terracio, New York University

Project Title: Skeletal Muscle Derived Stem Cells

*Targeted Investigation of Induced Pluripotent Stem Cells
and Other Derivation Approaches
Investigator-Initiated Research Projects
(IIRP) in Stem Cell Research*

CONTRACT TERM - JANUARY 1, 2009 THROUGH DECEMBER 31, 2011

Contract Number	Contract Amount	Principal Investigator	Project Title	Institution
C024402	\$ 1,080,000	Abeliovich, Asa	Human iPS Cell-Based Models for Neurodegeneration	The Trustees of Columbia University in the City of New York
C024403	\$ 1,080,000	Abeliovich, Asa	Intracellular Signaling Cascades in iPS Reprogramming	The Trustees of Columbia University in the City of New York
C024404	\$ 1,080,000	Bishop, David	The Congenital Erythropietic Porphyria: Evaluation of iPS Cells for Murine and Human Therapy	Mount Sinai School of Medicine
C024405	\$ 971,489	Bouhassira, Eric	Characterization of iPS Using a Novel High Throughput Replication Timing Assay	Albert Einstein College of Medicine of Yeshiva University
C024406	\$ 1,080,000	Feng, Jian	Using Improved iPS Derivation and Differentiation Methods to Study Parkinson's Disease	The Research Foundation of SUNY – Buffalo
C024407	\$ 1,079,937	Gelb, Bruce	Noonan Syndrome and Related Disorders: Stem Cells and RAS Pathway Signaling	Mount Sinai School of Medicine
C024408	\$ 1,080,000	Ghaffari, Saghi	Using a Novel Regulator of hES Cell Pluripotency in Generating iPS Cells	Mount Sinai School of Medicine
C024409	\$ 1,047,974	Goldman, Steven	iPS Cell Therapy for Diseases of Adult Acquired Demyelination	University of Rochester Medical Center
C024410	\$ 1,080,000	Lemischka, Ihor	Analyses of Pluripotency in Reprogrammed Induced Pluripotent Stem Cells	Mount Sinai School of Medicine
C024411	\$ 1,076,309	Moll, Ute	In Vivo Assessment of Tumorigenic Potential of iPS-Inducing Transcription Factors in Mouse Models	The Research Foundation of SUNY – Stony Brook
C024412	\$ 1,080,000	Sadelain, Michel	Exploring Human iPS Cells for the Hematopoietic and Genetic Correction of B-Thalassemia	Memorial Sloan-Kettering Cancer Center
C024413	\$ 1,068,031	Tabar, Viviane	In Vivo Function of Human iPS Derived Neural Precursors	Memorial Sloan-Kettering Cancer Center
C024414	\$ 1,000,000	Temple, Sally	Human RPE and Induced Pluripotent Stem Cells for Parkinson's Disease	Regenerative Research Foundation
C024415	\$ 1,080,000	Wichterle, Hynek	Human iPS Cells as a Model to Study ALS Pathogenesis	The Trustees of Columbia University in the City of New York
	<u>\$14,883,740</u>			

