

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
Galveston, TX 77555

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

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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					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT Unclassified	18. NUMBER OF PAGES 30	19a. NAME OF RESPONSIBLE PERSON USAMRMC
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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 four participating sites - 75% complete. HRPO has approved three sites to begin enrollment; 4th site protocol has been submitted and is under review
- C) Trial Conduct (to occur once enrollment begins until final subject completes protocol) 10%
- D) Sample Analysis 10%
- E) Data Analysis (to occur following completion of data collection) 0%
- F) Maintain accurate and responsible budget – 15%
- 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.

1. Major activities: To date, the protocol was written and approved by the UTMB IRB (IRB of record). UT-Southwestern, UTMB, and UT-Health Sciences Center Houston. Due to the tragic death of our colleague, Matt Rowan, at US-AISR, the protocol was assigned to a new PI, Julie Rizzo. The questions from the USAISR IRB have been submitted and we are awaiting review.
2. Twelve patients have been enrolled to date, data collected, and samples banked.
3. We will continue to enroll patients. Toward this end, we have identified several possible sites for enrollment as our enrollment has been slow and will be approaching them to gauge interest.

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.

1. Continue to screen and enroll patients at the three approved sites
2. Continue to collect data and samples
3. Begin measuring biomarkers in the collected samples
4. Continue to work with the US-AISR to obtain IRB and HRPO approval to start screening and enrolling patients.

- 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.

Although we do not have final approval for the US-AISR we are very close. We have worked to answer questions from the IRB and anticipate being able to move forward prior to the year's end.

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.

We have delayed purchasing reagents for measuring proteins until enough samples have been accumulated. Purchases will commence when ~75 samples are available for analysis (currently we have ~60 samples). By delaying the purchase until we are ready to analyze the samples, we will not be stuck with reagents that expire before we have a chance to utilize them.

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.*

Investigators met at the Shock Society annual meeting in June which was held in Austin, and at the ISBI meeting in Miami in August. We discussed the protocol and status of this project at the meeting.

- **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
<i>No change</i>	
Name:	Steven Wolf
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
Nearest Person Month Worked:	1
<i>No change</i>	
Name:	Charles Wade
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
<i>No change</i>	
Name:	Elizabeth Mann-Salinas PhD
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
<i>No change</i>	
Name:	David Herndon, MD
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
<i>No change</i>	
Name:	Andy Kudlicki
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
<i>No change</i>	
Name:	Yingxin Zhao
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
<i>No change</i>	

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

Current

W81XWH-14-2-0162 (Finnerty) 09/30/14-09/29/18 8%

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

1 R01 GM112936-01 (Finnerty) 01/15/15-12/31/19 15%

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

#71008 (Herndon) 01/01/12-12/31/16 5%

Shriners Hospitals for Children \$120,614

"Mechanisms of Improved Wound Healing & Protein Metabolism of Insulin & Metformin"

Goal: To understand the mechanisms by which insulin and metformin can improve wound healing and protein metabolism.

Aims: 1) Determine how insulin and metformin affect whole-body and organ function post burn on a clinical level. 2) Determine the mechanisms whereby insulin and metformin exert their effects post burn on a cellular level

Role: Principal Investigator

Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728

Overlap: None

P50 GM060338-15 (Herndon) 09/15/12-08/31/17 5%

National Institutes of Health \$250,000

"Mitigation of the Catecholamine Surge in Severely Burned Patients"

This is a program project grant that will study the efficacy, effects and mechanisms of the reduction in post-burn catecholamine surge by the non-selective beta-1 and beta-2 adrenergic antagonist, propranolol, in severely burned children and adults.

