Anatomical Society
Great Britain & Ireland

Summer Meeting of the Anatomical Society

with a symposium on

Axon-glial interactions in the CNS

July 20-22, 2010

University of Portsmouth

PROGRAMME

LOCATION

The meeting will be held at the University of Portsmouth (SEE TRAVEL DIRECTIONS ON PAGES 4-5, and weblink below for map).
http://www.port.ac.uk/aboutus/contact/maps/portsmouth/

ACCOMMODATION

Accommodation is on a B&B basis in en-suite rooms in Rees Hall (see weblink below for map).
http://www.port.ac.uk/aboutus/contact/universitybuildings/buildingname,92637,en.html
On arrival, delegates should obtain room keys and local information. A bar is available to guests until 11.00 pm.

TRAVEL FROM REES HALL (ACCOMMODATION) TO THE PORTLAND BUILDING (SCIENTIFIC MEETING)

15-20 min walk (see weblink for directions).
http://maps.google.co.uk/maps?f=q&source=s_q&hl=en&geocode=&q=from:+PO5+3AP+to:+PO1+3AH&sll=50.78869,-1.09716&sspn=0.000841,0.001719&dirflg=w&ie=UTF8&ll=50.778155,-1.109619&spn=0.053839,0.110035&z=13

SCIENTIFIC MEETING

The scientific meeting will be held in The Portland Building (see weblink below for map).
http://www.port.ac.uk/aboutus/contact/universitybuildings/buildingname,92551,en.html

Registration

Registration is from 08.00 on Tuesday 20th July in the Atrium, Portland Building.

Lectures

All lectures will be in the Lecture Theatre 1.53, The Portland Building.

Posters

The Poster Display Area is in the Atrium. Poster boards are 1m wide by 1m high. Posters should be mounted on the numbered boards at the start of the meeting on **Tuesday 20th July**. **There will be a formal Poster Discussion Session on Tuesday, 18.00-20.00, when presenters are requested to stand by their posters to discuss the poster**. This satisfies the requirements that the abstracts have undergone a form of peer review prior to publication in *Journal of Anatomy*.

Abstract Book

The full programme including the text of the abstracts will be available at the registration desk and on the Anatomical Society website.

CONFERENCE DINNER

The Conference dinner will be on Wednesday 21st July on board HMS Warrior (see weblink for map). President's drinks reception on the gundeck at 19.00, for dinner at 20.00.

http://www.hmswarrior.org/visiting/location.htm

Please note the dress code for dinner is Smart Casual, and NO STILETTOS OR VERY NARROW HEELED SHOES can be worn aboard HMS Warrior. HEELS SHOULD BE NO LESS THAN 1.5 cm^2

STUDENT EVENTS

Student Discussion Forum

Tuesday 20th July, students will hold a discussion forum at 13.00-14.00 in Lecture Theatre 1.53 in the Portland Building, on "*Academic CV Building: Teaching and Research*", by Dr Raj Ettarh and Prof Steve McHanwell. Buffet lunch available in the Atrium.

Student Social

Drinks at a local pub to be arranged on Tuesday 20th July from 20.00 onwards. This event is sponsored by the Anatomical Society.

President's Breakfast for students

Students holding an Anatomical Society PhD Studentship (and other students) are invited to breakfast with the President of the Anatomical Society Emeritus Professor Susan Standring on Wednesday 21st July at 7.30am in Rees Hall.

ANATOMICAL SOCIETY BUSINESS

Council Meeting of the Anatomical Society

Monday 19th July, 17.00-20.00, in the Garden Room, Rees Hall. Followed by Self-Service Dinner 20.15-22.00 in the Garden Room.

Committee Meetings

Other committee meetings as arranged will take place on Tuesday 20th July 2010, in Seminar Rooms 0.36 or 0.27, The Portland Building.

NOTICE OF AN EXTRAORDINARY GENERAL MEETING OF THE ANATOMICAL SOCIETY OF GREAT BRITAIN AND IRELAND

An Extraordinary General Meeting of the Anatomical Society of Great Britain and Ireland will be held in Lecture Theatre 1.53, Portland Building, University of Portsmouth at 12.00 noon on Tuesday 20th July 2010.

TRAVEL TO PORTSMOUTH

Portsmouth is well served by rail connections with London stations, and Heathrow, Gatwick and Southampton Airports.

By Train

London Waterloo (1hr 30mins) or London Victoria (2hrs 10mins) to PORTSMOUTH & SOUTHSEA (the main station for Portsmouth - not Portsmouth Harbour).
National Rail (external link) has more information.
Portsmouth and Southsea Station is within walking distance from Rees Hall (Accommodation) and The Portland Building (Scientific Meeting). Alternatively, you can get a taxi outside the train station.

By Air

Heathrow Airport.

Heathrow Airport Central Bus Station to Portsmouth: Coach 701 from Heathrow Central Bus Station (Stand 1) to Woking Rail Station, and train from Woking to Portsmouth and Southsea (2 hours)

Alternatively, Heathrow Express or London Underground from Heathrow to London, and London Underground for connections to Victoria or Waterloo Rail Stations, and rail to Portsmouth and Southsea.

Gatwick Airport.

Rail - direct train from Gatwick Airport to Portsmouth & Southsea (1hr 36 min).

Southampton International Airport.

Rail – train to via Southampton Central and change for Portsmouth
National Rail (external link) has more information.

ACCOMMODATION

Rees Hall, University of Portsmouth, Southsea Terrace, Southsea, Portsmouth PO5 3AP (see weblink below for map).
http://www.port.ac.uk/aboutus/contact/universitybuildings/buildingname,92637,en.html

SCIENTIFIC MEETING

The Portland Street, Portsmouth PO1 3AH (see weblink below for map).

http://www.port.ac.uk/aboutus/contact/universitybuildings/buildingname,92551,en.html

TRAVEL FROM REES HALL TO THE PORTLAND BUILDING

15-20 min walk (see weblink for directions).

http://maps.google.co.uk/maps?f=q&source=s_q&hl=en&geocode=&q=from:+PO5+3AP+to:+PO1+3AH&sll=50.78869,-1.09716&sspn=0.000841,0.001719&dirflg=w&ie=UTF8&ll=50.778155,-1.109619&spn=0.053839,0.110035&z=13

