Biostasis

PRESENTED BY:

Dr. Tristan McClure-Begley

Program Manager, DARPA

MODERATED BY:

Steve Redifer

2020-12-18

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https://www.hdiac.org

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Tristan McClure-Begley, Ph.D.
Program Manager
Biological Technologies Office
Defense Advanced Research Projects Agency

The problem we wish to solve

DoD Problem: On the battlefield, time is never on our side

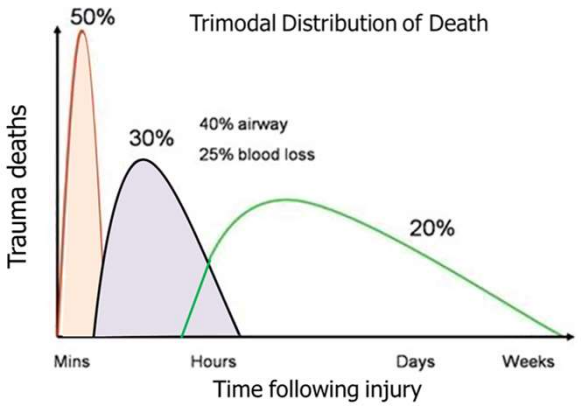
Distributed operations with minimal health infrastructure

Why do we (DoD) care?

Current strategies to treat individual warfighters suffering from trauma or acute infection are slow, reactive, and inadequate

Battlefield Trauma: Delays result in death

25% of combat deaths in Iraq and Afghanistan (2001-2011) considered "potentially survivable" *Military Times, 2013*



Trunkey DD, Trauma, Sci Am 1983; 249(2):20-7.

SoA: First aid, Blood transfusions, Medical Transport

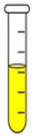
Logistics: Biological reagents and treatments are often labile

Growing number of products requiring temperature control

All Vaccines

10-15% Small Molecules

¾ of Biologics



Biological Samples, Reagents, Diagnostics

SoA: Depend on cold chain or cryopreservation

Infection: Disease onset is faster than treatment delivery

Example: severe sepsis can progress in hours to days and has a mortality rate of 25–50%

SoA: develop threat-specific vaccines & countermeasures which take time

Inside Biostasis

Biostasis Program goal: develop novel molecular interventions that will reversibly pause biological processes and protect the functional integrity of the biological system that has been paused.

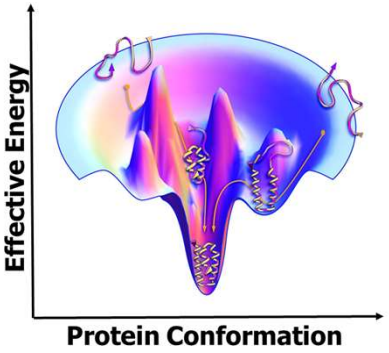
Vision: Develop a new class of interventions to effectively extend the window of time for treatment following injury or infection

Goals:

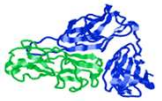
- Reversibly slow processes in live biological systems
- Scalable approach for preservation of simple cells to systems
- Demonstrate and deploy in austere conditions (no cold chain)

Approaches Pursued

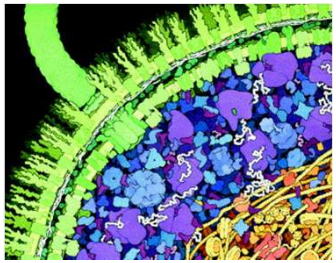
Concept	Solution?



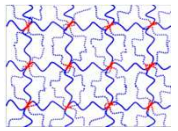
Protein Chaperoning:
Protein function is constrained by reducing conformational flexibility



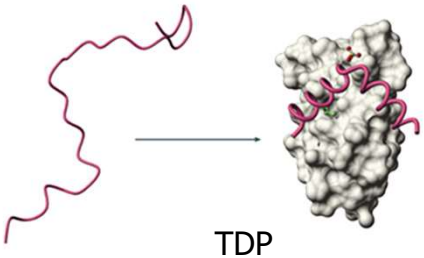
Promiscuous chaperones



Intracellular Crowding: Protein function and interaction with water is constrained when the interior of the cell is overcrowded



Intracellular Polymer



TDP
(tardigrade-disordered protein)

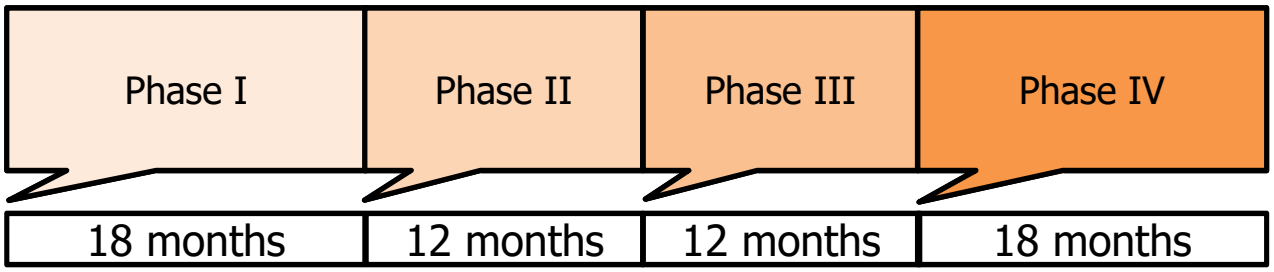
Tardigrade-disordered proteins (TDPs) stabilize cell functions and protect against freezing/desiccation stress.