Project Title: Core C: Human Subjects Core

Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of whether

blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials

Aims: To enroll patients, gather clinical data and measurements, and oversee the acquisition, compilation, and dissemination of all clinical and biological data, as well as to collect, catalogue, and distribute patient samples, and to perform basic protein and genetic analyses

Role: Co-Investigator

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

Overlap: None

P50 GM060338-15 (Herndon) 09/15/12-08/31/17 5%

National Institutes of Health \$110,396

"Mitigation of the Catecholamine Surge in Severely Burned Patients"

Project Title: Core A: Administrative Core

Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of whether blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials

Aims: To function as the administrative and organizational structure that coordinates the activities of the Research Center and facilitates its scientific mission

Role: Co-Investigator

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

Overlap: None

P50 GM060338-15 (Herndon) 09/15/12-08/31/17 2%

National Institutes of Health \$204,564

"Mitigation of the Catecholamine Surge in Severely Burned Patients"

Project Title: Project 1: Propranolol Effects, Clinical Outcomes and Quality of Life in the Severely Burned

Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of whether blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials

Aims: 1) To determine the effects of long-term propranolol administration on cardiac work as reflected by the product of heart rate and mean arterial blood pressure, and resting energy expenditure as reflected by resting oxygen consumption; 2) To determine the effects of long-term propranolol administration on muscle mass and muscle function, as reflected by lean body mass index and peak strength; 3) To assess changes in key biomarkers of inflammation and infection (C-Reactive Protein and Interleukin-6) in response to the long-term administration of propranolol; 4) To determine if propranolol administration improves psychosocial health (Quality of Life) when assessed one year post-burn

Role: Co-Investigator

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

Overlap: None

#79141 (Herndon) 01/01/13-12/31/16 5%

Shriners Hospitals for Children \$91,700

"Multi-Center Project: Safety and Efficacy of Propranolol in Severely Burned Children"

Goal: To test the safety and efficacy of propranolol in treating pediatric burn patients

Aims: We will determine the safety and efficacy of administration of propranolol for one year in severely

burned children in a multi-center study involving the 4 Shrine burn hospitals. Propranolol will be evaluated in comparison to the current standard of care. 1) Determine the safety and efficacy of 4mg/kg/day propranolol for reducing heart rate and rate pressure product. 2) Determine the effect of propranolol on muscle function by measuring peak strength and endurance. 3) Determine the effect of propranolol on infections, sepsis, systemic inflammation, and scarring. 4) Determine the effect of propranolol on quality of life assessed by the ABA/Shriners outcomes indicators.

Role: Co-Investigator

Contact: Carol Miller, Shriners Hospitals for Children, 409-770-6628

Overlap: None

#85310 (Herndon) 01/01/14-12/31/16 5%

Shriners Hospitals for Children \$160,000

"Effect of Severe Burn Injury and Propranolol on Adipose Tissue Metabolism"

Goal: We anticipate that this research will offer a more complete mechanistic insight as to the contributors to hypermetabolism following burn trauma and further our understanding of the role of adipose tissue metabolism in severe burn injury. The outcomes are expected to have an important positive impact because they will lay the foundation for a) improved nutrition support to further prevent muscle loss and improve physical function and b) the development of pharmacological interventions to specifically target adipose tissue abnormalities associated with burn injury.

Aims: 1) Determine the effects of a) severe burn injury and b) severe burn injury + propranolol on the activity and function of subcutaneous WAT. 2) Determine the relationship between adipose tissue metabolism and systemic lipid kinetics and oxidation.

Role: Co-Investigator

Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728

Overlap: None

*****End Date Extended*****

W81XWH-11-1-0835 (Herndon) 07/15/14-10/29/17 14%

American Burn Association \$87,694

"(PI Agreement) Protective Effects of Propranolol Following Severe Thermal Injury: A Safety and Efficacy Trial"

Goal: To determine parameters for the administration of propranolol to severely burned adults.

Aims: 1) To determine the dose at which propranolol will achieve reduction of cardiac rate pressure product during the acute post-injury period. 2) To evaluate the safety of propranolol administered to severely burned adult patients in the early post-injury period.

