AD_____

AWARD NUMBER: W81XWH-14-2-0162

TITLE: Identification and Validation of Established and Novel Biomarkers for Infections in Burns

PRINCIPAL INVESTIGATOR: Celeste C. Finnerty, PhD

RECIPIENT: The University of Texas Medical Branch at Galveston

REPORT DATE: October **2018**

TYPE OF REPORT: Annual

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	30 Sep 2017 - 29 Sep 2018

4. TITLE AND SUBTITLE

Identification and Validation of Established and Novel Biomarkers for Infections in Burns

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-14-2-0162

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Celeste C. Finnerty, PhD
Associate Professor, Department of Surgery
The University of Texas Medical Branch at Galveston
E-Mail: ccfinner@utmb.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
The University of Texas Medical Branch at Galveston
301 University Boulevard
Galveston, TX 77555-5302

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

Hypothesis: Plasma proteins, clinical data, and patient characteristics can be used to prospectively identify severely burned patients who are at risk for developing sepsis and other infections. Measurement of already identified biomarkers alongside novel biomarkers identified with discovery proteomics can improve identification of risk for infection and identify the early stages of infection prior to clinical detection. This multicenter study will enable us to identify novel biomarkers, validate whether the already identified biomarkers are appropriate, and establish a predictive model. **Rationale:** Our prior work has shown that severely burned patients who die from sepsis can be identified via their serum protein expression profile at the time of admission, that in the days prior to septic death there is an increase in serum biomarker expression, and that the use of both clinical and proteomic information as biomarkers improves the accuracy of patient survival prediction. Others have shown that procalcitonin is a good candidate marker of sepsis in burn patients. Clinical indices such as heart rate, mean arterial pressure, base deficit, temperature, and glucose levels more accurately identify sepsis in the burn patients than does the ABA consensus definition. **Methods:** 200 patients will be enrolled at four sites within the Burns Research in Texas Consortia. Blood samples will be taken daily, and clinical data recorded. **Specific Aims:** 1. Determine plasma proteomic biomarkers for the prediction and diagnosis of sepsis using mass spectrometry techniques; use stable isotope techniques to detect proteins for which assays do not exist. 2. Validate already identified markers of infection in a multicenter study 3. Develop a model of prediction of infection using clinical data and proteomic information. **Relevance:** 5% of combat-sustained casualties are burn injuries; ~20% of burn patients develop sepsis. This is a life-threatening disease which needs to be treated as early as possible. The studies described here will improve clinical care for the severely burned Wounded Warriors and other burn victims.

15. SUBJECT TERMS
Nothing Listed

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	16	19b. TELEPHONE NUMBER *(include area code)*

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

TABLE OF CONTENTS

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

Biomarkers predicting the development of sepsis and/or infections in burn patients have been proposed, but not validated. In our four site study, we are enrolling severely burned adults and collecting clinical data and blood samples in order to test already proposed biomarkers of infections and sepsis. Additionally we will use novel mass spectrometry techniques to identify heretofore unidentified biomarkers of infections and/or sepsis.

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

Sepsis, biomarkers, burns, infections, proteins, cytokines, mass spectrometry

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 and objectives 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.

A) Protocol Development (to occur prior to subject enrollment) – completion 100%
B) Obtain IRB approval for all five participating sites- 95%
C) Trial Conduct (to occur once enrollment begins until final subject completes protocol) 40%
D) Sample Analysis 0%
E) Data Analysis (to occur following completion of data collection) 0%
F) Maintain accurate and responsible budget – 50%
G) Publish research data 0%

What was accomplished under these goals?
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.

For UTMB: Five pediatric patients were enrolled. UTMB and SHC temporarily suspended burn research. Finally, samples for all 5 pediatric patients were lost due to negligence (described below).

For USAISR: Dr. Rizzo is the PI at USAISR and they have closed the study given the present burns research situation of UTMB. USAISR never enrolled a patient because the study got approved, then the PI got deployed, then research was put on hold at UTMB.

