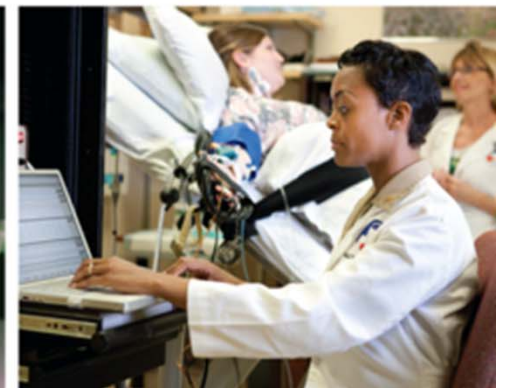
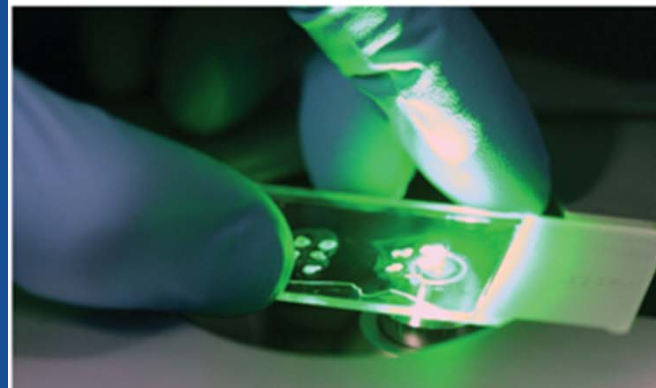
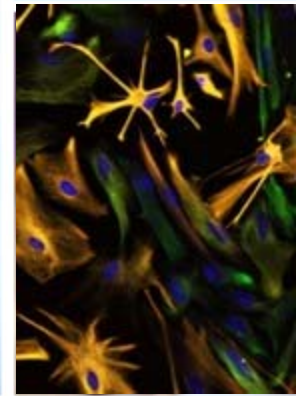
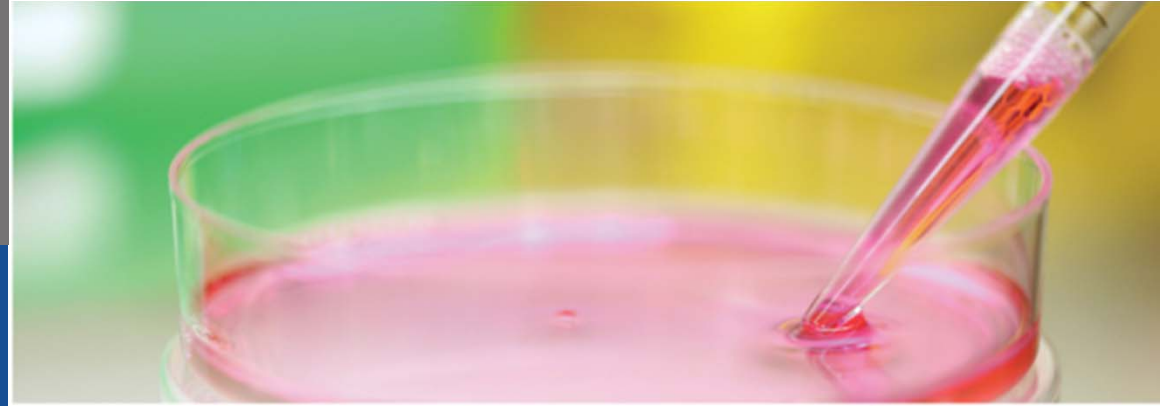




