



Connecticut Innovations

Connecticut Bioscience Collaboration Program

Annual Report Submitted by

The Jackson Laboratory

for

The Jackson Laboratory for Genomic Medicine

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I. SUMMARY

Pursuant to the Bioscience Collaboration, Operating and Funding Agreement between Connecticut Innovations, Incorporated and The Jackson Laboratory dated January 5, 2012, this report summarizes the activities for the year ending on December 31, 2013.

The Jackson Laboratory (JAX) began 2013 in approximately 11,200 gross square feet (gsf) of leased space on the University of Connecticut Health Center (UCHC) campus. Since that time, JAX has acquired and renovated an additional 8,200 gsf of office, laboratory, and administrative space both on and off the UCHC campus to meet its accelerated recruitment needs.

JAX continues to move quickly to establish the new genomic medicine research institute in Connecticut, working in partnership with the state's Bioscience Connecticut initiative. The Laboratory has reached its milestones for facilities planning and has exceeded the target for job creation for 2013. New employees continue to work in temporary quarters at the UConn Health Center campus and collaborations are underway with Connecticut researchers, hospitals and insurance companies to advance genomics research and improve patient care.

II. EXPENDITURES OF THE GRANT FUNDS AND FINANCIAL COMMITMENTS MADE BY JAX [Section 11.3(a)]

Schedule of Research and Training Expenditures. A summary of direct and indirect expenditures for research and training as well as the net amount charged to the Connecticut Innovation Grant for the 2013 calendar year is attached as Appendix 1.

Schedule of Research Services and Production Expenditures. A summary of direct and indirect expenditures for research services and products is attached as Appendix 2. At this time we do not have any expenditure related to these services for the 2013 calendar year.

Summary of Grant Information (Schedule 2). A summary of 2013 grant funding received by quarter and listed according to research and training and research services and products, as well as funds to be carried to 2013, is attached as Appendix 3.

Summary of Commitments. A summary of operational and capital commitments for the 2013 calendar year is attached as Appendix 4.

Additional financial information will be provided by June 30, 2014.

III. ACTIVITIES AND PERFORMANCE OF JAX GENOMIC MEDICINE [Section 11.3 (3)]

(i) Number and Salary Level of Employees and Senior Scientists

We are pleased to report that JAX has met and exceeded all of the goals set for its 2013 Operating Metrics as proposed in the Business Plan submitted on December 30, 2011 (**Table 1**). These metrics include (a) number of employees employed by JAX in the preceding year; (b) number of senior scientists employed by JAX in the preceding year; and (c) compliance with the Average Annual Wage Obligation in the preceding year. Of the 79 employees hired by JAX Genomic Medicine (JGM) in 2013, 48 are senior scientists and 24 of them were residents of Connecticut before joining JGM.

Table 1. JGM 2013 Operating Metrics

FY 2013	Proposed	Regular Employees	Other Employees**	Total	% Goal Met
Number of Employees	63	69.8	9.0	78.8	125%
Number of Senior Scientists	19	41.8	6.0	47.8	252%
Average Annual Wage*	\$81,445	\$124,703		\$111,860	137%

*125% of the Connecticut average annual wage measured by "Quarterly Census of Employment and Wages (QCEW)".

**These positions include visiting scientist, scholars, graduate students, post-doctoral fellows and are mostly funded by scholarships or stipends that are different in nature from the typical wages; therefore, their compensations are excluded from the average salary calculation for the regular employees; but, are included in the "Total" calculation.

Faculty Recruitment. In 2013, JGM continued to recruit from a global network of top-level researchers, and the new genomics institute continued to attract the attention of accomplished and ambitious scientists. Top-level principal investigators are among the scientific staff already in place in Connecticut:

- Charles Lee PhD, Director, JGM.** Dr. Charles Lee was appointed as the director of The Jackson Laboratory for Genomic Medicine in Farmington, Conn., in August 2013. He received his PhD from the University of Alberta (Canada) and completed research fellowships at Cambridge University (England) and Harvard Medical School. He then joined the faculty of the Department of Pathology at Brigham and Women’s Hospital / Harvard Medical School, last serving as the director of the Molecular Genetic Research Unit, director of the Cytogenetics Core at the Dana Farber - Harvard Cancer Center and associate professor at Harvard Medical School. He is widely noted for his discovery that copy number variation (CNV) is widespread in the human genome and is often associated with disease susceptibility or resistance. This discovery and his subsequent research led to the development of tools which clinicians around the world use to make accurate diagnoses of genetically based disorders. Dr. Lee has received numerous accolades and awards including the 2008 Ho-Am Prize in Medicine and a Chen Global Investigator Award from the International Human Genome Organization. He is also an elected fellow of the American Association for the Advancement of Science. He has authored more than 130 scientific papers and has held advisory roles for numerous national organizations including the Food and Drug Administration, the National Human Genome Research Institute, the American Society of Human Genetics and the American College of Medical Genetics.
- Jacques Banchereau PhD, Professor and Director of Immunological Sciences.** Dr. Jacques Banchereau, an internationally prominent immunologist, joined the JAX faculty in July 2013. Prior to joining JAX, Dr. Banchereau served as director of the Baylor Institute for Immunology Research, as the Caruth Chair for Transplantation Immunology at the Baylor Research Institute in Dallas, Texas, and most recently was a senior leader at the global pharmaceutical company Hoffmann-La Roche serving as chief scientific officer of the Nutley, N.J. campus and as senior vice president and head of the inflammation and virology discovery and translational areas.