For UTSW there is at the present no known PI for the site. Five patients enrolled at UTSouthwestern. Data will be analyzed and no further enrollment will take place.

For UTHSC-Houston
Thirteen adult patients enrolled. Data will be analyzed in Houston or UTMB depending on funding resources and laboratory resources.

(a) *Human Use Regulatory Protocols*

Describe the Regulatory Protocol and Activity Status (if applicable).
Describe the Protocol and Activity Status for sections a-c, as applicable, using the format described for each section. If there is nothing significant to report during this reporting period, state "Nothing to Report."

We are also moving toward electronic data extraction as opposed to hand extraction, and hope to have an automated process developed with the University's Institute for Translational Sciences and the UTMB Information Services team.

TOTAL PROTOCOLS (_1of 1_ total):

Protocol [HRPO Assigned Number]: Nothing to Report
Title: Identification and Validation of Established and Novel Biomarkers for Infection in Burns
Target required for clinical significance: 200
Target approved for clinical significance: Nothing to Report

SUBMITTED TO AND APPROVED BY:
- Any and all IRB documents will be forwarded to HRPO for approval of next steps or any further activity.

STATUS:
(i) Number of subjects recruited/original planned target: 200
Number of subjects screened/original planned target: >65
Number of patients enrolled/original planned target: 41/200
Number of patients completed/original planned target: 41 total to date

Forty one patients have been enrolled to date, data collected, and samples banked. (UTMB = 18; Shrine = 5; UTHSC-Houston = 13; UTSouthwestern = 5; USAISR = 0).

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review: Nothing to Report

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation: Nothing to Report

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.

This project will be closed to enrollment and only active for data analysis / report writing will be performed. Decision on where sample analyses, data analyses will take place, and funding resources needs to take place. Discussions will occur with the DOD scientific officers or relevant staff and site PIs.

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).

Nothing to report

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.

Nothing to report

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.

We had started to screen children for participation in the protocol. The ISR has had their IRB review the protocol and answered the questions; protocol was then resubmitted. Dr. Phalen has now taken over for Dr. Wolf at UT Southwestern.

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.

None

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.

Nothing to report

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.*

Nothing to report

- **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

- **Other Products**

  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."

Example:

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award).*

Name:	Finnerty, Celeste
Project Role:	PD/PI
Research Identifier (e.g., ORCID ID):	not applicable
Nearest Person Month Worked:	2
No change	
Name:	Steven Wolf
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
Nearest Person Month Worked:	1
No change	
Name:	Charles Wade
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
No change	
Name:	Elizabeth Mann-Salinas PhD
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
No change	
Name:	David Herndon, MD
Project Role:	Co-I

Research Identifier (e.g., ORCID ID): *No change*	not applicable
Name: Project Role: Research Identifier (e.g., ORCID ID): *No change*	Andy Kudlicki Co-I not applicable
Name: Project Role: Research Identifier (e.g., ORCID ID): *No change*	Yingxin Zhao Co-I not applicable

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.

See attached Other Support document, Attachment 1.

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)
Partner's contribution to the project (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.*

Nothing to report

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.

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.

CHANGES IN ACTIVE OTHER SUPPORT

Finnerty, Celeste

Dr. Finnerty has been on leave of absence since January 2019. She is not associated with any studies at this time. Information below was current as of December 2018.

Current

W81XWH-14-2-0162 (Finnerty) 09/30/14-09/29/19 1.20 cal mths
Dept of Defense $161,029
"Identification and Validation of Established and Novel Biomarkers for Infections in Burns"
Goal: To improve clinical care for the severely burned Wounded Warriors and other burn victims.
Aims: 1) To determine plasma proteomic biomarkers for the prediction and diagnosis of sepsis using mass spectrometry techniques; use stable isotope techniques to detect proteins for which assays do not exist; 2) To validate already identified markers of infection in a multicenter study; 3) To develop a model of prediction of infection using clinical data and proteomic information.
Role: Principal Investigator
Contact: Doug Medcalf, 301-619-2394, douglas.a.medcalf.civ@mail.mil
Overlap: None

W81XWH-15-1-0143 (Branski) 07/01/15-06/30/19 0.48 cal mths
Dept of Defense $387,803
"Growth Hormone Therapy for Muscle Regeneration in Severely Burned Patients"

Goal: To determine whether restoration of depleted GH levels post-burn will lead to prevention of lean body mass loss and bone mineral content, improve rehabilitation, and accelerate reintegration of severely burned patients.