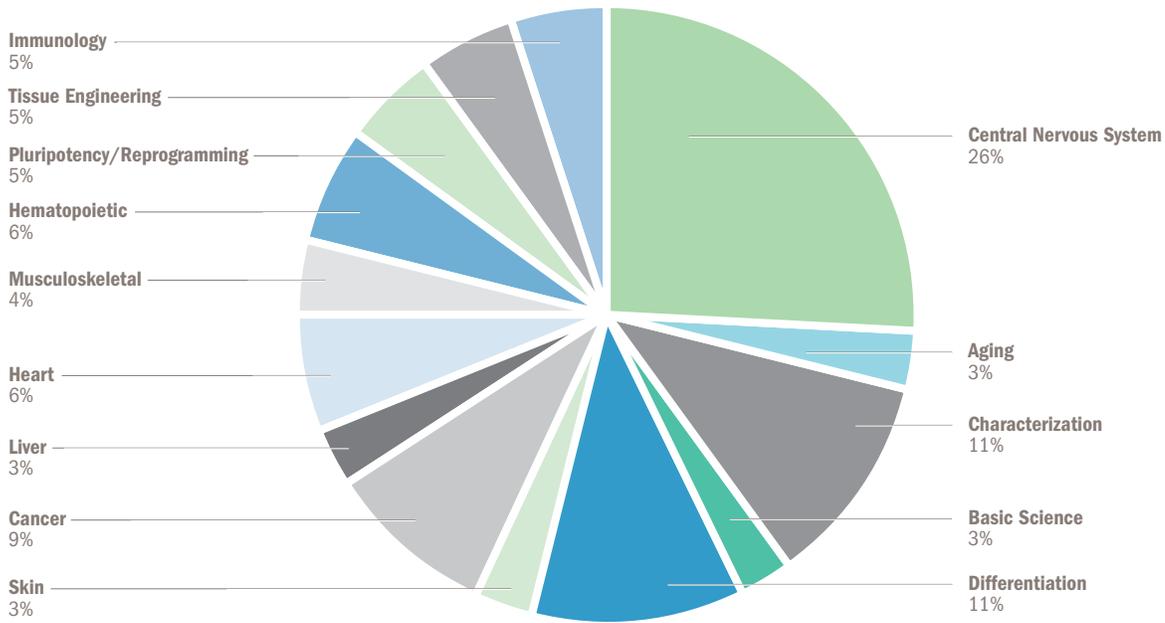
*Targeted Investigation of Induced Pluripotent Stem Cells
and Other Derivation Approaches
Innovative, Developmental and Exploratory Activities
(IDEA) in Stem Cell Research*

CONTRACT TERM - JANUARY 1, 2009 THROUGH DECEMBER 31, 2011

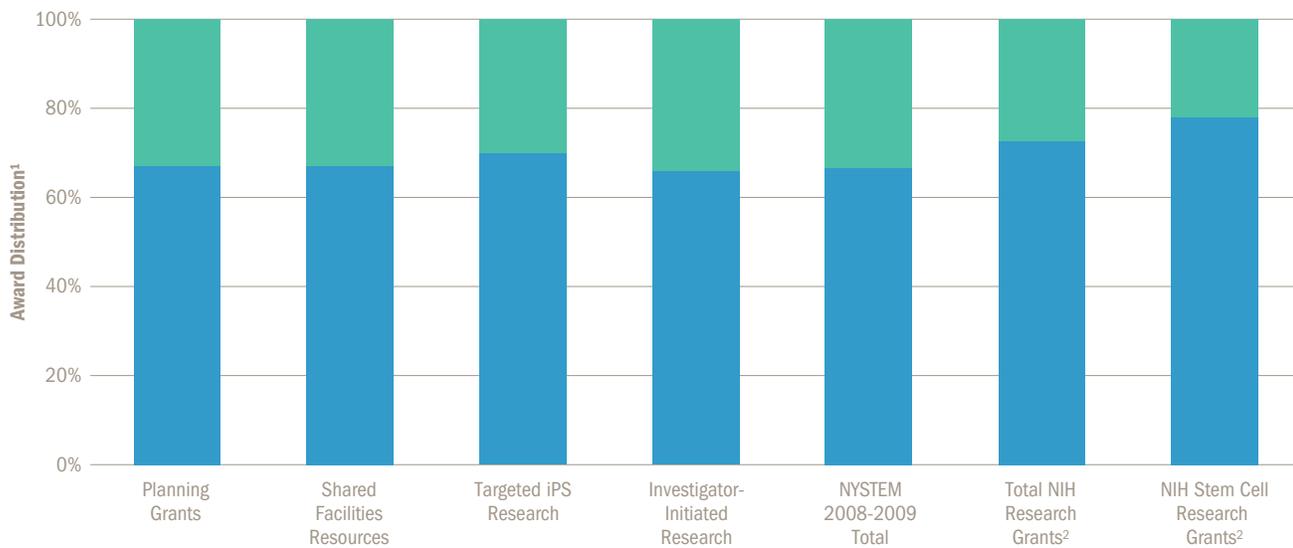
Contract Number	Contract Amount	Principal Investigator	Project Title	Institution
C024396	\$ 240,000	Evans, Todd	Stem Cell Activity and Human Longevity	Albert Einstein College of Medicine of Yeshiva University (Transfer to Weill Medical College)
C024397	\$ 240,000	Lu, Jonathan	The Development of Patient-Specific Cardiomyocytes Differentiated from Induced Pluripotent Stem Cells (iPS Cells) as a Cellular Model for Molecular, Cellular, and Electrophysiologic Characterization of Long QT Syndrome	The Trustees of Columbia University in the City of New York
C024398	\$ 240,000	Pruitt, Steven	Replication Errors in Hematopoietic Stem Cells	Health Research, Inc. – Roswell Park Cancer Institute
C024399	\$ 240,000	Salero, Enrique	Human Retinal Pigment Epithelial Multipotent Cells	Regenerative Research Foundation
C024400	\$ 228,840	Fortier, Lisa	Genetic Background and Efficient Generation of Induced Pluripotent Stem (iPS) Cells	Cornell University
C024401	\$ 240,000	Wang, Timothy	Induced Pluripotent Stem (iPS) Cells Derived from Mesenchymal Stem Cells	The Trustees of Columbia University in the City of New York
	<u>\$1,428,840</u>			