In his new role, Dr. Banchereau will focus on expanding the immunological research program at The Jackson Laboratory that was originally established by Nobel Laureate George Snell. Dr. Banchereau will expand the program across all three JAX

campuses, will lead the recruitment of new immunological investigators and will pursue areas of medical importance such as cancer immunobiology, autoimmunity and host responses to infectious diseases.

- **Reinhard Laubenbacher PhD, Professor, Computational Biology, JGM & UCHC Joint Faculty.** Dr. Laubenbacher is the first JGM faculty member appointed in collaboration with UCHC. He joined UCHC in May 2013 as visiting professor in the Department of Cell Biology and director of the Center for Quantitative Medicine. Prior to this appointment, he served as a professor at the Virginia Bioinformatics Institute and a professor in the Department of Mathematics at Virginia Tech since 2001. He was also an adjunct professor in the Department of Cancer Biology at Wake Forest University in Winston-Salem (NC) and affiliate faculty in the Virginia Tech Wake Forest University School of Biomedical Engineering and Sciences. In addition, Dr. Laubenbacher was professor of Mathematics at New Mexico State University. He has served as visiting faculty at Los Alamos National Laboratories, was a member of the Mathematical Science Research Institute at Berkeley in 1998, and was a visiting associate professor at Cornell University in 1990 and 1993. Dr. Laubenbacher's research focuses on the development of mathematical algorithms and their application to problems in systems biology with a particular focus on cancer systems biology, specifically in regard to the role that iron metabolism plays in breast cancer etiology.
- **George Weinstock PhD, Professor, Associate Director of Microbial Genomics.** Dr. Weinstock joined JGM on September 5th, 2013. He previously held appointments at Washington University in St. Louis (WUSTL) where he was associate director of The Genome Institute and a professor in the Departments of Genetics and Molecular Microbiology. In St. Louis, he established a microbial genomics and metagenomics division devoted to studying infectious diseases and the human microbiome. His group collaborates extensively with clinicians to apply genomic analyses to a wide range of medical problems. The goal of this research is to determine the role that the microbiome plays in health and disease with the aim of developing new diagnostic and therapeutic approaches. Dr. Weinstock's group played a leading role in the National Institute of Health's Human Microbiome Project. Dr. Weinstock also directs a number of human and mammalian genetics projects aimed at determining genetic causes of conditions such as retinitis pigmentosa and cheiloschisis (cleft lip). Prior to his appointment at WUSTL, Dr. Weinstock was co-director of the Human Genome Sequencing Center at Baylor College of Medicine in Houston where he was one of the leaders of the Human Genome Project.
- **Duygu Ucar PhD, Assistant Professor.** Dr. Ucar joined JGM on September 1st, 2013. A computational scientist who mines genetic databases to identify factors that regulate gene expression, Dr. Ucar completed a National Science Foundation Computing Innovation postdoctoral fellowship at the University of Iowa in the Department of Internal Medicine. Dr. Ucar joined JAX-Genomic Medicine after completing her second postdoctoral appointment at Stanford University in Stanford, CA where she completed research in the laboratories of Drs. Anne Brunet and Julie Baker.
- **Michael Stitzel PhD, Assistant Professor.** Dr. Stitzel joined the faculty of JGM as an assistant professor in September 2013 and is establishing a research program focusing on the genetics and epigenetics of islet dysfunction and type 2 diabetes. Dr. Stitzel arrived at JGM after completing a postdoctoral appointment at the National

Human Genome Research Institute in the laboratory of Francis S. Collins, MD, PhD, director of the National Institutes of Health.

Connecticut Residents. Among the 24 Connecticut residents currently employed by The Jackson Laboratory, 16 of them were hired in 2013. These include a number of key administrative and operational positions:

- **Manager, Environmental Health and Safety (EHS)** – Izabela Puskarz of West Hartford, Conn. Ms. Puskarz brings over 10 years of laboratory and EHS management experience to JGM including five years of research operation management at BioRelix, Inc. in New Haven, CT. Her primary responsibilities at JGM are to manage all tasks related to environmental health and safety and to provide laboratory management support to the research teams.
- **Clinical Services Project Manager** – Jennifer Bourne of East Haven, Conn. Ms. Bourne joined JGM as a project manager for the Clinical Services business unit. She has extensive experience in clinical services and has served as project manager, clinical test administrator, study director and project leader in various Connecticut-based clinical service companies. She is a graduate of the University of Connecticut and a certified project manager.
- **Sr. Software Engineer** – Anuradha Lakshminarayana of New Britain, Conn. Ms. Lakshminarayana has over 10 years of experience in scientific software development. In her role on the Computational Sciences team, she develops scientific software to support JGM’s research programs.
- **Sr. Scientific Writer** – Tara McLaughlin of Middletown, Conn. Dr. McLaughlin is a graduate of the University of Connecticut. Prior to her arrival at JGM, she worked at Hartford Hospital for 12 years in several capacities including senior scientist/grant writer, certified clinical research associate and project manager. She joined JGM as a sr. scientific writer working with JGM principal investigators to prepare grant submissions, manuscripts and other scientific materials.
- **Maintenance and Plant Utility Supervisor** – Scott Soderberg of Oakdale, Conn. Mr. Soderberg is a licensed operating stationary engineer and has served in various maintenance and supervisory roles at Pfizer Inc. in Groton, Conn. His team will be responsible for the maintenance and operation of all equipment and utilities in the new JGM facility currently under construction.

