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AWARD NUMBER: W81XWH-14-2-0160

TITLE: Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health, and Physical Performance

PRINCIPAL INVESTIGATOR: Oscar E. Suman, PhD

RECIPIENT: The University of Texas Medical Branch at Galveston
Galveston, TX 77555

REPORT DATE: October 2016

TYPE OF REPORT: Annual

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

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Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health, and Physical Performance

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W81XWH-14-2-0160

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Oscar E. Suman, PhD

Professor, Department of Surgery
The University of Texas Medical Branch at Galveston

E-Mail: oesuman@utmb.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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

8. PERFORMING ORGANIZATION REPORT NUMBER

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

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

10. SPONSOR/MONITOR'S ACRONYM(S)

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12. DISTRIBUTION / AVAILABILITY STATEMENT

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Prolonged inactivity accompanying stays in the burn intensive care unit (BICU) and hospital worsen muscle loss/weakness and lengthen hospitalization. We hypothesize that a personalized, structured, and quantifiable exercise program (MP10) will improve these variables over standard-of-care (SOC), as exercise has well-documented effects on maintaining/improving muscle strength, which should shorten hospitalization. Thus, we will characterize: (Aim 1) what is SOC throughout hospital stay across the US and (Aim 2) outcomes in burn in-patients. Over 4 years, we will enroll 96 patients (24 per site; MP10 n=64 and SOC n=32) aged 18-60 years with ≥30% TBSA burns. MP10 will begin ~4-5 days after the first surgery after admit (or when the burn surgeon deems mobilization safe) and continue for the entire BICU and hospital stay. MP10 will take place on weekdays in the morning and afternoon. In the morning, patients will participate in a 10-minute leg-crank ergometry session (Monark leg ergometer), starting with a load (watts) eliciting a 3-5 rating on the Borg Rated Perceived Exertion (RPE) scale. The number of revolutions in 10 minutes and minute-by-minute muscle and respiratory effort RPE will be noted. In the afternoon, patients will participate in a 10-minute arm crank ergometry session, which will be done similarly to lower body exercise. Endpoints are lean body mass, cardiopulmonary and muscle endurance, length of BICU, ventilator and hospital stay, and Quality of Life. Within- and between-group comparisons will be performed. A successful MP10 can be a platform for future rehabilitation programs in burns or trauma.

15. SUBJECT TERMS

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

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

TABLE OF CONTENTS

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

The title of this project is "Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health and Physical Performance". It has four sites: UTMB-Galveston, TX; AISR-San Antonio, TX; UTSW-Dallas, TX; UC-Davis. The prolonged inactivity that occurs in the burn intensive care unit (BICU) and hospital, results in worsening of muscle loss, muscle weakness, and in increased BICU and hospital stay. We need to reduce this time to speed up resuming normal physical activities, returning to work or to professional duties. To this end, we have two aims: **Aim 1**: to characterize, via a survey(s) the Standard of Care of in-patient care (BICUs, on ventilator, step down from BICU) across the U.S. **Aim 2**: to assess the efficacy of a personalized, structured, and quantifiable exercise program (MP10) implemented typically 4 to 5 days after the first surgical operation after admit (or when burn surgeon deems mobilization to be safe), and during the entire BICU, on ventilator and in-hospital stay in burned individuals.

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

Exercise, burns, standard of care, MP10, early exercise, lean mass, muscle strength, 6 minute walk

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.

Milestones:
Aim 1: to characterize, via a survey(s) the Standard of Care of in-patient care (BICUs, on ventilator, step down from BICU) at the 4 sites (UTMB-Galveston, USAISR, UTSW-Dallas, UC Davis)
Due: Y2 Report 14-Oct-2016 which covers SEP 15, 2015 to SEP 14, 2016.
Surveys were sent to all 4 sites and results were returned from all 4 sites. The results were presented at the International Society for Burn Injuries (AUG 29-SEP4, 2016) in Miami, FL. The manuscript summarizing and discussing the results is being written. We plan to submit to the Journal of Burn Care and Research or Burns Journal.

