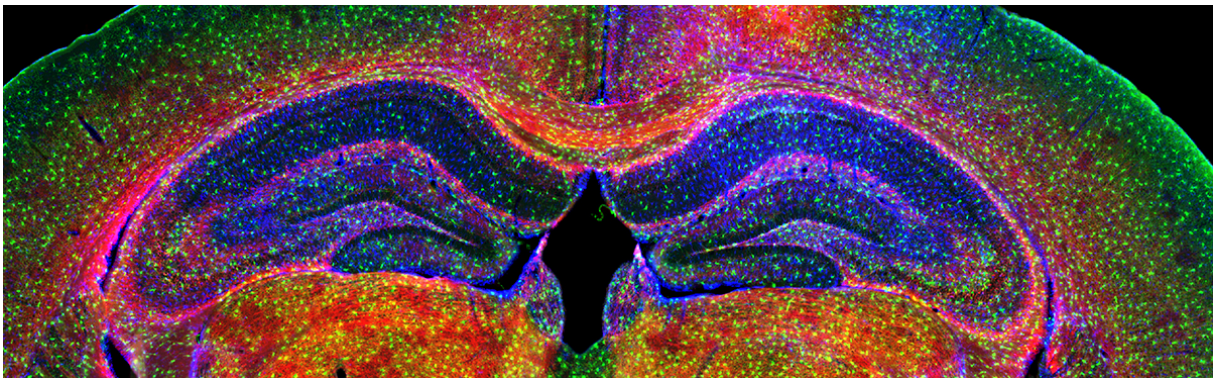
ITN EU-GliaPhD: 15 fully-funded 3-year PhD positions in NEUROSCIENCES –
"Training, Research and Raising of Public Awareness in Cell Biology and Pathology of Neuroglia"



Partners of the Marie Curie Innovative Training Network EU-GliaPhD are recruiting 15 highly motivated PhD candidates as Early-Stage Researchers (ESR) from the wide field of life sciences and engineering. The research, in which the young scientists will be trained, is centered on the role of neuron-glia interactions in brain function and pathology. The projects will focus on neuron-glia interactions in epilepsy, a complex brain disorder exhibiting several pathological events also seen in other CNS diseases. Addressing the role of glial cells in epilepsy research is a novel approach and has never been utilized in an international, collaborative training programme.

The brain is the most complex, but also the most vulnerable part of our body. "How does the brain work?" has been among the most frequently asked questions for more than centuries. Elucidation of molecular and cellular mechanisms of brain function is a prerequisite to understand its pathologies and to develop novel and better therapies. It is also essential to disseminate research results, to learn more about patients' priorities and to help them and their families in understanding the disease burden.

The EU-GliaPhD consortium has formed (1) to train the future generation of neuroscientists, (2) to enhance and improve the communication with the public, and (3) to establish inter-sectorial collaborations between academia and industry.

European neuroscientists joint forces with industrial partners to form the **EU-GliaPhD** network. In addition, partner organisations from the private sector contribute to training, dissemination, outreach and management. The training-by-research programme will be highly inter-sectorial to address academic AND industrial research requirements as well as to establish interactions with the public via social media and face-to-face with patients' organisations.

The research itself addresses mechanisms of cell-cell communication in the healthy and the diseased brain. The methodological approaches will cover mouse and human genetics, immunohistochemistry, molecular and cellular biology, advanced microscopy and electrophysiology *in vivo* and *in situ*, large neuronal ensemble recordings in freely moving animals, high throughput drug screening and development of novel research instrumentation.

Additional Information

Benefits

EU-GliaPhD is a Marie Curie Innovative Training Network (ITN) funded by the European Commission within the Horizon 2020 research and innovation program. The ESR/PhD positions will be offered by academic research institutions/universities and companies located in Germany, Italy, France, UK, Norway, Denmark and the Netherlands. Together with additional partners (patients' organization, science writing, microscopy and management) the consortium will provide cross-disciplinary training

in basic neurosciences for a new generation of neuroscientists who will exploit the power of emerging technological platforms to decipher the mechanisms of cell-cell interaction in the healthy and diseased brain.

How to apply:

Send your complete application as a single PDF file (5 MB max) to applications@eu-gliaphd.eu.

- a cover letter, stating your research motivation and interests; including relevant background. In addition, provide a ranked list of at least 3 ESR projects you would like to work on.
- CV (with list of publications or poster presentations)
- 2 letters of recommendation

Please **check your eligibility carefully** beforehand at www.eu-gliaphd.eu.

