Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is "None", please specify "None" as your response. "Not applicable" is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution:** The Trustees of the University of Pennsylvania

2. **Reporting Period (start and end date of grant award period):** 1/1/2010-12/31/2013

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Gearline R. Robinson-Hall, BSF

4. **Grant Contact Person's Telephone Number:** 215-746-6821

5. **Grant SAP Number:** 4100050912

6. **Project Number and Title of Research Project:** 2-Development of Laboratory Space at Penn Medicine – Research Infrastructure

7. **Start and End Date of Research Project:** 1/1/2011 – 3/1/2013

8. **Name of Principal Investigator for the Research Project:** Glen N. Gaulton, Ph.D.

9. **Research Project Expenses**.

   9(A) Please provide the total amount of health research grant funds spent on this project for the entire duration of the grant, including indirect costs and any interest earned that was spent:

   $ 1,250,000

   9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project	Cost
None			

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project
Gaulton, Glenn	Principal Investigator	1%
Soslowsky, Louis J	Co-Principal Investigator	1%

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
None		

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes___X_____ No_____

If yes, please indicate the source and amount of other funds:

University of Pennsylvania Perelman School of Medicine Special Purpose Funds: $750,000
University of Pennsylvania Facilities Renewal Funds: $185,000

Total-Other Funds: $935,000

11. Leveraging of Additional Funds

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Infrastructure Project:

Yes_____ No__X_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
None	☐NIH ☐ Other federal (specify:_____ _____) ☐ Nonfederal source (specify: _____)		$	$

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes____X_____ No_____

If yes, please describe your plans:

Now that the renovations for the Penn Center for Musculoskeletal Disorders (PCMD) and Comprehensive Neuroscience Center (CNC) are complete, we anticipate that Penn investigators will submit grants on multidisciplinary areas, primarily musculoskeletal disorders and neurosciences. We are confident that our investigators will continue to compete successfully for grant funding that will allow for further exploration in such important public health issues such as brain injury and rehabilitation, stroke, neurodegeneration, and tissue injury and repair.

12. Future of Research Project. What are the future plans for this research project?

This facility is of integral importance to the expansion of the PCMD and CNC at Penn. We anticipate that these centers will continue to support multiple research areas, develop collaborative outreach initiatives and programs, and support core resources.

13. New Investigator Training and Development. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes_____ No___X_____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male				
Female				
Unknown				
Total				

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic				
Unknown				
Total				

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian				
Other				
Unknown				
Total				

14. Recruitment of Out-of–State Researchers. Did you bring researchers into Pennsylvania to carry out this research project?

Yes_____X____ No_____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

We have recruited several new faculty members, who use the renovated space including:

- *X. Sherry Liu, Ph.D.* was recruited from Columbia University as a new tenure track faculty member. Her arrival greatly enhanced the orthopaedic bioengineering program by adding an expert in bone structure-function. Further, her expertise has allowed new research directions on the interfaces between tendon and bone, cartilage and bone, as well as fracture healing.
- *Foteini Mourkioti, Ph.D.* will be joining Penn as an Assistant Professor on July 1, 2014. She was recruited from Stanford University.

15. Impact on Research Capacity and Quality. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes____X_____ No_____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

The renovation of outdated workspace into a modern, open-plan laboratory area outfitted with 36 lab bench workstations and associated support areas has advanced the mission of the PCMD and CNC. The space provides critical support for and interaction between researchers, thereby facilitating the development of opportunities in the broader neurosciences and musculoskeletal research communities.

In addition, the newly renovated space included space for 2 research cores within the PCMD. In particular, the Biomechanics and Histology Cores were greatly expanded and enhanced, improving the ability of approximately 20 faculty members' research to be more efficient and effective. In part due to this project, the NIH P30 center grant was renewed that supports the PCMD with a perfect review score of "10" which included comments from the reviewers on the outstanding facilities. Further, just this past year, an NIH T32 institutional training grant was renewed (also with a perfect 10 score) that further supports the interactions with Bioengineering PhD students who train in orthopaedic bioengineering. PCMD has been able to recruit high quality trainees from across the country, several of which have competed successfully for prestigious NSF Graduate Research Fellowships.

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes_____ No____X_____

If yes, please describe the collaborations:

16(B) Did the research project result in commercial development of any research products?

Yes_____ No__X_____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes_____ No___X_____

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.