Aims: To determine the effects of recombinant human growth hormone (rhGH) supplementation on body composition, such as lean body mass loss and bone mineral content, and to assess if rehabilitation and subsequent reintegration of severely burned patients into society can be accelerated.
Role: Co-Investigator
Contact: Primary contact: Dr. Nicole Enman, Science Officer, CDMRP, Phone: (301) 619-7040, Email: nicole.m.enman.ctr@mail.mil
Overlap: None

1 KL2 TR001441-01 (Ameredes) 08/18/15-03/31/20 1.20 cal mths
National Institutes of Health $392,067
"UTMB Clinical and Translational Science Award (Linked Mentored Career Development Award)"
Goal: To provide mentored career development to early-stage investigators and develop individual and team-based translational research.
Aims: The Mentored Career Development component of our CTSA has the following specific aims: 1. To target the development of team-based and individual translational research; 2. To enhance and further develop the Academy of Research Mentors; and 3. To recruit new early-stage investigators as KL2 Scholars.
Role: Co-Investigator
Contact: David B. Wilde, 6701 Democracy Blvd, Bethesda, MD 20817, 301-435-0799, david.wilde@nih.gov
Overlap: None

#87300 (Finnerty) 01/01/17-12/31/18 0.60 cal mths
Shriners Hospitals for Children $26,111
"Cardiac Response to Burn Injury"

Goal: To understand the mechanism underlying burn-induced cardiac dysfunction which will assist in the identification of therapeutic interventions and ultimately reduce cardiovascular dependent morbidity and mortality in burn patients.

Aims: 1) To characterize the extent of cardiac hypertrophy post-burn; 2) To determine the contribution of beta-AR and/or PPARalpha signaling to burn-induced cardiac hypertrophy.

Role: Principal Investigator
Contact: Carole Miller, 815 Market Street, Galveston, TX 77550, cmiller@utmb.edu, 409-770-6728
Overlap: None

#85101 (Suzuki) 01/01/18-12/31/18 0.24 cal mths
Shriners Hospitals for Children $127,356
"Lentiviral vector-based GAS5 gene therapy for burn-associated opportunistic infection"

Goal: The results of these studies will provide a new gene therapy for controlling certain opportunistic infections in severely burned patients.

Aims: Aim 1 will determine the duration of improved host antibacterial defenses in severely burned mice subjected to GAS5-GT. Reduced GAS5 expression has been seen in Pheno2b macrophages accompanied with the impaired host antibacterial responses against MRSA infection. Therefore, Aim 2 will determine the mechanisms involved in the reduced GAS5 levels in Pheno2b macrophages from severely burned mice, focusing on nonsense-mediated RNA decay pathway that is a key RNA surveillance mechanism responsible for the rapid degradation of RNAs. Aim 3 will investigate the effect of human GAS5 lentivirus on the phenotypic change of peripheral blood monocytes from severely burned patients.

Role: Co-Investigator
Contact: Carole Miller, 409-770-6728
Overlap: None

CON26888 (Finnerty) 07/20/17-07/19/19 0.24 cal mths
Gillson-Longenbaugh Foundation $55,000
"Investigation of the Use of Stem Cells"

Goal: lnvestigation of the use of stem cells (incl adipose derived [ASC] & other stem cells & the stromal vascular fraction [SVF]) and related proteins (Secretome) to promote burn wound healing and to reduce or ameliorate (hypertrophic) scar formation, including both porcine & human clinical trials, and investigation of secretome to identify proteins enhancing cell migration, proliferation, & fibrotic gene expression.