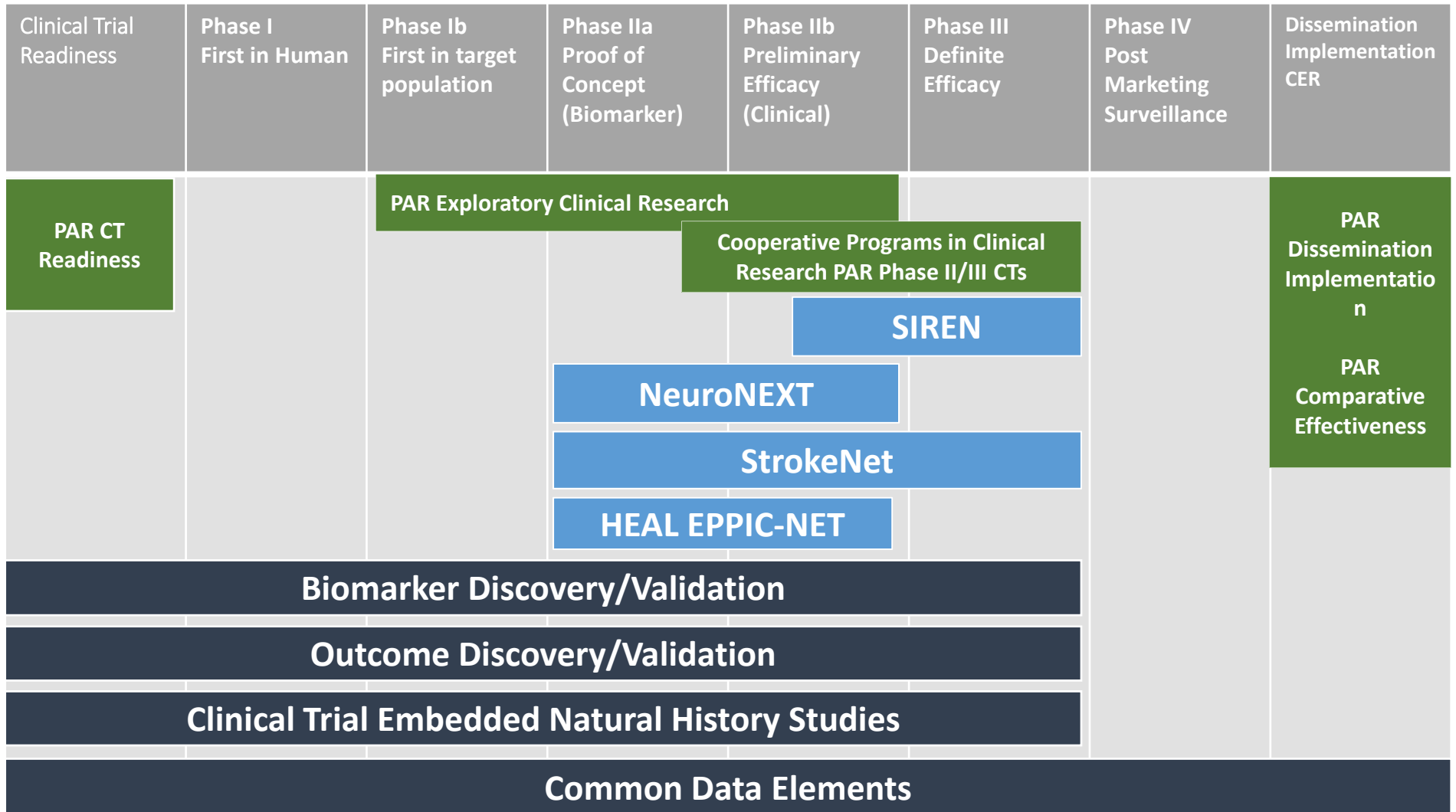
National Institute of
Neurological Disorders
and Stroke