(ii) **Status of Performance Expectations**

(a) *the number and dollar value of research grants obtained by JAX with respect to JGM from the federal government or from sources other than Connecticut;*

In 2013, JGM received five grant awards from the federal government worth a total value of \$3,187,195. In addition, JGM’s director received a \$7.5 million, five-year grant (2013-2017) from the government of South Korea to support a large-scale cancer genomics project. In collaboration with Seoul National University, the project will employ the latest sequencing technology and will use JAX Patient Derived Xenograft (PDX) mice to host and analyze human tumors. The goal of the project is to develop a standardized platform through which to evaluate the effectiveness of anticancer drug regimens using standardized clinical data collection and genomics sequencing procedures. Once established, the

platform will be used to guide cancer therapies that will be personalized for each patient according to the genetic profile of his or her specific cancer.

JGM faculty and investigators submitted over 30 grant proposals in 2013 to NIH and other funding agencies (**Table 2**) with a total value of all requested funding exceeding \$60 million. We have received award notices for a number of these grants including four of Dr. Lee's submissions (highlighted below). We anticipate additional awards will be made for some of these applications and will start generating additional revenue for JGM in 2014.

Table 2. JGM 2013 Grant Submissions

JAX Principal Investigator	SPONSOR	PRIME INSTITUTE/ COLLABERATOR	PROJECT TITLE	TOTAL FUNDING REQUESTED
Chuang, Jeffrey H	NIH/NHGRI		Combinatorial RNA Structural Features That Control RNA-Protein Binding	\$519,750
Chuang, Jeffrey H	NIH	UCHC	Molecular Genetic Studies of Families with Mitral Valve Prolapse	\$267,006
Chuang, Jeffrey H	NIH	UCHC	Phosphotyrosine Profiling to Predict Response of Lung Cancer to Targeted Therapy	\$548,100
Lee, Charles	NIH/NHGRI	Geisinger Clinic	A Unified Clinical Genomics Database	\$21,567
Lee, Charles	NIH/NHGRI		An Integrative Analysis of Structural Variation for the 1000 Genomes Project	\$8,236,904
Lee, Charles	NIH/NIAID	Mount Sinai School of Medicine	Genomic Determinants of Intrinsic Antiviral Host Defenses	\$191,365
Lee, Charles	NIH/NICHD	Massachusetts General Hospital	Gene Mutation and Rescue in Human Diaphragmatic Hernia	\$167,687
Lee, Charles	NIH/NIAID		Role of Non-antimalarial Drugs in the Development of Multidrug-resistant Malaria	\$3,280,970
Liu, Edison T	NIH/NCI		(PQD2) Chemotherapy Susceptibility Markers in Triple Negative Breast Cancer	\$519,750
Liu, Edison T	NIH/OD		Comprehensive Discovery of lncRNAs as Targets for Combinatorial Therapeutics	\$3,372,297
McKeon, Frank D	NIH/NCI	Brigham & Women's Hospital, Inc.	The Squamocolumnar Junction and Cervical Cancer	\$258,312
McKeon, Frank D	TJLINT		Cloning and Engineering of Human Liver Cells to Reconstitute the Liver of NRG-Fah ^{-/-} Mice	\$145,000
McKeon, Frank D	CTDPH		Mechanisms of Crohn's Disease Revealed by Patient-Specific Stem Cells	\$1,500,000
McKeon, Frank D	NIH/NHLBI		p63 ⁺ Stem Cells in Lung Regeneration	\$2,187,500
Ouyang, Zhengqing	NIH/NHGRI		Computational Methods for Genome-Scale Reconstruction of RNA Structure in Humans	\$494,200
Ruan, Yijun	ACS	UCHC	Survival Disparity in Breast Cancer: Population-Based Study of TN Subtype	\$295,338
Ruan, Yijun	NIH/NCI		Characterization of RNA-Chromatin Interactome by RNA-DNA Ligation and Sequencing	\$2,612,688
Ruan, Yijun	NIH/NHGRI		Workshop on Chromatin Interaction Analysis using Paired-End Tag Sequencing	\$162,000
Ruan, Yijun	NIH/NHGRI		Integrative Analyses of Multi-dimensional Networks of Transcription Regulation	\$6,224,683
Ruan, Yijun	NIH/NIMH		Genome-wide Mapping of Epigenetic Regulatory Units in Normal and RTT Brains	\$2,594,744
Ruan, Yijun	NIH/OD		Comprehensive Discovery of lncRNAs as Targets for Combinatorial Therapeutics	\$3,372,297
Stitzel, Michael L	NIH/NIDDK		Noncoding Variation in Human Pancreatic Islets and their Developmental Precursors	\$747,000
Weinstock, George M	NIH	UCHC	Frog Drug International Consortium	\$461,657
Weinstock, George M	NIH/NHGRI	UCHC	COP: A Center for Out-of-core Processing of NGS Data	\$525,000
Weinstock, George M	NIH/OD		Genetic Control of the Microbiome	\$16,279,451
Xian, Wa	ACS		The Origin of High-Grade Ovarian Cancer	\$30,000
Xian, Wa	CTDPH		Lung Stem Cells as Potential Therapy for COPD	\$750,000
Xian, Wa	DOD	Brigham & Women's Hospital, Inc.	SCOUT is the Early Precursor of High-Grade Ovarian Cancer	\$100,000
Xian, Wa	KIMMEL		Stem Cells in Barrett's Esophagus: Risk Assessment and Preemptive Therapeutics	\$200,000
Xian, Wa	KIMMEL		Rapid Identification and Targeting of Chemotherapy-Resistant Clones in Ovarian Cancer	\$200,000
Xian, Wa	NIH	UCHC	Iron Addiction and the Biology of Ovarian Cancer	\$161,650
Xian, Wa	NYSCF		Mechanisms of Stem Cell Mediated Lung Regeneration	\$1,500,000
Xian, Wa	NIH		(PQB4) Renewable Cancer Stem Cell Libraries for Heterogeneity and Drug Resistance	\$3,586,612
			Total	\$61,513,528

(b) patents and licensing agreements obtained by JAX with respect to JGM and other resultant commercial applications of JGM research;

JGM faculty submitted three patent applications in 2013 (**Table 3**). These patents represent innovations in stem cell technology, treatments of inflammatory disease and methods for analyzing RNA-chromatin interactions.