Role: Co-Principal Investigator

Contact: Susan M. Browning, MPH, Deputy CEO and COO, 312-642-9260

Overlap: None

R01 GM056687-16 (Herndon) 05/01/15-04/30/18 8%

National Institutes of Health \$698,088

"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: Co-Investigator

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

Overlap: None

W81XWH-15-1-0143 (Branski) 07/01/15-06/30/19 5%

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 10%

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

****End Date Extended****

2014-667 Suman MPI Pilot (Suman) 09/01/15-11/30/16 1%

Univ of Texas Medical Branch \$50,000

"Role of Satellite Cells in the Regeneration and Recovery of Skeletal Muscle after Burn Injury"

Goal: To establish a mechanistic role for skeletal muscle resident stem cells (satellite cells) in the muscle response to burn injury

Aims: 1. Determine the effect of satellite cell depletion on muscle recovery following burn injury. 2. Determine the effect of aerobic exercise on satellite cell content and muscle recovery in pediatric burn patients.

Role: Principal Investigator

Contact: Barbara H. Petit, 409-772-1285, bhpetit@utmb.edu

Overlap: None

*****New Award*****

CON25835 (Herndon; Finnerty) 03/10/16-03/09/17 5%
Gillson-Longenbaugh Foundation \$50,000
"Investigation of the Use of Stem Cells"
Goal: To explore the use of stem cells in burn treatment.
Aims: Investigation of the use of stem cells (including adipose-derived [ASC] and other stem cells and the stromal vascular fraction [SVF] and related proteins [Secretome] to promote burn wound healing and to reduce or ameliorate scar formation.
Role: Co-Principal Investigator
Contact: Gillson-Longenbaugh Foundation, 2121 Sage Rd # 120, Houston, TX 77056, (713) 668-3021
Overlap: None

*****New Award*****

UL1TR001439 (Tyler) 04/01/16-03/31/18 1%
Institute for Translational Sciences \$75,000
"Tumor Microenvironment and Cancer Immunotherapy Multidisciplinary Translational Team"
Goal: To support additional translational correlative studies that benefit from UTMB experts on the immunosuppressive tumor microenvironment, particularly vis-a-vis tumor-associated macrophages and cancer-associated fibroblasts.
Aims: 1) To identify early predictors of response to ipilimumab in the window of 6-8 weeks between the beginning of the checkpoint blockade immunotherapy and melphalan chemotherapy delivered by ILI.
Role: Co-Investigator
Contact: Liz Ruiz, 301 University Boulevard, Galveston, TX 77555-0264, 409-772-1920, ebruiz@utmb.edu
Overlap: None

Brasier, Allan

Current

1 UL1 TR001439-01 (Brasier) 08/18/15-03/31/20 40%
National Institutes of Health \$2,211,205
"UTMB Clinical and Translational Science Award"
Project Title: Translational Science Base
Goal: The mission of the UTMB CTSA hub is 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.
Aims: 1) To train a diverse workforce in the authentic skills needed to advance all phases of translational research; 2) To engage stakeholders across all phases of translational research and CTs; 3) To integrate quality systems through all types of translational research, including CTs in special populations; 4) To advance the conduct of translational research through MTT-based innovation.
Role: Project Leader
Contact: David B. Wilde, 6701 Democracy Blvd, Bethesda, MD 20817, 301-435-0799, david.wilde@nih.gov
Overlap: None

1 UL1 TR001439-01 (Brasier) 08/18/15-03/31/20 10%
National Institutes of Health \$386,021
"UTMB Clinical and Translational Science Award"
Project Title: Administrative Core
Goal: The mission of the UTMB CTSA hub is 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.
Aims: This core aims to provide administrative oversight and support for the UTMB CTSA.

Role: Principal Investigator
Contact: David B. Wilde, 6701 Democracy Blvd, Bethesda, MD 20817, 301-435-0799,
david.wilde@nih.gov
Overlap: None

*****Project and/or effort ended on the following award:*****

SR-09 (PI: Ansari, Naseem)

09/23/13-09/22/16

Herndon, David N

Current

#84090 (Herndon)	01/01/09-12/31/16	1%
Shriners Hospitals for Children	\$232,364	

"Special Shared Facility -- Mass Spectrometry Core"

This Core supports studies almost entirely performed in human patients and the results are directly pertinent to the nutritional/metabolic management of patients. This core will enable development of new methods of investigation to the study of metabolic response to burn injury. Also, the core laboratory is important in education and training in the use of stable isotope tracer methodology. This is accomplished by organizing continuing education courses and training of research fellows.