Aims: Investigation of the use of stem cells (incl adipose derived [ASC] & other stem cells & the stromal vascular fraction [SVF]) and related proteins (Secretome) to promote burn wound healing and to reduce or ameliorate (hypertrophic) scar formation, including both porcine & human clinical trials, and investigation of secretome to identify proteins enhancing cell migration, proliferation, & fibrotic gene expression.

Role: Principal Investigator
Contact: Lawrence I. Levy, 2121 Sage Road, Suite 120, Houston, TX 77056, llevy@thelevynet.com, (713) 668-3021

Overlap: This project overlaps with the "Stem Cells to Heal Burn Wounds and Reduce Hypertrophic Scarring (A)" project. The project is funded jointly by two sponsors.

#85116 (Fry) 01/01/18-06/30/19 0.12 cal mths
Shriners Hospitals for Children $15,200
"Myostatin alters satellite cell activity following a severe burn"

Goal: The central hypothesis is that burn injury-induced myostatin impairs satellite cell-mediated recovery and reduces muscle quality, and competitive inhibition of myostatin acutely following injury will prevent these changes.

Aims: Aim 1 will determine the time course of myostatin induction within skeletal muscles both proximal and distal to the burn injury site in a mouse model. Aim 2 will assess myostatin-derived adaptations in satellite cell activity and determine their contribution to muscle recovery.

Role: Research Scientist
Contact: Carole Miller, 815 Market Street, Galveston, TX 77550, cmiller@utmb.edu, 409-770-6728

****Suspended/Inactive Projects****

1 R01 GM112936-01 (Finnerty) 01/15/15-12/31/19 1.08 cal mths
National Institutes of Health $216,309
"Effects of Chronic Catecholamine Exposure on Post-burn Scarring"

Goal: Understanding the mechanisms underlying aberrant wound healing and scarring, and their reversal by propranolol, will lay the foundation to develop additional anti-scarring therapies for the severely burned.

Aims: Aim 1. Determine the effects of chronic catecholamine exposure and β-blockade on wound healing and hypertrophic scars. Aim 2. Quantitate the effects of β-blockade on scar composition. Aim 3. Determine the effects of β-blockade on β-AR expression, activity, and binding partners of dermal fibroblasts.

Role: Principal Investigator
Contact: Tseng, Hung H., 301-496-0810, tsengh@mail.nih.gov
Overlap: None

#70900 (Finnerty) 01/01/18-10/24/18 2.16 cal mths
Shriners Hospitals for Children $195,340
"Skin Substitutes for Wound Closure following Massive Burn Injuries"

Goal: To heal large burn wounds using adipose-derived stem cells or their by-products.

Aims: 1) To determine the impact of the application of stromal vascular fraction to the burn wounds of severely burned patients on wound healing and scar formation; 2) To determine whether the application of SVF to a burn wound has similar outcomes to applying enriched ASCs to a burn wound in terms of wound healing and scarring; 3) To test the utility of autologous and allogenic SVF or enriched ASCs seeded within acellularize dermis for healing burn wounds and/or reducing scarring.

Role: Principal Investigator
Contact: Carole Miller, 815 Market Street, Galveston, TX 77550, cmiller@utmb.edu, 409-770-6728
Overlap: None

#71000 (Herndon) 01/01/17-10/24/18 0.12 cal mths
Shriners Hospitals for Children $168,472
"Mechanisms of Improved Wound Healing & Protein Metabolism with Glucose Control"

Goal: To determine the effects of tightly regulating blood glucose levels with metformin in severely burned children.

Aims: 1) To determine how metformin affects whole-body and organ function post burn on a clinical level; 2) To determine the mechanisms whereby metformin exert their effects post-burn on a cellular level.

