Blood Preservation is Force Preservation

HTS Identifies Small Molecules That Sustain ATP in Whole Blood During Storage

MAJ Lisa-Maria Oberhuber-Kurth, MD

lisa-maria.v.oberhuber-kurth.fm@health.mil

August 4th, 2026

DHA
Defense Health Agency
RESEARCH & DEVELOPMENT ®

Disclaimer

The views, opinions and/or findings contained in this presentation are those of the author and do not necessarily reflect the views of the Department of War and should not be construed as an official DoW / Army position, policy or decision unless so designated by other documentation. No official endorsement should be made. Reference herein to any specific commercial products, process, or service by trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the U.S. Government.

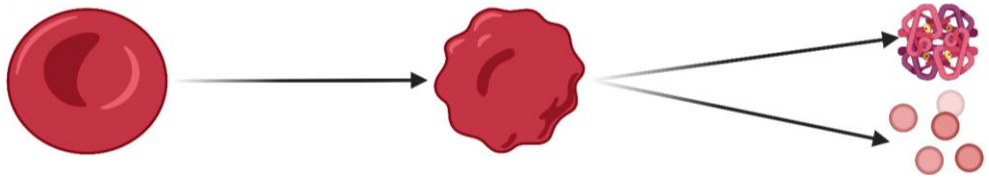
Disclosure Statement

The authors and contributors have no relevant financial relationships or conflicts of interest to disclose.

Agenda

- Problem Statement
- Study Design and Structure
- Results
- Next Steps & Outlook

The Problem: RBC Storage Lesion



Hours (0–24h)

Platelet activation ↑
α-granule release ↑
pH ↓
lactate ↑
Initial ATP ↓

Days 1–7

Plateletsdysfunction ↑
2,3-DPG ↓ → ↓ O_2 offloading
Factor V + VIII ↓
Echinocyte formation
Potassium leaks ↑