Table 3. JGM Patent Applications Submitted in 2013

<u>Inventor</u>	<u>Patent Application Number</u>	<u>Patent Title</u>
Wa Xian	61/792,027	Isolation of Non-Embryonic Stem Cells and Uses Thereof
Wa Xian	61/788,602	Treatment of Inflammatory Diseases
Yijun Ruan	61/873,928	Compositions for RNA-Chromatin Interaction Analysis and Uses Thereof

(c) collaborative agreements reached and maintained with colleges and universities in Connecticut and with research institutions in Connecticut, including agreements that foster participation in research opportunities by public and private colleges and universities and research institutions in Connecticut;

Agreements with Connecticut Colleges and Universities. In addition to the Collaborative Research Agreement with University of Connecticut (UConn) and University of Connecticut Health Center (UCHC) established in 2012, we are also in active discussions with other local institutions of higher education including Wesleyan University, Connecticut College and Connecticut Central Colleges to co-development seminars, lecture series and genomics courses.

Collaborative Research Agreement with Connecticut Children’s Medical Center. In April 2013, JAX entered into a Collaborative Research Agreement with Connecticut Children’s Medical Center (CCMC) in which the two organizations will jointly investigate the genetics of human cancers and the development of optimal individualized treatments using JAX cancer avatar models. In this program, JAX obtains human cancer tumors from CCMC and subsequently grows and multiplies these tumors in immune-compromised mice (the “avatars”). In consultation with CCMC clinical staff, JAX then applies various treatment regimens to the tumors collecting valuable information on the degree to which different treatment regimens are more or less effective on the basis of the tumor’s genetic profile. JAX is planning to make this information publically available, to empower clinicians to choose the most effective cancer therapies and to facilitate further advances in biomedical research.

Collaborative Research Agreement with Hartford Hospital. JAX is in the process of finalizing a Collaborative Research Agreement with Hartford Hospital. JAX and Hartford Hospital plan to utilize the JAX cancer avatar model to jointly investigate the genetics of human cancers and the development of optimal individualized treatments.

JAX Postdoctoral Program. JGM currently hosts 17 postdoctoral fellows, three of whom were recently nominated for the 2014 Blavatnik Award for Young Scientists

Regional Postdoctoral Competition. The Blavatnik Family Foundation holds this competition to recognize the most promising postdoctoral level scientists and engineers from NY, NJ and CT working in disciplines in the life sciences, physical sciences, mathematics and engineering. This year, JGM nominated Drs. Joel Wagner, Yizhou Li and Chenchen Zou. All JAX postdoctoral associates participate in training opportunities offered by the JAX Genomics Education Office including an annual “Whole Scientist” course focused on broadening postdoctoral training in research ethics, mentoring, teaching, science communication, management and entrepreneurship. The short course is followed by an academic year practicum in which the postdoctoral associates are encouraged to immerse themselves in one topic of particular interest. The office also assists the postdoctoral fellows with preparation of grant applications and hosts a science social forum in which the fellows meet to discuss current trends and to share mutual advice and support.

JAX Summer Student Program. As a pilot project, JAX offered a small Summer Student Program (SSP) at JAX GM in 2013 including three students from a local CT high school. JAX plans to expand the pilot program in 2014. In 2013, JAX received 880 applicants for the SSP, out of which 595 applicants indicated strong interest in completing an internship at JAX GM. Fifty of the applicants were CT residents.

(d) collaborative partnership established and maintained with businesses in Connecticut, including small businesses;

JAX continues to work with the UCHC, CCMC, Hartford Hospital and Saint Francis Hospital and Medical Center to create xenograft models from patient tumors. These models are then distributed to the cancer research community to accelerate the discovery and development of more effective anti-cancer therapies.

The Jackson Laboratory continues to discuss opportunities for collaboration with local insurance companies. Meetings and discussions have focused on ways to apply genomic technologies to improve health care outcomes and clinical decision making. We have spoken to representatives from Aetna Innovation Labs and Woman’s Health USA.

(e) the total amount of funding received by JAX with respect to JGM from sources other than CII, including a breakdown of amounts received from grants and from other sources;

Grant Funding. In 2013, JGM received five grant awards from the federal government worth a total of \$3,187,195. In addition, JGM’s Director received a \$7.5 million, five-year grant (2013-2017) from the government of South Korea.

Philanthropic Contributions. JGM received two gift pledges in 2013, one for \$500,000 in support of establishing an endowment and one for \$25,000 in support of JGM cancer avatar research activities.

JAX Organizational Effort and Contributions. JAX continued to make significant contributions to JGM by providing effort, resources, travel and infrastructure support in a number of areas including management, general administration, research administration, scientific services, clinical services and operation. The JAX Bar Harbor staff collectively spent over 25,600 hours on specifically identified JGM-related activities during 2013, representing the equivalent of approximately 14 FTEs and \$2 million in wages with benefits. JAX has also committed a total of \$533,300 (of which \$371,151 was spent in

2013) on renovations to the temporary facilities that were needed to accommodate the accelerated growth of JGM's scientific staff and program. Furthermore, JAX has committed funding from the 2013 budget (the expenses for which will be realized in 2014) to purchase three large scientific instruments to be located at the JGM temporary facility in Farmington. These instruments, including a PacBio RSII single molecule DNA sequencer (\$550,000), a Bio-Rad QX200 droplet digital PCR system (\$99,900) and a BD Fortessa cell analyzer (\$330,000), are critical to JGM's research activities. Overall, JAX has contributed and or committed over \$3.5 million in efforts, resources, travel and equipment to the establishment of JGM in 2013.

