A Focus on the Future: Current ADRC Projects

By James Leverenz, MD and Lindsey Beach

The ADRC strives to identify Alzheimer's biomarkers and to improve Alzheimer's treatments, and we currently have three important projects underway that look to fulfill these two primary goals. These projects are directly dependent on the clinical information we gather from research participants at annual ADRC Registry follow-up visits and lumbar punctures. Below is an overview of these ongoing ADRC projects; we hope this overview will give you a clear snapshot of the questions our center is asking and the answers we are pursuing.

Cerebrospinal Fluid (CSF) Proteome of Geriatric Dementia: CSF Protein Profiling of Central Nervous System (CNS) Insulin Activity *Project Leader:* Thomas Montine, PhD, Alvord Professor of Neuropathology, University of Washington, Department of Pathology, Division of Neuropathology

Recent small patient trials have suggested that improving insulin activity in the brain can improve or protect thinking abilities in patients with Alzheimer's disease (AD) or mild cognitive impairment (MCI). This project has three main goals to better understand these findings. The first goal is to identify markers in CSF that change when brain insulin activity is increased. The second goal is to examine these same markers in conditions, such as MCI and AD, where brain insulin activity appears to be impaired. And the third goal is to examine the presence of these markers in brain tissue obtained from the ADRC autopsy program. The overall objective of the project is to improve our understanding of the biological processes that that underlie the effect of insulin on brain functioning as people age.

Therapeutic Effects of Intra-Nasal Insulin Detemir *Project Leader:* Suzanne Craft, MD, Professor, University of Washington, Department of Psychiatry and Behavioral Sciences

This project also focuses on the insulin effects in the brain of aging and Alzheimer's disease (AD). It is a clinical trial, which is a study that looks at treatment responses in living patients. The project examines how insulin that is administered through the nose in the form of a spray may affect the thinking abilities of patients with MCI and AD. In addition to examining thinking abilities, the project also observes biomarkers associated with AD to see how they respond to the nasal spray treatment.

Modulation of Abeta Peptide Accumulation and Neuron Damage In Vivo with Adult Bone Marrow Transplants *Project Leader:* Christopher D. Keene, MD, PhD, Assistant Professor, University of Washington, Department of Pathology, Division of Neuropathology

This project uses an animal model to develop better treatments for Alzheimer's disease. More particularly, the project tests a new, unique method for reducing the accumulation of the amyloid-beta protein in the brains of mice. The investigators are attempting to refine and better understand a method known as a mini-bone marrow transplant, a method that appears to successfully remove amyloid-beta protein from the brains of mice. The overall goal of the project is to learn how these mini-bone marrow transplants have an effect on amyloid-beta in the brain and how this technique might ultimately be applied to patients with AD.

Upcoming ADRC Pilot Projects

Aerobic and Resistance Training in Prediabetic African Americans *Project Leader:* Jeannine Skinner, PhD

Dr. Skinner's project will compare the effects of exercise and health education on the thinking abilities, insulin sensitivity, and levels of Alzheimer's biomarkers in a group of African Americans with prediabetes. Learn more about Dr. Skinner's project in the next issue of Dimensions.

Quantification of Abeta and tau in CSF by LC-MS/MS *Project Leader:* Andrew Hoofnagle, MD, PhD

This project aims to develop a new type of biomarker analysis to help translate already-known Alzheimer's biomarkers into practical, day-to-day diagnostic tests that can be reliably used in caring for people with Alzheimer's.