AWARD NUMBER: W81XWH-16-2-0067

TITLE: Extremity Regeneration of Soft Tissue Injury Using Growth Factor-Impregnated Gels

PRINCIPAL INVESTIGATOR: Simon Talbot, MD

CONTRACTING ORGANIZATION: Brigham and Women's Hospital
Boston, Massachusetts 02115

REPORT DATE: October 2018

TYPE OF REPORT: Annual Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2018	Annual	30Sep 2017 -29 Sep 2018

4. TITLE AND SUBTITLE

Extremity Regeneration of Soft Tissue Injury Using Growth Factor-Impregnated Gels

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-16-2-0067

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Brigham and Women's Hospital
Boston, Massachusetts 02115

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Due to contamination of coccidioidomycosis within the animal facility, there was a delay of four months. Despite this, seven swine surgeries have been performed during this period, totaling 12 since the start of this study. We have now begun testing the optimal dose of VEGF and IGF in addition to completing the optimal ischemia studies. A total of five swine have been followed to completion at four months post-operatively. We continue to refine our post-operative protocol to minimize insensate traumas which have led to wound necrosis and ultimately euthanasia of four swine. Ongoing studies to evaluate nerve and vessel regeneration continue to be tested. There has been ongoing research and development on the alginate gels and growth factors through collaboration with the Wyss Institute.

15. SUBJECT TERMS Nerve and vessel regeneration. Growth factor: VEGF and IGF.					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT Unclassified	b. ABSTRACT Unclassified	c. THIS PAGE Unclassified	Unclassified	36	19b. TELEPHONE NUMBER *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

The overarching, long-term goal of this project is to develop technologies that maximize restoration of severely injured limbs by restoring muscle and nerve functions and avoiding amputation. This research specifically focuses on promoting regeneration of the injured host tissue by use of exogenous growth factors. A natural soft polymer gel material, alginate, has been fabricated to release two natural growth factors – vascular endothelial growth factor (VEGF) and insulin-like growth factor-1 (IGF-1). Repeated injections of growth factor-alginate material are performed following a surgically induced traumatic ischemic injury and followed with muscle biopsies and nerve conduction studies to track regeneration. Preliminary results from small animal studies show that this approach can promote expansion of the host cells, and enhance restoration of blood flow, regeneration of muscle tissue, and reconnection of nerves. Currently, this project is being tested in a large animal swine model for its effectiveness in restoring blood flow, muscle and nerve tissue, and connection of nerve to muscles. The project will extend development of the injectable gel into a prototype product, suitable for commercialization.

2. KEYWORDS: Provide a brief list of keywords (limit to 20 words).

Vascularized endothelial growth factor (VEGF)
Insulin-like growth factor-1 (IGF-1)
Alginate gel
Ischemia-reperfusion
Large animal model

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

The major goals of this project as stated in the Statement of Work include:

Subtask	Timeline in Months	Completion
Subtask 1.1: Submission of IACUC protocol for Aims 1 and 2	1-4	Completed
Subtask 1.2: Process and method development product	1-8	50%
Subtask 1.3: Development of a large animal model	4-8	Completed
Subtask 1.4: Development of assays (histology), functional studies (walking) and electrophysiology studies (EMG/NCS)	4-8	Completed
Subtask 1.5: Evaluation of dose-response relationship in limb transection model	8-12	Final surgery scheduled Dec, 2018; histology data pending
Subtask 2.1: Determine function of each of VEGF and VEGF+IGF1 on nerve regeneration	12-18	Scheduled to begin Spring, 2019
Subtask 2.2: Determine function of each VEGF and VEGF+IGF1 on ischemia-reperfusion	18-24	Scheduled to begin Spring, 2019
Subtask 2.3: Method and process qualification	18-24	50%
Subtask 2.4: Pilot (non-GLP) pharmacology-toxicity studies	20-24	10%

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

During the second year of study, accomplishments include performing seven large animal swine surgeries. We have now begun testing the optimal dose of gel based VEGF and IGF in addition to completing the optimal ischemia studies. A total of five swine have been followed to completion at four months post-operatively. We have continued to perform studies every three weeks with EMG, muscle biopsies and functional walking assessments through collaboration with USUHS and the Wyss Institute.

Of the seven swine surgeries performed during this study period, five swine have been euthanized due to complications. One swine was euthanized following cardiac arrest during anesthesia induction and four were euthanized during the post-operative period for insensate traumatic toe necrosis. The IACUC protocol was reevaluated and modified through multiple discussions with the USUHS veterinary and IACUC staff to reduce risks post-operatively. Changes include modified dressings and padded surfaces on the insensate limb. Limbs are now casted and changed weekly to minimize traumatic risk. Additional support staff will be present to monitor swine during the early post-operative period.

Ongoing histopathology processing and interpretation of muscle biopsies continues. Pigs with 0 hour ischemia had essentially no effects upon their musculature. Pigs with 4 hours of ischemia and transected-coapted sciatic nerve had marked changes in musculature size and developed fibrosis over time. In one procedural control animal, there were several examples over several weeks of muscles arranged in a ringbinden fashion, which is often demonstrated in neurogenic atrophy. At 3 and 6 weeks post-surgery, the growth factor appears mixed in effectiveness, however this has only been assessed in 3 pigs at the time of this report. Following further, at weeks 15 and 18 post-surgery, the medium dose growth factor appears to have less fibrosis and atrophy compared with the procedural control pig. However, due to low numbers, sample variation cannot be excluded and the sample may not be representative.