List the project goals, objectives and specific aims (as contained in the grant agreement). Summarize the progress made in achieving these goals, objectives and aims for the period that the project was funded (i.e., from project start date through end date). Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

The overall goal of this project was to renovate laboratory facilities in Stemmler Hall in support of Penn's Musculoskeletal Disorders and Comprehensive Neurosciences Centers. Research in the areas of musculoskeletal disorders and the neurosciences are important components of Penn Medicine's research strategic plan and fit with the school's mission of contributing to improved health outcomes for the citizens of the Commonwealth. These closely related, multidisciplinary research programs address important public health issues such as brain injury and rehabilitation, stroke, neurodegeneration, and tissue injury and repair. The PCMD and CNC were formed to integrate and strengthen the University of Pennsylvania's world class patient care, education, and research contributions in these fields. This project directly supported the research missions of

these centers by renovating wet laboratory space on the 4th floor of Stemmler Hall, which will enable the recruitment of 3-5 new investigators, promote interdisciplinary collaboration, and enhance the efficiency of musculoskeletal and neurosciences research. Encompassing 4,900 SF, the renovation project upgraded and enhanced outmoded wet laboratory space that had remained largely in its original state since Stemmler Hall was built in 1978.

The specific aims of this project included:

Specific Aim 1: Renovate approximately 4,900 sf in Stemmler Hall

Since its construction in 1978, laboratory space in Stemmler Hall had remained largely unchanged. As a result, the area targeted by this grant was outmoded and not configured in a way that supported efficient, modern research. For example, the laboratory was divided into many small rooms that stifled interaction among researchers and hindered efficient lab operations. The specific aim of this project was to renovate these outmoded laboratories to support Penn's Musculoskeletal Disorders and Neurosciences Programs, which are housed in adjacent space and require programmatic expansion. The renovation project resulted in a modern, open laboratory, tissue culture, and equipment space

Specific Aim 2: Expand research in Neurosciences and Musculoskeletal Disorders

Research in the neurosciences and musculoskeletal disorders are important components of Penn Medicine's research strategic plan and fit with the school's mission of contributing to improved health outcomes. The centers were formed to integrate and strengthen Penn's interdisciplinary, world-class patient care, education, and research capabilities in these areas, and this project represents an important step in a series of facilities projects being undertaken to enhance the resources available for these important initiatives. The renovation makes available space sufficient to support the recruitment of 3 – 5 investigators who will supplement those already working on neurosciences and musculoskeletal disorders in the adjacent areas.

In January 2003, Penn Medicine completed a comprehensive Strategic Plan. This plan was developed with extensive input from faculty, and bridges basic and clinical research in programmatic, as contrasted to historical departmental, themes. Indeed, key outcomes were the formation of the CNC and the PCMD. The CNC is dedicated to the advancement of the understanding of the brain, spine and peripheral nervous system. Developing effective treatments and therapies for these areas requires the expertise, dedication and cooperation of scientists from many fields of research. The research of CNC investigators spans the entire range of modern neuroscience, from fundamental molecular and cellular studies to translational and clinical research. A major goal of the CNC is to promote integrated basic, translational, and clinical research efforts. Research collaborations between numerous departments and disciplines allow the Penn CNC to approach these disorders from multiple perspectives and to move research more quickly from the 'bench to the bedside'. This research has profound implications for a broad range of human diseases, including but not limited to stroke, multiple sclerosis, epilepsy, HIV/AIDS, brain tumors, peripheral neuropathies, myopathies, neurodegenerative disorders such as Alzheimer's and Parkinson's Disease, and brain injury and repair.

The PCMD was formed to promote cooperative interactions among investigators to enrich the effectiveness of ongoing research and promote new research in the broad area of musculoskeletal disorders, with a particular focus on Musculoskeletal Tissue Injury and Repair. Musculoskeletal injuries affect 28 million Americans annually, resulting in the greatest number of physician office visits nationally, nearly twice the number of visits related to the circulatory system and four times the number related to the digestive system. Clearly, musculoskeletal injuries are a critical national health problem. The PCMD provides critical resources for established and new investigators across a wide spectrum of disciplines to address multidisciplinary research strategies for musculoskeletal problems. The Center facilitates the application of research themes, approaches and mechanistic paradigms that are consistent across many different musculoskeletal tissues, advancing research across tissue types and fostering collaborative research efforts that will ultimately benefit the public.

The important synergies among researchers working in neurosciences and musculoskeletal disciplines has been facilitated by the co-location of these programs in Stemmler Hall and Johnson Pavilion, two of the research facilities located on the heart of the Perelman School of Medicine campus. However, the ability of these scientists to work at their full potential and for the programs to recruit new faculty had been constrained by the lack of modernized available laboratory space. Due to the essential support provided by the DOH, this space has been renovated and now supports 3 newly recruited full time faculty, several orthopaedic surgeons who are part time in research, many lab staff, graduate students, undergraduate students and postdocs. Our scientists can now work to their full potential and expand research in neuroscience and musculoskeletal disorders.

