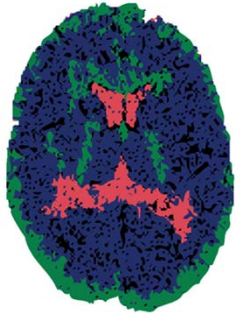


NIH SIREN  
Emergency  
Trials  
Network

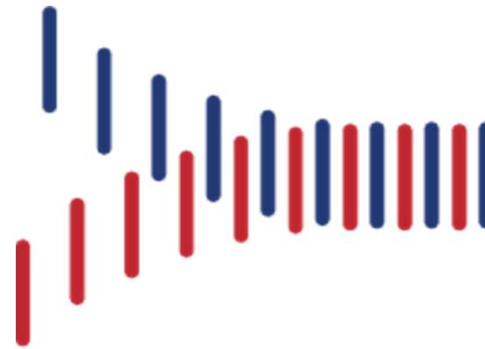
## Overview



# Neurological Emergencies Treatment Trials



Funded in 2017



NIH SIREN  
Emergency  
Trials  
Network



# Specific aims

1. diligently recruit, efficiently perform, and widely disseminate the most scientifically and **clinically important trials in emergency patient care**
2. create a **culture of clinical trials that is collaborative**, multidisciplinary, diverse and inclusive through leadership, openness, and engagement
3. **transform the emergency research enterprise** through innovative design, patient stakeholder engagement, better operational strategies

# Design principles and organizational values

- Focus on **early treatment**.
- Focus on **meaningful outcomes for patients**.
- Focus on **efficiency**.
- Focus on **collaboration**.
- Focus on **transforming the clinical trials enterprise**.

