AMERICAN BRAIN FOUNDATION
Research Advisory Committee Meeting
February 25, 2022
3:00 p.m. ET/ 2:00 p.m. CT/ 1:00 p.m. MT/ 12:00 p.m. PT
Conference Call

Zoom link:
https://aan.zoom.us/j/96728195662?pwd=WXB1UllQT25jcVY3SklyZFVNRDdCUT09

Committee Members	Robert Griggs, MD, Chair; Jose Biller, MD; Jose E. Cavazos, MD, PhD; Jacqueline French, MD; Na Tosha Gatson, MD, PhD; James Grotta, MD; Walter Koroshetz, MD; Mark Mehler, MD; Bruce Ovbiagele, MD, MSc, MAS; Ronald Petersen, MD, PhD; Eugene Scharf, MD; Gordon Smith, MD; Reisa Sperling, MD, MMSc; Phyllis C. Zee, MD; David Dodick, MD; Paul George, MD, PhD; Mary Post, MBA, CAE
Staff	Jane Ransom, ED; Julia Miglets-Nelson, PhD; Samantha Ross; Michelle Maxwell

AGENDA ITEM	PRESENTED BY
1. Call to Order **Approval of the December 3, 2021 minutes**	Robert Griggs, MD
2. Neuroinflammation Initiative Update	Jane Ransom
3. Strategic Discussion: Future Major Initiatives	
a. Brain Tumor	Na Tosha Gatson, MD, PhD
b. Discussion and Questions	
c. ALS and Neuromuscular	Robert Griggs, MD
d. Discussion and Questions	
e. Brain Health	David Dodick, MD
f. Discussion and Questions	
4. Clinical Research Training Fellowships	Julia Miglets-Nelson, PhD Robert Griggs, MD
Adjourn	

Meeting Materials:

- Minutes of December 3, 2021 (p. 2)
- Neuroinflammation Initiative Concept Paper (p. 4)
- Prospective Neuroinflammation Funders (p. 6)
- Next Generation Research Grants (p. 7)

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American Brain Foundation
Research Advisory Committee Meeting
December 3, 2021
3:00 p.m. ET / 2:00 p.m. CT / 1:00 p.m. MT / 12:00 p.m. PT
Conference Call

Meeting Minutes

In Attendance: Robert Griggs, MD, Chair; Raymond Roos, MD, Vice Chair; Carsten Bonnemann, MD; Na Tosha Gatson, MD, PhD; Mark Mehler, MD; Bruce Ovbiagele, MD, MSc, MAS; Ralph Sacco, MD; Gordon Smith, MD; Phyllis C. Zee, MD; David Dodick, MD; Christy Phelps

Staff: Jane Ransom; Julia Miglets-Nelson, PhD; Liam Moore

Excused: Jose Biller, MD; Jose E. Cavazos, MD, PhD; Jacqueline French, MD; Walter Koroshetz, MD; James Grotta, MD; Ronald Petersen, MD, PhD; Eugene Scharf, MD; Ira Shoulson, MD; Reisa Sperling, MD, MMSc; Paul George, MD, PhD; Mary Post, MBA, CAE

The meeting was called to order by Dr. Robert Griggs at 2:00 p.m. CT. The meeting minutes of October 1, 2021 were approved.

1. **Thank You to Departing Members:** Robert Griggs, MD thanked the departing members of the RAC: Carsten Bonnemann, MD; Merit Cudkowicz, MD, MSC; Ralph Sacco, MD; Ira Shoulsen, MD; and Raymond Roos, MD. Dr. Griggs also thanked Christy Phelps, who is leaving the Academy.

2. **2021 Research Program Report:** Julia Miglets-Nelson, PhD gave an update on the highlights of the research program in 2021. Despite the ongoing effects of the pandemic, this has been a very successful year for the research program, which included the following:

    - In June, the ABF released the RFA for the Cure One, Cure Many Award for early diagnosis of Lewy body dementia. The RFA was developed in collaboration with the AAN, the Alzheimer's Association, and the Michael J. Fox Foundation. Each of these partner organizations nominated leading scientists to serve on the selection committee. The committee received 21 letters of inquiry, and of these, 9 were invited to submit full proposals. The committee met on November 29, 2021 to select the award recipient, and the recipient will be announced publicly in early 2022 and featured at a session at the AAN's annual meeting in April.

