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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

REPORT DATE: October 2015

TYPE OF REPORT: Annual

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

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6. AUTHOR(S)
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The University of Texas Medical Branch at Galveston
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Galveston, TX 77555-5302

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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

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
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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 - 60% complete. HRPO has approved two sites to begin enrollment
C) Trial Conduct (to occur once enrollment begins until final subject completes protocol) 5%
D) Sample Analysis 0%
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). Under the University of Texas system reciprocity agreement, UTHSCH was able to utilize the UTMB IRB approval. Both UTMB and UTHSCH have been approved by HRPO to begin enrollment, which is now underway. UT-Southwestern and the USAISR are close to obtaining IRB approval; we anticipate receiving this shortly. Three patients have been enrolled, data collected, and samples banked.
2. We will continue to enroll patients and are on target to complete the study on time at this time.

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 UTMB and at UT-Health Science Center Houston / Memorial Hermann
2. Continue to collect data and samples
3. Begin measuring biomarkers in the collected samples
4. Continue to work with the US-AISR and UT-Southwestern 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.*

Northing 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 and UT-Southwestern to screen and enroll patients, we are very close. We have worked to answer questions from both institutions 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 ~20 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 US-AISR facility in San Antonio Texas for our quarterly Burns Research in Texas Consortium meeting. 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
Contribution to Project:	Dr. Finnerty has developed the IRB protocol and data collection sheets. She is also assembling the manual of operations for the trial. She has arranged the meeting between the co-I's from all four sites for the next reporting period.
Funding Support:	Not applicable
Name:	Steven Wolf
Project Role:	co-I
Research Identifier (e.g., ORCID ID):	not applicable
Nearest Person Month Worked:	1
Contribution to Project:	Dr. Wolf has participated in development of the IRB protocol and in obtaining IRB approval.
Funding Support:	Not applicable
Name:	Charles Wade
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
Nearest Person Month Worked:	1
Contribution to Project:	Dr. Wade has participated in development of the IRB protocol.
Funding Support:	Not applicable
Name:	Elizabeth Mann-Salinas PhD
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
Nearest Person Month Worked:	1
Contribution to Project:	Dr. Mann-Salinas has participated in development of the IRB protocol.
Funding Support:	Not applicable
Name:	David Herndon, MD
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
Nearest Person Month Worked:	1
Contribution to Project:	Dr. Herndon has participated in development of the IRB protocol and approved patient

	enrollment.
Funding Support:	Not applicable
Name:	Andy Kudlicki
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
Nearest Person Month Worked:	2
Contribution to Project:	Dr. Kudlicki has worked on developing the data analysis methods for this project
Funding Support:	Not applicable
Name:	Yingxin Zhao
Project Role:	Co-I
Research Identifier (e.g., ORCID ID):	not applicable
Nearest Person Month Worked:	2
Contribution to Project:	Dr. Zhou has worked on developing the mass spec analytical methods for this project
Funding Support:	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 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.

See Attachment 2.

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.

Attachment 1: Changes in Other Support for Senior/Key Personnel
Attachment 2: Quad Chart

CHANGES IN ACTIVE OTHER SUPPORT

Finnerty, Celeste

W81XWH-14-2-0162 (PI: Finnerty, Celeste) 09/30/14-09/29/18 8%
Dept of Defense $305,312
"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: This is the grant for which the progress report is being submitted.