# Multiple PI Leadership Plan - CCC

- Bill Barsan
- Robert Silbergleit
- Clif Callaway



# Multiple PI Leadership Plan - DCC

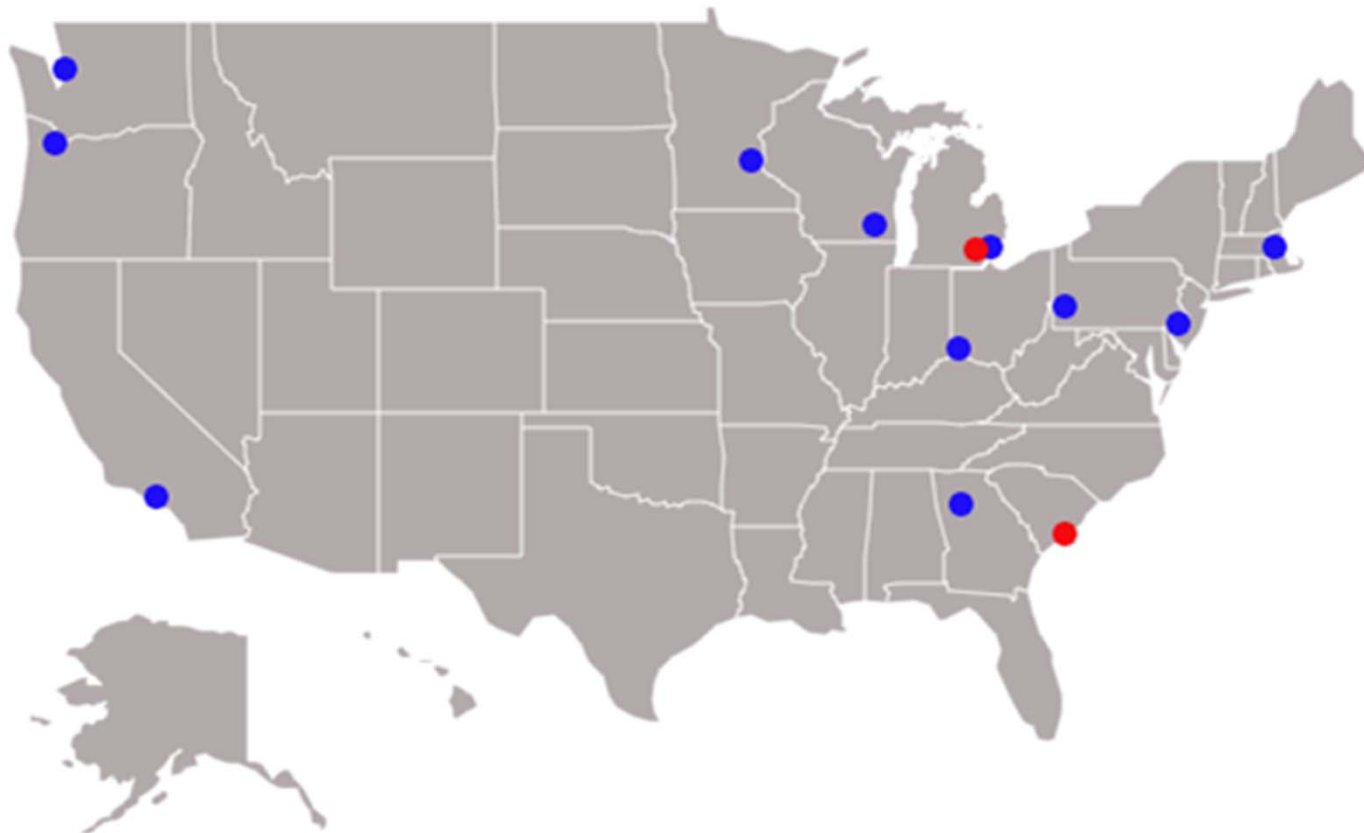
- Yuko Palesch
- Valerie Durkalski



# NIH Program Leadership

- Jeremy Brown (NINDS)
- Carolina Mendoza-Puccini (NINDS)
- George Sopko (NHLBI)
- Emily Tinsley (NHLBI)
- Robin Conwit (NINDS)
- Lupe Aquino (NCATS)





● Hub-Award ● Coordinating Center

**SIREN Grant Awards**

- Massachusetts General Hospital
- Temple University
- University of Pittsburgh
- Wayne State University
- University of Cincinnati
- Emory University
- Medical College of Wisconsin
- University of Minnesota
- University of Washington
- Oregon Health Sciences University
- University of California Los Angeles

**Coordinating Centers**

- University of Michigan
- Medical University of South Carolina



# Scope of Portfolio

Late learning phase or confirmatory phase trials

Patient oriented outcomes

Controlled efficacy to registry based RCT

Appropriate sized for our scalable network

Primary focus on neurological, cardiac, lung and blood (NINDS/NHLBI)

Secondary focus on other IC portfolios, and health services

Scientifically and Clinically Important Questions and Observations

Begin discussions with NIH program officers early

NIH program officers will evaluate the fit for the Institute

NIH Study Section

Institute Council

Trial Ideas (from anybody)

Clinical Trial Summary and Rough Budget

Revise

Grant application(s)

Grant Award

Institute Pre-approval to submit

Collaborative Grant Application and Protocol Development with input from Sites, Patients, and Others

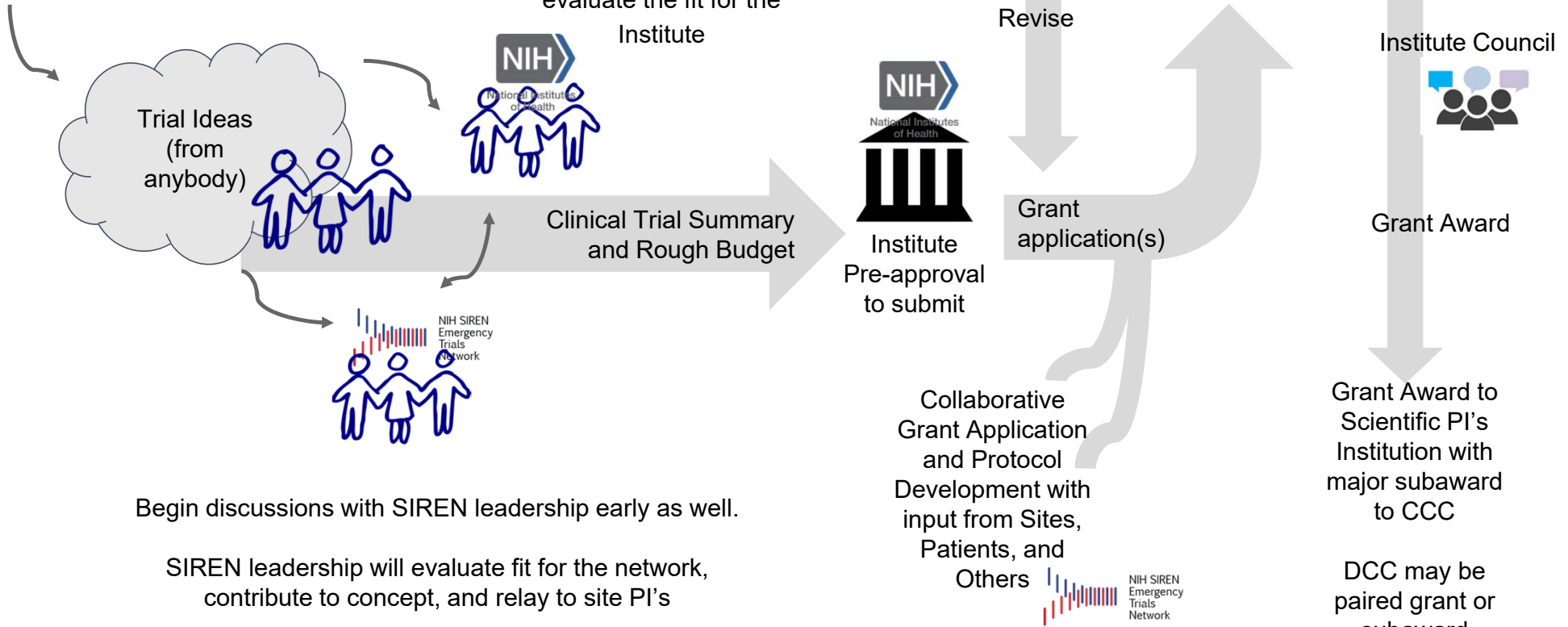
Grant Award to Scientific PI's Institution with major subaward to CCC

