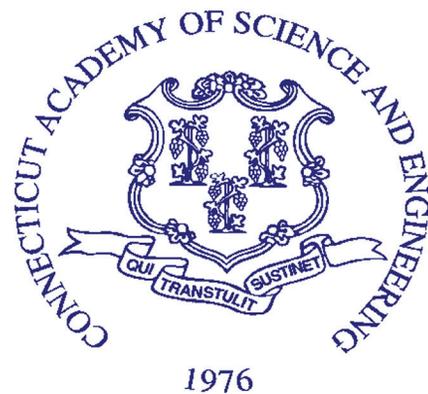


**CONNECTICUT STEM CELL
RESEARCH PROGRAM
ACCOMPLISHMENTS**

FEBRUARY 2013

A REPORT BY

**THE CONNECTICUT
ACADEMY OF SCIENCE
AND ENGINEERING**



FOR

THE

**CONNECTICUT DEPARTMENT OF
PUBLIC HEALTH**

AND

CONNECTICUT INNOVATIONS

CONNECTICUT STEM CELL RESEARCH PROGRAM ACCOMPLISHMENTS

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ORIGIN OF INQUIRY: THE CONNECTICUT DEPARTMENT OF
PUBLIC HEALTH
CONNECTICUT INNOVATIONS

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This study was initiated at the request of the Connecticut Department of Public Health and Connecticut Innovations, Inc., on September 3, 2012. The project was conducted by an Academy Study Committee with the support of Study Manager Maria Borowski, MA. The content of this report lies within the province of the Academy's Biomedical Research Technical Board. Martha Sherman, the Academy's Managing Editor, edited the report. The report is hereby released with the approval of the Academy Council.

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EXECUTIVE SUMMARY

Stem cell research has the potential for significant benefits to human health. Scientists are exploring the use of stem cells for the growth and development of tissues and organs, developing new drugs and studying genetic diseases.

In 2005, Connecticut joined California and New Jersey as the only states to allocate public funds for stem cell research ([Public Act 05-149](#)). The Connecticut Stem Cell Research Program was appropriated \$20M for grants-in-aid for embryonic or human adult stem cell research. Additionally, this act allocated a total of \$80M to be used over the course of seven years (2008-2015) from the state's Tobacco Settlement Fund to support additional stem cell research. The stated purpose of the program is to "support the advancement of embryonic and/or human adult stem cell research in Connecticut." While the political and scientific environments of today are quite changed from when the act was adopted, the need for funding stem cell research has not diminished.

At year six of the Connecticut Stem Cell Research Program, the Connecticut Department of Public Health (DPH) and Connecticut Innovations (CI) asked the Connecticut Academy of Science and Engineering (CASE) to conduct an analysis of the accomplishments of the program, and to report findings and recommendations to DPH and CI.

CONNECTICUT STEM CELL RESEARCH PROGRAM

DPH is tasked with overseeing the Connecticut Stem Cell Research Program and CI provides administrative support. The act enabling the program also mandated the creation of the Stem Cell Research Advisory Committee (SCRAC) that is chaired by the DPH commissioner. The committee is comprised of experts from the fields of stem cell research, bioethics, embryology, genetics, cellular biology and business or financial investments. A Stem Cell Research Peer Review Committee also was mandated for the purpose of reviewing all grant applications for scientific and ethical merit and to make recommendations on grant recipients to the SCRAC.

Five types of proposals have been accepted for funding consideration over the course of the program, each with its own criteria and award amounts:

- Core Facilities
- Established Investigators
- Group Projects, including Disease Directed Collaboration Group Projects (*starting in 2011*)
- Hybrid (*in 2006 only*)
- Seed

REVIEW OF ACCOMPLISHMENTS

To assess the stem cell research accomplishments, stem cell research leaders at each institution awarded grant funding completed a questionnaire and were interviewed, leaders of the Connecticut stem cell core facilities completed a questionnaire, and every Principal Investigator (PI) with grant funding awarded up through 2011 was asked to complete a survey. Notably, for the PI survey, a 98% response rate was achieved.