Project Title: Special Shared Facilities -- Mass Spectrometry Core

Goal: To maintain a mass spectrometry facility that enables the continued application of stable isotope methodology to the study of the response of humans to severe injury, stress, and rehabilitation. This includes service (routine sample analysis), method development (both analytical and theoretical), and education regarding stable isotope techniques.

Aims: This Core supports studies almost entirely performed in human patients and the results are directly pertinent to the nutritional/metabolic management of patients. This core will enable development of new methods of investigation to the study of metabolic response to burn injury. Also, the core laboratory is important in education and training in the use of stable isotope tracer methodology. This is accomplished by organizing continuing education courses and training of research fellows.

Role: Principal Investigator

Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728

Overlap: None

#84080 (Herndon)	01/01/11-12/31/16	1%
Shriners Hospitals for Children	\$120,279	

"Special Shared Facility: Clinical Research and Computer Research Support"

Goal: To support research that continues to improve treatment modalities and outcomes of severely burned patients.

Aims: To support research that continues to improve treatment modalities and outcomes of severely burned patients.

Role: Principal Investigator

Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728

Overlap: None

#71008 (Herndon)	01/01/12-12/31/16	1%
Shriners Hospitals for Children	\$120,614	

"Mechanisms of Improved Wound Healing & Protein Metabolism of Insulin & Metformin"

Goal: To understand the mechanisms by which insulin and metformin can improve wound healing and protein metabolism.

Aims: 1) Determine how insulin and metformin affect whole-body and organ function post burn on a clinical level. 2) Determine the mechanisms whereby insulin and metformin exert their effects post burn on a cellular level

Role: Principal Investigator
Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728
Overlap: None

#80100 (Herndon) 01/01/12-12/31/16 1%
Shriners Hospitals for Children \$17,749

"Administrative Core for Shrine Research"

Goal: To provide administrative support for Shriners Hospital research.

Aims: To provide support for Shrine related research. 1) Provide oversight of animal facility. 2) Provide oversight of administrative details regarding Shrine grants.

Role: Principal Investigator

Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728

Overlap: None

P50 GM060338-15 (Herndon) 09/15/12-08/31/17 8%
National Institutes of Health \$250,000

"Mitigation of the Catecholamine Surge in Severely Burned Patients"

This is a program project grant that will study the efficacy, effects and mechanisms of the reduction in post-burn catecholamine surge by the non-selective beta-1 and beta-2 adrenergic antagonist, propranolol, in severely burned children and adults.

Project Title: Core C: Human Subjects Core

Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of whether blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials

Aims: To enroll patients, gather clinical data and measurements, and oversee the acquisition, compilation, and dissemination of all clinical and biological data, as well as to collect, catalogue, and distribute patient samples, and to perform basic protein and genetic analyses

Role: Core Director

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

Overlap: None

P50 GM060338-15 (Herndon) 09/15/12-08/31/17 12%
National Institutes of Health \$110,396

"Mitigation of the Catecholamine Surge in Severely Burned Patients"

Project Title: Core A: Administrative Core

Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of whether blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials

Aims: To function as the administrative and organizational structure that coordinates the activities of the Research Center and facilitates its scientific mission

Role: Co-Investigator

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

Overlap: None

P50 GM060338-15 (Herndon) 09/15/12-08/31/17 8%
National Institutes of Health \$204,564
"Mitigation of the Catecholamine Surge in Severely Burned Patients"
Project Title: Project 1: Propranolol Effects, Clinical Outcomes and Quality of Life in the Severely Burned
Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of whether blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials
Aims: 1) To determine the effects of long-term propranolol administration on cardiac work as reflected by the product of heart rate and mean arterial blood pressure, and resting energy expenditure as reflected by resting oxygen consumption; 2) To determine the effects of long-term propranolol administration on muscle mass and muscle function, as reflected by lean body mass index and peak strength; 3) To assess changes in key biomarkers of inflammation and infection (C-Reactive Protein and Interleukin-6) in response to the long-term administration of propranolol; 4) To determine if propranolol administration improves psychosocial health (Quality of Life) when assessed one year post burn
Role: Principal Investigator
Contact: Scott D. Somers, PhD, Program Official, 301-594-3827, somerss@nigms.nih.gov
Overlap: None