Division of Clinical Research (DCR) – Networks 2019



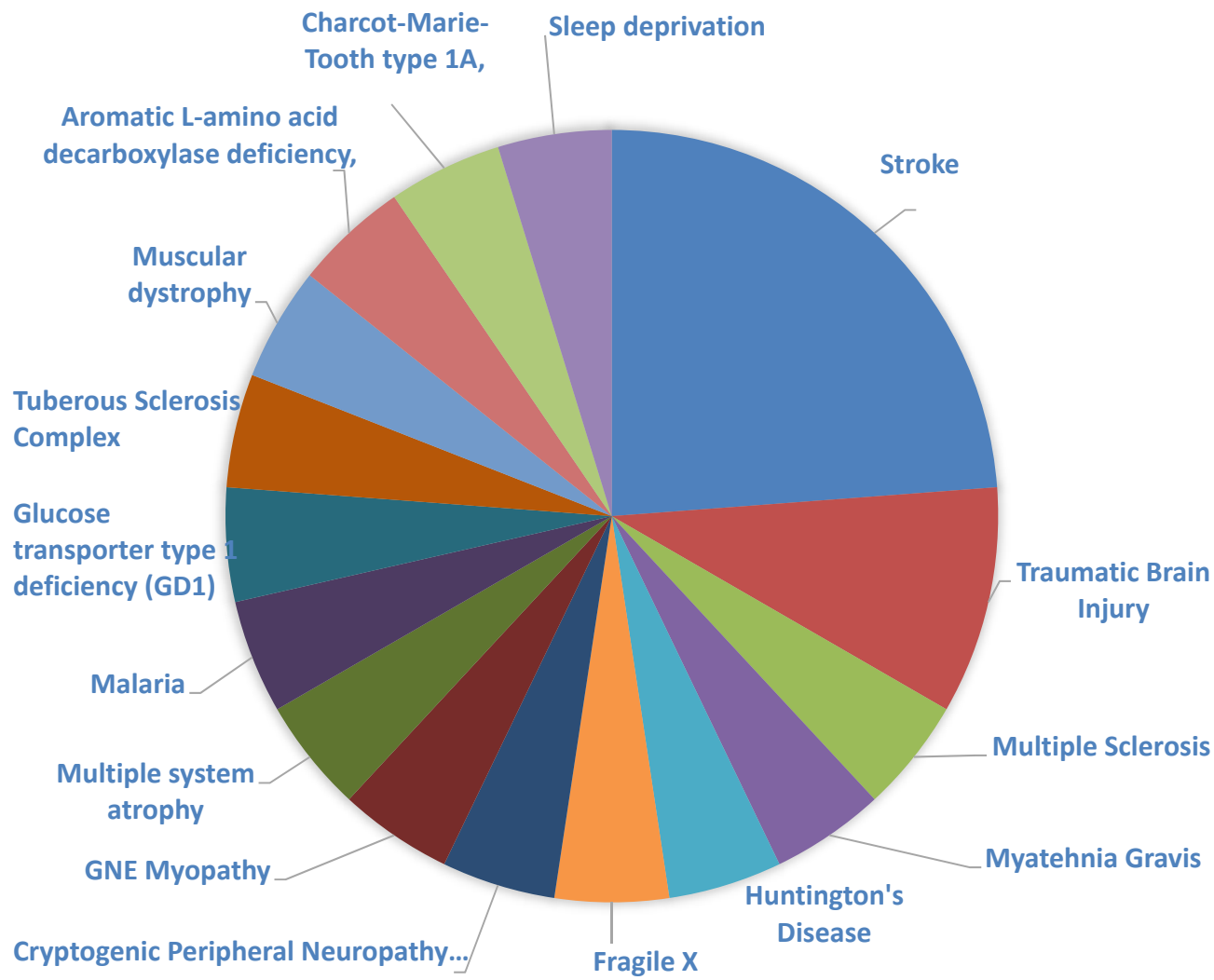
Robin Conwit, MD
Program Director, NINDS/NIH