In 2013, we continued to focus on successfully establishing JGM's operations as our top priority. The JAX Senior Management Team and key operational, technical and administrative staff continued to devote a significant amount of their efforts on the planning, organizing and implementing JGM's operations in 2013. Many of JGM's startup activities continued to be directly managed and supported by staff headquartered on the JAX Bar Harbor campus while JGM staff was establishing a local infrastructure. JAX Senior Management Team and key operational and administrative staff continue to make frequent visits to the JGM site in Farmington and to other locations in Connecticut to meet with local collaborators, Connecticut Innovations staff, contractors, policy makers and business leaders. JAX has absorbed all expenses for their travel and efforts.

Throughout the fiscal year, efforts dedicated to JGM were tracked by employees at The Jackson Laboratory who are organizationally separate from JGM; although the effort is not charged to the Connecticut Innovations grant. The areas that provided support, management and other services include:

Senior Management Team. The members of the JAX Senior Management Team, including Dr. Ed Liu, President & CEO; Dr. Charles Hewett, Executive VP; Mr. Michael Hyde, VP of External Affairs & Strategic Partnership; Dr. Robert Braun, VP of Research and Ms. Linda Jensen, CFO, have all devoted a significant portion of their efforts to planning, organizing and managing JGM's startup activities as well as recruiting key JGM administrative and scientific staff, developing collaborations and research programs and establishing relationships with local collaborators, Connecticut Innovations staff, contractors, policy makers and business leaders.

Fiscal Services. Recognizing the importance of good financial management to JAX and Connecticut Innovations, Fiscal Services provided extensive support to the organization's recruitment and training of a financial analyst located in Connecticut and dedicated to JGM activity. The financial analyst has been tasked with processing JGM's financial transactions in accordance with the Agreement and generating required financial reports. In addition, financial staff located in Bar Harbor developed and established processes and systems to obtain Connecticut Innovations approval of equipment purchases, to document and tag equipment, to track construction costs and to provide detailed information to Connecticut Innovations. Working with UCHC staff, Fiscal Services established a simplified billing process that allowed JGM scientists to easily use UCHC core services. Working with senior financial staff at Connecticut Innovations, we updated accounting guidelines and reporting formats to communicate financial performance metrics and to accommodate the scope of review required by outside auditors. Senior Bar Harbor financial staff supported JGM management

in budgeting and submitting grant applications. JGM management and scientists rely on the organization's enterprise resource management system for personnel and financial information. Working with a local JGM procurement agent at JGM, JAX Bar Harbor staff supported JGM faculty and scientists in selecting and acquiring equipment, materials and services needed to establish their laboratories.

Engineering and Facilities. Engineering and Facilities were responsible for the renovation, fit-out and management of the temporary facility including approximately 12,629 (gsf) of office space and 6,866 square feet of laboratory space. The team was also responsible for managing the budget and all other aspects of the new building construction. To accommodate the rapid expansion and growth of JGM research programs, JAX has invested approximately \$500,000 of its own money to renovate the 2nd floor of an office building on the UCHC campus. The renovation created approximately 2000 ft² of wet lab space in the UCHC Dowling South building.

Human Resources. The Human Resources team provided support for faculty recruitment, employee benefits and compensation, relocation, immigration, performance management, employee training and environmental health and safety services.

Information Technology. The Informatics Technology (IT) team worked with the UCHC IT team to establish high performance computing and networking capabilities and provided phone and video conferencing communication and personal computing/desk-top support. In 2013, the JAX IT team continued to provide support JGM in high performance computing (HPC) and data storage management to meet its growing demand for scientific computing.

Research Administration. Research Administration provided support for grant writing, review and submission, identified new funding opportunities, managed regulatory issues and managed sponsored projects.

Education. The JAX education group provided significant support to JGM in organizing a clinical genomics conference held in Farmington, CT on October 5th and 6th. The conference featured experts and thought leaders in clinical genomics and attracted an overflow crowd of over 130 participants. The team also supported JGM by developing postdoctoral and summer student internship programs.

Scientific Services. The JAX Bar Harbor scientific services team has provided support to JGM faculty and researchers in all core services areas including 1) imaging and microscopy; 2) flow cytometry; 3) animal model development; 4) histology; 5) computational sciences and 6) implementation of shared instrumentation while JGM continued to build up these core capabilities locally.

Clinical Services. Through the joint effort of JGM technical staff and JAX Bar Harbor operation staff, JGM established a CLIA-certified clinical genomics laboratory in September of 2013. Through an organization-wide effort, JGM successfully established clinical operations and obtained CLIA certification in a record 9 months.

In addition, Legal and Technology Transfer, Animal Health, and Communications divisions have all been intimately involved in planning and

developing programs and capabilities related to JGM's mission and have provided support on an as needed basis.

(f) spin-off businesses created in Connecticut as a result of commercialization of the research of JGM;

We are in exploratory discussions with several Connecticut institutions and industry partners regarding joint research ventures that may eventually result in spinoff activity. Some of the discoveries and inventions generated by JGM researchers, such as the ones described in section III (ii) (b), may have commercial application and hence may create spin-off opportunities.

