

**Project Title:** Imaging pancreatic amyloid with PET

**Abstract:** Post-mortem analyses detect pancreatic amyloid aggregates in most type-2 diabetes mellitus (T2DM) patients, but rarely in type-1 patients and non-diabetics. Despite the lapse of a century since this initial discovery, the causal or correlative role of amyloidosis in T2DM pathology has yet to be fully resolved.

Like the pancreas in T2DM, the Alzheimer's disease brain exhibits amyloid deposits at autopsy. The amyloid aggregates prototypical of Alzheimer's and T2DM are not identical, but sufficiently alike that the same histological stains are used for both. [11C]PiB is a recently developed PET tracer used to image cerebral amyloid and derived from Thioflavin-T, which is used to stain pancreatic amyloid. To our knowledge, pancreatic amyloid imaging has not been attempted.

We aim to assess the feasibility of imaging pancreatic amyloid deposits using PET with the amyloid-targeting radiotracer [11C]PiB. We will confirm that [11C]PiB penetrates pancreatic tissue and binds to amyloid by comparing microPET/CT and ex vivo measurements of radiotracer uptake with histological assays in transgenic mice expressing self-aggregating human amyloid. PET/CT will noninvasively measure pancreatic [11C]PiB uptake in healthy humans and T2DM patients, and binding will be related to metrics of disease severity.

These experiments will determine the potential for noninvasive measurement of pancreatic amyloid with [11C]PiB PET. The pilot data collected here will provide initial validation of our method and the basis for future grant applications to verify findings in a larger cohort and explore amyloid deposition in longitudinal studies to elucidate the role of amyloidosis in the onset and progression of T2DM.