Stemmler Hall was constructed in 1978 by Geddes Brecher Qualls and Cunningham. The 4th floor laboratory space covered by this project had seen little renovation since the building was built. The project was previously used as laboratory space with a small office suite. The scope of this project was to reconfigure existing laboratory space within the bounds of the original laboratory zone. These modifications included the removal of laboratory demising walls to "open up" the space into larger contiguous laboratory space and the reconfiguration of mechanical systems to support the new laboratory configuration. The proposed modifications did not modify the egress paths in any way. The resulting renovated laboratories included:

- Open laboratory area outfitted with 36 lab bench work stations and fume hoods distributed throughout;
- Two tissue culture rooms each with 2 6'-0" bio safety cabinets, CO2 incubators, refrigerators, work surface and sink;
- An equipment area to accommodate 4 laboratory grade refrigerators and 4 (-80) freezers; and
- Laboratory supply room

This configuration provides capacity for 3 – 5 faculty members to be recruited to the CNC/PCMD.

More specifically, the renovation activities completed during the term of this project included:

- Design: A preliminary feasibility study was developed for this project. Working in partnership with the CNC and PCMD, architectural drawings and construction documents were developed in preparation for bid and award of the construction project.
- Demolition: Existing walls, doors and flooring materials were removed. Existing fixed laboratory equipment was removed. Additional demolition was required in a portion of the area that had RF shielding. It should also be noted that this scope included the removal of a concrete "floating slab".
- Construction: Interior construction included the creation of new partitions, walls, flooring, ceiling systems, doors and hardware; specialty construction included laboratory casework and laboratory service fixtures, safety equipment, and fume hoods.
- Heating, Ventilation and Air Conditioning Systems: The former HVAC distribution systems (ductwork, piping, terminal boxes, air terminal devices, and reheat coils) serving the program area were completely demolished. New room distribution systems were supplied and installed as part of the project.
- Plumbing and Process Piping Systems: The plumbing distribution systems (water, natural gas, lab gas & vacuum, and compressed air) previously serving the project areas were completely demolished. New run-outs from the existing mains were added as part of the project.
- Electrical Systems were designed in accordance with all applicable codes, guidelines, and standards
- Fire Protection: the project area was fully sprinklered with a wet sprinkler system

Lastly, the 4th floor had a shielding slab installed over the structural slab which was inappropriate for the needs of the orthopaedic group. In addition, the layout of the floor with a series of small shielded rooms did not function well for their research. Demolition and reconstruction of their space permitted Penn to provide efficient lab planning and spaces specific to the functional needs of the researchers. An additional benefit of the renovation involved correcting some of the problems with the air systems on the floor and providing a safer environment for the occupants.

Construction on the 4th floor of Stemmler Hall was completed in April 2012, and the space was fully occupied. After occupancy, additional renovations in room 414 were initiated and completed between 7/1/12 and 3/1/13. These renovations included: removing the existing benches and utilities and damaged flooring, building a wall to accommodate equipment, installing data and electrical services for new benches, installation of shelving air and vacuum lines, purchasing and installing benches and seating for 10 work stations, installing new energy efficient lighting, repainting, and cleaning up the sink, fume hood and suite after the work was finished. Since March 2013, there were no additional physical updates to the infrastructure.

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be "No."

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
___X__No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
___X__No

If "Yes" to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both "No.")

18(C) How many hospital and health care professionals were involved in the research project?

_____Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____Number of subjects originally targeted to be included in the study
_____Number of subjects enrolled in the study

Note: Studies that fall dramatically short on recruitment are encouraged to provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:
_____Males
_____Females
_____Unknown

Ethnicity:
_____Latinos or Hispanics
_____Not Latinos or Hispanics
_____Unknown

Race:
_____American Indian or Alaska Native
_____Asian
_____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
_____White
_____Other, specify:_____
_____Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

19. Human Embryonic Stem Cell Research. Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?
_____Yes
__X___No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?
_____Yes
_____No

19(C) Please describe how this project involved human embryonic stem cells:

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication or paper submitted for publication, listed in the table, in a PDF version 5.0.5 (or greater) format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, and an abbreviated title of the publication. For example, if you submit two publications for Smith (PI for Project 01), one publication for Zhang (PI for Project 03), and one publication for Bates (PI for Project 04),

the filenames would be:

Project 01 – Smith – Three cases of isolated
Project 01 – Smith – Investigation of NEB1 deletions
Project 03 – Zhang – Molecular profiling of aromatase
Project 04 – Bates – Neonatal intensive care

If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1. None				☐Submitted ☐Accepted ☐Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes____X_____ No_____

If yes, please describe your plans:

With the opening of this newly renovated space, a large number of papers from highly productive collaborators have been submitted. Such submissions include:

