Pre-Clinical Evaluation of Red Blood Cells for Transfusion Workshop

Supporting a Strategic Research Agenda in Transfusion Medicine at NHLBI

RBC Products

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October 6-7, 2016
Establishing a Strategic Research Agenda
Division of Blood Diseases and Resources, NHLBI

NIH-wide Strategic Plan
NHLBI Strategic Vision Plan Goals
- Workshops
- Working Groups
- Symposia
- State of the Science
- Literature
- Scientific Conferences

Critical Needs

Portfolio Review
- Know what research and resources are currently supported

Strategic Priority Setting
- Continuously monitor and identify scientific priorities
- Identify and rectify gaps in research support

Encourage research training

Monitor progress using established metrics
Examples of NHLBI-initiated programs supporting RBC transfusion research

2006 through 2009

- RFA-HL-06-108: Continuation of TMH CTN (U01), Jun 2006
- RFA-HL-07-001: Pediatric Transfusion Medicine Academic Career Awards (K07), July 2006
- PA-07-385: Transfusion-Related Acute Lung Injury (TRALI) Basic Research (R01), Jul 2007
- PHS-2008-1 Topic 038: Omnibus SBIR Contract Solicitation - Production of Generic Modified Hemoglobin, Jul 2007
- RFA-HL-08-005: RBC Storage Lesion (R01), Mar. 2008
- PAR-10-033/034: Selected Topics in Transfusion Medicine (R21/R01), Nov. 2009

R01/R21 applications first received in Feb 2010

SBIR/STTR
Examples of NHLBI-initiated programs supporting RBC transfusion research

2010 through 2015

RFA-HL-12-004: Maximizing NHLBI Biologic Specimen Repository (R21) Feb. 2011


PAR-13-025/026: Selected Topics in Transfusion Medicine (R21/R01), Nov. 2012

RFA-HL-14-023: Clinical Research in the Prevention, Diagnosis, and Treatment of HIV-Related HLB Diseases in Adults and Children (R01), Oct. 2013

RFA-HL-14-024/029: Basic Research in the Pathogenesis of HIV-Related HLB Diseases in Adults and Children (R01/R21), Oct. 2013


RFA-HL-15-022: Stem Cell-Derived Blood Products for Therapeutic Use (R01), Nov. 2014


Date RFA/RFP/PAR released (Funding starts 1-2 year later)
Identification of scientific priorities
What’s in the [RBC] bag?
- Identify and quantify the components of RBC products to improve the quality, reproducibility, and robustness of these products

What are the relevant [RBC] transfusion triggers?
- Specific question: Are there specific conditions where a liberal RBC transfusion strategy results in lower rates of 30-day mortality as compared to a restrictive transfusion strategy?
- Specific question: What are the optimal RBC transfusion thresholds for adult and pediatric cancer patients undergoing chemotherapy that may improve functional status and quality of life?

How do we know if [a RBC transfusion] works?
- Establish appropriate, physiologically-relevant markers to determine transfusion effectiveness
- Specific question: In patients with critical illness, what is the best means to identify the degree to which anemia contributes to insufficient oxygen (O₂) delivery and the likelihood that O₂ delivery will be improved by RBC transfusion?

How can we make better [RBC] products?
- Specific question: Can the potency and/or safety of transfusable RBCs be improved?
- Specific question: What determines which individuals will develop RBC alloimmune responses resulting in clinically meaningful sequelae?
The NHLBI Strategic Vision
Released August 11, 2016

Accelerating our journey towards scientific and health advances in the next decade

Next Generation Scientists

Patients & Patients’ Families

Researchers, Investigators & Clinicians

Working together to define NHLBI’s research priorities for the next decade

UNDERSTAND HUMAN BIOLOGY
REDUCE HUMAN DISEASE
ADVANCE TRANSLATIONAL RESEARCH
DEVELOP WORKFORCE AND RESOURCES

https://www.nhlbi.nih.gov/about/documents стратегический взгляд

NIH National Heart, Lung, and Blood Institute
Examples of the NHLBI Strategic Vision Research Priorities Relevant to RBC transfusions

- What are the optimal red blood cell transfusion thresholds and optimal plasma transfusion strategies in both pediatric and adult patients?
  - Myocardial Ischemia in Transfusion (MINT) – Clinical Center PI, Jeff Carson (Rutgers Robert Wood Johnson Medical School) and Data Coordinating Center PI, Maria Brooks (University of Pittsburgh).

