21-22 March

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1st day Thursday March 21st 2019

Opening session and PIs lightning talks (Physiology Lecture Theatre)		***9h30- 10h25***
	Opening remarks	9h30 - 9h35
Susanna Mierau	Network Development in Cortical Circuits and Disruption in Rett Syndrome and Autism	9h35 - 9h40
Sara Morais da Silva	Studying the link between tumorigenesis, metabolism and the cell cycle in Drosophila melanogaster	9h40 - 9h45
Emma Cahill	Do you fear what I fear? rodent ultrasonic vocalisations in fear conditioning	9h45 - 9h50
Bio-Techne, Sponsor talk	In situ validation and spatial mapping of diverse striatal cells identified by scRNA-seq in the mouse brain at single-cell resolution	9h50 - 10h
Elisa Galliano	Neuronal plasticity: beyond the usual suspects	10h - 10h05
Erica Watson	Transgenerational epigenetic inheritance in mice	10h05 - 10h10
Leila Muresan	Image analysis for fluorescence microscopy	10h10 - 10h15
Ewa Paluch	Mechanobiology of cell shape control	10h15 - 10h20
Margherita Yayoi Turco	Stem cell biology of the maternal-fetal interface of human pregnancy	10h20 - 10h25
	Coffee break (Experimental Classroom)	***10h25 - 11h***
Session 1		***11h - 12h10***
	Physiology and stem cells 1 (Bryan Matthews room)	
Slatery, Erin	Towards the generation of chimaera-competent marmoset embryonic stem cells	11h - 11h15
Reiterer, Moritz	Organ-specific heterogeneity in endothelial cell hypoxia response	11h15 - 11h40
Siriwardena, Dylan Kassapa	Developing a platform for modeling primate placental development via generation and characterization of marmoset TSCs	11h40 - 11h55
Sowton, Alice	Metabolism of Obese Mitochondria with Inorganic Nitrate Supplementation – Preliminary Insights from Pilot Data	12h55 - 12h10
	Developmental biology 1 (Hodgkin-Huxley room)	
Campbell, Alexander Stuart	Identifying novel molecular mechanisms underlying lateral line sense organ development using an unbiased, comparative approach	11h - 11h15
Falo Sanjuan, Julia	Enhancer priming enables fast and sustained transcriptional responses to Notch signaling	11h15 - 11h40
Molè, Matteo	Integrin-mediated adhesion coordinates morphogenesis and survival of the epiblast upon implantation	11h40 - 11h55
Weberling, Antonia	Trophectoderm morphogenesis governs blastocyst remodelling upon implantation	11h55 - 12h10

	Lunch break (Experimental Classroom)	***12h15- 13h15***
Session 2		***13h15 - 14h45***
	Developmental biology 2 (Bryan Matthews room)	
Kyprianou, Christos	Sequential formation and resolution of rosettes drives formation of the pro-amniotic cavity in the early mouse embryo	13h15 - 13h30
Rodgers, Amanda	Placental Endocrine Malfunction Programs Metabolic Derangements in Offspring	13h30 - 13h45
Sanchez-Elexpuru, Gentzane	Zebrafish models of Multiple Sulfatase Deficiency	13h45 - 14h
Townson, Jonathan	Understanding Notch Intracellular Domain function and achieving precise spatial and temporal control of its release with optogenetics	14h - 14h15
Bergmann, Sophie	Unravelling the implanting primate embryo: SHOT-seq allows spatial transcriptome and methylome analysis	14h15 - 14h30
Greenhalgh, Ryan David	The role of viscoelasticity in axon guidance during development	14h30 - 14h45
	Mechanisms of neural development 1 (Hodgkin-Huxley room)	
Pillai, Eva	Mechanical regulation of chemical signalling in the developing Xenopus brain	13h15 - 13h40
Lau, Maggy Yu Hei	Morphological and Physiological Characterization of Identified Dopaminergic Neurons in the Mouse Olfactory Bulb and Midbrain	13h40 - 13h55
Supple, Jack	Binocular Fusion in Damselfly Descending Neurons	13h55 - 14h20
Badger, Benjamin	Autophagy in the brain	14h20 - 14h45
	Poster session and coffee break (Experimental Classroom)	***14h45 - 15h45***
	Plenary Session (Physiology Lecture Theatre)	***15h45 - 17h***
Sponsor talk	Cambridge Electronic Design	15h45 - 15h55
Cambridge Electronic Design plenary talk: Peter Lawrence	*Planar cell polarity, what it is, what it's for and something of how we think it works*	16h - 17h
	Wine reception (Experimental Classroom)	***17h***

2nd day Friday March 22nd 2019

Session 3		***9h30 - 10h40***
	Neurosignalling and Behaviour 1 (Bryan Matthews room)	
Banai Tizkar,Rana	The role of area 25 in producing anhedonia, its contribution to anxiety and its sensitivity to anti-depressants	9h30 - 9h45
Bujold, Philipe	Adaptive Economics: Exploring Choice Biases From the Brain's Perspective	9h45 - 10h10
Chaudhuri Vayalambrone, Prannoy	Characterising shifts in grid cell firing fields	10h10 - 10h25
Seak, Leo Chi U	Neural responses of revealed preference theory	10h25 - 10h40
	Mechanisms of neural development 2 (Hodgkin-Huxley room)	
Sipkova, Jana	The mechano-responsiveness of ephrin/Eph signalling in the topographic mapping of the Xenopus optic pathway	9h30 - 9h45
Becker, Julia	Stiffness alterations in spinal cord injury	9h45 - 10h
López Ramírez, Ana	Felodipine induces autophagy and clears neurotoxic proteins in mice and fish with pharmacokinetics amenable to repurposing in humans.	10h - 10h15
Memon, Ahsan	Fast Whole-cell 3D Super-resolution Imaging	10h15 - 10h30
Dunn, Alexander William Edward	Characterising pathological changes to neuronal network development in Rett Syndrome	10h30 - 10h45
	Coffee break (Experimental Classroom)	***10h45 - 11h15***
Session 4		***11h15 - 12h35***
	Physiology and stem cells 2 (Bryan Matthews room)	
Judge, Leia	The long and the short of it: Uncovering the role of long non-coding RNAs in the regulation of *Drosophila* neuroblast proliferation.	11h15 - 11h30
Garraud, Tess	Antenatal Glucocorticoids: Studies in the Chicken Embryo	11h30 - 11h55
Ross, Connor	Bananas about hypoblast - The derivation and functional characterisation of marmoset hypoblast stem cells.	11h55 - 12h10
Capatina, Nadejda	Effect of Endoplasmic Reticulum Stress on Trophoblast Cell Lineage Differentiation	12h10 - 12h35
	Neurosignalling and Behaviour 2 (Hodgkin-Huxley room)	
Fuchsberger, Tanja	Neuromodulation of Spike Timing-Dependent Plasticity in the Hippocampus	11h15 - 11h30
Stawicka, Zuzanna Monika	The role of anterior and posterior orbitofrontal cortex in emotional regulation.	11h30 - 11h55

Khorisantono, Putu	Neuroimaging of nutrient reward value and its effect on eating behaviour	11h55 - 12h10
Champion, Andrew	Combining structural and activity imaging in larval Drosophila	12h10 - 12h35

	Lunch break (Experimental Classroom)	***12h45 - 13h45***

Session 5 ***13h45 - 15h***

	Physiology and stem cells 3 (Bryan Matthews room)	
Strawbridge, Stanley	How does FGF signalling regulate the founding lineages of the mouse embryo?	13h45 - 14h
Mackinlay, Kirsty	Developing an in vitro Model of Post-Implantation Human Embryogenesis-Human Hypoblast Stem cell line derivation	14h - 14h15
Arman, Diana	Systemic and local signalling in nutrition-dependent reactivation of neural stem cells in *Drosophila*	14h15 - 14h30
Habib, Zaki	Structural and functional roles of the S5-S6 extracellular loop of $hNa_v1.5$ and β-subunits in Na^+ channel regulation	14h30 – 14h45
Pierson Smela, Merrick De Forest	Probing Gene Regulatory Networks in Human Primordial Germ Cell Specification	14h45 - 15h

	Neurosignalling and Behaviour 3 (Hodgkin-Huxley room)	
Feord, Rachael	Simultaneous spectral stimulation and two-photon neural activity imaging in a Drosophila colour processing neuropile, the medulla	13h45 - 14h10
Manchishi, Stephen Malunga	Molecular Signatures of Hypothalamic *Kiss1* Neurons	14h10 - 14h35
Jarzebowski, Przemyslaw	Neuronal target-specific hippocampal memory functions	14h35 – 14h50
Li, Chenguang	A computational study of variability in the lamprey spinal cord	14h50 -15h05

	Poster session and coffee break (Experimental Classroom)	***15h05 - 16h***

Plenary Session (Physiology Lecture Theatre) ***16h - 17h***

Foster talk: Steve Wilson *Breaking symmetry in the brain: from genes to circuits and behaviour*

	Drinks and Prizes (Experimental Classroom)	***17h - 17h30***

BioTechne Symposium Dinner (St Barnabas Church) ***19h - 22h***

1st day

PI's Lightning talks

Susanna Mierau

Network Development in Cortical Circuits and Disruption in Rett Syndrome and Autism

Multiple mutations have been identified in autism and related neurodevelopmental disorders that affect synaptic function. In Rett syndrome, loss of MeCP2, a chromatin remodeler, has opposing effects on excitatory synaptic maturation in excitatory and inhibitory cell populations in the cortex of the mouse model. Our work is focused on the effect of Mecp2-deficiency on network dynamics in developing cortical circuits using two-photon calcium imaging and multielectrode array recordings in cultured neurons. Our goal is to understand how synaptic changes lead to network level defects and identify new therapeutic targets for improving cortical function in these disorders.