Aim 2: to assess the efficacy of a personalized, structured, and quantifiable exercise program (MP10) implemented typically 4 to 5 days after the first surgical operation after admit (or when burn surgeons deems mobilization to be safe) and during the entire BICU, on ventilator and in-hospital stay in burn individuals. UTMB, UC-Davis and UTSW are enrolling patients. The USAISR is currently in the process of obtaining their IRB approval. For UTMB, a total of 24 subjects have been enrolled, which completes the 24 that were proposed for this site. We have requested permission to increase the number of subjects from 24 to an additional 72 for a total of

96. We have obtained verbal permission from Dr. Lai. We submitted official request to the UTMB IRB on October 12, 2016.

Due: Final Report 12-Dec-2018 Completion Date: 14-Sep-2018

Year 2 Key Milestones: Get site ready for study (completed); develop individual data forms and survey (completed); obtain IRB and HPRO approvals (completed for UTMB, UTSW and UC-Davis); register with clinicaltrials.gov (completed). Only USAISR is missing IRB approval at this date.

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
For Year 2: Period of September 15, 2015 to September 14, 2016
We focused on recruiting additional patients at UTMB as the lead site. Then we focused on each site obtaining HRPO and progressing with Aim 2, (in-patient exercise).

During this period at UTMB, a total of 24 patients had been enrolled and completed the MP10+SOC or SOC protocol as applicable. This met our recruitment goal. On October 6, we received IRB approval for assessment procedures, however, since we had met our enrollment goals, we requested to increase the number of subjects from 24 to 96 for UTMB. An amendment was sent to IRB on October 12, 2016. Approval is pending at this moment. Other accomplishments are the presentation of AIM ONE results at the International Society for Burn Injuries AUG 29 to SEP 4, 2016 in Miami, FL. From this presentation, a manuscript is being prepared. We anticipate submitting a manuscript for peer review in calendar year 2016.

SITE by SITE
Study Site: UTMB/SHC-GAL (Galveston, TX)
Study Coordinator: Jennifer Kemp, OTC
As of October 6, 2016, UTMB/SHC-GAL has IRB approval. Expiration date is 04/12/2016
They also have HRPO approval with an approval date of October 6, 2016 until September, 16, 2017. HRPO continuing review has started with communications with Kara Visser, Research Administrative Support at the Human Research Protection Office (HRPO), Office of Research Protections (ORP), US Army Medical Research and Materiel Command. We anticipate completing HRPO annual continuing review as soon as we get a response from our IRB on the increase in number of subjects.

Study Site: UC-Davis/SHC-NCA (Sacramento, CA) PI – Soman Sen, MD
Study Coordinator and Senior Therapist: Ingrid Parry, MS, PT
Study Coordinator: Lynda Painting, BS, CCRP, CCRC
Progress for UC-Davis; as of October 13, 2016 UCD/SHC-NCA has IRB approval. Expiration date is 02/24/2017
They also have HRPO approval with an approval date of 4/12/2016
They have four patients enrolled as of 10/13/2016

Progress for UC-Davis is that they have IRB approval and HRPO approval. They have also enrolled three subjects and continue to screen and enroll subjects.

Study Site: UT Southwestern (Dallas, TX) PI – Karen Kowalske, MD
Study Coordinator: Cindy Dolezal, PT, DPT
The study has IRB approval date of May 24, 2016 and HRPO approval date of April 29, 2016.
Progress for UTSW is that they have IRB approval and HRPO approval. They have also enrolled one subject the last week of September, randomized to the control group.

Study Site: USAISR PI-Julie Rizzo, MD
All activities are being devoted to obtain IRB approval. There were changes in PI from Dr. King to Dr. Cancio and now Dr. Rizzo. Dr. Rizzo has performed admirably and we are confident that once IRB approval and any other approval that the Army requires is obtained, enrollment will take place relatively smoothly. Request for approval and documents were submitted on October 6, 2016 to their IRB and HRPO.

What opportunities for training and professional development has the project provided?

"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."

"Nothing to Report." However, quarterly, we do get together with UTSW and USAISR key investigators of this project and discuss progress and issues. The next meeting will take place on January 2017 at the USAISR in San Antonio and we will attend. In addition, we will try to have a 4-site (all sites) meeting at the next American Burn Association in Boston in March 2017 to discuss progress and obstacles and plans for the final fourth year of grant. Finally, the project PI, Dr. Suman, gave a presentation on the timing of exercise at the International Society for Burn Injuries (AUG 29 to SEP 4, 2016) in Miami, FL. The MP10 methodology was presented and well received, as it highlighted the objective nature of the exercise prescription and significant outcome measures.

