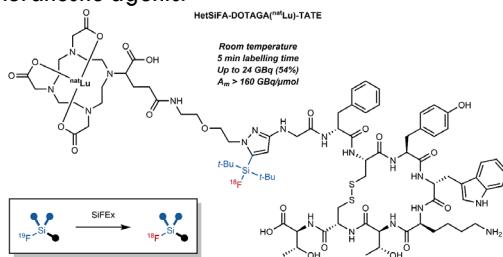


Dr. Thomas Singleton
Research Associate
Montreal Neurological Institute
Wednesday, March 8th 2023
11:00 a.m. to 11:50 a.m. in ENW 115

Peptidic theranostic radiopharmaceuticals based upon the silicon-fluoride bond

ABSTRACT

Radiolabeled peptides are an emergent family of imaging tools for the early diagnosis of certain cancers. In particular, the octapeptide TATE, incorporating positron-emitting isotopes, provides a powerful means of imaging somatostatin receptors (e.g. SSTR2) that are overexpressed on neuroendocrine tumors. Fluorine-18 is the preferred radioisotope for positron emission tomography (PET), but the typically harsh reaction conditions needed for its incorporation limit late-stage fluorination, and therefore, the development of ^{18}F -labeled peptides. This talk will describe a platform for the facile incorporation of ^{18}F using Heteroaromatic Silicon Fluoride Acceptors (HetSiFA's). HetSiFA's offer rapid ^{18}F incorporation under mild conditions via Silicon-Fluoride Exchange (SiFEx), making it ideal for the radiolabelling of complex molecular systems. He will report the design and synthesis of HetSiFA-DOTAGA(M)-TATE conjugates, and describe their theranostic potential for targeting SSTR2. Key features of their HetSiFA-TATE conjugates include excellent isolated decay-corrected radiochemical yields of up to 54% (max activity yield 24 GBq) and molar activity $>160 \text{ GBq}/\mu\text{mol}$ in 30 minutes. They also demonstrated facile incorporation of natural lutetium into the attached chelator as a mimic of the ^{177}Lu isotope commonly used for radioligand therapy. HetSiFA-DOTAGA(natLu)-TATE's show renal excretion and low defluorination under physiological conditions, suggesting a favorable pharmacokinetic profile for their potential application as new peptidic theranostic agents.



BIOGRAPHY

Thomas Singleton

Dr. Singleton received an Honours B.Sc. from Trent University in 2009 after working with Prof. Vreugdenhil for his undergraduate thesis, and a Ph.D. from McGill University in Materials Chemistry in 2015 with Prof. Chris Barrett. He subsequently held postdoctoral fellowships at the University of Manchester developing molecular machine catalysts (2015 – 2017 Royal Society Newton International Fellow with Prof. Dave Leigh) and the Montreal Neurological Institute (2017 – 2021 with Prof. Alexey Kostikov) developing novel radiotracers to expand the utility of PET imaging. He now works as a Research Associate at the Montreal Neurological Institute while also serving as Director of Discovery Chemistry with Fuzionaire Theranostics, a Texas-based startup, developing technology to allow the more rapid development of PET theranostics. A co-inventor on three patents and co-author of 12 peer-reviewed publications, Dr. Singleton's areas of experience include radiochemistry, materials, photochemistry and optics, and organic synthesis.