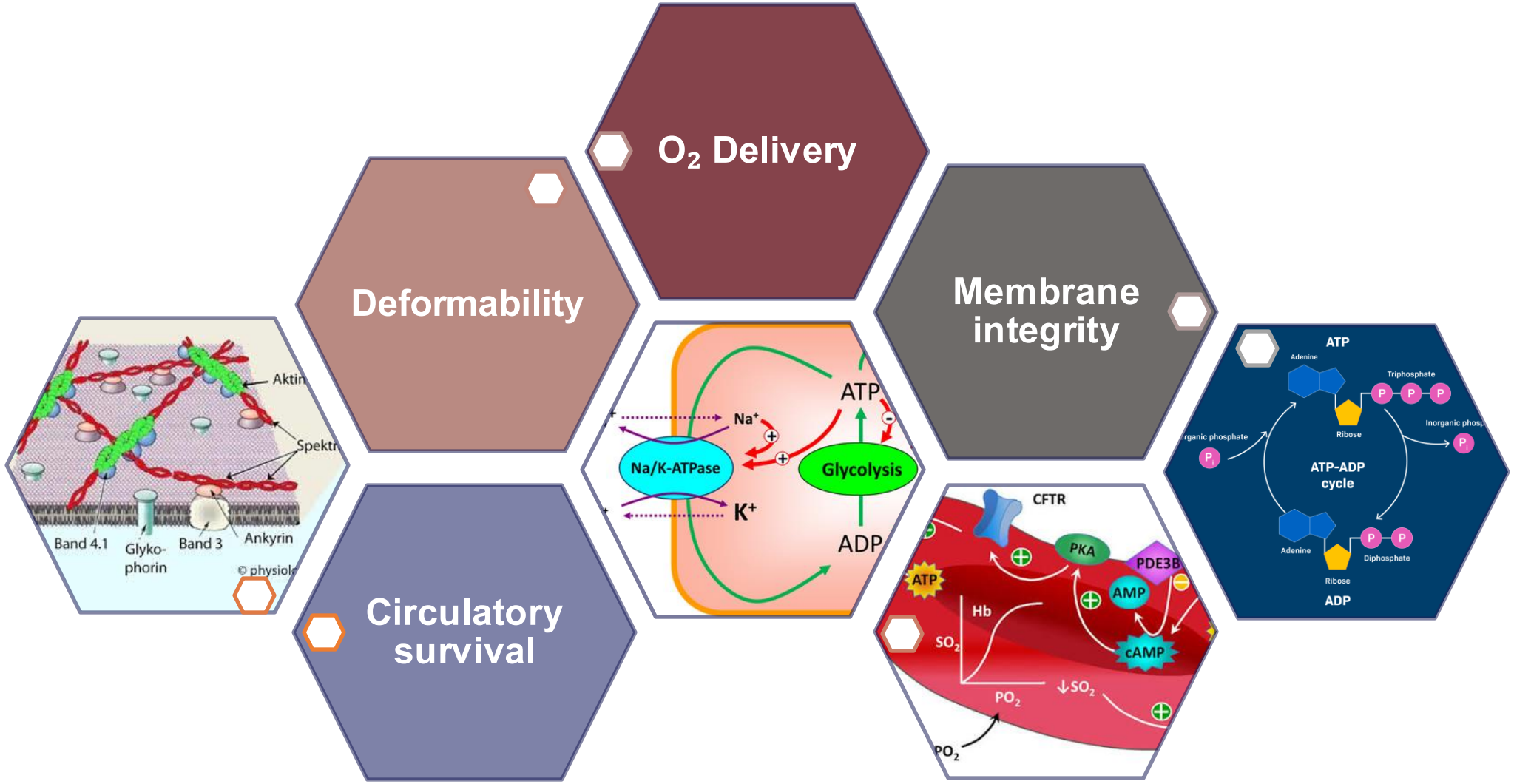
Days 7–14

2,3-DPG nearly depleted
RBC deformability ↓
Hemolysis ↑
free Hb ↑
→ NO scavenging ↑
Cytokine/ DAMP accumulation↑
Factor activity ↓

Days 14–21

Hemolysis ↑↑
Membrane vesiculation ↑
Potassium load ↑↑
PS exposure ↑
Bioactive lipids ↑
→ TRALI risk ↑

The Problem: Why Does ATP Matter?



Tactical Problem & Strategic Relevance

Long logistical chains

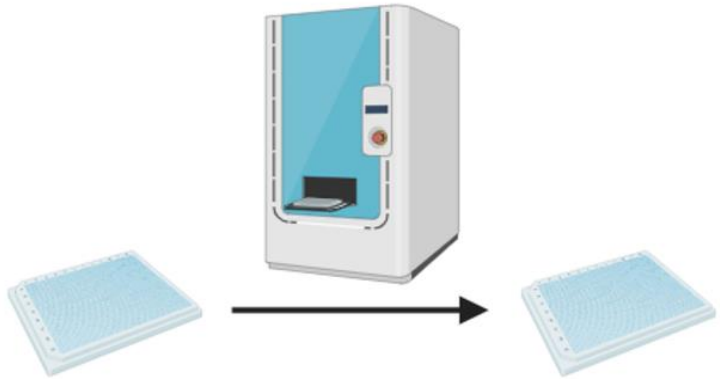
Extended shelf life = strategic flexibility

Future conflicts demand prolonged field care

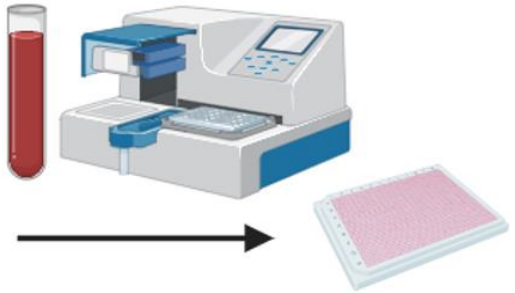
Hemorrhagic shock leaves no margin for poor blood quality