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

1. We will prepare and submit manuscript on the results of the 4-site survey on Exercise in the ICU. We anticipate submitting to the Journal of Burn Care and Research or to the Burns journal. We anticipate submitting in 2016.

2. For Aim2, we will continue to enroll, especially for UCD/SHC-NCA, UTSW and UTMB/SHC-GAL. We also anticipate enrollment to start very soon at USAISR. We will work very hard to bring USAISR to having full IRB approval (see section on **Actual or anticipated problems or delays and actions or plans to resolve them**).

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?

"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."

"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.

UTMB has enrolled 24 subjects, which is the proposed total number for this site. We requested and obtained verbal permission to increase total number of subjects from 24 to 96 (thus enroll 72 more patients during years 3 and 4). We have submitted this request to our IRB.

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.

At USAISR there have been numerous changes in personnel. The most noticeable one is that Sandra M. Escolas, PhD left San Antonio to become Director of the US Army Medical Research Unit-West in McChord, WA. She will remain involved, but we will have to communicate via phone, email, etc., and not in person. We may be able to meet during conferences or the PI (Dr. Suman) may travel there to discuss key issues related to psychosocial assessments once enrollment has reached 1/4 point (n=42 total). We are currently at n=28.

USAISR had not been able to hire a grants coordinator that could focus on the MP10 project. For a long time, Mr. Reginald Richards had been vital and key to keeping progress going. However, they have since brought in a new PI, Dr. Julie Rizzo, and another coordinator, Sonya Charo-Griego. She has been able to devote much effort to MP10, and they are closer than ever to receiving IRB approval.

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.

There is nothing to report for UTMB/SHC-GAL, and UTSW. However, for UCD/SHC-NCA, we may have to increase the amount allotted to this site, so they can complete obtaining DEXA. The costs are new and involve the DEXA itself and transport costs. We may have to decrease the amount of money allotted to UTSW based on enrollment progress (n=1 for UTSW) vs (n=3 for UC-Davis). This will be discussed with the program officer, Dr. Lai, as soon as the report is submitted. Finally, the potential continued shortage of personnel at USAISR specific to the MP10 project may have affected and if continued, will eventually affect expenditures. If continued, we will be seeking a budget amendment to increase funds for UTMB, particularly for personnel."

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

UTMB has enrolled 24 subjects, which is the proposed total number for this site. We requested and obtained verbal permission to increase total number of subjects from 24 to 96 (thus enroll 72 more patients during years 3 and 4). We have submitted this request to our IRB. The methods and outcomes measures have not changed.

Significant changes in use or care of vertebrate animals.

Not applicable.

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.

  "Nothing to Report."

  Books or other non-periodical, one-time publications.

  "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*

1. Oral presentation at the International Society for Burn Injuries (AUG 29 to SEP 4, 2016) in Miami, FL. The results of the Survey on Exercise Practice in the ICUs of the 4 sites were presented by Ingrid Parry, MS, PT. She is the study coordinator and PT at UC-Davis/SHC-NCA. She and the PI will also lead the preparation of the manuscript. The Survey results were the combined efforts of Ingrid Parry and Jennifer Kemp (OT from UTMB/SHC-GAL).

2. Finally, the project PI, Dr. Suman, gave a presentation on the timing of exercise at the International Society for Burn Injuries (AUG 29 to SEP 4, 2016) in Miami, FL. The MP10 methodology was presented and well received, as it highlighted the objective nature of the exercise prescription and significant outcome measures.

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**

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

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

Name:	*Oscar Suman*
Project Role:	*Project Director*
No change.	
Name:	*Michael Serghiou*
Project Role:	*Consultant*
No change.	
Name:	*Jennifer Kemp*
Project Role:	*Consultant*
No change.	
Name:	*Ronald Mlcak*
Project Role:	*Consultant*
No change.	
Name:	*Angela Agudelo*
Project Role:	*Clinical Research Coordinator*
Researcher Identifier (e.g. ORCID ID):	*not applicable*
Nearest person month worked:	*2 calendar months*
Contribution to Project:	*She has been the hands-on physical therapist and exercise trainer in the ICU.*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

See Attachment 1 for changes in active other support (page 13).