Through collaboration with the Wyss Institute, all processes to manufacture and test the alginate gel are being performed. This includes evaluation of oxidization, reduction, filtration, sterilization and reconstitution for production of the alginate gel. As the project continues, final product qualifications will be carried out for cross linking density, sterility, endotoxin and growth factor release of the final product. Documentation for standard operating procedures (SOPs) and forms to support manufacturing and characterization of the alginate material have been drafted. The Wyss has created working protocols and batch forms to record relevant information and to ensure that characterization has been conducted in a consistent and uniform manner. These documents will ultimately serve as the basis of the quality documentation that will be used to generate materials under Good Laboratory Practice (GLP) and then Good Manufacturing Practices (GMP).

At the start of this period, a fungal infection developed within the large animal facility requiring decontamination. This resulted in cancelling and postponing surgeries for four months. Combined with delays during year one while obtaining initial IACUC and ACURO approval, we remain behind on our overall goals. Our final surgical procedure to evaluate the dose-response relationship in limb transection was completed December of 2018. We plan to begin studies to determine function of each VEGF and VEGF+IGF1 on independent nerve regeneration and ischemia-reperfusion in March of 2019. Procedures will continue to be scheduled in closer succession to eliminate lost time however completion of these studies will carry into our third year of study.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

By December, 2018, we will have completed the our final procedure to determine optimal dose of alginate gel-based VEGF and IGF1. In the spring of 2019, we will begin procedures to determine the function of each of VEGF and VEGF+IGF1 on nerve regeneration and ischemia-reperfusion. The Wyss Institute will finalize their processing and manufacturing of the alginate based growth factor and finalize method and process qualification to support a pharmacology-toxicity study. This will be the basis for discussion with the FDA as we prepare to submit for an investigational new drug (IND).

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Refinement of the large animal model was developed through discussion with USUHS veterinary and IACUC staff to reduce risks of post-operative insensate traumatic wounds. Modifications include padded surfaces on the insensate limb, modified dressings and weekly casting. This has reduced the risk of a traumatic toe wound which resulting in several prior ethical euthanizations.

Overall, we expect this research to have significant impact with progression to commercialization of an injectable product to aid in muscle and nerve regeneration in traumatic injuries.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report.

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Several swine have developed insensate limb wound necrosis ultimately resulting in euthanasia. Through discussions with IACUC and veterinary staff, padded surfaces and dressings on the insensate limb have been modified. Post-operatively, a cast is placed on the insensate limb and changed weekly for sanitation. Additional support staff are present to monitor swine during the early post-operative period.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

A four-month delay was incurred at the start of this year while the large animal facility underwent decontamination for a fungal infection. This, combined with initial delays obtaining IACUC and ACURO approval during year one, have resulted in an overall delay in our study. Procedures are being scheduled in closer succession to eliminate lost time however completion of these studies will carry into our third year of study.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use or care of vertebrate animals.

Several swine have developed insensate limb wound necrosis ultimately resulting in euthanasia. Through discussions with IACUC and veterinary staff, modifications to post-operative care have been instituted. This includes a modified dressing on the insensate limb and padded flooring to minimize traumatic wounds. Post-operatively, a cast is placed on the insensate limb and changed weekly for sanitation. Additional support staff are present to monitor swine during the early post-operative period.

Significant changes in use of biohazards and/or select agents

Nothing to report.

6. **PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

  Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Poster Presentation at the Military Health System Research Symposium, August 2018.

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

- Nothing to report.

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *biospecimen collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Name: Simon Talbot
Project Role: Principal Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2.40
Contribution to Project: Directs and oversees all phases of the study.

Name: EJ Caterson
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1.20
Contribution to Project: Assistance with planning and surgical aspects of the study.

Name: Sarah Kinsley
Project Role: Research Assistant
Research Identifier:
Nearest person month worked: 12.0
Contribution to Project: Involved in coordination and ensuring each phase of the project remains on schedule, writing protocols, purchasing.

Name: David Mooney
Project Role: Co-Principal Investigator
Research Identifier:
Nearest person month worked: 0.24
Contribution to Project: Involved in management of Wyss Institute input to project.

Name: Ed Doherty
Project Role: Co-Principal Investigator
Research Identifier:
Nearest person month worked: 2.40
Contribution to Project: Involved in coordination of production of Wyss gels.

Name: Alexander Stafford
Project Role: Scientist
Research Identifier:
Nearest person month worked: 2.40
Contribution to Project: Involved in production of gels.

Name: Des White
Project Role: Research Associate
Research Identifier:
Nearest person month worked: 6.0
Contribution to Project: Involved in production of gels.

Name: Tracy Snyder
Project Role: Research Associate
Research Identifier:
Nearest person month worked: 12.0
Contribution to Project: Involved in production of gels.

Name: Leon Nesti
Project Role: Co-Principal Investigator
Research Identifier:
Nearest person month worked: 0.12
Contribution to Project: Involved in management of USUHS staff and laboratory including coordination of animal experimentation on site.

Name: Jody Richardson
Project Role: Research technician
Research Identifier:
Nearest person month worked: 12.0
Contribution to Project: Involved in day-to-day running and local coordination of activities.

Name: Jaira Vasconcellos
Project Role: Staff scientist
Research Identifier:
Nearest person month worked: 6.0
Contribution to Project: Involved in day-to-day running and local coordination of activities.

Name: Amal Nadel
Project Role: Program manager
Research Identifier:
Nearest person month worked: 1.20
Contribution to Project: Involved in coordination of activities through USUHS.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not

necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Please see the attached and updated DoD support forms for Dr. Simon Talbot and Dr. Dave Mooney.

