

## *The Judy Fund Sponsored Research Grants*

*Support from The Judy Fund has enabled thirteen teams of researchers to pursue the answers to important scientific questions about the causes of Alzheimer's disease, ways to prevent or detect the disease, and the best approaches for providing medical care for patients already affected by the disease or related disorders. These research studies have spanned the spectrum of scientific approaches for addressing these issues, and studies have provided important clues about the causes of Alzheimer's disease and ways to treat it. The following is a brief overview of each The Judy Fund sponsored research grant.*

For more information about the Alzheimer's Association's International Research Grants program, go to [http://www.alz.org/research/alzheimers\\_grants/overview.asp](http://www.alz.org/research/alzheimers_grants/overview.asp).

### **ZEN-15 – Marcia Gordon – Molecular Therapeutics to Mitigate Inflammation, Tauopathy and Degeneration**

Brain inflammation has been shown to play a role in the development and progression of Alzheimer's disease. These experiments are designed to investigate the effectiveness of seven novel anti-inflammatory therapies on preventing brain changes -- such as tangle formation and brain cell loss -- associated with Alzheimer's disease.

The studies will examine if new ways to regulate brain inflammation can prevent or slow the disease process. The investigators hope these findings will provide the evidence needed to move one or more of these approaches into human clinical trials.

### **ZEN-14 – Scott Brady - Signaling Pathways, Molecular Motors and Cell-Specificity in Alzheimer's Disease**

These experiments are designed to identify factors that make certain populations of nerve cells particularly vulnerable to damage and death in Alzheimer's disease. Therefore, protecting these nerve cells is critical to changing the course of the disease or even preventing the disease.

The results of these studies will provide insight into the molecular mechanisms of Alzheimer's disease, which can then lead to the development of novel therapeutics to prevent or slow disease progression.

### **ZEN-13 – Mark Tuszynski - MRI Guidance for BDNF Gene Delivery in Alzheimer's Disease**

These studies are developing a novel method to guide and deliver a protective protein directly into specific areas of the brain as a potential treatment for Alzheimer's disease. This protein, a growth factor, has the potential to prevent nerve cell loss and promote brain health.

The investigators also hope to show that this protein is safe when delivered directly into the brain. The intent of these preclinical studies is to pave the way to rapidly transition this growth factor into human clinical trials.

### **ZEN-11 – Randall Bateman - A Blood Isotope Labeled Amyloid-Beta Test for Alzheimer's Disease**

These studies are using novel methods to create a simple blood-based test to measure the levels and rates of clearance of beta-amyloid to help reliably detect and understand how this protein relates to the early stages of Alzheimer's disease.

These studies could lead to the development of the first ever blood-based biomarkers that could aid in the diagnosis of Alzheimer's disease, but most importantly could be used to monitor the effectiveness of treatments in clinical trials.

### **ZEN-10 – Suzanne Craft - Intranasal Insulin Analogue Effects on CSF and Imaging Biomarkers in MCI**

This pilot clinical trial will examine if intranasal administration of novel form of insulin can help prevent Alzheimer's-associated brain changes and cognitive decline in people with mild cognitive impairment (MCI) and early stage Alzheimer's disease. This study will provide critical data to determine if this therapy should move to more advanced clinical trials.

In addition, these studies may lead to a novel insulin-based therapy that could be used to help prevent or slow the progression of Alzheimer's disease.

### **ZEN-09 – Bradley Hyman - Untangling Tangles in Alzheimer's Disease**

These experiments examined how different forms of abnormal tau (neurofibrillary tangles or soluble tau) affect nerve cell damage and death in mouse models and human brain tissue. There are different hypotheses in the field as to the toxic form of tau. Identifying the damaging form will be essential to devising an effective treatment.

These studies provided new insight into the role of tau in Alzheimer's disease and suggest that soluble forms of tau called oligomers (multiple units of tau clumping together) are the toxic form. This information indicates that soluble oligomeric tau is an important target and novel therapies need to be developed to block the formation or to remove this form of abnormal tau.