#71008 (PI: Herndon, David N) 01/01/12-12/31/16 5%
Shriners Hospitals for Children $119,025
"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 GM060338-14 (PI: Herndon, David N) 09/15/12-08/31/17 5%
National Institutes of Health $118,743
"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 GM060338-14 (PI: Herndon, David N) 09/15/12-08/31/17 5%
National Institutes of Health $209,515
"Mitigation of the Catecholamine Surge in Severely Burned Patients"
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 biolgical 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 GM060338-14 (PI: Herndon, David N) 09/15/12-08/31/17 8%
National Institutes of Health $191,873
"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: 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 (PI: Herndon, David N) 01/01/13-12/31/15 5%
Shriners Hospitals for Children $98,119
"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

SR-09 (PI: Ansari, Naseem) 09/23/13-09/22/16 3%
LivioneX, Inc. $151,872
"Localized Topical Metal Modulation to Inhibit Burn Progression"
Goal: To determine if early down-regulation of inflammation via localized metal modulation soon afer the occurrence of the injury will speed healing and prevent the systemic effects that often occur post burn injury.
Aims: 1) To evaluate the efficacy of LF in the prevention of dermal full thickness burn in the porcine burn model; 2) To evaluate the effect of the time of initiating the treatment after burn injury, on reducing the progression of full thickness burns in the porcine model.

Role: Co-Investigator
Contact: Amit Goswamy, CEO, 104 Milani Court, Los Gatos, CA 95030, 408-398-3570, amit@livionex.com
Overlap: None

#85310 (PI: Sidossis, Labros) 01/01/14-12/31/16 5%
Shriners Hospitals for Children $158,182
"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:

******Previously reported. PI changed from Dr. Klein to Dr. Herndon.******
W81XWH-11-1-0835 PI Agreement (PI: Herndon, David) 07/15/14-10/29/15 15%
American Burn Association $87,694
"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 propanolol 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

******New award on 8/5/2014.******
5 R01 GM056687-15 (PI: Herndon, David N) 08/05/14-04/30/18 8%
National Institutes of Health $696,523
"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

******New award on 1/15/2015.******

1 R01 GM112936-01 (PI: Finnerty, Celeste) 01/15/15-12/31/19 15%
National Institutes of Health $259,620
"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

******New award on 7/1/2015.******

W81XWH-15-1-0143 (PI: Branski, Ludwik) 07/01/15-06/30/19 5%
Dept of Defense $384,660
"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: Darrell L. Beaver, 301-619-2195, darrell.l.beaver4.civ@mail.mil
Overlap: None

******New award on 8/18/2015.******

1 KL2 TR001441-01 (PI: Ameredes, Bill T.) 08/18/15-03/31/20 10%
National Institutes of Health $359,393
"UTMB Clinical and Translational Science Award (Linked Mentored Career Development Award)"
Goal: To provide mentored career development to early-stage incestigators 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:
Overlap: None

******Project and/or effort ended on the following grants.******

#80100 (PI: Herndon, David N) 01/01/12-12/31/14
Shriners Hospitals for Children
"Administrative Core for Shrine Research"

#71009 (PI: Suman, Oscar E) 01/01/12-12/31/16
Shriners Hospitals for Children
"Oxandrolone and propranolol will promote recovery in the severely burned"

#71007 (PI: Abate, Nicola) 01/01/12-12/31/14
Shriners Hospitals for Children
"Adipose Tissue Dysfunction as a Determinant of Insulin: Resistance after Burn Injury"

#84080 (PI: Herndon, David N) 01/01/11-12/31/16
Shriners Hospitals for Children
“Special Shared Facility: Clinical Research and Computer Research Support”

R01 GM087285 (PI: Jeschke, Marc) 09/30/10-08/31/15
NIH (Sunnybrook & Women’s, Toronto subcontract)
"Characterization of Burn-Induced Hepatic Apoptosis"

Herndon, David N

W81XWH-14-2-0162 (PI: Finnerty, Celeste) 09/30/14-09/29/18 1%
Dept of Defense $305,312
"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: This is the grant for which the progress report is being submitted.