Walking directions to Portsmouth, Hampshire PO1 3AH, UK

1.	Head **northeast** on **Bellevue Terrace/A288** toward **Pembroke Rd** Continue to follow A288	318 ft
2.	Continue onto **Jubilee Terrace**	240 ft
3.	Continue onto **King's Terrace/A288**	472 ft
4.	At **Kings Rd Roundabout**, take the **1st** exit onto **Museum Rd/B2154**	0.2 mi
5.	At **Cambridge Jct**, take the **1st** exit onto **Cambridge Rd/A3**	0.1 mi
6.	Turn **left** at **Burnaby Rd**	0.2 mi
7.	Turn **right** to stay on **Burnaby Rd**	203 ft
8.	**Burnaby Rd** turns **left** and becomes **Portland St**	253 ft
9.	Turn **right** at **St James's St** Destination will be on the right	108 ft

Programme of Events

Anatomical Society Business

Monday July 19

17.00-20.00 **Council Meeting of the Anatomical Society**
Garden Room, Rees Hall
Followed by Self-Service Dinner **20.15-22.00**

Tuesday July 20

12.00-13.00 **Extraordinary General Meeting of the Anatomical Society**
Lecture Theatre 1.53, The Portland Building

13.00-14.00 **Other committee meetings**
Seminar Rooms 0.36 or 0.27, The Portland Building

Summer Meeting of the Anatomical Society
The Portland Building, University of Portsmouth

Tuesday July 20

08.00-14.00 **Registration, *Atrium***

Education Symposium: "How Anatomy is Assessed"
Lecture Theatre 1.53

09.00-09.10 *Welcoming statements from the Chair,* Steve McHanwell (University of Newcastle),

09.10-09.40 **E1** John Morris (Oxford University)
How anatomy is assessed in Oxford

09.40-10.20 **E2** Claire Smith (University of Southampton)
How anatomy is assessed in Southampton

10.20-10.50 **E3** Joanne Wilton (University of Birmingham)
How anatomy is assessed in Birmingham

10.50-11.20 **E4** Tracey Wilkinson (Cardiff University)
How anatomy is assessed in Cardiff

11.20-11.50 **E5** Steve McHanwell (University of Newcastle)
The External Examiner system

12.00-13.00 **Extraordinary General Meeting of the Anatomical Society**
Lecture Theatre 1.53

13.00-14.00 **Buffet Lunch**
Atrium

13.00-14.00 **Student Forum**
Academic CV Building: Teaching and Research
Speakers Dr Raj Ettarh and Prof Steve McHanwell
Lecture Theatre 1.53

13.00-14.00 **Other committee meetings, as arranged**
Seminar Rooms 0.36 or 0.27

Symposium: *Axon-glial interactions in the CNS,* Lecture Theatre 1.53

Session 1. Axon-glial interactions in regulation of CNS myelination

14.00-14.10 *Welcoming statement from the Chair*, Arthur Butt (*University of Portsmouth, UK*)

14.10-14.50 **S1**
Klaus-Armin Nave *(Max Planck Institute of Experimental Medicine, Goettingen, Germany)*
The dual role of glia in myelination and axonal integrity

14.50-15.30 **S2**
Julia Edgar (*University of Glasgow, UK*)
MRI and histological characterisation of white matter changes in the CNS of the *Plp1*-gene overexpressing mouse model of Pelizaeus Merzbacher disease

15.30-16.00 **Tea**

16.00-16.40 **S3**
Sue Barnett (*University of Glasgow, UK*)
Myelination: a study of glial/axonal interactions

16.40-17.20 **S4**
Charles ffrench-Constant (*University of Edinburgh, UK*)
Integrins and the initiation of myelination

17.20-18.00 **S5**
Jacky Trotter (*University of Mainz, Germany*)
Src-kinases and myelination

18.00-20.00 **Posters and Welcome Reception, *Atrium***

Wednesday July 21

Symposium: *Axon-glial interactions in the CNS,* Lecture Theatre 1.53

Session 2. Axon-glial neurotransmitter signalling

09.00-09.40 **S6**
David Attwell (*University College London, UK*)
Control of myelination by neurotransmitters

09.40-10.20 **S7**
Maria Kukley *(University of Tuebingen, Germany*)
Synaptic communication between neurons and cells of oligodendroglial lineage

10.20-11.00 **S8**
Maria-Cecilia Angulo (*Univ Paris Descartes, Paris, France*)
GABAergic transmission of NG2 cells changes during postnatal development of the barrel cortex

11.00-11.30 **Coffee**

11.30-12.10 **S9**
Arthur Butt (*University of Portsmouth, UK*)
Astrocyte to pericyte signalling and neurovascular coupling in CNS white matter

12.10-12.50 **S10**
Bob Fern (*University of Leicester, UK*)
Astrocytes and ions, ischaemia and development

12.50-14.00 **Lunch**

14.00-14.40 **S11**
Carlos Matute (*Universidad del Pais Vasco, Leioa-Vizcaya, Spain*)
Neurotransmitter signalling in white matter pathology

14.40-15.20 **S12**
Alex Verkhratsky (*University of Manchester, UK*)
Neuroglia in neurodegenerative diseases

15.20-16.00 **Tea**

16.00- 17.30 **Symposium-related oral presentations**

16.00-16.15 **O1**
Roxanna Octavia Carare (*University of Southampton, UK*)
Lymphatic drainage of the brain and the pathology of Alzheimer's Disease

16.15-16.30 **O2**
Jerome Swinny (*University of Portsmouth, UK*)
Impact of early life environment on the functioning of the nucleus locus coeruleus: implications for stress and affective disorders

16.30-16.45 **O3**

Sassan Hafizi (*University of Portsmouth, UK*)
Tensin Intracellular Focal Adhesion Proteins: Expression and Roles in the Brain

16.45-17.00 **O4**
Virginia Bay (*University of Portsmouth, UK*)
Inward rectifier potassium channels: K^+ regulation in the optic nerve

17.00-17.15 **O5**
Michelle Ware (*University of Portsmouth, UK*)
Formation of early axon tracts in the chick embryonic brain

17.15-17.30 **O6**
Jo Begbie (*Oxford University, UK*)
Signalling between placodal neurons and cranial neural crest

19.00 Conference Dinner aboard the HMS Warrior
President of the Anatomical Society Drinks Reception

DRESS CODE: Smart Casual
NO STILETTOS OR VERY NARROW HEELED SHOES. HEELS SHOULD BE NO LESS THAN 1.5 cm^2

Thursday July 22
Symposium: *Axon-glial interactions in the CNS,* Lecture Theatre 1.53

09.00-13.00 **Session 3. Axon-glial interactions in axon growth and guidance**

09.00-09.40 **S13**
Frank Schubert (*University of Portsmouth, UK*)
Molecular mechanisms in the formation of the early axon scaffold

09.40-10.20 **S14**
Patricia Salinas (*University College London, UK*)
Wnt signaling in the regulation of neuronal circuit formation

10.20-11.00 **S15**
Guy Tear (*King's College London, UK*)
Axon guidance at the midline of the Drosophila central nervous system

11.00-11.30 **Coffee**

11.30-12.10 **S16**
Zubair Ahmed (*University of Birmingham, UK*)
Do glia mediate the axogenic effects of EGFR inhibitors?

