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TITLE: Identification of Mechanisms Underlying the Effects of Plasma Inclusive Resuscitation in Major Thermal Injury on Hemostasis and Vascular Homeostasis

PRINCIPAL INVESTIGATOR: Jeffrey W. Shupp, MD

CONTRACTING ORGANIZATION: MedStar Health Research Institute

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McLawhorn, Melissa M; Moffatt, Lauren T; Shupp, Jeffrey W

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MedStar Health Research Institute
108 Irving Street, NW
George Hyman Research Bldg. Rm. 304
Washington, DC 20010

8. PERFORMING ORGANIZATION REPORT NUMBER

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U.S. Army Medical Research and Development Command
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14. ABSTRACT

Recently, investigation is re-emerging on optimizing burn shock resuscitation. Areas of interest include a variety of strategies for reducing volume requirements. Colloid is being trialed in attempts to improve the response to vascular leakage, intravascular volume expansion and reduction of volume. Off-the-shelf colloid options include fresh frozen plasma (FFP). Many prescribers of FFP report great response in regards to intravascular volume expansion with minimal side effects. Little is known about the impacts of these transfusion products on thermally-injured patients. We hypothesize that a PIR alters coagulation homeostasis in a positive manner while combating the effects vascular endothelial dysfunction and modulating the inflammatory host response. This prospective, systematic, and comprehensive characterization of FFP and its impacts on hemostatic and inflammatory potential of burn patients will be broadly applicable because it will serve to advance the body of knowledge available on blood products.

15. SUBJECT TERMS

FFP, inflammation, endotheliopathy, burn injury, thermal injury, burn resuscitation

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

Reset

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1. INTRODUCTION:

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

The initial treatment of shock following thermal injury is swift infusion of isotonic crystalloids at a rate that is proportional to the percent total body surface area (TBSA) of cutaneous injury and the patient's pre-injury body weight. This often results in patients receiving in excess of 20 liters of fluid in the first 24 hours post-injury. Much of this massive volume then shifts to interstitial space causing edema-associated morbidities (pulmonary edema, burn depth progression, or compartment syndromes). Early resuscitation formulae included colloids that were introduced post-injury but for the most part these are of historic consideration as they were found to be inferior to the Brooke and Parkland methodologies. Recently, investigation is re-emerging on optimizing burn shock resuscitation. Areas of interest include a variety of strategies for reducing volume requirements (as would be needed in an austere environment—or where prolonged field care is required). Colloid is again being trialed in attempts to improve the response to vascular leakage, intravascular volume expansion and reduction of volume. Off-the-shelf colloid options include human serum albumin and fresh frozen plasma (FFP). Many prescribers of FFP report great response in regards to intravascular volume expansion with minimal side effects, though some reports exist of transfusion associated complications. Unfortunately, little is known about the impacts of these transfusion products on thermally-injured patients. Hence this proposal outlines a study that will elucidate the impact of a plasma-inclusive resuscitation (PIR) which will advance strategies for prolonged field care (i.e. freeze-dried plasma).

2. KEYWORDS:

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

Burn injury, thermal injury, burn resuscitation, fresh frozen plasma, inflammation, endotheliopathy, coagulopathy, resuscitation, systems biology, vascular homeostasis, transfusion reaction, extracellular vesicle

3. ACCOMPLISHMENTS:

The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.

What were the major goals of the project?

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

Major Task 1: Secure Regulatory Approval and Plan for Screening and Enrollment Coverage:
100%

Subtask 1: Clinical study/human subjects protocol preparation; data collection systems setup
100%

Subtask 2: Material and supply acquisition and on-call scheduling for screening; Staff

training for enrollment, sample acquisition, and data abstraction **100%**

Local IRB Approval and submission to HRPO: **100%**
Milestone Achieved: HRPO Approval

Major Task 2: Patient Enrollment and Sampling: **25%**

Subtask 1: Enroll patients and obtain complete sample sets as described **93.3%**

Subtask 2: Obtain clinical data and enter into database in real time **47%**

Subtask 3: Transfer samples to collaborating sites for assay **45%**

Subtask 4: Establish multi-donor pool of healthy human plasma **100%**

Milestone(s) Achieved: samples obtained and transferred for assay, clinical data set being compiled

Specific Aim 1: To assess changes in the inflammatory state of burn patients undergoing a resuscitation protocol that includes plasma transfusion

