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June 14, 2018

C. Munro Cullum, Ph.D., ABPP
Science Director, Texas Alzheimer's Research and Care Consortium

Dear Munro:

In our many previous EAC meetings to review and provide comment on the activities of TARCC, my EAC colleagues and I have noted on several occasions that our strongest advice is to leverage the Mexican American cohort to advance research in this understudied realm. Additionally, a primary goal noted for use of state funding should be to increase scientific productivity, and, to the extent possible, with an emphasis on more work in multi-site projects that utilize TARCC data. Another important accomplishment we were pleased to see was the implementation of the Compliance Committee that spent painstaking time reviewing individual TARCC cases from all sites and provided uniformity to the consensus diagnoses in the dataset. This, combined with the overhaul of the TARCC database interface which is underway, will greatly enhance the accessibility of TARCC data to participating sites and investigators and facilitate use of the valuable data that have been collected thus far. We see these steps as a natural and important progression for TARCC.

The Council approved in February 2018 a second round of the Investigator Grant Program (IGP) funding, which the EAC applauds. The IGP in its current iteration is a natural next-step to maximize the state appropriation, increase utilization of the now-mature TARCC database, and encourage unique and targeted expansion of the Mexican-American cohort through funding of the best science possible. This has the potential to ultimately lead, through meritorious science, to important discoveries and publications in high impact journals. A natural companion piece should be a TARCC- focused state conference on AD and neurodegenerative disorders, highlighting and encouraging research and collaboration across Texas.

This year, the EAC was charged with reviewing the top-ranked IGP applications that were thoroughly vetted through an NIH-like review system under the direction of the TARCC Scientific Director. The process you have employed to solicit, review, and score the applications TARCC received has been both rigorous and consistent with the high standards of peer review. The quality and number of out-of-state reviewers that have participated in your effort is significant and impressive, as was the response to the TARCC call for proposals, which resulted in 64 completed applications. Modeling the NIH scoring system as you did is fair and understandable, and provided an excellent format on which the EAC could make its funding recommendations.

My distinguished fellow members of the EAC recommend to you for funding a total of 13 grants, including two collaborative and 11 single site- driven projects. The individual site grants recommended reflect both mainstream and novel science, and the collaborative grants are unique and critical.

While we offer congratulations to those recommended for funding, it is important to note that a number of worthy projects will not be awarded due to funding limitations. Many important things are occurring in Texas AD research, and TARCC's efforts are to be commended. With this new direction for TARCC, we are even more enthusiastic about the forthcoming research discoveries from Texas and look forward for continued opportunities to assist TARCC as it continues to move ahead.

Sincerely,

Ronald C. Petersen

Ronald C. Petersen, Ph.D., M.D.
Mayo Clinic - Chair, TARCC External Scientific Advisory Committee

Signed on behalf of
Douglas Galasko, M.D. (UCSD), Kristine Yaffe, M.D. (UCSF) Gerard D. Schellenberg, Ph.D. (U. Penn)
rcp/djc

TARCC 2018 Investigator Grant Program

Grant Submission and Review Process

65 Applications received from 9 Texas medical schools

Baylor	7
TAMUHSC	5
Tx Tech	2
UNTHSC	7
UT Dell	2
UT Houston	6
UTHSC-SA	8
UTMB	9
UTSW	19

REVIEW PROCESS

The TARCC Scientific Director contacted leading experts in the field of Alzheimer's disease and related disorders who were asked to review 2 to 5 applications. In order to minimize the potential for conflicts of interest, all reviewers were from academic institutions (many from NIH-funded Alzheimer's Disease Centers) outside of Texas representing the fields of neurology, neuropsychology, neuropathology, neuroscience, and statistics. A total of 33 reviewers were identified and agreed to participate. Each application was assigned a primary and secondary reviewer based upon their area of expertise and focus of the application, with detailed multi-domain scoring in the style of an NIH review. Scoring was based upon scientific merit, programmatic relevance to the TARCC RFA, budgetary considerations, and overall TARCC research goals. The scientific review and scoring identified the highest-ranking applications for consideration by the External Advisory Committee.