Institutions and PIs reported on both direct accomplishments (i.e., an accomplishment as a result of a project funded by the program) and indirect accomplishments (i.e., an accomplishment where a resource, such as a core facility, was used for research or results from a funded project allowed researchers to acquire additional funding to continue research from other sources). Therefore, the accomplishments and outcomes cited in this report represent both direct and indirect accomplishments cited by the institutions and PIs surveyed for this study. Additionally, since accomplishments and outcomes of project research are for the most part reported following completion of a project, it is important to note that at the time of this study, the end of 2012, only 52% of grants awarded funding through 2011 had been completed.

To better assess the accomplishments and outcomes of the Connecticut Stem Cell Research Program moving forward, it is suggested that metrics for grant reporting and program review should be established and used on an ongoing basis. Grant reporting and program review requirements should be provided in advance to institutions and PIs, with such requirements memorialized in grant assistance agreements. This will assure consistent information is collected and reported for analysis.

In summary, accomplishments include

- leveraging funding received from the Connecticut Stem Cell Research Program to pursue/obtain additional funding for research from other sources;
- contributions and research outcomes in the form of published papers, new methodologies, etc. and direct achievements including patent applications, new technology, etc.;
- creation of new jobs in the state of Connecticut to support stem cell research; and
- development of partnerships and collaborations.

Major accomplishments of the Connecticut Stem Cell Research Program include

- 129 grants awarded through 2012, for a total of \$68.8M of the \$100M allocated for the program. The program's award funding is on target, with the remainder of the original \$100M allocation planned to be awarded by 2015.
- Leveraging the funding received from the Connecticut Stem Cell Research Program to pursue/obtain additional funds for stem cell research from other sources. Many of the PIs responded that as a result of the funding they received, they were able to pursue and/or obtain funding to either continue their research or expand their research endeavors. PIs reported the following related to additional funding from other sources:

CONNECTICUT STEM CELL RESEARCH PROGRAM ACCOMPLISHMENTS EXECUTIVE SUMMARY

- o 9 awards were funded and completed. Grant funding sources included the National Institutes of Health (NIH, 2 awards), corporations (3), private foundations (1), and other sources (3).
- o 33 awards are currently being funded with research in-process. Grant award sources include NIH (17), private foundations (7), public foundations (2), Department of Defense (1), National Science Foundation (1), corporations (1) and other sources (4).
- o 21 proposals were awaiting a funding decision as of November 2012. Possible grant sources include NIH (12), private foundations (6), public foundations (1), and other sources (2).

It is noted that stem cell research institutional leaders, consistent with the results of the PI survey, reported Connecticut Stem Cell Research Program funding awarded to their institutions has been a contributing factor in leveraging stem cell research funding from other sources.

Also, one of the SCRAC's objectives, as specified in the program's enabling legislation, was to develop a donated funds program to encourage funding from sources other than state appropriations. In the early years of the program, the development of a donated funds program to leverage state funding was explored. Initial findings were that potential funders would most likely require projects to be funded in an area of their interest. Under this assumption, unless the Connecticut Stem Cell Research Program was prepared to commit funds to the areas of interest of potential donors, the success of a donated funds program would probably be unlikely. In the future, perhaps creative approaches to seeking donated funds to match Connecticut's funding could be explored.

The universities receiving Connecticut Stem Cell Research Program funding (University of Connecticut (UConn)/University of Connecticut Health Center (UCHC), Wesleyan University, and Yale University) reported total grant awards for the period of 2007 - 2012 for the following: total institutional scientific research funding; total stem cell research funding; Connecticut Stem Cell Research Program funding; and stem cell research funding from other sources. Table 1-ES shows that for this period, Connecticut Stem Cell Research Program funding was 19.2% of total stem cell research funding awarded to these institutions. This indicates significant leveraging of Connecticut Stem Cell Research Program funding. This table also shows the scale of total stem cell research funding to total scientific research funding, and total Connecticut Stem Cell Research Program funding to total scientific research funding.