12.10-12.50 **S17**
Alicia Hidalgo (*University of Birmingham, UK*)
The glial regenerative response to central nervous system injury is enabled by pros-notch and pros-NF-kappa B feedback

13.00-14.00 **Lunch**

End of Meeting

List of Posters

P1 **Glia and the enteric nervous system of the mouse intestine**
Steve West, James Brown and Arthur M. Butt
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P2 **GSK3β is a master regulator of astrocytes in the rodent optic nerve**
Andrea Rivera and Arthur M. Butt
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P3 **TASK-1 channels in glial cells of the mouse CNS: implications for glial cell function**
Virginia Bay and Arthur M. Butt
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P4 **Inward rectifying potassium channel expression and localisation in mouse glial cells**
Csilla Brasko, Virginia Bay and A.M. Butt
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P5 **Inward rectifying potassium channel expression and localisation in human glioma cells**
Maria Papanikolaou, Csilla Brasko, Geoffrey Pilkington and Arthur M. Butt
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P6 **Localisation of inhibitory synaptic markers and GABAergic receptors in different glial populations in the CNS**
Victoria Stanford, Virginia Bay, Arthur M. Butt, Jerome D Swinny
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P7 **Immunohistochemical analysis of tensin protein expression in the mammalian brain**
Florence Escosio, Emma James, Salman Goudarzi, Jerome D. Swinny and Sassan Hafizi
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P8 **Distinct GABA-A receptor subunits label noradrenergic and non-noradrenergic cell-types in the locus coeruleus**
Nicole Corteen and Jerome D. Swinny
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P9 **Generation of GABAergic neurons in the early fetal human neocortex**
Nahidh Al-Jaberi
Newcastle University

P10 **Increasing diameter of retinal ganglion cell axons in rat, cat and ferret and the influence of light deprivation**

Gary Baker[1], Christophe Guibal[1] and Glen Jeffery[2]
[1] *Department of Optometry & Visual Science, City University London*
[2] *Institute of Ophthalmology, University College London*

P11 **Permissive effects of NG2 glia on neurite outgrowth in vitro: Implications for retinoic acid signalling**

Elizabeth Janet Pawson, Rebekah Wigley, Stephen McMahon and Jonathan Corcoran
Wolfson CARD, Guy's Campus, Kings College London, UK

P12 **Metastasis studies of the blood-brain barrier using in vitro models**

Kathryn Fry and Geoffrey Pilkington
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P13 **Immunotoxin Ablation of NG2 and GD3A: potential novel approach to glioma treatment**

Samantha Higgins, Arthur Butt and Geoffrey Pilkington
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P14 **Targeting GD3/GD3A in Novel Therapy Development for Glioma**

Suzanne Birks, Darek Gorecki and Geoffrey Pilkington
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P15 **Influence of Hypoxia on Cellular Biology in CD133-expressing Glioma Cells**

Qian An, Laura Donovan and Geoffrey Pilkington
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P16 **A Functional Study of CD44 and CD155 in Glioma Invasion**

Zaynah Maherally and Geoffrey Pilkiington
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P17 **Glycogen synthase kinase 3 expression in murine tissues**

Alvise Calamai, Anthony Cullen and Raj Ettarh
School of Medicine & Medical Sciences, University College Dublin

P18 **A quantitative investigation of transcriptional activity in syncytiotrophoblast nuclei during human gestation**

Norah Mary Elisabeth Fogarty, TM Mayhew, AC Ferguson-Smith, GJ Burton
Department of Physiology, Development and Neuroscience, University of Cambridge

P19 **Leptin and leptin receptors in the rat and human carotid body**

Andrea Porzionato
Section of Anatomy, Department of Anatomy and Physiology, University of Padova

P20 **Proposition of a new statistical method for facial reconstruction in forensic medicine**

Odile Plaisant
Paris Descartes University

Abstracts

Symposium Speakers

S1 The dual role of glia in myelination and axonal integrity

Klaus-Armin Nave

Max Planck Institute of Experimental Medicine, Goettingen, Germany

Glial cells that engage with neurons and their long axonal processes are a feature of virtually all nervous systems. However, the mechanisms by which neurons and glia communicate are only poorly understood. We are interested in the interaction of neurons with oligodendrocytes and Schwann cells, both highly specialized glial cells of the CNS and PNS, respectively, and best known for making myelin. In an attempt to identify the neuronal signals that recruit these glial cells to axons and trigger myelination, we identified NRG1 type III as the critical axonal growth factor for myelination by Schwann cells. Unexpectedly, we also found that oligodendrocytes myelinate axons independently of NRG1/ErbB signaling, although they rely on the same intracellular PI3K-AKT-mTOR) signaling pathway to fine-tune myelin membrane growth. While 'saltatory' impulse propagation is one of the key concepts of neurophysiology, we discovered in several mouse mutants that myelinating glia serve more principle functions. Oligodendrocytes support axonal transport, long-term integrity and ultimately axon survival, all of which appears independent of myelin itself. The underlying mechanisms are not understood, but we have obtained indirect evidence for a critical role of sirtuins and a metabolic support of myelinated axons. Such metabolic support may be even more important for myelinated axons, as they are deprived from free access to the extracellular milieu.