Distribution of Funded Investigator-Initiated and Targeted Research by Focus Area

TOTAL \$69,731,279



Geographic Distribution of Grants Awarded in 2008-2009

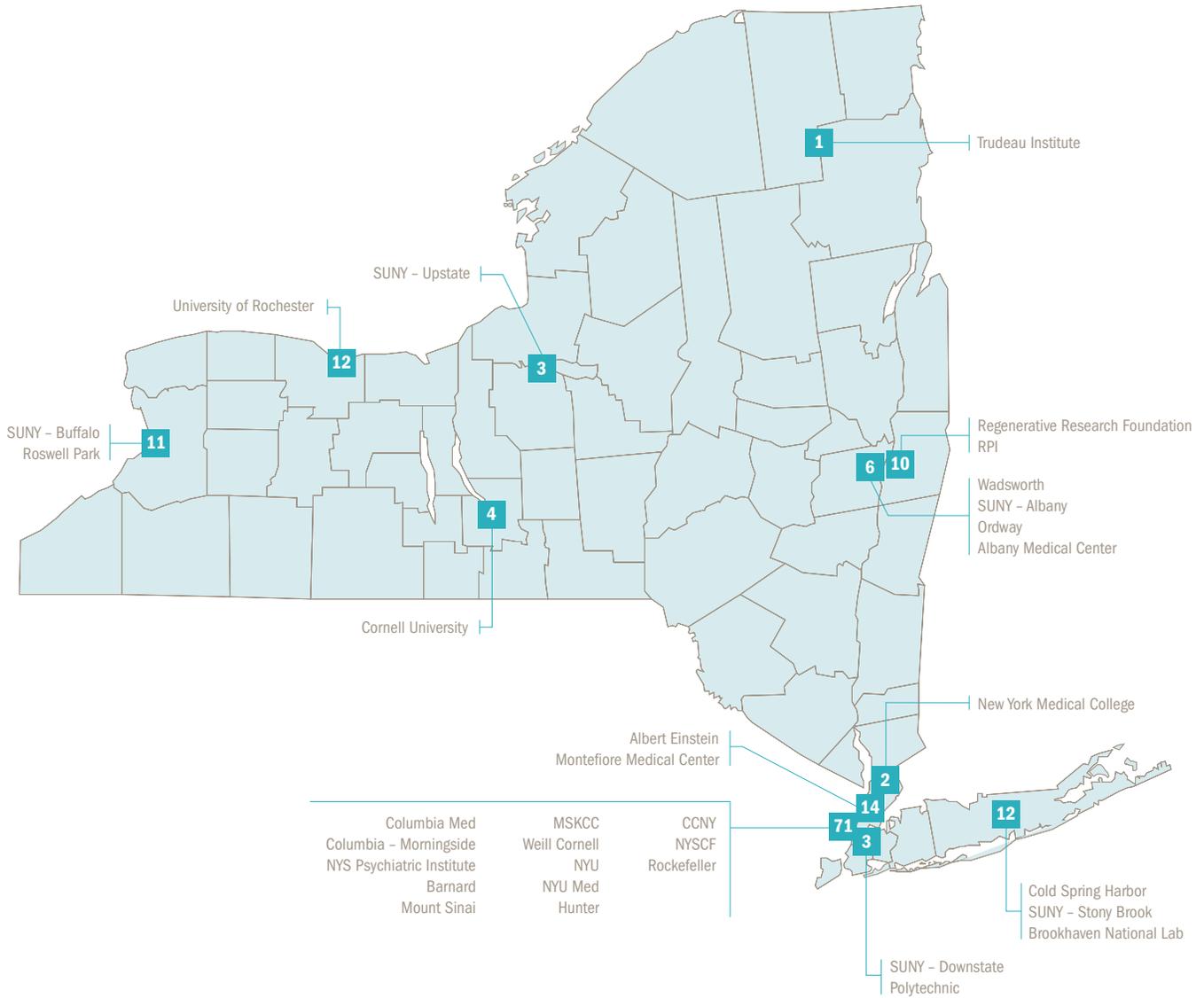


¹Downstate: Westchester County, Five Boroughs and Long Island; Upstate: the remainder of New York State

²Source: NIH 2007 award data