TABLE 1-ES: CONNECTICUT STEM CELL RESEARCH PROGRAM FUNDING AS COMPARED TO TOTAL STEM CELL RESEARCH FUNDING AND TOTAL SCIENTIFIC RESEARCH FUNDING (2007 – 2012)

		Period: 2007 - 2012					
	Total Institutional Scientific Research Funding	Stem Cell Research Funding			Total Stem Cell Research Funding v. Total Institutional Scientific Research Funding (%)	CT Stem Cell Research Funding v. Total Scientific Research Funding (%)	CT Stem Cell Research Funding v. Total Stem Cell Research Funding (%)
		Total Stem Cell Research Funding	CT Stem Cell Research Funding	Stem Cell Research - Other Sources			
UConn/UCHC*	\$1,258,300,000	\$120,558,813	\$32,663,813	\$ 87,895,000	9.58%	2.60%	27.09%
Wesleyan	\$ 33,481,000	\$ 4,518,278	\$ 2,128,278	\$ 2,390,000	13.50%	6.36%	47.10%
Yale	\$3,429,403,018	\$233,373,746	\$34,054,964	\$199,318,782	6.81%	0.99%	14.59%
Total	\$4,721,184,018	\$358,450,837	\$68,847,055	\$289,603,782	7.59%	1.46%	19.21%

* Note: UConn/UCHC Connecticut Stem Cell Research Funding includes one grant award of \$1,290,499 to Chondrogenics in 2011 (\$831,185 of this award is sub-contracted to UCHC)

- Contributions and research outcomes: These outcomes included creation of stem cell-related companies, articles published in peer-reviewed journals, contributions to the general knowledge base in stem cell biology, and the development of outreach and training programs.
 - o PI's reported 166 peer-reviewed articles and journals, 59 new research methods, 45 new theories, 24 new laboratories, 55 novel human stem cell lines, 17 new practices (clinical, tools, instruments, procedures/techniques), 9 patent applications, 7 software/databases, and 2 licenses, as outcomes of Connecticut Stem Cell Research Program funding.
 - o Wesleyan continues to progress on a stem cell-based therapy for Temporal Lobe Epilepsy, as reported at the Biosciences and Economy Forum for the General Assembly Appropriations Committee on September 24, 2012. Additionally, Wesleyan's stem cell research leadership reported 18 peer-reviewed research papers/journal articles published and one new stem cell line. Three of the five stem cell-dedicated laboratories at Wesleyan are funded by the Connecticut Stem Cell Research Program. Wesleyan's reported accomplishments/outcomes are those that can be attributed both directly and indirectly to the Connecticut Stem Cell Research Program.
 - o Yale stem cell research leadership reported 470 papers published, 192 invention disclosures, 132 patent applications, and 26 licenses obtained. Yale is researching the use of stem cells for treating Parkinson's disease; repairing damage of the central nervous system; building blood vessels to treat congenital heart defects; creating living, growing blood vessels from scratch; and rebuilding a heart. Yale Core Facilities have developed training classes to help support the researchers requesting stem cell lines. To date, approximately 300 Yale-affiliated scientists have been certified in stem cell culture, cell imaging and gene knockdown through the Yale Core Facilities. Yale's Stem Cell Research Center includes 12,776 square feet of laboratory and administrative space in the university's 120,000 square foot Amistad Building. Yale's reported accomplishments/outcomes are those that can be attributed both directly and indirectly to the Connecticut Stem Cell Research Program.
 - o UConn/UHC stem cell leadership reported the start-up of three companies; derivation of four stem cell lines with distribution to 227 recipients in the United States and worldwide; 150 publications, including journal articles, book chapters, public media and presentations; 15 training sessions on human embryonic stem cell (hESC) culture for 100 researchers and graduate students; and production of patient-specific induced pluripotent stem cells (iPSCs) using cutting-edge techniques that do not require any manipulation of human embryos. UConn noted in its 2013 Program Report Card for the General Assembly that recently published articles in medical literature cite progress toward treatment of patients with serious health issues, including promising results in cancer, multiple sclerosis, and severe periodontal diseases. UConn's reported accomplishments/outcomes are those that can be attributed both directly and indirectly to the Connecticut Stem Cell Research Program. The UConn Stem Cell Institute includes 7,600 square feet of laboratory, administrative and incubator space for stem cell research in the 120,000 square foot UHC Cell and Genome Sciences Building. It is noted that UConn/UHC's construction/renovation of the

building was dependent upon the establishment of the Connecticut Stem Cell Research Program.

