

Date of submission:  
Project title:

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

### PROJECT

Title:

Development of new molecular tracers as tools for imaging neurological disease

Planned start date (month/year):

October 2010

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

University of Glasgow

University first supervisor: contact details

Name: Dr Andrew Sutherland  
Department: Chemistry  
Address: WestCHEM, Joseph Black Building, University Avenue, Glasgow, G12 8QQ  
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Second academic supervisor/ other university or other people in primary university involved with project

Name: Dr Lutz Schweiger  
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Address: School of Medical Sciences, John Mallard Scottish Pet Centre, Foresterhill, Aberdeen, AB25 2ZD.  
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Industry

Molecular Neuroimaging (MNI)

Industry main contact details

Name: Dr Gilles Tamagnan  
Address: Molecular Neuroimaging, L.L.C., 60 Temple Street, Suite 8A, New Haven, Connecticut 06510, USA.  
Email: [gtamagnan@mnimaging.com](mailto:gtamagnan@mnimaging.com)

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

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

This proposal requires a student with a chemistry degree and with research experience in synthetic organic chemistry (MSci degree or equivalent). Essential skills include the ability to carry out synthetic transformations and the purification and analysis of compounds using standard techniques such as IR, NMR and UV spectroscopies as well as mass spectrometry. Previous experience in using HPLC would also be useful.

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

The translocator protein 18 kDa (TSPO, formerly known as the peripheral benzodiazepine receptor) is found at high levels in the kidney, lung, heart and at low concentration in the brain. TSPO is associated with initial inflammatory processes in the early stages of neurological diseases such as Parkinson's and Alzheimer's diseases and after brain injury caused by stroke or head trauma. TSPO has therefore significant potential as a marker of regions affected by these conditions. While radioligands have been developed for TSPO these suffer from high nonspecific binding and relatively low brain uptake.

The aim of this project is to develop a new generation of molecular tracers which can act as effective imaging agents for TSPO. A new synthetic approach for the preparation of a small library of compounds based on the phenoxyphenylacetamide core structure will be developed and tested for affinity with TSPO. This will allow the development of a structure activity relationship model ultimately generating a lead compound which can radiolabelled for in vivo imaging of TSPO. An additional feature of this research programme will be the design of target compounds with multi-labelling positions allowing these compounds to be used for either PET and SPECT imaging (In collaboration with Dr Sally Pimlott, University of Glasgow). The structures of these compounds also have the potential to fluoresce and thus may find application in optical imaging. A significant portion of this PhD studentship will be carried out in the department of chemistry (GU), thus further strengthening the collaboration between the ScotCHEM and SINAPSE pooling initiatives.

The research will be carried out in collaboration with Molecular NeuroImaging, MNI, a company based in Connecticut who develop radioligands as tools for drug development for neurodegenerative and neuropsychiatric disorders (Dr Gilles Tamagnan). MNI will consult on the key objectives of the research programme as well as provide a placement for the PhD student to experience the use of clinical trials and PET/SPECT radiochemistry in an industrial setting.

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

1. L. Stevenson, S. L. Pimlott and A. Sutherland, A New Approach for the Synthesis of the Peripheral Benzodiazepine Ligand, PK11195, *Tetrahedron Lett.*, 2007, **48**, 7137-7139.
2. S. L. Pimlott, L. Stevenson, D. J. Wyper and A. Sutherland, Rapid and Efficient Radiosynthesis of [<sup>123</sup>I]-PK11195, A SPECT Tracer for Peripheral Benzodiazepine Receptors, *Nucl. Med. Biol.*, 2008, **35**, 537-542.
3. L. Stevenson, A. A. S. Tavares, A. Brunet, F. I. McGonagle, D. Dewar, S. L. Pimlott and A. Sutherland, New Iodinated Quinoline-2-carboxamides for SPECT Imaging of the Translocator Protein, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 954-957.