1. Beason, DP, Hsu, J.E., Marshall, S.M., McDaniel, A.L., Temel, R.E., Abboud, J.A., Soslowsky, L.J.: Hypercholesterolemia Increases Supraspinatus Tendon Stiffness and Elastic Modulus Across Multiple Species. J Shoulder Elbow Surg, 22(5):681-6, 2013. (PCMID 3525802).
2. Dunkman, A.A., Buckley, M.R., Mienaltowski, M.J., Adams, S., Thomas, S.J., Satchell, L, Kumar, A., Pathmanathan, L., Beason, D.P., Iozzo, R.V., Birk, D.E., Soslowsky, L.J.: Decorin Expression Is Important for Age-Related Changes in Tendon Structure and Mechanical Properties. Matrix Biol, 32(1): 3–13, 2013. (PMCID 3615887).
3. Reuther, K.E., Thomas, S.J., Sarver, J.J., Tucker, J.J., Lee, C.S., Gray, C.F., Glaser, D.L., Soslowsky, L.J.: Effect of Return to Overuse Activity Following an Isolated Supraspinatus Tendon Tear On Adjacent Intact Tendons and Glenoid Cartilage in a Rat Model, J Orthop Res, 31(5):710-5, 2013. (PMCID 3641891)
4. Connizzo, B.K¸ Sarver, J,J, Birk, D.E,, Soslowsky, L.J: Effect of Age and Proteoglycan Deficiency on Collagen Fiber Re-Alignment and Mechanical Properties in Mouse Supraspinatus Tendon, J Biomech Eng, 135(2):021019, 2013. NIHMS498863

5. Connizzo, B.K., Yannascoli, S.M, Soslowsky, L.J.: Structure–function relationships of postnatal tendon development: A parallel to healing, Matrix Biol, 32(2):106-16 2013. (PMC3615149)
6. Dourte, L.M., Pathmanathan, L, Mienaltowski, M.J., Jawad, A.F., Birk, D.E., Soslowsky, L.J.: Mechanical, compositional, and structural properties of the mouse patellar tendon with changes in biglycan gene expression, J Orthop Res, 31(9):1430-7, 2013. NIHMS519538
7. Buckley, M.R., Dunkman, A.A., Reuther, K.E., Kumar, A., Pathmanathan, L., Beason, D.P., Birk, D.E., Soslowsky, L.J.: Validation of an Empirical Damage Model for Aging and In Vivo Injury of the Murine Patellar Tendon, J Biomech Eng, 135, 041005-1, 2013. NIHMS498871
8. Reuther, K.E., Thomas, S.J., Evans, E.F., Tucker, J.J., Sarver, J.J., Ilkhani-Pour, S., Gray, C.F., Voleti, P.B., Glaser, D.L., Soslowsky, L.J.: Returning to Overuse Activity Following a Supraspinatus and Infraspinatus Tear Leads to Joint Damage in a Rat Model, J Biomech, 46(11):1818-24, 2013. (PMCID 3713088)
9. Buckley, M.R., Sarver, J.J., Freedman, B.R., Soslowsky, L.J.: The Dynamics of Collagen Uncrimping and Lateral Contraction in Tendon and the Effect of Ionic Concentration, J Biomech, 46(13):2242-9, 2013. (NIHMS508128)
10. Ahmadzadeh, H., Connizzo, B.K., Freedman, B.R., Soslowsky, L.J., Shenoy, V.B.: Determining the Contribution of Glycosaminoglycans to Tendon Mechanical Properties with a Modified Shear-Lag Model, J Biomech, 46(14):2497-503, 2013. NIHMS514212
11. Caro, A.,Tucker, J., Dunkman, A., Yannascoli, S., Soslowsky, L.J.: Efficacy of Various Analgesics on Shoulder Function and Rotator Cuff Tendon to Bone Healing in a Rat (Rattus norvegicus) Model, JAALAS, in press, 2013.
12. Buckley, M.R., Huffman, G.,R., Iozzo, R.V., Birk, D.E., Soslowsky, L.J.: The Location-Specific Role of Proteoglycans in the Flexor Carpi Ulnaris Tendon, Connective Tissue Research, 54(6):367-73, 2013.
13. Beason, D.P.; Tucker, J.J.; Edelstein, L.; Lee, C.S.; Abboud, J.A.; Soslowsky, L.J.; Rat Rotator Cuff Tendon-to-Bone Healing Properties are Adversely Affected by Hypercholesterolemia, J Shoulder Elbow Surg, in press, 2013.
14. Connizzo BK, Yannascoli SM, Tucker JJ, Caro AC, Riggin CN, Mauck RL, Soslowsky LJ, Steinberg DR, Bernstein J.: The Detrimental Effects of Systemic Ibuprofen Delivery on Tendon Healing Are Time-Dependent, Clin Orthop Relat Res., in press, 2013.
15. Dunkman, A., Buckley, M.R., Mienaltowski, M.J., Adams, S.M., Thomas, S.J., Satchell, L., Kumar, A., Pathmanathan, L., Beason, D.P., Iozzo, R.V., Birk, D.E., Soslowsky, L.J.: The Tendon Injury Response Is Influenced by Decorin and Biglycan, Ann Biomed Eng, in press, 2013.
16. Buckley MR, Evans EB, Matuszewski PE, Chen YL, Satchel LN, Elliott DM, Soslowsky LJ, Dodge GR.: Distributions of types I, II and III collagen by region in the human supraspinatus tendon, Connect Tissue Res, 54(6):374-9, 2013.
17. Thomas SJ, Reuther KE, Tucker JJ, Sarver JJ, Yannascoli SM, Caro AC, Voleti PB, Rooney SI, Glaser DL, Soslowsky LJ.: Biceps Detachment Decreases Joint Damage in a Rotator Cuff Tear Rat Model, Clin Orthop Relat Res, in press, 2013