- How can we “reprogram” the immune system to improve outcomes of allogeneic cell therapies, tissue and organ transplants, and regenerative strategies, and to diminish allogeneic responses to essential biologic replacement therapies?

- Development of safe, well-functioning designer platelets and red blood cells from stem or progenitor cells, as well as the large-scale production of these products, are needed for therapeutic and diagnostic uses.

- What technical improvements in the collection, preparation, storage, and processing of blood products would improve their potency, safety, and lifetime? What biomarkers or other characteristics predict stability during storage and successful transfusion?
Harness advances in “Omics” technologies and system biology approaches to:

- Further our understanding of RBC biology
- Inform efforts to develop transfusion products from stem cells or their progenitors
- Better understand the effect of processing, storage conditions and donor variability
- Evaluate correlations between “what’s in the bag” and 24h in vivo recovery evaluations and other measures of RBC effectiveness
- Evaluate novel additive solutions or storage strategies
Encourage investigator-initiated research

- Two NHLBI Program Announcements with review (PARs) are currently available to investigators interested in submitting R01 or R21 applications, respectively, that address research topics in blood banking and transfusion medicine.
- Does not support clinical trials in phase II or above (see other FOAs).
- Review Panel with appropriate expertise led by CSR.
- Funding per NHLBI funding payline:

These FOAs will use the Cycle I and Cycle III standard receipt dates only.

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Recently Released FOAs to Support Clinical Trials Phase II and above at NHLBI

- **Multisite Clinical Trials phase II and above FOAs**

- **Single site Clinical Trials phase II and above FOA**

  - Applications should provide the information that will allow for both science AND operational feasibility to be evaluated by peer review

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NHLBI Supported Career Awards (K Series)

- Mentored research training programs for junior investigators:
  - Mentored Research Scientist Development Award
    - Parent (K01) – limited to applications in epidemiological, biostatistical, outcomes or implementation research
    - Promoting Faculty Diversity (K01)
  - Mentored Clinical Scientist Development Award (K08)
  - Mentored Patient-Oriented Research Career Development Award (K23)
  - Mentored Quantitative Research Career Development Award (K25)
  - Pathway to Independence Award (K99/R00)

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Small Business Innovation Research (SBIR) **PA-16-302** R43/R44
Small Business Technology Transfer (STTR) **PA-16-303** R41/R42

**PHASE I – R41, R43**
- Feasibility Study
- $150K* and 6-month (SBIR)
- *or* 12-month (STTR) Award

**PHASE II – R42, R44**
- Full Research/R&D
- $1 M* and 2-year Award (SBIR & STTR)

**Competing Renewals**
NHLBI SBIR Phase IIB Bridge Awards (**HL-16-009**)
Small Market Awards: SBIR Phase IIB (**HL-17-012**)

**PHASE III**
- Commercialization Stage
- Use of non-SBIR/STTR Funds

*These dollar amounts are provided as a guideline and will vary as a function of the research being proposed.*
*Contact Phyllis Mitchell for questions (301-435-0065)*
NHLBI Small Business Targeted Funding Opportunities

- Human Cellular Models for Predicting Individual Responses to CFTR-Directed Therapeutics (SBIR HL-15-027)
- Stem Cell-Derived Blood Products for Therapeutic Use: Technology Improvement (SBIR Phase II HL-15-030)
Contact us
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