S2 MRI and histological characterisation of white matter changes in the CNS of the *Plp1*-gene overexpressing mouse model of Pelizaeus Merzbacher disease

F. Gruenenfelder[1], T. Ruest[2], W. Holmes[3], T.J. Anderson[1], J.A. Barrie[1], M.C. McCulloch[1], K-A. Nave[4], D. Dewar[2], J. Penderis[1], J.M. Edgar[1]

[1]Applied Neurobiology Group, Institute of Comparative Medicine, Faculty of Veterinary Medicine, University of Glasgow, Glasgow, UK. [2]Division of Clinical Neuroscience and [3]Glasgow Experimental Magnetic Resonance Imaging Centre, Faculty of Medicine, University of Glasgow, Glasgow, UK.

[4]Dept. of Neurogenetics, Max Planck Institute of Experimental Medicine, Hermann-Rein-Strasse 3, D-37075 Goettingen, Germany

Duplication of the X-linked *PLP1* gene, which encodes the major membrane protein of CNS myelin, is the most frequent cause of the leukodystrophy, Pelizaeus-Merzbacher disease (PMD). Transgenic mice with extra copies of the wild type *Plp1* gene are valid models of PMD due to gene duplication. Homozygous *Plp1* transgenic mice (line #72; Readhead et al., 1994) are defined by an approximate 2-fold overexpression of *Plp1* mRNA. Mice appear normal until around post-natal day 90 (P90) when they start to display a mild ataxia and develop seizure activity. The aim of this study was to characterise, using diffusion magnetic resonance imaging and histology, white matter changes in this model. High resolution, ex-vivo, diffusion tensor imaging of the brain at P120, revealed widespread changes in diffusion parameters including fractional anisotropy and axial and radial diffusion, compared to wild type brains. Changes were observed in all major white matter tracts and also in the cerebral cortex. To examine the nature and evolution of the underlying microstructural alterations, we undertook electron microscopic and immunohistochemical analyses of the corpus callosum of the *Plp1* transgenic mouse at

P40, P60, P90 and P120. Initial myelination of the corpus callosum was followed by progressive demyelination from around P60. Despite the fact that oligodendrocyte precursors (OPCs; NG2 or PDGFRα +ve cells) were present in the demyelinated corpus callosum, there was no evidence of effective remyelination. Consequently, almost all axons were devoid of a myelin sheath by P120. Focal axonal swellings were observed occasionally, butt most axons appeared normal at all ages. Densities of microglia/macrophages and astrocytes increased progressively compared to wild type values, in parallel with the evolution of demyelination. The DTI changes observed in the P120 *Plp1*-transgenic mouse reflect microstructural changes associated with demyelination. The reason why remyelination fails in this model is not known, but may reflect both cell-intrinsic and cell-extrinsic factors. The model provides a tool with which to identify factors involved in remyelination failure and in which to assess therapies aimed at restoring myelination.

Funding: Multiple Sclerosis Society Scotland (JME), University of Glasgow, Faculty of Medicine and Faculty of Veterinary Medicine Scholarships (TR and FG).

Reference List: 1. Readhead C, Schneider A, Griffiths IR, Nave K-A (1994) Premature arrest of myelin formation in transgenic mice with increased proteolipid protein gene dosage. Neuron 12: 583-595.

S3 Myelination: a study of glial/axonal interactions

Sue Barnett

Clinical Neurosciences, University of Glasgow, GBRC, Glasgow G128TA

Astrocytes are one of the major glial cell types that maintain homeostasis in the undamaged CNS. After injury and disease astrocytes become 'reactive', and prevent regeneration. However, it has also been suggested that astrocytes can become "activated" and promote regeneration. We have identified astrocyte treatments that result in either an increase or a decrease in the amount of myelinated fibres which correlated with the "status" of the astrocyte using myelinating cultures. These cultures are comprised of glia and CNS axons, which over time recapitulate all stages of glial/axonal interaction from neuronal survival and neurite extension to oligodendrocyte proliferation and differentiation. The cultures culminate in the ensheathment of axons and formation of myelin internodes interspaced with nodes of Ranvier containing the correct location of nodal proteins. Our data illustrates that the "reactivity status" of astrocytes can influence the myelinating capacity of oligodendrocytes and that these cells should be considered as important targets in promoting myelination in demyelinating diseases. We will also present our preliminary data on following myelination in these cultures over time using time lapse in which neurospheres made from a GFP mouse (*B-actin* promoter) have been add to the "myelinating" cultures from wild type mice. Further work is ongoing to follow glia/axonal contact in the intact spinal cord using a small animal imaging (LaVision, Biotec, a 2 photon microscope). Neurospheres generated from the *B-actin* GFP mouse were transplanted into the non-labelled hypomyelinated tracts of the *shiverer* mouse (*shi*, resulting in defects in myelin) to assess the feasibility of following glia/axonal contact over time. This is a useful phenotype as it allows us to transplant fluorescent protein tagged oligodendrocyte precursors lacking the *shiverer* mutation which can myelinate the hypomyelinated axons. Data will be presented of our *ex vivo* results to date.

S4 Integrins and the initiation of myelination

Charles ffrench-Constant (*University of Edinburgh, UK*)

S5 Src-kinases and myelination

Jacqueline Trotter
Molecular Cell Biology, Department of Biology, Johannes Gutenberg University of Mainz, 55128 Mainz, Germany

During CNS myelination, oligodendrocytes extend membrane processes towards an axonal ontact site, polarise their cytoskeleton and ensheathe the axon resulting in a compacted multilamellar myelin sheath. Regulation of trafficking of myelin lipids and proteins in time and space is thus essential for myelination. The src-family tyrosine kinase Fyn is expressed by oligodendrocytes and Fyn-deficient mice are hypomyelinated and express lower levels of one of the myelin protein MBP. Mutant mice lacking MBP are also strongly hypomyelinated. MBP mRNA is transported in RNA granules to oligodendroglial processes in a translationally silenced state mediated by trans-acting factors such as heterogeneous nuclear ribonucleoprotein (hnRNPs) binding to the MBP mRNA, preventing ribosomal subunit binding and thus inhibiting translation. Release of this translational repression is thus essential for myelination. We are studying targets of activated Fyn in oligodendrocytes and have identified hnRNPA2 and hnRNP F as targets. Phosphorylation of these proteins is linked to release of the translational inhibition of MBP mRNA. Fyn kinase activation in oligodendrocytes results in the localized translation of MBP mRNA at sites of axon-glial contact and myelin deposition. Oligodendrocyte precursor cells (OPC) also express the src family kinase Lyn which is down-regulated as the cells mature and exhibits binding partners distinct from Fyn.