*Planning Grants for Emerging Opportunities
and Consortia Development for Stem Cell Research*

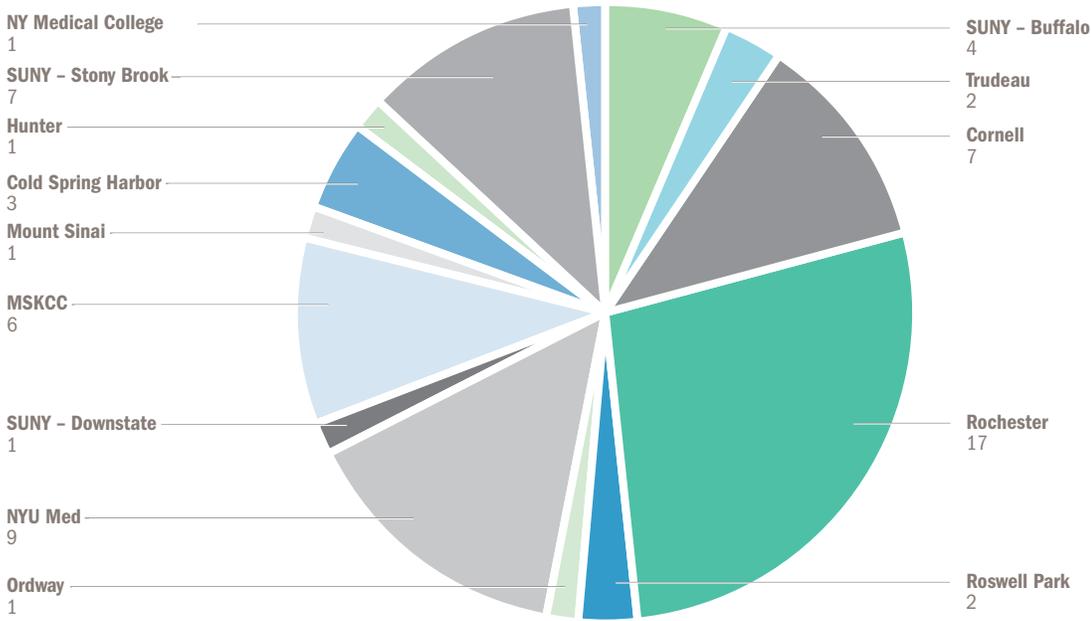
CONTRACT TERM - NOVEMBER 1, 2008 THROUGH OCTOBER 31, 2009



Numbers inside squares represent the total number of awards from all funding mechanisms approved for the institutions at that location.