#84090 (PI: Sidossis, Labros) 01/01/09-12/31/16 1%
Shriners Hospitals for Children $241,498
"Special Shared Facility -- 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: Co-Investigator
Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728
Overlap: None

******End date extended.******
W81XWH-09-2-0194 (PI: Wolf, Steven E) 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

#84080 (PI: Herndon, David N) 01/01/11-12/31/16 1%
Shriners Hospitals for Children $6,000
"Special Shared Facility: Clinical Research and Computer Research Support"
Goal: To provide research and computer support.
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

#71006 (PI: Suman, Oscar E) 01/01/12-12/31/16 1%
Shriners Hospitals for Children $121,965
"Amino acid supplementation in recovery from severe burn"
Goal: To determine if amino acid supplementation combined with exercise training leads to greater improve¬ments 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

#71008 (PI: Herndon, David N) 01/01/12-12/31/16 1%
Shriners Hospitals for Children $119,025
"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 (PI: Herndon, David N) 01/01/12-12/31/15 1%
Shriners Hospitals for Children $56,882
"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

Grant 10000.2723 (PI: Herndon, David N) 08/01/12-12/31/15 1%
Shriners Hospitals for Children $55,366
"Grant 10000.2723-Carl C. & Marie Jo Anderson Foundation"
Goal:
Aims: The specific aims of this grant are to characterize stem cells isolated from the amnion and the

adipose tissue and to utilize these cells for wound healing.
Role: Principal Investigator
Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728
Overlap: None

P50 GM060338-14 (PI: Herndon, David N) 09/15/12-08/31/17 12%
National Institutes of Health $118,743
"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 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 GM060338-14 (PI: Herndon, David N) 09/15/12-08/31/17 8%
National Institutes of Health $209,515
"Mitigation of the Catecholamine Surge in Severely Burned Patients"
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 biolgical 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 GM060338-14 (PI: Herndon, David N) 09/15/12-08/31/17 8%
National Institutes of Health $191,873
"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

#79141 (PI: Herndon, David N) 01/01/13-12/31/15 1%
Shriners Hospitals for Children $98,119
"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 (PI: Sidossis, Labros) 01/01/14-12/31/16 1%
Shriners Hospitals for Children $158,182
"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

CON23000 (PI: Herndon, David N) 01/30/14-12/31/16 1%
Novartis Pharma. Corp. Milestone dependent
"Protocol BVS857X2201: "Multiple Ascending, Sequential, Placebo-controlled, Doubleblind 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 Corporaiton; One Health Plaza 438/3409F, East Hanover, NJ 07936-1080. 862-778-2595
Overlap: None

Previously reported. PI changed from Dr. Klein to Dr. Herndon.
W81XWH-11-1-0835 (PI: Herndon, David) 07/15/14-10/29/15 2%
American Burn Association $87,694
"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 propanolol 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

New award on 8/5/2014.
R01 GM056687-15 (PI: Herndon, David N) 08/05/14-04/30/18 15%
National Institutes of Health $696,523
"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:

New award on 9/15/2014.
W81 XWH-14-2-0160 (PI: Suman, Oscar E) 09/15/14-09/14/18 1%
Dept of Defense $212,695
"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

New award on 1/1/2015.
#79144 (PI: Herndon, David N) 01/01/15-12/31/19 1%
Shriners Hospitals for Children $18,000
"Multi-Center Grant: System for Feedback of Patient Oriented Outcomes in Children with Burns"
Goal: To develop and test the effectiveness of a feeback 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 instuments with subjects 11-18 years of age; 2) To conduct a randomized clinical trail 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

******New award on 1/15/2015.******

1 R01 GM112936-01 (PI: Finnerty, Celeste) 01/15/15-12/31/19 1%
National Institutes of Health $259,620
"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

******This is the competing renewal of a previously reported award.******

2 R01 HD049471-10 (PI: Suman, Oscar E) 02/01/15-01/31/20 1%
National Institutes of Health $372,860
"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

******This is a reissue of a previous award (H133A120091) when the granting agency (NIDRR) was transferred from ED to DHHS (as NIDILRR).******

90DP0043-02-00 (PI: Herndon, David N) 04/01/15-09/29/17 10%
National Institute on Disability, Independent Living, and $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

New award on 7/1/2015.