Major Task 3: Measure inflammatory markers: **0%**

Subtask 1: RNA isolation and whole genome microarray analysis (PAXgene blood) **0%**

Subtask 2 (Aim 1a. Understand the inflammatory potential of plasma products): Inflammatory marker protein panel quantification including IL-1b, IL-6, IL-10, IL-12p70, TNF-α, TNF-α R1/R2 and sIL-6 receptor (blood samples and FFP satellites/samples) **0%**

Milestone(s) Achieved (Aim 1b. Identify and characterize a further modulation of the host response by FFP administration in the setting of major thermal trauma): Inflammatory data obtained and integration with clinical and other data

Specific Aim 2: To assess changes in the vascular homeostasis and endothelial function of burn patients undergoing a resuscitation protocol that includes plasma transfusion

Major Task 4: Measure markers of endothelial integrity and assess plasma composition for extracellular vesicles: **3.5%**

Subtask 1 (Aim 2b. To determine the hemostatic potency of EVs present in the transfused FFP units and relate this potency to alterations in the parameters assessing endotheliopathy in each patient): Extracellular vesicle measurements in blood samples and FFP satellites/samples **5%**

Subtask 2 (Aim 2a. To evaluate the level of "endotheliopathy" (endothelial dysfunction) at baseline and after plasma transfusion): Marker protein level quantification including CD-138, sTM, neutrophil elastase-antitrypsin complex, sP-selectin (blood samples and FFP

satellites/samples) **0%**

Subtask 3 (Aim 2a): Vascular leakage quantification including fibrinogen, α2-macroglobulin, VEGF, and ceruloplasmin (Saliva) **10%**

Milestone(s) Achieved: Endothelial function data obtained and integration with clinical and other data

Specific Aim 3: To assess the trajectory of clot stability in burn patients undergoing a resuscitation protocol that includes plasma

Major Task 5 (3a. To evaluate the relationship between thrombin generation intensity (procoagulant potential) and clot stability in the burn patient receiving plasma resuscitation. 3b. To determine whether observed changes in clot stability are solely derived from the transfused product): Measure markers and assessments of coagulation **18%**

Subtask 1: Mine transcriptome data for related differential gene expression (see protein markers) **0%**

Subtask 2: Marker protein level quantification and functional assays including α-TAT, fibrin monomer, D-Dimer, PAI-1, factors II, V, VII, VIII, IX, X, AT, TFPI, PC, XI, XII, plasminogen, FXIII, TAFI, C1 esterase inhibitor, etc. (blood samples and FFP) **39%**

Subtask 3: Data analysis and integration **15%**

Milestone(s) Achieved: Coagulation data obtained and integration with clinical and other data

Major Task 6: Data analysis and integration using systems biology approaches **2.5%**

Subtask 1: Analyze data and integrate assay results, clinical data and outcomes, functional assay results, and relationships between FFP and patient samples **5%**

Subtask 2: Produce reports and manuscripts **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.

Major Activities:

- 12 patients were enrolled into this study during this reporting year, this includes the

completion of real time TEG, ROTEM, and platelet aggregometry. Of these 12, three did not consent or will likely need to be replaced to obtain a full data set.

- Continuing review approved by local MedStar Health Research Institute IRB on 6/21/2022 and submitted to HRPO 7/8/2022
- Healthy human control plasma pool was created at UVM.
- Additional shipments were sent out to the University of Vermont with samples for 16 of 28 patients shipped.
    - UVM began assaying shipped samples with significant process made on thrombin generation, protein level, and functional assays.
- MWHC has optimized the methodology for protein extraction from saliva specimens.

Enrollment Table

	Year 01				Year 02				Year 03				Year 04			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Projected	0	0	3	2	3	2	3	3	3	4	4	3	0	0	0	0
Actual	0	0	0	0	5	3	9	6	4	4	1	3				

- Number of subjects recruited/original planned target: 352/50
- Number of subjects screened/original planned target: 1821/n/a
- Number of patients enrolled/original planned target: 32/50
- Number of patients completed/original planned target: 28/30

Key Results/Outcomes Findings:

