



October 16, 2018

Maria C. Freire, Ph.D.
 President and Executive Director
 Foundation for the National Institutes of Health, Inc.
 11400 Rockville Pike, Suite 600
 North Bethesda, MD 20852

*Established by
 Evelyn F. McKnight
 to Alleviate Memory Loss
 in the Aging.*

Executive Director

Amy Porter
 Alexandria, VA
 aporter@mcknightbrf.org
 202-302-9849

Trustees

- J. Lee Dockery, M.D.
Gainesville, FL
- Michael L. Dockery, M.D.
Charlotte, NC
- Richard S. Isaacson, M.D.
New York, NY
- Susan L. Pekarske, M.D.
Tucson, AZ
- Nina Ellenbogen Raim, M.D., J.D.
Miami Beach, FL
- Gene G. Ryerson, M.D.
Gainesville, FL
- Madhav Thambisetty, M.D., PhD.
Ellicott City, MD
- Robert M. Wah, M.D.
McLean, VA

Corporate Trustee

Melanie A. Cianciotto
 SunTrust Bank

Project Title:	Research Partnership in Cognitive Aging III
Term:	7 years
Funding Amount:	\$5,000,000

Dear Dr. Freire,

This Letter of Agreement (“Agreement”) sets forth the terms under which the McKnight Brain Research Foundation (“Organization”) will provide continued funding in support of our Research Partnership in Cognitive Aging (hereinafter referred to as “Project”), a public-private partnership coordinated by the Foundation for the National Institutes of Health, Inc. (“FNIH”), a Maryland 501(c)(3) not-for-profit organization. Hereinafter, Organization and the FNIH are referred to individually as a “Party” and collectively as the “Parties.” Organization is providing funding with the understanding that the funds will not be used to promote any Organization products or services.

The purpose of the FNIH pursuant to 42 U.S.C. 290b is to support the mission of the National Institutes of Health (“NIH”) by organizing and administering research programs; supporting education and training of new researchers; organizing educational events and symposia; and administering a series of funds that support a wide range of health challenges.

The purpose of the Project is to fund a research grant making program in partnership with the National Institute on Aging (“NIA”). Specifically, funding would support an initiative, approved in concept by the NIA’s National Advisory Council on Aging in May 2018, to establish a *Network for Identification, Evaluation and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age*.

Although chronological age itself remains the strongest predictor of age-related cognitive decline and many forms of dementia, it has become clear that there are protective factors against these outcomes that are poorly understood. These

factors have often been described as imparting resilience to age-related changes in brain structure or neuropathology, building of cognitive and/or brain reserve that would oppose such age-related changes or frank pathology, or else augmenting other types of cognitive and brain function that would be beneficial. Some of these protective factors might suggest important intervention strategies.

At least two research groups in the U.S. have identified individuals who, despite their advanced age, have the cognitive performance of individuals 20 to 30 years younger. Although these so-called cognitive “super agers” are believed to constitute a very small minority of older individuals, they represent an unparalleled resource in which to study the behavioral, environmental, health, neural and genetic profiles that lead to sustained cognitive and brain function in advanced age. The opportunity to study these individuals in depth is expected to reveal important information about the factors that are critical for maintenance of function, as well as the factors that do not figure prominently. This initiative will require a multi-site, systematic effort to identify individuals with sustained cognitive function in advanced age. Once established, the network is expected to yield a research cohort of sufficient size to enable important research to be performed and key questions to be answered.

The current scope of the Project is as set forth in the proposal entitled “*Establishing a Network for Identification, Evaluation and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age Proposal*” provided in Attachment A.

1. **Term:** The term of this Agreement (“Term”) shall begin on the date last signed below (“Effective Date”) and terminate the later of a) the date Organization has remitted all Funds to the FNIH and b) May 1, 2025, unless this Agreement is terminated earlier pursuant to Section 9.
2. **Funding:** Organization desires to assist the Project by providing funding to the FNIH as set forth below:
 - a. **Funding Amount:** Organization agrees to provide the FNIH with a total commitment of five million US Dollars \$5,000,000 (the “Funds”), payable according to the following schedule:

Organization’s funding is conditioned upon NIA’s investment of at least \$5 million in grant funding in this research partnership over the five-year period.