    - There was significant growth and interest in the early career clinical research training grants funded through our next Generation Research Grants program, from both applicants and funding partners. In 2021, the ABF awarded nine recipients, including researchers in ALS, multiple sclerosis, Parkinson's, neuromuscular disease, epilepsy, and cognitive aging, and provided funding to a total of 25 researchers, including those in the second and third year of their awards. The ABF also secured partnerships and funding for 18 grants to be awarded in 2022, including five new awards in partnership

with the Association for Frontotemporal Degeneration, Muscular Dystrophy Association, Amgen, and Hearst Foundations and Eisai, and two awards which were previously funded and administered outside of the ABF's collaboration with the AAN: the Lawrence Brass CRTS in Stroke and the CRTS in Tourette Syndrome; going forward, these awards will be administered by the AAN. Applications for the 2022 awards were due on October 1, and the ABF received 64 applications for 18 awards.

- The ABF piloted a new funding mechanism in collaboration with the AAN by offering a $50,000 seed grant promoting diversity, equity, and inclusion in autism research. This grant was open to a researcher at any career level; the ABF received eleven applications.

3. **Neuroinflammation Initiative:** Robert Griggs, MD introduced the neuroinflammation proposal that was drafted by Na Tosha Gatson, MD, PhD. The next step is to translate the idea into something that is appealing to both donors and scientists.

   David Dodick, MD, thanked Na Tosha Gatson, MD, PhD for the draft. The potential impact of the neuroinflammation initiative dovetails well the ABF mission of Cure One, Cure Many. It cuts across so many mechanisms and illustrates why the ABF and the AAN are uniquely positioned to do this work. The draft proposal gives confidence to our donors, and the initiative shows donors how neuroinflammation and mechanisms interact with individual disease states.

   Raymond Roos, MD emphasized that the challenge now is deciding how specific a focus the ABF should present to potential donors and partners at this stage. Neuroinflammation is important to many areas, but the ABF wants to target those topics that are most innovative and have the greatest potential to be transformative.

   Mark Mehler, MD emphasized the need for detail in the proposal about neuroinflammation as a rapidly evolving concept that is much broader than was initially thought. It involves a continuum from early development to later stages of aging and has both beneficial and deleterious effects. Research is showing that cell types can be modulated in dramatic ways that can influence normal brain functions, disease outcomes, the continuum from brain to body and back. The proposal should do more to emphasize the exciting aspects of studying neuroinflammation as a brave new world, specifically, that understanding neuroinflammation has implications for everything from maternal-fetal modulation of normal biology, early onset disease, late onset disease, and manipulation of molecules and cells in ways that can dramatically affect disease. This initiative can also help us define the ways in which inflammation is not unidirectional, and that it can be good or bad or both at once. This is an extremely rich area, with the ability to define a new discipline across the age spectrum.

   Jane Ransom shared learnings from the LBD initiative, in particular that the ABF's partner funders want to be part of developing the direction of an initiative like this one. She suggested that the ABF begin engaging potential partners at this early stage in order to get them invested in the idea and motivated to donate later.

   Gordon Smith, MD, asked about the giving objective; is it supposed to be an X-prize, or to raise funds around a suite of other funding mechanisms?

   Raymond Roos, MD confirmed that it is not an X-prize. The goal is for successful applicants to apply as a consortium with at least two PIs.

Adjourned 2:59 p.m. CT.

AMERICAN BRAIN FOUNDATION

Harnessing Neuroinflammation:
A cross-cutting mechanism of brain disease and the aging brain

The American Brain Foundation (ABF) is launching a major funding initiative to support research to understand neuroinflammation as an underlying mechanism of brain disease and brain health. Neuroinflammation contributes to numerous diseases and affects all stages of life, from fetal development to aging. Multiple national and international organizations in neurology have highlighted the need for research on neuroinflammation. To date, however, there has been no concerted, major national research effort.

The ABF is seeking research and funding partners to launch a multi-year, multi-million-dollar research initiative that will begin making awards to researchers in 2024. This effort will be administered in collaboration with the American Academy of Neurology (AAN). This initiative will focus on both revolutionary (high risk/high reward) as well as evolutionary (high quality, incremental) research proposals.