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

Organization: University of California – Davis
Location: 1850 Research Park Dr. Ste. 300, Davis, CA 95618-6153
Contribution to the Project: Collaboration

Organization: The University of Texas Southwestern Medical Center at Dallas
Location: 5323 Harry Hines Blvd., Dallas, TX 75390-9105
Contribution to the Project: Collaboration

Organization: US Army Institute of Surgical Research
Location: 3698 Chambers Pass, Ft. Sam Houston, TX 78234-6315
Contribution to the Project: Collaboration

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.

Attachment 1: Changes to Active Other Support
Attachment 2: IRB Approval for n=24. Presently waiting for approval for an additional n=72. The methods and outcomes measures have not changed.

Early Mobility/Exercise Program (MP10) in the Burn Intensive Care Unit (ICU) Decreases Hospital Stay and Fatigue, and Improves Mental Health and Physical Performance

Log 13214039 Award # W81XWH-14-2-0160 Report period: 15-SEP-15 to 14-SEP-16

PI: Oscar E. Suman **Org: The Univ of Texas Medical Branch/Shriners Hospital-Galveston** **Award Amount:** $1,079,350.00

Study/Product Aim(s)

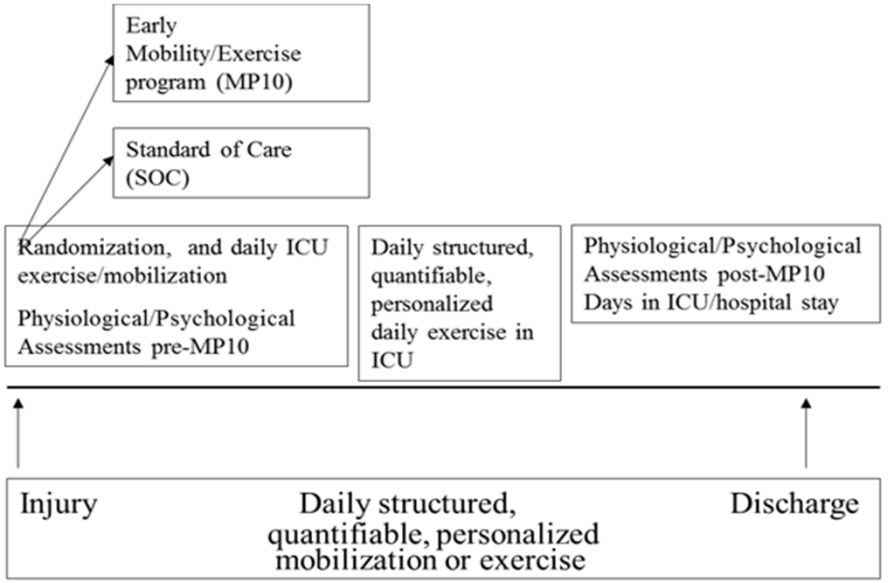
- **Objectives**: 1. decrease length of hospital stay 2. improve physiological and psychological outcomes
- **Aim 1**: Characterize SOC in the ICU in each of the 4 sites. **Aim 2**: Test the hypothesis that early exercise in the ICU will significantly improve outcomes compared to SOC.
- **Outcomes**: decreased ICU/hospital stay, improved lean mass, aerobic capacity/muscle endurance and fatigue scores.

Approach

Over 4 years, we will enroll 96 patients (24 per site; MP10 n=64 and SOC n=32) aged 18–60 years with ≥30% TBSA burns. Patients in MP10 will participate in a 10-minute leg-crank and a 10-minute arm crank ergometry session. Endpoints are lean body mass, cardiopulmonary and muscle endurance, length of BICU, ventilator and hospital stay, and Quality of Life.