Sara Morais da Silva

Studying the link between tumorigenesis, metabolism and the cell cycle in Drosophila melanogaster

Bub3 is a spindle assembly checkpoint protein with a role in the correct chromosomal distribution between cells in mitosis. Lower expression levels of this protein lead to tumorigenesis in Drosophila larvae. A genetic modifier screen has identified several metabolic modulators of this tumour growth. My aim is to identify the role of these candidate genes in the cross-talk between metabolism, tumorigenesis and the cell cycle.

Emma Cahill

Do you fear what I fear? rodent ultrasonic vocalisations in fear conditioning

Having joined PDN in September, Dr Cahill studies the mechanisms of fear and anxiety. She is interested in the differences between emotionally-driven behaviour that is learned and that which is innate. Using molecular biology, pharmacology and modified behavioural tasks, she aims to figure out how the brain changes in response to experience and how those responses are controlled.

Elisa Galliano

Neuronal plasticity: beyond the usual suspects

The ability of nerve cells to modify themselves in a process called neuronal plasticity is one of the characteristics that make the brain millions of times more powerful and capable of learning than any supercomputer. We are particularly interested in the ways in which the brain responds to sensory stimuli from the environment and uses such experiences to plastically modify itself at a cellular and circuit level. We investigate signalling, plasticity and behaviour in the olfactory bulb (Maggy Lau, Gaia Bianchini and Yasmeen Cooper) and in the cerebellum (Tessa Bienfait, Harry Bestwick and Ben Grodzinski).

Erica Watson

Transgenerational epigenetic inheritance in mice

Folate deficiency is famously associated with neural tube defects yet folate metabolism plays a much larger role in development and health. We previously showed that defects in folate metabolism in mice has transgenerational effects on the development of their grandprogeny and great grandprogeny. The goal of our research is to explore genetic, epigenetic and developmental mechanisms behind the multigenerational inheritance of these phenotypes (e.g., growth phenotypes, congenital malformations). Understanding how folate metabolism conveys memory to the next generation will better inform us about the mechanisms behind the inheritance of non-communicable disease risk.

Leila Muresan

Image analysis for fluorescence microscopy

Leila Muresan is a RSE EPSRC fellow, hosted by Cambridge Advanced Imaging Centre. Her objective is to support research in the School of Biology by developing image analysis solutions for light microscopy, with special emphasis on super-resolution microscopy and lightsheet microscopy. She will be joined in June by a research associate working on space varying deconvolution for lightsheet microscopy and multi-modal registration.

Ewa Paluch

Mechanobiology of cell shape control

The Paluch lab investigates the basic principles of cell shape control. Cell shape is ultimately the result of mechanical forces acting on the cell membrane. To investigate cell shape regulation, it is thus essential to investigate how cells control their own physical properties. We combine molecular and cell biology, quantitative imaging, biophysics and modelling to understand cell shape control across scales, from molecular processes to cell-scale behaviour. We are particularly interested in cell shape changes during cell migration and division, and during developmental fate transitions.

Margherita Yayoi Turco

Stem cell biology of the maternal-fetal interface of human pregnancy

The placenta, the extra-embryonic organ derived from the trophectoderm, sustains the mammalian embryo during its development in utero. Disorders of pregnancy that arise from abnormal placental development result in considerable maternal and infant mortality. Understanding the molecular and cellular mechanisms underlying the development of the human placenta and its interactions with the endometrium, the lining of the uterus has been challenging. We have recently derived 3D culture systems of both sides of the maternal-fetal interface that phenotypically and functionally recapitulate their tissue of origin. We aim to use these organoids combined with single cell genomics, Crispr/Cas9 genome editing and tissue engineering to unravel the fundamental biology of how these two organs function and cooperate to establish a successful pregnancy.

Erin Slatery

1st year PhD student - Boroviak lab

Towards the generation of chimaera-competent marmoset embryonic stem cells

Conventional human and nonhuman primate pluripotent stem cells (PSCs) transcriptionally correspond to the postimplantation epiblast. Recently, several groups have reported culture conditions supporting a putative naïve pluripotent (preimplantation epiblast-like) state in human pluripotent cells (Gafni et al., 2013; Takashima et al., 2014; Theunissen et al., 2014; Ware et al., 2014; Duggal et al., 2015; Guo et al., 2017). However, naïve human PSCs cannot be tested for functional equivalence to the preimplantation epiblast in chimera contribution assays for ethical reasons. In my PhD project, I seek to generate naïve pluripotent marmoset PSCs and evaluate their ability to contribute to normal development in vivo. The specific aims of my proposal are to: (i) refine culture conditions promoting a naïve pluripotent state in marmoset PSCs; (ii) carry out joint profiling of chromatin accessibility, DNA-methylation and transcriptome in naïve marmoset PSCs for direct comparison to the in vivo preimplantation epiblast; (iii) functionally define the essential, primate-specific regulators of naïve pluripotency in gain- and loss-of function candidate screens, (iv) assess survival, incorporation and pluripotency maintenance of naïve marmoset PSCs in mouse blastocysts; and (v) examine the contribution of naïve marmoset PSCs to marmoset chimeras.

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Physiology and stem cells 1

Moritz Reiterer

3rd year PhD student - Branco and Johnson labs

Organ-specific heterogeneity in endothelial cell hypoxia response

The microvasculature is a heterogeneous, dynamic and versatile component of the systemic circulation, with a unique ability to locally self-regulate and to respond to organ demand and systemic stimuli. ECs from different organs display considerable variation but it is currently not clear whether this is intrinsically determined or a result of microenvironmental cues.

We compared the hypoxia response of primary murine lung microvascular EC (lMVEC), which we have largely explored in the context of metastatic disease and pulmonary hypertension, to those of the brain (bMVEC), a network of very distinct environment and demands. Unexpectedly, bMVECs lose viability earlier and more dramatically when exposed to 1% O2 than lMVEC. This correlates with increased expression of the autophagic protein BNIP3. Hypoxic bMVECs also show metabolic dormancy and are unresponsive to mitochondrial toxins. Furthermore, hypoxic bMVECs display only modest increases in glycolytic rate, compared to lMVECs, in keeping with comparatively mild induction of hypoxia-induced transcription factor HIF-1α (regulator of the switch to glycolysis). Overall, bMVEC have a reduced and attenuated hypoxia response compared to lMVEC.

To investigate if these differences are due to environmental reprogramming, we subsequently cultured these cells at physiological oxygen levels. Cells cultured at 10% O2 (average O2 in lung) and 5% O2 (physiological O2 in brain) showed a metabolic response to hypoxia (1% O2) that was strikingly different, both between the two EC types and within the same cells cultured at different atmospheres. In all cases, higher O2 exposure elevated baseline OXPHOS in favor of glycolysis. At 10% O2, the response to hypoxia in bMVEC was still impaired compared to lMVEC, but when cultured at 5% O2, this was reversed; bMVECs showed a quick and pronounced increase in glycolytic rate upon hypoxia, whereas lMVECs displayed no further increase, suggesting 5% O2 is already hypoxic for a lMVEC.

These results show that microvascular plasticity and responses are intrinsic, but to a large extent reprogrammable by environmental priming. This knowledge is central in understanding and treating a myriad of insults to the microvasculature, such as surgery, wounding or circulating therapeutics.

Dylan Kassapa Siriwardena

1st year PhD student - Boroviak lab

Developing a platform for modeling primate placental development via generation and characterization of marmoset TSCs

The mammalian placenta is essential for embryo survival and development by mediating all interactions between the mother and embryo. To accommodate the developing embryo, placental development begins at day 5 post-fertilization with the specification of trophoblast cells along the outer blastula. Trophoblast development and differentiation are essential for embryo implantation into the uterine tissue, maternal vascular remodeling, and nutrients and waste exchange between mother and embryo. Consequently, defects in trophoblast specification and differentiation can lead to numerous developmental disorders include pre-eclampsia or placenta accreta. Despite the essential role of trophoblasts during early embryonic development, there is a lack of accurate in vitro human trophoblast stem cell (TSC) models. Moreover, current murine TSC models have been shown to misrepresent human TSCs, due to significant transcriptional differences between the mouse and human preimplantation embryo. TSCs also represents an ideal model for early embryonic lineage specification, due to their indefinite self-renewal capacity and multipotency. In fact, in humans and primates, trophoblast specification constitutes the first cell fate decision made by cells within developing embryo at the 16-cell stage. However, current extraction protocols yield small numbers of cells and in vitro culture may select for non-representative trophoblast clones. Consequently, we aim to generate and characterize marmoset TSCs for in vivo implantation to develop a platform for modeling primate embryonic model system. Specifically, we have generated TSCs from marmoset blastocysts and early placental tissues. Marmoset TSCs will be characterized on a genetic, epigenetic, and transcriptional level to confirm trophoblast lineage differentiation and gain insights into trophoblast specifications. Moreover, key trophoblastic regulators will be identified and functionally characterized in our TSCs in vitro using CRISPR/Cas9 genome editing. In vivo functional characterization will be conducted via the injection and culture of labelled marmoset TSCs in marmoset embryos

Alice Sowton

1st year PhD student - Murray lab

Metabolism of Obese Mitochondria with Inorganic Nitrate Supplementation – Preliminary Insights from Pilot Data

Diabetic cardiomyopathy is an important but poorly understood clinical cause of cardiovascular mortality in diabetic patients that occurs in the absence of cardiovascular risk factors such as coronary artery disease or hypertension. It is understood to be associated with altered cardiac metabolism, but whether this is causal in the development of the condition or a consequence of the pathology remains to be determined. In order to investigate the metabolic progression and associated mitochondrial changes of the condition, we have designed a longitudinal study over 12 months using mice fed a diabetogenic, high-fat high-sugar diet. Simultaneously, we are also investigating the potential for dietary supplementation with inorganic nitrate to slow progression of the metabolic abnormalities. In preparation for this, and in order to assess the impact of the diet alone, we carried out a pilot study, where C57Bl/6J mice (N=8/group) were fed either a high-fat, high-sugar diet or standard laboratory chow for 4 weeks before mitochondrial function in heart, soleus, gastrocnemius and liver was assessed by high-resolution respirometry. Phenotypic measurements were collected throughout the study including weekly body mass, food and water intake and fed and fasted blood glucose concentrations. Analysis is still ongoing, but this talk will highlight the preliminary findings from the pilot study, to indicate the impact high-fat high-sugar feeding exerts on systemic glucose handing and mitochondrial function.