S6 Control of myelination by neurotransmitters

Ragnhildur Káradóttir, Aryna Luzhynskaya, Iben Lundgaard, Zhen Wang , Nicola Hamilton, Johanne Rinholm, Linda Bergersen, Charles ffrench-Constant and David Attwell
University College London

Activation of neurotransmitter receptors on oligodendrocyte lineage cells is known to damage the cells and cause failure of myelin development, or demyelination, in pathological conditions such as cerebral palsy, spinal cord injury, stroke and multiple sclerosis. However, neurotransmitter receptors may also positively regulate myelination. We investigated myelination of dorsal root ganglion axons by cortical oligodendrocyte precursor cells, and myelination in cultured cortical slices, to study how glutamate and GABA receptors regulate myelination, and how this process fails in pathological conditions. In the absence of added neuregulin, myelination of DRG axons was not affected by blocking action potentials with TTX, nor by blocking glutamate's ionotropic receptors. With added neuregulin, myelination was increased by 50%, TTX reduced myelination by ~50%, and the NMDA receptor blocker MK-801 reduced myelination by ~80%. Thus, added neuregulin switches the mode of myelination, from a mode that is independent of action potentials and glutamate release to a mode that depends on action potentials and activation of NMDA receptors. This effect of neuregulin was associated with a 4-fold increase in the current response of patch-clamped oligodendrocyte lineage cells to NMDA, with no effect on the response of these cells to kainate, and no effect on the response of neurons to either NMDA or kainate. These data suggest that neuregulin acts by upregulating NMDA receptor expression in oligodendrocytes and their precursors, making them more sensitive to glutamate which is released from axons by action potentials. In cortical slices made from P7 rat brains, myelination of intracortical axons proceeds over a 2 week period in culture. Including the $GABA_A$ receptor blocker GABAzine, from days 3-14 in vitro, approximately doubled the number of oligodendrocyte lineage cells present, but did not affect the myelination produced. In contrast the $GABA_B$ receptor blocker CGP35348 had no effect on the number of oligodendrocyte lineage cells, but decreased myelination by ~40%. These data suggest that

endogenous GABA acts on $GABA_A$ receptors to suppress oligodendrocyte precursor proliferation, and on $GABA_B$ receptors to increase myelination. If cortical slices were cultured in low glucose medium, the number of oligodendrocyte lineage cells was reduced, as was myelination. The number of cells and myelination could be rescued if L-lactate was added to the medium, and pH imaging demonstrated lactate uptake into oligodendrocytes. These data suggest that, when myelination occurs in conditions of low glucose, the presence of lactate (either from astrocytes or from the blood) could reduce the impairment of myelination that would otherwise occur. Together, these data are consistent with neurotransmitters playing an important role in regulating myelination.

Supported by the Wellcome Trust, European Research Council, Royal Society, EU (Leukotreat) and MRC.

S7 Synaptic communication between neurons and cells of oligodendroglial lineage

Maria Kukley
Centre for Integrative Neuroscience, University of Tuebingen and University Clinic Bonn, Germany

Vesicular release of neurotransmitter is the universal output signal of neurons in the brain. It had been generally believed that fast transmitter release is restricted to nerve terminals that contact postsynaptic cells in the gray matter. In our recent study we have shown that the neurotransmitter glutamate is also released at discrete sites along axons in white matter in the absence of neurons and nerve terminals. The propagation of single action potentials along axons leads to rapid vesicular release of glutamate, which is detected by ionotropic glutamate receptors on local oligodendrocyte precursor cells, OPCs. Axonal release of glutamate is reliable, involves highly localized calcium microdomain signaling and is strongly calcium cooperative, similar to vesicle fusion at synapses. Interestingly, synaptic input largely disappears as soon as OPCs differentiate into pre-myelinating oligodendrocytes (NG2-, DM20/PLP+). Uncaging experiments and tracer loading revealed that pre-myelinating oligodendrocytes still express a substantial number of AMPA/kainate receptors and many branching processes but spontaneous and stimulated synaptic currents are largely absent. Mature myelinating oligodendrocytes completely lack AMPA/kainate receptors and respond to uncaging and synaptic stimulation with glutamate transporter currents. Our data show that neurons selectively synapse onto only one of several coexisting developmental stages of oligodendroglial cells. Therefore, we believe that neurons specifically signal to OPCs and are able to modulate transmitter output by regulating the local release machinery in a manner specific to the developmental stage of the postsynaptic glial cell.

S8 GABAergic transmission of NG2 cells changes during postnatal development of the barrel cortex

María Cecilia ANGULO
Inserm U603, Paris, France; CNRS UMR8154; Univ. Paris Descartes, Paris, France

Oligodendrocyte precursors, also called NG2 cells, constitute the endogenous pool of progenitors for oligodendrocytes during developmental myelination, but also for adult myelin repair in demyelinating diseases. In recent years, reports have demonstrated that NG2 cells receive functional synaptic contacts from inhibitory and excitatory neurons in gray and white matter. It is presumed that adult NG2 cells retain this synaptic input. In the present work, we analysed the synaptic activity of NG2 cells in acute slices of the barrel cortex of NG2-DsRed transgenic mice during the first postnatal (PN) month, the period of active myelination in this region. Spontaneous synaptic activity appears after P3 and was

mainly GABAergic, sensitive to the $GABA_A$ receptor antagonist GABAzine. However, a drastic frequency decrease of GABAergic synaptic events occurred after PN14. Moreover, miniature postsynaptic currents (mPSCs) were not detected at PN21-28, even when the potent secretagogue ruthenium red was bath applied. In contrast, mPSCs having fast rise times and slow decay times were easily observed at PN7-14, suggesting a decrease in the number of synaptic inputs onto NG2 cells during development. However, NG2 cells still receive GABAergic inputs from interneurons in the adult cortex. These inputs do not rely on the presence of functional synapses; instead, they involve a form of GABA spillover. Indeed, low-frequency extracellular stimulation revealed that $GABA_A$ receptor activation of NG2 cells at late developmental stages mediates transient responses with unusually slow kinetics. In addition, the effect of the low-affinity competitive $GABA_A$ receptor antagonist TPMPA on the amplitude of averaged currents was significantly greater in the fourth PN week, indicating that the concentration reaching $GABA_A$ receptors in older mice is lower than in young mice where GABA is released in a synaptic cleft. Finally, trains of stimuli (100 Hz) resulted in a response that was potentiated by GAT-1 GABA transporter antagonist NNC711 in the fourth, but not in the second PN week. The absence of miniature events as well as the higher sensitivity of evoked responses to NNC711 and TPMPA in the fourth PN week with respect to the second PN week supports the notion that $GABA_A$ receptor-mediated responses in NG2 cells from older mice arise from an extrasynaptic mode of diffuse transmission mediated solely by GABA spillover from neuronal terminals.