Timeline and Cost

Activities CY	1	2	3	4
a. Construction and development of Survey to characterize SOC; b. submit for peer-reviewed publication				
Implement MP10+SOC vs SOC, obtain IRB, HRPO, register for clintrials,gov, enroll patients				
Submit manuscripts, present posters or oral presentations				
Estimated Budget ($K)	296,093	254,824	261,734	266,699



Goals/Milestones

CY1 Goal – IRB and HRPO approval for UTMB/SHC-GAL; UTSW; and UCD/SHC-NCA

Survey completion to characterize SOC completed by UTMB/SHC-GAL; UTSW; and UCD/SHC-NCA

CY2 Goals – MP10 enrolling at UTMB/SHC-GAL; UTSW; and UCD/SHC-NCA

Submission of abstract on Survey to ISBI

CY3 Goal – Continuation of MP10

CY4 Goal – Continuation of MP10

Analysis of data, submission of abstracts to ABA or other critical care meetings. Submission of manuscript.

Comments/Challenges/Issues/Concerns

- Aim ONE completed. Still waiting for IRB/HRPO approval from USAISR. UTMB to increase n from 24 to 96. This site only.

Budget Expenditure to Date

Projected expenditure: 550,917

Actual expenditure: $210,538

Updated: OCT 12 -2016

CHANGES IN ACTIVE OTHER SUPPORT

Suman, Oscar E.

W81 XWH-14-2-0160 (Suman) 09/15/14-09/14/18 1.56 cal mths
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: 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.

#71006 (Suman) 01/01/12-12/31/16 0.48 cal mths
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 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: Principal Investigator
Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728
Overlap: None

#71009 (Suman) 01/01/12-12/31/16 1.44 cal mths
Shriners Hospitals for Children $148,999
"Oxandrolone and propranolol will promote recovery in the severely burned"

Goal:

Aims: The following aims will allow the testing of the major hypothesis.
Aim 1: Is to test the hypothesis that the catabolic (lean mass, protein synthesis and protein breakdown) response can be ameliorated by therapeutic use of the testosterone analog, oxandrolone combined with the therapeutic use of the propranolol over a treatment period of 1 year.
Aim 2: Is to test the hypothesis that the hypermetabolic (heart rate, blood pressure, resting energy expenditure) response can be ameliorated by therapeutic use of the testosterone analog, oxandrolone combined with the therapeutic use of the propranolol over a treatment period of 1 year.
Aim 3: To identify factors (cytokines in blood and urine) and potential mechanisms involved in these hypermetabolic and catabolic process in response to the administration of both treatment drugs. We will determine whole-body physiologic changes, as well as clinical, and

biochemical changes over the 1 year study period.

Role: Principal Investigator

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

Overlap: None

2 R01 HD049471-10 (Suman) 02/01/15-01/31/20 2.16 cal mths
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: Principal Investigator

Contact: Valerie Maholmes, valerie.maholmes@nih.gov, 301-496-1514, 6100 Executive Blvd, Rockville, MD 20852

Overlap: None

******End date extended******

2014-667 Suman MPI Pilot (Suman) 09/01/15-11/30/16 0.12 cal mths
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

W81XWH-09-2-0194 (Wolf/Suman) 09/30/09-10/29/16 0.24 cal mths
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: Principal Investigator

Contact: American Burn Association, 312-642-9260

Overlap: None

#71008 (Herndon) 01/01/12-12/31/16 0.60 cal mths
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: Co-Investigator
Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728
Overlap: None

P50 GM060338-15 (Herndon) 09/15/12-08/31/17 1.68 cal mths
National Institutes of Health $204,564
"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: 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 0.96 cal mths
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: 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 0.24 cal mths
National Institutes of Health $250,000
"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 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 0.24 cal mths
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: Co-Investigator

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

Overlap: None

2 R01 GM056687-14 (Herndon) 08/05/14-04/30/18 0.48 cal mths
National Institutes of Health $727,000
"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

1 R01 GM112936-01 (Finnerty) 01/15/15-12/31/19 0.60 cal mths
National Institutes of Health $216,309
"Effects of Chronic Catecholamine Exposure on Post-burn Scarring"

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

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

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

90DP0043-02-00 (Herndon) 04/01/15-09/29/17 0.24 cal mths
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: Co-Investigator
Contact: Cate Miller, Administration for Community Living, One Massachusetts Ave, Washington, DC 20201-1401, 202-357-1000
Overlap: None

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

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

Aims: To determine the effects of recombinant human growth hormone (rhGH) supplementation on body composition, such as lean body mass loss and bone mineral content, and to assess if rehabilitation and subsequent reintegration of severely burned patients into society can be accelerated.