(g) businesses that are located in Connecticut as a result of JGM;

None to report for the current reporting year.

(h) the establishment and implementation of policies to promote minority local and small business participation using the guidelines developed by the State of Connecticut;

JAX strongly supports the use and promotion of local, small and minority business enterprises as contractors and vendors and this project will be no exception.

JAX has filed an affirmative action plan as an employer with the Connecticut Commission on Human Rights and Opportunities (CHRO) and has required its JAX-Genomic Medicine Construction Manager at Risk to develop a voluntary compliance plan outlining the project's diversity goals. We have specifically outlined targets for awarding contracts to small business and minority business enterprises. This voluntary compliance plan has been incorporated into an affirmative action plan filed with CHRO and Connecticut Innovations and has provided voluntary compliance plan monitoring.

To date the project is meeting or exceeding target goals of awarding 25% of contract value to Small Business Enterprise (SBE) firms and 6.35% to Minority Business Enterprise firms, achieving 25.8% and 18.5% of contract value respectively. The Purchasing and Receiving Policy 30-30-3003 is attached in Appendix 5.

(i) the establishment and implementation of a program to conduct workforce recruitment activities at public and private colleges and universities and community colleges in Connecticut, regardless of their size, which request the participation of JAX.

A program aimed at recruitment from both public and private colleges and universities, as well as from community colleges in the area, regardless of whether they request participation or not, is currently under development. JGM site director, Yu-Hui Rogers, has been serving on the project advisory board of the Connecticut Health & Life Sciences Career Initiative (HL-SCI) which is a Connecticut state funded program to create fifteen new certified or degree programs within the seven participating state and community colleges including Capital Community College, Gateway Community College, Manchester Community College, Middlesex Community College, Norwalk Community

College, Charter Oak State College and Eastern Connecticut State University. The goal of the program is to create programs that align with industry credentials and help the HL-SI participants find positions in the industry. Ms. Rogers has also had discussions with Tunxis Community College, Goodwin College and Central Connecticut State University administrators on potentially developing job training programs specifically for JGM.

(iii) Employee Positions and Funds Required for Equipment for Next Annual Disbursement

This information, representing 125 employees and \$10,218,000 in equipment, is presented in **Table 4**.

Table 4. Employee Positions and Funds Required for Equipment for Next Annual Disbursement

Position	# Employees	Equipment	2014 Budget
Senior Scientist	51	IT Equipment	\$4,197,000
All Other	74	Scientific Equipment	\$6,021,000
Total Employees	125	Total Equipment	\$10,218,000

(iv) Status of JAX’s Relocation to the Facility and Progress of Construction Activities

JGM has continued to make significant progress towards the construction of The Jackson Laboratory for Genomic Medicine’s permanent facility. In this reporting year, contractor procurement for the 183,500 square foot facility was completed with a Construction Manager at Risk Guaranteed Maximum Price contract awarded in late January 2013. All major state and local development permits have been received including DEEP flood management, wetlands, construction dewatering permits, CDOT traffic permits, along with the OBSI building permit. A successful and well attended ground-breaking for the building took place on January 17, 2013, with over 300 attendees. As of December 31, 2013 nearly \$64 million of work was completed on the \$135 million facility (representing 47% of the construction budget). The new JGM research center will be ready for occupancy in October 2014.

JAX has selected the following firms to work on the project, with preference given to Connecticut-based contractors when possible:

- Gilbane Inc., a New England construction firm with a district office in Glastonbury Conn., is managing the program and has guided the project through the design development phase, meeting all established milestones to date. Gilbane has extensive experience developing complex research and life-science facilities including the UConn Pharmacy Laboratory and various research facilities at Pfizer and Bayer, as well as a new U.S. Center for Disease Control public health laboratory and a research facility for the National Institute of Allergy and Infectious Diseases.
- A team of comprised of Centerbrook Architects (Centerbrook, Connecticut), BVH Integrated Services (of Bloomfield, Connecticut), Tsoi/Kobus & Associates (Cambridge, Massachusetts) and BR+A (Watertown, Massachusetts) is providing the architectural and engineering design work for the facility. These firms were selected

for their demonstrated expertise in designing scientific research space and for their commitment to low-impact, environmentally-friendly design.

- The Whiting-Turner Contracting Company is the project's construction-management firm. The company, with a regional office in New Haven, Conn oversees site preparation, utilities development and overall building and site construction efforts. At the end of 2013, Whiting Turner subcontractors have incorporated over 250,000 person-hours into the building, all without a single lost time incident, and are overseeing a contractor workforce of 270 CT tradesman daily.

(v) **Status of JAX's Activities at the Facility**

While JGM's permanent building is under construction, JGM researchers have been actively conducting research in the temporary facility. The main activities included i) fundamental research in the areas of genomic structure and variation, biology of the genome and computational biology; ii) translational research in cancer biology, cancer treatment options based on JAX PDX mouse models, human immunology, stem cells and human microbiomes; iii) clinical translation using the most advanced genomic technologies for developing new diagnostics. In addition to the accomplishments described in other sections above, four high impact scientific publications have resulted from these activities in 2013. They are listed below:

Publications of which JGM faculty are the senior or co-senior authors:

- Crum CP, Herfs M, Ning G, Bijron JG, Howitt BE, Jimenez CA, Hanamornroongruang S, **McKeon FD**, **Xian W**. 2013. Through the glass darkly: intraepithelial neoplasia, top-down differentiation and the road to ovarian cancer. *J Pathol* 231:402-412.
- Chen D, Fu LY, Zhang Z, Li G, Zhang H, Jiang L, Harrison AP, Shanahan HP, Klukas C, Zhang HY, **Ruan Y**, Chen LL, Chen M. 2013. Dissecting the chromatin interactome of microRNA genes. *Nucleic Acids Res*. 2013 Dec 18.