Summary of changes for Dr. Dave Mooney:

- Current: Alliance for Regenerative Rehabilitation Research and Training Grant
- Current: Engineering Skeletal Muscle with Biodegradable Hydrogels
- Current: Scaffolds Mimicking Antigen Presenting Cells
- Current (was pending): Material Engineered Scaffold Vaccines
- Current (was pending): Biomaterial Cancer Vaccines that Generate Patient-Specific Antigen In Situ
- Pending: Developing the Captured Antigen Presentation System as vaccine against bovine tuberculosis.
- Pending: Novel Mast Cell Stabilizers for the Management of the Diabetic Foot Ulceration
- Pending: Biomaterial-based Therapeutic Melanoma Vaccine
- Completed, now previous: Prolonged Field Care with Platform Wound Device
- Completed, now previous: Role of Macrophages in Impaired Wound Healing in Diabetes
- Completed, now previous: Hydrogels to Promote Tendon Healing
- Completed, now previous: Infection Mimicking Biomaterials for Vaccination against Gonadotropin Releasing Hormone
- Completed, now previous: Engineering skeletal muscle with biodegradable hydrogels.
- Completed, now previous: Biomaterial-based breast cancer vaccine.

Summary of changes for Dr. Simon Talbot:

- Completed: A novel protocol for upper extremity restoration by transplantation with intent for tolerance induction
- Pending: A novel approach to upper extremity amputation to augment volitional motor control and restore proprioception
- Pending: Cells and rejection in vascularized composite

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)

<u>Partner's contribution to the project</u> (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Organization name: United States Uniformed Health Services
Location of Organization: Associated with Walter Reed Military Medical Center in Bethesda, MD
Partner's Contribution to the project: Facilities and collaboration

Organization name: Wyss Institute for Biologically Inspired Engineering
Location of Organization: Associated with Harvard University. Located in Boston, MA
Partner's Contribution to the project: Collaboration and in-kind support developing the alginate and growth factor.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

Extremity Regeneration of Soft Tissue Injury Using Growth Factor Impregnated Gels

Log Number: DM153165
Award Number: W81XWH-16-2-0067

PI: Simon G. Talbot, MD **Org:** Brigham and Women's Hospital **Award Amount:** $2.1 M

Study/Product Aim(s)

Hypothesis: Injection of growth factor impregnated hydrogels can restore blood flow, promote muscle and nerve regeneration, and restore nerve connections to muscle.

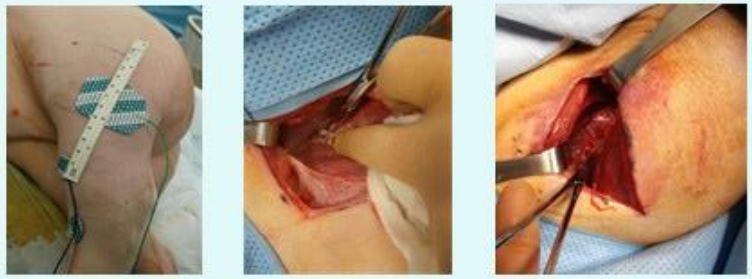
• Aims: Evaluate biocompatibility and efficacy of alginate gel-based delivery of VEGF and IGF-1 in a large animal model of limb injury including ischemia-reperfusion and nerve transection-repair in support of future human clinical studies.

Approach

Experiment 1: Determine optimal ischemia time and optimal growth factor dose in large animal model.

Experiment 2: Determine effect of VEGF and IGF-1 on nerve regeneration.

Experiment 3: Determine effect of VEGF and IGF-1 on ischemia-reperfusion.



L to R: Preoperative EMG. Femoral artery. Sciatic nerve and braches.

Accomplishment: Performed two surgeries in modified large animal model and completed ischemic duration studies.

Timeline and Cost

Activities	2017	2018	2019
Determine optimal ischemia time and optimal growth factor dose in large animal model.			
Determine effect of VEGF and IGF-1 growth factor on nerve regeneration.			
Determine effect of VEGF and IGF-1 growth factor on ischemia-reperfusion.			
Estimated Budget ($K)	733	702	665

Updated: 10/03/2018

Goals/Milestones

CY17 Goal – Determine optimal ischemia time and growth factor dose
☑Develop large animal model
☑Submit to IACUC and ACURO
☑Begin experiment 1 on 20 animals
☑Modify IACUC protocol to minimize postoperative risks
☑Preliminary testing of alginate gel confirms consistency of product

CY18 Goal – Determine effect of growth factor on nerve regeneration
☑Complete experiments to determine ischemia time
☑Begin dose experiments on 15 animals

CY19 Goal – Determine effect of growth factor on ischemia-reperfusion
☐ Experiment 3 on 15 animals.
☐ Develop IND application to FDA

Comments/Challenges/Issues/Concerns

• Increasing number of surgeries to meet goal completion date

Budget Expenditure to Date

Projected Expenditure:
Actual Expenditure: $1,128,439 (incl subcontracts $ 621,863)

9. APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

- DoD Support document for Simon Talbot
- DoD Support document for David Mooney

Other Support, Simon Talbot

Current

Title:	*A novel approach to lower extremity amputation to augment volitional motor control and restore proprioception*
Time Commitment:	6.5% effort
Supporting Agency:	US Department of Defense
Grants Officer:	Elena G. Howell, DOD, 820 Chandler St, Fort Detrick, MD, 21702-5014, 301-619-6871
Performance Period:	July 2017-June 2021
Level of funding:	$2,383,103
Project's Goals:	The goal of this project is to develop and validate a new surgical technique to lower extremity amputation that incorporates agonist-antagonist myoneural interfaces
Specific aims:	1. To define a standardized approach to the performance of a novel operative procedure for both below knee (BKA) and above knee (AKA) amputations 2. To measure the degree of volitional motor activation and excursion achievable in the residual limb constructs, and to determine the optimal configuration and design of such constructs 3. To describe the extent of proprioceptive and other sensory feedback achievable through the employment of these modified surgical techniques 4. To validate the functional and somatosensory superiority of the proposed amputation technique over standard approaches to BKA and AKA 5. To develop a modified acute postoperative rehabilitation strategy suited to this new surgical approach
Overlap:	This technology is equivalent but is based on upper rather than lower limbs.