Division of Clinical Research Programs



Early Phase Clinical Trials: Current Portfolio

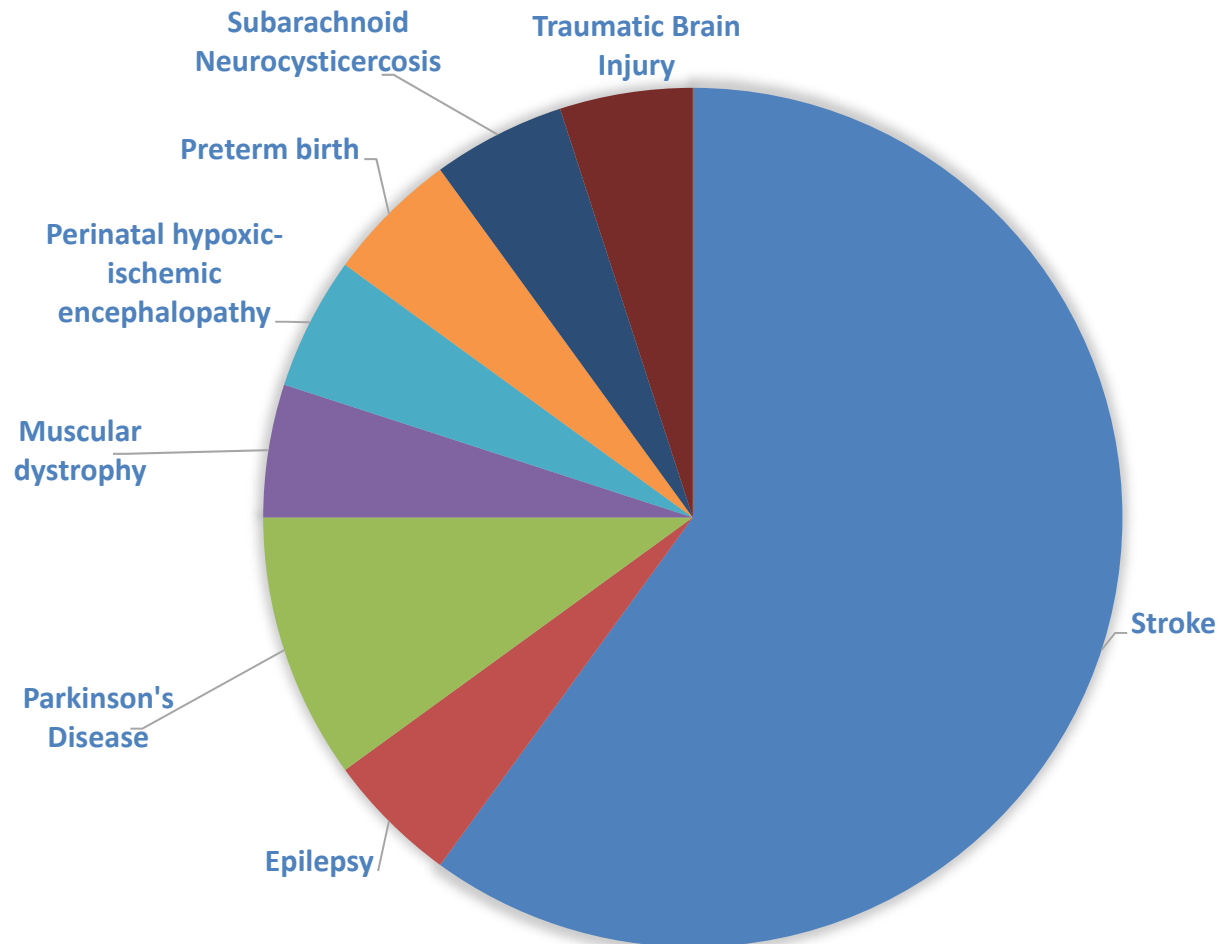
