My participation as a Williams Scholar will allow me to further expand on my evolving research interests in the mechanisms of age-related glucose intolerance as well as learn more about gerontological research and the endocrinology of aging. This work is critical given the growing numbers of older people and high rates of type 2 diabetes in this population. Impaired glucose tolerance (IGT) is also common in elderly people and is an early stage in the progression to diabetes. However, relatively little is known regarding the pathophysiology of age-related changes in glucose tolerance.

Multiple risk factors for diabetes associated with aging likely predispose older people to develop glucose intolerance and increased insulin resistance. However, in elderly people, pancreatic β-cell function is impaired, and compensatory hyperinsulinemia does not occur.

Further loss of β-cell function as well as increased insulin resistance and increased hepatic glucose production (HGP) may lead to the eventual development of IGT and diabetes, although the exact sequence of events remains unclear.

Metformin is an effective treatment for type 2 diabetes and is thought to act by suppressing basal HGP and possibly improving insulin sensitivity. Recently, the Diabetes Prevention Program showed that both lifestyle and metformin interventions reduced the incidence of the development of diabetes in Americans with IGT. Metformin was effective in people less than age 60 but unexpectedly did not reduce the progression to diabetes in people greater than age 60. This surprising finding led to the development of the following objectives for my research proposal:

1. To examine the magnitude of impairment of HGP, insulin secretion, and insulin sensitivity in older people with IGT compared to younger people with IGT.

2. To determine if metformin improves insulin secretion in people with IGT, and, if so, whether this effect is less in older than younger people with IGT.

3. To determine if metformin decreases basal HGP in people with IGT, and, if so, whether this effect is less in older than younger people with IGT.

An improved understanding of the metabolic alterations associated with aging is important for the continued development of preventive and therapeutic strategies for this population at high risk for the development of diabetes and its complications.

My background thus far for a career in academic endocrinology has included strong clinical endocrinology training, the University of Michigan Master's Program in Clinical Research Design and Statistical Analysis, and mentored clinical research training supported by an individual National Research Service Award from the National Institutes on Aging. To build on this foundation, the ADA-ASP Young Investigator Innovation Award in Geriatric Endocrinology will allow me to pursue independent research interests with continued mentorship by a team of dedicated investigators with expertise in both geriatric medicine and diabetology. This award will also allow me to obtain formal training in gerontological research as well as to develop joint geriatric medicine and endocrinology clinical conferences and educational resources. In addition to the ongoing support of my mentorship team, the ADA-ASP award will greatly facilitate my continued evolution into an independent physician-scientist with a career in academic geriatric endocrinology.