Role: Principal Investigator
Contact: Carole Miller, 815 Market Street, Galveston, TX 77550, 409-770-6728, cmiller@utmb.edu

90DPBU0003-03-00 (Herndon) 09/30/17-09/29/22 0.24 cal mths
Natl Inst on Disability, Independent Living, and Rehab $297,619
"Effects of anabolic steroids and blockade of chronic catecholamine mediated stress on psychosocial, growth, scar, and physiologic outcomes after massive burn injury"

Goal: Our long-term outcomes multicenter study fill a gap and provide knowledge about the prevalence of emotional and physical disabilities among pediatric or adult survivors of burns suffered during childhood and evaluating the impact of advancements in burn care and rehabilitation on survivors' quality of life and reintegration.

Aims: Data collection for Specific Aim 1: NIDILRR Questionnaire which includes demographic data, VR-12(Veterans RAND), PHQ(Patient Health), CIQ(Community Integration), SL(Satisfaction with life Scale),5-D Itch Scale, etc. Specific Aim 2: Blood samples or buccal swabs. Genomic DNA will be isolated using a DNA extraction kit. The adrenergic and androgen receptors will be evaluated for clinically and functionally relevant SNP's. Specific Aim 3: Physical Activity Monitors will assess the daily activity levels of patients. Specific Aim 4: Fasting plasma glucose and fasting plasma insulin.

Role: Principal Investigator
Contact: Federal Project Officer: Dr. Kenneth Wood, 330 C Street SW, 2511B, Washington, DC 20201, (202) 275-7469; GMS: Patricia Barrett 202-795-7303, patricia.barrett@acl.hss.gov or Marlene Spencer 202-795-7422, marlene.spencer@acl.hhs.gov.

Overlap: None

2P50 GM060338-16 (Herndon) 09/01/17-05/02/18 0.36 cal mths
National Institutes of Health $175,110
"Modulation of the Post-burn Catabolic Response by Modification of Androgen and Glucocorticoid Pathways"
Project Title: Project 1. Clinical, Functional, and Biochemical Outcomes in Response to Androgen and Oxidative Stress Modulation

Goal: To identify pharmacological and non-pharmacological strategies to counter maladaptive responses to burns to improve patient recovery.

Aims: 1) To determine the effects of long-term OX administration on clinically relevant outcomes, as reflected by growth rate and growth arrest, length of hospital stay and psychosocial health; 2) To assess the effects of long-term OX on bone and muscle mass and their function, as reflected by strength and cardiopulmonary endurance; 3) To determine the effects of long-term OX on oxidative stress and the glucocorticoid response, as reflected by oxidant and antioxidant concentrations.

Role: Project Leader
Contact: Scott D. Somers, PhD, Program Official, 45 Center Drive, Bethesda, MD 20814, 301-594-3827, somerss@nigms.nih.gov

2P50 GM060338-16 (Herndon) 09/01/17-05/02/18 0.36 cal mths
National Institutes of Health $228,572
"Modulation of the Post-burn Catabolic Response by Modification of Androgen and Glucocorticoid Pathways"
Project Title: Core C. Human Subjects Core

Goal: To identify pharmacological and non-pharmacological strategies to counter maladaptive responses to burns to improve patient recovery.

Aims: 1) To enroll patients, gather clinical data and measurements and oversee the acquisition, compilation, and dissemination of all clinical and biological data; 2) To collect, catalogue, and distribute patient samples; 3) To perform basic protein and genetic analyses.

Role: Core Director

Contact: Scott D. Somers, PhD, Program Official, 45 Center Drive, Bethesda, MD 20814, 301-594-3827, somerss@nigms.nih.gov

2P50 GM060338-16 (Herndon) 09/01/17-05/02/18 0.36 cal mths
National Institutes of Health $159,966
"Modulation of the Post-burn Catabolic Response by Modification of Androgen and Glucocorticoid Pathways"
Project Title: Core A. Administrative Core

Goal: To identify pharmacological and non-pharmacological strategies to counter maladaptive responses to burns to improve patient recovery.

