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TITLE: Mesenchymal Stem Cells for Treatment of ARDS Following Trauma

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CONTRACTING ORGANIZATION: The Regents of the University of California, San Francisco

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14. ABSTRACT

The acute respiratory distress syndrome (ARDS) is a life-threatening medical condition in which the lung is injured or inflamed to the degree that it cannot properly exchange gases and oxygenate the body. ARDS can be caused by a variety of conditions including trauma, severe blood loss, multiple or large volume blood transfusions, burns, and infections. The development of therapeutics that can limit the severity and/or progression of lung injuries that lead to ARDS and death is an immediate clinical need in both military and civilian sectors. Experimental studies carried out in small and large animals have demonstrated that specialized cells called mesenchymal stromal cells (MSC) can effectively reduce inflammation in multiple diseases including ARDS. The overall objective of this proposal is to carry out a randomized, blinded, placebo-controlled, multicenter phase 2b trial to test the therapeutic potential of allogeneic bone-marrow derived MSC for treating ARDS, with a major focus on civilian trauma patients. The specific aims of this project are: **Specific Aim 1**. To test the clinical efficacy of intravenously delivered allogeneic human MSC in patients with ARDS. **Specific Aim 2.** To test the mechanisms by which MSC reduce acute lung injury in patients with ARDS.

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1. INTRODUCTION:

The acute respiratory distress syndrome (ARDS) is a life-threatening medical condition in which the lung is injured or inflamed to the degree that it cannot properly exchange gases and oxygenate the body. ARDS can be caused by a variety of conditions including infections, trauma, severe blood loss, multiple or large volume blood transfusions, burns, and the inhalation of chemical poisons or smoke. According to the National Heart Lung and Blood Institute, approximately 190,000 people in the U.S. will develop ARDS each year, with a death rate ranging from 25–40%. Recent studies from the Department of Defense Iraq Trauma Registry (DoDTR) reported that ARDS developed in a large number of severely wounded warfighters and was associated with higher death rates. To date, there have been few advances in the treatment of major trauma related conditions such as ARDS. The development of therapeutics that can limit the severity and/or progression of lung injuries that lead to ARDS and death is an immediate clinical need in both military and civilian sectors. Experimental studies carried out in small and large animals have demonstrated that specialized cells called mesenchymal stromal cells (MSC) can effectively reduce inflammation in multiple diseases including ARDS. The overall objective of this proposal is to carry out a randomized, blinded, placebo-controlled, multicenter phase 2b trial to test the therapeutic potential of allogeneic bone-marrow derived MSC for treating ARDS. The specific aims of this project are: **Specific Aim 1**. To test the clinical efficacy of intravenously delivered allogeneic human MSC in patients with ARDS. **Specific Aim 2.** To test the mechanisms by which MSC reduce acute lung injury in trauma patients with ARDS. Subsequently emerging evidence suggests that the incidence of ARDS following trauma has declined, probably related to changes in resuscitation practices with the reduced use of crystalloid fluids and balanced transfusion of blood products. In order to study all patients with ARDS after trauma as well as to meet enrollment goals over the defined study period, after the discussion with the Department of Defense, the inclusion criteria for this phase 2b trial have been broadened to include all causes of ARDS for testing MSCs for both trauma and medical causes of ARDS.

2. KEYWORDS: Acute respiratory distress syndrome, pulmonary edema, trauma, pneumonia, sepsis

3. ACCOMPLISHMENTS:

- **What were the major goals of the project?**

During Year 3, our major goals were as follows:

1. Revise the protocol with changes in the inclusion criteria and minor revisions and clarification in study procedures.
2. IRB regulatory submissions, which mainly included the following tasks: Obtain the central IRB approvals for local consent context for all sites; Obtain IRB renewal approval from sIRB (VUMC); Submit a protocol amendment to sIRB at Vanderbilt University regarding minor protocol and consent revision, as well as Site-PI change at ZSFG, and obtain IRB approval for electronic consent instruments for remote consenting.
3. Submit IND amendment and annual progress report to the FDA under IND 15331
4. Submit the local consent context to the DoD HRPO to obtain the approval from the DoD. Obtain USARMC HRPO approvals for all recruitment sites
5. Set up electronic consent for all sites through Vanderbilt RedCap. Submit electronic consent forms to sIRB (VUMC) and obtain IRB official approvals for remote consenting

6. Finalize and beta test the case report forms with the data management system and develop data dictionary and additional data quality checking tools.
7. Finalize each site-specific MSC preparation and MSC infusion protocol, based on the approved MSC preparation and infusion protocol which are included in the current Clinical Protocol.
8. Delivery of the first batch of MSCs and run the necessary testing at local sites prior to the initiation of the trial and delivery of MSC to local sites
9. Set up a plan for monthly teleconference with the study investigators and study coordinators at all participating sites
10. Training of coordinators and investigators with a conference call and meetings by conference call. Webinar educational sessions to introduce the data management system to investigators, BMT staff (randomization) and study coordinators
11. Begin enrollment of patients at two sites: UCSF and ZSFG. Expand enrollment to include U. Texas Houston, OHSU, Vanderbilt, U. Washington Harborview Seattle
12. Add University of California Davis Medical Center as a new participating site
13. Hold DSMB teleconference in July 2020.
14. Develop a clinical trial website for this STAT trial

- **What was accomplished under these goals?**

Goal #1: Revise the protocol with changes in the inclusion criteria and minor revisions and clarification in study procedures. – completed

During the past reporting year, we have amended the Clinical Protocol twice, and we have also updated the related study documents for this Phase 2b trial listed as below:

Clinical Protocol:

The Clinical Protocol has been revised in March 2020 (Protocol No: UCSF-hMSC-ARDS-P1P2-11, dated March 17, 2020) and July 2020 (Protocol No: UCSF-hMSC-ARDS-P1P2-12, dated July 17, 2020). All the changes have been listed in Protocol Amendment 1 (dated March 17, 2020) and Protocol Amendment 2 (dated July 13, 2020). Some significant protocol revisions include:

- We have expanded of recruiting ARDS patients with from PaO_2/FiO_2 < 200 mmHg to PaO_2/FiO_2 < 250 mmHg and New exclusion criteria for patients with recent tocilizumab treatment
- We have added a new participating site: University of California Davis Medical Center (UCD, Sacramento, CA). The Site-Principal Investigator is Rachael Callcut, MD.
- We have updated the Study Product Preparation Protocol (Clinical Protocol – Appendix E). This is the Standard Operation Procedure developed by the UCSF Clinical Bone Marrow Transplant Facility, and is used as the template for all sites.
- We have updated the Study Product Infusion Protocol (Clinical Protocol – Appendix H).
- We have revised and clarified some minor study procedure changes which were summarized in Clinical Protocol Amendment 1 and 2.

Investigator Brochure:

The Investigator Brochure has been updated to reflect the changes of the Clinical Protocol. During the past reporting year, we developed two versions of Investigator Brochure: Version 11 (dated March 17, 2020) and Version 12 (dated July 13, 2020; current version).

Informed Consent Form (ICF):

We are using the Vanderbilt IRB as the single IRB (sIRB) at Vanderbilt University Medical Center (VUMC) for this Phase 2b trial. Per the Vanderbilt IRB's guidelines, the consent forms at each site includes two parts: main consent (Part 1) to be used for all seven sites, and local consent context form (Part 2) which has site-specific language. The main consent has been updated (version 1.5, dated June 24, 2020) and approved by the sIRB at UVMC on August 3, 2020. This main consent form has also been translated into Spanish and Russian, and approved by the sIRB.

All recruitment sites have developed site-specific consent forms. The local consent forms for all 7 participating sites have been approved by the sIRB at VUMC and the Department of Defense. During the past year, we have made a very minor modification on this consent by indicating a less volume of DNA/RNA blood collection in the part 2 ICF. We have also changed the site PI's information in the ZSFG's part 2 ICF. The current versions of the local consent context forms (Part 2) are listed as below:

- University of California San Francisco (UCSF): dated 04/03/2020
- Zuckerberg San Francisco General Hospital & Trauma Center (ZSFG): dated 02/24/2020
- University of Texas Health Science Center at Houston (UTHSCH): dated 04/03/2020
- University of Washington, Harborview Medical Center (Harborview): dated 04/03/2020
- Oregon Health & Science University (OHSU): dated 04/03/2020
- Vanderbilt University Medical Center (VUMC): dated 04/03/2020
- University of California Davis (UCDavis): dated 06/03/2020

Case Report Form (CRF):

We have updated the case report forms to reflect the new changes in the Clinical Protocol. The current version is dated July 13, 2020.

Statistical Analysis Plan (SAP):

We have updated the Statistical Analysis Plan to reflect the new changes in the Clinical Protocol. The current version is dated July 13, 2020.

Goal #2: Submissions to single IRB at VUMC, which mainly included but not limited to the following tasks: (1) Obtain the central IRB approvals for local consent context for all sites; (2) Obtain IRB renewal approval from sIRB (VUMC); (3) Submit a protocol amendments regarding minor protocol and consent revision, as well as Site-PI change at ZSFG; (4) Obtain IRB approval for electronic consent instruments for remote consenting. – completed.