2018 Active Grants



Total: 21

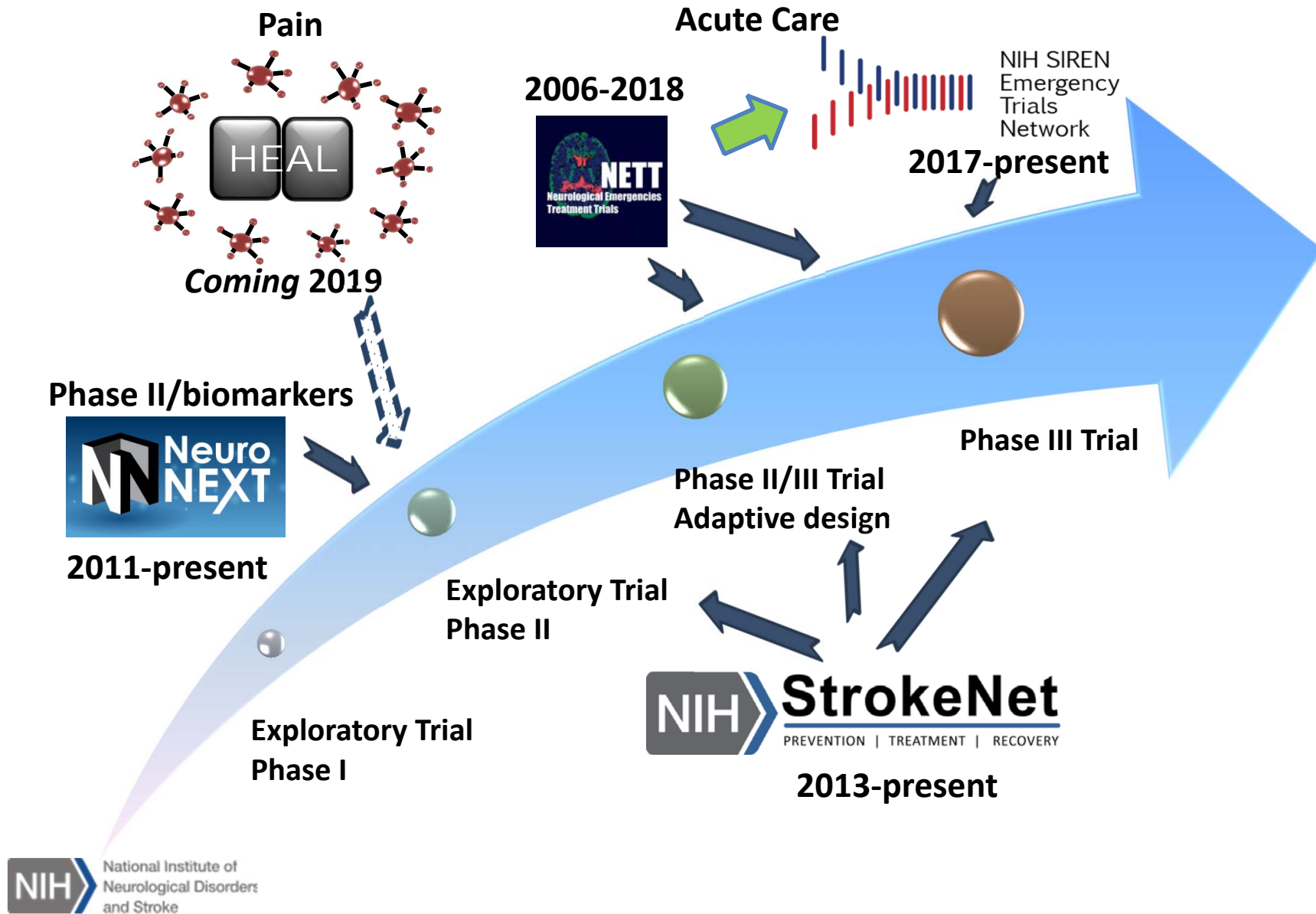
Efficacy Clinical Trials: Current Portfolio