o Core Facility Development

- ◇ Yale University established and maintains five state-of-the-art core laboratories that are located at Yale's Stem Cell Research Center in the Amistad Building, including: Human Embryonic Stem Cell (hESC) Core, Cell Imaging Core, Cell Manipulation Core, Genomics Core, and Fluorescence Activated Cell Sorting (FACS) Core. The cores offer key stem cell technologies to Yale stem cell researchers and stem cell laboratories at other institutions in Connecticut. The Core facility has been in operation since 2007 and includes 1,836 square feet of space. Since 2007, the Yale Core Facilities have been awarded \$5,300,000 in Core Facility grant funding from the Connecticut Stem Cell Research Program.
- ◇ The UConn Stem Cell Core facility at UCHC (UCHC Core Facility) that is shared with Wesleyan has been in operation since 2007. The Core Facility's 3,600 square foot lab space was renovated in 2010, and is located in UCHC's Cell and Genome Sciences Building. Since 2007, the UCHC Core Facility has been awarded \$5,650,000 in Core Facility grant funding from the Connecticut Stem Cell Research Program.
- Creation of new jobs in the state of Connecticut to support stem cell research. Over the funded years of the program, employment and staffing have steadily increased. It was reported in the PI survey response that 222 researchers and support staff supporting their Connecticut stem cell research grant were new to the stem cell research field; and that approximately 92 staff hired to support the grant awards relocated to Connecticut.
- Development of partnerships and collaborations. PIs reported 15 separate collaborations that were made possible directly from this funding, and when asked about the importance of collaborations, 82 respondents classified it as either very important or important.
- Activities such as retreats, workshops and conferences are held annually by the stem cell research community in Connecticut. Connecticut also sponsors StemCONN, a major biennial stem cell conference that is attended by stem cell experts from Connecticut, other states and countries. These types of activities provide a collaborative environment for stem cell research in Connecticut.
- Based on information provided through this study's surveys, interviews and questionnaires, there were no royalty payments due to the state in accordance with provisions of the grant award assistance agreements.

In summary, the Connecticut Stem Cell Research Grant Program has increased stem cell research capacity in the state of Connecticut, established stem cell core facilities, attracted research professionals to the state, and created numerous occupation opportunities along the continuum of scientific research-related employment.

As noted in this report, basic science comprises most of the funded research grants. The accomplishments identified in this report illustrate that the program is poised to build on these

results and move toward clinical translation while maintaining basic research still needed in this emerging field.

RECOMMENDATIONS

The following recommendations are offered for consideration regarding identifying and reporting on the accomplishments and performance of the Connecticut Stem Cell Research Program to assure accountability of the state's public investment in stem cell research. The recommendations encompass the following: Annual Program Review, Program Administration, Core Facilities, and Funding.

- 1. Annual Program Review:** Conduct an annual review of the Connecticut Stem Cell Research Program to assess
 - program operations, including administrative operations, and proposal peer review and the selection award process;
 - progress of all grantees awarded funding for in-process and completed projects; and
 - overall accomplishments and benefits to the institutions that receive Connecticut Stem Cell Research Program funding. Each institution should be asked to provide an annual report that identifies the overall accomplishments that resulted from Connecticut Stem Cell Research Program funding, including additional grant funding from other sources that can be attributed to the program, an update on recruitment and retention of stem cell-related faculty and staff, infrastructure improvements to support stem cell research, and a projection on the program's continuing benefits for the upcoming year.

The purpose of the annual review process would be to

- adapt award criteria to position the program based on lessons learned, past achievements, and scientific developments;
- adjust funding levels between the types of grant funding to capitalize on current needs for basic, translational and clinical research;
- address funding gaps and redirect funds where needed to support research goals;
- benchmark the program with similar programs in other areas of the country to support decisions including those related to the investment and management of public funds used for scientific research; and
- identify best practices for management and investment of public funds in support of stem cell research.

The requirements of the current grantee Annual Technical and Fiscal Progress Report, and Final Report should be modified to include annual review process metrics and data, to be determined, for grantees and their institutions. This requirement should be included in the annual Request for Proposals and in grantee assistance agreements.