Required Research Experiences

- RESEARCH FIELD
  Biological sciences › Neurobiology - Epilepsy Research
  Life Sciences › Neurosciences
  Computer Science › Informatics/Bioinformatics
  Engineering
- YEARS OF RESEARCH EXPERIENCE
  1 - 4

Offer Requirements

- REQUIRED EDUCATION LEVEL
  Biological Sciences: Master Degree or equivalent at start of project
  Life Sciences: Master Degree or equivalent at start of project
  Computer Sciences: Master Degree or equivalent at start of project
- REQUIRED LANGUAGES
  ENGLISH: Excellent

Map Information

See website www.eu-gliaphd.eu.

EURAXESS offer ID: 722053

Each position will be appointed between January and November 2017 for 36 months and dedicated to the following projects/partner labs:

USAAR

ESR 1: Role of glial transmitter receptors in epileptic network function *in vivo*
ESR 2: Molecular and cellular mechanisms of pathological network function in mouse models of absence epilepsy

Frank Kirchhoff
CIPMM, Universitaet des Saarlandes
frank.kirchhoff@uks.eu
http://physiology.uni-saarland.de/Kirchhoff/Kirchhoff_Research.html,
http://www.kirchhoff-lab.de

CNR

ESR 3: Reciprocal signalling between specific GABAergic interneurons and astrocytes
ESR 4: Neuron-glia interactions in neurovascular coupling

Giorgio Carmignoto
Consiglio Nazionale delle Ricerche
giorgio.carmignoto@ bio.unipd.it
http://www.biomed.unipd.it/ricerca/gruppi-di-ricerca/astroglia-signalling-in-brain-function/

FINCB

ESR 5: Acute glia dysfunction associated to seizures and status epilepticus

Marco de Curtis
Fondazione IRCCS Istituto Neurologico "Carlo Besta"
marco.decurtis@istituto-besta.it
http://www.istituto-besta.it/Area-Ricerca.aspx?doc=Elenco-Strutture Organizzative&IdSOSD=IdNeurofisiologiaEEpilettologiaSperimentale

http://www.istituto-besta.it/Area-Ricerca.aspx?doc=Elenco-Unita-Operative&IdUO=UO-EPILETTOLOGIACLINICAENEUROFISIOLOGIASPERIMENTALE

CdF

ESR 6: Role of astroglial connexins in epileptogenesis and temporal lobe epilepsy

Nathalie Rouach
College de France
E-Mail nathalie.rouach@college-de-france.fr
http://www.college-de-france.fr/site/en-cirb/rouach.htm

INSERM

ESR 7: Ca2+ signalling and motility of microglial cells

Etienne Audinat
Institut National de la Santé et de la Recherche Médicale
etienne.audinat@parisdescartes.fr
http://www.biomedicale.parisdescartes.fr/neurophysiologie/laboratory-members/audinat/

UKB

ESR 8: Mechanisms underlying uncoupling of astrocytes in the epileptic brain

Christian Steinhäuser
Universitaetsklinikum Bonn
christian.steinhaeuser@ukb.uni-bonn.de
https://www.izn.uni-bonn.de

UKB

ESR 9: Dynamic physiological and morphological responses of astroglial networks

Christian Henneberger
christian.henneberger@ukb.uni-bonn.de
https://www.izn.uni-bonn.de

AMC

ESR 10: Noncoding RNAs (ncRNAs) and inflammation: new strategies to target epileptogenesis

Eleonora Aronica
Academisch Medisch Centrum bij de Universiteit van Amsterdam
E.Aronica@uva.nl
https://www.amc.nl/web/research/who-is-who-in-research/who-is-who-in-research.htm?p=456

CU

ESR 11: Nature of the GABA transporter GAT1 malfunction in thalamic astrocytes in absence epilepsy

Vincenzo Crunelli
Cardiff University
crunelli@cardiff.ac.uk
http://www.cardiff.ac.uk/people/view/61023-crunelli-vincenzo

AU

ESR 12: Astrocytic plasticity and dysfunctions in the cortical “initiation site” of absence seizures

Rheinallt Parri
Aston University
parrihr@aston.ac.uk
http://www.aston.ac.uk/lhs/staff/az-index/parrihr

OUS

ESR 13: The role of K+ buffering and water channels in epilepsy

Kjell Heuser
Oslo Universitetssykehus HF
kjell.heuser@ous-hf.no;
http://ous-research.no/home/tauboll/Group%20members/7075