- UVM has completed a normal range study to define the level of variation in the empirical parameter values characterizing lytic and coagulant potential.
    - These studies should provide a context in which to evaluate alterations in the dynamics observed in burn patients as well as providing data for the refinement and validation of our computational model integrating coagulant and lytic processes.
- An ongoing analysis focused on coagulation effects and hemostatic trajectories in enrolled patients, which could be driven by a number of factors including prophylactic doses of enoxaparin.
    - Several different coagulation factors have been measured across timepoints and in relation to FFP dosing.
    - In one analysis, patients were grouped according to level of enoxaparin measured in plasma at different timepoints.
    - The below charts report initial viscoelastic results. (BD=Blood Draw)
        - Prolongation of the BD 4 clot time is observed in the following comparisons under all 4 assay conditions: BD 4 (all patients) to BD 2 (all patients), BD 4 Group 1 (high enoxaparin) to BD 2 Group 1 (prior to enoxaparin), BD 4 Group 1 to BD 4 Group 2 (comparing effect of high vs low enoxaparin)
        - When Group 2 patients are compared at BD 2 and BD 4, no difference in CT (or any other parameter) is observed suggesting that the presence of enoxaparin in Group 1 patients accounts for the observed differences

No TPA	BD2	BD4	BD4 Group 1	BD4 Group 2
CT (s)	187 ± 33	281 ± 98%	353 ± 81&	209 ± 46*
α (degrees)	64 ± 8	59 ± 7	55 ± 7&	64 ± 4
MCF (mm)	22 ± 6	26 ± 5	28 ± 4&	25 ± 6*
LT (s)	---	---	---	---
AUC (mm*s)	141000 ± 43000	164000 ± 31000	173000 ± 24000&	159000 ± 38000
Normalized AUC (%)	100	100	100	100

BD 4 group 1 (E>0.1 U/mL)
(100, 102, 106,
110, 115, 122)

BD4 group 2 (E<0.1U/mL)
108, 112, 114, 116,
117,118

+ TPA	BD2	BD4	BD4 Group 1	BD4 Group 2
CT (s)	189 ± 33	287 ± 100%	361 ± 81&	214 ± 50*
α (degrees)	65 ± 7	58 ± 10%	52 ± 10&	64 ± 4*
MCF (mm)	19 ± 6	19 ± 5	19 ± 4	20 ± 5
LT (s)	1543 ± 946	1345 ± 692	1027 ± 211	1662 ± 876
AUC (mm*s)	37000 ± 57000	17000 ± 14000	10000 ± 4000&	23000 ± 18000
Normalized AUC (%)	23 ± 29	10 ± 7	6 ± 3&	14 ± 9

Significant differences

% - BD4 vs BD2 (n=12 pairs)
& - BD4 group 1 vs BD2 group 1 (n=6 pairs)
* - BD4 group 1 vs BD4 group 2 (n=6 vs 6)
? - BD4 group 2 vs BD2 group 2 (n= 6 pairs)

+ TPA + TM	BD2	BD4	BD4 Group 1	BD4 Group 2
CT (s)	197 ± 37	297 ± 102%	374 ± 78&	220 ± 53*
α (degrees)	64 ± 6	56 ± 9%	50 ± 8&	62 ± 5*
MCF (mm)	20 ± 6	22 ± 5	22 ± 4&	22 ± 6
LT (s)	3037 ± 1349	2923 ± 813	2449 ± 399	3398 ± 870*
AUC (mm*s)	60000 ± 51000	49000 ± 24000	38000 ± 12000	59000 ± 30000
Normalized AUC (%)	41 ± 26	30 ± 12	22 ± 6	36 ± 13*

BD 4 group 1 (E>0.1 U/mL)
(100, 102, 106,
110, 115, 122)

BD4 group 2 (E<0.1U/mL)
108, 112, 114, 116,
117,118

+ TPA + PTCI	BD2	BD4	BD4 Group 1	BD4 Group 2
CT (s)	187 ± 34	283 ± 95%	353 ± 73&	212 ± 50*
α (degrees)	66 ± 6	58 ± 9%	53 ± 8&	64 ± 4*
MCF (mm)	19 ± 6	20 ± 4	19 ± 4	20 ± 5
LT (s)	1150 ± 814	1059 ± 371	901 ± 138	1217 ± 473
AUC (mm*s)	30000 ± 55000	12000 ± 7000	10000 ± 4 000	15000 ± 9000
Normalized AUC (%)	18 ± 27	7 ± 3	5 ± 2	9 ± 4

Significant differences

% - BD4 vs BD2 (n=12 pairs)
& - BD4 group 1 vs BD2 group 1 (n=6 pairs)
* - BD4 group 1 vs BD4 group 2 (n=6 vs 6)
? - BD4 group 2 vs BD2 group 2 (n= 6 pairs)

