

Title: Development of F-18 labeled human IAPP analogs for imaging pancreatic islet amyloid deposits by PET

PI: Hariprasad Gali, Ph.D.

Agency: Presbyterian Health Foundation (Seed Grant)

Funding Period: 09/01/2008 through 08/31/2009

#### Abstract

Diabetes is a major health care issue that is reaching epidemic proportions. The most common form of diabetes is Type 2 diabetes, which affects about 90 to 95 percent of all patients diagnosed with diabetes. The pathogenesis of Type 2 diabetes is complex and in most instances clearly requires defects in both pancreatic beta-cell function and insulin sensitivity. A growing body of evidence from recent studies suggests that formation of islet amyloid deposits is a major contributor to the progressive loss of beta cells. These deposits are found in almost all diabetic patients. Islet amyloid is mainly composed of a 37-amino acid islet amyloid polypeptide (IAPP or amylin). Amyloidogenicity of the human IAPP is known to be due to its 20–29 amino acid region. Therefore, this region of human IAPP would be an excellent target for development of diagnostic and therapeutic agents for this disease. The overall goal of this project is to develop small peptide conjugates that bind human IAPP(20-29) with high affinity and inhibit amyloid formation. These conjugates when labeled with fluorine-18 enables positron emission tomography (PET) imaging facilitating both diagnosis and therapy. Non-invasive assessment of islet amyloid deposits would provide an important tool for both therapeutic interventions and better understanding of the natural history of the disease. Specific Aims: 1) Synthesize, radiolabel, and characterize a series of small peptide conjugates that bind human IAPP(20-29). 2) Evaluate *in vitro* binding using synthetically grown islet amyloid fibrils and determine their inhibition coefficient for amyloid formation. 3) Select a lead candidate and perform *in vivo* biodistribution and pharmacokinetic studies in normal mice. 4) Perform *in vivo* dynamic microPET imaging studies with the lead candidate.