**Characterizing an 18F-Growth Hormone Secretagogue Probe for Positron Emission Tomography Imaging of Cardiac Growth Hormone Secretagogue Receptor**

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**Introduction:** Cardiovascular disease affects 1.6 million Canadians and nearly one-third of these patients have heart failure (HF). Patients with HF require repeat hospital admissions for inpatient acute care, accounting for the highest readmission rates in the country[1], and presenting a significant economic burden. Currently, HF is diagnosed using circulating biomarkers that are not cardiac-specific, and thus there is critical need for a biomarker that is endogenous to myocardial tissues. One potential biomarker is the growth hormone secretagogue receptor (GHSR), which binds the peptide hormone ghrelin. Activation of GHSR has various downstream effects, including protection of cardiomyocytes[2]. GHSR is expressed on the surface of cardiomyocytes and has been shown to be elevated in end-stage heart disease in humans[3,4]. This study employs Positron Emission Tomography (PET) imaging of GHSR expression using a novel 18F-Growth Hormone Secretagogue (18F-GHS), named 18F-[Tyr4,Lys5(2-FP)]G7039 (18F-G-7039), that binds to GHSR with strong affinity in vitro. This work characterizes 18F-G-7039 for in vivo imaging of cardiac GHSR expression as a biomarker for HF. We expect that the 18F-GHS PET probe will specifically bind cardiac GHSR and will sensitively detect changes in GHSR expression.

**Methods:** Whole body probe uptake was assessed by biodistribution in healthy female C57BL/6 mice in a fasted or fed state. The mice were injected i.v. via tail vein with 9-10 MBq of 18F-G-7039 and sacrificed at 1h (n=2), 2h (n=3), and 4h (n=2) when fasted and 1h (n=5), 2h (n=5), and 4h (n=5) when fed. Radioactivity in organs was calculated as % injected dose per gram of tissue sampled (%ID/g). Blood plasma samples, gathered from fasted (n=8) and fed (n=17) mice, were assessed for ghrelin levels by Luminex multiplex assay. For imaging, GHSR wildtype (GHSR+/+, n=5) and GHSR null (GHSR-/-, n=3) mice were injected with 9-10 MBq of 18F-G-7039 and scanned in an Inveon preclinical PET scanner (Siemens Medical Solutions) for 90 min and subsequently scanned in a clinical Revolution Computed Tomography (CT) scanner (General Electric) followed by biodistribution. Data analyses were performed using one-tailed t-test, two-way ANOVA and Tukey’s test, where significance was set at p<0.05.

**Results:** Plasma ghrelin levels are slightly elevated in fasted mice. Probe uptake was predominantly distributed to the lung, spleen, liver, and intestine in both fasted and fed mice. These results are supported by imaging.

**Conclusions:** We are characterizing a novel PET probe to target cardiac GHSR in vivo and have demonstrated its use. Future studies will quantify receptor expression in cardiac and pulmonary tissues and will evaluate 18F-G-7039 metabolites in whole blood.

**References:**