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project. Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

Penn's capacity to conduct research on a variety of musculoskeletal and neurological diseases should be positively impacted by the project, thereby indirectly affecting individuals of all ages, genders and ethnic groups as the new research capacity is converted into discoveries of societal benefit.

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None.

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes__X_____ No_____

If "Yes" to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is "No.")

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a. Title of Invention: Shoulder Torque and Range of Motion Device [Penn Invention Disclosure W5325]

b. Name of Inventor(s): Joseph J. Sarver, Louis J. Soslowsky

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention): The invention relates to a device for measuring shoulder stiffness and range of motion. Specifically, the invention relates to a device for measuring shoulder stiffness and range of motion in human subjects, and methods for making and using thereof.

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes X___ No___

If yes, indicate date patent was filed:

Patent application filed, provisional patent application 61/302,375 "Shoulder Torque and range motion device", was filed 02/08/2010. US National Phase application, 13/577, 589, filed 08/07/2012, is still pending.

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes _____ No __X__
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No___X

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes_____ No ___X

If yes, describe the commercial development activities:

==========

a. Title of Invention: RNAi-therapeutic approaches for (FOP) [Penn Invention Disclosure Y6216/S4145]

b. Name of Inventor(s): Frederick S. Kaplan, Eileen M. Shore

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention): This invention is directed to mutated Activin A type I receptor proteins (ACVR1) and isolated nucleic acids encoding same. The invention also relates to compositions and methods for siRNA-based regulation of mutated ACVR1 expression in the treatment of Fibrodysplasia Ossificans Progressiva (FOP).

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes X___ No___

If yes, indicate date patent was filed:

Patent application " siRNA-based therapy of fibrodysplasia ossificans progressive (FOP), US National phase application 13/654,208, filed Oct 17, 2012, is still pending.

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes ____ No__X__
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No__X

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes___ No__X

If yes, describe the commercial development activities:

==========

a. Title of Invention: Production of aligned nanofibrous materials with a spatially varying orientation [Penn Invention Disclosure Y6050]

b. Name of Inventor(s): Robert L. Mauck, Matthew B. Fisher, Brendon M. Baker, Amy M. Silverstein, Jason Alan Burdick

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention): Provided are materials comprising layers of anisotropically aligned fibers, the alignment of which fibers may be adjusted so as to give rise to circumferentially-aligned fibers that replicate the fiber alignment of native fibrous tissue, such as the meniscus or the annulus fibrosis. Also provided are laminates formed from the disclosed materials, as well as methods of fabricating the disclosed materials and laminates.

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes X___ No____

If yes, indicate date patent was filed:

Patent application "aligned fibrous materials with spatially varying fiber orientation and related methods" provisional patent 61/594,551 was filed February 3, 2012; 13/422,027 a continuation-in-part application titled same, was filed 03/16/2012

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes ____ No__X__
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No___X

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes_____ No___X

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes____X_____ No_____

If yes, please describe your plans:

We will continue to investigate potential commercial applications and associated processes for work aided by this research project.

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Glen N. Gaulton, Ph.D.	Professor, Department of Pathology and Laboratory Medicine Executive Vice Dean and Chief Scientific Officer
eRA COMMONS USER NAME (credential, e.g., agency login) gaulton	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Southern California	B.S.	1974	Biology
University of California, Santa Barbara	Ph.D.	1981	Biochem. & Mol. Biol.