The central IRB at Vanderbilt University Medical Center (PI – Todd Rice, MD) is the central IRB, and all 7 sites (UCSF, ZSGH, OHSU, UTHSCH, Harborview, OHSU, VUMC, UCDavis) have agreed to this plan and obtained the reliance approval from their institutional IRBs. The UCSF IRB is responsible for the regulatory issues for two recruitment sites: UCSF and ZSFG.

During the past reporting period, we have conducted the following regulatory activities with the central IRB at Vanderbilt University:

1. **IRB Amendment 4:** **Submission date:** 08/20/2019 **Approval date:** 10/17/2019

   Description: We submitted the revised local consent document for UCSF site for two minor changes: (1) Fixing a telephone typo; (2) Adding the Bills of Rights, which is required for the California site. We have also submitted the new local consent for four sites: 1. Zuckerberg San

Francisco General Hospital & Trauma Center; 2. Harborview Medical Center; 3. Oregon Health & Science University (Portland, OR); 4. The University of Texas Health Sciences Center at Houston/Memorial Hermann-Texas Medical Center. The Vanderbilt team, per central IRB's guideline, has submitted their local consent context separately.

2. **IRB Amendment 5:** **Submission date**: 11/19/2019 **Approval date:** 11/25/2019

   Description: We submitted the local consent context for Oregon Health & Science University to Vanderbilt IRB.

3. **IRB Amendment 6:** **Submission date**: 11/26/2019 **Approval date:** 12/12/2019

   Description: We identified a formatting error in the local consent context of three sites (UCSF, ZSFG, UW) and submitted the updated versions. We received approval notice on January 2, 2020.

4. **IRB Amendment 7:** **Submission date:** 01/24/2020 **Approval date:** 02/07/2020

   Description: We submitted the revised local consent document for UTH regarding treatment and compensation for injury per the DoD HRPO's request.

5. **IRB Renewal:** **Submission date:** 02/27/2020 **Approval date:** 03/19/2020

   Description: We submitted the IRB renewal request to the sIRB at VUMC for the following 5 sites: UCSF, ZSFG, UTHSCH, Harborview and OHSU. The new IRB expiration date is March 18, 2021.

6. **IRB Amendment 8:** **Submission date:** 03/28/2020 **Approval date:** 03/24/2020

   Description: We submitted the amendment to add VUMC as a new recruitment site and requested the review and approval of local consent context for VUMC.

7. **IRB Amendment 9:** **Submission date:** 04/10/2020 **Approval date:** 04/23/2020 (05/14/2020 notice received)

   Description: We submitted the IRB amendment for the following changes: (1) Updated Clinical Protocol with Protocol Amendment 1; (2) Updated IRB application form to reflect clinical protocol revision and study procedure optimization; (3) Updated Investigator Brochure to reflect the minor protocol revision; (4) Submission of FAQ Set 1 regarding the adjustment for COVID-19 pandemic and the clarification of Clinical Protocol; (5) Submission of updated Statistical Analysis Plan (minor revision of statistical modeling for primary end point); (6) Submission of updated Case Report Form; (7) Report the site-PI revision at Zuckerberg San Francisco General Hospital & Trauma Center. Dr. Carolyn Hendrickson's 1572 form and CV is attached; (8) Submission of updated consent forms regarding the reduction of blood collection for genetic testing; (9) Submission of translated consent form in Spanish language for all 6 recruitment sites; (10) Submission of remote electronic consent instruments for 6 sites, including: surrogate consent for (English and Spanish) and patient re-consent form (English and Spanish); (11) Submission of non-English short forms of consenting for Oregon Health & Science University. We received the approval notice by email on 05/14/2020.

8. **IRB Amendment 10:** **Submission date:** 07/16/2020 **Approval date:** 08/03/2020

   Description: We submitted the amendment for the following changes: (1) Updated Clinical Protocol (version 12) with Protocol Amendment 2; (2) Updated IRB application form to reflect clinical protocol revision; (3) Updated Investigator Brochure to reflect the minor protocol revision; (4) Updated Statistical Analysis Plan to reflect protocol changes; (5) Updated Case Report Form; (6) Submission of the new 28-day and 6-month telephone survey scripts, as well as the revised 60-day telephone survey script; (7) Submission of revised master consent form (English and Spanish versions) for better clarification of day 28 and day 60 measurements, as well as the new master consent form in Russian; (8) Revised E-consent instruments for 6 sites (UCSF, ZSFG, UTHSCH, Harborview, OHSU, VUMC), which are matched with master consent revisions.

9. **IRB Amendment 11:** **Submission date:** 07/30/2020 **Approval date:** 08/05/2020

   Description: We submitted the amendment to add University of California Davis Medical Center (UCDavis) a new recruitment site and requested the review and approval of local consent context for UCDavis.

10. **IRB Amendment 12:** **Submission date:** 08/25/2020 **Approval date:** 08/26/2020

    Description: We submitted the DSMB recommendation issued on 08/11/2020 to the sIRB. The DSMB recommendation is attached in Appendix A.

Goal #3: Submit IND amendment and annual progress report to the FDA under IND 15331 – completed

During the past reporting year, we have submitted the two IND amendments to the FDA for this trial. Please note that no formal approval notices was required for these submissions.

1. **IND 15331 #0021:** **Submission date:** 03/22/2020

   This IND amendment submission included the following tasks and updates:
   - Submission of amended Clinical Protocol (Version 11).
   - Report of site PI change at ZSFG with the updated 1572 form and signed by Dr. Carolyn Hendrickson.
   - Submission of Annual Progress Report for the past year.
   - Submission of revised Investigator Brochure and Statistical Analysis Plan.
   - Submission of the Information Amendment for the updated key personnel list for 6 sites and research laboratory facilities.

2. **IND 15331 #0022:** **Submission date:** 07/31/2020

   This IND amendment submission included the following tasks and updates:
   - Submission of amended Clinical Protocol (Version 12)
   - Submission of new participating site – UCDavis, with the signed 1572 form signed by site PI, Dr. Rachael Callcut.

- Submission of the updated Investigator Brochure and Statistical Analysis Plan.

Goal #4: Submit the local consent context to the DoD HRPO to obtain the approval from the DoD. Obtain USARMC HRPO approvals for all recruitment sites – Completed

During the past reporting period, we have had the following communications with the DoD:

1. **Site addition – ZSFG:** The local study documents (including part 2 of ICF) from ZSFG were submitted on 11/19/2019 and approved on 12/09/2019.

2. **Site addition – UTHSCH:** The local study documents (including part 2 of ICF) from UTHSCH were submitted on 12/11/2019 and approved on 02/11/2020.

3. **Site addition – Harborview:** The local study documents (including part 2 of ICF) from Harborview were submitted on 12/12/2019 and approved on 02/11/2020.

4. **Site addition – OHSU:** The local study documents (including part 2 of ICF) from OHSU were submitted on 12/16/2019 and approved on 03/04/2020.

5. **Site PI change at ZSFG:** We reported the site PI change at ZSFG to the HRPO by email on March 3, 2020. However, we were unable to submit this request to sIRB and stamped the revised local consent form because the Vanderbilt IRB suggested us to hold the submission of site PI change until we submitted and obtained the continuing renewal approval, in consideration of IRB processing of Site PI change might delay the submission of continuing renewal (concurrent IRB submissions for the same site would not be allowed). During the site PI transition, Dr. Michael Matthay has overseen the enrollment and study activities at ZSFG.

6. **Continuing Renewal:** On April 20, 2020, we submitted the Continuing Review Submission Forms and the supporting documents for 5 participating sites (UCSF, ZSFG, UTHSCH, Harborview, OHSU).

7. **Site addition – VUMC:** The local study documents from VUMC were submitted on 01/30/2020, stamped ICF was submitted on 03/24/2020, and the DoD HRPO approved on 04/24/2020.

8. **Protocol Amendment 1 – All sites and Site PI change at ZSFG**: The IRB amendment regarding Clinical Protocol Amendment 1 was approved by the sIRB at VUMC on April 23, 2020 and we received the approval notice on May 14, 2020. On May 20, 2020, we submitted the following approved study documents to the DoD HRPO:

   Global study documents for all sites:
   - IRB submission form and IRB approval notice;
   - Clinical Protocol (Version 11, dated 03/17/2020) and Protocol Amendment 1 listing all proposed protocol changes;
   - Updated Investigator Brochure (Version 11, dated 03/17/2020);
   - Revised Case Report Form (dated 03/17/2020);
   - Updated Statistical Analysis Plan (dated 03/19/2020);
   - FAQ set 1 (dated 04/09/2020);

Consent documents:

- New Spanish master consent form (Part 1) for all participating sites;
- Revised local consent context (Part 2) for all participating sites
- New Electronic consent forms for all participating sites, which are created and stored in Vanderbilt REDCap.

Supporting documents for Site PI change at ZSFG

- Re-submitting the Form 1572 and CV for the new site-PI Dr. Carolyn Hendrickson.

We received the DoD HRPO's approval notice regarding the site PI change on June 8, 2020.