The External Advisory Committee, under the direction of Dr. Ron Petersen, reviewed the scoring results of the scientific review members. The EAC, led by Dr. Petersen, each reviewed the highest-rated submissions and convened via teleconference to discuss and make funding recommendations to the TARCC Scientific Director. Each scientific review member and the EAC members received a nominal honorarium upon completion of their TARCC grant review duties.

The Council Chair was notified of the funding recommendations by the TARCC Scientific Director on June 14, 2018.

2018 TARCC EXTERNAL ADVISORY COMMITTEE

Ron Petersen	Mayo Clinic
Douglas Galasko	University of California at San Diego
Gerald Schellenberg	University of Pennsylvania School of Medicine
Kristine Yaffe	University of California at San Francisco

2018 SCIENTIFIC REVIEWERS

Erin Abner	University of Kentucky
Beau Ances	Washington University School of Medicine
Floyd Bloom	Scripps Research Institute
Mark Bondi	University of California at San Diego
Adam Brickman	Columbia University Medical Center
Meryl Butters	University of Pittsburgh
Melanie Chandler	Mayo Clinic
Derin Cobia	Brigham Young University
Julia Crook	Mayo Clinic
Carlos Cruchaga	Washington University School of Medicine
Charlie Decarli	University of California at Davis Health Science Center
Ramon Diaz-Arrastia	University of Pennsylvania School of Medicine
Kevin Duff	University of Utah Health Sciences
Sarah Farias	University of California at Davis Health Science Center
Chris Filley,	University of Colorado at Denver
Neill Graff-Radford	Mayo Clinic
Michael Greicius	Stanford University
John Hardy	University College London
Larry Honig	Columbia University Medical Center
Sterling Johnson	University of Wisconsin Madison
Robert Kane	University of Maryland and Georgetown University
C. Dirk Keene	Washington University School of Medicine
Maria Kounnas	University of California at San Diego
Joel Kramer	University of California at San Francisco
Richard J. Kryscio	University of Kentucky
Walter Kukull	University of Washington
Brendan Lucey	Washington University School of Medicine
Jennifer Manly	Columbia University Medical Center
Subbiah Pugazhenthi	University of Colorado at Denver
David Salmon	University of California at San Diego
Mary Sano	Mount Sinai School of Medicine
Kathleen Welsh-Bohmer	Duke University School of Medicine
Lei Yu	Rush University

TEXAS ALZHEIMER'S
RESEARCH AND CARE CONSORTIUM
A project of the Darrell K Royal Texas Alzheimer's Initiative

2018 RFA Review Template

Application #:

Principal Investigator(s):

Scoring Guide:

1 – Exceptional	4 – Very Good	7 – Fair
2 – Outstanding	5 – Good	8 – Marginal
3 – Excellent	6 – Satisfactory	9 – Poor

1. OVERALL IMPACT

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, impactful influence on research in AD and related neurodegenerative disorders in Texas, in consideration of the following review criteria. An application does not need to be strong in all categories to be judged likely to have major scientific impact. Proposals that utilize or build upon TARCC resources will be given priority (please see special emphasis section 3).

Overall Impact – Score:
Write a short summary here of the factors that informed your Overall Impact score:

2. SCORED REVIEW CRITERIA

Reviewers will consider each of the review criteria below in the determination of scientific and technical merit, giving a separate score for each item.

1. Significance – Score:
Strengths • **Weaknesses** •

2. Investigator(s) – Score:
Strengths •

Weaknesses

-

3. Innovation – Score:
Strengths • **Weaknesses** •

4. Approach – Score:
Strengths • **Weaknesses** •

5. Environment and Resources – Score:
Strengths • **Weaknesses** •

3. SCORED SPECIAL EMPHASIS REVIEW CRITERIA

Reviewers will consider each of the special review criteria below in the determination of giving a separate score for each item.