Role: Co-Investigator
Contact: Primary contact: Dr. Nicole Enman, Science Officer, CDMRP, Phone: (301) 619-7040, Email: nicole.m.enman.ctr@mail.mil
Overlap: None

Herndon, David N.
#84090 (Herndon) 01/01/09-12/31/16 0.12 cal mths
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 0.12 cal mths
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 0.12 cal mths
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 0.12 cal mths
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 0.96 cal mths
National Institutes of Health $204,564
"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: 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 1.44 cal mths
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 0.96 cal mths
National Institutes of Health $250,000
"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 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 0.24 cal mths
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 0.12 cal mths
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 0.12 cal mths
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 0.12 cal mths
Novartis Pharma. Corp. Clinical Trial
"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

******End date extended******
W81XWH-11-1-0835 (Herndon) 07/15/14-10/29/17 0.24 cal mths
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 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

#79144 (Herndon) 01/01/15-12/31/19 0.12 cal mths
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 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

90DP0043-02-00 (Herndon) 04/01/15-09/29/17 1.20 cal mths
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

R01 GM056687-16 (Herndon) 05/01/15-04/30/18 1.80 cal mths
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 0.12 cal mths
Gillson-Longenbaugh Foundation $50,000
"Investigation of the Use of Stem Cells"
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: UTMB Development Office
Overlap: None

W81XWH-09-2-0194 (Wolf/Suman) 09/30/09-10/29/16 0.12 cal mths
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 0.12 cal mths
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 0.12 cal mths
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: This is the grant for which the progress report is being submitted.

W81XWH-14-2-0162 (Finnerty) 09/30/14-09/29/18 0.12 cal mths
Dept of Defense $161,029
"Identification and Validation of Established and Novel Biomarkers for Infections in Burns"

Goal: To improve clinical care for the severely burned Wounded Warriors and other burn victims.

Aims: 1) To determine plasma proteomic biomarkers for the prediction and diagnosis of sepsis using mass spectrometry techniques; use stable isotope techniques to detect proteins for which assays do not exist; 2) To validate already identified markers of infection in a multicenter study; 3) To develop a model of prediction of infection using clinical data and proteomic information.

Role: Co-Investigator

Contact: Doug Medcalf, 301-619-2394, douglas.a.medcalf.civ@mail.mil

Overlap: None

1 R01 GM112936-01 (Finnerty) 01/15/15-12/31/19 0.12 cal mths
National Institutes of Health $216,309
"Effects of Chronic Catecholamine Exposure on Post-burn Scarring"

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

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

Role: 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 0.12 cal mths
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 0.12 cal mths
Dept of Defense $387,803
"Growth Hormone Therapy for Muscle Regeneration in Severely Burned Patients"

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

Aims: To determine the effects of recombinant human growth hormone (rhGH) supplementation on body composition, such as lean body mass loss and bone mineral content, and to assess if rehabilitation and subsequent reintegration of severely burned patients into society can be accelerated.

Role: Co-Principal Investigator

Contact: Primary contact: Dr. Nicole Enman, Science Officer, CDMRP, Phone: (301) 619-7040, Email: nicole.m.enman.ctr@mail.mil

Overlap: None

UL1TR001439 (Tyler) 04/01/16-03/31/18 0.12 cal mths
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

Lee, Jong

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

2016-2018 ETEP (Lee) 05/01/16-06/30/18 0.60 cal mths
Texas Higher Education Coordinating Board $54,500
"Emergency and Trauma Care Education Partnership Program"

Goal: To provide salary and training support for fellows enrolled in the UTMB/Shriners Hospital Surgical Critical Care Fellowship program.

Aims: To provide salary and training support for fellows enrolled in the UTMB/Shriners Hospital Surgical Critical Care Fellowship program.

Role: Principal Investigator

Contact: Fu-An Lin, PhD, Program Director, Academic Quality and Workforce Division, 512-427-6211, fu-an.lin@thecb.state.tx.us

Overlap: None

P50 GM060338-15 (Herndon) 09/15/12-08/31/17 0.48 cal mths
National Institutes of Health $250,000
"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 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 0.12 cal mths
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: Co-Investigator

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

Overlap: None

W81 XWH-14-2-0160 (Suman) 09/15/14-09/14/18 0.12 cal mths
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: This is the grant for which the progress report is being submitted.