P50 GM060338-15 (Herndon) 09/15/12-08/31/17 2%
National Institutes of Health \$167,744
"Mitigation of the Catecholamine Surge in Severely Burned Patients"
Project Title: Project 9: Effects of Propranolol on Hypermetabolism
Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of whether blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials
Aims: 1) To define the short- and long-term effects of propranolol on a) the development of hepatic steatosis, b) the rate of peripheral lipolysis and systemic FFA availability, and c) very low density lipoprotein-triglyceride (VLDL-TG) kinetics in severely burned patients; 2) To define the short- and long-term effects of propranolol on muscle protein synthesis and breakdown rates, and b) elucidate the mechanisms responsible for the observed propranolol induced alterations in muscle protein metabolism in severely burned patients; 3) To determine the correlations between changes in hepatic steatosis and muscle protein metabolism with changes in body composition and energy expenditure, insulin resistance, and inflammation
Role: Principal Investigator
Contact: Scott D. Somers, PhD, Program Official, 301-594-3827, somerss@nigms.nih.gov
Overlap: None

#79141 (Herndon) 01/01/13-12/31/16 1%
Shriners Hospitals for Children \$91,700
"Multi-Center Project: Safety and Efficacy of Propranolol in Severely Burned Children"
Goal: To test the safety and efficacy of propranolol in treating pediatric burn patients
Aims: We will determine the safety and efficacy of administration of propranolol for one year in severely burned children in a multi-center study involving the 4 Shrine burn hospitals. Propranolol will be evaluated in comparison to the current standard of care. 1) Determine the safety and efficacy of 4mg/kg/day propranolol for reducing heart rate and rate pressure product. 2) Determine the effect of propranolol on muscle function by measuring peak strength and endurance. 3) Determine the effect of

propranolol on infections, sepsis, systemic inflammation, and scarring. 4) Determine the effect of propranolol on quality of life assessed by the ABA/Shriners outcomes indicators.

Role: Principal Investigator

Contact: Carol Miller, Shriners Hospitals for Children, 409-770-6628

Overlap: None

#85310 (Herndon) 01/01/14-12/31/16 1%
Shriners Hospitals for Children \$160,000

"Effect of Severe Burn Injury and Propranolol on Adipose Tissue Metabolism"

Goal: We anticipate that this research will offer a more complete mechanistic insight as to the contributors to hypermetabolism following burn trauma and further our understanding of the role of adipose tissue metabolism in severe burn injury. The outcomes are expected to have an important positive impact because they will lay the foundation for a) improved nutrition support to further prevent muscle loss and improve physical function and b) the development of pharmacological interventions to specifically target adipose tissue abnormalities associated with burn injury.

Aims: 1) Determine the effects of a) severe burn injury and b) severe burn injury + propranolol on the activity and function of subcutaneous WAT. 2) Determine the relationship between adipose tissue metabolism and systemic lipid kinetics and oxidation.

Role: Principal Investigator

Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728

Overlap: None

CON23000 (Herndon) 01/30/14-12/31/16 1%
Novartis Pharma. Corp. Clinical Trial

"Protocol BVS857X2201: "Multiple Ascending, Sequential, Placebo-controlled, Double-blind Study to Assess Safety, Tolerability and Efficacy of BVS857 in Severe Burn Patients""

Goal: 1) Evaluate the safety and tolerability of BVS857 in adult severe burn subjects. 2) Evaluate the effect of BVS857 on lean body mass (LBM) by DXA scan in adult severe burn subjects after 12 weeks of dosing (Groups 2, 3 and 4 only).