9. **Protocol Amendment 2 – All sites:** The IRB amendment regarding Clinical Protocol 2 was approved by the sIRB at VUMC on 07/16/2020 and approved by sIRB on 08/03/2020. On August 7, 2020, we submitted the following approved study documents to the DoD HRPO:

   Global study documents for all sites:

   - IRB submission form and IRB approval notice;
   - Clinical Protocol (Version 12, dated 07/13/2020) and Protocol Amendment 2 listing all proposed protocol changes;
   - Updated Investigator Brochure (Version 12, dated 07/13/2020);
   - Revised Case Report Form (dated 07/13/2020);
   - Updated Statistical Analysis Plan (dated 07/13/2020);

   Consent documents:

   - Revised master consent form (Part 1) to reflect the protocol changes, in both English and Spanish versions, for all participating sites
   - Revised Electronic consent forms for all participating sites to be consistent with the updated master consent form.

   We received the DoD HRPO's approval notice regarding this protocol revision on September 18, 2020.

10. **Site addition – UCDavis:** The local study documents (including part 2 of ICF) from UCDavis were submitted on 08/29/2020. We received and responded the review clarifications on 09/21/2020. This site addition submission was approved by the DoD HRPO on October 10, 2020.

Goal #5: Set up electronic consent for all sites through Vanderbilt RedCap. Submit electronic consent forms to sIRB (VUMC) and obtain IRB official approvals for remote consenting – Completed.

REDCap is the only system approved for E-consenting by central IRB at Vanderbilt University. We have built the E-consent forms for all 7 participating sites and obtained the sIRB's approval for E-consent forms. This E-consent portal is now active and plays a critical role in patient recruitment during COVID-19 pandemic.

Goal #6: Finalize and beta test the case report forms with the data management system and develop data dictionary and additional data quality checking tool. - Completed

During the past reporting period, the case report form has been updated to reflect the current protocol changes and the additional data collection for COVID-19 information.

The electronic data base system has been developed and maintained by Quesgen Inc. The Project Manager at UCSF, Hanjing Zhuo, oversees (blinded) the database development and data management. The data management features for data validation and query creation have been completely built in the system. The beta testing have been completed by the Data Manager and the Study Coordinators. The portals of study randomization and data entries are actively in use now.

Goal #7: Each site to finalize their site-specific MSC preparation and MSC infusion protocol, based on the approved MSC preparation and infusion protocol which are included in the current Clinical Protocol. – In progress

Each site should have developed site-specific study product preparation SOP and infusion SOP, based on the IRB-approved SOP template (in Clinical Protocol Appendices E and H). Five of the 7 sites (UCSF, ZSFG, OHSU, UTHSCH, VUMC) have completed site-specific SOP development regarding study product preparation and study product infusion. Harborview has finalized their study preparation SOP and UC Davis is working closely with UCSF BMT lab to finalize their SOPs.

Goal #8: Delivery of the first batch of MSCs and run the necessary testing at local sites prior to the initiation of the trial and delivery of MSC to local sites

The University of Minnesota MSC production site has completed the production of the clinical-grade MSCs. Currently, the inventory at University of Minnesota has approximately 11.6 billion MSCs, and it supports 4 sites (UCSF, ZSFG, OHSU, UTHSCH) which are open for enrollment.

The mock test of MSC preparation at Vanderbilt met satisfactory criteria (e.g. viability expected, recovery that matched viability, et al) and the clinical grade MSCs have been delivered to VUMC. VUMC is anticipated to start screening and enrollment in the week of October 19, 2020.

UC Davis is finalizing their study product preparation SOP. The MSCs for the mock test have delivered to the local site. If the results of MSC mock run is satisfactory, it is anticipated that the clinical grade MSCs will be shipped to the site within 2 weeks.

UC Washington and Harborview Hospital – We are working with their cell therapy laboratory to complete all of the mock testing, including manual counting of the MSC viability. We anticipate that this site can open in the very near future.

Goal #9: Set up a plan for monthly teleconference with the study investigators and study coordinators at all participating sites – Completed.

We have scheduled a regular one-hour monthly teleconference with the study investigators, study coordinators and Stem Cell Lab personnel at all participating sites (second Tuesday of every month) for study progress updates and discussions. The Science Officer Sandy Snyder has been invited to attend this teleconference. Meanwhile, a weekly email regarding study progress has been scheduled to sent to all research personnel.

Goal #10: Training of coordinators and investigators with a conference call and meetings by conference call. Webinar educational sessions to introduce the data management system to investigators, BMT staff (randomization) and study coordinators – In progress

We provided the study initiation training for the VUMC, OHSU, and UC Davis. We have also provided constant consultation by phone calls and emails for any research related questions. We have also distributed the study related documents and SOPs to help each recruitment site to initiate the study recruitment.

Instead of setting up webinar educational sessions, we have developed three separate User Manuals to provide step-by-step instruction for: (1) E-consent portal through VUMC REDCap; (2) Study randomization portal through QuesGen system; (3) Data entry portal through QuesGen system. We have also created the mock databases for each user so they can practice and be familiar with the systems. The CCC at UCSF and QuesGen team is available for consultation.

We will continue to provide necessary training and consultation to facilitate the study initiation and conduction.

Goal #11: Begin enrollment of patients at two sites: UCSF and ZSFG, and then expand enrollment to include U. Texas Houston, OHSU, Vanderbilt, U. Washington Harborview Seattle and UC Davis – In progress

During the past reporting period, we have opened the following sites:

- UCSF – Screening initiated date: 11/26/2020
- ZSFG – Screening initiated date: 12/30/2020
- UTHSCH – Screening initiated date: 04/17/2020
- OHSU – Screening initiated date: 05/28/2020

As of October 13, 2020, we have enrolled a total of 36 patients into this Phase 2b trial: 5 from UCSF, 22 from UCSF-ZSFG, 5 from OHSU and 4 from UTHSCH.

We anticipate beginning enrollment at Vanderbilt University Medical Center in the week of October 19, 2020, and beginning enrollment at University of California Davis Medical Center in late October. We are also working closely with University of Washington Harborview Seattle to solve their technical issues with regards to the MSC mock run, so we can activate this site in the next reporting period.

Goal #12: Add University of California Davis Medical Center as a new participating site

An opportunity arose in the Spring of 2020 to apply for funding from the California Institute of Regenerative Medicine to add UC Davis to our participating hospitals. This application was approved by DoD, and CIRM awarded us the funding in late June 2020. Thus, a new goal was to add UC Davis to the participating hospitals later in the calendar year 2020.

Goal #13: Hold DSMB teleconference in July 2020 - completed.

The DSMB 6-month interval teleconference was scheduled on August 11, 2020. After review of the materials submitted to the Board and reviewed during the open session, including a review of recent protocol amendments along with a report of baseline characteristics, SAEs, and narratives of the 8 participant deaths, the Board recommends that the study continue as amended.

Goal #14: Develop clinical trial website – completed.

We have developed a study website (www.stattrial.com) to track enrollment, exchange study related documents, post FAQ and maintain personnel directory for all participating sites.

- **What opportunities for training and professional development has the project provided?** Carolyn Hendrickson, MD, MAS and Lucy Kornblith, MD, MAS have become proficient at leading a challenging clinical trial including screening, consent, enrollment and overseeing all of the details of the trial at ZSFG. They are both Assistant Professors so this is an excellent professional development experience for them. Both Drs. Hendrickson and Kornblith have NIH K awards and Dr. Matthay is their primary mentor.

- **How were the results disseminated to communities of interest?** Nothing to report.

- **What do you plan to do during the next reporting period to accomplish the goals?**
  1. Identify and solve the technical problems in MSC mock run at the U Wash Harborview Cell Therapy Center in Seattle
  2. Clinical grade MSCs delivery to UC Davis and Harborview and U. Wash Cell Therapy Center in Seattle
  3. Expand site activation and enrollment at UC Davis and Harborview U. Washington
  4. Continue to provide education and support for study conduct at all sites

4. IMPACT:

- **What was the impact on the development of the principal discipline(s) of the project?** Nothing to report.

- **What was the impact on other disciplines?** Nothing to report.

- **What was the impact on technology transfer?** Nothing to report.

- **What was the impact on society beyond science and technology?** Nothing to report.

5. CHANGES/PROBLEMS:

- **Changes in approach and reasons for change**

A. Protocol Amendment 1 (dated 03/17/2020) included the following changes, and all of them were considered as minor revisions.

i. To confirm study product eligibility, an arterial blood gas will be obtained within 90 minutes prior to beginning the baseline stability period, instead of required prior to the study product infusion, during the last 30 minutes of the baseline stability period. Based on our experience from the first three enrolled patients, study product preparation is very time consuming (1-1.5 hours), and it is not feasible for us to get the cells ready for infusion after we obtain the arterial blood gas during the last 30 minutes of baseline stability period.

ii. We clarify that the collection of arterial blood gas collection at hours 6, 12, 18, 24, 30, and 36 hours will accept "+/- 1 hour" of time window; and the arterial blood gas of day 2, 3 and

7 could be anytime of the day. This clarification will optimize the study processing without affecting scientific rationale.

iii. In Clinical Protocol Section 9.4, we deleted the following sentence: "If the patient is on vasopressin, investigators will be instructed not to titrate the vasopressin dose during this 2-hour period." Vasopressin is commonly used in critically ill patients for blood support and is usually given at a dose that is not being frequently changed.

iv. In Clinical Protocol Section 9.4, we have revised the flowchart of screening, enrollment and study product administration process by fixing a typo. We deleted "Continue to monitor for stability within the eligibility window of 120 hours from ARDS onset" and replaced with "Continue to monitor vital signs, ventilator parameters and for adverse events".

v. We have made some changes in Biospecimens for Biological Endpoint Measurements, including:
   - Revise freezer temperature for storing biospecimens
   - Expand time window of biospecimen collection
   - Reduce volume of blood collection for future DNA/RNA extraction

   The rationale for the minor revisions for biospecimen collection is to optimize the process and reduce the un-necessary blood collection.

vi. We have revised the statistical modeling by adding two stratification variables in Protocol Section 11.2. This change was recommended by the DSMB during the study initiation review.

vii. We have updated the Appendix E: Study Product Preparation Protocol (UCSF site), which is the template for all other sites. This preparation protocol has been updated after conducting the mock test at UCSF, and has been expanded to provide more operational details for the purpose of optimizing the preparation process.