6. Relevance to TARCC Funding Priorities – Score:

The TARCC 2018 grant cycle is particularly interested in but not limited to:

- *Studies of MCI and AD in Hispanics*
- *Biomarkers of disease onset/progression*
- *Multidimensional diagnostic/prediction models*
- *Advances in neuroimaging*
- *Advances in assessment of cognitive decline*
- *Use of technology to aid in detection and monitoring of behavior*
- *Use of technology in advancing dementia assessment, monitoring, and/or caregiving*
- *Advances in caregiving, with a focus on collaboration and innovation*
- *Advances in therapeutic interventions*

Strengths

-

Weaknesses

-

7. Utilization of Existing TARCC Resources, Data, and/or Cohort – Score:

Collaborative proposals involving more than one TARCC site and those that utilize the existing TARCC database are encouraged. Additionally, individual or multi-site proposals that build upon or create a Hispanic TARCC clinical cohort for use in specific studies (e.g., that include biomarkers of disease onset/progression as noted above) are particularly encouraged.

Strengths

-

Weaknesses

-

Which data items from the application do you feel have value for the TARCC data core to capture centrally?

-

Which tissue samples from the application do you feel have value for the TARCC tissue bank to capture centrally?

-

4. FINAL NOTES AND/OR COMMENTS

8. Any additional comments. This could include comments on Human Subjects, Vertebrate Animals, Data Management, Data Sharing Plans, Deliverables, Timelines, and/or any other areas of special note or concern. Reviewers can also make suggestions for collaborative proposals if two or more applications address similar issues and might benefit from being combined.
Strengths • **Weaknesses** • **Is the budget and period of support a fair representation of the resources that would be needed to accomplish the project's scope?** •

TARCC 2018 Investigator Grant Program

Summary information on grants recommended for funding

COLLABORATIVE GRANTS RECOMMENDED FOR FUNDING

Longitudinal Continuation of TARCC Hispanic Cohort
UT Southwestern, UT Health Science Center San Antonio, Texas Tech Univ Health Science Center, UT Dell
(collaborative multi-site)
John Hart, Jr., M.D. $2,117,376
The proposal continues the TARCC Hispanic cohort across 4 TARCC sites to better understand neurodegenerative in Hispanics. Annual evaluations will include neurological, neuropsychological, cerebrospinal, MRI morphometrics, and resting-state fMRI measures.

Assessing the utility and effectiveness of monitoring technology for reducing caregiver burden for Alzheimer's Disease
Texas A&M Univ Health Science Center, Univ of North Texas Health Science Center, UT Dell
(collaborative multi-site)
Marcia Ory, Ph.D. $439,999
This proposal examines the effectiveness, usability, and user satisfaction of a patient tracking device via a wearable smartwatch for the patient matched with smartphone app for the caregiver that has communication, physical activity and impact monitoring, and tracking technology.

SINGLE SITE GRANTS RECOMMENDED FOR FUNDING

Immune profile investigations of Alzheimer's Disease
UT Southwestern
Ryan Huebinger, Ph.D. (Junior Investigator) $216,562
This proposal will compare cerebrospinal fluid and blood cells between patients with Alzheimer's Disease and Healthy Controls recruited from the TARCC cohort to examine the molecular and cellular differences of immunity related to anti-Abeta and anti-tau antibody production (through antibody genetics and the impact of innate cell expansion and CD4+ T cell contraction).

Tau seeding and strain identification across the spectrum of Alzheimer's Disease and Lewy Body pathology
UT Southwestern
Trung Nguyen, Ph.D. (Junior Investigator) $208,068
This proposal will provide a comparison of detailed alpha-synuclein and tau brain pathology of Alzheimer's Disease and Lewy Body disease by evaluating well-characterized human brains from the UT Southwestern Neuropathology Laboratory Brain Bank. Some of the brains from the brain bank may be TARCC participants.