Publications of which JGM faculty co-authored:

- Zhang Y, Wong CH, Birnbaum RY, Li G, Favaro R, Ngan CY, Lim J, Tai E, Poh HM, Wong E, Mulawadi FH, Sung WK, Nicolis S, Ahituv N, **Ruan Y**, Wei CL. 2013. Chromatin connectivity maps reveal dynamic promoter-enhancer long-range associations. *Nature* 504: 306-310.
- Kieffer-Kwon KR, Tang Z, Mathe E, Qian J, Sung MH, Li G, Resch W, Baek S, Pruett N, Grøntved L, Vian L, Nelson S, Zare H, Hakim O, Reyon D, Yamane A, Nakahashi H, Kovalchuk AL, Zou J, Joung JK, Sartorelli V, Wei CL, Ruan X, Hager GL, **Ruan Y**, Casellas R. 2013. Interactome maps of mouse gene regulatory domains reveal basic principles of transcriptional regulation. *Cell* 155: 1507-1520.

IV. SCHEDULE OF THE SHARES OF STOCK [Section 11.3 (c)]

Not applicable for the current reporting year.

V. STATUS OF ACTIVITIES AND PROGRAMS CONTEMPLATED BY THE COLLABORATIVE RESEARCH AGREEMENT [Section 11.3 (d)]

Affiliation Agreement. JAX has established an Affiliation Agreement with the University of Connecticut School of Medicine (SOM) and Dental Medicine (SDM). The Affiliation Agreement provides a mechanism to expand the opportunities for JAX and UCHC scientists to participate in genomic science and systems biology research and to teach science at UCHC. This affiliation enables eligible JAX scientists to seek affiliated faculty appointments in the SOM and residence-track faculty appointments in the SDM. Processes for applying for these joint appointments and for granting them are ongoing as new JGM faculty are recruited. Several JGM faculty members including Drs. Edison Liu, Yijun Ruan and Jeff Chuang have submitted their application for joint appointments. Several JGM faculty members have either recruited or are in the process of recruiting UConn graduate students to work in their laboratories

Submission of Joint Grant Proposals. Researchers from JAX, UConn and UCHC have been actively collaborating in the development of research proposals and have been seeking joint grant funding. Below is a list of joint grant proposals submitted by JAX, UConn and UCHC in 2013 (Table 5).

Table 5. JAX and UConn/UCHC Joint Grant Proposals Submitted in 2013

JAX CONTACT PI	MULTI OR PRIME PI	SPONSOR	PRIME INSTITUTE	PROJECT TITLE
Chuang, Jeffrey H	Sarfrazi	NIH	UCHC	Molecular Genetic Studies of Families with Mitral Valve Prolapse
Chuang, Jeffrey H	Mayer	NIH	UCHC	Phosphotyrosine Profiling to Predict Response of Lung Cancer to Targeted Therapy
Ruan, Yijun	Brent Graveley/UCHC	NIH/NHGRI	JAX	Integrative Analyses of Multi-dimensional Networks of Transcription Regulation
Ruan, Yijun	Swede	ACS	UCHC	Survival Disparity in Breast Cancer: Population-Based Study of TN Subtype
Weinstock, George M	Malone	NIH	UConn - Storrs	Frog Drug International Consortium
Weinstock, George M	Moraru	NIH/NHGRI	UCHC	COP: A Center for Out-of-core Processing of NGS Data
Xian, Wa	Torti	NIH	UCHC	Iron Addiction and the Biology of Ovarian Cancer

The Institute for Systems Genomics. As one of the founding members of the Institute for Systems Genomics at the University of Connecticut, we have been deeply involved in the planning of the organization including the graduate program and its curriculum. We intend to be a full partner in this exciting initiative that will integrate genomics with engineering, mathematics, biology, medicine and agricultural sciences. Both our faculty and leadership will participate in the launch and implementation of the institute, which has the strong potential to change the course of graduate education. This synergy exemplifies how the presence of The Jackson Laboratory for Genomic Medicine is contributing to Connecticut's intellectual capital for the benefit of all parties involved.

VI. APPENDICES

Appendix 1 Schedule of Research and Training Expenditures

Appendix 2 Schedule of Research Services and Production Expenditures

Appendix 3 Schedule 2, Summary of Grant Information

Appendix 4 Summary of Commitments

Appendix 1-Schedule of Research and Training Expenditures

Research & Training

THE JACKSON LABORATORY - GENOMIC MEDICINE
 Schedule of Connecticut Innovations Incorporated Grant Expenditures
 For Year ended 2013
 Research & Training Expenditures