Screening Design

Add compound

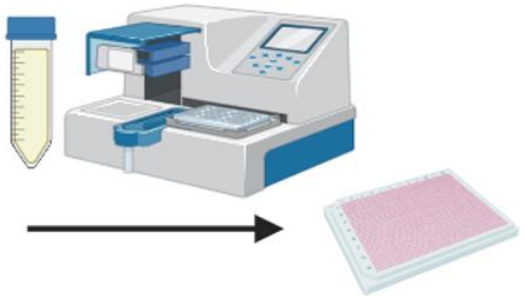


Add diluted whole blood

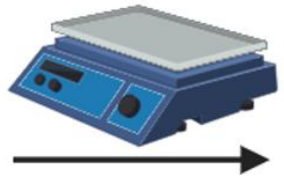


Store in fridge

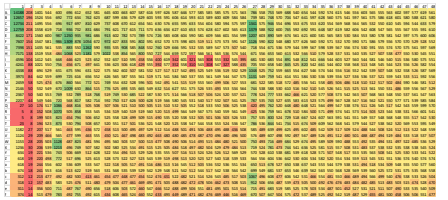
Add ATP Standard



Add CellTiter-Glo

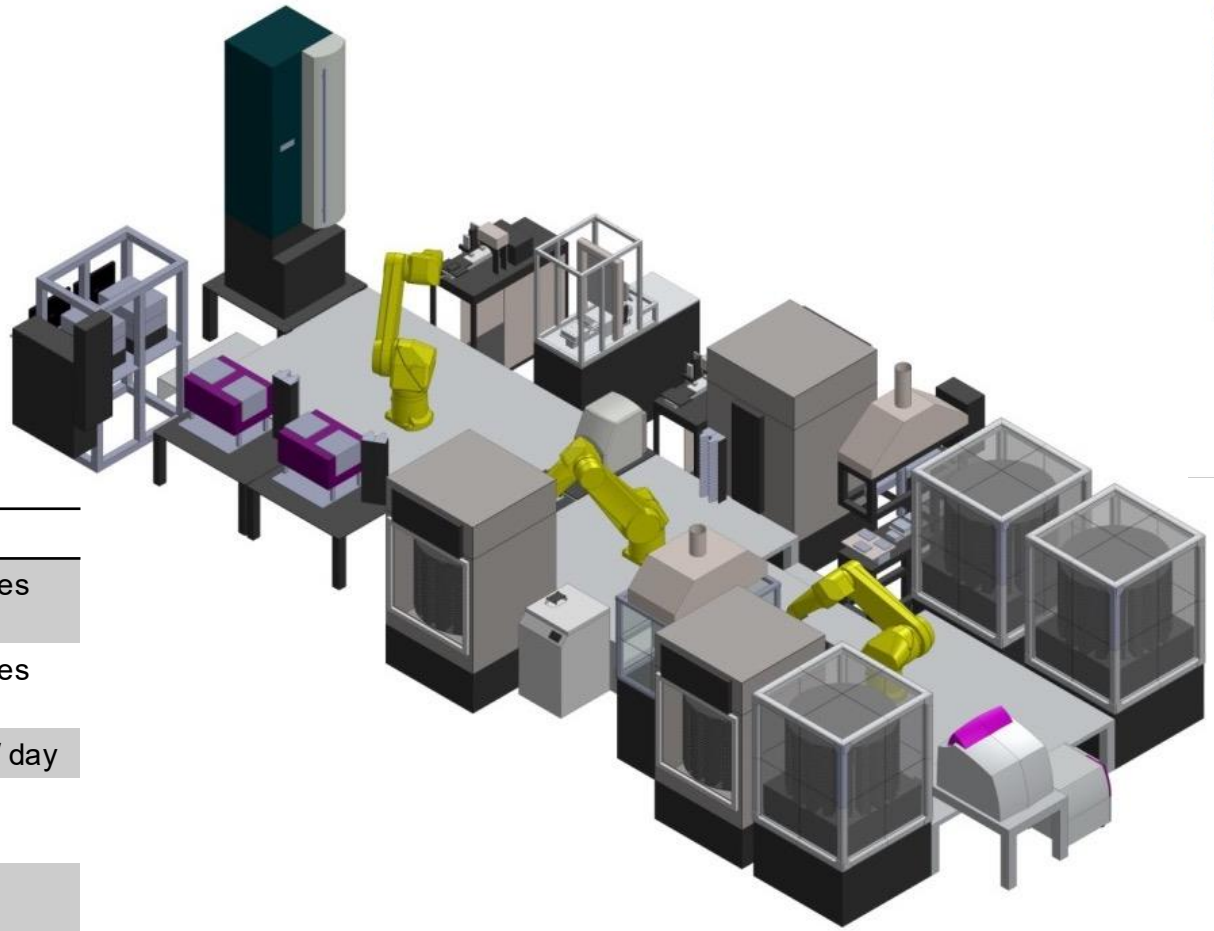


Shake

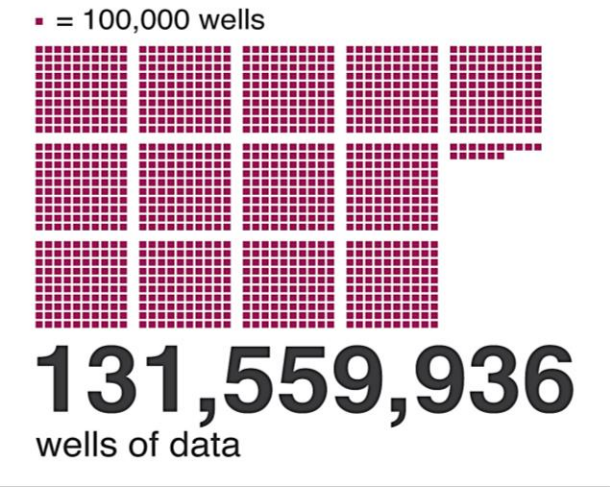


Read luminescence

NCATS high-throughput screening (HTS)



Parameter	Value
Assay Plate Storage	1,134 plates
Compound Plate Storage	2,079 plates
Throughput	~480 plates/ day
Low Volume Dispensers	3
Compound Transfer Devices	3
Plate Readers	6