W81XWH-15-1-0143 (Branski) 07/01/15-06/30/19 0.24 cal mths
Dept of Defense $387,803

"Growth Hormone Therapy for Muscle Regeneration in Severely Burned Patients"

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

Aims: To determine the effects of recombinant human growth hormone (rhGH) supplementation on body composition, such as lean body mass loss and bone mineral content, and to assess if rehabilitation and subsequent reintegration of severely burned patients into society can be accelerated.

Role: Co-Investigator

Contact: Primary contact: Dr. Nicole Enman, Science Officer, CDMRP, Phone: (301) 619-7040, Email: nicole.m.enman.ctr@mail.mil

Overlap: None

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Institutional Review Board
301 University Blvd.
Galveston, TX 77555-0158

06-Oct-2016

MEMORANDUM

TO: Oscar Suman
Surgery-Burn 145120

FROM: Aristides Koutrouvelis, MD
Institutional Review Board, Chairman

RE: Continuing Study Approval

IRB #: IRB # 14-0432

TITLE: Randomized, Controlled, Multicenter Study of the Effect of In-Patient Exercise Training on Length of Hospitalization, Mental Health, and Physical Performance in Burned Patients

DOCUMENTS: Protocol, Version Date: June 30, 2016

The UTMB Institutional Review Board (IRB) reviewed the above-referenced research protocol at a convened meeting on 16-Sep-2016. Having met all applicable requirements, the research protocol is approved for continuation for a period of 12 months. The approval period for this research protocol begins on 06-Oct-2016 and lasts until 16-Sep-2017.

The research protocol cannot continue beyond the approval period without continuing review and approval by the IRB. In order to avoid a lapse in IRB approval, the Principal Investigator must apply for continuing review of the protocol and related documents before the expiration date. A reminder will be sent to you approximately 90 days prior to the expiration date.

The approved number of subjects to be enrolled is 24.00. The IRB considers a subject to be enrolled once s/he signs a Consent Form. If, additional subjects are needed, you first must obtain permission from the IRB to increase the approved sample size.

If you have any questions, please do not hesitate to contact the IRB office via email at IRB@utmb.edu.

Note: There are no consent/permission/assent with this submission as the site has met the IRB target accrual. Per communications with Dr. Suman, an amendment to increase enrollment along with revised consent/permission/assent forms will be submitted upon approval of this continuing review.

General Instructions

To maintain IRB approval in good standing, please observe the following requirements:

1. The research consent form(s) (if applicable) with the date of the IRB approval is available in infoED. Please use the IRB stamped consent form(s) with the current approval/expiration dates and make additional copies as they are needed.
2. All subjects must sign the consent form before undergoing any research study procedures, including screening procedures unless this requirement has been waived by the IRB. When conducting research involving children, a child assent form must be reviewed with and signed by the child (if applicable) in addition to obtaining a signed parental permission form unless these requirements are waived by the IRB. A photocopy of the signed consent form(s) should be given to each participant. The copy of the consent form(s) bearing original signature(s) should be kept with other records of this research for at least six years past the completion of the research study.
3. Obtain prior IRB approval for any modifications including addition of new recruiting materials, changes in research personnel or site location, sponsor amendments or other changes to the protocol or associated documents. Only those changes that are necessary to avoid an immediate apparent hazard to a subject may be implemented without prior IRB approval.
4. Report all adverse events, protocol violations, DSMB reports, external reports and study closures promptly to the IRB.
5. Make study records available for inspection. All research-related records and documentation may be inspected by the IRB for the purpose of ensuring compliance with UTMB policies and procedures and federal regulations governing the protection of human subjects. The IRB has authority to suspend or terminate its approval if applicable requirements are not strictly adhered to by all research study personnel.
6. When enrolling subjects who do not speak or read English, in research involving therapeutic or prophylactic interventions or invasive diagnostic procedures, a bilingual translator must be continuously available to facilitate communications between research personnel and a subject. If a bilingual translator will not always be available, it may be unsafe for an otherwise eligible candidate to participate in the research if that person does not speak and read English.