W81XWH-15-1-0143 (PI: Branski, Ludwik) 07/01/15-06/30/19 1%
Dept of Defense $384,660
"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: Darrell L. Beaver, 301-619-2195, darrell.l.beaver4.civ@mail.mil

Overlap: None

Project and/or effort ended on the following grants.

W81XWH-12-1-0429 (PI: Enkhbaatar, Perenlei) 09/27/12-09/26/16
Dept of Defense
"Vitamin E Supplementation in Burn Patients"

OTHER SUPPORT

Kudlicki, Andrzej

Active

P20DA024157 (PI: Cunningham, Kathryn) 09/30/07-12/31/13 0.75 cal mths
"Translational Center for Serotonin and Stimulant Addiction" $829,243
Goal: To address a set of shared questions on serotonin (5-HT) plasticity and involvement in vulnerability to addiction and relapse.
Aims: 1) To provide bioinformatics and biophysics support and consultation; 2) To provide support for the Center for Addiction Research database.
Role: Co-Investigator
Contact: Minda Lynch, 601 Executive Blvd., Rockville, MD 20852, 301-435-1322, minda.lynch@nih.gov
Overlap: None

HHSN268201000037C (PI: Kurosky, Alexander) 8/15/10-8/14/15 0.60 cal mths
(N01-HV-00245) $1,290,385
NIH/National Heart Lung and Blood Institute
"UTMB-NHLBI Proteomics Center for Airway Inflammation"
Goal: To enhance and develop innovative proteomic technologies and apply them to relevant biological questions that will advance our knowledge of heart, lung, blood and sleep, health and disease.
Aims: 1) Develop separation and array-based proteomic technologies to facilitate and enhance protein expression/PTM studies of asthma, COPD, and respiratory viruses; 2) Investigate the pathways and mechanisms of action of airway diseases in lung tissue (mucosal) and blood leukocytes to identify critical causative pathways and possible targets for therapeutic interventions; 3) Apply proteomic technologies to three clinical applications, related to asthma, COPD, and respiratory viruses. These studies include measures of protein/peptide expression arising from multiple oxidative stressors, e.g., pollen antigens (NADPH oxidases), ultra-fine carbon particles (air pollution mimetic), and respiratory syncytial virus (RSV); 4) Develop and verify diagnostic and prognostic biomarkers for disease severity and treatment sensitivity for allergy/asthma, COPD, and RSV infection.
Role: Co-Investigator
Contact: Kristiane E. Cooper, 6701 Democracy Blvd., Bethesda, MD, 20817, 301,435-6674, kristi.cooper@nih.gov
Overlap: None

UL1TR000071 (PI: Brasier, Allan) 7/14/09-03/31/2014 1.68 cal mths
"UTMB Clinical and Translational Science Award" $600,000
Goal: To support the translational goals of exemplar multidisciplinary translational teams (MTTs), generally organized around our successful NIH-funded interdisciplinary research centers.
Aims: 1) Facilitate translational research as a rigorous discipline; 2) Develop translational research training programs at all levels in the graduate continuum; 3) Effectively conduct and bridge step 1 translational research (T1) to steps T2 and T3; and 4) Interface productively with the national CTSA Consortium. The Bioinformatics Core develops computational models of inflammation pathways.
Role: Co-Investigator
Contact: David B. Wilde, 6701 Democracy Blvd., Bethesda, MD, 20817, wilded@mail.nih.gov, 301-435-0790
Overlap: None

Pending

None

Other Support
Charles E. Wade, Ph.D. – University of Texas Health Science Center at Houston

Active:

Title:	Pragmatic Randomized Optimal Platelet and Plasma Ratio (PROPPR)
Time Commitment:	20% (Co-Investigator)
Supporting Agency:	National Heart, Lung, and Blood Institute (5U01HL077863)
Agency Contact:	Dr. Gail Pearson, pearsong@nhlbi.nih.gov 31 Center Drive RKL2 Rm.8104, Bethesda, MD 20892, 301-435-0510
Performance Period:	10/2010-09/2014
Annual Direct Costs:	$3,051,148
Project Goals:	To conduct a Phase III multi-site, randomized trial comparing the efficacy and safety of 1:1:1 transfusion ratios of plasma and platelets to red blood cells, with a 1:1:2 ratio in trauma patients.
Specific Aims:	1) To separately compare as co-primary outcomes, 24-hour mortality and 30-day mortality between 1:1:1 and 1:1:2 groups adjusting for clinical site. 2) To compare subjects predicted to have a massive transfusion and randomized to the 1:1:1 or 1:1:2 ratio groups on a variety of ancillary clinical outcomes measured from randomization to initial hospital discharge after adjusting for site. 3) To develop models characterizing TIC and inflammation in enrolled patients at ED admission. 4) To assess the effect of coagulation and inflammatory models on primary and ancillary outcomes. 5) To develop models characterizing the dynamics of TIC in order to identify mechanistic drivers and sequelae of coagulation and inflammation, AND to characterize the natural history of the coagulation/inflammatory milieu in enrolled subjects.
Overlap:	None

Title:	Emerging Technology Fund
Time Commitment:	8% (Co-Investigator)
Supporting Agency:	State of Texas
Agency Contact:	Office of the Governor, Jonathan W. Taylor, jonathan.taylor@governor.state.tx.us P.O. Box 12068, Austin, TX 78711, 512-936-0501
Performance Period:	9/2008-8/2016
Annual Direct Costs:	$600,000
Projects Goals:	To provide an unparalleled advantage in the research, development, and commercialization of emerging technologies, by recruiting and hiring world class surgeons, scientist, and clinicians for the Center for Translational Injury Research.
Specific Aims:	1) To help companies take ideas from concept to development to ready for the marketplace. 2) To create public-private partnerships which leverage the unique strengths of universities, federal government grant programs, and industry. 3) To provide funds for Texas higher education institutions to recruit the best research talent in the world.
Overlap	None

Title:	Checklist and Decision Support in Nutritional Care in Burned Patients
Time Commitment:	2% (Site Principal Investigator)
Supporting Agency:	Department of Defense, USAMRMC (Subaward of UTSouthwestern)
Agency Contact:	Cheryl Anderson, grants.mgt@uthsouthwestern.edu

	5323 Harry Hines Blvd., Dallas, TX 75390-9105, 214-648-4494
Performance Period:	10/2012-09/2016
Annual Direct Costs:	$23,931
Project Goals:	To propose a system that reports feeding rate both hourly and across time to give providers a checklist to monitor whether recommended calories are being given.
Specific Aims:	1) To determine under what precise conditions compliance with nutritional goals are not met in severely burned adults 2) To find strategies to address identified gaps in feeding 3) To develop and test a system that incorporates the above strategies
Overlap:	None

Title:	Vitamin E Supplementation in Burn Patients
Time Commitment:	2% (Site Principal Investigator)
Supporting Agency:	Department of Defense, USAMRMC (Subaward of UTMB)
Agency Contact:	Andrew Hall, ahall@utmb.edu 301 University Blvd., 3.100H, Galveston, TX 77555, 409-772-8556
Performance Period:	10/2012-09/2016
Annual Direct Costs:	$52,534
Project Goals:	To determine if the administration of high doses of alpha-tocopherol will prevent or restore levels of vitamin E in adipose tissue and reverse the oxidative state in burned patients.
Specific Aims:	1) To determine the degree that supplemental vitamin E will attenuate alpha-tocopherol depletion 2) To determine if supplemental vitamin E reduces markers of oxidative stress in burned patients 3) To collect preliminary data to establish the relationship between oxidative stress and pulmonary pathophysiology and fatty liver after burn injury
Overlap:	None