Library Selection

NPC

FDA-Approved Drugs

n=2,678

Screened at 5 doses
(33.3 nM – 20.8 µM)
Donor 1

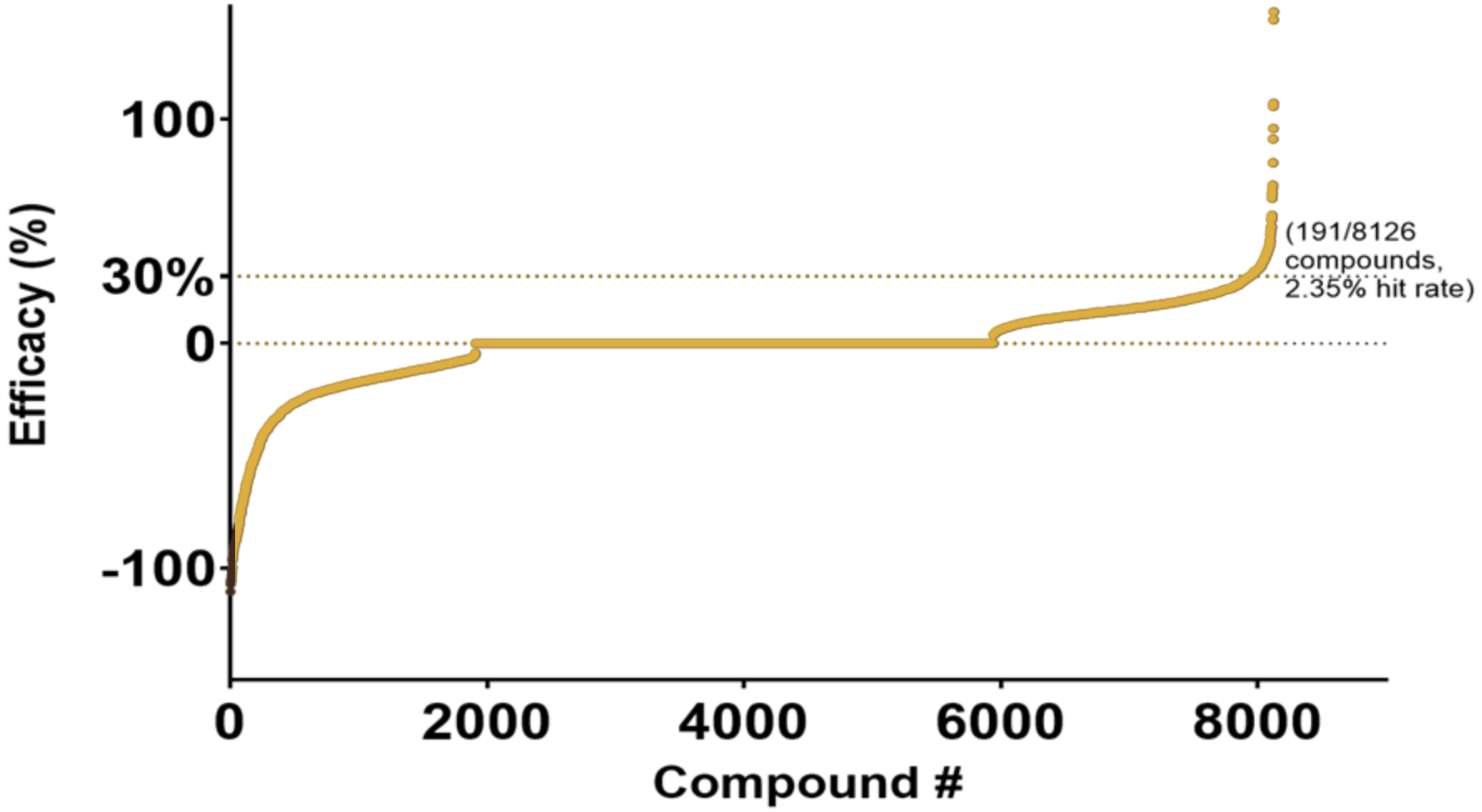
NPACT

Known Bioactive Compounds

