

Date of submission:
Project title:

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

PROJECT

Title:

Potential MRI indices of functional recovery after focal cerebral ischaemia treated with neural stem cells

Planned start date (month/year):

October 2010

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

Glasgow

University first supervisor: contact details

Name: Keith Muir
Department: Clinical Neurosciences
Address: Institute of Neurological Sciences, Southern General Hospital, Glasgow G51 4TF
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Phone: 0141 201 2494

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

Prof Mhairi Macrae, Division of Clinical Neurosciences, University of Glasgow

Industry

ReNeuron Ltd

Industry main contact details

Name: Dr John Sinden
Department:
Address: ReNeuron Group plc, 10 Nugent Road, Surrey Research Park, Guildford GU2 7AF
Email: John-Sinden@reneuron.com
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Key Other Industry people involved with Project including Industry Supervisor (if different to Industry main contact above)

Dr Paul Stroemer, Head of Preclinical Research, ReNeuron Limited

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

Neuroscience

Summary of proposed project (approximately 200 words):

The neural stem cell product CTX0E03 is a conditionally immortalised cell line developed for treatment of ischaemic stroke. Preliminary clinical trials are scheduled to commence in the near future. Evidence from rodent focal ischaemia models supports enhanced functional recovery when CTX0E03 cells are implanted directly into the putamen adjacent to the site of ischaemic injury, in a paradigm of late treatment (4 weeks post ischaemia), using motor assessments such as tape removal.

Further clinical development of stem cell therapies will inevitably only be possible in small clinical trials and the development of biomarkers of cell action will be key. At present it is thought that few cells survive, yet exert beneficial functional effects, so direct imaging of grafted cells is unlikely to prove valuable, and potential markers of cell effects on neuronal organisation are required.

In a rodent focal ischaemia model, potential MRI markers will be sought in a study that will follow the late direct intraputaminial injection of CTX0E03 cells 4 weeks after focal ischaemia by serial brain imaging and neurobehavioural studies, initially exploring diffusion tensor imaging, high resolution structural MRI, and ¹H MRS. Functional recovery in the somatosensory cortex will be serially monitored using fMRI and forepaw stimulation. In addition quantitative T2* maps will be used the temporal evolution of cerebral angiogenesis.

Key references (up to five):

1. Gray JA, Grigoryan G, Virley D, Patel S, Sinden JD, Hodges H. Conditionally immortalized, multipotential and multifunctional neural stem cell lines as an approach to clinical transplantation. *Cell Transplant*. 2000;**9**:153-68.
2. Pollock K, Stroemer P, Patel S, Stevanato L, Hope A, Miljan E, Dong Z, Hodges H, Price J, Sinden JD. A conditionally immortal clonal stem cell line from human cortical neuroepithelium for the treatment of ischemic stroke. *Exp.Neurol*. 2006;**199**:143-55.
3. Ding G, Jiang Q, Li L, Zhang L, Zhang ZG, Ledbetter KA, Gollapalli L, Panda S, Li Q, Ewing JR, Chopp M. Angiogenesis detected after embolic stroke in rat brain using magnetic resonance T2*WI. *Stroke* 2008;**39**:1563-8.
4. Ding G, Jiang Q, Li L, Zhang L, Zhang ZG, Ledbetter KA, Panda S, Davarani SP, Athiraman H, Li Q, Ewing JR, Chopp M. Magnetic resonance imaging investigation of axonal remodeling and angiogenesis after embolic stroke in sildenafil-treated rats. *J.Cereb.Blood Flow Metab* 2008.
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