Early Mobility/Exercise Program (MP10) in the Burn Intensive Care Unit (ICU) Decreases Hospital Stay and Fatigue, and Improves Mental Health and Physical Performance

Log 13214039 Award # W81XWH-14-2-0160 Report period: 15-SEP-15 to 14-SEP-16

PI: Oscar E. Suman **Org: The Univ of Texas Medical Branch/Shriners Hospital-Galveston** **Award Amount:** $1,079,350.00

Study/Product Aim(s)

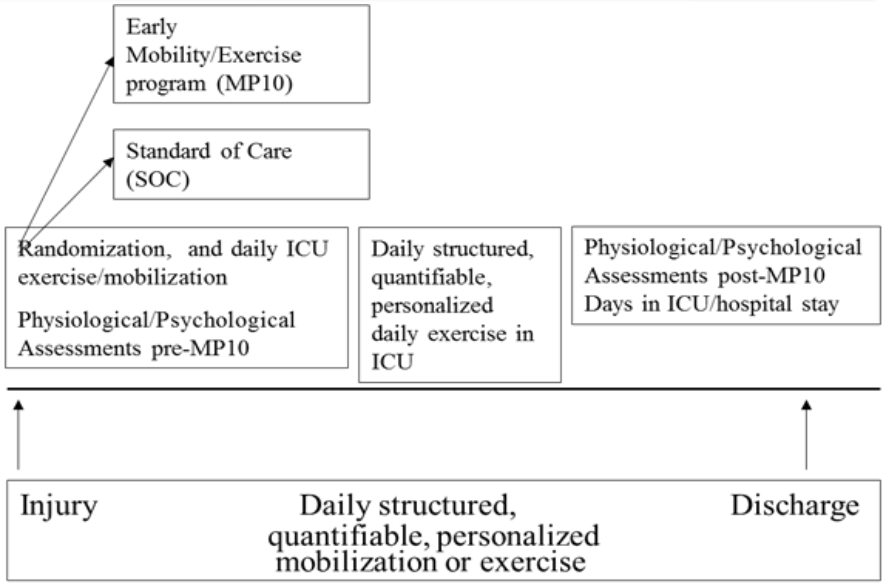
- **Objectives**: 1. decrease length of hospital stay 2. improve physiological and psychological outcomes
- **Aim 1**: Characterize SOC in the ICU in each of the 4 sites. **Aim 2**: Test the hypothesis that early exercise in the ICU will significantly improve outcomes compared to SOC.
- **Outcomes**: decreased ICU/hospital stay, improved lean mass, aerobic capacity/muscle endurance and fatigue scores.

Approach

Over 4 years, we will enroll 96 patients (24 per site; MP10 n=64 and SOC n=32) aged 18–60 years with ≥30% TBSA burns. Patients in MP10 will participate in a 10-minute leg-crank and a 10-minute arm crank ergometry session. Endpoints are lean body mass, cardiopulmonary and muscle endurance, length of BICU, ventilator and hospital stay, and Quality of Life.

Timeline and Cost

Activities CY	1	2	3	4
a. Construction and development of Survey to characterize SOC; b. submit for peer-reviewed publication				
Implement MP10+SOC vs SOC, obtain IRB, HRPO, register for clintrials,gov, enroll patients				
Submit manuscripts, present posters or oral presentations				
Estimated Budget ($K)	296,093	254,824	261,734	266,699



Goals/Milestones

CY1 Goal – IRB and HRPO approval for UTMB/SHC-GAL; UTSW; and UCD/SHC-NCA

Survey completion to characterize SOC completed by UTMB/SHC-GAL; UTSW; and UCD/SHC-NCA

CY2 Goals – MP10 enrolling at UTMB/SHC-GAL; UTSW; and UCD/SHC-NCA

Submission of abstract on Survey to ISBI

CY3 Goal – Continuation of MP10

CY4 Goal – Continuation of MP10

Analysis of data, submission of abstracts to ABA or other critical care meetings. Submission of manuscript.

Comments/Challenges/Issues/Concerns

- Aim ONE completed. Still waiting for IRB/HRPO approval from USAISR. UTMB to increase n from 24 to 96. This site only.

Budget Expenditure to Date

Projected expenditure: 550,917

Actual expenditure: $210,538

Updated: OCT 12 -2016