Title	*Psychosocial predictors of VCA outcomes*
Time Commitment	12.5% effort (PI)
Supporting Agency	US Department of Defense
Grants Officer	Sandra Rosario, USAMRAA, 843 Chandler St, Fort Detrick, MD 21740, (301) 619-4063
Performance Period	07/1/2017-06/30/2020
Level of funding	$563,380
Project's Goals	The goal of this project is to determine key factors in determining outcomes for VCA patients.
Specific aims	Specific Aim 1: To evaluate prospectively collected data on the International Registry of Hand and Composite Tissue Transplantation (demographics, medical/surgical factors) to determine variables associated with transplant 'success.' Specific Aim 2: To develop a model based on expert opinion, focusing on psychosocial parameters, to help objectify the psychosocial evaluations of hand transplant patients. Specific Aim 3: To validate the model developed in Aims 1 and 2 in actual patients from the several large volume centers where complete data is available.
Overlap	None

Title:	*Extremity regeneration of soft tissue injury using growth factor-impregnated gels (W81XWH-16-2-0067)*
Time Commitment:	10% effort
Supporting Agency:	US Department of Defense
Grants Officer:	Elena G. Howell, DOD, 820 Chandler St, Fort Detrick, MD, 21702-5014, 301-619-6871
Performance Period:	09/30/2016-09/29/2019
Level of funding:	$2,100,000
Project's Goals:	The goal of this project is to investigate the use of growth-factor impregnated hydrogels for the improvement of nerve regeneration and limb function.
Specific aims:	The specific aims of this grant are to determine if the use of injectable hydrogel combined VEGF and IGF-1 can improve nerve growth in a large animal model, and thereafter to determine dose, scheduling, and produce a product for FDA approval.
Overlap:	None

Previous

Title:	*Engineering skeletal muscle with biodegradable hydrogels (4R01DE013349-16)*
Time Commitment:	5% effort
Supporting Agency:	National Institutes of Health
Grants Officer:	Gabriel Hidalgo, NIDCR, 6705 Rockledge Drive, Bethesda, MD 20892-7986
Performance Period:	08/28/2014-06/30/2017
Level of funding:	$91,629
Project's Goals:	The goal of this project is to test and further refine the use of biodegradable hydrogels in ischemia tissue and denervated tissue to improve tissue viability and recovery.
Specific aims:	The aims are to examine the ability of alginate gel-based delivery of VEGF and IGF-1 to enhance engraftment and function of a denervated tibialis anterior muscle, in young and aged mice and in a rabbit gracilis muscle transfer model.
Overlap:	Although the concept of tissue transfer and viability is central, there is no overlap between this animal model and the proposed clinical translational project.

Title:	*Design and testing of a robotic system to perform microscale anastomosis (URAD)*
Time Commitment:	5% effort
Supporting Agency:	The Charles Stark Draper Laboratory
Grants Officer:	Mary Luther, Draper Laboratory, 555 Technology Square, Cambridge, MA 02139-3563, (617) 258-2361
Performance Period:	July 2013-June 2014
Level of funding:	$110, 000
Project's Goals:	The project goals were to develop micro-robotic technology for microsurgery.
Specific aims:	The aims were to miniaturize and improve fidelity of micro-instruments through the development of micro-sensors and to modify existing robotic control systems for this purpose.
Overlap:	None

Title:	*A novel protocol for upper extremity restoration by transplantation with intent for tolerance induction (W81XWH-12-2-0037)*
Time Commitment:	5% effort
Supporting Agency:	US Department of Defense
Grants Officer:	Elena G. Howell, DOD, 820 Chandler St, Fort Detrick, MD, 21702-5014, 301-619-6871
Performance Period:	09/30/2012-09/29/2017
Level of funding:	$ 2,005,315
Project's Goals:	The goal of this project is to induce tolerance to upper extremity allografts in four human transplant recipients through a mixed chimerism approach.
Specific aims:	(1) To perform upper extremity transplantation followed two months later by delayed bone marrow transplantation in four subjects; (2) To determine whether mixed lymphohematopoietic chimerism reduces the immune response to upper extremity allografts by in vitro analysis of recipient T- cell subtypes and function, allowing for reduction or withdrawal of immunosuppression after upper extremity/bone marrow transplantation; (3) To study the outcomes of upper extremity allotransplantation in a cohort of four patients for a period of one year post-transplant.
Overlap:	None

Pending

Title:	*A novel approach to upper extremity amputation to augment volitional motor control and restore proprioception (W81XWH-12-2-0037)*
Time Commitment:	TBD
Supporting Agency:	US Department of Defense
Grants Officer:	Elena G. Howell, DOD, 820 Chandler St, Fort Detrick, MD, 21702-5014, 301-619-6871
Performance Period:	July 2018-June 2022
Level of funding:	$3,000,000
Project's Goals:	The goal of this project is to develop and validate a new surgical technique to upper extremity amputation that incorporates agonist-antagonist myoneural interfaces
Specific aims:	1) To define a standardized approach to the performance of a novel operative procedure for both below elbow (BEA) and above elbow amputations (AEA) 2) To measure the degree of volitional motor activation and excursion achievable in the residual limb constructs, and to determine the optimal configuration and design of such constructs 3) To describe the extent of proprioceptive feedback achievable through the employment of these modified surgical techniques 4) To validate the functional and somatosensory superiority of the proposed amputation technique over standard approaches to BEA and AEA 5) To develop a modified acute postoperative rehabilitation strategy suited to this new surgical approach
Overlap:	None
Title	*Cells and rejection in vascularized composite(W81XWH-18-1-0785)*
Time Commitment:	TBD
Supporting Agency:	US Department of Defense
Grants Officer:	Elena G. Howell, DOD, 820 Chandler St, Fort Detrick, MD, 21702-5014, 301-