Alexander Stuart Campbell

1st year PhD student - Baker lab

Identifying novel molecular mechanisms underlying lateral line sense organ development using an unbiased, comparative approach

Electroreception is an ancient division of the lateral line sensory system of fishes and aquatic-stage amphibians that enables the detection of weak electric fields in water, mostly used for hunting live prey. It was lost in the ancestors of frogs and teleost ray-finned fishes (the lab models Xenopus and zebrafish lack electroreception), and evolved independently at least twice within teleosts. In all fishes and aquatic-stage amphibians, the lateral line has a mechanosensory division that detects local water movement. In non-teleost jawed vertebrates, electroreceptor cells reside within 'ampullary organs' in fields on the head that flank lines of 'neuromasts' containing mechanosensory hair cells. Ampullary organs and neuromasts originate from lateral line placodes that elongate over the head to form sensory ridges (neuromasts form first, along the centre of the ridge; ampullary organs form later, on its flanks). To identify genes involved in ampullary organ vs. neuromast development, the lab previously used differential RNA-seq in late-larval stages of a chondrostean ray-finned fish, the Mississippi paddlefish, to generate a lateral line organ-enriched gene-set (Modrell et al., 2017, eLife 6: e24197). This contains ~45 genes encoding transmembrane receptors and ligands. I am cloning cDNA fragments of these genes in an experimentally tractable chondrostean, the sterlet (Acipenser ruthenus, a sturgeon), and performing in situ hybridisation to determine which are expressed within developing lateral line organs and whether this is conserved between ampullary organs and neuromasts. I will subsequently target the most interesting genes for CRISPR-mediated knockout. I also plan to compare the expression and function of validated genes in Xenopus and zebrafish, whose lateral line placodes only form neuromasts. Overall, this unbiased, cross-species approach should identify novel signalling pathways important for the development of hair cells and/or electroreceptors, and determine whether such mechanisms are conserved or lineage-specific.

Julia Falo Sanjuan

3rd year PhD student - Bray lab

Enhancer priming enables fast and sustained transcriptional responses to Notch signaling

Information from developmental signaling pathways must be accurately decoded to generate transcriptional outcomes. In the case of Notch, the intracellular domain (NICD) transduces the signal directly to the nucleus. How enhancers decipher NICD in the real time of developmental decisions is not known. Using the MS2/MCP system to visualize nascent transcripts in single cells in Drosophila embryos we reveal how two target enhancers read Notch activity to produce synchronized and sustained profiles of transcription. By manipulating the levels of NICD and altering specific motifs within the enhancers we uncover two key principles. First, increased NICD levels alter transcription by increasing duration rather than frequency of transcriptional bursts. Second, priming of enhancers by tissue-specific transcription factors is required for NICD to confer synchronized and sustained activity; in their absence, transcription is stochastic and bursty. The dynamic response of an individual enhancer to NICD thus differs depending on the cellular context.

Matteo Molè

Postdoc - Zernicka-Goetz lab

Integrin-mediated adhesion coordinates morphogenesis and survival of the epiblast upon implantation

Implantation is a critical stage of embryogenesis, during which the embryo establishes primary contacts with the maternal endometrium. During this process, the embryonic lineage (epiblast) undergoes a major morphogenetic change transforming the disorganised group of pluripotent stem cells of the blastocyst into a highly structured epithelium with a defined apico-basal polarity surrounding a central cavity, the future amnion.

Here, we find that the transition of epiblast from apolar to a fully polarised epithelium is characterised by a fine-tuned spatial segregation between the contractile acto-myosin cytoskeleton and integrin receptors, in a mutually exclusive pattern. By conditional genetics, we show that integrins exert an inhibitory effect on the cytoskeleton to ensure initiation of contractility precisely at the future apical site. While dispensable for the establishment of the epiblast apico-basal axis, these interactions are essential for the subsequent maintenance of apico-basal polarity and for the correct secretion of vesicles to the nascent site of lumenogenesis. In addition to acting as primary linkage to the internal cytoskeleton of the cells, we find that integrin signalling finely tunes the balance between survival and apoptotic death upon exit from naïve pluripotency. Combining pharmacological activation with conditional genetics of integrin receptors, we were finally able to restore survival and promote morphogenesis of the integrin-deficient epiblast, highlighting the key essential building blocks, which underlie epiblast morphogenesis upon implantation.

Antonia Weberling

1st year student - Zernicka-Goetz lab

Trophectoderm morphogenesis governs blastocyst remodelling upon implantation

The shape of mammalian embryos changes dramatically upon implantation. During mouse embryonic development, the implanting blastocyst remodels to transform into a cylindrical-like structure, the egg cylinder. Particularly, the polar trophectoderm expands to form the extra-embryonic ectoderm, while the primitive endoderm differentiates into the visceral endoderm, which envelops both epiblast and the newly formed extra-embryonic ectoderm. Despite the fact that mouse embryonic development has been studied for more than five decades extensively, the molecular and cellular events driving the blastocyst to egg-cylinder transition remain unknown. In this study, we reveal that precise positional information regulates trophectoderm morphogenesis, which in turn orchestrates the blastocyst to egg cylinder metamorphosis. Specifically, we show that positional information provided by the epiblast results in different fate acquisition from polar and mural trophectoderm. That is followed by the establishment of a tissue boundary, at the respective interface. Formation of this tissue boundary is indispensable for polar trophectoderm expansion to extra-embryonic ectoderm. Furthermore, we demonstrate that the last step of egg cylinder transformation is governed by forces generated during the folding of the newly formed extra-embryonic ectoderm resulting in cell shape changes driven expansion of the primitive endoderm. Thereby, we reveal a connection between positional information and proper tissue morphogenesis during embryogenesis.

Christos Kyprianou

Postdoc - Zernicka-Goetz lab

Sequential formation and resolution of rosettes drives formation of the pro-amniotic cavity in the early mouse embryo

Murine embryo development can be divided into three major phases; the pre-implantation, peri-implantation and post-implantation stages. Immediately after implantation of the blastocyst to the uterine tissue, the embryo undergoes a dramatic transformation transitioning from the cavitated blastocyst to an egg cylinder comprised of three tissues; the epiblast (EPI), the extraembryonic ectoderm (ExE) abutting the EPI and the visceral endoderm (VE) monolayer covering both EPI and ExE. One of the major morphogenetic events that take place once egg cylinder forms is the emergence of the proamniotic cavity (PAC); a cavity spanning through the egg cylinder in both EPI and ExE. Careful characterisation of the EPI and ExE tissues during the time of PAC formation revealed that the process to get this cavity involves the two pre-existing cavities of the EPI and ExE and the reorganisation of the intervening tissue between them to allow them to unify. The ExE architecture, as directed by the underlying basement membrane through integrin-mediated signalling, is essential in the correct progression of the two cavities through the intervening tissue. More specifically, the regular architecture of the ExE allows formation of epithelial rosette structures that when next to a cavity, resolve in a way that the cavity is allowed to extend. This resolution of the rosettes is mediated by polarised recruitment and secretion of podocalyxin-filled vesicles in the lateral cell membranes of rosette cells at the rosette-cavity interface.

Amanda Rodgers

1st year PhD student - Sferruzzi-Perri lab

Placental Endocrine Malfunction Programs Metabolic Derangements in Offspring

INTRODUCTION: Studies have shown that the mother's environment (diet, stress, oxygen levels and maternal BMI) can affect placental growth and birthweight, and program the offspring's long term health. However, the precise role of the placenta, the site of materno-fetal nutrient transfer and source of metabolism-modulating hormones, in the developmental programming of the offspring is unknown. Utilizing a newly-developed mouse model where placental endocrine malfunction was selectively induced by loss of the imprinted growth gene, insulin-like growth factor 2 in only the endocrine zone (junctional zone) of the placenta (Jz-Igf2UE), this project aimed to identify the role of placental endocrine function in the metabolic health of offspring. We hypothesised that placental endocrine malfunction will program metabolic impairments in the offspring.

METHODS: TpbpaCre females were crossed with Igf2-floxed males to produce entire litters with Jz-Igf2UE (leaving the placental transport zone, fetus and mother un-manipulated). Litters of the reverse parental cross (Igf2-floxed females mated to TpbpaCre males; no change in Igf2) were used as controls. After birth, litters were reduced to 3 females and 3 males and from weaning pups were fed a normal chow or a high sugar and fat (HFHS) diet (>6 litters/genotype/diet). Insulin tolerance tests were performed at 12 weeks of age and metabolic organs collected at 13 weeks for molecular and biochemical analyses. T-tests on litter means or a representative pup/litter were used to determine significant differences between Jz-Igf2UE and control within each diet ($P<0.05$). Only data from female pups are presented.