NPI

ESR 14: Development, improvement and optimization of electrophysiological equipment for glia physiology

Hans Reiner Polder
NPI electronic - Electronic Instruments for the Life Science
sales@npielectronic.com
www.npielectronic.de

HLU

ESR 15: Interaction of interneurons and astrocytes for epileptogenesis and identification of novel modulatory drugs as putative AEDs

Morten Grunnet, Trine Nygaard Jørgensen
H. Lundbeck A/S
MGRU@lundbeck.com; TNR@lundbeck.com
https://lundbeck.com/dk

(to be placed on the website)

Position	Host institution	PhD enrolment	Start date	Duration	
ESR1	P1-USAAR	Y (at USAAR)	early 2017	36 months	

Project Title:

Role of glial transmitter receptors in epileptic network function *in vivo*

Objectives:

The aim of this project is to provide information about **communication mechanisms between neuronal and glial cell populations** in an animal model of temporal lobe epilepsy. Glial network activities will be assessed primarily as Ca^{2+} signals since these have integrative functions. Electrical activity such as extracellular field activity in slice preparations or EEG recordings from experimental animals will be used for complementation and confirmation.

Methodology:

Electrophysiology of acute brain slices and *in vivo* imaging of Ca^{2+} signals using two-photon laser-scanning microscopy (2P-LSM) will be employed as well as telemetric EEG recordings and behavioural analysis. Molecular and immunohistochemical techniques will be applied to determine the extent of receptor knockout and subsequent changes in the adjacent neighbourhood.

Position	Host institution	PhD enrolment	Start date	Duration	
ESR2	P1-USAAR	Y (at USAAR)	early 2017	36 months	

Project Title:

Molecular and cellular mechanism of pathological network function in mouse models of absence epilepsy

Objectives:

To evaluate the role of distinct **glial transmitter receptors in the generation and duration of absence seizures** in respective animal models.

Methodology:

Knockout mice with inducible gene deletion will be investigated by *in vivo* 2P-LSM using intracellular Ca^{2+} as indicator of glial network activity. After induced gene ablation, chemical seizures will be evoked. Ca^{2+} signals as well as EEGs will be recorded in the affected mice. In addition, molecular and immunohistochemical techniques will be applied to determine and quantify the extent of receptor knockout and subsequent changes in the adjacent neighbourhood.

Position	Host institution	PhD enrolment	Start date	Duration
ESR3	P2-CNR	Y (at U Padova)	early 2017	36 months
Project Title: Reciprocal signalling between specific GABAergic interneurons and astrocytes				

Objectives:

The aim of this project is to obtain insights into the cellular and molecular mechanisms at the basis of the reciprocal **signalling between astrocytes and GABAergic interneurons** (INs) in slices of the **entorhinal and temporal cortices as well as the hippocampus** in normal and epileptic mice. Does GABA released from specific interneuron subtypes activate astrocytes? Does GABA activate Ca^{2+} signals in astrocytic processes? Do astrocytes modulate GABAergic synaptic transmission?

Methodology:

Experiments will be performed in brain slices obtained from different genetically modified mouse lines expressing fluorescent proteins or Ca^{2+} sensitive dyes in specific neuronal and glial cell populations.

Position	**Host institution**	**PhD enrolment**	**Start date**	**Duration**	
ESR4	P2-CNR	Y (at U Padova/Milano)	early 2017	36 months	

Project Title:

Neuron-glia interactions in neurovascular coupling

Objectives:

Activation of astroglia by neuronal signals plays a central role in the **control of cerebral blood flow** (CBF, neurovascular coupling). How does **epileptiform activity, in the acute and chronic state**, affect Ca^{2+} levels in astroglial endfeet and how could a defect in astroglial activation impair the CBF response to seizures? Neurons can suffer a metabolic disruption that may firstly, **impair the ability of neurons to function** properly and thus leading to seizure cessation, and secondly, lead to the neuronal death associated with chronic epilepsy.

Methodology:

A combination of electrophysiology and Ca^{2+} imaging techniques at high spatial and temporal resolution will be employed to monitor simultaneously neuronal activity and Ca^{2+} signals of both neurons and astroglia in acute brain slices, isolated brain preparations, and *in vivo* experiments.