n=5,035

Screened at 4 doses
(0.25 – 20.8 µM)
Donor 2

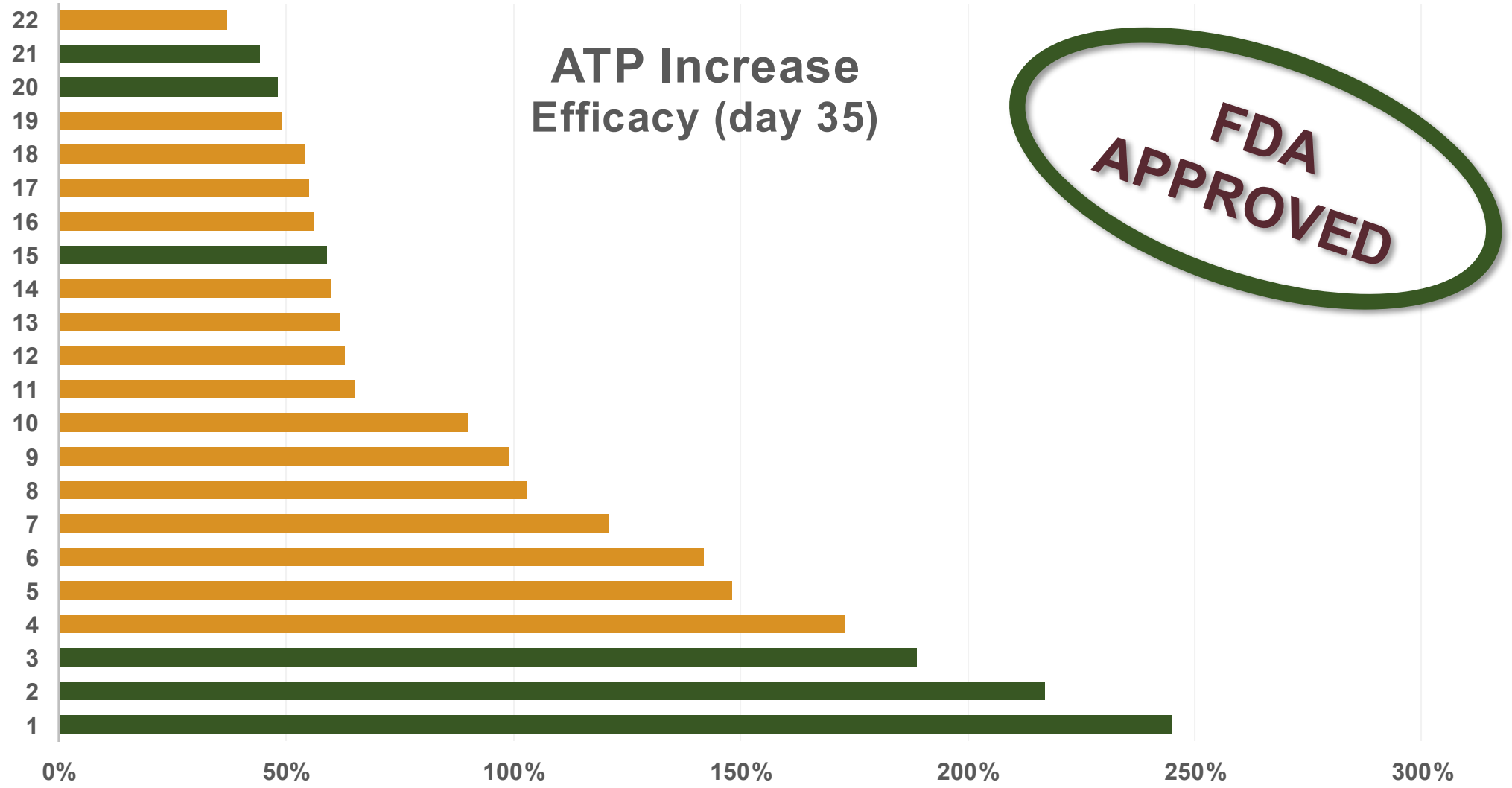
Efficacy across NPACT and NPC Libraries



NPC: Donor 1, screened at 5 