RESULTS: Compared to controls, Jz-Igf2UE females were insulin resistant on both a chow and HSHF diet. On a chow, but not HSHF diet, Jz-Igf2UE females had less adiposity and elevated pancreas insulin content compared controls. This was related to a greater increase in adiposity and no elevation in pancreas insulin content with a HSHF diet in Jz-Igf2UE females, compared to controls. There were significant differences in the abundance of growth and metabolic signalling proteins in the liver between Jz-Igf2UE and control on both a chow and HSHF diet.

CONCLUSION: Placental endocrine malfunction (via Jz-Igf2UE) impacts the future metabolic health of the female offspring. Analyses of male offspring are underway.

Gentzane Sanchez-Elexpuru

Postdoc - Fleming lab

Zebrafish models of Multiple Sulfatase Deficiency

Multiple Sulfatase Deficiency (MSD) is a rare and currently untreatable inherited metabolic disorder. It is caused by mutations in the SUMF1 gene which encodes formylglycine generating enzyme (FGE), an enzyme that post-translationally activates all cellular sulfatases in the endoplasmic reticulum (ER).

With at least 8 sulfatases exhibiting their function in the lysosome, MSD pathology results in a unique form of lysosomal storage disorder (LSD). Patients suffering from MSD show a neurodegenerative course of disease, mental retardation, hepatosplenomegaly, shortening of stature and corneal clouding, ichthyosis and skeletal changes. Recently, two SUMF1 null zebrafish lines have become available. Our overall aim is to use these models of MSD to identify novel compounds that show disease rescue. For that purpose, we are first characterizing the two SUMF1 null zebrafish lines. We have performed a detailed survival analysis and biochemical analysis of the sulfatase activities. We are also analysing the histopathology to determine which tissues are most severely affected by the mutation and we are evaluating the lysosomal function. These results will provide a suitable model for compound screening to identify agents which prolong survival. These compounds will be used for further development as potential treatments for the disease.

Jonathan Townson

1st year PhD student - Bray lab

Understanding Notch Intracellular Domain function and achieving precise spatial and temporal control of its release with optogenetics

The Notch signalling pathway is highly conserved and important for multiple developmental processes. A number of diseases, including cancers, result from defects in the pathway. Activation of transmembrane receptor leads to release of the intracellular domain (NICD) that traffics to the nucleus where it activates transcription of target genes. Despite its simplicity, there remain many unanswered questions about what levels and duration of signalling are required to elicit an effective response. Two approaches have been taken to investigate these questions. The first is to investigate specific features of NICD to determine their significance for the formation of active transcription complexes and their effects on chromatin accessibility. The second is to investigate strategies to release NICD in a carefully controlled spatial and temporal manner, optogenetic tools have been employed to achieve this.

Sophie Bergmann

Research Assistant - Boroviak lab

Unravelling the implanting primate embryo: SHOT-seq allows spatial transcriptome and methylome analysis

Implantation is a crucial event during the early embryonal development in mammals, as it allows the embryo to attach, and subsequently extraembryonic cells to invade the maternal uterus. Unfortunately, the process of implantation in our own species has remained enigmatic, due to ethical reasons making early human postimplantation stages inaccessible for study. In this project, we aim to delineate the dynamics of implantation using the non-human primate marmoset as a model for primate embryogenesis. We have developed a new protocol for spatial methylome and transcriptome sequencing (SHOT-seq) in the implanting primate embryo. SHOT-seq combines laser capture microdissection with joint singlecell methylome and transcriptome profiling. Carnegie stage 5 (pre-gastrulation postimplantation embryo) and 6 (early gastrulating embryo) marmoset embryos are cryosectioned and subjected to 4colour immunofluorescence labelling. At the moment we are working on an image reconstruction pipeline to render high-resolution, 3D models of the early postimplantation primate embryo. Importantly, our approach preserves the spatial identity of each multi-omics sample within the reconstructed embryo. SHOT-seq will be a powerful tool to faithfully track the embryonal lineages and derivatives in the implanting primate embryo and to identify regulatory associations between transcriptome and methylome.

Ryan David Greenhalgh

1st year PhD student - Franze lab

The role of viscoelasticity in axon guidance during development

Recently, tissue elasticity has been demonstrated to be critical in regulating axon guidance during Xenopus optic pathway development. Stiff substrates facilitate straight and fast growth of axon bundles, stiffness gradients lead to axons turning towards the soft side, and soft substrates lead to slowed growth and axon unbundling. However, biological tissues are viscoelastic materials with not only an elastic but also a viscous component. Here, Xenopus eye primordia were grown on polyacrylamide hydrogels with tuneable elasticity and viscosity. In contrast to soft elastic substrates, axon growth is facilitated on soft viscoelastic substrates, suggesting that substrate viscosity represents another important parameter regulating axon growth. Methods are now being developed to rapidly probe the viscoelasticity of brain tissue in vivo to understand role of viscous forces in axon guidance in the developing brain.

Eva Pillai

3rd year PhD student - Franze lab

Mechanical regulation of chemical signalling in the developing Xenopus brain

During nervous system development, growing neurons respond to chemical as well as mechanical signals in their environment. We found that axons of the optic tract grow along stiffness gradients in the developing Xenopus brain. Mechanosensitive ion channels (MSCs) are key players in transducing these mechanical cues into intracellular signals. Pharmacological blocking of MSCs and knockdown of the MSC, Piezo1, caused severe pathfinding errors in the developing Xenopus optic tract. In addition to directly impacting axon growth, downregulation of Piezo1 also dramatically altered the expression of semaphorin3A (Sema3A), a chemical guidance cue known to be critical in optic tract axon pathfinding. Our results thus indicate that the expression of chemical guidance cues may be modulated by tissue mechanics during development. As mechanical changes occur throughout development and during ageing and injury, this study could allow us to better understand how chemical signalling may be influenced by tissue mechanics during these processes.

Maggy Yu Hei Lau

MPhil - Jones lab

Morphological and Physiological Characterization of Identified Dopaminergic Neurons in the Mouse Olfactory Bulb and Midbrain

In the mammalian brain, heterogeneity exists between dopaminergic (DA) neuronal classes on grounds of morphology, physiology, connectivity and gene expression. The majority of DA neurons reside in the midbrain (Substantia Nigra pars compacta, SNc and the Ventral Tegmental Area, VTA), the olfactory bulb (OB) and the diencephalon. Midbrain DA neurons exhibit different protein expression, neurotransmitter co-release and projection target patterns (Morales and Margolis, 2017). In the olfactory bulb, DA neurons are found to exist in two subclasses, categorized by the presence of an axon initial segment (Galliano et al., 2018). Given the heterogeneity of DA neurons within and across brain regions, how do we characterize physiological heterogeneity under the same recording conditions? Can we attribute physiological differences within neuronal subclasses in the SN, VTA and OB to their morphology and protein expression?

To tackle this question, we performed whole-cell patch clamp recording in acute slices of midbrain and OB taken from juvenile DAT-tdTomato transgenic mice (P14-37). Under identical conditions, current clamp experiments were performed to examine single-spike properties (spiking threshold, amplitude, width and afterhyperpolarization) and continuous firing properties (input-output spiking frequency, spiking frequency by time, interspike intervals and first action potential delay). The effect of tonic signalling on physiological properties of DA neurons was also examined by the application of synaptic transmission blockers picrotoxin (100uM) and DNQX (10uM), blocking $GABA_A$, AMPA and kainite receptor-mediated currents.

Preliminary data shows that the application of synaptic blockers increased the input-output firing frequency of DA neurons in the OB. The next step forward will be to look at the effects of synaptic blockers in the SN and VTA; and to determine whether heterogeneity in DA neurons within each brain region is related to their morphology.

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Jack Supple

3rd year PhD student - Franze and Gonzalez-Bellido labs

Binocular Fusion in Damselfly Descending Neurons

Dragonflies and Damselflies both perform complex visually guided aerial manoeuvres for prey capture, albeit with distinct visual adaptations and hunting strategies. For instance, most Dragonfly species well-studied to date track and attack their prey from below using a single fused (holotopic) dorsal fovea, whilst Damselflies have conspicuously separated eyes with frontward-facing foveas and attack their prey in a frontal assault, with many species able to stalk up to and capture stationary prey in this manner. At the core of these divergent behaviours is the information processing task of transforming visual representations of prey into motor commands. In Dragonflies, a small set of 16 bilaterally symmetric Target Selective Descending Neurons (TSDNs) efficiently encode prey position and direction of movement as a population vector and are thought to form a reactive control mechanism stabilising the prey within the dorsal fovea for interception. Thus, TSDNs serve as an ideal handle to test how sensorimotor transformation of these animals may have diverged from their common ancestor. To investigate this, we have identified and recorded from TSDNs of the Banded Demoiselle (Calopteryx splendens). The receptive fields of these neurons show directional and spatial tuning properties for object movement reminiscent of Dragonfly TSDNs. Although the receptive fields in Calopteryx also tend to be centred at the midline, they usually expand across both hemifields, potentially reflective of the increased ocular disparity between Damselfly eyes compared to the fused holotopic ocular arrangement of the Dragonfly dorsal fovea. Experiments comparing binocular and monocular inputs to Calopteryx TSDN receptive fields suggests that individual TSDNs receive binocular input, and that at least 2 types of TSDNs only respond when both eyes are stimulated at the same time, i.e. binocular facilitation. Binocular facilitation is present in cats and monkey neurons highly sensitive to disparity, called “binocular only neurons”.