Position	Host institution	PhD enrolment (Y/N)	Start date	Duration	
ESR5	P3-FINCB	Y (at U Milano/Pavia)	early 2017	36 months	

Project Title:
Glia dysfunction associated to seizures and status epilepticus in animal models and humans

Objectives:

Sustained seizure activity alters both **glial function and blood-brain barrier permeability**. These changes may promote tissue adjustments that influence the process of **epileptogenesis**. Here, it will be tested whether seizures worsen epileptogenesis through glia-mediated mechanisms. For analysis the *ex vivo* isolated **whole guinea pig brain** preparation as well as *in vivo* rodent models will be used. Access to post-surgical human tissue from the local Epilepsy Surgery Program is available. Inflammatory and blood-brain barrier molecules will be studied with detailed histochemical and molecular evaluation of cellular and subcellular astro- and microglial markers.

Methodology:

Neurophysiological, histological and molecular techniques will be employed. The ESR will be trained to run *in vivo* video-EEG experiments on chronic animal models of temporal lobe epilepsy and *in vitro* experiments on brain slices and on the isolated guinea pig brain preparation. The research will compare human tissue obtained from epilepsy surgery (temporal lobe epilepsies and focal cortical dysplasias) and animal models to identify the role of seizure activity on astro/microglia activation. **7T magnetic resonance imaging studies** (including DTI and high-resolution spectroscopy) of animal model and human post-surgical and experimental tissue will be used.

Position	Host institution	PhD enrolment	Start date	Duration	
ESR6	P4-CdF	Y (at U Paris)	early 2017	36 months	

Project Title:

Role of astroglial connexins in epileptogenesis and temporal lobe epilepsy

Objectives:

Astrocytes form plastic networks mediated by gap junction channels formed by connexins 43 (Cx43) and 30 (Cx30). Such astroglial networks are thought to limit neuronal network activity during epileptiform bursts. The aim is to investigate how **Cx-mediated astroglial networks influence neuronal excitability** and population activity at the cellular and molecular levels.

Methodology:

Electrophysiological (patch-clamp, field recordings and **multielectrode array**) and imaging techniques will be employed *ex vivo* and *in vivo* in Cx30 and Cx43- deficient mice. The underlying mechanisms involving Cx30 and Cx43 regulations will be studied, focusing on potassium buffering, glutamate uptake, gliotransmitter release, and regulation of extracellular space volume. We will particularly investigate the respective contribution of channels (gap junction and hemichannels) and non-channel functions of each astroglial connexin. For this purpose, we will use either transgenic mice or novel engineered **astrocyte-targeted lentiviral vectors** *in vivo*, expressing in astrocytes dominant negative Cx isoforms (Cx30T5M and/or Cx43G138R), which block selectively the channel function of Cxs.

Position	Host institution	PhD enrolment (Y/N)	Start date	Duration	

ESR7	P5-INSERM	Y (at U Paris)	early 2017	36 months	

Project Title:

Ca^{2+} signalling and motility of microglial cells

Objectives:

Microglial cells have been mostly studied for their roles in pathological conditions. However, they also interact with neurons and astrocytes in physiological conditions, notably during brain development where they influence the structural and functional maturation of synaptic networks. The present project will aim at analyzing **Ca^{2+} signalling and motility of microglial cells during postnatal development** of the mouse somatosensory cortex to understand better their interactions with developing neurons in physiological and pathological conditions.

Methodology:

New genetic and imaging tools will be used to study Ca^{2+} signals of microglia *in situ* and *in vivo* in response to neuronal activity and during their tissue surveillance. A combination of electrophysiological (patch clamp) and imaging (video microscopy, 2P-LSM) techniques will be used in acute cortical slices and *in vivo*. We will first identify the **signalling pathways responsible for the recruitment of microglia** at maturating synapses. We will then study how **an inflammatory challenge and febrile seizures** influence interactions between neurons and microglia during cortical development.

Position	**Host institution**	**PhD enrolment**	**Start date**	**Duration**	
ESR8	P6-UKB	Y (at UKB)	early 2017	36 months	

Project Title:

Mechanisms underlying uncoupling of astrocytes in the epileptic brain

Objectives:

In human temporal lobe epilepsy (TLE), patients with hippocampal sclerosis (HS) show **lack of gap junction coupling among astrocytes**. In a TLE mouse model, **unilateral intracortical kainate injection**, morphological and functional changes that **reproduce** those seen in **chronic human HS**. Importantly, uncoupling of astrocytes occurs already within 4 h after onset of **status epilepticus (SE),** thus preceding changes in neurons and generation of recurrent seizures. However, the **mechanisms underlying SE-induced uncoupling** are unclear.