A. Personal Statement

The interests of the Gaulton laboratory focus on an increased understanding of the molecular processes that regulate the infection and pathology of retroviruses, such as HIV, the impact of these infections on the immune system, and the detection of these infections using novel imaging and diagnostic approaches. More specifically, the laboratory has investigated the effects of human and, as experimental models, murine retroviruses during active infection of adult, pediatric and neonatal subjects. Recent results have identified the primary mechanisms whereby retroviruses induce cell destruction through cell-cell fusion, also know as syncytia formation. The laboratory has pioneered the use of magnetic resonance imaging (MRI) techniques to detect HIV infection within cells and is now applying these techniques to in vivo, whole body imaging of active infections. Lastly, using state-of-the-art engineering technology, the laboratory is developing highly sensitive yet mobile, hand-held devices to detect HIV infection in blood and other body fluids. These devices are critical for diagnosing new infections, and to monitor HIV levels in patients undergoing active therapy and/or participating in vaccine trials. Dr. Gaulton also serves as the Chief Scientific Officer at Penn Medicine. In this role he is responsible for developing and implementing the institutional strategic plan in scholarship and research training for the Perelman School of Medicine.

Academic Appointments

1985-1991	Asst. Professor, Dept of Pathology and Laboratory Medicine, U.Penn, Sch. of Med., Phila, PA
1991-1998	Associate Professor (with tenure), Department of Pathology and Laboratory Medicine, U.Penn
1993-1998	Assoc. Dean and Dir., Combined Degree and Physician Scholar Prgms., U.Penn Sch. of Med.
1995-1998	Director, Biomedical Graduate Studies, University of Pennsylvania
1998-	Professor, Department of Pathology and Laboratory Medicine, U.Penn, School of Medicine

1998-2006	Vice Dean for Research and Research Training, University of Pennsylvania School of Medicine
2006-	Executive Vice Dean and Chief Scientific Officer, University of Pennsylvania School of Medicine

Honors and Awards

1986-1990	National Multiple Sclerosis Society, Harry Weaver Scholar
1990-	American Association of Immunologists
1991-1996	Leukemia Society of America Scholar
1994	University of Pennsylvania Leonard Berwick Teaching Award
1996	University of Pennsylvania Christian and Mary Lindback Teaching Award

C. Selected Peer-reviewed Publications

Additional recent publications of importance to the field (in chronological order)

2. Majka, M., Rozmyslowicz, T., Lee, B., Honczarenko, M., Gaulton, GN, Pietrzowski, Z., Poncz, M., Gewirtz, A.M., Silberstein, L. and Ratajczak, M.Z. 1999. R5 HIV Inhibitory Chemokines are Secreted by Human Bone Marrow CD34+ Cells and Interferon Upregulates their Expression. J. Clin. Invest. 104: 1739-1749. 10606628.
3. Majka, M., Rozmyslowicz, T., Honczarenko, M., Ratajczak, J., Wasik, M.A., Gaulton, GN, and Ratajczak, M.Z. 2000. Biological significance of the expression of HIV-related chemokine coreceptors (CCR5 and CXCR4) and their ligands by human hematopoietic cell lines. Leukemia 14: 1821-1832. 11021758.
4. Majka, M., Rozmyslowicz, T., Ratajczak, J., Dobrowsky, A., Pietrzowski, Z., Gaulton, GN, Janowska-Wieczorek, A., and Ratajczak, M.Z. 2000. The limited infectability by R5 HIV of CD34+ cells from thymus, cord and peripheral blood and bone marrow is explained by their ability to produce β chemokines. Experimental Hematology. 28: 1334-1342. 1146155.
5. Rozmyslowicz, T., Majka, M., Kijowski, J., Murphy, S.L., Conover, D.O., Poncz, M., Ratajczak, J., Gaulton, GN and Ratajczak, M.Z. 2003. Platelet- and megakaryocyte-derived microparticles transfer CXCR4 receptor to CXCR4-null cells and make them susceptible to infection by X4-HIV. AIDS 17: 33-42. 12478067.
6. Levinson A.I., Zheng Y., Gaulton GN, Song D., Moore J., and Pletcher H.. 2003. Intrathymic Expression of Neuromuscular Acetylcholine Receptors and the Immunpathogenesis of Myasthenia Gravis. Immunol. Res., 27:399. 12857984.
7. Levinson A.I., Zheng Y., Gaulton GN, Moore J., and Pletcher H., Song D., and Wheatley L.M. 2003. A new model linking intrathymic acetylcholine receptor expression and the pathogenesis of myasthenia Gravis. In Myasthenia gravis and related disorders. Ann. N.Y. Acad. Sci. 998:257-265. 14592882.
8. Landers, CM., Dugger, N., Quadros, M., Hoffman, P. M., and Gaulton, GN. 2004. Neuropathogenic murine leukemia virus TR1.3 induces selective syncytia formation of brain capillary endothelium. Virol. 321: 57-64. 15033565.
9. Murphy, SL, Honczarenko, MJ, Dugger, NV, Hoffman, PM and Gaulton, GN. 2004. Disparate regions of envelope protein regulate syncytium formation versus spongiform encephalopathy in neurological disease induced by murine leukemia virus TR. J. Virol. 78: 8392-8399. 152542.