Aims: This study is designed as a proof of concept of BVS857 in adult subjects with severe burn. The purpose of the study is to determine the efficacy, safety and tolerability of BVS857 in adult burn subjects in addition to assessing the bioavailability of BVS857 following s.c. administration in this population.

Role: Principal Investigator

Contact: Annett Ellis, Sr. Outsourcing Mgr; Novartis Pharmaceuticals Corporation; One Health Plaza 438/3409F, East Hanover, NJ 07936-1080. 862-778-2595

Overlap: None

*****End Date Extended*****

W81XWH-11-1-0835 (PI Agreement) (Herndon) 07/15/14-10/29/17 2%
American Burn Association \$87,694

"(PI Agreement) Protective Effects of Propranolol Following Severe Thermal Injury: A Safety and Efficacy Trial"

Goal: To determine safety parameters for the administration of propranolol to severely burned adults.

Aims: 1) To determine the dose at which propranolol will achieve reduction of cardiac rate pressure product during the acute post-injury period. 2) To evaluate the safety of propranolol administered to severely burned adult patients in the early post-injury period.

Role: Principal Investigator

Contact: Susan M. Browning, MPH, Deputy CEO and COO, 312-642-9260

Overlap: None

#79144 (Herndon)	01/01/15-12/31/19	1%
Shriners Hospitals for Children		
\$19,145		
"Multi-Center Grant: System for Feedback of Patient Oriented Outcomes in Children with Burns"		
Goal:	To develop and test the effectiveness of a feedback system for patient reported outcomes in children with burns	
Aims:	1) To establish and perform pilot tests of a "data through put system" on the basis of the BOQ instruments with subjects 11-18 years of age; 2) To conduct a randomized clinical trial at 4 SHC burn centers among clinical practices with and without the feedback of BOQ information and recommendations within each of the 4 sites	
Role:	Principal Investigator	
Contact:	SHC Boston: Martha Lyndon, RN, BS, 617-371-4808, mlyndon@shrinenet.org	
Overlap:	None	
90DP0043-02-00 (Herndon)	04/01/15-09/29/17	10%
Natl Inst Disability, Independent Living, and Rehab Rsrch \$298,400		
"Modulation of catabolism mediated by catecholamine in severely burned children: Analysis of outcomes at hospital discharge, 6 months, 1, 2, 5, 10, 15 and 20 years post-injury"		
Goal:	This Pediatric Burn Center will conduct clinical research studies that aim to modulate the catabolic and hypermetabolic response to burn trauma and improve long-term burn outcomes in children	
Aims:	We propose to assess in children with severe burns: 1) the efficacy of propranolol administered for 1 year post-burn to diminish the effects of catecholamine to reduce the hypermetabolic and catabolic response 2) the efficacy of the combination of oxandrolone plus propranolol administered for 1 year post-burn to diminish the effects of catecholamine to reduce the hypermetabolic and catabolic response.	
Role:	Principal Investigator	
Contact:	Cate Miller, Administration for Community Living, One Massachusetts Ave, Washington, DC 20201-1401, 202-357-1000	
Overlap:	None	
R01 GM056687-16 (Herndon)	05/01/15-04/30/18	15%
National Institutes of Health		
\$698,088		
"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	
Overlap:	None	