Title:	Postdoctoral Training in Trauma and Hemorrhagic Shock
Time Commitment:	10% (Primary Mentor, no salary support)
Supporting Agency:	NIH/NIGMS (T32GM008792)
Agency Contact:	Scott Somers, Ph.D., somerss@nigms.nih.gov 45 Center Dr. Rm 2As.49H, MSC 6200, Bethesda, MD 20892, 301-594-3827
Performance Period:	07/2012-06/2017
Annual Direct Costs:	$331,296
Project Goals:	The goal of the program is to prepare researchers to become academically competitive, translational scientists (both MD's and PhD's) who can design and execute laboratory models to test clinically-relevant hypotheses, collaborate with other scientists to enhance the basic understanding of the problem they are studying, initiate clinical trials, and clinically translate this information.
Specific Aims:	This Trauma Research Training Program will train postdoctoral students during a two year research fellowship. By the conclusion of their training, each fellow should be able to: 1) critically analyze available published data; 2) formulate a focused hypothesis; 3) design and perform necessary experiments to test the hypothesis; 4) analyze results to state appropriate conclusions and modify experimental strategies; 5) effectively present the results of their research both orally and in writing (by manuscript); and 6) prepare a competitive research proposal.
Overlap:	None

Title:	Combination therapies for the mitigation of musculoskeletal pathologic damage in

	a novel model of severe injury and disuse
Time Commitment:	5% (Principal Investigator)
Supporting Agency:	Department of Defense (CDMRP)
Agency Contact:	help@cdmrp.org 1077 Patchel St., Fort Detrick, MD 21702-5024, 301-682-5507
Performance Period:	04/01/2013-03/31/2016
Annual Direct Costs:	$157,800
Project Goals:	The goal of this project is to determine if the combination of exercise and the use of insulin or oxandrolone will synergistically improve muscle strength, bone health, and subsequent function to improve quality of life in burn patients.
Specific Aims:	1) Characterize the effect of resistance exercise on muscle and bone health in a validated model of burn and disuse 2) Evaluate the effect of resistance exercise in combination with currently used pharmacological therapies on muscle and hone health in a validated model of burn and disuse. 3) Determine the interrelationship between muscle and bone after re-ambulation following pharmacological interventions and exercise.
Overlap:	None

Title:	Identification and Validation of Established and Novel Biomarkers for Infections in Burns
Time Commitment:	2% Co-Principal Investigators
Supporting Agency:	The University of Texas Medical Branch at Galveston/DOD USAMRAA (W81XWH-14-0162)
Agency Contact:	Celeste Finnerty, Ph.D./Doug Medcalf, douglas.a.medcal.civ@mail.mill, 301-619-2394
Performance Period:	09/2014-09/2018
Annual Direct Goals:	$48,851
Project Goals:	The 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.
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.

Title:	Prehospital Resuscitation on Helicopter Study (PROHS)
Time Commitment:	20%
Agency:	NIH/NHLBI
Agency PoC:	Gail Pearson, M.D., 301-435-0510, pearsong@mail.nih.gov
Performance Period:	1/2015-12/2017
Role:	Principal Investigator
Level of Funding:	$2,383,399
Goals:	The goal of this project is to perform a multicenter prospective observational study of air ambulance-based prehospital resuscitation regimens currently utilized at 9 participating sites.
Specific Aims:	a) Compare routinely collected prehospital vital signs and demographics, prior to in-transit resuscitation to assess whether groups were similar at baseline. b) Compare in-hospital mortality and time to death between

groups, adjusting for potential confounders including center.
c) Assess additional outcomes of interest, including amount of products infused and subsequent need for early hospital transfusion.