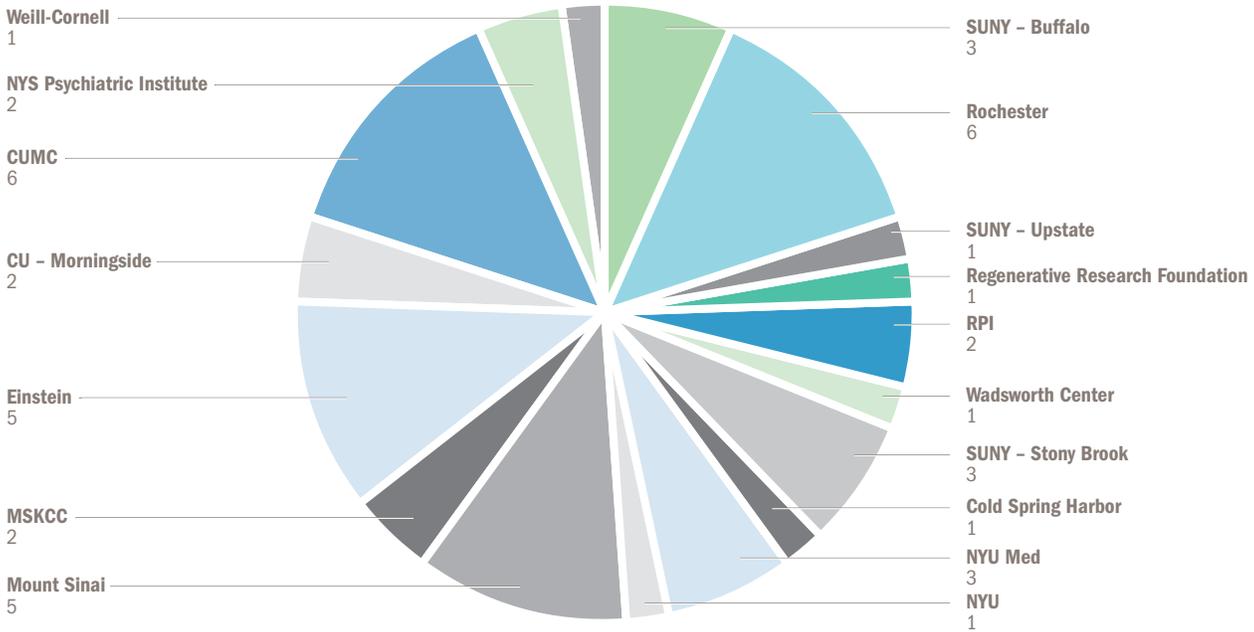
Institutional Development Awards – Individual Investigators Funded Through Bridge or Supplemental Funding at Each Institution

APPROVED JANUARY 2008



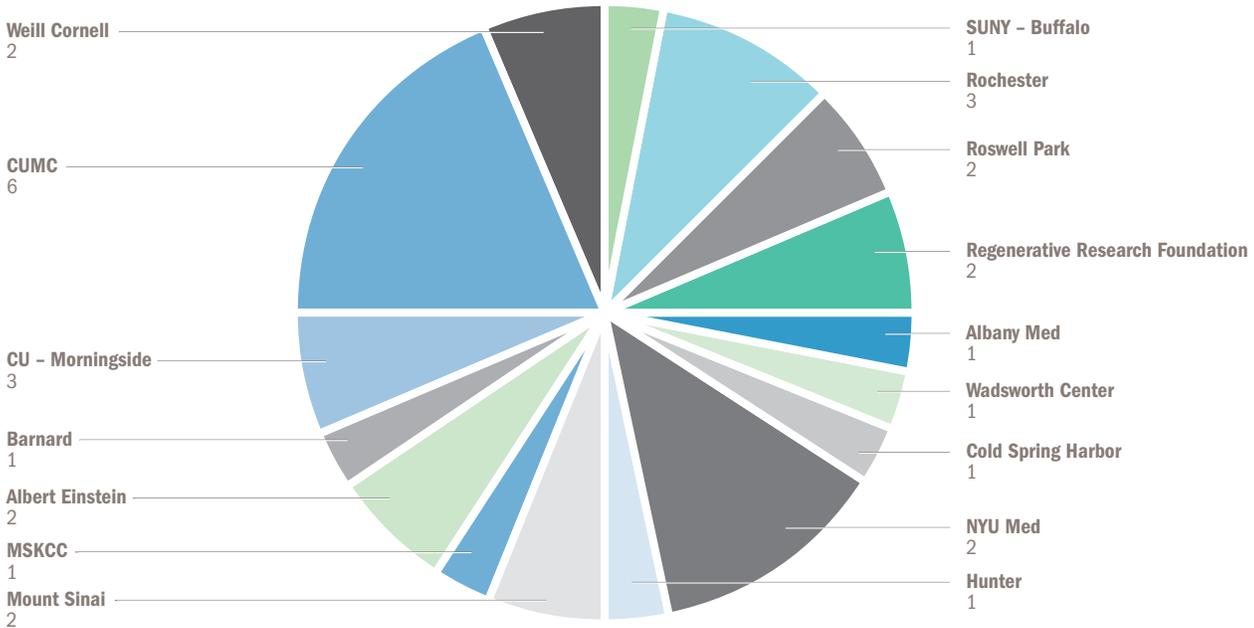
Investigator-Initiated Research Projects (IIRP) in Stem Cell Research Awards – Investigators Funded per Institution