doses, 1:5 dilution ranging from 20.8 µM to 33.3nM

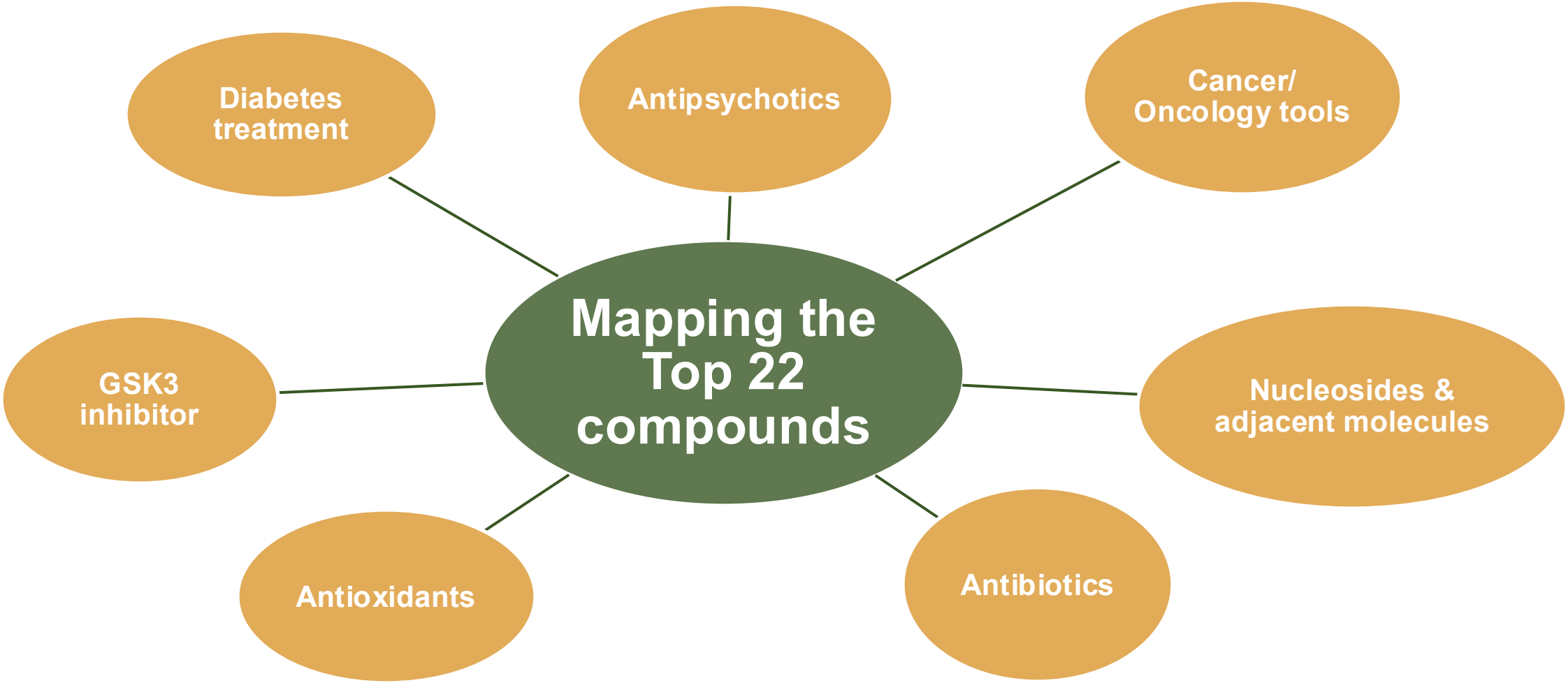
NPACT: Donor 2, screened at 4 doses, 1:5 dilution ranging from ~20.8 µM to 0.25 µM