S9 Astrocyte to pericyte signalling and neurovascular coupling in CNS white matter

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Cerebral blood flow is directly coupled to neuronal activity in the brain. Brain capillaries lack smooth muscle and pericytes situated around the blood vessels are believed to play a key role in regulating local perfusion. Astrocytes contact both neurons and blood vessels, and release transmitters such as glutamate and ATP, which are known regulators of cerebral blood flow. Several pathways for the release of neurotransmitters by astrocytes have been proposed, including exocytosis. In this paper, we examine the mechanisms of communication between astrocytes and pericytes in situ, in isolated intact rodent optic nerves from mice in which NG2 drives the expression of DsRed. Astrocytes contact nodes of Ranvier, the site of action potential propagation in myelinated axons, and we show electrical activity in axons evokes raised calcium in astrocytes via ATP and glutamate release. In turn, we provide evidence of vesicular release of ATP and glutamate from astrocytes, and that vesicular release of ATP regulates pericyte intracellular calcium and capillary tone. In addition, we show that glutamate decreases the ATP-evokes rise in pericyte calcium. The results suggest a dynamic mechanism by which astrocytes couple local blood flow to neuronal activity, by the release of ATP or glutamate to regulate the contractile tone of pericytes.

S10 Astrocytes and ions, ischaemia and development

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Ion regulation in astrocytes has been extensively examined in cell culture preparations but little it known about how astrocytes regulate the extracellular space of the CNS in situ. Ion regulation of the

extracellular space if of particular importance during development because maintained excitability is a necessary condition for the formation of appropriate neural connection and for the control of cell fate. Action potential conduction in the axons of the developing optic nerve is required if mature visual connections are to form. Astrocytes in the rat optic nerve are post-mitotic at birth and express the mature cell marker GFAP. Using ion-sensitive dyes loaded into astrocytes in this preparation at post-natal day 0-2, we have found that ion and pH regulation has unique properties. In particular, HCO3-dependent net acid extrusion was accomplished by SLC26A3, an electrogenic anion exchanger not previously found in any neural cell type. This transporter was able to stabilize astrocytes pH under ischaemic conditions lasting 60 min. HCO3-independent acid extrusion was achieved by V-ATPase and Na-H exchange in a ratio of 2:1. This expression pattern of pH regulatory transporters is most similar to that found in epithelial cells and indicates an intermediate phenotype between mature astrocytes and their neurepithelial origins in the fetus.

S11 Neurotransmitter signalling in white matter pathology

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Glutamate is the principal excitatory neurotransmitter in the central nervous system (CNS), but it is also a potent neurotoxin that can kill nerve cells. Glutamate damages oligodendrocytes, like neurons, by excitotoxicity which is caused by sustained activation of AMPA, kainate and NMDA receptors. Glutamate excitotoxicity depends entirely on calcium overload of the cytoplasm and can be initiated by disruption of glutamate homeostasis. Thus, inhibition of glutamate uptake in isolated oligodendrocytes in vitro and in the optic nerve in vivo, is sufficient to trigger cell death which is prevented by glutamate receptor antagonists. In turn, activated, but not resting microglia, can compromise glutamate homeostasis and induce oligodendrocyte excitotoxicity which is attenuated by AMPA/kainate antagonists or by the blockade of the system x_c^- antiporter present in microglia. On the other hand, non-lethal, brief activation of glutamate receptors in oligodendrocytes rapidly sensitizes these cells to complement attack. Intriguingly, these effects are exclusively mediated by kainate receptors which induce calcium overload of the cytosol and the generation of reactive oxygen species. In addition, ATP signaling can trigger oligodendrocyte excitotoxicity via activation of calcium-permeable P2X7 purinergic receptors expressed by these cells. Sustained activation of P2X7 receptors *in vivo* causes lesions that are reminiscent of the major features of multiple sclerosis (MS) plaques, i.e., demyelination, oligodendrocyte death, and axonal damage. In turn, treatment with P2X7 antagonists of chronic experimental autoimmune encephalomyelitis, a model of MS, reduces demyelination and ameliorates the associated neurological symptoms. Together, these results indicate that ATP can kill oligodendrocytes via P2X7 activation and that this cell death process contributes to EAE. Importantly, P2X7 expression is elevated in normal-appearing axon tracts in MS patients, suggesting that signaling through this receptor in oligodendrocytes may be enhanced in this disease. Thus, P2X7 receptor antagonists may be beneficial for the treatment of MS. Altogether, these observations reveal novel mechanisms by which altered glutamate and ATP homeostasis can trigger oligodendrocyte death. This knowledge may generate new therapeutic avenues to treat more efficiently acute and chronic white matter pathology.

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S12 Neuroglia in neurodegenerative diseases

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The human brain circuitry is formed by neuronal networks embedded into astroglial syncytia. The astrocytes perform numerous functions providing for overall brain homeostasis, assisting in neurogenesis, determining the micro-architecture of the grey matter and defending the brain through evolutionary conserved astrogliosis programmes. Astroglial cells are engaged in neurological diseases determining the progression and outcome of neuropathological process. Astrocytes are specifically involved in various neurodegenerative diseases including Alzheimer's disease, Amyotrophic lateral sclerosis, Parkinson's disease and various forms of dementia. Recent evidence suggest that early stages of neurodegenerative processes are associated with atrophy of astroglia, which causes disruptions in synaptic connectivity, disbalance in neurotransmitter homeostasis and neuronal death through increased excitotoxicity. At the later stages astrocytes became activated and contribute to neuro-inflammatory component of neurodegeneration.