Overlap: None

Pending:

Title: Impact of Microvesicule Pro-Inflammatory and Pro-Coagulant Properties on Sepsis-Induced Endothelium Dysfunction
Time Commitment: 3%
Agency: NIH
Agency PoC: Not Available
Performance Period: 02/2016-01/2020
Role:
Level of Funding: $378,624
Goals: The overall goal of this research proposal is to assess phenotypic and pathophysiological implications of pro-inflammatory and pro-coagulant MVs as strong biomarkers of sepsis-induced vascular dysfunction and coagulation abnormalities.
Specific Aims: The first aim of this proposal is to isolate and characterize neutrophil MVs, endothelium MVs, monocyte MVs and platelet MVs in rats challenged with LPS-induced endothelial dysfunction. The second aim is to assess the pro-inflammatory and pro-coagulant effects of characterized MVs, isolated from LPS and/or saline-treated rats, administered intravenously in healthy rats (non-treated with LPS). The third aim is to assess the effects of pharmacological interventions to overcome deleterious effects of characterized MVs on vascular function.
Overlap: None

Title: Glycocalyx biomarkers to predict progressive intracranial hypertension after severe TBI
Time Commitment: Not Available
Agency:
Agency PoC:
Performance Period:
Role: Co-Investigator
Level of Funding: $150,000
Goals: The proposal seeks to measure the shed component of the microvascular barrier/ Glycocalyx as a predictor of the edemagenic status of the post-TBI neurovascular unit.
Specific Aims: 1) Determine the time course of syndecan-1 release and COP in patients with severe TBI, and correlate this with pressure-time ICH exposure derived from the TRACK-TBI database/bio-bank. 2) Test whether the degree of microvascular barrier disruption predicts responsiveness to standard therapies for ICH as measured by Tier 2-3 Brain Trauma Foundation interventions and TIL/PILOT scores.
Overlap: None

Title: Thrombelastography-guided Resuscitation of Pediatric Trauma and Associated Coagulopathy

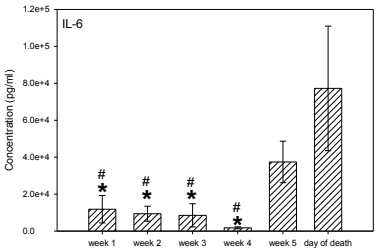
Time Commitment:	5%
Agency:	NIH/National Institute of Child Health and Human Development
Agency PoC:	Valerie Maholmes, Ph.D., maholmev@mail.nih.gov
Performance Period:	09/2015-08/2020
Role:	Co-Investigator
Level of Funding:	$2,923,556
Goals:	Transfer the current adult hemostatic resuscitation practices to pediatric trauma care, based upon prospectively collected data and outcomes linked to TBI, rather than just "shrinking" the protocols based on weights.
Specific Aims:	1) Define the time-course of TAC in pediatric trauma resuscitations (highest level of activation). 2) Implement study evaluating the effects of TEG-based resuscitation on clinical outcomes after traumatic brain injury. 3) Determine if TEG based hemostatic resuscitation results in structural preservation of GM/WM volumetrics after severe TBI.

Title: Identification and validation of established and novel biomarkers for infections in burns
ERMS: 13214046 **Task Title:** Year 1, Annual report 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.



A

B

Gold Standard Predictor Model*				
Actual class	Survivors	Non-survivors	Total cases	Percent correct
Survivors	270	18	288	93.8
Non-survivors	21	23	44	52.3
Total	291	41	332	
Clinical and Proteomic Predictor Model^				
Actual class	Survivors	Non-survivors	Total cases	Percent correct
Survivors	277	11	288	96
Non-survivors	8	36	44	81
Total	285	47	332	

*The 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%). ^The 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: 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

Updated 29-Oct-15

Goals/Milestones

CY15 Goals – Protocol development, Regulatory approval, patient Enrollment following HRPO approval.
- ❑ IRB approval for all 4 sites – *two are complete, two submitted*
- ❑ HRPO approval *obtained for 2 sites*
- ☐ Enroll patients at all 4 sites – *we have begun screening at 2 sites (3 patients are enrolled)*
- ☐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: $413,881
Actual Expenditure: $95,376