Results: Hits

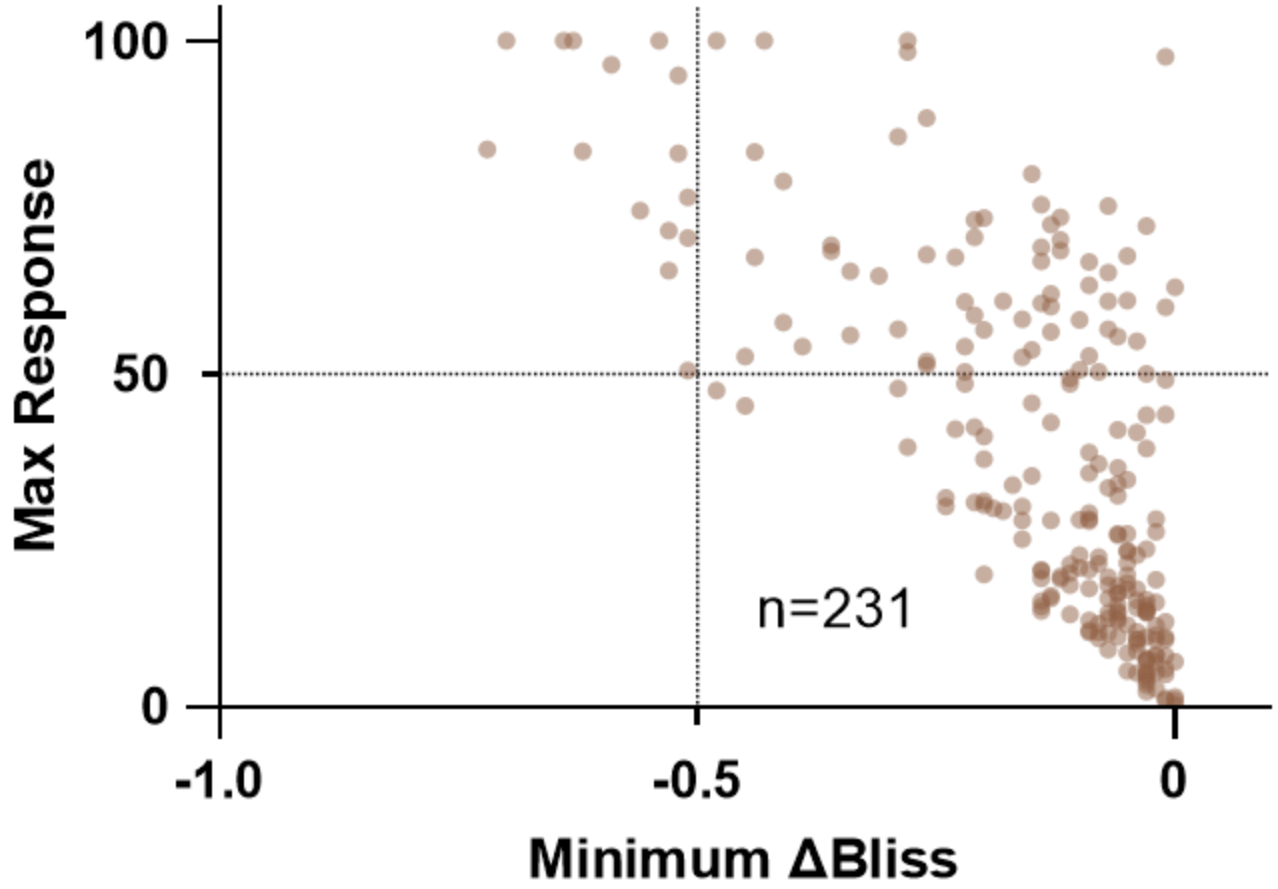


FDA APPROVED

Actual use of the substances



Results: Hits & Synergies



Matrix Screening Results:

15 Synergistic Combinations

Next Steps & Outlook

Immediate: In Vitro Validation

- Confirm top hits in expanded donor cohort (n=10)
- Dose-response optimization (IC50) for top 3 compounds
- Extended storage validation up to 56 days (CBC, hemostasis, metabolism)

Medium Term: In Vivo Studies

- **RBC labeling optimization for post-transfusion recovery (PTR24)**
- <u>Rabbit model:</u> 24h in vivo survival of modified vs. control RBCs

Long Term: Clinical Translation

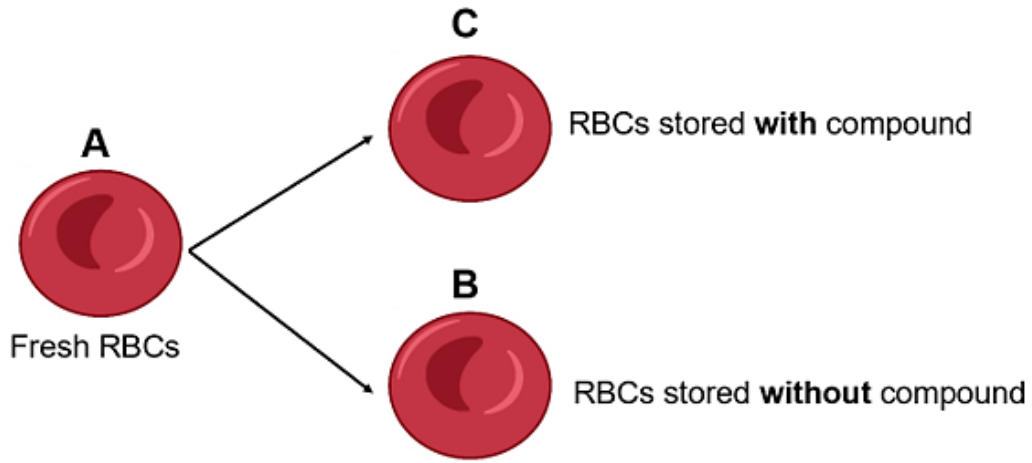
- Leverage FDA-approved compound status for accelerated regulatory pathway

Next Steps & Outlook

Medium Term: In Vivo Studies

RBC labeling optimization for post-transfusion recovery (PTR24)

Rabbit model: 24h in vivo survival of modified vs. control RBCs



Acknowledgements

NCATS
COLLABORATE. INNOVATE. ACCELERATE.

