TRANSLATIONAL MOLECULAR IMAGING

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Translational Molecular Imaging (TMI) develops novel imaging technologies and acts as a regional hub for molecular imaging research. Operating over three sites: the CRUK Scotland Institute, the West of Scotland PET Centre at Beatson Cancer Hospital and the Scotland Total-Body PET Facility, jointly managed with the University of Edinburgh. Our facilities house state-of-the-art PET radiochemistry and imaging equipment. Within the TMI, there is expertise in several key areas including PET chemistry, preclinical PET/MR imaging, clinical imaging and advanced image analysis. The TMI drives collaborative imaging research across our networks with a focus on developing and applying innovative imaging technologies, such as new PET radiotracers and MRI methodology for visualising cancer biology.

Projects in the TMI range from standard imaging studies where we facilitate access to imaging technology to much wider scale projects where the TMI acts as a collaborative partner in, for example the development of novel imaging agents or *in vivo* molecular phenotyping of new genetically engineered mouse models. The unique research environment at the CRUK Scotland Institute enables collaboration using its world-class cancer models to develop imaging biomarkers for new applications in tumour classification and personalised cancer therapy.

PET radiochemistry

We provide expertise and technology for the versatile development and labelling of a whole range of PET-labelled molecules. We have negotiated a Collaboration Agreement with the local Greater Glasgow and Clyde Health Board for open access to Glasgow's PETtrace 800 16.5MeV cyclotron, based at the PET Radiopharmaceutical Production Unit (RPU) in the West of Scotland PET Centre. We provide a range of radiolabelling collaborative opportunities around rapid carbon-11 and fluorine-18 labelling of novel PET radiotracers on our two automated multipurpose Synthra radiosynthesizers. These laboratories have the full range of radio-analytical equipment including a gamma-spectrometer, four HPLC instruments, gas-chromatography systems, radio-TLC scanner and pH-meters. Access to cold chemistry for precursor synthesis is by collaboration with the School of Chemistry (Sutherland). Since 2017, we have synthesized 18 PET radiotracers and we have developed five carbon-11 synthons (^{11}CO, $^{11}CO_2$, $H^{11}CN$, [^{11}C]CH_3I and [^{11}C]methyltriflate) with one more in development ([^{11}C]formaldehyde). This provides one of the most versatile radiolabelling laboratories in the world for carbon-11 development.

We have continued to support the extensive imaging programmes in the TMI with radiotracers such as [^{11}C]acetate, [^{18}F]fluoro-ethyl-tyrosine (FET), [^{18}F]terafluoroborate (TFB), [^{18}F]fluorodeoxyglucose (FDG), [^{11}C]methionine, (4S)-4-(3-[^{18}F]Fluoropropyl)-L-glutamate (FSPG), [^{11}C]leucine and [^{11}C]nicotinamide. To support our collaborative partners at the Edinburgh Imaging Facility, we have enabled radiosynthesis and quality control methods for production of [^{18}F]fluoroproline and [^{18}F]LW233 for on-going preclinical studies. These tracers, which target collagen synthesis and translocator protein (TSPO) respectively, are now available for cancer imaging studies in Glasgow.

In 2024, in collaboration with the University of Edinburgh we helped establish the UKRI/MRC Scotland Total-body PET Facility. This is now a national PET imaging facility, one of only three total-body PET scanners in the UK. This successful award also granted us inaugural membership in the national PET imaging platform (NPIP) and as a result, the Translational Molecular Imaging Facility is engaging in collaboration on new national projects focusing on total-body PET development. Additionally, this grant is supporting three new positions in radiochemistry and image analysis.

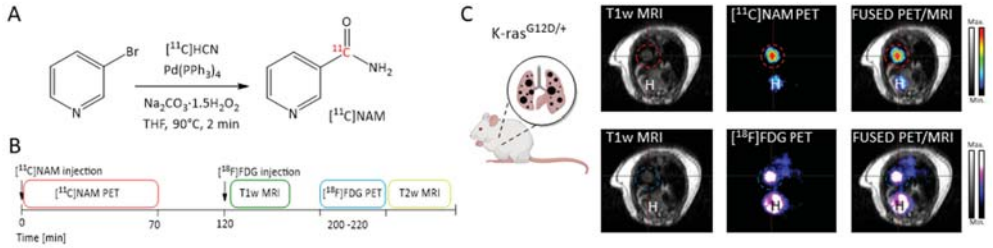

Figure 1. Tracing proliferating potential of lung tumours using [^{11}C]Nicotinamide. (A) Synthesis of [carboxyl-^{11}C] nicotinamide from 3-bromopyridine and hydrogen [^{11}C]cyanide by palladium catalysed reaction. (B) Dual-tracer sequential imaging protocol with [^{11}C]nicotinamide and [^{18}F]FDG. Dynamic PET was acquired between 0 and 70 min post-injection of 35 ± 5 MBq of [^{11}C]NAM per mouse and static PET was acquired between 80-100 min post-injection of 10 ± 2 MBq of [^{18}F] FDG/mouse with anatomical T1 and T2-weighted MRI. (C) Example of transversal T1-weighted MRI images, and PET images for [^{11}C]NAM (tumour circled red) at 30 min p.i. and [^{18}F]FDG (tumour circled blue) at 90 min p.i. in a K-ras$^{G12D/+}$ lung cancer model (n = 4 mice). H indicates [^{18}F] FDG PET signal from the heart.

Preclinical and translational imaging

In 2024, we supported research at our sister Institute at CRUK Cambridge to develop optimal timing and imaging of [^{18}F]FDG in tumours models (Hesketh *et al.*, 2024, *Mol Imaging Biol*) and optimising image co-registration methods (Lefebvre *et al.*, 2024). The latter was part of a series of UK-wide projects developed through the CRUK Radiation Centres of Excellence (RadNet) programme. We have also supported Thomas Bird's group to characterise mouse models of hepatocellular carcinoma (HCC) (Muller *et al.* 2025, in press). Building on collaborative work with Saverio Tardito, we continued development of [^{11}C]nicotinamide, vitamin B3, in this case as a biomarker of highly proliferative lung cancer (Figure 1).