### **IIRG-09 – Bradford Dickerson - Quantitative Neuroanatomic Biomarkers for Dementia Differential Diagnosis**

Often it is difficult to distinguish between different dementias, especially very early in the assessment process when symptoms are very mild and can mimic age-related decline. These studies used advanced brain imaging (MRI, fMRI) to create distinct "signatures" of brain changes that can help predict and diagnose Alzheimer's disease from other dementias.

These studies have led to the development of novel brain image analyses that can aid in the differential diagnosis of Alzheimer's from other dementias, as well as from changes seen in normal aging. The scanning and analyses developed here will also be useful in determining the effectiveness of treatments in clinical trials.

#### **ZEN-08 – William Jagust - The Detection of Alzheimer's Disease in Normal Older People**

This investigation used advanced brain imaging and sensitive cognitive testing in cognitively healthy older adults to detect early brain changes associated with Alzheimer's disease. They also investigated if increased cognitive activity is protective against the development of Alzheimer's disease.

The results of these studies have suggested that beta-amyloid accumulates in the brain very early, along with structural changes in the brain, all before symptoms appear. These imaging studies have helped outline a series of events leading to clinical dementia. Most importantly, enhanced cognitive activity was associated with lower levels of beta-amyloid in the brain. These findings suggest we have a method for early detection of amyloid build-up in the brain, allowing for a possible early treatment with potential therapies to prevent or slow the disease. In addition, this work has provided new information on the relationship between lifestyle factors and Alzheimer's risk.

#### **ZEN-07 George Perry - Mitochondrial Abnormalities in Alzheimer's Disease**

These studies examined how dysfunction in cellular structures important for energy production - called mitochondria -- may contribute to Alzheimer's-associated brain changes.

The results indicated that certain forms of beta-amyloid cause an abnormal cellular distribution of mitochondria leading to nerve cell dysfunction. These studies have shed light on the molecular mechanisms underlying nerve cell damage and death in Alzheimer's disease and suggest a potential novel therapeutic target.

#### **ZEN-06 – Ramon Diaz-Arrastia - Elevated Homocysteine as a Risk Factor for Progression from MCI to Alzheimer's Disease**

These studies have examined if elevated levels of a molecule called homocysteine, resulting from vitamin B12 and folic acid deficiencies, increases the risk of developing Alzheimer's disease in people with mild cognitive impairment (MCI).

Results of this work have provided novel information on the importance of elevated homocysteine being associated with brain cell death and an increased risk for converting from MCI to Alzheimer's Disease. These studies found no benefit of vitamin therapy in advanced stage Alzheimer's, but a trend was seen that earlier intervention may be more therapeutic and might be beneficial in prevention trials. More studies are needed to determine why homocysteine is elevated in Alzheimer's disease.

#### **ZEN-05 – Bruce Lamb - Gene-Environment Interactions in Alzheimer's Disease Mouse Models**

These studies used multiple genetically-engineered mouse models of Alzheimer's disease to study how environmental factors, such as diet and cholesterol levels, interact with increased genetic risk for developing Alzheimer's disease.

The results of these studies suggest that genetic background plays an important, but complex role in interacting with environmental risk factors of developing Alzheimer's disease.

#### **PIO-04 – Phillip Sloane - Improving Medical Care of Assisted Living Residents with Dementia**

These studies developed and implemented research-based “best practices” in clinical care of people with Alzheimer's disease who are residing in assisted-living facilities.

The results of these studies showed that monitoring and dispensing medications could be improved by using trained aides as effectively as licensed nurses. Additionally, improved dental care was implemented through education. The quality of life for individuals with dementia could be greatly improved by receiving consistent medications and by improving oral hygiene.

#### **IIRG03 – Edward Koo - APP- Induced gene transcription: Role in Alzheimer's Disease**

These studies examined how an important protein, Amyloid Precursor Protein (APP), and its metabolites can modify the expression of other genes. APP is the parent molecule from which beta-amyloid is formed. Beta-amyloid is a protein fragment that clumps into plaques, a hallmark of Alzheimer's disease.

Results of these studies showed that APP metabolism can up-regulate another gene that is involved in abnormally modifying tau protein, which forms tangles, the other important hallmark of Alzheimer's disease in the brain. These studies have helped us understand the underlying cascade of events in Alzheimer's-associated brain changes, and have set the ground work for identifying specific therapeutic targets for the treatment of Alzheimer's disease.