2014 NINDS Benchmarks for Epilepsy Research

History and evolution

Ray Dingledine, Chair

Brandy Fureman, co-Chair

Epilepsy Research Benchmarks Stewards

2000-2015

Disclosure

Name of Commercial Interest	Type of Financial Relationship
NeurOp, Inc	Founder, Board of Directors

History of the Benchmarks

Curing Epilepsy 2000: Focus on the Future

- White House-initiated conference
- Developed the first Epilepsy Research Benchmarks
- “No seizures, no side effects”

Curing Epilepsy 2007: Translating Discoveries into Therapies

- Developed 2007 Benchmarks
- New emphasis on comorbidities and SUDEP

Curing the Epilepsies 2013:

- Developed 2014 benchmarks
- Refined focus on comorbidities

2014 NINDS Benchmarks for Epilepsy Research

I. *Understand the causes of the epilepsies and epilepsy-related neurologic, psychiatric, and somatic conditions.*

II. *Prevent epilepsy and its progression.*

III. *Improve treatment options for controlling seizures and epilepsy-related conditions without side effects.*

IV. *Limit or prevent adverse consequences of seizures and their treatment across the lifespan.*

Epilepsy Research Benchmarks Stewards

- ***Began*** as a group of researchers who volunteered after the first Curing Epilepsy conference to promote and track progress in areas highlighted by the Benchmarks
  - Report research advances and opportunities to NINDS
  - Raise awareness of the Benchmarks among researchers, including junior investigators entering the field
  - Forge partnership with AES to integrate the Benchmarks into Annual Meeting programs and materials
- ***Now*** an AES committee, working in partnership with NINDS
  - Enhanced visibility of Stewards' activities
  - Increased opportunities for AES members to participate
  - Achieves further integration of the Benchmarks as shared framework for guiding and tracking research progress

Past Stewards

Matthew Anderson
Jocelyn Bautista
*Anne Berg**
Edward Bertram
*Amy Brooks-Kayal**
Chad Carlson
Marc Dichter
*Jerome Engel**
Jackie French
Tracy Glauser
Bruce Hermann
Molly Huntsman
Ruben Kuzniecky
John Langfitt
*Brian Litt**
Dan Lowenstein**
Solomon Moshé
Patricia Shafer
Alexander Rotenberg
Elson So
*Susan Spencer**
John Swann
Carl Stafstrom
H. Steve White
Karen Wilcox

** Benchmarks Area Co-Chairs*

*** founding Benchmarks chair*

2014 AES/NINDS
Epilepsy Research Benchmarks Stewards

Chair: Ray Dingledine

NINDS co-chair and liaisons: Brandy Fureman, Cara Long, Vicky Whittemore

AES staff: Margaret Jacobs

I. Understand the causes of the epilepsies and epilepsy-related neurologic, psychiatric, and somatic conditions.

Co-Chairs: Heather Mefford, Rochelle Caplan

Madison Berl, Bernard Chang, Jack Lin
Annapurna Poduri, Andrey Mazarati

II. Prevent epilepsy and its progression.

Co-Chairs: Aristea Galanopoulou, Michael Wong

Devin Binder, Adam Hartman, Elizabeth Powell, Avtar Roopra, Richard Staba, Annamaria Vezzani

III. Improve treatment options for controlling seizures and epilepsy-related conditions without side effects.

Co-Chairs: Dennis Dlugos, Gregory Worrell

Kathryn Davis, Beate Diehl, Patrice Jackson-Ayotunde, Andres Kanner, Tobias Loddenkemper, Michael Rogawski, William Stacey, Sridhar Sunderam, Jerzy Szaflarski

IV. Limit or prevent adverse consequences of seizures and their treatment across the lifespan.

Co-Chairs: W. Curt LaFrance, Jr., Alica Goldman

Miya Asato, Timothy Benke, Robert Doss, Daniel Drane, Samden Lhatoo, Alison Pack, Tanvir Syed

Research progress highlights 2010-2014

(I) Novel causes of epilepsy

- Advances in genetics (next generation sequencing and role of de novo mutations)
- Autoimmune mechanisms (NORSE, etc)

(II) Preventing epileptogenesis

- Strong evidence base for roles of REST, mTOR, TrkB, and inflammatory pathways
- Studies in animal models show promise for antiepileptogenic interventions