Aims: 1) To set the overall scientific direction of the P50 Burn Center and oversee the scientific progress of each Center component; 2) To provide financial management for projects, cores, and the overall Center; 3) To provide administrative support to the Human Subjects and Biostatistics cores and facilitate investigator access to core resources; 4) To disseminate P50 Center findings, promote Center research, and initiate Center communications/reporting.

Role: Co-Investigator

Contact: Scott D. Somers, PhD, Program Official, 45 Center Drive, Bethesda, MD 20814, 301-594-3827, somerss@nigms.nih.gov

R01 GM056687-17 (Herndon) 08/05/14-05/02/18 0.12 cal mths
National Institutes of Health $593,582
"Mechanisms of fenofibrate alone or combined with propranolol in burned patients"

Goal: This long-term clinical trial will advance the understanding of burn-induced tissue-specific signaling pathways, alterations in clinical indices such as insulin resistance, body composition, and scarring, and may
improve clinical outcomes of burn patients, and by extension also improve these in other hypermetabolic and hypercatabolic states.

Aims: Aim 1: will characterize the effects of fenofibrate and propranolol on muscle protein metabolism, regional lipid metabolism, and insulin resistance, after severe burn. Aim 2a: will test the efficacy of these agents on wound closure, wound infection, graft rejection, and scarring (the modified Vancouver and Seattle scar scales). Aim 2b, will determine whether these agents alter wound protein turnover and healing rates by using stable isotope techniques. Aim 2c, will use fibroblasts isolated from skin and scar biopsies to study molecular signaling pathways related to wound healing and scar development. Aim 3: will test the hypothesis that the mechanistic results of SA1 and SA2 are highly associated with improvements in outcomes vital in the acute stage: inflammatory response as reflected by interleukin-6, as well as result in improvements in long term outcomes: lean body mass, resting energy expenditure, cardiac function and quality of life.

Role: Principal Investigator
Contact: Scott D. Somers, PhD, Program Official, 301-594-3827, somerss@nigms.nih.gov

******Effort or Project Ended******

5UL1TR001439 (Kudlicki) 10/01/18-03/31/19

Kudlicki, Andrzej

Current

W81XWH-14-2-0162 (Finnerty) 09/30/14-09/29/19 3.6 cal mths
Dept of Defense $161,029
"Identification and Validation of Established and Novel Biomarkers for Infections in Burns"
Goal: To improve clinical care for the severely burned Wounded Warriors and other burn victims.
Aims: 1) To determine plasma proteomic biomarkers for the prediction and diagnosis of sepsis using mass spectrometry techniques; use stable isotope techniques to detect proteins for which assays do not exist; 2) To validate already identified markers of infection in a multicenter study; 3) To develop a model of prediction of infection using clinical data and proteomic information.
Role: Co-Investigator
Contact: Doug Medcalf, 301-619-2394, douglas.a.medcalf.civ@mail.mil
Overlap: None

******New******

3UL1TR001439 (Urban) 10/01/18-03/31/19 7.8 cal mths
National Institutes of Health $472,172
"CTSA Supplement"
Aims: 1) To enhance the capacity for data sharing via the development of a registry of burns and trauma patients to facilitate the study of opioid use disorders in burns and other trauma patients. 2) To generalize this approach for our other CTSA patient populations by utilizing the infrastructure / process established in Aim 1.

Role: PI of Supplement
Contact: David B. Wilde; wilded@mail.nih.gov; Phone: 301-435-0790

5P50DA03393504 (Cunningham) 09/01/13-04/30/19 0.6 cal mths
NIH/NIDA $136,017
Translational Addiction Sciences Center, Core A