	619-6871
Performance Period:	July 2018-June 2020
Level of funding:	TBC
Project Goals:	This research aims to determine the relative contribution of donor versus recipient-derived T cells in VCA rejection, elucidate if monitoring pathogenic T cell clones in the circulation can be used as a rejection biomarker, and establish the correlation of rejection in sentinel flaps and clinical VCA allografts to determine the clinical utility of sentinel flaps as remote site rejection biomarkers.

OTHER SUPPORT

MOONEY, DAVID J.

CURRENT

Title: Material Research Science and Engineering Center (MRSEC) (DMR-1420570)
Time Commitment: .01 calendar months
Supporting Agency: National Science Foundation, (PI:Weitz,D.)
Name and address of funding agency's Procuring Contracting/Grants Officer: Daniele Finotello, DMR Division of Material Research, MPS Director for Mathematical and Physical Science, 4201 Wilson Blvd., Arlington, VA 22230
Performance Period: 11/01/14-10/31/20
Level of Funding: $100,000
Brief description of project's goals: This center identifies new research areas, and trains and retains students in materials science and engineering.

Title: Polymeric Matrices with Defined Cell Adhesion (R01DE013033-17)
Time Commitment: 1.52 calendar months
Supporting Agency: National Institutes of Health (NIH/NIDCR)
Name and address of funding agency's Procuring Contracting/Grants Officer: Nadya Lumelsky, PhD., Director of Tissue Engineering and Regenerative Research Programs, Room 618, 6701 Democracy Blvd, Bethesda, MD, 20892-4878
Performance Period: 07/14/14-05/31/19
Level of Funding: $312,724 Current Annual Direct Costs
Brief description of project's goals: The aim of this proposal is to develop materials to enable the regeneration of bony tissues for reconstructive dental and craniofacial applications.

Title: Extremity regeneration of soft tissue injury using growth factor impregnated gels (W81XWH-16-2-0067)
Time Commitment: .12 calendar months
Supporting Agency: Department of Defense
Name and address of funding agency's Procuring Contracting/Grants Officer: Elena G. Howell, Grants Officer, 820 Chandler Street, Fort Detrick, MD 21702-5014.
Performance Period: 9/30/16-09/29/19
Level of Funding: $168,517 Current Annual Direct Costs
Brief description of project's goals: The Programmable Nanomaterials (PNM) platform of the Wyss Institute for Biologically Inspired Engineering at Harvard University will develop a biomaterial for delivery of growth factors to promote limb regeneration. This project will be a component of a larger collaborative project in which these materials are used in a large animal model (animal work to be done at collaborators lab). The PNM will perform the studies and collect data required to file an IND application with the FDA at the completion of these studies. *Subcontractor to Brigham and Women's Hospital.*

Title: A New Platform for Burn Treatment and for Delayed Evacuation of Service Members (W81XWH-16-1-0784)
Time Commitment: 0.01 calendar month
Supporting Agency: DOD (Sub from Eriksson/BWH)
Name and address of funding agency's Procuring Contracting/Grants Officer: Grants Mgmt. Specialist/Grants Officer, Assistance Agreements Branch 1, U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick, MD 21072
Performance Period: 09/30/16-08/31/19
Level of Funding: $54,165 Current Annual Direct Costs
Brief description of project's goals: Develop a new device capable of providing high, local concentrations of antibiotics to severe burns, in order to prevent and eliminate infections. *Subcontractor to the Metis Foundation.*

Title: Mechanisms of Prosthetic Arterial Graft Failure (R01HL021796)
Time Commitment: 1.2 calendar months
Supporting Agency: National Institutes of Health (NIH/NHLBI)
Name and address of funding agency's Procuring Contracting/Grants Officer: Gary H. Gibbons, M.D., Director of the National Heart Lung and Blood Institute, Building 31, Room 5A52, 31 Center Drive MSC2486, Bethesda, MD 20892.
Performance Period: 02/01/17-01/31/2022
Level of Funding: $113,574 Current Annual Direct Costs
Brief description of project's goals: Dr. Mooney's laboratory will develop the cryogel system for sustained delivery of therapeutic agents from the grafts. The laboratory will design the hydrogels, synthesize and characterize. They will collaborate closely with the LoGerfo laboratory in the animal studies in which these materials are tested. *Subcontractor to Beth Israel Deaconess Medical Center.*

Title: 3D Models of Immunotherapy (U01CA214369)
Time Commitment: 1 calendar month
Supporting Agency: National Institutes of Health (NIH/NCI)
Name and address of funding agency's Procuring Contracting/Grants Officer: Marta Owusu, National Cancer Institute, BG 9609 MSC 9760, 9609 Medical Center Drive, Bethesda, MD 20892-9760
Performance Period: 4/1/17-3/31/22
Level of Funding: $109,977 Current Annual Direct Costs
Brief description of project's goals: At the completion of this project we will have developed and thoroughly characterized novel, 3D models of both mouse and human biology that will replicate the vaccination site and vascularized tumors.