2018 Active Grants



Total: 20

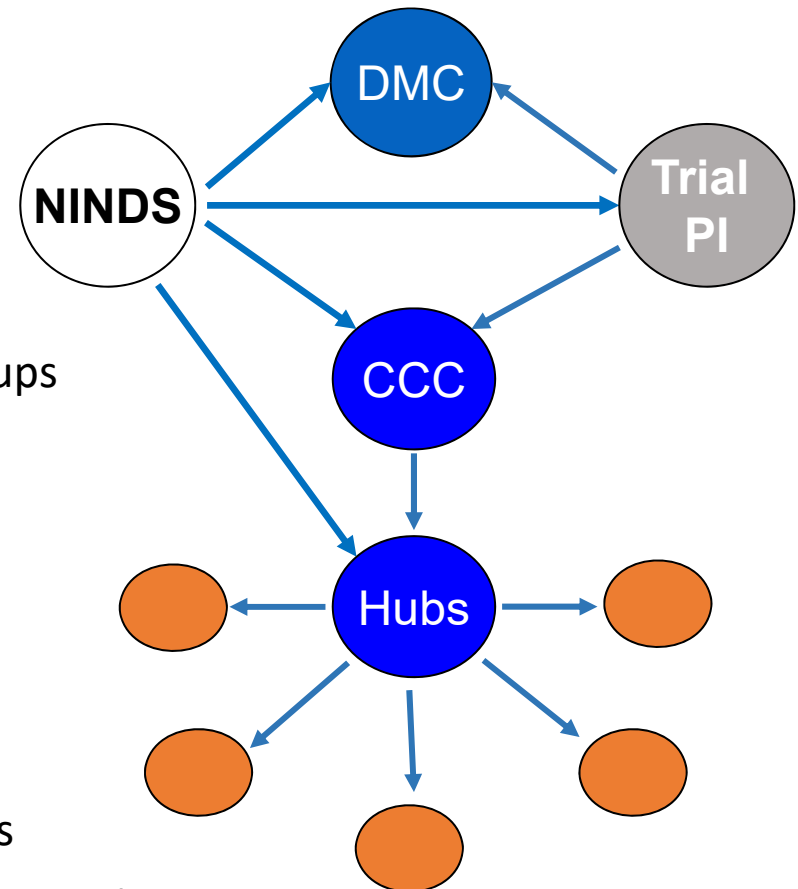
NINDS Networks



NINDS Networks



Organizational and Funding Structure

- Increased trial quality
- Balanced portfolio
 - Allows logical ordering of incoming trials
 - Creates a pipeline for future trials
- Stable infrastructure and research capacity
 - Improved subspecialty input via working groups
 - Stable funding for research and training
- Improved data sharing
 - Single data center with uniform governance
 - Fosters the use of CDEs
- Manages trials competing for similar patients
 - Commitment to consider **ALL** eligible patients
- Coordinates with non-profits, industry, and international partners
- Trains the next generation of clinical trialists






NINDS Networks

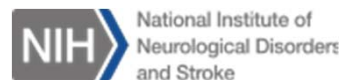
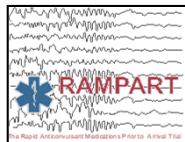
NETT Clinical Trial Activities

- 2006-2018
- 22 Hub centers (17 funded) each with 3-5 satellite spoke hospitals, a coordinating center, and a data coordinating center
- Emergency neurology network that conducted large, simple, phase III trials for acute injuries commonly treated in the emergency room  



Completed:

- **RAMPART**- Rapid Anticonvulsant Medication Prior To Arrival Trial (N=1024) 
- **ALIAS** –Albumin Therapy for Neuroprotection in Acute Ischemic Stroke (N=841) 
- **ProTECT III** - Progesterone for Traumatic Brain Injury (N=882)
- **SHINE** – Stroke Hyperglycemia Insulin Network Effort Trial (N=1151)
- **POINT** – Platelet-Oriented Inhibition in New TIA Trial (N=4892) 
- **ATACH II** – Antihypertensive Treatment of Cerebral Hemorrhage (N=1000)
- **ESETT**- Established Status Epilepticus Treatment Trial (N=478)




NINDS Networks

Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT)



Overview

- 2011 - present
- 25 regional sites, data and clinical coordinating centers
- Designed to advance the field by accelerating biomarker and therapy development

 Coordinating Center

 Site Award



<https://neuronext.org/>

NINDS Networks

NeuroNEXT Clinical Trial Activities

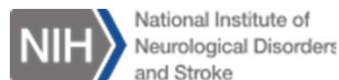


Completed:

- **SUPER BABY** Spinal Muscular Atrophy Biomarker Study (N=53) 
- **SPRINT MS** Ibudilast in Progressive Multiple Sclerosis (N=255) 
- **Beat MG** Rituximab in Myasthenia Gravis (N=52)
- **RHAPSODY** 3K3A-APC in Acute Stroke (N=110)
- **STAIR** SRX246 for irritability in Huntington's Disease (N=105)

Ongoing:

- **CYTO-C** Cytochrome C as Biomarker in Glioblastoma Multiforme (N=200)
- **FX LEARN** AFQ056 (Novartis) for language learning in Fragile X (N=100)
- **Top CSPN** Topiramate for Cryptogenic Peripheral Neuropathy (N=125)
- **MAGINE** ManNAc for GNE Myopathy (N=50)



NINDS Networks

The NINDS Stroke Clinical Trial Network (NIH StrokeNet)