Diastolic dysfunction and the development of dementia
UT Health Science Center San Antonio
Alicia Parker, M.D. $220,000
This proposal will examine the connection between diastolic heart problems as assessed by echocardiogram, brain structure and function changes as assessed by brain imaging, and cognitive impairment as assessed by neuropsychological testing. Participants will be recruited from the TARCC cohort and clinics at UTHSC-SA.

Blood biomarker for Alzheimer's Disease & disease progression: Phospholipids
UT Southwestern
Dwight German, Ph.D. $484,237
This proposal will develop a method to identify a blood biomarker for Alzheimer's Disease using a new advanced lipidomic approach with brain-derived blood exosomes using blood samples from the TARCC biobank.

Development of a blood test for Alzheimer's disease diagnosis
UT Health Science Center at Houston
Sandra Pritzkow, Ph.D. (Junior Investigator) $220,000
By using a cyclic amplification technique, this proposal seeks to develop a sensitive and objective laboratory-based diagnosis of Alzheimer's Disease through the detection of misfolded Abeta oligomers circulating in blood using samples from the TARCC biobank.

SINGLE SITE GRANTS RECOMMENDED FOR FUNDING - CONTINUED

Epigenetic risk factors for age at onset of Alzheimer's & MCI and metabolic dysfunction among non-Caribbean Hispanics and non-Hispanic whites
Univ of North Texas Health Science Center
Robert Barber, Ph.D. $710,804
This proposal will measure genomic DNA methylation and perform RNA sequence analysis of 600 samples from the TARCC biobank in order to understand the relationship between cognitive decline and metabolic dysfunction, and how it may differ in Mexican-Americans and non-Hispanic whites.

Establishing novel blood-based biomarkers for Alzheimer's Disease in the Texas Alzheimer's Research and Care Consortium
UT Health Science Center San Antonio
Mitzi Gonzales, Ph.D. (Junior Investigator) $220,000
This proposal will use 3,164 baseline serum samples from the TARCC biobank to examine biomarkers of neurodegeneration (tau, NFL, UCHL1, GFAP, sCD-14, YKL-40), their association with diagnostic accuracy and cognitive outcomes data in the TARCC database, and their association with APOE genotype.

Brain targeted RNAi therapy for Alzheimer's Disease
Univ of North Texas Health Science Center
Sangram Raut, Ph.D. (Junior Investigator) $211,970
In a mouse model, this proposal will examine the effects of using the brain enzyme Glycogen synthase kinase-3 to disrupt two key pathogenic factors in Alzheimer's Disease – amyloid precursor protein APP and tau.

Probing the role of glial endocytic genes and ROS on AB42-induced neurotoxicity
Baylor College of Medicine
Hugo Bellen, D.V.M., Ph.D. $383,020
Using flies and mice, this proposal seeks to determine which specific glial-endocytic genes contribute to both lipid droplet accumulation and Abeta 42 sequestration and will use this information to create a simpler mouse model of Alzheimer's Disease that can be used in research for pre-clinical modeling.

Stem cell-derived anti-inflammatory treatment for Alzheimer's disease
UT Health Science Center at Houston
Ines Moreno-Gonzalez, Ph.D. (Junior Investigator) $220,000
In a mouse model, this proposal will use stem cell neural precursors to develop a new approach for treating Alzheimer's Disease using a non-invasive intravenous therapy.

Multi target combinatory therapy for Alzheimer's Disease
UT Medical Branch at Galveston
Rakez Kayed, Ph.D. $220,000
Using an FDA-approved drug, FK506 (Tacrolimus, an immunosuppressive drug that promotes the proliferation of T cells), along with an anti-tau oligomer, this proposal will examine the effectiveness of the combined therapy in a mouse model of Alzheimer's Disease.

RECOMMENDED COLLABORATIVE GRANTS TOTAL: $2,557,375.00

RECOMMENDED SINGLE SITE GRANTS TOTAL: $3,314,661.00

RECOMMENDED COLLABORATIVE AND SINGLE SITE GRANTS TOTAL: $5,872,036.00