- i. Payment 1: \$1,000,000, payable on or before June 1, 2019, within thirty (30) days after receipt of an invoice as described in Section 2.c;
- ii. Payment 2: \$1,000,000, payable within thirty (30) days after receipt of an invoice, such invoice may be issued on or after May 1, 2020;
- iii. Payment 3: \$1,000,000, payable within thirty (30) days after receipt of an invoice, such invoice may be issued on or after May 1, 2021;
- iv. Payment 4: \$1,000,000, payable within thirty (30) days after receipt of an invoice, such invoice may be issued on or after May 1, 2022; and

- v. Payment 5: \$1,000,000, payable within thirty (30) days after receipt of an invoice, such invoice may be issued on or after May 1, 2023.
- b. *Use of Funds:* The FNIH shall use the Funds provided by Organization solely for the purpose of funding the Project, including the FNIH's direct and related indirect costs; indirect costs shall be limited to five (5) percent of each payment received.
- c. *Time and place of payment:*

Invoices relating to this Agreement may be sent to:

Melanie A. Cianciotto
Corporate Trustee
McKnight Brain Research Foundation
SunTrust Bank
200 S. Orange Avenue
SOAB-10
Orlando, FL 32801
407-237-4485
Melanie.Cianciotto@suntrust.com

Copy to:

Amy Porter
Executive Director
McKnight Brain Research Foundation
8733 Plymouth Road
Alexandria, VA 22308
202-302-9489
aporter@mcknightbrf.org

Payments shall be made according to the schedule in Section 2.a. and delivered via check by Organization to:

Foundation for the NIH
c/o Maria C. Freire, Ph.D.
11400 Rockville Pike, Suite 600
North Bethesda, MD 20852

Or sent via electronic transfer to:

SunTrust Bank
1 Park Place
Atlanta, GA 30303
Account #: 209004037
Routing #: 055002707
ABA#: 061-000-104
SWIFT Code: SNTRUS3A
For the account of the Foundation for NIH

3. **Content and Administration:** The FNIH will provide funds to the NIA for use in funding the Project, consistent with a Memorandum of Understanding to be put in place between NIA and FNIH. Organization acknowledges and agrees that NIA will establish and coordinate the grant-making program and will have responsibility for and control over the solicitation, funding, and administration of any contracts or agreements related to the Project.
4. **Organization's Communications:**
 - a. **Communication About the Project:** The Parties agree that interaction and communications about the Project shall be coordinated by or through the FNIH throughout the life of the Project. The FNIH will provide Organization with progress reports and other updates on the Project, based on materials and information provided by the NIA, and may participate in and/or authorize communications between the NIA and Organization as indicated in Section 4b.
 - b. **Communication with NIA:** Organization understands and acknowledges that the NIA is a government agency and therefore Organization is prohibited from unduly influencing the NIA. Organization represents that it has not made any attempt to unduly influence the NIA or any government agency and will not communicate directly with the NIA with respect to the Project without the inclusion or prior written consent of the FNIH, which will not be unreasonably withheld. Organization may also receive Project progress reports and site visit invitations directly from the NIA, in addition to reports and updates to be provided by the FNIH, and will include the FNIH in its response to any such NIA communications.
 - c. **Communication with Awardee:** To the extent any Project funds are provided to an Awardee (as defined below), Organization represents that it has not made and will not make any attempt to unduly influence the Awardee. Further, Organization will not communicate with an Awardee with regard to the Project without the prior written consent of the FNIH, except when such communications have been arranged by the FNIH (or by NIA with the inclusion of the FNIH) in order to provide progress reports and other Project updates to Organization.. "Awardee" shall mean any person(s) or institution(s), recommended or approved by the NIA to perform activities for the Project with support in whole or in part to be provided by funds raised or to be raised by the FNIH.
5. **Disclosures:** The Organization's participation in the Project may be disclosed at any time by the FNIH, but (except as required by process or law) the FNIH may not disclose the details of Organization's Funds or other rights and obligations of Organization under the Project without Organization's prior written permission. Subject to Section 7, Organization may disclose the existence of the Project and Organization's participation in the Project at any time after the official public announcement of the Project by the FNIH (or the NIH).