 Coordinating Center

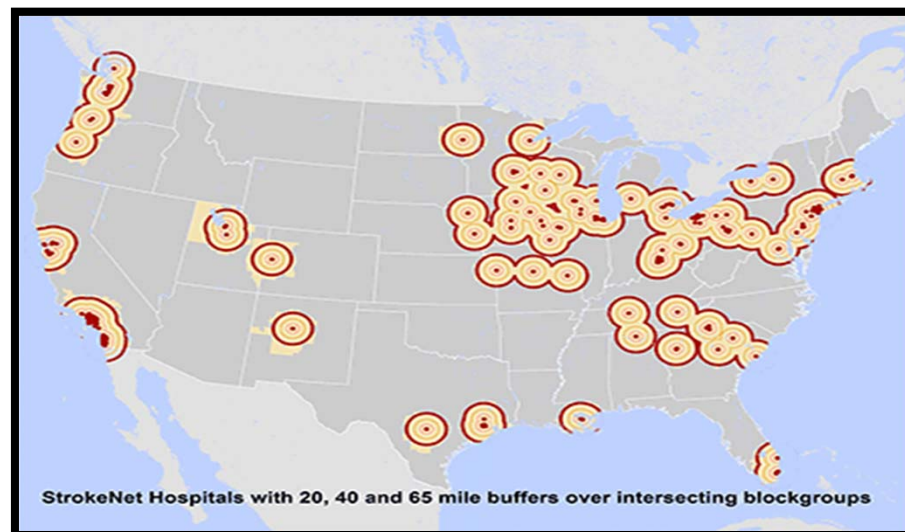
 Site Award

Overview

- 2013 - present
- 29 regional centers (24 funded) with 432 satellite stroke hospitals, a coordinating center, and a data coordinating center
- Phase 2 and phase 3 clinical trials and biomarker studies to advance acute stroke **treatment, prevention, and recovery**

NINDS Networks

Population coverage of “Hub & Spoke” model




| Characteristic | Distance from StrokeNet Center | | | | | | Total (50 States) | % of Total |
|-------------------------|--------------------------------|------------|----------------|------------|----------------|------------|-------------------|------------|
| | 20 Mile Radius | % of Total | 40 Mile Radius | % of Total | 65 Mile Radius | % of Total | | |
| Total Population | 120,758,537 | 38.3% | 157,727,442 | 50.0% | 189,572,542 | 60.1% | 315,219,560 | 100.0% |
| Male (adult) | 44,518,863 | 38.1% | 58,121,547 | 49.8% | 70,121,776 | 60.1% | 116,781,403 | 100.0% |
| RACE | | | | | | | | |
| White | 80,374,323 | 34.5% | 109,783,225 | 47.1% | 136,388,020 | 58.5% | 233,168,413 | 100.0% |
| Hispanic/Latino | 24,695,940 | 44.6% | 29,719,245 | 53.6% | 33,189,395 | 59.9% | 55,429,828 | 100.0% |
| Black | 18,115,454 | 45.9% | 21,868,666 | 55.4% | 24,323,226 | 61.7% | 39,451,870 | 100.0% |
| Asian | 9,952,233 | 65.3% | 11,108,254 | 72.9% | 11,888,761 | 78.0% | 15,244,082 | 100.0% |
| Other | 8,048,767 | 53.3% | 9,567,560 | 63.3% | 10,560,177 | 69.9% | 15,111,418 | 100.0% |
| American Indian | 509,505 | 20.0% | 675,804 | 26.5% | 866,548 | 34.0% | 2,550,780 | 100.0% |
| Pacific Islander | 197,664 | 37.6% | 235,546 | 44.8% | 267,158 | 50.8% | 526,408 | 100.0% |

NINDS Networks

StrokeNet Clinical Trials Activities

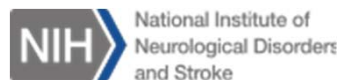


Completed:

- **MISTIE-3** Minimally Invasive Surgery for ICH evacuation trial (N=500) *
- **i-DEF** Deferoxamine mesylate treatment for ICH trial (N=293) *
- **DEFUSE-3** Delayed endovascular therapy for select patients (N=182) 
- **TeleRehab** Home based telerehabilitation stroke recovery trial (N=124)

Ongoing:

- **CREST-2** Treatment of asymptomatic carotid stenosis (N=2480) *
 - **CREST-H** Hemodynamic impairment ancillary study in CREST-2 (N=500)
- **ARCADIA** Apixaban vs. aspirin for cryptogenic stroke (N=1100)
- **MOST** Optimization of thrombolysis ischemic stroke trial (N=1200)
- **Sleep-SMART** Treatment of obstructive sleep apnea (N=3062)
- **TRANSPORT-2** Transcranial direct stimulation stroke recovery trial (N=129)
- **I-ACQUIRE** Intensive infant rehabilitation for pediatric stroke (N=240)



NINDS Networks

Strategies to Innovate Emergency Care Clinical Trials Network (SIREN)