Peptide Engineering

Technical tasks and time frame

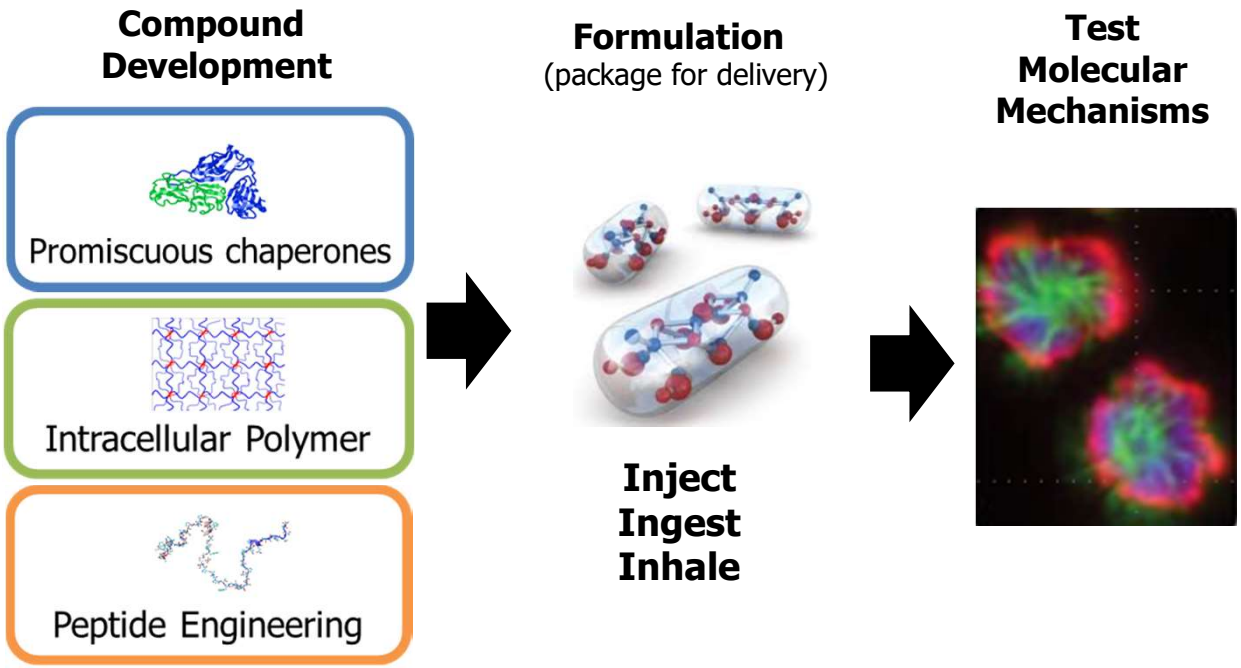
1. Design, Build and Test reversible Biostasis interentions

2. Determine Safety, Efficacy and Generalizability of Biostasis



Task 1: Design, Build, and Test Reversible Biostasis Interventions

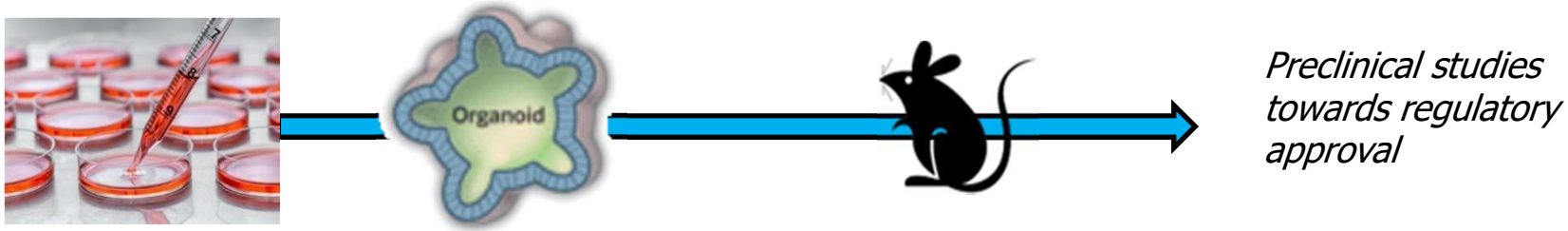
Our eventual goal is to *develop interventions that pause and/or slow biological systems*



Task 2: Determine Safety, Efficacy, and Generalizability of Biostasis

Our eventual goal is to *test interventions from Task 1 in biological systems of increasing complexity and along the way determine the generalizability of interventions.*

Determine in vivo biostasis activity and establish safety



Determine generalizability: Intervention should produce stasis in any human relevant system

Table 1: Progression of Model Complexity and Potential DoD applications by phase

Phase	Model System	Primary Metrics (capability test)	Potential DoD application
I	Simple cell/in vitro system, human cells	Stasis induction and viable cell recovery at 60%.	Biological reagents & therapeutics without cold chain
II	Complex human cell systems, organoids or tissue	Stasis induction and viable cell recovery at 85%.	Blood product, cell-based sensors/diagnostics
III	Human organoid or tissue	Stasis induction and viable cell recovery at 98%.	Tissue preservation
IV	Animal	Stasis induction and tolerance in animal model	Trauma and acute infection

Section 1.3 – "End" of Phase Demonstration

- "Prior to the end of each phase, performers will be required to demonstrate the ability of their approach(es) to initiate and maintain Biostasis in their model system of choice."

- "Ideally, this demonstration should be presented as a single, large-scale experiment that details the methods used to measure biological activity, the degree and duration of stasis induced, and the mechanisms by which stasis is produced and reversed."

- "Challenges to the system will be selected by the performers in consultation with DARPA, and should be consistent with a desired end-user application space. It is not required that performers set aside a specific period of time for a demonstration, rather, the demonstration should be a test of Biostasis capability by the end of the phase."

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