B. Protocol amendment 2 (dated 07/13/2020) included the following changes:

i. We have added University of California Davis Medical Center as a new participating site. This plan has been pre-approved by the Department of Defense. We have also obtained funding from the California Institute for Regeneration Medicine (CIRM) to support UC Davis site for this trial. We obtained the approvals from the sIRB at VUMC and DoD HRPO, W also reported this site to the FDA.

ii. We have revised the inclusion criteria. So instead of recruiting ARDS patients with PaO2/FiO2 < 200 mmHg, we have now increased the qualified PaO2/FiO2 to < 250 mmHg. By increasing the PaO2/FiO2, we want to increase the opportunity recruit more COVID-19 patients with ARDS into the trial. The Chair of our DSMB, Taylor Thompson, MD agrees with this change.

iii. We have added "Received tocilizumab within the last 7 days" as a new exclusion criteria. Because of potential unknown adverse events with blockade of IL-6, these patients will be excluded from this trial.

iv. Co-enrollment in randomized clinical trials of supportive therapies such as proning will be allowed after approval from the Scientific Review Committee (includes the Principal Investigator and two other study investigators) and the Chair of the DSMB. With respect to patients with SARS-CoV-2 infection, co-enrollment in randomized clinical trials of other interventions such as pharmacologic therapies and convalescent plasma will be considered on a trial by trial basis in concert with the Scientific Review Committee and the Chair of the DSMB. The use of treatments through Emergency Use Authorization (EUA) and Expanded Access Program (EAP) studies shall not be considered an exclusion. The

consideration of co-enrollment with other experimental therapy trials that target patients requiring ICU level of care must be evaluated by the Scientific Review Committee and request approval from the Chair of the DSMB. Patients who are enrolled in clinical trials targeting outpatients or patients admitted to the acute care floor with trial endpoints assessed before admission to the Intensive Care Unit will be eligible for participation. Co-enrollment into multiple trials are common in COVID-19 patients. This revision provides the necessary flexibility of patient recruitment without sacrificing the safeguard of patient safety and scientific rigor.

v. We have remove limitation of prone position for stable baseline criteria because prone position is often a standard care in patients with COVID-19.

vi. To reduce confusion, we have clarified the telephone interviews at 28 days and 60 days in patients who are discharged from the hospital prior to 60 days.

vii. We have clarified and emphasized the timepoints regarding the study procedures throughout the updated Clinical Protocol, in order to make sure there is transparency and consistence across all participating sites.

viii. We have deleted the following sentence: "If the patient does not have an arterial line, an arterial line will be placed for hemodynamic monitoring prior to administration of the hMSCs." We do not plan to insert an arterial line if the patient does not have one.

ix. We have added several data points related to COVID-19 to be collected, e.g., COVID-19 test and related therapies, co-enrollment with other experiment therapy trials or treatment, lab tests. These fields are critical for our trial which is related to COVID-19 patients.

x. We have updated the Study Product Infusion Protocol (Appendix H) to adapt the enrollment of COVID-19 patients.

- **Actual or anticipated problems or delays and actions or plans to resolve them**

During the past reporting year, the site activation and recruitment at University of Washington Harborview Medical Center and the Vanderbilt University Medical Center has delayed due to the following reasons: Both sites have been slow to have their cell therapy laboratories become competent for the SOP and measuring the MSC viability. Both of these issues have been resolved for Vanderbilt and are in the process of resolution for U. Washington Harborview for their cell therapy center.

- **Changes that had a significant impact on expenditures - None**

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

As mentioned above, instead of recruiting ARDS patients with PaO2/FiO2 < 200 mmHg, we have now increased the qualified PaO2/FiO2 to < 250 mmHg. By increasing the PaO2/FiO2, we want to increase the opportunity recruit more COVID-19 patients with ARDS into the trial. We have revised the Clinical Protocol to reflect this change. The updated protocol has been approved by the central IRB at Vanderbilt, the FDA under IND 15331, and by the DoD HRPO.

There is nothing to report for human subjects, vertebrate animals, biohazards, or select agents.

C. PRODUCTS:

- **Publications, conference papers, and presentations:** Nothing to report.

- **Website(s) or other Internet site(s):** www.stattrial.com
- **Technologies or techniques:** Nothing to report.
- **Inventions, patent applications, and/or licenses:** Nothing to report.
- **Other Products**: Nothing to report.

D. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:

- **What individuals have worked on the project?**

UCSF - UCSF Moffitt-Long Hospital and Zuckerberg San Francisco General Hospital & Trauma Center (San Francisco, CA):

Michael A. Matthay MD
Project Role: Principal Investigator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 4.80
Contribution to Project: Revised the FDA approved Clinical Protocol and Investigator Brochure for submission to the Vanderbilt cIRB; communicated with all of the sites (6 sites in addition to UCSF) by conference calls and by emails and phone calls; supervised the preparation of the case report form and submitted to our data management firm (Quesgen); working on the plans for a central IRB at Vanderbilt with Hanjing Zhuo and Kathleen Liu; worked with UCSF Research Management Services (Sara Yturralde) on the budget for UCSF and the other sites; communicated with FDA by email and by conference call (November 30, 2018 – Tal Salz, CBER); communicated with the Dave McKenna, MD at the University of Minnesota regarding details for production of the mesenchymal stromal cells for the trial; worked on selecting the DSMB for the trial.

Kathleen D. Liu, MD, PhD, MAS
Project Role: Co-Investigator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.56
Contribution to Project: Worked with Dr. Matthay to write and edit the Clinical Protocol; advised Dr. Matthay on the plans for a central IRB at Vanderbilt and spoke directly with the Head of that cIRB, Dr. Todd Rice; helped plan completion of Statement of Work Tasks and the case report form; helped to oversee Hanjing Zhuo, the project manager. Dr. Liu also worked Melanie McMillan and Lizette Caballero on finalizing the laboratory SOPs for preparing the MSC and placebo infusion products. She is available to oversee study product infusion in the Parnassus ICU.

Carolyn Calfee, MD MAS
Project Role: Co-Investigator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 1.05
Contribution to Project: Worked with Dr. Matthay on editing the clinical protocol, the screening form, and Case Report Form and overseeing delivery of study product to patients in the UCSF Parnassus ICU. She is also on the consent team.

Carolyn Hendrickson, MD, MAS
Project Role: Co-Investigator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.92
Contribution to Project: Worked with Dr. Matthay to prepare the Clinical Protocol and the case report form and the screening form and to initiate mock screening. She is the primary

site investigator at ZSFG and is Medical Director of the ZSFG Medical ICU.

Rachael Callcut, MD, MAS
Project Role: Co-Investigator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.30
Contribution to Project: Worked with Dr. Matthay to write and edit the Clinical Protocol and to edit the case report form for the cIRB and for mock screening. She is the Site Director at UC Davis.

Jeffrey Gotts, MD, PhD
Project Role: Co-Investigator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.00
Contribution to Project: Worked with Dr. Matthay to write and edit the Clinical Protocol and to edit the case report form for the cIRB.

Hanjing Zhuo, MD, MPH
Project Role: Project Manager
Research Identifier 0000-0003-3039-8155:
Nearest person month worked: 0.0
Contribution to Project: Worked with Dr. Matthay to write and edit the Clinical Protocol and the Investigator Brochure, and to edit the case report form and to set up the cIRB with Vanderbilt for this trial. She is the primary Project Manager for this STAT trial and works closely with Dr. Matthay.

Serena Ke, BS
Project Role: Coordinator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 3.14
Contribution to Project: Worked on preparing the case report form and screening form for the trial and also the laboratory and study manuals for the trial.

Brian Daniel
Project Role: Coordinator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.00
Contribution to Project: Worked on the clinical protocol and case report form development.

Kevin Delucchi, BS, PhD
Project Role: Statistician
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.72
Contribution to Project: Prepared the statistical plan for the clinical protocol with attention to the FDA-requested expansion of the statistical plan with more details.

Shibani Pati, MD, PhD
Project Role: Co-Investigator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 1.08
Contribution to Project: Working on standardizing laboratory assays for the MSCs for this trial including plans to test the viability and other features of the bone marrow derived MSCs from the University of Minnesota.