10. Levinson AI, Song D, Gaulton GN, and Zheng. 2005. The intrathymic pathogenesis of myasthenia gravis. Clin Dev. Immunol. 11: 215-220. 15559366.
11. Lin G., Murphy, SL, Gaulton GN, and Hoxie JA. 2005. Modification of a viral envelope glycoprotein cell-cell fusion assay by utilizing plasmid encoded bacteriophage RNA polymerase. J Virol. Methods. 128: 135-142. 15941597.
12. Murphy, SL, Landers, CM, Honczarenko, MJ and Gaulton, GN. 2006. Linkage of reduced receptor affinity and superinfection to pathogenesis of TR1.3 murine leukemia virus. J. Virol. 80: 4601-4609. 16611920.
13. Murphy, SL and Gaulton, GN. 2007. TR1.3 Viral Pathogenesis and Syncytia Formation are Linked to Env-Gag Cooperation. J Virol. 81(19):10777-85. 1763219.
14. Rozmyslowicz T, Wroblewski K, Moodley J and Gaulton GN. "A Decrease in the Cellular Phosphodiester to Phosphomonoester Lipid Ratio is Characteristic of HIV-1 Infection", Curr. HIV Res., 2010, 8, 355-363.
15. Rozmyslowicz T, Murphy SL, Conover DO and Gaulton GN. "HIV-1 infection inhibits cytokine production in human thymic macrophages" accepted for publication, Exp. Hematol. 2010, 38, 1157-1166.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Soslowsky, Louis J.	Fairhill Professor
eRA COMMONS USER NAME (credential, e.g., agency login) SOSLOWSKY	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Columbia University, New York, NY	B.S.	1982-1986	Engineering Mechanics
Columbia University, New York, NY	M.S.	1986-1987	Engineering Mechanics
Columbia University, New York, NY	Ph.D.	1987-1991	Eng. Mech., Biomechanics

A. Personal Statement

My research program is focused on structure-function relationships in tendon and ligament and mechanisms of injury, healing, repair, and regeneration of tendons and ligaments. Current project areas include the use of transgenic mouse models for structure-function and healing studies, understanding mechanisms of scarless healing in fetal tendons, and use of the rat model to investigate fundamental mechanisms of rotator cuff injury and repair and associated joint damage. These studies are multi-disciplinary in nature, have a strong basis in mechanics, with other assays such molecular biology, biochemistry, histology, imaging, and in vivo assessments being utilized, often in animal model systems.

B. Positions and Honors

Positions and Employment

1991-96	Asst Professor, Orthopaedic Surgery and Mech. Eng. and Appl. Mech., University of Michigan
1991-97	Faculty Member, Bioengineering Program, University of Michigan
1996-97	Associate Director, Orthopaedic Research Laboratories, University of Michigan
1997-97	Associate Professor, Orthopaedic Surgery, Department of Surgery, University of Michigan
1997-04	Assoc Prof, Orthopaedic Surg (primary) and Bioengineering (secondary), Univ. of Pennsylvania
1997-	Member, Graduate Groups of Bioengineering and MEAM, University of Pennsylvania
1997-	Member, Institute for Medicine and Engineering, University of Pennsylvania
1997-	Director of Orthopaedic Research, University of Pennsylvania
2002-	Vice Chair for Research, Department of Orthopaedic Surgery, University of Pennsylvania
2004-	Professor, Dept of Orthop Surg (primary) and Dept of Bioeng. (secondary), Univ. of Pennsylvania
2006-	Member, Institute for Translational Medicine and Therapeutics, University of Pennsylvania

2006- Founding Director, Penn Center for Musculoskeletal Disorders, University of Pennsylvania

2008- Fairhill Professor, Perelman School of Medicine, University of Pennsylvania