New Award

CON25835 (Herndon; Finnerty)	03/10/16-03/09/17	1%
Gillson-Longenbaugh Foundation	\$50,000	
"Investigation of the Use of Stem Cells"		
Goal: To explore the use of stem cells in burn treatment.		
Aims: Investigation of the use of stem cells (including adipose-derived [ASC] and other stem cells and the stromal vascular fraction [SVF] and related proteins [Secretome] to promote burn wound healing and to reduce or ameliorate scar formation.		
Role: Co-Principal Investigator		
Contact: Gillson-Longenbaugh Foundation, 2121 Sage Rd # 120, Houston, TX 77056, (713) 668-3021		
Overlap: None		
W81XWH-09-2-0194 (Suman/Wolf)	09/30/09-10/29/16	1%
American Burn Association	\$188,414	
"Community-Based Exercise Rehabilitation in Severely Burned Adults"		
Goal: To assess the efficacy of implementing a 12-week structured and supervised community-based exercise program (COMBEX) started at hospital discharge.		
Aims: The central hypothesis of this proposal is that exercise-induced physical and psychosocial benefits obtained during a supervised and structured community-based exercise program in severely burned adults will improve physical function, and quality of life relative to the Standard of Care.		
Role: Co-Investigator		
Contact: Susan M. Browning, MPH, Deputy CEO and COO, 312-642-9260		
Overlap: None		
#71006 (Suman)	01/01/12-12/31/16	1%
Shriners Hospitals for Children	\$136,063	
"Amino acid supplementation in recovery from severe burn"		
Goal: To determine if amino acid supplementation combined with exercise training leads to greater improvements in liver and plasma lipid concentrations, muscle lipid metabolism, and insulin resistance, than exercise alone during rehabilitation in burn children.		
Aims: In these aims, we will determine if EAA supplementation combined with exercise training yields greater improvements in the following outcomes than exercise alone: 1) liver and plasma triglyceride (TG) concentrations; 2) muscle lipid metabolism (fat oxidation, concentrations of TG and fatty acid intermediates, number of mitochondria and mitochondrial oxidative capacity); 3) insulin resistance.		
Role: Co-Investigator		
Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728		
Overlap: None		
W81 XWH-14-2-0160 (Suman)	09/15/14-09/14/18	1%
Dept of Defense	\$218,828	
"Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health and Physical Performance"		
Goal: To obtain a successful, quantifiable exercise program (MP10) which can be a platform for future rehabilitation programs in burns or trauma.		
Aims: 1) To characterize what is Standard of Care throughout hospital stay across the US. 2) To characterize outcomes in burn inpatients.		
Role: Co-Investigator		
Contact: Doug Medcalf, 301-619-2394, douglas.a.medcalf.civ@mail.mil		
Overlap: None		

W81XWH-14-2-0162 (Finnerty) 09/30/14-09/29/18 1%
 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

1 R01 GM112936-01 (Finnerty) 01/15/15-12/31/19 1%
 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: Co-Investigator
 Contact: Tseng, Hung H., 301-496-0810, tsengh@mail.nih.gov
 Overlap: None

2 R01 HD049471-10 (Suman) 02/01/15-01/31/20 1%
 National Institutes of Health \$374,520
 "Oxandrolone and Exercise: A Potent Therapy in the Rehabilitation from Burns"
 Goal: To identify evidence-based therapeutic interventions that are clinically effective in the rehabilitation and recovery of severely burned children.
 Aims: 1) To determine the physiological therapeutic efficacy of exercise training/rehabilitation plus oxandrolone relative to exercise alone; 2) To determine the biochemical consequences of combined exercise training/rehabilitation and oxandrolone relative to those of exercise alone.
 Role: Co-Investigator
 Contact: Valerie Maholmes, valerie.maholmes@nih.gov, 301-496-1514, 6100 Executive Blvd, Rockville, MD 20852
 Overlap: None

W81XWH-15-1-0143 (Branski) 07/01/15-06/30/19 1%
 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-Principal Investigator

Contact: Primary contact: Dr. Nicole Enman, Science Officer, CDMRP, Phone: (301) 619-7040,

Email: nicole.m.enman.ctr@mail.mil

Overlap: None

*****New Award*****

UL1TR001439 (Tyler) 04/01/16-03/31/18 1%
Institute for Translational Sciences \$75,000

"Tumor Microenvironment and Cancer Immunotherapy Multidisciplinary Translational Team"

Goal: To support additional translational correlative studies that benefit from UTMB experts on the immunosuppressive tumor microenvironment, particularly vis-a-vis tumor-associated macrophages and cancer-associated fibroblasts.

Aims: 1) To identify early predictors of response to ipilimumab in the window of 6-8 weeks between the beginning of the checkpoint blockade immunotherapy and melphalan chemotherapy delivered by ILI.