Jason Abbott, BS
Project Role: Laboratory Manager
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.00
Contribution to Project: Organizing specimen tubes and bar coding for this trial and working with Dr. Pati on the MSC laboratory assays

Xiaohui Fang
Project Role: Laboratory analysis of MSCs for viability and functional characteristics
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.00
Contribution to Project: Testing properties of MSCs with in vitro assays and potency assays

Stuart Gibb, PhD
Project Role: Research assistant
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.00
Contribution to Project: In the past he worked with Dr. Pati on standardizing laboratory assays for the MSCs for this trial but he has left UCSF for another position

Alpa Mahuvakar
Project Role: Research assistant
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 1.02
Contribution to Project: Worked with Dr. Pati on laboratory assays for the MSCs for this trial.

Erin E Ross
Project Role: Coordinator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 3.49
Contribution to Project: Prepare and test the screening forms and practicing obtaining consents with Dr. Matthay.

Margaret Luk
Project Role: Post award grant manager
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.40
Contribution to Project: Worked with Dr. Matthay for organizing the personnel contributions to this grant and preparing the quarterly report.

Jones, Chayse Marie
Project Role: Lab Assistant
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 1.91
Contribution to Project: Assisting with cell analyses.

Haoqian, Zhang
Project Role: Specialist 2
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 3.6

Contribution to Project: Worked to characterize all clinical doses from the MSC Trial.

Dennis Hua
Project Role: Post award grant manager
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.90
Contribution to Project: Worked with Dr. Matthay for organizing the personnel contributions to this grant and preparing the quarterly report.

University of Harborview Medical Center (Seattle, WA)
Bryce Robinson, MD
Project Role: Site Principal Investigator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.60
Contribution to Project: communicated with overall PI, Michael A. Matthay, MD and Clinical Coordinating Center at UCSF by conference calls and by emails and phone calls; supervised the reliance to a central IRB at Vanderbilt, and the preparation of site-specific regulatory documents for submission to the central IRB at Vanderbilt University, the FDA and the Sponsor, the Department of Defense.

Oregon Health & Science University (Portland, OR)
Martin Schreiber, MD
Project Role: Site Principal Investigator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.60
Contribution to Project: communicated with overall PI, Michael A. Matthay, MD and Clinical Coordinating Center at UCSF by conference calls and by emails and phone calls; supervised the reliance to a central IRB at Vanderbilt, and the preparation of site-specific regulatory documents for submission to the central IRB at Vanderbilt University, the FDA and the Sponsor, the Department of Defense.

University of Texas Health Sciences Center at Houston/Memorial Hermann (Houston, TX)
Laura Moore, MD
Project Role: Site Principal Investigator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.60
Contribution to Project: communicated with overall PI, Michael A. Matthay, MD and Clinical Coordinating Center at UCSF by conference calls and by emails and phone calls; supervised the reliance to a central IRB at Vanderbilt, and the preparation of site-specific regulatory documents for submission to the central IRB at Vanderbilt University, the FDA and the Sponsor, the Department of Defense.

Vanderbilt University Medical Center (Nashville, TN)
Lorraine Ware, MD
Project Role: Site Principal Investigator
Research Identifier: 0000-0003-3039-8155
Nearest person month worked: 0.60
Contribution to Project: communicated with overall PI, Michael A. Matthay, MD and Clinical Coordinating Center at UCSF by conference calls and by emails and phone calls;

supervised the reliance to a central IRB at Vanderbilt, and the preparation of site-specific regulatory documents for submission to the central IRB at Vanderbilt University, the FDA and the Sponsor, the Department of Defense.

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period? –** The PI is Dr. Matthay and his updated Other Support is included in this report.

- **What other organizations were involved as partners?** Nothing to report.

E. SPECIAL REPORTING REQUIREMENTS:

- **COLLABORATIVE AWARDS:** Not applicable.
- **QUAD CHARTS:** Not applicable.

F. **APPENDICES:**

1. DoD (STAT) trial DSMB recommendation (dated August 11, 2020)

2. Active other support of the PI: Michael A. Matthay, MD

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

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55 Fruit Street, Bulfinch 148
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Boyd Taylor Thompson M.D.
Medical Director, PETAL CCC
Director, Translational Research
Division of Pulmonary and Critical Care Medicine,
Massachusetts General Hospital
Professor of Medicine, Harvard Medical School

DoD (STAT) Trial DSMB Recommendations
August 11, 2020 3-4 PM EDT

DSMB:
B. Taylor Thompson, MD, DSMB Chair
Jason Sperry, MD, MPH
Michael Harhay, PhD

Dear Dr Matthay,

After review of the materials submitted to the Board and reviewed during the open session, including a review of recent protocol amendments along with a report of baseline characteristics, SAEs, and narratives of the 8 participant deaths, the Board recommends that the study continue as amended.

Respectfully Submitted,

B. Taylor Thompson MD
Chair, DoD (STAT) Trial DSMB

SUPPORT
MATTHAY, MICHAEL A.

Current

Title: *Prevention and Early Treatment of Acute Lung Injury*
Time Commitments: *0.45 Calendar*
Supporting Agency: *NIH/NHLBI, U01 HL123004*
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: *Gayle Jones*
Performance period: *6/17/2014-04/30/2021*
Level of funding: *Direct Cost*
Project Goals: *Overlap: No scientific or budgetary overlap with the proposed PRMRP proposal*
To test new treatments for acute lung injury in patients enrolled in the Emergency Department and in the Intensive Care Unit.
Specific Aims: *The specific aim is to test new therapeutic approaches to testing the preventative or early treatment value of novel treatments in patients admitted to the Emergency Department at risk for ARDS or new treatments for ARDS in patients in the intensive care unit in primarily phase 3 designs.*
Overlap: *No scientific or budgetary overlap with the proposed PRMRP proposal*

Title: Mesenchymal Stem Cells for Treatment of ARDS Following Trauma
Time Commitments: 4.60 Calendar
Supporting Agency: *Department of Defense W81XWH-17-1-0631*
Address:
US Army Medical Research Acquisition Activity
820 Chandler ST
Fort Detrick MD 21702-5014
Contracting/Grants Officer: *Kevin R. Moore*
Performance Period: *9/15/2017-9/14/2021*
Level of funding: *Direct Cost*
Project Goals: The overall objective of this proposal is to carry out a randomized, double-blind, placebo-controlled multicenter phase 2b trial to test the therapeutic potential of allogenic bone-marrow derived MSC for treating ARDS in trauma patients.
Specific Aims: ***Specific Aim 1.*** To test the clinical efficacy of intravenously delivered allogeneic human MSC in trauma patients with ARDS. ***Specific Aim 2***. To test the mechanisms by which MSC reduce acute lung injury in trauma patients with ARDS
Overlap: *None*

Title: Novel Paracrine Mechanism for Cell-Based Therapy of Injured Lungs
Time Commitments: 0.45 Calendar
Supporting Agency: *University of Texas Health Science Center at Tyler/NIH R01 HL134828*
Address:
University of Texas Health Science Center at Tyler
11937 U.S. Highway 271
Tyler, TX 75708-3154
Contracting/Grants Officer: *Dena Walton*
Performance Period: *9/1/2017-8/31/2021*
Level of funding: *Direct Cost*
Project Goals: The results of these experiments will provide novel insights into how mesenchymal stem (stromal) cells enhance the resolution of alveolar edema in human lungs harvested from brain dead donors, an important scientific and clinical question.
Overlap: *None*

Title: Piceantannol entrapped albumin nanoparticles (PANPs) to combat ALI/ARDS
Time Commitments: 0.12 Calendar
Supporting Agency: Nano Biotherapeutics / NIH
Address:
Cell Biologics, Inc
2201 W Campbell Park Dr
Chicago, IL 60612
Contracting/Grants Officer: Jeanne Chang
Performance Period: 09/15/2017-06/30/2021 (NCE)
Level of funding: Direct Cost
Project Goals: This project is being done at UCSF in order to carry out the goals of specific aim 3, which is to test the efficacy of picetannol, an anti-inflammatory compound that is prepared as part of entrapped albumin nanoparticles (PANPs), to treat acute lung injury that occurs in the acute respiratory distress syndrome.
Overlap: *None*

Title: Precision Medicine in the Acute Respiratory Distress Syndrome
Time Commitments: 0.12 Calendar
Supporting Agency: *NHLBI/R35HL140026 (Calfee)*
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: *Manda C Richards*
Performance Period: *1/16/18-12/31/2024*
Level of funding: *Direct Cost*
Project Goals: To identify molecular endotypes of ARDS with distinct clinical and biological profiles, including integration of environmental exposure data and identification of differential treatment responses; to develop practical models for endotype identification; and to test biological mechanisms in an experimental human lung model.
Role: Co-Investigator
Overlap: *None*

Title: Angiopoietin/Tie signaling regulation of vascular leakage in lung inflammation
Time Commitments: 0.15 Calendar
Supporting Agency: *NHLBI/R01 HL143896 (McDonald)*
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: *Tammi Simpson*
Performance Period: *7/1/2018-5/31/2022*
Level of funding: *Direct Cost*
Project Goals: To determine the contributions of angiopoietin-1(Ang1) and angiopoietin-2 (Ang2), and their receptors, Tie1 and Tie2 (Tek), to the regulation of vascular leak in lung injury and inflammation.
Role: Co-Investigator
Overlap: *None*
Title*: Integrated Health, Behavioral and Economic Research on Current and Emerging Tobacco Products*
Time Commitments: *0.12 Calendar*
Supporting Agency: NIH/NHLBI, U54HL147127 (Glantz)
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer*: Judy Sint*