(II) New and improved animal models

- Infantile spasms, TSC/cortical dysplasia, viral encephalitis, zebrafish, comorbid conditions

(III) Understanding network activity

- New tools and algorithms to measure and analyze seizure-related activity
- Potential biomarkers of epileptogenicity
- Development of devices for seizure prediction and control

(IV) Comorbidities

- Evidence for shared pathogenicity and impact of chronic seizures and their treatment
- Potential mechanisms and therapeutic targets beginning to emerge

(IV) SUDEP

- Identification of risk factors
- New surveillance efforts will enable further research

Teed up

- 2-4 page reviews of progress since 2013 in each benchmark area, to be published in *Epilepsy Currents* April 2016
- Recruiting new Benchmark Stewards

2014 NINDS Benchmarks for Epilepsy Research

I. Understand the causes of the epilepsies and epilepsy-related neurologic, psychiatric, and somatic conditions.

A. Identify new genes and pathways associated with the epilepsies and epilepsy-related conditions.

B. Identify new infectious, immune, age-related, environmental, or other causes and risk factors associated with the epilepsies and epilepsy-related conditions.

C. Determine whether factors related to age, gender, race/ethnicity, socioeconomic status, and other features of specific populations affect risk and mechanisms of epilepsy and epilepsy-related conditions.

D. Determine whether the bi-directional relationships that exist between the epilepsies and several co-occurring conditions (e.g., neuropsychiatric or neurodevelopmental disorders) result from the same underlying causal mechanisms, interacting mechanisms, or are a consequence of the first presenting condition.

2014 NINDS Benchmarks for Epilepsy Research

II. Prevent epilepsy and its progression.

A. Understand epileptogenic processes involved in epilepsies with neurodevelopmental origins, including those due to genetic or presumed genetic causes.

B. Understand epileptogenic processes involved in the development of epilepsy following traumatic brain injury, stroke, brain tumor, infections, neurodegeneration, or other insults to the brain.

C. Identify biomarkers that will aid in identifying, predicting, and monitoring epileptogenesis and disease progression, including markers early after injury/insult that identify those people at risk for epilepsy.

D. Develop or refine models aligned with the etiologies of human epilepsies to enable improved understanding of epileptogenesis and rigorous preclinical therapy development for epilepsy prevention or disease modification.

E. Identify new targets and develop interventions to prevent or modify epileptogenesis and the progression of epilepsy and epilepsy related conditions.

2014 NINDS Benchmarks for Epilepsy Research

III. Improve treatment options for controlling seizures and epilepsy-related conditions without side effects.

A. Understand the initiation, propagation, and termination of seizures at the network level in different forms of epilepsy.

B. Identify biomarkers for assessing or predicting treatment response, including markers that may identify specific populations likely to have good outcomes or develop adverse responses.

C. Develop or refine models aligned with etiologies and clinical features of human epilepsies, especially treatment resistant forms, to enable improved understanding of ictogenesis and preclinical development to improve seizure control with fewer side effects.

D. Identify, develop, and improve interventions to detect, predict, prevent, or terminate seizures, including approaches suitable for use in the home and other non-medical settings.

E. Identify, develop, and improve anti-seizure therapies that target novel or multiple seizure mechanisms.

F. Develop, improve, and implement interventions for effective self-management, including treatment adherence.

G. Develop and validate objective patient-centered outcome metrics for clinical studies.

2014 NINDS Benchmarks for Epilepsy Research

IV. Limit or prevent adverse consequences of seizures and their treatment across the lifespan.

A. Understand and limit adverse impacts of seizures on quality of life, including effects on neurodevelopment, mental health, intellectual abilities, and other neurological and non-neurological functions.

B. Understand and limit adverse impacts of anti-seizure treatments (medical, surgical, or other interventions) on quality of life, including effects on neurodevelopment, mental health, intellectual abilities, and other neurological and non-neurological functions.

C. Understand risk factors and mechanisms involved in non-epileptic seizures (NES). Develop effective approaches for earlier and accurate diagnosis and treatment.

D. Identify causes, risk factors, and potential preventive strategies for sudden unexpected death in epilepsy (SUDEP) and other epilepsy-related mortality (for example, suicide) in people with epilepsy.

E. Identify the impact of pharmacological treatment of the epilepsies on fetal and neonatal development. Develop strategies to control seizures in pregnancy without causing harm to either the mother or child.