“Synthesis and Evaluation of Metal-Specific Chelating Radioligands”

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Early detection of neurodegenerative diseases (NDs) has remained challenging for clinicians. To improve diagnostic confidence across the ND spectrum, there is considerable research devoted to the discovery of potential biomarkers of disease onset and progression. Neurodegenerative Diseases (NDs) have the common feature of progressive loss of structure and function of neurons resulting from different protein aggregates responsible for the various diseases. Alzheimer’s Disease (AD), the most prevalent ND, is characterized by amyloid plaques (composed of amyloid ß (Aß) protein) and neurofibrillary tangles (composed of tau protein) within the hippocampal and cortex regions of the brain. Parkinson’s Disease (PD), the second most common ND, is caused by dopaminergic neuronal loss within the basal ganglia, which controls voluntary movement, as a result from α-synuclein (α-syn) aggregation within the same region. Biologically relevant transition metals such as iron, copper, and zinc are reportedly accumulating and causing the aggregation of known neurotoxic protein aggregates at sites afflicted by neurodegenerative diseases. Detecting such metal ions may provide a means of early detection of these otherwise hard to diagnose diseases through the use of positron emission tomography (PET) imaging agents. Radiopharmaceuticals available today for imaging of the central nervous system (CNS) are limited to those imaging the mid- to late-stages of CNS disease progression. The objective of this work is to design and analyze novel PET tracers that bind physiological transition metals (Cu, Zn, and Fe) which are hypothesized to accumulate abnormally in the brain early in NDs. Known metal chelators will be radiolabeled and used in preclinical animal studies to determine brain uptake, binding kinetics, metabolism, biodistribution, and be evaluated in both diseased brains and healthy controls. This presentation focuses on current efforts to radiolabel the FDA approved iron chelator, Deferiprone.