Performance period: *9/1/2013-8/31/2023*
Level of funding: *Direct Cost (Project 1: Calfee)*
Project Goals: To provide a comprehensive assessment of the impact of varying e-cigarette characteristics on acute lung injury by combining data from cell culture, mouse models, and humans, including testing different device and e-liquid characteristics
Role: Co-Investigator
Overlap: None

Title: *Aerosol Delivery of Surfactant for ARDS*
Commitments: *0.12 Calendar*
Supporting Agency: KAER Biotherapeutics Corp/NIH
Address:
926 S. Andreasen Dr., Ste 105
Escondido, California 92029
Contracting/Grants Officer: *Donovan B. Yeates (CEO)*
Performance Period: *9/15/2018-6/30/2020*
Level of Funding: *Direct Cost*
Project Goals: Dr. Matthay will continue to work closely with Dr. Yeates to advise him on the practical aspects of the KAER surfactant delivery device with 1-2 annual visits to KAER therapeutics in San Diego.
Overlap: *None*

Title*: ARREST RESPIRATORY FAILURE DUE TO PNEUMONIA (ARREST PNEUMONIA)*
Time Commitments: *0.45 Calendar*
Supporting Agency: NIH/Stanford University UG3HL14722
Address:
Stanford University
3172 Porter Drive
Palo Alto CA 94304
Contracting/Grants Officer*: Sharon Collum*
Performance period: *9/1/19-3/31/2024*
Level of funding: *Direct Cost*
Project Goals: Dr. Michael Matthay will serve as an Executive Committee Member providing expertise in the design and conduct of multicenter clinical trials in patients at risk for lung injury.
Overlap: No scientific or budgetary overlap.

Title*: Mesenchymal Stromal Cells for ARDS (COVID Positive and COVID negative)*
Time Commitments: *0.24 Calendar*
Supporting Agency: CIRM
Address:
1999 Harrison Street, Suite 1650
Oakland, CA 94612
Contracting/Grants Officer*: Doug Kearney*
Performance period: *7/1/20-6/30/2022*
Level of funding: *Direct Cost*
Project Goals: Support the addition of the University fo California at Davis as a clinical site for enrolling 20 patients from 2020 to 2022 into an ongoing phase 2B trial of Mesenchymal Stromal Cells (MSCs) for the treatment the actue respiratory distress syndrome (ARDS), including both COVID-19 positive and COVID-19 negative patients.
Overlap: No scientific or budgetary overlap.

Title: University of California, San Francisco (UCSF) CIRM Alpha Stem Cell Clinic
Time Commitments: 2.52 calendar
Supporting Agency: CIRM
Address:

1999 Harrison Street, Suite 1650
Oakland, CA 94612
Contracting/Grants Officer: Michael Worden
Performance Period: 10/1/2019-11/30/2021
Level of funding:
Project Goals To address these gaps and expand clinical trial activity in cell therapies, the specific aims for an Alpha Stem Cell Clinic at UCSF at the above locations will be designed to accelerate the temple of pre-award planning, clinical trial activation, patient accrual and trial completion, expand access to these therapies by under-represented populations with disorders in the Alpha Stem Cell Network, and to establish a disease team approach that promotes participation in the CIRM Alpha Stem Cell Network trials
Overlap: *None*

Title*: Integrated Health, Behavioral and Economic Research on Current and Emerging Tobacco Products*
Time Commitments: *0.12 Calendar*
Supporting Agency: NIH/NHLBI, U54HL147127 (Glantz)
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer*: Judy Sint*
Performance period: *9/1/2013-8/31/2023*
Level of funding: *Direct Cost (Supplemental Funds)*
Project Goals: To provide a comprehensive assessment of the impact of varying e-cigarette characteristics on acute lung injury by combining data from cell culture, mouse models, and humans, including testing different device and e-liquid characteristics
Role: Co-Investigator
Overlap: None

Title*: Task Order: Identifying Treatable Targets in ARDS*
Time Commitments: *0.48 Calendar*
Supporting Agency: Genentech
Address:
One DNA Way, Mail Stop 245C
South San Francisco, CA 94080
Contracting/Grants Officer*: Dana Tolari*
Performance period: *12/1/2019-12/31/2022*
Level of funding: *Direct Cost*
Project Goals:
Role: Co-Investigator
Overlap: None

Pending

Title: Molecular profiling of ARDS edema fluid: a window to an injured lung.
Commitments: 0.12 Calendar
Supporting Agency: Stanford/NIH
Address:
Stanford University
3172 Porter Drive
Palo Alto CA 94304
Contracting/Grants Officer: Anitra Johnson
Performance period: 4/1/2020-3/31/2021
Level of funding: Direct Cost
Project Goals: We will deliver clinical data and biologic data on 20 patients with ARDS each year to be included in the studies and analyses that Dr. Rogers will do on mechanisms of acute lung injury in ARDS.

Overlap: No scientific or budgetary overlap. If all the pending applications are funded, the PI will adjust his efforts accordingly to stay in compliance.

Title: ENaC-α mediates lung fluid clearance and capillary barrier function in pneumonia
Commitments: 0.19 Calendar
Supporting Agency: Augusta University/ NIH
Address:
1120 15th Street
Augusta, GA 30912
Contracting/Grants Officer: Sandy Ferguson
Performance period: 7/1/2020-6/30/2020
Level of funding: Direct Cost
Project Goals: The experiments in the ex vivo perfused human lung preparation will provide valuable data for evaluating the efficacy of these agonists of sodium transport and barrier function in a clinically relevant model of bacterial pneumonia in the ex vivo perfused human lung.
Overlap: No scientific or budgetary overlap. If all the pending applications are funded, the PI will adjust his efforts accordingly to stay in compliance.

Title: Novel small-molecule therapies for CF
Commitments: 0.24 Calendar
Supporting Agency: NIH-NIDDK
Address:
9000 Rockville Pike
Bethesda, MD 20892
Contracting/Grants Officer:
Performance period: 6/1/2020-5/31/2021
Level of funding: Direct Cost
Project Goals: This is a proposal to continue our Cystic Fibrosis (CF) Research and Translation Core Center at the University of California, San Francisco and collaborating institutions. The focus of our Core Center remains the discovery and evaluation of novel small-molecule therapies for CF.
Role: Co-Investigator
Overlap: No scientific or budgetary overlap. If all the pending applications are funded, the PI will adjust his efforts accordingly to stay in compliance.

Title: Lung endothelial microRNA-1, a novel therapeutic target in ARDS
Commitments: 0.24 Calendar
Supporting Agency: Yale/NIH
Address:
New Haven
CT, 06520
Contracting/Grants Officer: Teresa Bohan
Performance period: 7/1/2022-6/30/2024
Level of funding: Direct Cost
Project Goals: The proposed studies in this NIH R01 application with Dr. Takyar will test a promising new therapeutic approach in our clinically relevant ex vivo perfused human lung preparation
Overlap: No scientific or budgetary overlap. If all the pending applications are funded, the PI will adjust his efforts accordingly to stay in compliance.

Title: Activation of plasmin(ogen)-S protein-host receptors cascade in COVID-19
Time Commitments: 0.24 calendar
Supporting Agency: UTHCT/NIH
Address:
9000 Rockville Pike

Bethesda, MD 20892
Contracting/Grants Officer:
Performance Period: 9/1/20-8/31/2021
Level of funding: Direct Cost
Project Goals: The results of these experiments will provide novel insights into mechanisms relevant for COVID-19 lung injury.
Overlap: *None*

Title: ENaC is an important target in SARS-Cov2-induced ARDS
Time Commitments: 0.24 calendar
Supporting Agency: NIH/Emory
Address:
9000 Rockville Pike
Bethesda, MD 20892
Contracting/Grants Officer:
Performance Period: 12/1/20-11/30/2025
Level of funding: Direct Cost
Project Goals: Provide human lung cells in primary culture as described and fixed tissue after SARS-Cov2 infection for microscopy.
Overlap: *None*

Title: ARREST RESPIRATORY FAILURE DUE TOPNEUMONIA (ARREST PNEUMONIA)
Time Commitments: 0.24 calendar
Supporting Agency: NIH/Stanford
Address:
9000 Rockville Pike
Bethesda, MD 20892
Contracting/Grants Officer:
Performance Period: 9/1/20-8/31/2024
Level of funding: Direct Cost
Project Goals: Dr. Joe Levitt at Stanford is leading a multicenter trial (ARREST) to test inhaled beta agonist / steroid versus placebo for actue respiratory failure NHLBI UH3
Overlap: *None*

Previous

Title: Study Chair for PETAL/ASTER
Commitments: 0.60 Calendar
Supporting Agency: MGH/NIH
Address:
55 Fruit St,
Boston MA 02114
Contracting/Grants Officer: Lynne A Benoit
Performance period: 6/1/2019-4/30/2020
Level of funding:
Project Goals: I will function as Chair for this clinical trial working on all aspects of protocol development, implementation and monitoring of the trial in conjuction with the Clinical Coordinating Center at Massachusetts General Hospital in Boston and the Lung Division at the NHLBI.**
Overlap: No scientific or budgetary overlap. If all the pending applications are funded, the PI will adjust his efforts accordingly to stay in compliance.