Benjamin Badger

3rd year PhD student - Brand lab

Autophagy in the brain

Autophagy is the process by which cytosolic material is sent to the lysosome for destruction, and has been observed to be capable of lipid redistribution. We investigated the formation of lipid droplets in the larval Drosophila brain and find that neural stem cell but not glial autophagy is necessary for glial lipid droplet formation upon larval starvation. We propose a mechanism by which lipids are freed from membranes via autophagy in neural stem cells and are transported to the glia for storage.

Cambridge Electronic Design Plenary talk:

Peter Lawrence

Planar cell polarity, what it is, what its for and something of how we think it works

Short Biography: Peter Lawrence has a long standing interest in the formation of patterns in development and would like to know how genes act to achieve pattern through the interaction of cells. For the last twenty years or so, in collaboration with José Casal in Cambridge, Gary Struhl at the HHMI, Columbia University, NY and David Strutt in Sheffield, They have been investigating the development of the larval and adult abdomen. He was a student of Sir V. B. Wigglesworth in the Zoology Department at the University of Cambridge from 1962-65. After a Harkness Fellowship held in 1966-67 in the USA, he returned to the Genetics Department. He was at the MRC Laboratory of Molecular Biology in Cambridge from 1969-2006. In 2006, instead of giving up research after turning 65 he returned to the Zoology Department at the University of Cambridge. In 1992 he published The Making of a Fly (Blackwell Scientific Publications, Oxford).

Abstract: The talk will mainly be about our attempts to understand planar cell polarity (PCP) and a biased and simplified selection of the ideas and models that have emerged. Drosophila stands way out as the best model organism, its genetics, its methodology of making mosaics and its oriented cell hairs and bristles have provided the means of discovery.

2nd day

Rana Banai Tizkar

1st year PhD student - Roberts lab

The role of area 25 in producing anhedonia, its contribution to anxiety and its sensitivity to anti-depressants

Depression is a heterogenous illness with many facets including anhedonia (e.g. lack of feeling pleasure) and rumination (e.g. increased negative emotion) and is mostly comorbid with anxiety. Studies investigating therapeutic avenues for depression suggest a causal link between activity of subgenual anterior cingulate cortex including area 25 and depression. However, the precise functions of this area are as yet unknown. Investigating the role of area 25 in anhedonia, previous findings in our lab have shown that overactivation of this area using Dihydrokainic acid (DHK) has led to partial anhedonia (motivational and anticipatory but not consummatory) in an appetitive Pavlovian task. This overactivation also has led to increased cortisol levels and anxiety-like behaviour in an aversive context compared to saline. However, increased cortisol levels when achieved by peripheral injection of cortisol could not produce a complete form of the anhedonia induced by area 25 overactivation. On the other hand, a peripheral injection of ketamine, an experimental antidepressant was observed to ameliorate anhedonia but not the cortisol and anxiety-like behaviour. All these observations suggest that there is some form of interaction between networks underlying anhedonia and anxiety. One of the aims of the current project is to understand the nature of this interaction. First, I am going to extend these findings by using progressive ratio (PR) instead of appetitive Pavlovian task to study if ketamine can ameliorate the blunting of motivational anhedonia as it did for anticipatory anhedonia. The progressive ratio task measures how willing the animal is to work for reward. Moreover, the previous lab's results suggests that the PR task is sensitive to both activation and inactivation of area 25, with responding being both blunted and increased, respectively. Second, I am going to infuse ketamine directly into area 25 to determine whether this area is a possible site of action through which ketamine exerts its antidepressant effects. I shall also measure the timeframe of any antidepressant effect when infused centrally. Third, I am going to infuse cortisol directly into area 25 to study if and how cortisol might affect the activity in this area in order to determine what might lead to activation of this area normally. In all tasks, physiological measurements such as cortisol levels will also be measured since previously cortisol has been shown to be increased following area 25 activation.

Philipe Bujold

3rd year PhD student - Schultz lab

Adaptive Economics: Exploring Choice Biases From the Brain's Perspective

A neuron's curse is that at every given time it is faced with a yes/no decision. It has evolved to be the optimal decision-unit in the brain, and together with around 86 billion of its neighbours, the neuron keeps us alive, helps us cooperate with other individuals, and allows us to successfully compete with each other when resources get scarce. Where it fails at optimizing, however, is when the neuron - together with its neighbours - steps out of the realm of evolution, and onto the floor of the New York Stock Exchange.

Metaphors aside, it is now widely accepted that humans, at least in economic contexts, are not as 'rational' as once believed. Our biological brick-and-mortar makes us distort reward values, misinterpret probabilities, or ignore crucial information altogether. But while we violate many of the classical models of economic behaviour, the fields of behavioural and neuroeconomics have provided some much-needed insight into 'why'. Here I will address the biological basis of some of our 'irrational behaviour', building on the puzzling finding that humans, when presented with overt probability information, tend to overvalue low probabilities and undervalue high ones; but invert this misrepresentation when probabilities are instead unknown and must be learned from experience. Having shown that this odd but persistent reversal is in fact a behavioural bias shared amongst primates, I argue that instead of being 'irrational' our flexible behaviour is in fact evolutionarily adaptive - and can be successfully modelled to improve economic predictions.

Prannoy Chaudhuri Vayalambrone

1st year PhD student - Krupic lab

Characterising shifts in grid cell firing fields

Grid cells in the medial entorhinal cortex (MEC) have been found to fire at particular locations such that each cell's firing fields are arranged in a hexagonal pattern extending throughout the enclosure. It has been suggested that grid cells play a major role in forming the brain's "cognitive map", and that they enable navigation by providing cues for path integration. Experiments in rats have shown that exposure to novel environments causes these patterns to expand in scale; subsequent repeated exposure to these environments causes the scale to decrease to the level seen in similar familiar environments. These results demonstrate that grid cells do not provide a constant spatial metric, which complicates the idea that they are used in path integration. During a recent pilot study in the lab, one rat was made to freely forage in a novel environment for a single three-hour session. This novel environment had dimensions identical to a highly familiar environment. The results appear to show that grid scale decreases over the course of this single session. This would imply that grid cells are able to achieve their canonical properties online. These preliminary results will be presented during the talk, followed by a brief discussion of hypotheses to test using data from future experiments and using previously published models of grid cell firing.

Leo Chi U Seak

1st year PhD student - Schultz lab

Neural responses of revealed preference theory

Revealed preference theory is an important economic theory that illustrates choices and decision making of individuals among bundles of goods. Previous studies show that when there are bundles of goods, individuals would make a trade-off for one good in order to get some of the other. Although some research show how values are coded in human brain, the neural activity during choices of bundles of goods remains unclear. Here, we probed the neural responses in human during choices of bundles using functional magnetic resonance imaging (fMRI). By analyzing the fMRI scans when human subjects were making decision between different types and amount of milkshake bundles, we found that brain structure involved in reward value coding and decision making, including striatum, midbrain and orbital frontal cortex, are activated on par with revealed preference theory.

Jana Sipkova

1st year PhD student - Franze lab

The mechano-responsiveness of ephrin/Eph signalling in the topographic mapping of the Xenopus optic pathway

Neuronal development is mediated by chemical as well as mechanical signals. One important group of chemical guidance cues are the membrane-bound ephrins and their receptors, Ephs, which rely on cell-cell contact to mediate downstream signalling. Ephrin/Eph signalling is crucial in retinal ganglion cell (RGC) axon sorting at the optic tectum during Xenopus retinotectal pathfinding. However, it is still unknown whether this signalling pathway is also mechanosensitive, and how potential mechanical cues, such as tissue stiffness, could be integrated with ephrin/Eph signalling during topographic mapping to the tectum. In this study, I am investigating how mechanical signals influence retinal axon growth and mapping through the ephrin/Eph signalling system, using in vitro cell cultures on soft substrates and in vivo pathfinding analyses.

Julia Becker

1st year PhD student - Franze lab

Stiffness alterations in spinal cord injury

Spinal cord injury is a devastating condition that may lead to loss of limb movement, sensation and bladder control. Despite intense research over the last few decades, treatment is still very limited. Most research to date has focused on biochemical signalling. However, recent studies have hinted that mechanics might play an important role in spinal cord regeneration: axonal growth patterns are influenced by the stiffness of the environment and spinal cord significantly softens after injury. It is yet unknown whether these changes in stiffness might pose a mechanical barrier axon regrowth. Using atomic force microscopy, I will investigate the stiffness of spinal cord tissue inside and around a lesion at various time points after injury and compare this to the stiffness of healthy spinal cord. I will test whether artificially modifying the stiffness of the damaged spinal cord or modifying mechanosensing in spinal cord cells improves regeneration of neurons after spinal cord injury. Our studies will be carried out in a cervical contusion model in rats which closely mimics the pathology seen in the human spinal cord after injury.

Ana López Ramírez

Postdoc - Fleming lab

Felodipine induces autophagy and clears neurotoxic proteins in mice and fish with pharmacokinetics amenable to repurposing in humans.

Neurodegenerative diseases like Alzheimer's disease, Parkinson's disease and Huntington's disease manifest with the accumulation of toxic proteins within neurons. There are now numerous data showing that autophagy upregulation enhances the clearance of such proteins and ameliorate their toxicities in animal models. Accordingly, we and others have sought existing compounds used in humans that may induce autophagy in the brain. A key challenge with this approach is to assess if any hits identified can induce neuronal autophagy at concentrations that would be seen in humans taking the drug for its conventional indication. Here we report that felodipine, an L-type calcium channel blocker and anti-hypertensive drug, can induce autophagy and clear mutant huntingtin, mutant tau and mutant alpha-synuclein in mouse and zebrafish at corresponding plasma concentrations similar to those that would be seen in humans taking the drug. This is associated with neuroprotection in mice and fish, suggesting the promise of this compound for use in neurodegeneration.

