TRANSLATIONAL MOLECULAR IMAGING (TMI)

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The Translational Molecular Imaging facility has been renamed and relaunched to reflect its extended capabilities and broad new scope. The purpose of this new unit is to enable the clinical translation of novel molecular imaging approaches from preclinical cancer models at the Institute into innovative clinical trials. Investment from the Beatson Cancer Charity of £240k/year is allowing critical infrastructure investment in radiochemistry, including recruitment of a Senior PET Chemist, Dmitry Soloviev.

PET Radiochemistry

The Cyclotron Facility at Gartnavel Hospital currently supports routine production of FDG (fluorodeoxyglucose) and a small number of other fluorine-18-labelled clinical tracers. In 2017 we recruited a new Senior PET Chemist, Dmitry Soloviev, who brings world-class expertise in carbon-11 labelling of metabolites for cancer imaging. Carbon-11 is a highly versatile radiolabel, allowing tracing of many endogenous metabolic pathways. We are building new capacity at the Radiopharmaceutical Unit of the West of Scotland PET Centre by providing a new radiochemistry platform that will facilitate the development of new carbon-11- and fluorine-11-labelled PET probes. We are upgrading the cyclotron and ancillary radiochemistry equipment to work with carbon-11-labelled gaseous products and are installing two identical, universal and automatic $^{11}C/^{18}F$ synthesisers (Synthra GmbH, Germany) in the R&D and GMP radiolabelling suites (Fig. 1). Any radiotracer developed for preclinical research will be available for rapid translation to human studies at the Radiopharmaceutical Unit in Gartnavel Hospital. Installation of the two synthesisers is planned for 2018, and the first new tracers – [^{11}C]acetate, [^{18}F]fluoro-ethyl-tyrosine (FET) and [^{11}C]methionine – will be

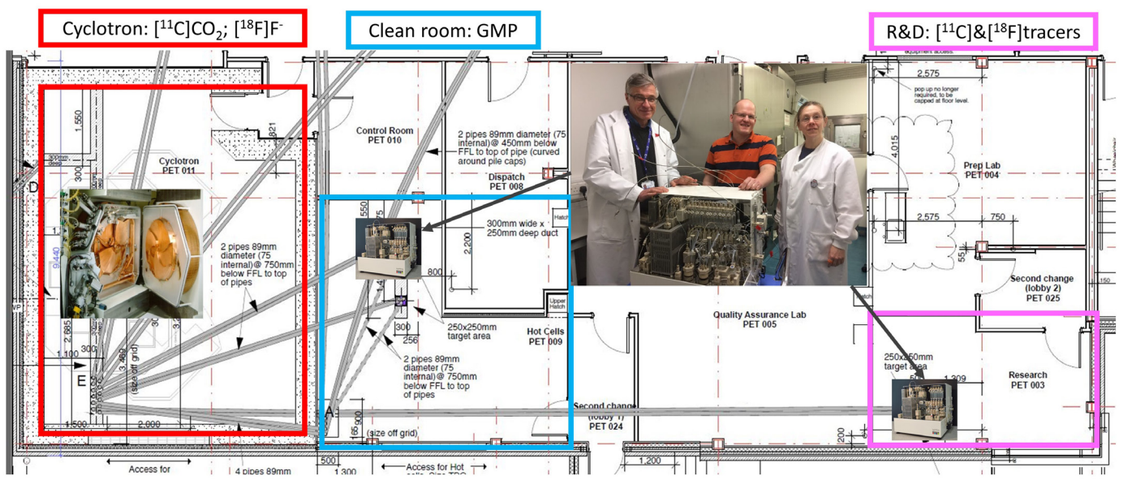

Figure 1
Blueprint for the installation of two identical and universal $^{11}C/^{18}F$ synthesisers (SYNTHRA GmbH, Germany) at the cyclotron facility of the Radiopharmaceutical Unit of the West of Scotland PET Centre, Gartnavel Hospital, allowing rapid clinical translation of new PET radiopharmaceuticals. R&D: development and production of radiotracers for preclinical research. GMP: production of the pharmaceutical-grade material for clinical studies.