Methodology:

We will use reporter mice for Cx43 expression (Cx43kiECFP), immunodetection with antibodies recognizing distinct Cx43 phosphorylation sites and mass spectrometry to find out whether reduced expression or post-translational modification of Cx43 account for decreased coupling in TLE. Preliminary data indicate a role for **pro-inflammatory cytokines** in SE-induced gap junction blockade. Using **mice lacking** the **corresponding receptors (TLR4 KO, IL-R1 KO, TNF-R1 KO, IL-R1/TNF-R1 dKO**) or applying receptor antagonists (LPS-RS, IL-1ra, XPro1595) the underlying mechanisms will be explored.

Position	**Host institution**	**PhD enrolment**	**Start date**	**Duration**	

ESR9	P6-UKB	Y (at UKB)	early 2017	36 months	

Project Title:

Dynamic physiological and morphological responses of astroglial networks

Objectives:

Diffusion of signalling molecules in astroglial syncytia does not only depend on properties of gap junctions, but also on **diffusion within individual astrocytes and therefore their complex morphology**. Changes of astrocyte morphology that modify the tortuosity of intracellular space will affect diffusion of a molecule within that cell and also to neighbouring cells. Induction of epilepsy or LTP in acute hippocampal slices results in changes of astrocyte morphology and, at the same time, intracellular diffusivity. We will explore whether restructuring of astrocytes could lead to formation or pruning of gap junctions, and how acute astrocyte morphology changes affect diffusion and signal propagation within astrocyte networks.

Methodology:

We will use our recently established **computer model** of fluorescent dye **coupling between astrocytes** for predictions of signal propagation that will then be tested experimentally by combing 2P-LSM and patch-clamp recordings. These experiments will reveal how morphology and intracellular diffusion of astrocytes shape astrocyte networks in control and epileptic hippocampus.

Position	**Host institution**	**PhD enrolment**	**Start date**	**Duration**	
ESR10	P7-AMC	Y (at AMC)	early 2017	36 months	

Project Title:

Noncoding RNAs (ncRNAs) and inflammation: new strategies to target epileptogenesis

Objectives:

To examine the **non-coding (nc) RNA expression profile** of intracellular and extracellular **miRNAs** upon exposure to inflammatory molecules in human astrocytes. To study **the ncRNA expression profile of glial enriched/ inflammation-associated miRNAs in selected hippocampal subregions and in blood samples after induction of status epilepticus in animal models**.

Methodology:

To study the effect of silencing or overexpression of ncRNAs involved in the regulation of **astrocyte-mediated inflammatory response on ictogenesis** *in vitro* (hippocampal slices) and *in vivo* (experimental models of acute and chronic seizures). In this proposal the translational regulation of astroglial proteins involved in inflammatory responses will be investigated using human astrocyte cultures. In particular the effect of inhibition or overexpression of specific short **ncRNAs** (microRNAs; miRNAs) and long ncRNA on the production of inflammatory mediators in cultured human astrocytes will be evaluated. In addition, miRNA and long ncRNA expression profiles upon exposure to inflammatory molecules in human astrocytes as well as from selected hippocampal subregions and in blood samples after induction of *status epilepticus* in animal models will be determined.

Position	**Host institution**	**PhD enrolment**	**Start date**	**Duration**	

ESR11	P8-CU	Y (at CU)	early 2017	36 months	

Project Title:

Nature of the GABA transporter GAT1 malfunction in thalamic astrocytes in absence epilepsy

Objectives:

Increased tonic GABAA receptor inhibition in the thalamus is necessary and sufficient for **induction of seizures of experimental absence epilepsy** (AE). Drugs that increase GABA levels elicit and aggravate absence seizures (ASs) in normal individuals and in AE patients. Although tonic inhibition results from malfunction of the **astroglial GABA transporter GAT1**, there are no genetic abnormalities of the GAT1 gene. Here, it will be investigated *in situ* and *in vivo* whether thalamic GAT1 malfunction in genetic animal models of AE results from either **1) abnormal phosphorylation, 2) failure of trafficking to the outer astrocytic membrane**, and/or **3) misplaced localization** with respect to synaptic or extrasynaptic regions of the GABAergic synapses between thalamic reticular and thalamocortical neurons.

Methodology:

Experiments will involve 3H-GABA uptake, biotinylation experiments and live trafficking of fluorescence-tagged GAT1 in thalamic slices and in cultures of pure thalamic astrocytes) as well as immunogold EM localization of GAT1 transporter, $GABA_B$ and δ-subunit containing $GABA_A$ receptor and in thalamic regions.