Ahsan Memon

1st year PhD student - O'Holleran lab - CAIC

Fast Whole-cell 3D Super-resolution Imaging

3D Super resolution (SR) microscopy is an advanced optical imaging technique that retains the advantages of fluorescence imaging, whilst enabling the resolution of structures at length scales that are particularly relevant to biological activities. Despite their current successes, 3D SR techniques have been limited to relatively small axial depths (~500nm) which have to be scanned in a series of 'discrete' layers and put back together digitally to achieve whole cell imaging. My project focuses on two main areas, firstly, by building on CAIC's successes of live super-resolution I will investigate using a new 3D technology "light-field imaging" that has the potential to image a whole cell in a single measurement plane, secondly, I will incorporate optical tweezers so that experiments can be performed that require active perturbation - such as bringing two cells into contact in suspension. Such experiments allow superresolution to be performed whilst simulating physiologically relevant scenarios of cell interaction. The final aim of the PhD will be to image an entire eukaryotic cell at ~50nm isotropic resolution while manipulating the position of the cell (or associated probe) with optical tweezers.

Alexander William Edward Dunn

MPhil - Paulsen lab

Characterising pathological changes to neuronal network development in Rett Syndrome

In Rett syndrome, young girls develop normally for 6-18 months before severe regression of cognitive, linguistic and sensory-motor abilities. This is caused by loss-of-function mutations in the MECP2 gene which is also implicated in synaptic development. In the cortex for example, MECP2 mutation causes premature development of NMDA receptors in inhibitory PV cells whilst delaying development in excitatory pyramidal cells. However, it is not yet known how these synaptic effects culminate in changes at the level of neuronal networks. These cell-type specific alterations to NMDA receptor development could alter the balance between excitatory and inhibitory activity, thus affecting activity-dependant plasticity in the network. For example, Inhibitory interneuron activity may have an effect on the synchrony of activity of functionally connected cells. We record spontaneous activity using microelectrode arrays in wild-type and Mecp2 deficient mouse cortical cell cultures. We aim to detect differences in the development of network topology in cultures of dissociated cells. This may have implications for pharmaceutical interventions that inhibit prematurely-developed PV cells to restore network activity.

Leia Judge

1st year PhD student - Brand lab

The long and the short of it: Uncovering the role of long non-coding RNAs in the regulation of *Drosophila* neuroblast proliferation.

Long non-coding RNA (lncRNA) refers to a class of RNAs longer than 200 nucleotides which are found to have no significant potential to code proteins. lncRNAs are thought to have mechanistically diverse functions in the cell, and in the nucleus have been shown to regulate gene expression in a transcript-dependent manner either in *cis* or in *trans* by recruiting chromatin-modifying complexes and enhancers to promoters of target genes and facilitation of long-distance genomic interactions (Yan et al., 2017; Nwigwe et al., 2015; Petruk et al., 2006).

LncRNAs are believed to have great biological significance in relation to both normal homeostatic processes and disease states, such as cancer (Delas and Hannon, 2017). Given that >80% cancer-associated SNPs are now known to occur in non-coding regions of the genome, it is clear much is to be learned about the pathological roles of these molecules (Cheetham et al., 2013). However, the role of specific lncRNAs in regulation of both normal and cancer stem cells is not yet clear.

Targeted DamID of proliferating neuroblasts identified a lncRNA which is highly upregulated in proliferating neuroblasts and is specific to neuroblasts compared to their differentiated progeny. Previous work in the Brand lab has identified a potential role for this lncRNA in orchestrating neuroblast reactivation following cellular quiescence, however the exact nature of this role has yet to be elucidated. A combination of developmental timing analysis, genetic perturbations (MiMIC lines and MARCM/FlpStop clones) and analytic techniques (RNA smFISH, RNA Dam-ID and scRNA-seq) are currently being employed in order to resolve the role of this novel lncRNA in neuroblast proliferation regulation

Tess Garraud

3rd year PhD student - Giussani lab

Antenatal Glucocorticoids: Studies in the Chicken Embryo

The late gestation glucocorticoid surge initiates maturational changes in the fetus vital for birth (Liggins.Reprod Fertil Dev. 6(2):141-50, 1994). This is mimicked in fetuses at risk of pre-term birth by maternal administration of synthetic glucocorticoids (Liggins & Howie. Pediatrics 50(4):515-25, 1972). Antenatal glucocorticoid treatment (AGT) reduces mortality and morbidity associated with pre-term birth, but there are concerns about adverse cardiovascular effects on the offspring. There is also a lack of sufficient evidence for the synthetic glucocorticoid of choice for this treatment. Using an integrative approach in the chick embryo, combining cardiac functional and mechanistic analysis, we provide evidence for direct effects on the fetal heart of clinically relevant doses of two synthetic glucocorticoids: Dexamethasone (Dex) and Betamethasone (Beta).

Connor Ross

1st year PhD student - Boroviak lab

Bananas about hypoblast - The derivation and functional characterisation of marmoset hypoblast stem cells.

To develop our understanding of mammalian embryogenesis, the mouse has served as the canonical model to interrogate the mechanisms of early embryonic development. With the advancement of single-cell transcriptomics, we have discovered that the developmental trajectory of the early primate development greatly differs from that of the rodent paradigm. Elucidating the underlying molecular mechanisms of primate development will assist in understanding human embryogenesis.

To understand how the early ICM bifurcates, specifies and develops to form the epiblast and hypoblast in primates, we want to elucidate the mechanisms of hypoblast specification in marmoset (Callithrix jaccus) embryos. Thus, to study the endogenous signalling pathways and transcription factors involved in hypoblast specification, maintenance and lineage progression, deriving hypoblast stem cells from late marmoset blastocysts in Japan offer an in vitro model. Stable hypoblast stem cell lines will be analysed using single-cell RNA seq and cross-referenced against our pre and postimplantation datasets. The most promising cultures will be "blueprinted" to gauge which stage of development these cells faithfully capture. Finally, hypoblast stem cells that recapitulate the preimplantation lineage will be assessed for their lineage-intrinsic differentiation capacity to generate yolk sac endoderm and extraembryonic mesoderm.

Nadejda Capatina

3rd year PhD student - Burton lab

Effect of Endoplasmic Reticulum Stress on Trophoblast Cell Lineage Differentiation

A diet high in fat, a stressful lifestyle, malnutrition, and excessive drug or alcohol use can induce endoplasmic reticulum (ER) stress at the cellular level. The unfolded protein response (UPR) is activated upon ER stress and primarily aims to restore cell homeostasis. Evidence suggests the UPR pathways are also involved in differentiation of stem cells, and so ER stress may have broad impact. The present project aims to test whether ER stress induced by environmental cues affects trophoblast stem cell (TSC) differentiation, and if so to elucidate the mechanistic pathways involved. I am employing two strategies to address this question: an in vitro mouse TSC model and three in vivo mouse models. Four inducers of ER stress are used in vitro: pharmacological inducers of pure ER stress tunicamycin and thapsigargin, and the more physiological calcium ionomycin salt and homocysteine. Induction of ER stress, stemness and differentiation of TSCs is monitored using RT-qPCR, western blotting and immunofluorescence. Data show that TSCs differentiate upon ER stress and that Foxo3a and Notch1 transcription factor expression is regulated by Perk sensor of UPR. Further, Notch1 is involved in regulating Gcm1 expression and thus establishment of the labyrinth layer for nutrient delivery to the developing mouse. Furthermore, treatment of wild-type morulas with homocysteine results in 25% of the embryos not having a blastocoel. This might have important implications for the treatment of infertility as there are numerous studies showing that infertile individuals have increased levels of homocysteine in seminal plasma, fallopian tubes, and blood. Two additional in vivo models are used to induce genetic ER stress. Immunofluorescence and confocal imaging in the Eif2s1tm1RjK in vivo model demonstrate that Foxo3a translocates to nuclei of trophectoderm (TE) cells only, upon genetic ER stress induction confirmed by Grp78 quantification. 25% of Eif2s1tm1RjK the mutant embryos do not have a blastocoel and there are fewer TE cells in the mutant blastocysts as compared to wild-type counterparts. This supports the in vivo homocysteine treatment data and suggests that ER stress leads to a decreased placental stem cell pool. The inner cell mass is unaffected. The last in vivo model employs generation of Perk knock-out driven by Cdx2 promoter and thus conditional deletion of Perk in the TE cells only. Blastocyst morphology and cell numbers at 3.5 dpc are analysed. In summary, the data show that ER stress plays an important role in trophoblast stem cell differentiation and elucidates potential mechanisms that could be targeted to treat conditions as infertility, miscarriage, and fetal growth restriction.

Tanja Fuchsberger

Postdoc - Paulsen lab

Neuromodulation of Spike Timing-Dependent Plasticity in the Hippocampus

Introduction

Spike timing-dependent plasticity (STDP) is a physiologically relevant form of Hebbian learning, in which near coincident pre- and postsynaptic firing induces plasticity: Long term potentiation (LTP) is induced when the presynaptic spike precedes postsynaptic firing, and long term depression (LTD) when postsynaptic firing precedes the presynaptic spike (Bi and Poo, 1998). However, these plasticity rules are profoundly influenced by neuromodulators (Seol et al., 2007), which can affect memories and behavioural outcome. Studies from our lab have shown that modulatory input that arrives even after plasticity induction can change plasticity rules; the application of dopamine after the induction converts LTD into LTP (Brzosko et al., 2015). This suggests that during the induction of plasticity, a synaptic molecular tag is set, through which modulatory signals can act. In this study we investigate the underlying molecular mechanism.