6. **No Relation to Organization's Business; Compliance with Law and Ethical Business Practices:** The Organization and the FNIH acknowledge and agree that the Organization's funding of the Project is not in any way conditioned upon any present or future business relationship between the Organization and the FNIH.
7. **Organization Involvement and Recognition:** Organization will be acknowledged for its partnership with the NIH and the FNIH and recognized for its contributions, including being listed as an FNIH donor in the FNIH annual report. In FNIH promotional materials related to the Project or in recognition for its contributions, Organization's name will appear as set forth in the first paragraph above or as approved by Organization in writing. The FNIH will work with Organization to appropriately acknowledge Organization in such communications regarding the Project and on the FNIH's web site, www.fnih.org. The FNIH agrees to share drafts of such communications with Organization, and shall normally allow Organization five (5) business days to review and comment on it, prior to its public availability or dissemination. Organization agrees to review communications for correct attribution, affiliations and/or participation of Organization with the Project. Any additional feedback from Organization on the text of the communications will be considered in good faith but not guaranteed to be incorporated into the final copy. The FNIH will disseminate or provide a final copy of such communications to Organization, which Organization agrees to disseminate to its key audiences through social media, email communications, etc. It is understood that Organization will share the final version of all print and electronic communications materials regarding the Project, including news releases, with the FNIH for review, comment, and approval prior to public availability or dissemination.
8. **Early Termination:** This Agreement may be terminated prior to the end of the Term under either of the following circumstances:
 - a. In the event of a material breach, the non-breaching Party will notify the breaching Party in writing of the breach and include a description of the material breach ("Notice of Breach"). If the breaching Party fails to rectify the breach to the reasonable satisfaction of the non-breaching Party by thirty (30) business days from receipt of the Notice of Breach, the non-breaching Party may immediately terminate the Agreement on written Notice (as provided below) to the breaching Party.
 - b. In the event the NIH/NIA decides to close the Project prior to Organization remitting all Funds due, or otherwise for reasonable cause, the FNIH may, in its own discretion, terminate this Agreement on thirty (30) days' Notice to Organization. In such circumstance, the Organization will have no further obligation to the FNIH under this Agreement except to the extent the FNIH requires Funds to cover FNIH costs to close the Project, provided in no event will the total Funds to be paid by Organization to the FNIH under this Agreement exceed the total commitment of Funds set forth in Section 1.a.
9. **Disposition of Unused Funds:** Upon termination of this Agreement, in the event there are uncommitted and unexpended Funds, the FNIH shall with Organization's written consent redirect them to another FNIH project or purpose or, at Organization's request, return all uncommitted Funds to Organization. Expiration or termination of the funding

will not affect any rights or obligations which have accrued prior thereto. For avoidance of doubt, Funds allocated to FNIH direct and indirect costs for Project management are committed funds and the FNIH shall retain any interest earned on the Funds.

10. **Notices:**

- a. **Generally:** Any notice in connection with this Agreement ("Notice") will be in writing and deemed given as of the day it is: (i) Delivered to the receiving Party by an internationally recognized express delivery service, recipient signature required; (ii) Delivered to the receiving Party by first class registered or certified mail; or, (iii) If delivered by email, acknowledged by the receiver by return email, addressed as set forth below:

To Organization:

Amy Porter
Executive Director
McKnight Brain Research Foundation
8733 Plymouth Road
Alexandria, VA 22308
202-302-9489
aporter@mcknightbrf.org

Copy to:

Melanie A. Cianciotto
Corporate Trustee
McKnight Brain Research Foundation
SunTrust Bank
200 S. Orange Avenue
SOAB-10
Orlando, FL 32801
407-237-4485
melanie.Cianciotto@suntrust.com

To the FNIH:

Foundation for the NIH
Attn: Grants and Contracts Department
11400 Rockville Pike, Suite 600
North Bethesda, MD 20852
Email: Contracts@fnih.org
with copy to Development@fnih.org
Telephone: 301-594-7121

- b. **Changes to Notice:** Either Party may change the persons eligible to receive Notice, or the address where Notice must be sent, by giving Notice to the other Party.