DCC may be paired grant or subaward depending on Institute

Begin discussions with SIREN leadership early as well.

SIREN leadership will evaluate fit for the network, contribute to concept, and relay to site PI's

SIREN will NOT be a layer of scientific peer review



# Potential Sources of Trials

Early referrals from program officers at NIH

Investigators contacting us directly

SIREN initiated/generated trials

(addressing needs, portfolio gaps, IC priorities)

(retreats/workshops)

Industry partnerships (SBIRs)

# Current and Pipeline SIREN trials

## Current:

Hyperbaric Oxygen Brain Injury Trial (HOBIT)

Brain Oxygen Optimization in Severe TBI-Phase 3 (BOOST3)

## Pipeline:

ICECAP (Influence of Cooling Duration on Outcome in Cardiac Arrest Patients)

CHEST PAIN (Comparative Health Effectiveness of Strategies Testing Pain Assessment of Ischemia Noninvasively)

# HOBIT (Hyperbaric Oxygen Brain Injury Trial)

PIs: Gaylan Rockswold, William Barsan, Byron Gajewski, Renee Martin

Adaptive Phase 2 trial evaluating 7 different dose tiers for Hyperoxia in severe TBI (GCS 3-8); 200 patients

Primary outcome: > 50% probability of success in a Phase 3 trial

Work began on HOBIT in 2014

First grant submitted 4/2016

Funded in 9/2017

# BOOST3 (Brain Oxygen Optimization in Severe TBI—Phase 3)

PIs: Ramon Diaz-Arrastia, William Barsan, Lori Shutter, Sharon Yeatts

Phase 3 trial to determine whether management strategies based on brain tissue oxygen monitoring and ICP management improves outcome from severe TBI (GCS 3-8) compared to management based on ICP alone; 1094 patients

Primary Outcome: Sliding dichotomy GOS-E at 6 months

Work began in 2015

Funded in 7/2018

# ICECAP (Influence of Cooling Duration on Outcome in Cardiac Arrest Patients)

PIs: Will Meurer, Rob Silbergleit, Romer Geocadin, Sharon Yeatts, Ramesh Ramakrishnan

Phase 3 trial to characterize the duration/response curve for hypothermia in comatose survivors of cardiac arrest; will determine this for both shockable and non-shockable rhythms

Primary Outcome: mRS at 90 days following cardiac arrest

Original design part of the ADAPT-IT project 2010-2015

Grant submitted and reviewed 2018; Resubmission in process

# CHEST PAIN (Comparative Health Effectiveness of Strategies Testing Pain Assessment of Ischemia Noninvasively)

PIs: Alan Storrow, David Maron, Clif Callaway, Valerie Durkalski

Non-inferiority trial comparing an in hospital noninvasive testing strategy vs outpatient follow up in patients with low risk chest pain

Primary outcome: All cause mortality at 30 days; 16,700 patients

Grant submitted and reviewed in 2018; Resubmission in process



QUESTIONS?