Title: Michigan-Pittsburgh-Wyss Resource Center: Supporting Regenerative Medicine in Dental, Oral and Craniofacial Technologies (U24DE026915) (Kohn, D.)
Time Commitment: .9 calendar months

Supporting Agency: NIH/NIDCR
Name and address of funding agency's Procuring Contracting/Grants Officer: Gabriel Hidalgo hidalgoge@nidcr.nih.gov Phone: 301-827-4630
Performance Period: 3/1/17-2/29/20
Level of Funding: $82,953 Current Annual Direct Costs, $69,670 in Supplemental (ITP) Direct Costs
Brief description of project's goals: Our project aims to address the problem of dental disease. Dental caries affects 60-90% of school-age children and the vast majority of adults worldwide, which impact long-term oral health causes significant economic impact. Developing reliable and affordable therapeutic strategies for treating dental diseases is an important area of investigation**.**
Supplement: To identify, develop and validate a high-pressure carbon dioxide process to terminally sterilize the final alginate/VEGF/ IGF product.

Title: MSC Encapsulations with Thin Gel Coating (R01EB023287)
Time Commitment: 1 calendar month
Supporting Agency: National Institutes of Health (NIH/NIBIB)
Name and address of funding Agency's Procuring Contracting/Grants Officer: Florence Turska Email: ft7p@nih.gov Phone: 301-496-9314
Performance Period: 9/15/17-6/30/20
Level of Funding: $133,333 Direct Costs
Brief description of project's goals: Here, we propose to further develop this new technology, and to study its utility in context of hematopoietic stem cell therapy (HSCT). We have put together a unique team to address the hypothesis underlying this project, with leaders in microfluidics technology (Weitz), biomaterials (Mooney), and hematopoietic stem cell (HSC) biology and HSCT (Scadden).

Title: Biomaterial Cancer Vaccines that Generate Patient-Specific Antigen In Situ (R01CA223255)
Time Commitment: 1 calendar month
Supporting Agency: National Institutes of Health (NIH/NCI)
Name and address of funding Agency's Procuring Contracting/Grants Officer: Marianne Galczynski, Marianne.galczynski@nih.gov, NCI, Bethesda MD, Phone: 240-276-6300
Performance Period: 11/1/17-10/31/22
Level of Funding: $228,750 Current Annual Direct Costs
Brief description of project's goals: This project will result in the development of new, Patient-specific vaccination strategy that does not require personalized manufacturing.

Title: Material Engineered Scaffold Vaccines
Time Commitment: .01 calendar months
Supporting Agency: Novartis
Name and address of funding agency's Procuring Contracting/Grants Officer: Novartis Institutes for Biomedical Research, Attn: General Counsel, 250 Massachusetts Avenue, Cambridge, MA 02139

Performance Period: 3/2/18-3/2/20
Level of Funding: $397,878 Current Annual Direct Costs
Brief description of project's goals: Research and development of PLG engineered vaccine scaffolds containing autologous tumor necrotic tumor lysate, GM-CSF and Novartis Adjuvants and Novartis Other Molecules up to and including pre-clinical toxicology assessment.

Title: Alliance for Regenerative Rehabilitation Research and Training Grant (AR3T) (P2CHD086843)
Time Commitment: .12 calendar months
Supporting Agency: Eunice Kennedy Shriver National Institute of Child Health & Human Development (NICHD) (PI; Ambrosio, F.)
Name and address of funding Agency's Procuring Contracting/grants Officer: Ralph M. Nitkin, PhD, Deputy Director NCMRR, Rockville, MD 20847
Performance Period: 07/30/18-06/30/20
Level of Funding: $56,000 (Harvard subcontract)
Brief description of project's goals: Robotic actuator for in vivo muscle stimulation. Development of a soft robotic device which can deliver various mechanical parameters to severely injured murine skeletal muscle in a controlled manner with adaptability of ultrasound imaging during stimulation.

Title: Engineering Skeletal Muscle with Biodegradable Hydrogels (2R01DE013349)
Time Commitment: .77 calendar month
Supporting Agency: National Institute of Health (NIH/NIDCR)
Name and address of funding agency's Procuring Contracting/Grants Officer: April Harrison, harrisona@mail.nih.gov, Phone: 301-827-4628, 6701 Democracy Blvd, Bethesda, MD, 20892-4878
Performance Period: 07/06/18-06/30/23
Level of Funding: $385,804 (Current Annual Direct Costs)
Brief description of project's goals: The aims of this proposal are to engineer skeletal muscle by developing biodegradable hydrogels, which mediate transplanted cell population of damaged muscle, in concert with delivery of growth factors that mediate revascularization and reinnervation of the damaged muscle.

Title: Scaffolds Mimicking Antigen Presenting Cells
Time Commitment: .6 calendar months
Supporting Agency: DHHS/FDA
Name and address of funding agency's Procuring Contracting/Grants Officer:
Performance Period: 09/20/18-08/31/21
Level of funding: $326,099 Current Annual Direct Costs
Brief description of project's goals: The specific objectives for this project are (1) Establish SOPs for APC-ms synthesis. This will include identifying MSR critical quality attributes (CQAs) for functional APC-ms and understanding how critical process parameters (CPPs) in MSR

synthesis affect those CQAs (2) Develop a process to directly and selectively conjugate surface cues onto lipid bilayers, via click chemistry, to simplify and modularity of APC-ms assembly and function. (3) Characterize residual APC-ms materials during T cell processing, and perform a thorough in vivo safety assessment. The successful achievement of these aims will immediately address key issues related to using APC-ms as an ex vivo T-cell expansion platform.