Position	**Host institution**	**PhD enrolment**	**Start date**	**Duration**	
ESR12	P9-AU	Y (at AU)	early 2017	36 months	

Project Title:

Astrocytic plasticity and dysfunctions in the cortical “initiation site” of absence seizures

Objectives:

The underlying cellular, **molecular and synaptic abnormalities of the putative “cortical initiation site” of absence seizures** is largely unknown, and limited data is confined to that from neuronal recordings. Here, we will test the hypothesis that the underlying dysfunction at the initiation site is astrocytic.

Methodology:

The project will start by investigating the relative **hyperexcitability** of astrocytes compared to neurons, using patch-clamp recordings, alone or combined with Ca^{2+} imaging, thereby providing a systematic characterization of astrocytic and neuronal dysfunctions in this cortical area. Using selective **optogenetic stimulation** (light activation of the opto-alpha1 adrenergic receptor and ChR2 targeted cell type-selectively to astrocytes and neurons), the mechanisms of intercellular communication will be investigated in non-epileptic animals and in genetic models of AE.

Position	**Host institution**	**PhD enrolment**	**Start date**	**Duration**	
ESR13	P10-OUS	Y (at OUS)	early 2017	36 months	

Project Title:

The role of K^+ buffering and water channels in epilepsy

Objectives:

Early astrocyte changes after status epilepticus may precipitate epileptogenesis. Therefore, the aim of this project is to investigate whether **administration of potential drugs against K^+ and water channels** shortly after chemically induced status epilepticus (SE) can **attenuate morphological and molecular changes in brain glial cells** and improve the clinical prognosis in terms of lowering frequency and severity of seizures. Is there a time window in the early phase of epileptogenesis in which it is possible to rescue astrocytic changes by administrating drugs effecting astroglia functions?

Methodology:

Defined drug targets are already suggested from current studies, but **will also be deduced from genetic profiling data** of patients. For analysis chemical and genetic animal models will be investigated by molecular, histochemical, electrophysiological and imaging techniques.

Position	Host institution	PhD enrolment	Start date	Duration	
ESR14	P11-NPI	Y (at USAAR)	early 2017	36 months	

Project Title:

Development, improvement and optimization of electrophysiological equipment for glia physiology

Objectives:

Astrocytes display special electrophysiological properties with a low input resistance and extensive intercellular gap junctional coupling. Therefore, these cells require special recording equipment. Our goal is to **develop such specialized equipment of amplifiers suitable for intracellular recordings with an almost complete electronic compensation of the recording electrode**.

Methodology:

Electrophysiological recording instruments will be improved (based on an active bridge circuit combined with an improved compensation of the stray capacitance) and optimized for easy combination in simultaneous single and dual-cell patch clamp as well as sharp microelectrode recordings, in multisite extracellular recordings, in recordings with ion sensitive electrodes, for drug application with high spatiotemporal resolution, for rapid concentration-clamp based techniques, and precise single and multiple stimulation protocols. **A fast drug application device with high temporal resolution** will be developed and optimized for advanced optical recording techniques. For both new instruments will also be combined with glass fiber probes to allow **optogenetic manipulations**. In addition, **electroporation-based protocols** will be developed for selectively labelling or transfecting single identified neurons and glial cells.

Position	Host institution	PhD enrolment	Start date	Duration	
ESR15	P12-HLU	Y at U Copenhagen	early 2017	36 months	

Project Title:

Interaction of interneurons and astrocytes for epileptogenesis and identification of novel modulatory drugs as putative AEDs

Objectives:

Fast spiking interneurons have an important function for general inhibitory neuronal input and are very important for proper synchronization of connected circuits in the brain. Dysfunctional interneurons have been associated with a number of CNS mediated diseases involving general hyperactivity such as epilepsy. In addition, cognitive impairment has also been associated with lack of proper interneuron function. The overall aim of this project is to obtain an understanding of the **role of fast spiking interneurons in chronic animal models of epilepsy and to investigate possible dynamics between interneurons and glia cells** under these conditions. A second aim is to identify targets that could constitute new innovative entries into treatment of epilepsy.

Methodology:

Experiments will be divided between *ex vivo* slice recordings and *in vivo* single unit recordings. **High-throughput drug-screening will occur in *in vitro* assays** using purified astrocyte or organotypic slice cultures. Since a common co-morbidity in epilepsy is cognitive impairment, the direct consequences of the epileptogenic phenotype will be expanded to also investigate **cognitive consequences of the induced hyperexcitability**. These experiments will be behavioural assessment in assays such as novel object recognition and set-shifting.