C. Selected Peer-reviewed Publications (2013 and 2014 only from >140 peer-reviewed publications)

18. Connizzo, B.K., Yannascoli, S.M, Soslowsky, L.J.: Structure–function relationships of postnatal tendon development: A parallel to healing, Matrix Biol, 32(2):106-16 2013. (PMC3615149)
19. Dourte, L.M., Pathmanathan, L, Mienaltowski, M.J., Jawad, A.F., Birk, D.E., Soslowsky, L.J.: Mechanical, compositional, and structural properties of the mouse patellar tendon with changes in biglycan gene expression, J Orthop Res, 31(9):1430-7, 2013. NIHMS519538
20. Buckley, M.R., Dunkman, A.A., Reuther, K.E., Kumar, A., Pathmanathan, L., Beason, D.P., Birk, D.E., Soslowsky, L.J.: Validation of an Empirical Damage Model for Aging and In Vivo Injury of the Murine Patellar Tendon, J Biomech Eng, 135, 041005-1, 2013. NIHMS498871
21. Reuther, K.E., Thomas, S.J., Evans, E.F., Tucker, J.J., Sarver, J.J., Ilkhani-Pour, S., Gray, C.F., Voleti, P.B., Glaser, D.L., Soslowsky, L.J.: Returning to Overuse Activity Following a Supraspinatus and Infraspinatus Tear Leads to Joint Damage in a Rat Model, J Biomech, 46(11):1818-24, 2013. (PMCID 3713088)
22. Buckley, M.R., Sarver, J.J., Freedman, B.R., Soslowsky, L.J.: The Dynamics of Collagen Uncrimping and Lateral Contraction in Tendon and the Effect of Ionic Concentration, J Biomech, 46(13):2242-9, 2013. (NIHMS508128)
23. Ahmadzadeh, H., Connizzo, B.K., Freedman, B.R., Soslowsky, L.J., Shenoy, V.B.: Determining the Contribution of Glycosaminoglycans to Tendon Mechanical Properties with a Modified Shear-Lag Model, J Biomech, 46(14):2497-503, 2013. NIHMS514212
24. Caro, A.,Tucker, J., Dunkman, A., Yannascoli, S., Soslowsky, L.J.: Efficacy of Various Analgesics on Shoulder Function and Rotator Cuff Tendon to Bone Healing in a Rat (Rattus norvegicus) Model, JAALAS, in press, 2013.
25. Buckley, M.R., Huffman, G.,R., Iozzo, R.V., Birk, D.E., Soslowsky, L.J.: The Location-Specific Role of Proteoglycans in the Flexor Carpi Ulnaris Tendon, Connective Tissue Research, 54(6):367-73, 2013.
26. Beason, D.P.; Tucker, J.J.; Edelstein, L.; Lee, C.S.; Abboud, J.A.; Soslowsky, L.J.; Rat Rotator Cuff Tendon-to-Bone Healing Properties are Adversely Affected by Hypercholesterolemia, J Shoulder Elbow Surg, in press, 2013.
27. Connizzo BK, Yannascoli SM, Tucker JJ, Caro AC, Riggin CN, Mauck RL, Soslowsky LJ, Steinberg DR, Bernstein J.: The Detrimental Effects of Systemic Ibuprofen Delivery on Tendon Healing Are Time-Dependent, Clin Orthop Relat Res., in press, 2013.
28. Dunkman, A., Buckley, M.R., Mienaltowski, M.J., Adams, S.M., Thomas, S.J., Satchell, L., Kumar, A., Pathmanathan, L., Beason, D.P., Iozzo, R.V., Birk, D.E., Soslowsky, L.J.: The Tendon Injury Response Is Influenced by Decorin and Biglycan, Ann Biomed Eng, in press, 2013.

29. Buckley MR, Evans EB, Matuszewski PE, Chen YL, Satchel LN, Elliott DM, Soslowsky LJ, Dodge GR.: Distributions of types I, II and III collagen by region in the human supraspinatus tendon, Connect Tissue Res, 54(6):374-9, 2013.
30. Thomas SJ, Reuther KE, Tucker JJ, Sarver JJ, Yannascoli SM, Caro AC, Voleti PB, Rooney SI, Glaser DL, Soslowsky LJ.: Biceps Detachment Decreases Joint Damage in a Rotator Cuff Tear Rat Model, Clin Orthop Relat Res, in press, 2013
31. Dunkman AA, Buckley MR, Mienaltowski MJ, Adams SM, Thomas SJ, Kumar A, Beason DP, Iozzo RV, Birk DE, Soslowsky LJ. The Injury Response of Aged Tendons in the Absence of Biglycan and Decorin, Matrix Biol, in press, 2013.
32. Freedman, B.R., Sarver, J.J., Buckley, M.R, Voleti, P.D., Soslowsky, L.J Biomechanical and structural response of healing Achilles tendon to fatigue loading following acute injury, J Biomech, in press, 2013.
33. Riggin CN, Sarver JJ, Freedman BR, Thomas SJ, Soslowsky LJ.: Analysis of Collagen Organization in Mouse Achilles Tendon Using High-Frequency Ultrasound Imaging, J Biomech Eng, in press, 2013.
34. Freedman BR, Gordon JA, Soslowsky LJ. The Achilles Tendon: Fundamental Properties and Mechanisms Governing Healing, Muscles, Ligaments and Tendons Journal in press, 2014.
35. Reuther KE, Thomas SJ, Tucker JJ, Sarver JJ, Gray CF, Rooney SI, Glaser DL, Soslowsky LJ.: Disruption of the anterior-posterior rotator cuff force balance alters joint function and leads to joint damage in a rat model, J Orthop Res, in press, 2014