Title: *The GOLD STUDY: Goal of open lung ventilation in donors*
Time Commitments: *0.45 Calendar*
Supporting Agency: NIH/NHLBI, R01HL126176

Address:
NHLBI /VUMC
3319 West End Avenue, STE 100
Nashville TN 37203
***Contracting/Grants Officer**: Libby D. Salberg*
***Performance period:** 5/1/2016-5/31/2021*
Level of funding:
Project Goals: Dr. Matthay has laboratory will be responsible for processing the human lungs collected and studied in Aim 2 of this application. Dr. Matthay himself will also oversee the conduct of the trial as described in Aim 1 in conjunction with Dr. Ware at Vanderbilt.
***Overlap:** None*

Title: Mechanistic roles of Cytochrome P4501A enzymes in hyperoxic lung injury
***Time Commitments:** 0.45 Calendar*
***Supporting Agency:** NIH/NHLBI R01HL129794/ Baylor College of Medicine*
Address:
Baylor College of Medicine
One Baylor Plaza, BCM310
Houston, TX 77030-3411
***Contracting/Grants Officer:** Leanne B. Scott, Ph.D*
***Performance Period:** 04/01/2016-03/31/20*
Level of funding:
Project Goals: Mechanistic roles of cytochrome P4501A enzymes in hyperoxic lung injury
These analyses will specifically relate to the mouse studies with the metabolomics data and the planned proteomic studies.
***Specific Aims:** To study biomarkers as reliable indices of acute lung injury.*
***Overlap:** None*

Title: University of California, San Francisco (UCSF) CIRM Alpha Stem Cell Clinic
Time Commitments: 2.52 calendar
Supporting Agency: CIRM/CHORI
Address:
1999 Harrison Street, Suite 1650
Oakland, CA 94612
Contracting/Grants Officer: Michael Worden
Performance Period: 10/01/2017-09/30/2019
Level of funding:
Project Goals To address these gaps and expand clinical trial activity in cell therapies, the specific aims for an Alpha Stem Cell Clinic at UCSF at the above locations will be designed to accelerate the temple of pre-award planning, clinical trial activation, patient accrual and trial completion, expand access to these therapies by under-represented populations with disorders in the Alpha Stem Cell Network, and to establish a disease team approach that promotes participation in the CIRM Alpha Stem Cell Network trials
***Overlap:** None*

Title: Pulmonary Hypertension in ARDS study (To define the clinical and biological correlates of pulmonary hypertension and increased pulmonary dead space in patients with ARDS.)
***Time Commitments:** 1.2 calendar*
***Supporting Agency:** Bayer AG*
Address:
Bayer AG
Aprather Weg 18a
D-42113 Wuppertal
GDWRC/building WUP 431 2 223
***Contracting/Grants Officer:** Hubert Trübel*
***Performance Period:** 7/1/17-6/30/19*
Level of funding:

Project Goals: To determine the relationship of elevated pulmonary arterial pressures and elevated dead space to respiratory outcomes, 28 day mortality and biological markers of lung and systemic injury
Specific Aims: To determine incidence of pulmonary hypertension in ARDS patients and whether it identifies patients with a higher mortality along with measurement of pulmonary dead space and biologic markers of inflammation and lung injury.
Overlap: *None*

Title: Targeting Angiopoietin-2 in ARDS
Time Commitments: 0.21 calendar
Supporting Agency: *NHLBI/University of Pennsylvania (R01 HL137006)*
Address:
Office of Research Services
3451 Walnut St, 5th Floor Franklin Building
Philadelphia PA 19104-6205
Contracting/Grants Officer: *Amy Camilleri*
Performance Period: *2/1/18-2/28/18*
Level of funding:
Project Goals: The major goals are to test the role of angiopoietin-2 (ANG2) as a predictor of acute respiratory distress syndrome (ARDS) risk and evaluate early anti-ANG2 therapy to decrease lung leak in an ex vivo lung perfusion model of human disease.
Overlap: None

Title: *Quantification and Biomarkers of Short-Term Pulmonary Effects of Tobacco Smoke Exposure: Infection-Related Acute Lung Injury*
Time Commitments: *0.60 calendar*
Supporting Agency: *NIH/FDA*
NCI Contact Center
BG 9609 MSC 9760
9609 Medical Center Drive Bethesda, MD 20892-9760
Contracting/Grants Officer: *Rebecca Brightful*
Performance period: *09/01/2013-08/31/2018*
Level of funding:
Project Goals: *To quantify the association between cigarette smoke exposure and the development of acute lung injury in patients with severe infection and in mouse models of infection-related ALI, and to develop new biomarkers for tobacco-related acute lung injury*
Specific Aims: *The specific aims are to test the biological and clinical predictors of developing ARDS in patients at risk for developing ARDS who smoke cigarettes versus those who do not and identifying biomarkers that may be associated with the increased risk. One aim also tests the effects of cigarette smoke exposure in mice to determine if they are more susceptible to acute lung injury from endotoxin or bacterial lung infection.* ***Overlap:*** *No scientific or budgetary overlap with the proposed PRMRP proposal*

Title: *Resolution of Clinical Lung Injury*
Time Commitments: *0.12 calendar (NO COST EXTENSION)*
Supporting Agency: *NIH/NHLBI, R37 HL051856*
Address:
NIH/NHLBI Information center
P.O Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: *Charmaine Prasad*
Performance Period: *04/01/2011-03/31/2018*
Level of funding:
Project Goals: *To study the pathogenesis of acute lung injury and ARDS, with an emphasis on alveolar epithelial fluid clearance, through the use of clinical studies.*
Specific Aims: *The specific aims are to study the the pathogenetic and prognostic value of biomarkers in patients with ARDS, to test the effect of human edema fluid from ARDS patients in both an in vitro model of cultured human alveolar epithelial type 2 cells and new therapeutics for acute lung injury in an isolated perfused human lung*

preparation.
Overlap: *No scientific or budgetary overlap with the proposed PRMRP proposal*

Title: *Allogeneic Human Mesenchymal Stem Cells for the Treatment of Acute Lung Injury*
Time Commitments: *0.12 calendar (NO COST EXTENSTION)*
Supporting Agency: *NIH/NHLBI, U01 HL108713*
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: *Kimberly Stanton*
Performance period: *09/01/2011-06/30/2018*
Level of funding:
Project Goals: *To test the safety and efficacy of human mesenchymal stem cells for the treatment of severe acute lung injury.*
Specific Aims: *The specific aim is to test the therapeutic value of intravenous human bone marrow derived mesenchymal stem cells for the treatment of 60 patients with moderate to severe ARDS for safety and limited efficacy endpoints, using a 2:1 randomization with a double blind design. There is also an aim to study the biologic markers of injury that may be altered in the plasma and bronchoalveolar lavage in the placebo versus treated patients.*
Overlap: *No scientific or budgetary overlap with the proposed PRMRP proposal*

Title: Genetic risks for ALI in ARDSnet and the iSPAAR Consortium
Time Commitments: 0.6 calendar
Supporting Agency: NIH/NHLBI RC2 HL101779/University of Washington
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: Michael Blackwell (University of Washington)
Performance Period: 9/30/2009-8/31/2012
Level of Funding:
Project Goal: To identify genetic factors contributing to the pathogenesis of ARDS.
Specific Aims: **To study DNA and plasma for biological factors that predict outcomes in ARDS patients.**
Overlap: None

Title: Treatment of Pulmonary Edema in Organ Donors
Time Commitments: 0.6 calendar
Supporting Agency: NIH/NHLBI R01 HL088263/VUMC (subcontract)
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: Libby Salberg (VUMC)
Performance Period: 2/01/2008 -01/31/2013
Level of Funding:
Project Goal: To test aerosolized albuterol a beta agonist to improve lung function in brain dead subjects.
Specific Aims To carry out a randomized trial of inhaled albuterol versus placebo to increase lung utilization for lung transplantation.
Overlap: None

Title: Sedation Management in Pediatric Patients with Acute Respiratory Failure

Time Commitments: 0.6 calendar
Supporting Agency: NIH/NHLBI U01HL086622 /University of Pennsylvania (subcontract)
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: Sheila R. Atkins (University of Pennsylvania)
Performance Period: 4/1/2008-3/31/2013
Level of Funding:
Project Goal: To test a sedation strategy to improve clinical outcomes in children with acute respiratory failure who were being mechanically ventilated.
Specific Aims: To use a cluster design to test a protocolized sedation strategy to increase ventilator free days in pediatric patients with acute respiratory failure.
Overlap: None

Title: Lung Fluid Balance and Mesenchymal Stem Cells
Time Commitments: 2.4 calendar
Supporting Agency: NIH/NHLBI R01HL051854
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: Dianna Jessee (GMO)
Performance Period: 9/30/2008-6/30/2013
Level of Funding:
Project Goal: To study the mechanisms by which mesenchymal stem cells reduce lung injury in experimental models.
Specific Aims: To study the efficacy and mechanisms of mesenchymal stem cells in mouse models of acute lung injury.
Overlap : None