Mark Henderson, PhD
Biology Group Lead

Kat Landler, BS
Post-Baccalaureate Fellow

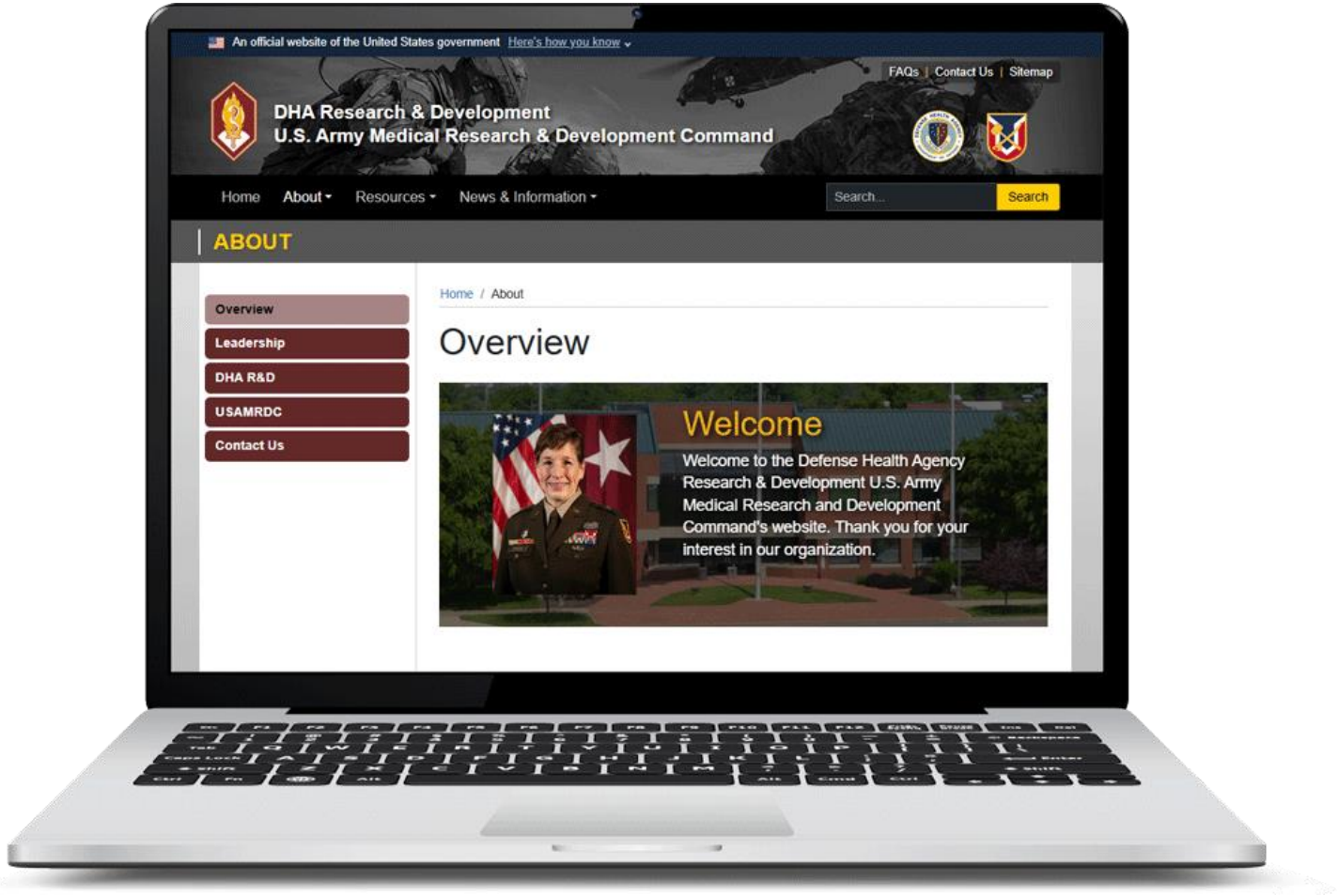
Evan Ross, MD
Adam Meledeo, PhD
Kristin Cardenas, PhD

Questions

Stay Connected and Informed

To learn more visit us at:

https://mrdc.health.mil/



Sources

- Högman, C. F., de Verdier, C.-H., Ericson, Å., Hedlund, K., & Sandhagen, B. (1987). Studies on the Mechanism of Human Red Cell Loss of Viability during Storage at +4°C in vitro. *Vox Sanguinis*, *48*(5), 257–268. https://doi.org/10.1111/J.1423-0410.1985.TB00181.X
- B. S. Karon, C. M. van Buskirk, E. A. Jaben, J. D. Hoyer, and D. D. Thomas, "Temporal sequence of major biochemical events during blood bank storage of packed red blood cells.," *Blood Transfusion*, vol. 10, no. 4, pp. 453–461, Mar. 2012, doi: 10.2450/2012.0099-11.
- J. Hess and A. D'Alessandro, "Red blood cell metabolism and preservation," July 2022, doi: 10.1002/9781119719809.ch14.
- T. Yoshida, M. Prudent, and A. D'Alessandro, "Red blood cell storage lesion: causes and potential clinical consequences.," *Vox Sanguinis*, vol. 17, no. 1, pp. 27–52, Jan. 2019, doi: 10.2450/2019.0217-18.
- A. D'Alessandro *et al.*, "Metabolomics of AS-5 RBC supernatants following routine storage.," *Vox Sanguinis*, vol. 108, no. 2, pp. 131–140, Feb. 2015, doi: 10.1111/VOX.12193.
- Marin *et al.*, "Metabolic rejuvenation upgrades circulatory functions of red blood cells stored under blood bank conditions.," *Transfusion*, 2021, doi: 10.1111/trf.16245.
- Ortiz, J. C., Griffin, I., Kazakova, S. V., et al. (2024). *Transfusion-related errors and blood product wastage reported to NHSN Hemovigilance Module, 2014–2022.* Transfusion. DOI: 10.1111/trf.17775
- Eastridge BJ et al. *Death on the battlefield (2001–2011): implications for the future of combat casualty care.* J Trauma Acute Care Surg. 2012;73(6 Suppl 5):S431–7.
- *US Army blood program: 2025 and beyond.* Transfusion. DOI: 10.1111/TRF.13338
- *Airborne! UAV delivery of blood products and medical logistics for combat zones.* (2023). Transfusion. DOI: 10.1111/trf.17329