

Date of submission:  
Project title:

1



## SINAPSE PhD Project Proposal Template for PhDs with Industry starting in 2010

### PROJECT

Title:

PET Isotope Mediated Release and Labelling of Radiotracers

Planned start date (month/year):

October 2010

SINAPSE Centre (i.e. primary university to which this studentship will be attached):

Edinburgh

University first supervisor: contact details

Name: Professor Mark Bradley  
Department: School of Chemistry  
Address: West Mains Road, Edinburgh, EH9 3JJ  
Email: mark.bradley@ed.a.cuk  
Phone: 0131-650-4820

Second academic supervisor/ other university or other people in primary university involved with project

Name: Dr Christophe Lucatelli  
Department: CRIC  
Address: 47 Little France Crescent, Edinburgh, EH16 4TJ  
Email: christophe.lucatelli@ed.ac.uk  
Phone: 0131 242 9239

Industry

NHS Lothian Research and Development

Industry main contact details

Name: Professor David Newby  
Department: NHS Lothian R&D, QMRI  
Address: 47 Little France Crescent, Edinburgh, EH16 4TJ  
Email: D.E.Newby@ed.ac.uk  
Phone: 0131 242 3330

Key Other Industry people involved with Project including Industry Supervisor (if different to Industry main contact above)

Date of submission:  
Project title:

2



**Likely background of suitable student (eg. Neuroscience, MR Physics, Chemistry, Engineering, Informatics, Psychology) and essential skills required prior to starting this PhD:**

**Synthetic Chemist, Chemical Engineer must have an interest in *in vivo* radionuclide imaging and translational activities. Must be prepared to work across-sites and research schools.**

**Summary of proposed project (approximately 200 words):**

The focus of this project will be to develop a one-step labelling procedure suitable for the rapid and efficient labelling of a variety of probes with  $^{18}\text{F}$  fluoride or  $^{68}\text{Ga}$ . The key steps of all the proposed approaches will be:

- (a). The generation of labelled material *via a variety of PET-isotope mediated cleavage processes*, giving rise to highly pure and concentrated samples.
- (b). The probes can be peptides thus allowing the approach to be applicable generically while the pre-probes can be made *en masse* and cleaved just when required
- (c). The liberation will be rapid and carried out in a flow manner.

Three routes will be explored:

- (i). The desired peptide pre-probe will be synthesised by solid phase methods, conjugated to a boronate carboxylic acid and then cleaved and purified. This will subsequently be captured onto a catechol derivatised resin. Treatment of the captured probe (ideally a macroporous PS) with the fluoride source will cleave the probe off the support and give the stable boron fluoride label.<sup>1,2</sup>
- (ii). The desired peptide pre-probe will be conjugated to an azido group, purified and captured onto a sulfonyl chloride resin that has been derivatised with an propargyl alcohol, using a Cu(I) catalysed [3+2] cycloaddition<sup>5</sup>. Treatment with the fluoride source will again cleave the probe off the support.
- (iii). As above the peptide will be synthesised, purified and then immobilised back on to a solid support. In this case the Ga(III) will induce co-ordination followed by resin mediated ester cleavage to give the desired liganded complex in solution.

**Key references (up to five):**

1. Peptides and Peptide Hormones for Molecular Imaging and Disease Diagnosis, X. Chen, Chem Review, 2010 in press.
2. Synthesis, purification, and aqueous stability of a fluorescent [18F]-labelled aryltrifluoroborate, D.M. Perrin, J. Fluorine Chemistry, 2008, 349.
3. Arylfluoroborates and Alkylfluorosilicates as Potential PET Imaging Agents: High-Yielding Aqueous Biomolecular  $^{18}\text{F}$ -Labeling, D.M. Perrin, J. Organic Chemistry, 2008, 4662.
4. Facile Synthesis of Cyclic Tetrapeptides from Nonactivated Peptide Esters on Metal Centers, W. Beck, Angewandte Chemie, 1998, 1086.
5. Click Chemistry for  $^{18}\text{F}$ -Labeling of RGD Peptides and microPET Imaging of Tumor Integrin  $\alpha_v\beta_3$  Expression, Z. B. Li, Bioconjug. Chem. 2007, 1987.