11. **Responsible Personnel:** The primary contacts for the Project are:

Organization Contacts:

a. Amy Porter
Executive Director
McKnight Brain Research Foundation
8733 Plymouth Road
Alexandria, VA 22308
202-302-9489
aporter@mcknightbrf.org

Copy to:

b. J. Lee Dockery, MD
Chair, Board of Trustees
McKnight Brain Research Foundation
5200 S. W. 25th Blvd.; Unit #3215
Gainesville, FL 32608
352-377-5872
jld007@cox.net

Copy to:

c. Melanie A. Cianciotto
Corporate Trustee
McKnight Brain Research Foundation
SunTrust Bank
200 S. Orange Avenue
SOAB-10
Orlando, FL 32801
407-237-4485
Melanie.Cianciotto@suntrust.com

The FNIH Contacts:

a. Julie Wolf-Rodda
(or current) Senior Vice President of Development
301-402-6027
jwolf-rodde@fnih.org

b. Alison Drone
(or current) Development Officer
301-443-2103 adrone@fnih.org

c. Donald M. Hill
(or current) Chief Financial Officer
301-435-6246
dhill@fnih.org

d. Abbey Meltzer
(or current) Vice President of Communications
301-435-4103
ameltzer@fnih.org

Address for all FNIH Contacts above:
11400 Rockville Pike, Suite 600
North Bethesda, MD 20852

12. General Provisions

- a. **Amendments and Waivers:** Any term of this Agreement may be amended or waived only with the written consent of both Parties.
- b. **Assignment:** The Organization may not assign or subcontract any part of its duties, obligations, or rights hereunder without the prior written consent of the FNIH, which the FNIH may grant or withhold in its sole discretion.
- c. **No Third-Party Beneficiaries:** Nothing in this Agreement is intended to confer on any person other than the FNIH or the Organization or their respective successors or permitted assigns, any rights, remedies, liabilities or obligations under or by reason of this Agreement.
- d. **Integration:** This Agreement, including any exhibits and/or attachments hereto, constitutes the sole Agreement of the Parties and supersedes all oral negotiations and prior writings with respect to the subject matter hereof.
- e. **Choice of Law and Forum:** The laws of the State of Maryland shall govern the validity, interpretation, construction and performance of this Agreement, without giving effect to the principles of conflict of laws. The forum of any disputes shall be a court located in the State of Maryland and each Party hereby consents to the jurisdiction and forum of such court.
- f. **Legal Fees:** If any dispute arises between the Parties with respect to the matters covered by this Agreement which leads to a proceeding to resolve such dispute, the prevailing party in such proceeding shall be entitled to receive its reasonable attorney's fees, expert witness fees and out-of-pocket costs incurred in connection with such proceeding, in addition to any other relief it may be awarded.
- g. **Severability:** If one or more provisions of this Agreement are held to be unenforceable under applicable law, the Parties agree to renegotiate such provision in good faith. If the Parties cannot reach a mutually agreeable and enforceable replacement for such provision, then: (i) Such provision shall be excluded from this Agreement; (ii) The balance of the Agreement shall be interpreted as if such provision were so excluded; and, (iii) The balance of the Agreement shall be enforceable in accordance with its terms.
- h. **Survival:** The provisions of this Agreement which expressly or by their nature survive termination of this Agreement will remain in effect after the termination of this Agreement. For the avoidance of doubt, Sections 5 through 13 shall survive termination of this Agreement.
- i. **Advice of Counsel:** Each Party acknowledges that, in executing this Agreement, such Party has had the opportunity to seek the advice of independent legal counsel,

and has read and understood all of the terms and provisions of this Agreement. This Agreement shall not be construed against any Party by reason of the drafting or preparation hereof.