PENDING

Title: Developing the Captured Antigen Presentation System (CAPS) as vaccine against bovine tuberculosis
Time Commitment: .01 calendar months
Supporting Agency: International Development Research Center
Name and address of funding agency's Procuring Contracting/Grants Officer: pending
Performance Period: 06/15/18-12/31/19 *(in negotiations)*
Level of funding: $311,485 Direct Costs
Brief description of project's goals: The ultimate aim of the proposed work is to develop an effective, safe and cost-effective vaccine against bovine TB.

Title: Novel Mast Cell Stabilizers for the Management of the Diabetic Foot Ulceration
Time Commitment: .01 calendar months
Supporting Agency: NIH (subcontractor to BIDMC)
Name and address of funding agency's Procuring Contracting/Grants Officer: pending
Performance Period: 4/1/19-3/31/24
Level of Funding: $40,168
Brief description of project's goals: The goal of our part of the project will incorporate protective hydrogels that allow for a sustained release to the underlying epidermis and dermis. We have previously demonstrated that degradable, injectable alginate gels can provide sustained SP delivery. In this project, we will instead develop bandage-like hydrogels fabricated from alginate to deliver SP.

Title: Biomaterial-based therapeutic melanoma vaccine
Time Commitment: .6 calendar months
Supporting Agency: NIH (subcontractor to DFCI)
Name and address of funding agency's Procuring Contracting/Grants Officer: pending
Performance Period: 4/1/19-3/31/24
Level of Funding: $345,506
Brief description of project's goals: The Wyss Institute will use its expertise in biomaterials and translation to conduct process and method development to support pre-clinical data generation to support the IND submission. In addition, the Wyss Institute will develop a GMP process for the vaccine component of the product which will be supplied to the DFCI for clinical testing when combined with the human lysate portion of the vaccine.

PREVIOUS

Title: Prolonged Field Care with Platform Wound Device
Time Commitment: .01 calendar months
Supporting Agency: DOD/(Eriksson/Applied Tissue Technologies, Inc.)
Name and address of funding agency's Procuring Contracting/Grants Officer: Grants Mgmt.
Specialist/Grants Officer, Assistance Agreements Branch 1, U.S. Army Medical Research Acquisition
Activity, 820 Chandler Street, Fort Detrick, MD 21072
Performance Period: 1/1/17-9/6/18 (early termination of subcontract in process)
Level of Funding: $103,550 Direct Costs
Brief description of project's goals: Dr. Mooney will develop antibiotic/hydrogel formulations designed to deliver topical antimicrobials to severe blast/burn wounds. He will test these formulations in vitro, and will provide precise descriptions of the antibiotic/hydrogel formulations to Applied Tissue Technologies.

Title: Role of Macrophages in Impaired Wound Healing in Diabetes (1DP3DK108224-01)
Time Commitment: 1 calendar month
Supporting Agency: National Institute of Health (NIH/NIDDK)
Name and address of funding Agency's Procuring Contracting/grants Officer: Theresa Jones, M.D.,
Division Diabetes Endocrinology, and Metabolic Diseases, 6707 Democracy Blvd., Bethesda, MD
20892-4878
Performance Period: 09/30/15-08/31/18
Level of Funding: $132,871
Brief description of project's goals: The aim of this proposal is to develop and test the ability of biomaterials capable of localized, sequential release of factors to first recruit macrophages, and then direct these cells to enhance healing in both *in vitro* engineered skin models and in diabetic, neuropathic rodent wounds. *Subcontractor to Beth Israel Deaconess Medical Center.*

Title: Hydrogels to Promote Tendon Healing (A21448)
Time Commitment: .01 calendar months
Supporting Agency: Novartis Pharmaceuticals Corporation
Name and address of funding Agency's Procuring Contracting/grants Officer: Dr. Michael Hoever, Director – Operational Alliances, Novartis Pharma AG, PO Box CH4002 Basel, Switzerland.
Performance Period: 09/01/14-08/31/18
Level of Funding: $398,246
Brief description of project's goals: The aim of this project is to develop controlled release polymers for drugs that promote tendon regeneration.

Title: Infection Mimicking Biomaterials for Vaccination against Gonadotropin Releasing Hormone (GnRH)
Time Commitment: .01 calendar months
Supporting Agency: Found Animals Foundation
Name and address of funding Agency's Procuring Contracting/grants Officer: Becky Cyr, Program

Manager Michelson Prize and Grants, Found Animals Foundation, Post Office Box 66370, Los Angeles, CA 90066.
Performance Period: 11/21/14-11/20/17
Level of Funding: $216,092
Brief description of project's goals: The aim of this proposal is to develop a biomaterial-based vaccine against GnRH that can be injected via needle and syringe.

Title: Engineering skeletal muscle with biodegradable hydrogels (5R01DE013349-14)
Time Commitment: .77 calendar month
Supporting Agency: National Institute of Health (NIH/NIDCR)
Name and address of funding Agency's Procuring Contracting/grants Officer: Nadya Lumelsky, PhD., Director of Tissue Engineering and Regenerative Research Programs, Room 618, 6701 Democracy Blvd, Bethesda, MD, 20892-4878
Performance Period: 07/01/12-06/30/18
Level of Funding: $538,722
Brief description of project's goals: The aims of this proposal are to engineer skeletal muscle by developing biodegradable hydrogels, which mediate transplanted cell population of damaged muscle, in concert with delivery of growth factors that mediate revascularization and reinnervation of the damaged muscle.