Role: Co-Investigator

Contact: Liz Ruiz, 301 University Boulevard, Galveston, TX 77555-0264, 409-772-1920, ebruiz@utmb.edu

Overlap: None

*****Project and/or effort ended on the following award:*****

Grant 10000.2723 (PI: Herndon, David N) 08/01/12-12/31/15

Kudlicki, Andrzej

Current

W81XWH-14-2-0162 (Finnerty) 09/30/14-09/29/18 10%
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

5P50DA03393504 (Cunningham) 09/01/13-04/30/18 5%
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-HT_{2A} receptor (5-HT_{2AR}) and 5-HT_{2CR} localized to prefrontal-striatal-thalamic circuitry. Our premise is that restoration of the 5-HT_{2AR}:5-HT_{2CR} 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

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

Title: Identification and validation of established and novel biomarkers for infections in burns

ERMS: 13214046

Task Title: Year 2, Quarter 3 QC

Award No. W81XWH-14-2-0162



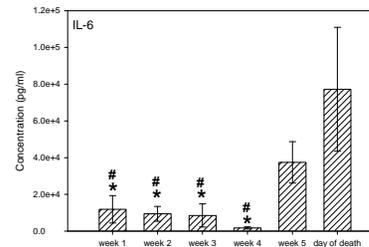
PI: Celeste C Finnerty PhD

Org: University of Texas Medical Branch

Award Amount: \$1,349,662.00

Problem, Hypothesis and Military Relevance

- After burn injury, development of sepsis and other infections is masked due to the pathophysiology of the burn injury itself.
- Early detection of infection is needed to initiate early treatment – the only intervention that improves survival.
- Many biomarkers have been identified, but these have not been validated in multicenter studies with appropriate statistical analysis. Furthermore, these targets have largely been identified because they have been successful in other diseases. More appropriate biomarkers may exist but have not been identified.



Gold Standard Predictor Model ¹				
Actual class	Survivors	Non-survivors	Total cases	Percent correct
Survivors	270	18	288	53.8
Non-survivors	21	23	44	52.3
Total	291	41	332	

Clinical and Proteomic Predictor Model ²				
Actual class	Survivors	Non-survivors	Total cases	Percent correct
Survivors	277	11	288	81
Non-survivors	8	36	44	81.8
Total	285	47	332	

¹The percent TBSA, age, and the presence of inhalation injury were used as features in MARS. Model selection was by 10-fold cross validation. The variable importance in the final model was percent TBSA (100%), the presence of inhalation injury (71%), and age (46%). ²The clinical gold standards (percent TBSA, age, and the presence of inhalation injury) and proteomics measurements were used as features in MARS modeling. Model selection was by 10-fold cross validation.

A

B

A: Patients who die of sepsis have higher IL6 expression from the time of admission; as the patients begin to become septic, IL6 and 9 other cytokines undergo significant perturbations (#, * indicate p<0.05 compared to week 5 and day of death respectively). B Accuracy of the gold standard clinical predictor model is improved by incorporating proteomic predictors (from 52 to 81% predicted correctly).

Timeline and Cost

Activities	FY	14	15	16	17
Obtain IRB approval		█			
Aim 1 Enroll patients; discovery proteomics			█		
Aim 2 validate known and new biomarkers				█	
Estimated Budget (\$K)		428K	409K	328K	337K

Goals/Milestones

CY15 Goals – Protocol development, Regulatory approval, patient Enrollment following HRPO approval.

IRB approval for all 4 sites

HRPO approval

Enroll patients at all 4 sites

Serum and clinical data collection for patients

CY16 Goal – patient enrollment and data analysis

Enroll a total number of 200 patients for the study

Discovery proteomics of serum samples and clinical data analysis

CY17 Goal – patient enrollment, data analysis, model validation

Enroll a total number of 200 patients for the study

Validate known and new biomarkers

Develop a model for prediction of infection

Budget Expenditure to Date

Projected Expenditure: \$837,000

Actual Expenditure: \$211,789

Updated 28-October-2016