Goals: The Translational Addiction Sciences Center (TASC) is comprised of a translational team bridging from molecules to cells to animals to humans with the long-term research goal to definitively reveal the role of 5-HT in addiction neurobiology and to integrate this knowledge into the dominant theoretical constructs of addiction.
Aims: The central research theme of the TASC is that impulsive action and cue reactivity are mechanistically-linked to disrupted 5-HT signaling through the 5-HT2A receptor (5-HT2AR) and 5-HT2CR localized to prefrontal-striatal-thalamic circuitry. Our premise is that restoration of the 5-HT2AR:5-HT2CR balance will repair corticostriatal deficits and ameliorate relapse.
Role: Co-investigator
Contact: Yvonne Walker, Guide Liaison, OEA/NIDA/NIH/DHHS, 6001 Executive Blvd, Bethesda, MD 20852, Phone: 301.402.5239, Fax: 301.443.0538, email: Yvonne.walker@nih.gov
Overlap: None

****End Date Extended****

5R01GM11213103 (Rowicka) 07/01/14-06/30/19 15%
NIH $450,000
Decoding Genome Instability by Combining Accurate Mapping and Predictive Modeling
Goal: We test the hypothesis that that the majority of the observed DSBs can be attributed to at least one of three main, non-mutually exclusive endogenous causes: collapse of fork due to 1) stalling on DNA secondary structures or 2) RTCs, or 3) co-transcriptional R-loop formation.
Aims: 1) Quantify how fork stalling on DNA secondary structures impacts DSB formation; 2) Estimate the contribution of RTCs to DSB formation; and 3) Clarify the influence of R-loops on DSB formation.
Role: Collaborator
Contact: Peter Lyster, email: lysterp@nigms.nih.gov, phone: 301-451-6446
Overlap: None

Zhao, Yingxin

Current

W81XWH1420162 (Finnerty) 9/30/2014 – 9/29/2019 1.2 cal mths
US Army, Department of Defense $1,349,662
"Identification and Validation of Established and Novel Biomarkers for Infections in Burns"
Goal and Specific Aims: 1. Determine plasma proteomic biomarkers for the prediction and diagnosis of sepsis using mass spectrometry techniques; and 2. Validate already identified markers of infection in a multicenter study; and develop a model of prediction of infection using clinical data and proteomic information.
Role: Co-Investigator
Contact: Elena G. Howell, Grants Officer, (301) 619-6871, elena.g.howell.civ@mail.mil
Overlap: None

5 UL1 TR001439-04 (Urban) 8/18/2015 – 3/31/2020 1.2 cal mths
NIH/NCATS $19,887,129
"UTMB Clinical and Translational Science Award (CTSA)"
Goal: UTMB CTSA seeks to support the health goals of the nation by generating, testing and disseminating integrative team science, education and best practices through stakeholder involvement at all stages
Specific Aims: 1. Train a diverse workforce in the authentic skills needed to advance all phases of translational research; 2. Engage stakeholders across all phases of translational research and CTs; 3. Integrate quality systems through all types of translational research, including CTs in special populations; and 4. Advance the conduct of translational research through multi-disciplinary team (MTT)-based innovation.
Role: Co-Investigator
Contact: David B. Wilde, Program Officer, (301) 435-0799, david.wilde@nih.gov
Overlap: None

1 R21 AI133454-01A1 (Zhao/Brasier) 6/1/2018 – 5/31/2020 2.4 cal mths
NIH/NIAID $446,422
"N-linked Glycosylation of Matrisome and Pulmonary Fibrosis"
Goal: To determine the contribution of BRD4-XBP1-HBP to the pathomechanism underlying lung fibrosis.
Specific Aims: 1. To characterize how the BRD4-XBP1-HBP axis regulates intracellular proteostasis and matrisome N-glycosylation in human small airway epithelial cells during TGFβ-induced fibrosis; and 2. To characterize the link between BRD4-XBP1-HBP activation and matrisome N-glycosylation in TGFβ-induced lung fibrosis.
Role: Contact PI
Contact: Michael Minnicozzi, Program Officer, (240) 627-3532, michael.minnicozzi@nih.gov
Overlap: None

******Effort or Project Ended******

Award 1804422 (Motamedi)	5/1/2018-4/30/2021
DMS1361318 (Brasier, Kimmel, Levine)	9/1/2014-8/31/2018

Brasier, Allan, Consultant – left institution in July 2018