Methods

Whole-cell patch-clamp recordings were performed on acute slices of hippocampal CA1 pyramidal neurons using Schaffer collateral stimulation. After a baseline period, STDP was induced by repeated pairings of EPSPs and single postsynaptic action potentials and EPSPs were monitored for at least 40 min after the pairing protocol. This protocol was combined with 2-photon imaging for simultaneous detection of calcium transients.

Results

We show that calcium permeable AMPA receptors are required for the dopamine-induced conversion of LTD into LTP. This is mediated via signalling through the calcium-sensitive adenylate cyclases (AC) 1/8. Alternatively, synaptic stimulation could be replaced by a postsynaptic burst 10 min after the induction protocol, which was sufficient to convert LTD into LTP in the presence of dopamine.

Zuzanna Monika Stawicka

3rd year PhD student - Roberts lab

The role of anterior and posterior orbitofrontal cortex in emotional regulation.

While the orbitofrontal cortex has sometimes been described as a single functionally homogenous area, differences in connectivity, as well as functional differences in certain tasks, suggest that the anterior and posterior sub-regions may play different roles in emotional regulation. My work in the last years has focused on examining effects of selective inactivations of the anterior and posterior sub-regions in the common marmoset on a range of tasks aimed at studying various aspects of emotion. This includes appetitive and aversive Pavlovian conditioning, approach-avoidance decision-making, and learning from positive and negative feedback.

Putu Khorisantono

1st year PhD student - Grabenhorst lab

Neuroimaging of nutrient reward value and its effect on eating behaviour

In order to regulate the consumption of nutrients through food, the brain's reward system plays a large role in shaping eating behaviour to make eating a pleasurable act. However, this may also contribute to overconsumption of nutrients, causing an energy imbalance that leads to obesity and comorbid diseases. Therefore, we need to understand the role of this mechanism in regulating eating behaviour. We aim to investigate basic nutrient processing of fatty, and sweet stimuli in taste areas such as the hypothalamus and insula in addition to whether different nutrients are processed differently in the reward processing areas such as the striatum, orbitofrontal cortex and amygdala. Healthy participants will undergo a session of functional Magnetic Resonance Imaging (fMRI) while they receive various liquid reward stimuli (in the form of milkshakes) and perform psychophysical ratings and subjective valuations of the stimuli. On a separate day, they are invited to take part in a food-tasting experiment where their real-life eating behaviour is monitored for a single meal. We hope to use the individual differences in neural processing of rewards to explain individual differences in observed eating behaviour. The results would have great implications in obesity research

Andrew Champion

3rd year PhD student - Cardona lab

Combining structural and activity imaging in larval Drosophila

Connectivity-guided investigation of neural circuits underlying behavior is often infeasible for complex systems because wiring diagrams derived from structural imagining alone may not sufficiently constrain the number of plausible circuit hypotheses. Combining structural imaging of synaptic connectivity with functional information from activity imaging can further constrain this hypothesis space. We present computational methods and tools that enable cross-referencing of structural and activity imaging of explant larval Drosophila central nervous systems. These methods include segmentation and detection of nuclei and other structures in electron microscopy, deconvolution of multi-view light sheet imaging of GCaMP activity indicators, cell body detection in light sheet microscopy, and registration between electron and light sheet microscopy volumes. Augmenting synaptic wiring diagrams with activity maps via these methods relates circuit structure and function at the cellular level on a per-behavior basis.

Stanley Strawbridge

Postdoc - Smith's lab

How does FGF signalling regulate the founding lineages of the mouse embryo?

The second cell fate decision in the mouse embryo is Inner Cell Mass (ICM) segregation into Epiblast and Primitive Endoderm (PrE). It is known that PrE specification is driven by Fibroblast Growth Factor (FGF) 4 secretion from the ICM and nascent Epiblast. However, the mechanism(s) of FGF4 communication remain unclear in this context. To decipher the method of FGF4 communication in the early embryo, we modulated FGF4 levels by injecting either FGF4+/+ or FGF4-/- embryonic stem cells (ESCs) into 8-cell stage host embryos and assessed lineage proportions at the blastocyst stage. We found that donor ESCs impede host contribution to the ICM, and its derivatives, by combined spatial crowding and FGF4 signaling, in accordance with a mathematical model of cell population dynamics. Finally, we established a single-molecule imaging platform to quantify binding kinetics of FGF4 and its receptor, which provide a foundation to investigate cell-cell communication in the early embryo.

Kirsty Mackinlay

1st year PhD student - Zernicka-Goetz lab

Developing an in vitro Model of Post-Implantation Human Embryogenesis- Human Hypoblast Stem cell line derivation

Although in vitro fertilisation allows pre-implantation human development to be closely studied, our understanding of post-implantation human development is comparatively poor. The need to develop a greater understanding of the first weeks of human embryogenesis is two fold: not only is the body plan established during this period, but it is also the time during pregnancy associated with the highest rates of miscarriage. Thus, there is a need to develop system that is easily amenable to genetic and molecular manipulation and does not depend on the availability of donated human embryos. As has been demonstrated for mouse embryogenesis, this could be achieved via a stem cell-based model that cocultures stem cell equivalents of the embryonic (epiblast) and the extra-embryonic (trophoblast and hypoblast) lineages of the early human embryo. However, first, a human hypoblast stem cell line must be developed. This project hypothesises that this can be achieved by exposing naive human pluripotent stem cells (hPSCs) to developmentally relevant molecular cues. Naive hPSCs are preferable to the conventionally used 'primed' human embryonic stem cells, as their pluripotent state bears a greater resemblance to the preimplantation epiblast from which the hypoblast derives in vivo. Accordingly, to address this initial objective within the project, I have demonstrated that hypoblast markers are upregulated in naive hPSCs in response to simultaneous Activin, LIF, and WNT signalling pathway activation

Diana Arman

1st year PhD student - Brand lab

Systemic and local signalling in nutrition-dependent reactivation of neural stem cells in *Drosophila*

Stem cells exist primarily in a quiescent state but can be reactivated to generate new cells in response to various conditions, and the balance between quiescence and reactivation is crucial for maintaining a healthy organism. Here we focus on *Drosophila* neural stem cells (NSCs), which are quiescent between embryonic and larval phases of proliferation (Ito & Hotta, 1992), and are reactivated during larval growth in response to nutrition via the fat body (Britton & Edgar, 1998), which acts as a sensor organ analogous to liver and adipose tissue in vertebrates (Colombani et al., 2003). Previous work has shown that in response to essential amino acids from the larval diet sensed by the fat body, blood-brain barrier glia secrete insulin-like peptides, which bind to the insulin/insulin-like growth factor receptor on underlying NSCs and activate the PI3K/Akt pathway, thereby triggering NSC proliferation (Chell & Brand, 2010; Speder & Brand, 2014; Sousa-Nunes et al., 2011). However, the signal secreted by the fat body in response to dietary amino acids further leading to reactivation of NSCs is yet to be fully determined. Building upon previous work (Liu & Brand, unpublished), we use Targeted DamID, a powerful technique which allows cell- and tissue-specific transcriptional profiling *in vivo* (Southall et al., 2013). We compare transcriptional profiles of fat bodies in fed, starved, and newly-hatched larvae to determine specific changes in expression of genes encoding signals released by the fat body in response to dietary amino acids. Further, we examine how the fat body-derived signal is received by blood-brain barrier glia and transmitted to the NSCs to trigger their reactivation from quiescence.

Zaki Habib

1st year PhD student - Huang lab

Structural and functional roles of the S5-S6 extracellular loop of hNa$_v$1.5 and β-subunits in Na$^+$ channel regulation

Voltage-gated sodium ion channels (Nav) are central to action potential initiation through regulating entry of sodium ions into excitable cells to cause cell membrane depolarization. Human voltage-gated sodium ion channels (hNav) contain four homologous domains (DI-IV). Each domain contains six transmembrane alpha-helices each connected by extracellular or intracellular loops of varying lengths. Helices S5 and S6 from each domain are symmetrically-arranged forming the pore at the centre. The extracellular pore loops that connect the S5 and S6 helices within each domain extend over the pore forming a turret-like structure and play a role in ion selectivity and permeation. Mutations in the pore-forming α subunit have been implicated in multiple cardiac disorders and this project concerns the effects of several mutations in the extracellular loop region of hNav1.5 that have been associated with Brugada Syndrome (BrS). Of these, the R878C mutation involving the extracellular region of DII displayed a total loss of sodium current (*i*Na), despite normal levels of plasma membrane channel expression compared to wild-type. The E1441Q mutation at the extracellular region of DIII is also associated with BrS although it has not been extensively studied. E1441Q showed normal membrane expression and yet a total loss of hNav1.5 channel current (*i*NA) in common with the earlier report regarding R878C. Salt bridge formation due to the close proximity (<4Å) between the R878 and E1441 residues as a potential mechanism for causing BrS was also analysed by forming a double mutation R878E/E1441R, however, the function of the hNa$_v$1.5 was not rescued even though this mutant channel was also expressed in the membrane.