Title: Stromal stem cells of human placenta for the treatment of Acute Lung Injury
Time Commitments: 0.6 calendar
Supporting Agency: NIH/NHLBI R43HL108327/Plasalus LLC
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: Frans A Kuypers (Plasalus)
Performance Period: 8/1/12-5/31/2014
Level of Funding:
Project Goal: To test the efficacy of human placental mesenchymal stem cells for reducing lung injury in both in vitro and in vivo models of lung injury.
Specific Aims : To use human type 2 cells and the ex vivo perfused human lung preparation to test the efficacy of human placental stem cells for reducing lung injury from endotoxin.
Overlap: None

Title: Clinical Research Network for the Treatment of Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS)
Time Commitments: 0.6 cal
Supporting Agency: NIH/NHLBI HHSN268200536166C

Address: NHLBI, NIH
Rockledge II building, Rm 6016
6701 Rockledge Drive MSC 7902
Bethesda MD 20892-7902
Contracting/Grants Officer: Scott Bredow (NHLBI)
Performance Period: 12/1/2011-6/30/2014
Level of Funding:
Project Goal:To test in phase 3 trials new treatments for acute lung injury and ARDS.
Specific Aims: To enroll patients in randomized clinical trials in the NHBLI ARDS Network.
Overlap: None

Title: Metabolic Response to Acute Injury in Alveolar Epithelium and ARDS
Time Commitments: *0.12 calendar*
Supporting Agency: Stanford /American Thoracic Society, 60995841-117524
Address:
Stanford University Office of Sponsored Research 3160 Porter Drive, Suite 100
Palo Alto, CA 94304-8445
Contracting/Grants Officer: Teresa Tom
Performance Period: 11/30/14-11/29/15
Level of Funding:
Project Goal: *To study the metabolic factors released by human alveolar epithelial type 2 cells in culture and to supply pulmonary edema fluid for metabolomics studies.*
Specific Aims: *The specific aim is to determine the metabolic abnormalities that may have pathogenetic or prognostic significance in cultured human epithelial type 2 cells exposed to cytomix (pro-inflammatory stimulus) and to test the metabolic abnormalities in undiluted edema fluid from patients with hydrostatic versus acute lung injury (ARDS).*
Overlap: *No scientific or budgetary overlap with the proposed PRMRP proposal*

Title: Gene-modified mesenchymal stem (stromal) cells for Treatment of the Acute Respiratory Distress Syndrome **A125202**
Time Commitments: 0.6 calendar
Supporting Agency: NIH/NHLBI U54HL119893/UCLA
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: Mary Haskins (UCLA)
Performance Period: 3/1/15-2/29/2016
Level of Funding:
Project Goal: *Our primary objective will be to carry out proof of principle studies to determine which combination of genes for KGF, Ang-1, and TIMP3 transfected into MSCs will produce the most therapeutically effective conditioned media (CM) for treating ARDS using pre-clinical models of pneumonia and sepsis in mice and severe pneumonia and lung injury in our novel ex vivo perfused human lung.*
Specific Aims: *Specific aim is to determine to potential therapeutic efficacy of an enriched conditioned media from transfected MSCs for reducing in vitro lung endothelial and epithelial injury and then test the conditioned media in an endotoxin model of lung injury in mice.*
Overlap: *No scientific or budgetary overlap with the proposed PRMRP proposal*

Title: The inflammasome: A Novel Biomarker in ALI/ARDS
Time Commitments: .12 calendar
Supporting Agency: NIH/NHLBI R01 HL112747/Brigham & Women's Hospital
Address: NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105

Contracting/Grants Officer: Stephanie Redfield (Brigham & Women's Hospital)
Performance Period: 5/15/2012-4/30/2016
Level of Funding:
Project Goal: *To determine the predictive value of biomarkers of the inflammasome in acute lung injury.* ***Specific Aims:*** *To test the predictive value of plasma levels of biomarkers of the inflammasome on developing ARDS in at risk patients plus to determine the modifying effect if any on these biomarkers of treatment with statins.*
Overlap: None

Title: *Recipient Epidemiology and Donor Evaluation Study-III *REDS-III) –Domestic Sites*
Time Commitments: *1.8 calendar*
Supporting Agency: *NIH/NHLBI, HHSN2681100051*
Address:
NIH/NHLBI Information center
P.O Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: *Michael Spears*
Performance period: *03/15/2011-08/31/2016*
Level of funding:
Project Goals: *To assure safe and effective blood banking and transfusion medicine practices through a comprehensive, multi-targeted strategy involving basic, translational, and clinical research to improve the benefits of transfusion while reducing its risks.*
Specific Aims: *The specific aim is to test clinical criteria for determining if patients who have blood product transfusions who develop pulmonary edema have TACO or TRALI or ARDS from a usual risk factor (not blood products) by reviewing specific patient cases from three hospitals with a consensus panel.*
Overlap: *No scientific or budgetary overlap with the proposed PRMRP proposal*

Title: *Gene-modified mesenchymal stem (stromal) cells for Treatment of the Acute Respiratory Distress Syndrome*
Time Commitments: *0.3 calendar*
Supporting Agency: *UC/CAI grant, 20130924SFM*
Address:
11000 Kinross Avenue, Suite 211 Los Angeles, CA 90051
Contracting/Grants Officer: *Susan Waelder*
Performance period: *03/01/2015-02/28/2017*
Level of funding:
Project Goals: *Our primary objective will be to carry out proof of principle studies to determine which combination of genes for KGF, Ang-1, and TIMP3 transfected into MSCs will produce the most therapeutically effective conditioned media (CM) for treating ARDS using pre-clinical models of pneumonia and sepsis in mice and severe pneumonia and lung injury in our novel ex vivo perfused human lung.*
Specific Aims: *Specific aim is to determine to potential therapeutic efficacy of an enriched conditioned media from transfected MSCs for reducing in vitro lung endothelial and epithelial injury and then test the conditioned media in an endotoxin model of lung injury in mice.*
Overlap: *No scientific or budgetary overlap with the proposed PRMRP proposal*

Title: *TIMP-3 For Viral Induced Acute Lung Injury*
Time Commitments: *0.8 calendar*
Supporting Agency: *Amgen, 2013583306*
Address:
Extramural Research Alliances (ERA)
Amgen, Inc.
One Amgen Center Drive Thousand Oaks, CA 91320
Contracting/Grants Officer: *Scott Simonet*
Performance period: *12/03/2013-06/02/2017*
Level of funding*:*
Project Goals: *To test a new therapy with TIMP-3 for influenza pneumonia and lung injury.*
Specific Aims: *To evaluate the potential therapeutic value of inhibiting TIMP-3 to reduce acute lung injury from PR8 H1N1 influenza in mice.*
Overlap: *No scientific or budgetary overlap with the proposed PRMRP proposal*

Title: *Identification of Patients at High Risk for the Development of ALI with Clinical and Biological Predictors*
Time Commitments: *Effort as needed*
Supporting Agency: *U Penn Subcontract/Glaxo Smith Kline, Galaxy ALI (subcontract)*
Address:
Glaxo Smith Kline
709 Swedeland Road
King of Prussia, PA 19406
Contracting/Grants Officer*: Susan Russell*
Performance period: *06/26/2012-07/31/2017*
Level of funding:
Project Goals: *To identify clinical and biological predictors of ALI in a cohort of patients with sepsis*
Specific Aims: *The aim is to determine the biological predictors of ARDS in the plasma of sepsis patients in the Emergency department at risk for developing ARDS.*
Overlap: *No scientific or budgetary overlap with the proposed PRMRP proposal*

Title: *Cigarette Smoke Exposure and Acute Lung Injury After Severe Blunt Trauma*
Time Commitments: *0.30 calendar*
Supporting Agency*: NIH/NHLBI, R01 HL110969*
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: *Charmaine Prasad*
Performance period: *12/15/2011-11/30/2017*
Level of funding:

Project Goals: *To determine the biologic effects of cigarette smoke exposure that increase susceptibility to acute lung injury after severe trauma.*
Specific Aims: *The specific aim is to determine the effect of cigarette smoke on increasing the risk of ARDS in major trauma patients, including accounting for passive versus active cigarette smoke exposure and alcohol use. There is also one aim designed to test the relationship of the microbiome in the airways at baseline and on days 2-4 sampled by bronchoalveolar lavage to cigarette smoke exposure and to the development of ARDS in major trauma patients.*
Overlap: *No scientific or budgetary overlap with the proposed PRMRP proposal*

Title: Molecular Endotypes of ARDS: Identification, Biology, and Differential Response to Therapy
Time Commitments: *0.6 calendar*
Supporting Agency: *NIH/NHLBI R01 HL131621*
Address:
NHLBI Health Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
Contracting/Grants Officer: *Sunshine Wilson*
Performance Period: *3/15/2016-1/15/18*
Level of funding:
Project Goals: *To identify endotype-specific treatment responses and differences in endotype biology within ARDS*
Specific Aims: *To test biologic and clinical variables in ARDS patients to identify clinically meaningful phenotypes that would be more specific for therapeutic targets.*
Overlap: None