UT SOUTHWESTERN MEDICAL CENTER

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The Darrell K Royal Research Fund for Alzheimer's Disease
PO Box 5839
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Dear Mrs. Edith Royal, the DKR Fund Board of Directors, and Scientific Review Committee:

It is my great pleasure to submit this progress report for the scientific research project entitled: *The role of a novel AIF3 isoform in dementia,* which was supported by DKR fund.

Dementia severely interferes with daily life of patients. Neuronal cell death is a key feature in dementia and causes problems with memory, thinking and behavior. Unfortunately so far no effective treatment is available. The goal of our study is to understand the role of newly identified apoptosis inducing factor isoform (AIF3) in dementia. During the first year award period, we found that AIF3 was induced in dementia-associated diseases. Induction of AIF3 expression leads to progressive neuronal cell death, supporting our hypothesis that AIF3 is induced in dementia-related human diseases and might promote dementia pathogenesis. Attached please find the detailed progress report for the first year award period. The continued support will ensure the successful completion of this project, which might yield a new therapeutic target for the treatment of dementia.

Sincerely,

Yingfei Wang

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The Role of a Novel AIF3 Isoform in Dementia (Progress Report 2016)

Dementia severely interferes with daily life of patients. Neuronal cell death is a key feature in dementia and causes problems with memory, thinking and behavior. Unfortunately so far no effective treatment is available. The goal of our study is to understand the role of newly identified apoptosis inducing factor isoform (AIF3) in dementia.

Previously, we found that AIF3 was induced in Parkinson's disease (PD) patients with dementia. During the first year award period, we showed that AIF3 expression was induced in the human cortex and hippocampus tissues from AD patients at both mRNA and protein levels. The expression of AIF3 was also further confirmed by the Sanger sequencing. In parallel, we have also successfully set up the controlled cortical impact (CCI) traumatic brain injury mouse model in our lab. So far, we found that AIF3 was not obviously induced in brain 1 day after traumatic brain injury under the current conditons we tested. We are continuously testing AIF3 expression in multiple other traumatic brain injury conditions and other time points. Nevertheless, these data indicate that AIF3 is induced in AD and PD patients with dementia. In order to study the role of AIF3 in vivo, we have just established a tamoxifen inducible mouse model to overexpress AIF3 in the adult mouse brain. Next we will further study its direct role in dementia. The project is undergoing on schedule as we planned. Our current progress data support our hypothesis that AIF3 is induced in dementia-related human diseases and might promote dementia pathogenesis.