Title: Stimuli Responsive, Reloadable, Drug Eluting, Smart Hydrogels for Graft Targeted Immunosuppression in Vascularized Composite Allotransplantation (MR141089)
Time Commitment: .50 calendar months
Supporting Agency: DoD (subcontract from University of Pittsburg, PI: Gorantla, V.)
Name and address of funding Agency's Procuring Contracting/grants Officer: Elena Howell, Grants Mgmt. Specialist/Grants Officer, Assistance Agreements Branch 1, U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick, MD 21072
Performance Period: 07/1/15-06/30/17
Level of Funding: $94,497
Brief description of project's goals: The aim of this proposal is to develop targeted release of embedded anti-rejection therapies (TREAT) technology that will allow for predictable and reliable loco-regional immunosuppression in grafts without systemic toxicity.

Title: Biomaterial-based breast cancer vaccine (5R01EB015498-01A1)
Time Commitment: .76 calendar month
Supporting Agency: National Institute of Health (NIH/NIBIB)
Name and address of funding Agency's Procuring Contracting/grants Officer: Dr. Jessica Tucker, Division of Discovery Science and Technology, Bldg. 2 DEM, Room 200, 6707 Democracy Blvd., Bethesda, MD 20892-4878
Performance Period: 04/01/13-09/30/17 (NCE)
Level of Funding: $293,265
Brief description of project's goals: The aim of this proposal is to create a new approach to breast cancer vaccines, in which biomaterials that can be introduced into the body in a minimally invasive manner are used to program, in situ, host dendritic cells to generate a potent immune response.

Title: Human anti-MICA monoclonal antibodies for melanoma immunotherapy (MRA 269516)
Time Commitment: .12 calendar months
Supporting Agency: Melanoma Research Alliance (Subcontract from DFCI, PI: Wucherpfennig, K.)
Name and address of funding Agency's Procuring Contracting/grants Officer: Louise M. Perkins, Ph.D., The Melanoma Research Alliance Foundation, 1101 New York Avenue, NW, Suite #620, Washington, DC 20005
Performance Period: 05/01/15-04/30/17
Level of Funding: $100,000
Brief description of project's goals: The aim of this project is to develop antibody responses to modulate tumor tolerance mechanisms.

Title: iPSC-derived repair-responsive fibroblasts to heal diabetic foot ulcers (5R01DK098055)
Time Commitment: .24 calendar months
Supporting Agency: National Institute of Health (NIH/NIDDK) (Sub from BIDMC, PI: Garlick, J.)
Name and address of funding Agency's Procuring Contracting/grants Officer: Theresa Jones, M.D., Division Diabetes, Endocrinology, and Metabolic Diseases, 6707 Democracy Blvd., Bethesda, MD 20892-4878
Performance Period: 08/01/12-1/31//17
Level of Funding: $52,212
Brief description of project's goals: The aim of this proposal is to differentiate and characterize fibroblast cell lines from iPSC reprogrammed from diabetic foot ulcers to fibroblasts laboratory. 2. Develop polymeric delivery vehicles for the cell transplantation studies in the mouse and rabbit models.

Title: Building the hematopoietic stem cell niche (5R01EB14703-04)
Time Commitment: .75 calendar month
Supporting Agency: National Institute of Health (NIH/NIBIB)
Name and address of funding Agency's Procuring Contracting/grants Officer: Rosemary Hunziker, PhD., Division of Discovery Science and Technology, Bldg. 2 DEM Room 235, 6707 Democracy Blvd, Bethesda, MD 20892-4878
Performance Period: 09/15/11-07/30/16
Level of Funding: $541,625
Brief description of project's goals: The aim of this proposal is creating 3D model of hematopoiesis, in which mesenchymal stem cells (MSCs) and other cells of the osteoblast lineage, and vascular cells have been hypothesized to play a key role in the hematopoietic stem cell (HSC) niche.

Title: Novel therapeutic approaches for the Management of Foot Ulceration (R24DK091210-01A1)
Time Commitment: .36 calendar months

Supporting Agency: National Institute of Health (NIH/NIDDK) (sub from BIDMC, PI: Veves, A.)
Name and address of funding Agency's Procuring Contracting/grants Officer: Theresa Jones, M.D., Division Diabetes Endocrinology, and Metabolic Diseases, 6707 Democracy Blvd., Bethesda, MD 20892-4878
Performance Period: 4/01/12-3/31/14
Level of Funding: $75, 000
Brief description of project's goals: The aim of this proposal is to establish a collaborative team with expertise in bioengineering, basic and translational research to develop new biomaterials that will improve diabetic foot ulceration healing.

Title: Engineering Capillary Networks (5R01HL069957)
Time Commitment: 1.00 calendar months
Supporting Agency: National Institute of Health (NIH/NHLBI)
Name and address of funding Agency's Procuring Contracting/grants Officer: Martha Lundberg**,** Ph.D., Program Director, Tissue Engineering and Regenerative Medicine Two Rockledge Center, Room 9146, MSC 7940 6701 Rockledge Drive Bethesda, MD 20892-7956
Performance Period: 5/13/10-4/30/15
Level of Funding: $481,407
Brief description of project's goals: The aims of this proposal are to investigate the mechanisms and delivery of stem cells with growth factors to provide sustained angiogenic stimulus in the ischemic limb using SCID mice and rabbit models of diabetes.

Title: Programming dendritic cells in concert with morphagen delivery for periodontal regeneration (5R01DE019917)
Time Commitment: 1.00 calendar months
Supporting Agency: National Institute of Health (NIH/NIDCR)
Name and address of funding Agency's Procuring Contracting/grants Officer: Nadya Lumelsky, PhD., Director of Tissue Engineering and Regenerative Research Programs, Room 618, 6701 Democracy Blvd, Bethesda, MD, 20892-4878
Performance Period: 6/1/09-5/31/14
Level of Funding: $584,239
Brief description of project's goals: The goal of this application is to develop polymers that can simultaneous ameliorate inflammation and promote bone regeneration via delivery of inductive molecules.