

AMERICAN DIABETES ASSOCIATION-ASP YOUNG INVESTIGATOR AWARD IN GERIATRIC ENDOCRINOLOGY



AWARD RECIPIENT

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PROJECT

"FETUIN-A, ADIPOSITY, AND INCIDENT DIABETES IN OLDER PERSONS"

MENTORSHIP TEAM

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Obesity and diabetes mellitus have reached epidemic proportions. This is especially concerning among older adults because they bear the highest prevalence of both conditions, and are at highest risk for associated consequences such as cardiovascular and kidney diseases. While changes in diet and physical activity patterns have likely contributed to the ever increasing burden of obesity and diabetes, their impact is heterogeneous, and biochemical mechanisms contributing to this risk remain poorly understood.

Recently, novel insights to mechanisms leading to obesity and diabetes have been provided by the study of adipocytokines. Adipocytokines molecules are produced by fat cells, secreted into the blood stream, and are hypothesized to regulate glucose metabolism in peripheral tissues. In contrast, fetuin-A is produced by hepatocytes and secreted into the blood stream. Higher serum fetuin-A levels are associated with insulin resistance, increased body weight, and dyslipidemia in experimental animals. Conversely, fetuin-A gene knock-out mice are insulin sensitive, resistant to weight gain, and have less adiposity. In vitro studies demonstrate that fetuin-A binds the insulin receptor on muscle and fat cells and inhibits the action of insulin, resulting in insulin resistance in these target tissues. We previously demonstrated that higher fetuin-A levels are associated with insulin resistance and the metabolic syndrome in cross-sectional studies in humans. However, in comparison to adipocytokines, the potential effects of fetuin-A on incident diabetes risk and longitudinal change in body composition in humans is unknown.

With the support of the American Diabetes Association (ADA)-ASP Young Investigator Award in Geriatric Endocrinology, I will conduct an ancillary study nested within the National Institutes of Health-funded Health, Aging, and Body Composition (Health ABC) Study. Health ABC recruited black and white adults aged 70 to 79 years and extensively measured body composition and glucose metabolism. I will measure serum fetuin-A levels in blood specimens that were obtained at the baseline study visit. Subsequently, participants were followed longitudinally for six years and evaluated repeatedly for development of diabetes and changes in body composition.

We propose to take advantage of this rich resource to address the following aims:

1. To determine the cross-sectional and longitudinal associations of serum fetuin-A concentrations and incident diabetes in community-dwelling older persons.
2. To determine the cross-sectional and longitudinal associations of serum fetuin-A concentrations with adiposity and muscle mass among community-dwelling older persons.

In addition, the support of the ADA-ASP Young Investigator Award in Geriatric Endocrinology will foster my development as an independent leader in the clinical investigation at the interface of geriatric medicine, endocrinology, and nephrology. Through the guidance of my mentorship team, this award will enable me to acquire the additional training and mentored research experience I require to achieve this goal.