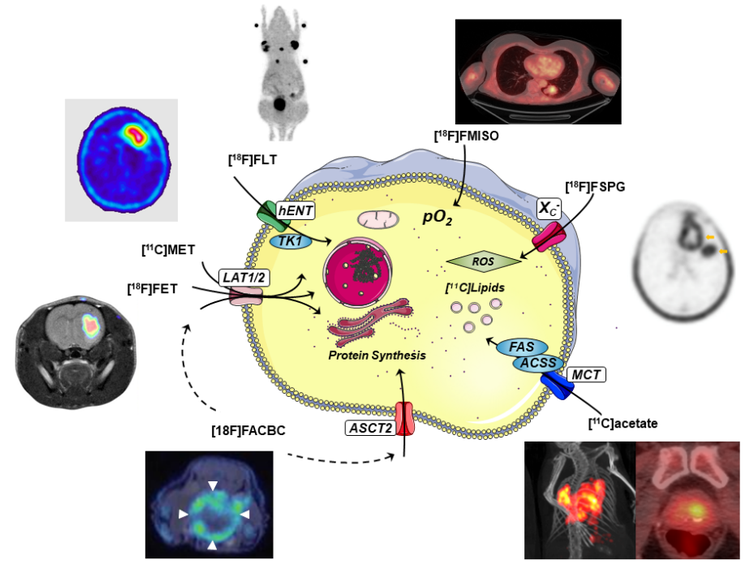

Figure 2
Positron emission tomography images, and cellular uptake mechanisms for several radiotracers for translational cancer imaging. ACE, [^{11}C]acetate; ACSS, acetyl-coenzyme A synthetase; ASCT2, neutral amino acid transporter, SLC1A5; FACBC, trans-1-amino-3-[^{18}F]-fluorocyclobutane-carboxylic acid; FAS, fatty acid synthase; FET, [^{18}F]fluoroethyltyrosine; FLT, 3′-deoxy-3′[^{18}F]-fluorothymidine; FMISO, [^{18}F] fluoromisonidazole; FSPG, (4S)-4-(3-[^{18}F]fluoropropyl)-l-glutamate; hENT, human equilibrative nucleoside transporter, SLC29A1; LAT1/2, large neutral amino acids transporters, SLC7A5 and SLC7A8; MCT, monocarboxylate transporter, SLC16A1; MET, [^{11}C]methionine; pO2, partial pressure of oxygen; ROS, reactive oxygen species; TK1, thymidine kinase 1; X_c–, cystine/glutamate transporter, SLC7A11.

available for preclinical studies in May. The list of available radiotracers will be gradually expanded according to the demands of the preclinical and translational imaging research projects. Parallel GMP production of the same tracers will be established for early-phase clinical trials.

Preclinical and Translational Imaging

PET imaging allows non-invasive assessment of specific biological processes, such as glycolysis, fatty acid synthesis, proliferation, redox, hypoxia, amino acid uptake, and protein and nucleotide synthesis (Fig. 2). Together with MRI, which provides functional and high-contrast soft tissue images, PET can monitor the effectiveness of novel cancer therapies and increase understanding of tumourigenesis at the molecular level. Our new facility will drive *in vivo* imaging research projects from preclinical models through to clinical implementation.

In 2017, the preclinical facility recruited new personnel and expanded equipment capabilities. A talented Senior Scientific Officer, Emma Johnson, has joined the group to support preclinical imaging studies, and we have installed an automatic gamma counter, cryomicrotome and multi-mouse anaesthetic platform for high-throughput tumour characterisation, complementing the non-invasive imaging available with our state-of-the-art NanoScan PET/MRI scanner. We redesigned, renovated and extended the laboratory to facilitate this increased workflow.

This year, in collaboration with Hing Leung, we explored whether PET could monitor the effects of androgen deprivation therapy in prostate cancer. We observed reduced uptake of [^{18}F] FACBC, a novel SLC7A5 and SLC1A5 transporter tracer, in castrate-resistant compared to castrate-sensitive prostate cancer orthografts, suggesting that FACBC could be used for detecting the emergence of treatment resistance. This work was presented at the World Molecular Imaging Conference in Philadelphia. This year we will be exploring the role of PET/MRI in phenotyping subtypes of colon cancer and studying metabolic progression in breast and pancreatic tumourigenesis.

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