- j. **Non-Waiver of Rights**: The failure of either Party to insist upon performance of any provision of this Agreement, or to exercise any right, remedy or option provided herein, shall not be construed as a waiver of the right to assert any of the same at any time thereafter.
 - k. **Rights and Remedies Not Exclusive**: Unless otherwise expressly provided herein, no right or remedy of a Party expressed herein shall be deemed exclusive, but shall be cumulative with, and not in substitution for, any other right or remedy of that Party.
 - l. **Counterparts**: This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together will constitute one and the same instrument.
 - m. **Interpretation**: The captions and headings used in this Agreement are solely for the convenience of the Parties, and shall not be used in the interpretation of the text of this Agreement. Each Party has read and agreed to the specific language of this Agreement; therefore no conflict, ambiguity, or doubtful interpretation shall be construed against the drafter.
 - n. **Limitation of Liability**: The duties of the FNIH and the Organization shall be confined to those expressly set forth herein, and no implied duties are assumed by or may be asserted against either Party hereunder. The Parties shall not be liable for any error of judgment or mistake of law or for any loss arising out of any act or omission, including, without limitation, any act or omission in the performance of its duties under this Agreement, except to the extent liability or loss arises from the willful misfeasance, bad faith or gross negligence of such Party. As used in this Section, the term "FNIH" shall include the FNIH, its affiliates and their respective directors, officers and employees, and the term "Organization" shall include Organization, its affiliates and their respective directors, officers and employees.

Under no circumstances shall the Parties be liable to each other for any special, indirect, punitive, or consequential damages of any kind (including but not limited to lost profits, income, savings, business, or goodwill) in connection with any matter arising under or relating to this Agreement, regardless of whether such liability is based on breach of contract, tort (including negligence), strict liability, breach of warranty, or any other theory, even if such Party has been advised of the possibility of such damages.
 - o. **Relationship of Parties**: Nothing in this Agreement creates a partnership or joint venture between the Parties (e.g., use of the term "partnership").
13. **Suspension of Rights**: Organization's rights, and the FNIH's obligations to Organization, under this Agreement shall be suspended during the period covered by any canceled or delayed payment.

[SIGNATURES BEGIN ON THE NEXT PAGE]

The FNIH and Organization shall indicate acceptance of this Agreement and certification that these funds will be used in support of the indicated Project by having an authorized representative of the FNIH and Organization sign this Agreement.

Sincerely,

McKnight Brain Research Foundation

By: Amy Porter

Name: Amy Porter

Title: Executive Director

Date: October 16, 2018

Foundation for the National Institutes of Health, Inc.

By: Maria C. Freire

Name: Maria C. Freire, Ph.D.

Title: President and Executive Director

Date: 10-23-18

JLR 10-22-18

DA 10-22-18

KAK 10/22/18

**Attachment A
Proposal**

**Establishing a Network
for Identification, Evaluation and Tracking
of Older Persons with Superior Cognitive Performance
for Their Chronological Age**

The Need

With a rapidly growing aged population, maintenance of cognitive function has become increasingly critical for the health, welfare and well-being of United States citizens. According to a recent survey conducted by the AARP, virtually all adults age 40+ believe maintaining or improving brain health is important; three-quarters of adults age 40+ are concerned about their brain health declining in the future.

Although chronological age itself remains the strongest predictor of age-related cognitive decline and many forms of dementia including Alzheimer's disease (AD) and Alzheimer's disease and related dementias (ADRD), it has become clear that there are protective factors against these outcomes that are poorly understood. These factors have often been described as imparting resilience to age-related changes in brain structure or neuropathology, building of cognitive and/or brain reserve that would oppose such age-related changes or frank pathology, or else augmenting other types of cognitive and brain function that would be beneficial. Some of these protective factors might suggest important intervention strategies.

At least two research groups in the U.S. have identified individuals who, despite their advanced age, have the cognitive performance of individuals 20 to 30 years younger. Although these so-called cognitive "super agers" are believed to constitute a very small minority of older individuals, they represent an unparalleled resource in which to study the behavioral, environmental, health, neural and genetic profiles that lead to sustained cognitive and brain function in advanced age. The opportunity to study these individuals in depth is expected to reveal important information about the factors that are critical for maintenance of function, as well as the factors that do not figure prominently. Examples of relevant research questions include but would not be limited to:

- Do cognitive super agers demonstrate exceptional performance for their age in cognitive domains other than memory?
- Do cognitive super agers have social networks and/or personality factors that distinguish them from typical agers?
- What factors—behavioral, neural and/or genetic—distinguish cognitive super agers from typical agers and what factors are shared between cognitive super agers and those who show decline/impairment?

