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Radiochemistry

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Radionuclides are important tools for tracing biological, chemical, and physical processes. The National Superconducting Cyclotron Laboratory (NSCL) and the upcoming Facility for Rare Isotope Beams (FRIB) have the potential to supply unique radioisotopes that are otherwise difficult to produce. The challenge of obtaining these rare isotopes from NSCL and FRIB is in the need for rigorous chemical or physical purification of sub-nanogram quantities of individual elements from a complex mixture of spallation and fragmentation products. The purpose of my research is to parse and purify the stock of co-produced radionuclides to obtain both high radionuclidic purity and high specific activity for application in basic science, medical, chemical and biological research. Of particular interest are transition and rare earth radiometals for use in the development of new diagnostics and therapeutics against invasive disease.

Radiometals in Medicine – Research into the molecular identity of cancerous and other malignant cells has identified biological vectors that can seek out disease sites in vivo. In order to trace the biodistributions and pharmacokinetics of these new vectors, preclinical Positron Emission Tomography (PET) has expanded beyond the organic and pseudo-organic radionuclides (^{11}C, ^{13}N, ^{14,15}O, ^{18}F) to include a host of longer-lived and unconventional radiometals (e.g. ^{44}Sc, ^{45}Ti, ^{52}Mn, ^{64}Cu, ^{89}Zr, and ^{140}Nd). Beyond receptor- and epitope-based PET, radiometals also facilitate development of metal-based drugs, allow tracing of the native and mimetic nature of metals in the body, can be used to track nanoparticle drug delivery vehicles, and in some cases have unique exploitable decay properties (e.g. ^{140}Nd in Figure 1 below). Further, the diagnostic metals are often isotopically matched to therapeutic nuclides, motivating a rapid transition from diagnostic imaging to targeted radionuclide therapy.

A new water-cooled beamstop at NSCL will provide access to a selection of radiometals including ^{47}Sc, a therapeutic analog to the positron emitter ^{44}Sc. ^{47}Sc forms following ^{47}Ca decay (Figure 2), which is co-produced in high yield during ^{48}Ca irradiations at NSCL.

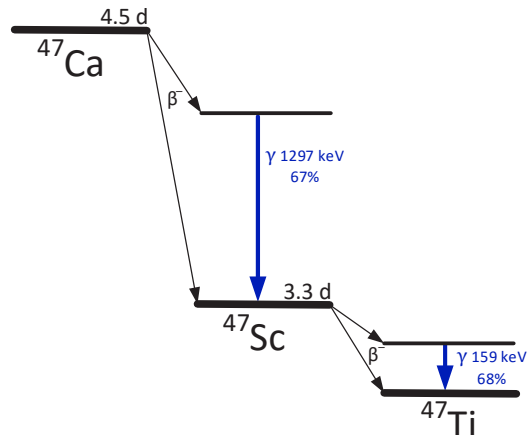

Figure 2: A simplified decay scheme for ^{47}Ca and ^{47}Sc. The low energy beta particles from ^{47}Sc are therapeutic, and the 159 keV gamma ray has an appropriate energy for imaging with single photon computed tomography (SPECT).

Isolation of ^{47}Ca allows production of a ^{47}Sc generator that extends the usable lifetime of ^{47}Sc in addition to providing it in high purity and with high specific activity.

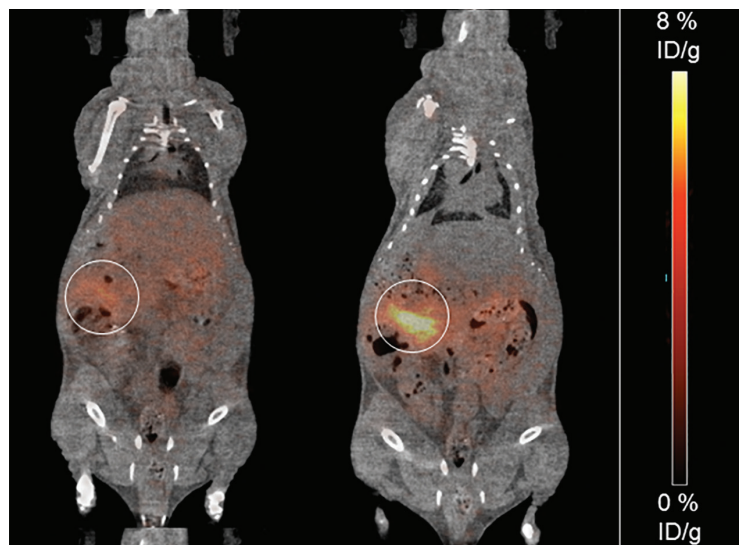

Figure 1: (left) Pre- and (right) post-mortem PET/CT scan of a mouse 16h after injection with a somatostatin receptor 2 (sst2) targeting peptide, DOTA-LM3, labeled with ^{140}Nd. The white circle is drawn over the pancreas (sst2 +) where the difference in the pre- and post-mortem pancreatic signal is due to rapid diffusion of ^{140}Nd's short-lived daughter nuclide, ^{140}Pr, from the highly perfused pancreas into the blood stream. With further development, similar techniques with ^{140}Nd may be used to determine the* in vivo *internalization status of labeled therapeutics.

Selected Publications

ImmunoPET/MR imaging enables specific detection in vivo *of* Aspergillus fumigatus *infection*, Rolle, A-M, *et al*., *Proc Natl Acad Sci* **2016**, *113(8)*, E1026–E1033.

Measurement of the branching ratio for the beta decay of ^{14}O, Voytas PA, *et al*., *Phys. Rev. C* **2015**, *92*, 065502.

Novel Preparation Methods of ^{52}Mn for ImmunoPET Imaging, Graves, SA *et al*., *Bioconjug. Chem.* **2015**, *26(10)*, 2118-2124.

Bringing radiotracing to titanium-based antineoplastics: solid phase radiosynthesis, PET and ex-vivo evaluation of antitumor agent [^{45}Ti](salan)Ti(dipic), Severin, GW *et al*., *J. Med. Chem.* **2015**, *58(18)*, 7591-7595.

The impact of weakly bound ^{89}Zr on preclinical studies: Non-specific accumulation in solid tumors and aspergillus *infection*, Severin, GW *et al*., *Nucl. Med. Biol.* **2015**, *42(4)*, 360–368.