Need for Research
Nearly every major pediatric, adult, and geriatric neurological and neuropsychiatric disorder involves complex and unique changes in the body's immune response. Understanding the continuum between autoimmunity and immunodeficiency at the molecular, cellular, and systems levels will allow us to more precisely target diseases as disparate as multiple sclerosis, brain tumor, epilepsy, Parkinson's Disease, Huntington's Disease, Alzheimer's Disease, stroke, Amyotrophic Lateral Sclerosis, migraine, neuropathy, traumatic brain injury, meningitis, and COVID-19 associated brain disease. Together, these diseases affect 60% of the US population and at least 3 billion people worldwide, and attack the essence of what makes us human: thought, speech, emotion, and movement.

Neuroinflammation is a crucial underlying mechanism that contributes to each of these neurological diseases and many therapeutic breakthroughs in neurological disease have targeted mediators of inflammation and the immune system. Inflammation is also thought to play a role in mental health conditions such as depression as well as the deleterious effects on the brain from chronic stress.

Neuroinflammation is of such importance to the field of neuroscience, the future of brain diseases, and the aging of the brain, that the thematic emphasis of a recent European Academy of Neurology annual meeting focused on Neuroinflammation. In addition, the US National Institutes of Health convened a workshop on disease-promoting chronic inflammation to identify the challenges and needs in the development of clinically feasible strategies for monitoring a person's inflammation status before, during and after disease occurrence.

To date, however, there has been no large-scale, coordinated research effort to understand the precise mechanisms of inflammatory mediated mechanisms involved in brain disease and age-related brain pathology. This understanding is essential to identifying potential therapeutic targets and developing targeted pharmacological approaches acting at different points along these inflammatory cascades.

Our Approach and Partnerships
The American Brain Foundation is a national charitable foundation that funds world-class research on diseases and disorders of the brain and nervous system. Our mission is to bring researchers and donors together to cure brain diseases and disorders. Understanding the shared mechanisms that underlie many neurological diseases has been the guiding principle of the research funded by the American Brain Foundation (ABF). We believe that a cure for one will lead to a cure for many.

The ABF is backed by the 36,000 neurologists of the American Academy of Neurology (AAN), our founder and research partner. The largest organization of neurologists in the world, AAN will supply its top scientists to vet research proposals for the *Harnessing Neuroinflammation* initiative, assuring that only those proposals that have the potential to result in truly transformational and translational advances will be supported. The awards issued from this funding initiative will also be administered by the AAN.

Timeline
The ABF is currently meeting with potential partners for this project who are interested in helping to shape the scope and goals of the initiative. An advisory committee consisting of scientists from the ABF, the AAN, and our partner organizations will convene later this year, and we seek to begin awarding funds in 2024.

Research Funding Priorities
The American Brain Foundation's *Harnessing Neuroinflammation* initiative will prioritize revolutionary and evolutionary proposals that seeks to advance knowledge in one of the following critical domains:

- Determine the role of immune cells and their subsets in the development of chronic brain disease
- Develop detection platforms and instruments that can perform multiple measurements of genetic, epigenetic and protein inflammation biomarkers related to brain disease
- Design and analyze population studies based on molecular, cellular and 'trans-omics' data
- Analyze and discover inflammatory biomarkers from metabolome, microbiome, secretome, proteome and other large biological data resources
- Develop computational platforms and tools to integrate and analyze cross-platform measurements of inflammatory markers
- Determine whether chronic brain disease and disability are diminished by therapeutic interventions that target high-value inflammation molecules or pathways

Our emerging revelations regarding the neuroprotective and neural regenerative role of neuroinflammation, the systemic modulators and signaling pathways of neuroinflammation, as well as the interactive cellular species and bioactive niches mediating neuroinflammation will allow these initiatives to develop dynamic, evolving, and multifaceted treatment regimens to harness the extraordinary potential of immunotherapy for mitigating – and even curing – some of the most pernicious brain disorders.