APPROVED DECEMBER 2008



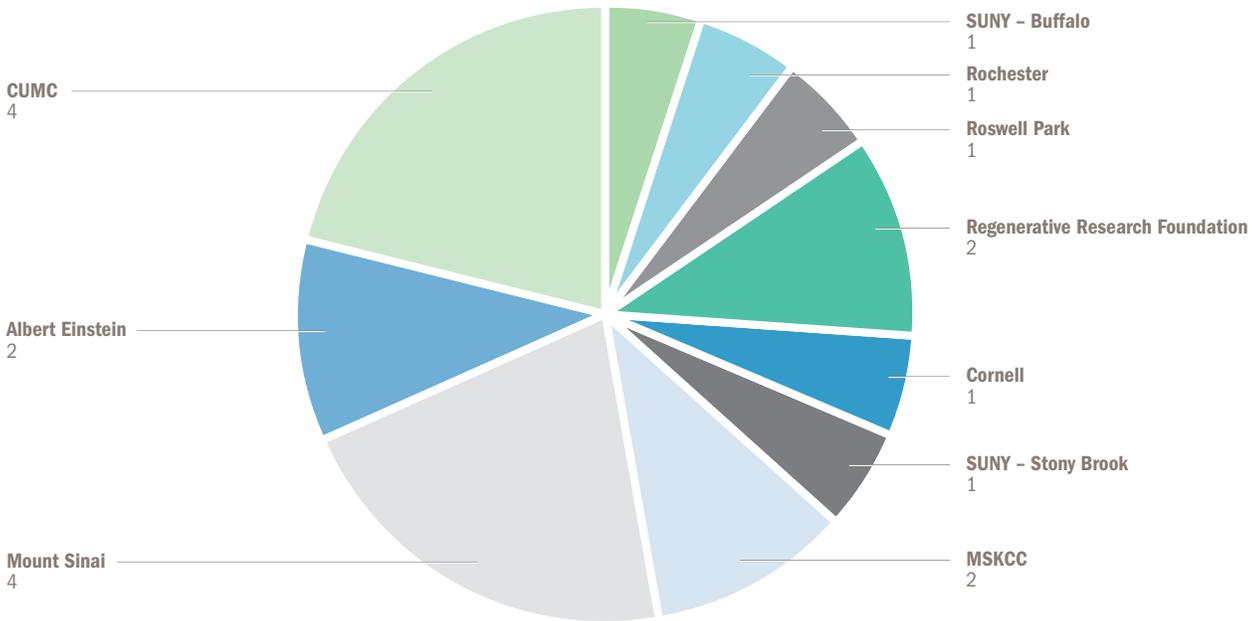
*Innovative, Developmental and Exploratory Activities (IDEA)
in Stem Cell Research Awards – Investigators Funded per Institution*

APPROVED DECEMBER 2008



*Targeted Investigation of Induced Pluripotent Stem Cells and
Other Derivation Approaches – Investigators Funded per Institution*

APPROVED DECEMBER 2008





Empire State Stem Cell Board
NYSTEM/New York State Stem Cell Science
Wadsworth Center, New York State Department of Health
Box 509, Empire State Plaza
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State of New York
David A. Paterson, Governor
Department of Health
Richard F. Daines, M.D., Commissioner