Overview

- Established in 2017
- Co-Funded with NHLBI
- 11 regional centers with 50 satellite ER sites, coordinating and data center
- SIREN improves the outcomes of patients with neurologic, cardiac, respiratory, hematologic and traumatic emergencies by identifying effective treatments administered in the earliest stages of critical care

<https://siren.network/>

NINDS Networks

SIREN Clinical Trial Activities



NIH SIREN
Emergency
Trials
Network

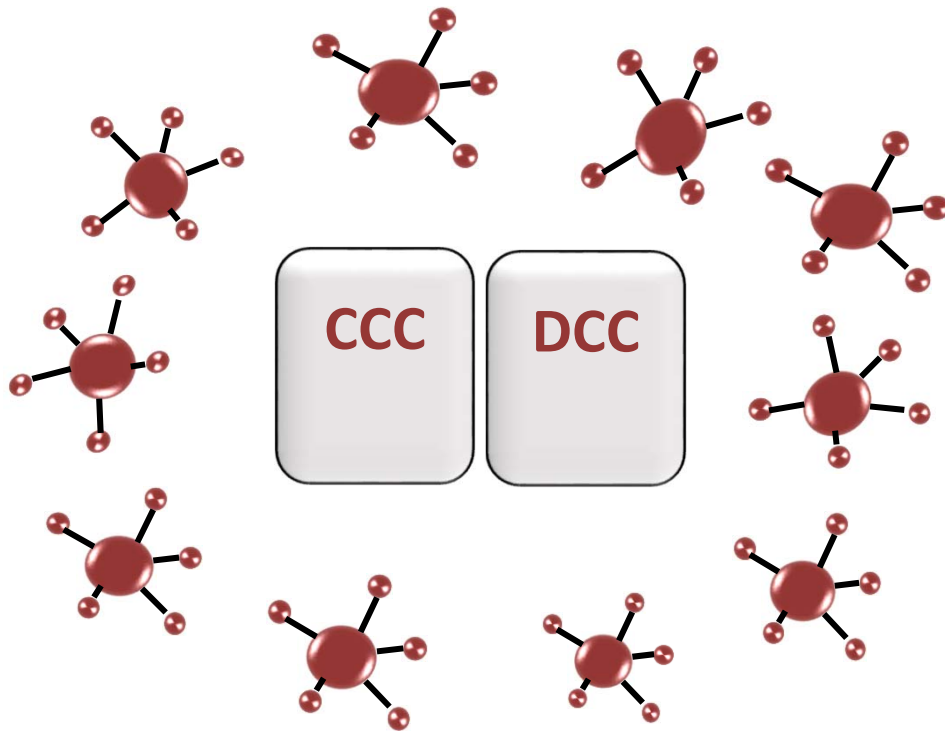
Ongoing:

- **HOBIT** Hyperbaric oxygen therapy in severe TBI (N=200)
 - Signal of efficacy: to determine whether there is a > 50% probability of hyperoxia treatment
 - Dose selection: to select the combination of treatment parameters (pressure +/- intervening normobaric hyperoxia)
- **BOOST** Brain oxygen optimization in severe TBI (N=1094)
 - Whether PbTO₂ monitoring vs ICP monitoring results in improved neurological outcomes measured by the GOS-E



NINDS Networks

HEAL: NINDS Early Phase Pain Investigation Clinical Network (EPPIC-NETT)



Overview

- FOA in Dec 2018
- Phase II studies
- Infrastructure applications in Feb 2019
- Anticipated funding in July 2019
- A cornerstone of the NIH's Helping to End Addiction Long-term (HEAL) Partnership.
- Provides a robust and readily accessible infrastructure for the rapid implementation and performance of high-quality Phase 2 clinical trials to test promising novel pain therapeutics

NINDS Networks

Network Efficiencies

- Most trials completed enrollment ahead of schedule (N=3) or on-time (N=13), and without need for additional funding
- Able to assess feasibility before funding trials
- Efficient management of competing trials
- Reduced need for *de novo* monitoring site visits
- Workforce stability facilitates quicker trial activities initiation
- Able to combine large meetings (e.g. Steering Committee and Investigator meetings) providing \$100Ks in additional saving
- Innovative master agreement contracting reduced F&A costs across trials
- Successfully training fellows and junior faculty
- Effectively involving smaller non-research hospitals in clinical research