AMERICAN BRAIN FOUNDATION

Neuroinflammation Initiative

Prospective Funding Partners

ALS Association*

Alzheimer's Association*

Alzheimer's Research UK

American Epilepsy Society*

American Heart Association/American Stroke Association*

Association for Frontotemporal Degeneration*

Biogen

Bristol Myers Squibb

Chan Zuckerberg Initiative

Cure Alzheimer's Fund

CURE Epilepsy

Dementia Discovery Fund

I AM ALS

McKnight Brain Research Foundation*

Muscular Dystrophy Association*

National MS Society*

Novartis

*current ABF Next Generation Research Grants partner

AMERICAN BRAIN FOUNDATION

Status of Next Generation Research Grants, 2022-2024

2022 Awards	
Confirmed	
Award	**Partner**
CRTS in ALS	ALS Association
Richard Olney CSDA in ALS	ALS Association
CRTS in Lewy Body Disease	Alzheimer's Association & Mary Groff Charitable Trust
Susan Spencer, MD CRTS in Epilepsy	American Epilepsy Society & Epilepsy Foundation
CTRS in Cognitive Aging and Age-Related Memory Loss (x2)	McKnight Brain Research Foundation
CRTS in Parkinson's Disease	Parkinson's Foundation
Katzman CRTS in Alzheimer's	Alzheimer's Association
(NEW) CRTS in Migraine	Amgen
(NEW) CRTS in Frontotemporal Degeneration	Association for Frontotemporal Degeneration
CSDA in Myasthenia Gravis	Myasthenia Gravis Foundation of America
(NEW) CRTS in Muscular Dystrophy (x2)	Muscular Dystrophy Association
CRTS in Neuromuscular Disease	Muscle Study Group
(NEW) CRTS in Neurodisparities	Hearst Foundation & Eisai, Inc.
Lawrence Brass Stroke CRTS	American Heart Association
CRTS in Tourette Syndrome	Tourette Association of America
CSDA in MS	National MS Society (external)
2023 Awards	
Confirmed	
Award	**Partner**
CRTS in ALS and Related Disorders	CReATe Consortium
CTRS in Cognitive Aging and Age-Related Memory Loss (x2)	McKnight Brain Research Foundation
Lawrence Brass Stroke CRTS	American Heart Association
Susan Spencer, MD CRTS in Epilepsy	American Epilepsy Society & Epilepsy Foundation
CRTS in Parkinson's	Parkinson's Foundation
(NEW) CRTS in Peripheral Neuropathy (x2)	Foundation for Peripheral Neuropathy
(NEW) CRTS in Mal de Debarquement Syndrome	Mal de Debarquement Foundation

CRTS in ALS	ALS Association
Richard Olney CSDA in ALS	ALS Association
CRTS in Frontotemporal Degeneration	Association for Frontotemporal Degeneration
Pending	
CRTS in Neuromuscular Disease	Muscle Study Group
CRTS in Migraine	Amgen
CSDA in MS	National MS Society (non-AAN)
CRTS in Tourette Syndrome	Tourette Association of America
CRTS in Neurodisparities	TBD
CRTS in Muscular Dystrophy (x2)	Muscular Dystrophy Association

2024 Awards	
Confirmed	
Award	**Partner**
CTRS in Cognitive Aging and Age-Related Memory Loss (x2)	McKnight Brain Research Foundation
Lawrence Brass Stroke CRTS	American Heart Association
CRTS in Parkinson's	Parkinson's Foundation
CRTS in ALS	ALS Association
Richard Olney CSDA in ALS	ALS Association
Katzman CRTS in Alzheimer's	Alzheimer's Association
Pending	
CRTS in Neuromuscular Disease	Muscle Study Group
CRTS in Lewy Body Disease	Alzheimer's Association & Mary Groff Charitable Trust
Susan Spencer, MD CRTS in Epilepsy	American Epilepsy Society & Epilepsy Foundation
CRTS in Frontotemporal Degeneration	Association for Frontotemporal Degeneration
CRTS in Peripheral Neuropathy (x2)	Foundation for Peripheral Neuropathy
CRTS in Mal de Debarquement Syndrome	Mal de Debarquement Foundation
CRTS in Migraine	Amgen
CSDA in MS	National MS Society (non-AAN)
CRTS in Tourette Syndrome	Tourette Association of America
CRTS in Muscular Dystrophy (x2)	Muscular Dystrophy Association
CRTS in Neurodisparities	TBD
(NEW) CRTS for URiM Researcher	TBD
(NEW) CRTS in Child Neurology	TBD