<u>Expenditures</u>	<u>Salaries</u>	<u>Benefits</u>	<u>Other</u>	<u>(Recovery)</u>	<u>Total</u>
1. Direct Research & Training Activities Note: excludes grants, gift, and endowment funded activities. [7027100 JGM Research & 7027101 - JGM New Investigators]	\$ 1,775,909	\$ 591,698	\$ 1,787,641	n/a	\$ 4,155,248
a. Research training programs					
<u>Activity #</u>	<u>Description</u>				
b. Unrecovered shared scientific services, research technology platforms, and other core services [Name of Service]	n/a	n/a	n/a	n/a	n/a
c. Courses and Conferences [Clinical Genomics in the 21st Century, Farmington, CT]	\$ -	\$ -	\$ 30,761	n/a	\$ 30,761
Total Direct Cost of Research & Training	[sum of 1a., 1b, and 1c]				<u>\$ 4,186,010</u>
2. Indirect Cost related to research and training overhead					
a. Connecticut General & Administrative costs specific to research [7027510 - JGM Research Administration]	\$ 368,708	\$ 91,802	\$ 386,925		847,435
b. Connecticut General & Administrative Costs General allocated to Research & Training [7027500 - JGM Administration & 7027600 JGM Development] Allocated to Research & Training based on R & T direct costs/total direct costs	780,466	243,388	342,302		\$ 1,366,156 73.19%
c. Facilities Cost [7027520 - JGM Facilities & Utilities] Allocated to Research & Training based on sqft	\$ 135,041	\$ 42,249	\$ 334,539		\$ 511,829 86.80%
d. Indirect Research & Training costs sum of allocated indirect costs					<u>\$ 2,725,420</u>
e. Indirect cost recovery and training grants excluding reimbursement for general administration costs not included above					139,240.39
f. Net amount charged to CII grant					<u>\$ 6,772,189</u>

Appendix 2-Schedule of Research Services and Production Expenditures

Research Services & Production

THE JACKSON LABORATORY - GENOMIC MEDICINE

Schedule of Connecticut Innovations Incorporated Grant Expenditures

For Year ended 2013

Research Services & Production

<u>Expenditures</u>	<u>Salaries</u>	<u>Benefits</u>	<u>Other</u>	<u>Total</u>
1. Direct Costs related to research services & products.				
a. Direct Costs of delivering service or product [Service or product]	N/A	N/A	N/A	N/A
b. Costs of product development - Clinical & Core Services [7027140 JGM Scientific Services, 7027400 JGM Clinical Sequencing, 7027405 JGM Clinical Comp Science, 7027410 JGM Clinical Services Direct and 7027450 JGM Clinical Product Develop]	573,228	162,061	903,197	\$ 1,638,487
c. Costs of outreach/customer service, etc.product development [7027455 JGM Customer & Tech Support and 7027460 JGM Sales & Marketing]	-	-	676	\$ 676
Total direct cost				<u>\$ 1,639,162.97</u>
2. Indirect Cost related to research services and products				
a. Connecticut General & Administrative costs specific to research services and products [Accounting Units included in this pool]	N/A	N/A	N/A	N/A
b. Connecticut General & Administrative Costs General allocated to Research Services & Products [7027500 JGM Adm and 7027600 JGM Development] Allocated to Research Services & Products based on RSP direct costs/total CT direct costs	285,948	89,173	125,413	500,534 26.81%
c. Facility costs [7027520 JGM Facility & Utility] Allocated to Research Services & Training based on sqft	20,536	6,425	50,875	77,836 13.20%
Total indirect costs				<u>\$ 578,370</u>
Revenue from Products & Services (up to amount expended)				N/A
f. Net amount charged to CII grant				<u>\$ 2,217,532.88</u>

Appendix 3-Schedule 2, Summary of Grant Information

Schedule 2

Summary

THE JACKSON LABORATORY - GENOMIC MEDICINE

Schedule of Connecticut Innovations Incorporated Grant Expenditures

For Year ended 2013

Balance of Grant monies carried forward into year	\$ 2,640,555
Annual Grant payments received in year:	
Quarter 1	\$ 1,852,500
Quarter 2	\$ 1,852,500
Quarter 3	\$ 1,852,500
Quarter 4	\$ 1,852,500
 Total amounts available for research and operations of JAX Genomic Medicine	 <u>\$ 10,050,555</u>
 Research & Training expenditures	 \$ 6,772,189
Research Services & Product expenditures	\$ 2,217,533
 Total Expenditures paid from CII Grant	 <u>\$ 8,989,722</u>
 Balance of grant monies carried to next year (if available funds exceeds expenditures)	 <u>\$ 1,060,833</u>
 Amount of expenditures carried to next year (if expenditures exceed available funds)	 <u>\$ -</u>

Appendix 4
THE JACKSON LABORATORY - GENOMIC MEDICINE
Schedule of Connecticut Innovations Incorporated Grant Expenditures
For Year ended 2013

Outstanding Purchase Order Commitments

Operational Commitments by Activity

7027100 JGM Research	\$ 35,811
7027101 JGM New Investigator	\$ 156,680
7027500 JGM Administration	\$ 42,587
7027510 JGM Research Administration	\$ 26,853
7027520 JGM Facilities & Utilities	\$ 68,840
Add services	Total
	<u>\$ 330,771</u>

Clinical Services Commitments by Activity

7027400 JGM Clinical Sequencing	\$ 43,387
7027405 JGM Clinical Comp Sciences	\$ 4,342
7027410 JGM Clinical Services Direct	\$ 495
	<u>\$ 48,224</u>

Capital Commitments by Activity

71-08324 Genomic Medicine	\$ 68,654,032
71-08335 Genomic Med Temp Office/Lab	\$ 10,218
71-08338 Genomic Med Temp Office FF&E Adm	\$ 2,369,162
71-08371 Genomic Med Temp Lab CGSB	\$ 79,505
71-08642 ASB Temporary Space Phase II	\$ 208,058
	Total
	<u>\$ 71,320,975</u>

Total Purchase Order Operational and Capital Commitments \$ 71,699,970

Outstanding Faculty Commitments

Faculty Funding Commitments as of December, 2013	Total	<u>\$ 24,136,522</u>
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Total Commitments	<u>\$ 95,836,492</u>
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