S13 Molecular mechanisms in the formation of the early axon scaffold

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In all vertebrates, the first neurons set up a well-conserved array of longitudinal, transversal and commissural axon tracts. At the core of this early axon scaffold is the ventral longitudinal tract system, formed by the medial longitudinal fascicle (MLF) and the tract of the postoptic commissure (TPOC). The MLF is the first tract to develop in most vertebrates. It originates from neurons at the ventral midbrain-forebrain boundary which extend their axons strictly caudad, along the ventral midline. The transversal tract aligning the midbrain-forebrain boundary is the tract of the posterior commissure (TPC). Neurons contributing to the TPC are located ventrally, intermingled with the MLF neurons. We are interested in the patterning mechanisms that determine the fate of the early neurons, and in the cues that guide their axons along well-defined paths. Our results indicate that the differential expression of homeobox genes, controlled by patterning signals, is involved in the fate determination of MLF neurons, while repulsion by semaphorins and netrins guides MLF and TPC axons.

S14 Wnt signaling in the regulation of neuronal circuit formation

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The establishment and maintenance of an appropriate balance between excitatory and inhibitory synapses is crucial for normal brain function. An imbalance in this equilibrium has been implicated in a number of developmental disorders such as mental retardation, autism and schizophrenia. Wnt proteins play a crucial role in neuronal connectivity by regulating axon guidance, dendritic development and synaptic assembly. However, the specific role for Wnts in excitatory and inhibitory synapses has not been reported. Here we demonstrate that Wnt7a, a key synaptic organizer, specifically regulates the formation of excitatory synapses in the hippocampus by stimulating the formation of dendritic spines, the postsynaptic loci of excitatory glutamatergic synapses. We recently found that Wnt7a, expressed at the peak of synaptogenesis, increases the number of synapses in hippocampal neurons. Wnt7a directly

signals to axons to stimulate the recruitment of presynaptic components. But Wnt7a also increases the apposition of pre- and synaptic markers, specifically the number excitatory but inhibitory synapses. Electrophysiological recordings revealed that Wnt7a increases the frequency and amplitude of miniature postsynaptic currents (mEPSCs) without affecting mIPSCs. Conversely, Wnt blockade with secreted antagonists causes a reduction in mEPSC frequency, again without affecting mIPSCs. Consistent with a role for Wnts in excitatory synaptogenesis, Wnt7a stimulates dendritic spine morphogenesis whereas deficiency in Wnt signaling as observed in the double *Wnt7a; Dvl1* mutant mice results in defects in spine morphogenesis. Importantly, specific postsynaptic activation of Wnt signaling increases the size of spines and the frequency and amplitude of mEPSCs, with no change in mIPSCs. Together, these results indicate that Wnt7a signals directionally to the pre and postsynaptic sides and that postsynaptic Wnt signaling regulates spine size. We propose that Wnt signaling plays an important role in the establishment and maintenance of a balance of excitatory and inhibitory neurotransmission through the regulation of dendritic spine morphogenesis.

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S15 Axon guidance at the midline of the Drosophila central nervous system

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The study of axon guidance at the midline of the central nervous system in the *Drosophila* embryo has allowed the identification and study of genes directing axonal growth. Both ipsilateral and contralateral projecting neurons in the *Drosophila* central nervous system are guided by a number of repellent and attractant cues. The Netrins have previously been shown to act as the major attractants bringing axons towards the midline while Slit acts as a repellent cue signalling through the Roundabout (Robo) receptor to steer axons away from the midline. Commissural neurons express *robo* but are insensitive to Slit prior to crossing the midline and become responsive to Slit after crossing. This differential sensitivity occurs through Commissureless (Comm), which regulates Robo protein distribution in the axon. The initial simple model of a balance of the Netrin attractant and Slit repellent guiding axons at the midline has recently become complicated by the discovery of additional midline guidance pathways and mechanisms, such as robo2, DsCam and turtle. We are using genetic and bioinformatic approaches to identify further axon guidance molecules. The latter has identified a set of transmembrane proteins that contain combinations of conserved extracellular protein domains previously found in known axon guidance molecules which are expressed in the *Drosophila* CNS during axon extension. A genetic approach has identified mushroom bodies defect (mud) as having an activity to guide commissural axons in the absence of Netrin signalling. Our data suggests a function for Mud protein in the polarisation of axonal outgrowth in response to guidance information. Genetic interaction studies show that Mud is acting downstream of some, but not all, of the pathways known to be required for midline guidance.

S16 Do glia mediate the axogenic effects of EGFR inhibitors?

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EGFR inhibitors are reported to act directly on neurons to attenuate inhibitory ligand signalling derived from components of the glial scar and degraded myelin. For example, inhibitory ligand binding to NgR on axonal growth cones increases Ca^{2+} influx which transactivates EGFR, leading to activation of the Rho/ROCK inhibitory signalling cascade by an unknown mechanism (Koprivica et al., 2005). According to this assertion, EGFR blockade by two EGFR inhibitors (AG1478 and PD168393) promotes CNS neurite/axon regeneration solely by paralysis of inhibitory signalling. However, we and others have demonstrated that optimal conditions for regeneration of CNS neurites/axons in the presence of inhibitory ligands, requires concomitant stimulation of axon growth and blockade of inhibitory signalling through intramembranous proteolysis (RIP) of $p75^{NTR}$/TROY and both are induced by neurotrophic factors (NTF) (Ahmed et al., 2005a, b, 2006a, b; Logan et al., 2006; Fischer et al., 2004a; Fischer et al., 2004b). RhoA is inactivated and protects axon growth cones from collapse by retarding actin depolymerisation (Ahmed et al., 2006b; Ahmed et al., 2006a; Logan et al., 2006). Since axons blinded to CNS growth inhibitors by EGFR kinase antagonist-mediated disinhibition require an additional stimulus for driving growth, we suggest that EGFR inhibitors are likely to act off-target to drive RGC axon regeneration possibly through the release of NTF from glia which induce both RIP and axogenic protein synthesis in axons and neuronal somata. On-target axogenic AG1478/PD168393 effects require the presence of the phosphorylated (p) EGFR substrate to be localised within axotomised RGC somata and their injured axons, and predict lowered or absent pEGFR titres in neurons and their axons when they are regenerating and that these small molecule antagonists will be ineffective in the absence of the EGFR substrate. However, our findings support the contention that off-target and indirect glial-mediated effects mediate AG1478/PD168393-stimulated axogenesis, since our experiments show that none of the above predictions are borne out. We have shown that axogenesis/neuritogenesis is unrelated to EGFR kinase inactivation but is mediated through Trk activation by glia-derived NGF, BDNF, NT-3 found in the conditioned medium of mixed primary dorsal root ganglion and retinal cultures exposed to AG1478 plus myelin. Release of NTF has the dual action of driving axogenesis and disinhibiting neurite outgrowth, at least in part, by NTF-induced RIP of $p75^{NTR}$/TROY.