- An ongoing composition analysis of Factor data suggests a significant difference between pre-plasma administration values (BD2) and post-plasma resuscitation levels (BD4) for Factors II, VII, VIII, X, XI, XII, and Antithrombin
- Enoxaparin levels at BD4 allowed for grouped comparison. Groups 1 had values >0.1U/ml and Group 2 had values less than 0.1U/ml

Factor	BD2	BD4	BD4 Group 1	BD4 Group 2
II	89 ± 22	69 ± 18%	66 ± 17&	72 ± 20
V	106 ± 24	103 ± 23	105 ± 10	102 ± 33
VII	111 ± 29	71 ± 23%	75 ± 14&	67 ± 30?
VIII	304 ± 150	205 ± 66%	195 ± 39	214 ± 88
IX	130 ± 38	114 ± 33	119 ± 15	109 ± 46
X	89 ± 18	71 ± 16%	72 ± 9	70 ± 22?
XI	136 ± 44	97 ± 30%	92 ± 21&	101 ± 39
XII	89 ± 16	63 ± 13%	63 ± 12&	62 ± 14?
AT	84 ± 14	63 ± 14%	68 ± 9&	59 ± 18?
PC	66 ± 22	59 ± 22	65 ± 20	53 ± 24?
TFPI	111 ± 40	121 ± 34	145 ± 32	98 ± 13*
FBGN (mg/dL)	342 ± 89	423 ± 91	433 ± 76	414 ± 110

Red indicates that the mean for that time point is outside the range of all 56 healthy human control plasmas
BD = blood draw

BD 4 Group 1(>0.1 U/mL) (100,102,106, 110, 115, 122)

BD4 Group 2 (<0.1U/mL) 108, 112, 114, 116, 117,118

Significant differences

% - BD4 vs BD2 (n=12 pairs)
& -- BD4 group 1 vs BD2 group 1 (n=6 pairs)
? - BD4 group 2 vs BD2 group 2 (n=6 pairs)
* - BD4 group 1 vs BD4 group 2 (n=6 vs 6)

All current data analyses are ongoing and preliminary. Stronger conclusions will be informed by an increased number of patients as they are added as well as additional assays completed using the current population.

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.

Given staffing changes due to resignation from the institutions during the past year an additional 8 staff members (with limited laboratory exposure) were trained by to become proficient in simple sample processing, real time thromboelastography and rotational thromboeslastometry, platelet aggregometry, and bar coded freezer management. This has been accomplished through group and one-on-one training

Members of the UVM/MWHC team meet routinely for a lab meeting to discuss ongoing data analysis and priorities for ongoing task completion.

As part of their participation at the American Burn Association conference, attendees had the opportunity to learn more about coagulopathies in burn injury via the education forum entitled "Understanding Coagulopathies as Related to Burn Injury: Research Findings and Clinical

Implications".

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.

During the next quarter of the final year, it is expected the last patients will be enrolled and all samples shipped to assaying sites at UVM or WRAIR. This allows the focus of the research team will move to be assay completion and data analysis.

It is anticipated that multiple abstracts will be developed in the final year leading to manuscripts.

Clinical data and auditing will be completed in upcoming 2 quarters to allow for complete systems biology integration with the assay data.

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

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

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

Nothing to Report

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

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

Nothing to Report

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

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

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

Nothing to Report

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

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

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

Nothing to Report

5. CHANGES/PROBLEMS:

The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official 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.

No major changes to the objectives or scope were undertaken during the reporting period.

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

Disposition of samples including shipping was delayed to UVM due to inconsistency with the ability to scan datamatrix barcode once samples were frozen. Sample accountability is crucial to

meeting study objectives. Study site has contacted the freezer management vendor to troubleshoot and it was determined the cause due to the size and clarity of the datamatrix barcode. A new barcode printer was purchased (using non-study funding) to ensure label clarity.
In the event that samples are unable to scan, a two person double check of the pulled specimens will be completed using the box map.

Reagent supply chain delays have also slowed down the assay progress from some biomarkers, particularly PAI-1. No other vendors were available but this shipment has now arrived and assays are moving forward.

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

Nothing to Report

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

Significant changes in use or care of human subjects

No major changes.

Significant changes in use or care of vertebrate animals

Not Applicable.

Significant changes in use of biohazards and/or select agents

Not Applicable.