It is suggested that the reporting metrics and data be developed in consultation with the stem cell research leadership of the institutions/companies that receive program

funding. Based on initial lessons learned from this review, suggestions for future metrics for reporting on accomplishments and outcomes include the following:

- Institutional Research Funding: research award funding as presented in this report should continue to be reported annually so as to clearly show the leveraging of state funding with that from other sources, and to show the scale of stem cell research in relation to total scientific research being conducted at participating universities and companies. Financial reporting terminology and periods should be identified and used by all reporting institutions so that consistent and accurate information can be used for analysis.
 - Staffing and Job Creation: Suggested data to be reported include the following:
 - o Project staffing and jobs created should be reported on a full-time-equivalent basis
 - o Wages paid, which would be useful for conducting an economic impact analysis of the program in the future
 - o New staff relocating to Connecticut as a result of project funding
 - Training Programs: number and types of training programs provided, and the number of participants and where they are from
 - Accomplishments and Outcomes: Many research accomplishments and outcomes occur after the completion of a project, and therefore after a final project report is submitted by the PI. Therefore, consideration should be given to requiring ongoing annual reporting by PIs for grants that have been completed for as long as the program continues and is subject to regular review or for a period of time as determined, with this requirement being a condition of grantee assistance agreements.
2. **Program Administration:** Program staff designated to manage and oversee the Connecticut Stem Cell Research Program should continually seek to improve the administration of the program and bring uniformity to the grant funding procedures and annual reporting processes.

Staff would

- manage program operations;
- identify key high-level metrics for the annual review of program accomplishments and administrative performance, in consultation with the program's leadership, including the SCRAC, and the Peer Review Committee;
- manage the annual review process, including reporting to the SCRAC, state agencies, CGA, research institutions, and others as appropriate;
- establish relationships between states and/or institutions based on a mutual need for the sharing and reporting of common metrics in collaboration with stem cell researchers and institutional leaders; and
- research best practices for scientific research grant funding, economic development, and institutional practices and processes in collaboration with stem cell researchers and institutional leaders.

3. **Core Facilities:** Consistent with the Core Facilities award goals as described in the most recent Request for Proposals, the Core Facilities at the Yale Stem Cell Center and the Stem Cell Core at UCHC should continue to transition from a reliance on Connecticut Stem Cell Research Program funding to a self-sustaining enterprise serving a broader and deeper range of users, including researchers and labs from other institutions, businesses and entities within the state, regionally and nationally to further support both continued scientific progress in the stem cell field and economic development.

Connecticut's core facility administrators should

- assess user satisfaction with current core facility services and technology and identify services and technology that may be needed in the future;
 - increase collaborative activities between the leaders of the core facilities to ensure that future activities are explored and agreement reached on joint strategies to efficiently make these activities available, while respecting the need for each core facility to focus on approaches unique to their institution's strategic plan;
 - implement outreach plans to increase visibility and use of the facilities by researchers, students and educators, and the general public; and
 - seek to increase the share of core facility revenue from fee-based services and other grant funding sources.
4. **Funding:** Enact legislation to stabilize research funding to further strengthen the state's preeminence in the stem cell field for a sufficient period of time to enable research institutions and others receiving Connecticut Stem Cell Research Program funding to
- commit to expand infrastructure necessary for stem cell research;
 - increase the capacity of institutions to leverage funding from other sources; and
 - recruit and retain stem cell researchers and staff

It is suggested that the legislation provide for a multi-year (such as five years), rolling funded program that would require legislative action to terminate the program. Termination would only take effect following a trailer of the full funded period (i.e., in the case of a 5-year program, then at the end of the 5th year – so as to provide for a commitment of 5 years of funding prior to termination taking effect). Also, consideration should be given to including in the legislation a formula to determine the annual level of funding to be provided, such as with the first five years at a set level, with each subsequent year then being increased at a rate of "x%", or to provide the General Assembly with the option to increase such annual amount of funding by a to-be-determined inflation factor.

CONCLUDING REMARKS

An important aspect of the state's economic development strategy is to further strengthen the state's competitive position in scientific research and development through its support of biomedical and stem cell research, and expansion into genomics and personalized medicine, as evidenced by 2013 legislation proposed by the governor.

The state should consider establishing one entity responsible for administering the state's public investments in scientific research-related grant funding, including the existing biomedical and stem cell research programs as well as the proposed genomics research initiative, and others as may be determined. A centralized administrative structure would effect efficiencies in management, establish a source for scientific research policy advice, and bring uniformity to the grant funding procedures and annual reporting processes to assure accountability of public funding of the state's scientific research initiatives.