- Are cognitive super agers able to “tolerate” amyloid and/or tau accumulation in the brain without accompanying cognitive decline/impairment?
- Do autopsy data reveal structural and neurochemical signatures in cognitive super agers that differ from typical agers?
- What is the trajectory of age-related performance across multiple domains in the cognitive super agers? Are these trajectories highly individualized? Or associated with stability or change in the neural environment (activation, connectivity, white matter integrity, etc.)?

The Network

In April 2017, the National Institute on Aging (NIA), in partnership with the McKnight Brain Research Foundation (MBRF) and the Foundation for the National Institutes of Health (FNIH), conducted the Cognitive Aging Summit III, the specific focus of which was the concepts of cognitive reserve and resilience. The Summit brought together a multidisciplinary group of investigators with shared interest in research on age-related cognitive decline as well as cognitive reserve and resilience, as compared to cognitive impairment or dementia. Recommendations from the Summit included the specific suggestion to establish a network to study cognitive “super agers” which would help to escalate the research enterprise for discovery of factors for resilience, reserve, compensation, and/or preservation of cognition. Because the numbers of individuals identified and followed at any one site to date are small, a structure to allow uniform identification of individuals and uniform data collection would allow the field to push forward more quickly in our understanding of factors that promote sustained cognitive health and those that are not of primary importance.

*The NIA's National Advisory Council on Aging recently approved a concept to establish a **Network for Identification, Evaluation and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age**. This initiative will require a multi-site, systematic effort to identify individuals with sustained cognitive function in advanced age. Once established, the network will yield a research cohort of sufficient size to enable important research to be performed and key questions to be answered.*

Milestones would be incorporated into the early phases of the research to insure operationalization of criteria for cognitive super agers and to develop the plan for identification of these individuals at multiple sites. Based on estimates from one U.S. site, between 5-10% of 80+ aged individuals who self-identify for possible study inclusion would truly meet the eligibility requirements to be enrolled as cognitive super agers. Current criteria to identify cognitive super agers are based on memory performance that is comparable to individuals 20-30 years younger and appears to represent maintenance of this function into older age. In other words, the super agers are not individuals of superior intellect from early in life, but rather are exhibiting a notable lack of decline or impairment in memory performance with advancing age.

Harmonization protocols and uniformity in identifying and evaluating multiple variables (imaging, blood biomarkers, social and personality assessment, lifestyle factors, cognitive

assessment, genetic/epigenetics evaluation, etc.) would escalate data collection and allow comparison across sites, including internationally. Histopathological examination of brain tissue in individuals who come to autopsy would be an important component. Recruiting close family members (siblings, parents if possible) who do not show the same sustained cognitive performance, but perhaps more typical age-related cognitive decline would provide for an important comparison group.

The proposed initiative would provide for establishment of a network to identify, evaluate, and track cognitive super agers within the U.S. across multiple sites; plans for identification of these individuals on an international basis could be encouraged as well.

The Opportunity

The McKnight Brain Research Foundation has been an essential and generous partner to the National Institute on Aging and the Foundation for the National Institutes of Health for more than a decade. The FNIH now invites the MBRF to renew its commitment to the Research Partnership in Cognitive Aging and help to fund the establishment of the *Network for the Identification, Evaluation and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age*.

A \$5 million commitment from the MBRF will provide essential support to the Network. Payable in equal annual installments over a five-year period beginning in 2019, this gift would leverage the federal investment necessary to meet the anticipated budget need of approximately \$20 million.

With support from the McKnight Brain Research Foundation, this initiative can serve to improve our understanding of healthy aging, accelerate discovery of the causes and risk factors associated with disease and disability among older adults, and open a new path for discoveries and improved brain health for our aging population.