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 at this time.

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 at this time.

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

Nothing to Report at this time.

- **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. Describe the technologies or techniques were shared.

Nothing to Report at this time.

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. 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 at this time.

- **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;*
  - *physical 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 at this time.

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:	*Jeffrey W. Shupp, MD*
Project Role:	*Principal Investigator*

Nearest person month worked: 1
Contribution to Project: Dr. Shupp provided overall oversight and guidance related to appropriateness of subject enrollment and removed subjects from continued sample collection if milestones were not met. He is working with the UVM team, Dr. Moffatt and Ms. McLawhorn on routine data review and analysis.

Name: Lauren Moffatt, PhD
Project Role: Lab and Admin Manager
Nearest person month worked: 1
Contribution to Project: Dr. Moffatt provided laboratory oversight and assisted with saliva assay troubleshooting. She generated required reporting for the award along with Ms. McLawhorn.

Name: Melissa McLawhorn
Project Role: Project Manager
Nearest person month worked: 3
Contribution to Project: Ms. McLawhorn provided clinical oversight and assistance for all aspects of protocol implementation including subject enrollment, sample processing, data monitoring, and ICF completion. She interfaces with regulatory personnel with IRB and HRPO. With the MWHC staff members and Dr. Moffatt she has overseen and evaluated the proficiency of newly hired clinical and laboratory staff.

Name: Sarah Burkey
Project Role: Clinical Research Coordinator
Nearest person month worked: 2
Contribution to Project: Ms. Burkey monitored for eligible subjects, performed informed consents, processed samples, and collected clinical data. She worked with Ms. McLawhorn on data monitoring and shipments. She has left the project as of March 2022.

Name: Mounica Bevara
Project Role: Clinical Research Coordinator
Nearest person month worked: 1
Contribution to Project: Ms. Bevara monitored for eligible subjects, performed informed consents, processed samples, and entered clinical data.

Name: Cara Delatore
Project Role: Clinical Research Coordinator
Nearest person month worked: 3
Contribution to Project: Ms. Delatore monitored for eligible subjects, performed informed consents, processed samples, and collected clinical data. She assisted Ms. McLawhorn on integrating the TEG machine into the sample processing plan. She is working with Ms. Ross on data monitoring.

Name: *Lou'ay Hussein*
Project Role: *Lab Technician*
Nearest person month worked: *2*
Contribution to Project: *Mr. Hussein monitored for eligible subjects, performed informed consents, processed samples, and collected clinical data. He worked with Dr. Moffatt to troubleshoot initial*

Name: *Mary Oliver*
Project Role: *Lab Technician*
Nearest person month worked: *2*
Contribution to Project: *Mr. Hussein monitored for eligible subjects, performed informed consents, processed samples, and collected clinical data.*

Name: *Connor Scannell*
Project Role: *Lab Technician*
Nearest person month worked: *1*
Contribution to Project: *Mr. Scannell monitored for eligible subjects, performed informed consents, processed samples, and collected clinical data.*

Name: *Eriks Ziedins*
Project Role: *Lab Technician*
Nearest person month worked: *1*
Contribution to Project: *Mr. Ziedins monitored for eligible subjects, performed informed consents, processed samples, and collected clinical data.*

Name: *Alison Ross*
Project Role: *Research Assistant*
Nearest person month worked: *3*
Contribution to Project: *Ms. Ross has aided Ms. McLawhorn in the revision of the REDCap data base and clinical data entry and audit. She has aided the Clinical Research Coordinators with patient enrollment and lab processing.*

Name: *Thomas Orfeo, PhD*
Project Role: *UVM subcontract Principal Investigator*
Nearest person month worked: *2*
Contribution to Project: *Dr. Orfeo has been initiating assay protocols and experimental systems at UVM. He is overseeing the team at UVM on establishing normal human donor pool, assay completion and analysis.*

Name: *Maria Cristina Bravo, PhD*
Project Role: *Faculty Scientist*
Nearest person month worked: *2*
Contribution to Project: *Dr. Bravo has been completing assays and compiling data for analysis and discussion with the MWHC team.*

Name: *Matthew Gissel*

Project Role:	*Research Specialist*
Nearest person month worked:	*2*
Contribution to Project:	*Mr. Gissel has worked with Drs. Bravo and Orfeo on completing assays and compiling data for analysis and discussion with the MWHC team.*

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.

Nothing to report.

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 Principal Investigator (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.