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S17 The glial regenerative response to central nervous system injury is enabled by pros-notch and pros-NF-kappa B feedback

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Injury to the central nervous system (CNS) induces the proliferation of ensheathing glial cells, leading to axonal re-enwrapment and functional recovery, in a wide range of organisms from cockroaches to humans. However, the gene network enabling this regenerative glial response - while avoiding

tumorigenesis - is unknown. Using stabbing injury and in vivo gene manipulation in Drosophila, here we show that two positive feedback loops involving Pros-Notch and Pros-Dorsal/NF κ B underlie the glial proliferative response. While Pros and Notch positive ensheathing glia rarely proliferate in the unstabbed CNS, injury induces signaling by Eiger/TNF through Dorsal/NF κ B to trigger their proliferation. Pros negatively regulates the cell cycle and promotes glial differentiation, while Notch and Dorsal/NF κ B positively promote proliferation. The balance of opposing functions maintains glial cells on the brink of dividing, enables them to respond to injury, and to re-establish cell cycle arrest. Breakdown of these feedback loops resulted in loss of the injury response and in tumourigenesis. Time-lapse analysis showed that vacuoles emerged in axonal bundles after stabbing, some of which were filled with glial projections and subsequently repaired. Increasing glial number by gain of function of Notch reduced wound-size and the extent of injury-induced apoptosis. These results show that the proliferative glial response is regenerative, and it can be manipulated to facilitate neuropile repair. Given the widespread evolutionary conservation of gene networks, our findings are likely to provide valuable insights for mammalian models of CNS regeneration.

Symposium-related oral presentations

O1

Roxanna Octavia Carare (*University of Southampton, UK*)
Lymphatic drainage of the brain and the pathology of Alzheimer's Disease

O2

Jerome Swinny (*University of Portsmouth, UK*)
Impact of early life environment on the functioning of the nucleus locus coeruleus: implications for stress and affective disorders

O3

Sassan Hafizi (*University of Portsmouth, UK*)
Tensin Intracellular Focal Adhesion Proteins: Expression and Roles in the Brain

O4

Virginia Bay (*University of Portsmouth, UK*)
Inward rectifier potassium channels: K^+ regulation in the optic nerve

O5

Michelle Ware (*University of Portsmouth, UK*)
Formation of early axon tracts in the chick embryonic brain

O6

Jo Begbie (*Oxford University, UK*)
Signalling between placodal neurons and cranial neural crest

Posters

P1 **Glia and the enteric nervous system of the mouse intestine**
Steve West, James Brown and Arthur M. Butt
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P2 **GSK3β is a master regulator of astrocytes in the rodent optic nerve**
Andrea Rivera and Arthur M. Butt
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P3 **K2P channel expression and function in optic nerve glia**
Virginia Bay and Arthur M. Butt
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P4 **Inward rectifying potassium channel expression and localisation in mouse glial cells**
Csilla Brasko, Virginia Bay and A.M. Butt
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P5 **Inward rectifying potassium channel expression and localisation in human glioma cells**
Maria Papanikolaou, Csilla Brasko, Geoffrey Pilkington and Arthur M. Butt
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P6 **Localisation of inhibitory synaptic markers and GABAergic receptors in different glial populations in the CNS**
Victoria Stanford, Virginia Bay, Arthur M. Butt, Jerome D Swinny
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P7 **Immunohistochemical analysis of tensin protein expression in the mammalian brain**
Florence Escosio, Emma James, Salman Goudarzi, Jerome D. Swinny and Sassan Hafizi
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P8 **Distinct GABA-A receptor subunits label noradrenergic and non-noradrenergic cell-types in the locus coeruleus**
Nicole Corteen and Jerome D. Swinny
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P9 **Generation of GABAergic neurons in the early fetal human neocortex**
Nahidh Al-Jaberi
Newcastle University

P10 **Increasing diameter of retinal ganglion cell axons in rat, cat and ferret and the influence of light deprivation**
Gary Baker[1], Christophe Guibal[1] and Glen Jeffery[2]
[1] *Department of Optometry & Visual Science, City University London*
[2] *Institute of Ophthalmology, University College London*

P11 **Permissive effects of NG2 glia on neurite outgrowth in vitro: Implications for retinoic acid signalling**
Elizabeth Janet Pawson, Rebekah Wigley, Stephen McMahon and Jonathan Corcoran
Wolfson CARD, Guy's Campus, Kings College London, UK

P12 **Metastasis studies of the blood-brain barrier using in vitro models**
Kathryn Fry and Geoffrey Pilkington
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P13 **Immunotoxin Ablation of NG2 and GD3A: potential novel approach to glioma treatment**
Samantha Higgins, Arthur Butt and Geoffrey Pilkington
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P14 **Targeting GD3/GD3A in Novel Therapy Development for Glioma**
Suzanne Birks, Darek Gorecki and Geoffrey Pilkington
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P15 **Influence of Hypoxia on Cellular Biology in CD133-expressing Glioma Cells**
Qian An, Laura Donovan and Geoffrey Pilkington
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P16 **A Functional Study of CD44 and CD155 in Glioma Invasion**
Zaynah Maherally and Geoffrey Pilkiington
Institute of Biomedical and Biomolecular Science (IBBS), Department of Pharmacy and Biomedical Science, University of Portsmouth

P17 **Glycogen synthase kinase 3 expression in murine tissues**
Alvise Calamai, Anthony Cullen and Raj Ettarh
School of Medicine & Medical Sciences, University College Dublin

P18 **A quantitative investigation of transcriptional activity in syncytiotrophoblast nuclei during human gestation**
Norah Mary Elisabeth Fogarty
Department of Physiology, Development and Neuroscience, University of Cambridge

P19 **Leptin and leptin receptors in the rat and human carotid body**
Andrea Porzionato
Section of Anatomy, Department of Anatomy and Physiology, University of Padova

P20 **Proposition of a new statistical method for facial reconstruction in forensic medicine**
Odile Plaisant
Paris Descartes University

P21 **Course di clinical topographic neuroanatomy**
De Caro Raffaele
Section of Anatomy, Dep. Humana Anatomy and Physiology, University of Padova