Merrick De Forest Pierson Smela

MPhil - Surani lab

Probing Gene Regulatory Networks in Human Primordial Germ Cell Specification

Human primordial germ cells (hPGCs) are the precursors to gametes, and are specified early in post-implantation embryonic development in response to BMP signaling. Although this stage of development is infeasible to study directly in human embryos, primordial germ cell-like cells (PGCLCs) can be derived using a stem cell-based model system. This system enables the study of regulatory networks involved in hPGC specification. In this work, human embryonic stem cell lines were edited to conditionally overexpress or deplete transcription factors and RNA binding proteins hypothesized to be involved in hPGC specification. The stem cell lines were then induced to form PGCLCs, the conditional systems were activated, and the phenotypic effects were observed. The conditional systems were chosen to give highly rapid responses, allowing time-resolved experiments to identify direct targets of the proteins of interest.

Rachael Feord

3rd year PhD student - Franze and Wardill labs

Simultaneous spectral stimulation and two-photon neural activity imaging in a Drosophila colour processing neuropile, the medulla

The fruit fly, Drosophila melanogaster, has emerged as a key model in vision research. Despite extensive characterisation of motion vision, very little is known about how flies process colour information. We have developed a novel setup that will enable us to accurately dissect the different components of the Drosophila visual system responsible for processing colour. Using flies that express neural activity indicators, we can track visual responses to a projected colour stimulus via a two-photon imaging system. Our visual stimulation setup consists of a customised projector system using a monochromator as its light source to produce many colours (narrow bands of light) across the spectrum. The visual stimulus is projected on a specialised screen material that scatters wavelengths of light across the spectrum equally at all locations of the screen, thus enabling presentation of spatially structured stimuli. Furthermore, the calibration process of the irradiance and spectral contents of the visual stimulus has been automated to allow rapid development of a variety of stimuli. A key feature of our setup is the introduction of specialised bandpass optical filters (or combinations thereof) in two separate locations to allow for the presentation of a visual stimulus with minimal detection of light resulting from the stimulus by the microscope gallium arsenide phosphide (GaAsP) detectors. Using this setup, we are characterising spectral responses, intensity-response relationships, and receptive fields of neurons in the early visual system of a variety of genetically modified strains of Drosophila.

Stephen Malunga Manchishi

3rd year PhD student - Colledge lab

Molecular Signatures of Hypothalamic *Kiss1* Neurons

Kisspeptins, acting upstream of gonadotropin releasing hormone (GnRH) neurons, have emerged as master hormones in the control of reproduction, essential in the control of puberty onset and ovulation. In mice, two distinct populations of kisspeptin-producing neurons (*Kiss1* neurons) are predominant in the hypothalamus; in the arcuate nucleus (ARC) and in the anteroventral periventricular nucleus (AVPV). While the two populations share some similarities in their transcriptome, including co-transmitters and receptors, they also show molecular and physiological differences. For example, despite both populations expressing the oestrogen receptor, Erα, they exhibit opposite responses to oestrogen exposure: the AVPV *Kiss1* population being stimulated, while the ARC *Kiss1* population is inhibited. Many studies have also shown heterogeneity of *Kiss1* neurons within the ARC population; for example, the middle or caudal (mARC or cARC) but not rostral (rARC) regions of ARC *Kiss1* neurons have been shown to be responsible for pulsatile GnRH secretion, suggesting that heterogeneity within the ARC could be spatial. In this study, we compared the transcriptomic profile of cARC, rARC and AVPV *Kiss1* neurons in mice in dioestrus, using RNA-seq from a pool of cells. PCA plots showed clear clustering of the AVPV samples and both the ARC samples in a cluster together, indicating considerable differences between AVPV and ARC groups. The caudal and rostral ARC appear more similar as the differences were not statistically significant after adjusting for multiple testing using FDR (Benjamin-Honchberg).

Przemyslaw Jarzebowski

1st year PhD student - Paulsen lab

Neuronal target-specific hippocampal memory functions

Hippocampus is critical for forming and recall of memory. It is well-connected with multiple brain structures: populations of pyramidal neurons located in the ventral Cornu Ammonis 1 (vCA1) of the hippocampus send projections to the nucleus accumbens, the medial prefrontal cortex and the amygdala – brain regions involved in emotional processing. I am investigating the functional role of these distinct projections in the memory for appetitive and aversive locations.

Chenguang Li

MPhil - Parker lab

A computational study of variability in the lamprey spinal cord

Swimming in the lamprey is a repetitive behavior that looks very similar between individuals. However, it is unclear whether the apparent similarity extends to the neuronal level, down to the circuitry governing muscle cell activation in the spinal cord. In addition, the lamprey spinal cord is highly plastic and able to recover from paralysis following complete spinal cord transection. Previous work from the Parker Lab suggests that cellular and synaptic properties vary, and that in animals that have recovered locomotor function the spinal cord differs significantly from its pre-lesioned state. Thus, variability in the roles of neurons and their connections could be of interest, both when looking between individuals and within one individual. In this project, I use small recurrent neural networks (ten or fewer hidden-layer neurons) to model motor units in the lamprey spinal cord and train them to mimic swimming with oscillatory behavior. I then re-train the same networks on “lesioned” data to study how solutions diverge based on the sets of training data used or initial network states. I find that, despite the simplicity of the task, small network sizes, and the similarity of network outputs, there is little consistency in the solutions obtained. That is, given a specified architecture and identical sets of training data, models will generally converge toward dissimilar circuitries dependent on initialization states. I have analyzed relationships between variabilities in network performance, trained parameters, and network dynamics in an attempt to understand how each of these factors may exist in corresponding biological systems, and consequently affect our interpretation of data obtained from physiological experiments.

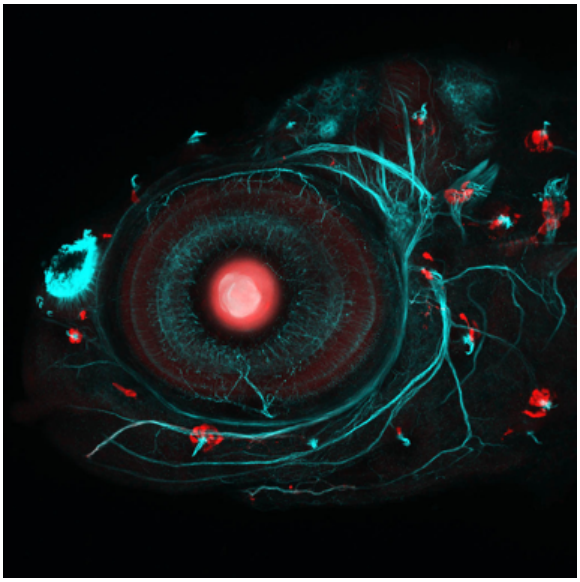
Plenary / Foster talk

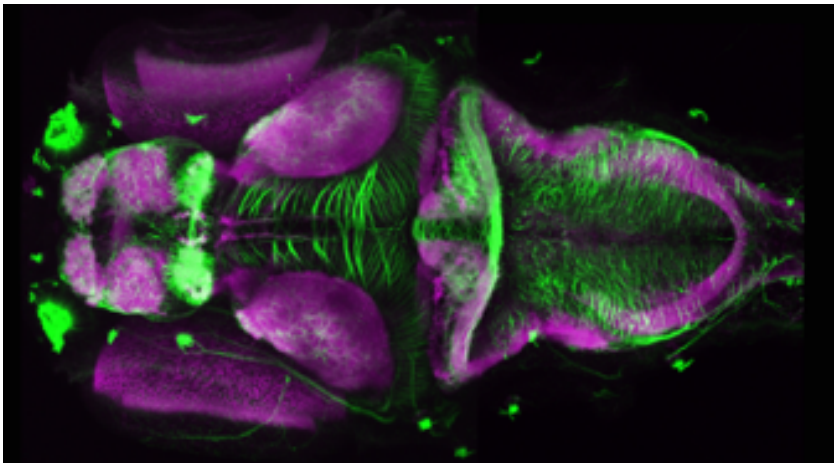
Professor Steve Wilson

Breaking symmetry in the brain: from genes to circuits and behaviour

Short Biography: Steve Wilson is Professor of Developmental Genetics and Vice-dean for Research at UCL in London. Ever since his post-doc at the University of Michigan with Steve Easter, his research has been focused on brain development using zebrafish as a model system. He established an independent research group in 1992 and moved to UCL in 1998 as a Wellcome Trust Senior Research Fellow, was appointed Professor of Developmental Genetics in 2002 and Vice-Dean for Research in 2007. Steve was elected to the Academy of Medical Sciences in 2002 and to EMBO in 2005. He is Deputy Editor in Chief for the journal Development and Chaired the Wellcome Trust Basic Science Interview Committee until 2016. He won the Remedios Caro Almeida Prize in Developmental Neurobiology in 2009.

Abstract: It is likely that the nervous systems of all bilaterally symmetric animals are left-right asymmetric with respect to processing of information and control of behaviour. However, we know very little about how asymmetries arise in development, how they are encoded in circuits and what their importance is for nervous system function. We use developmental, genetic, imaging and behavioural approaches to study habenular asymmetry in zebrafish to address these issues. One focus is to determine the mechanisms that lead to neurons on the left and the right acquiring different character and establishing different circuit connectivity between left and right sides of the brain. We have also been using optogenetic approaches to characterise functional properties on neurons on left and right and assessing how genetic mutations affecting laterality affect circuitry. In parallel we are developing behavioural assays to assess how habenular circuit asymmetry affects behaviour.





Poster session

Effie Christoforou

Endocrine zone overgrowth in the mouse placenta alters nutrient transport to the fetus

Bethany Aykroyd

The role of Igf2 in regulating the endocrine capacity of the mouse placenta

Igor de Almeida

Shedding light on the embryo: Extension of single-molecule imaging in the Z dimension for 3D cell cultures and embryos.

Hazel Walker

Development of a fluorescent Cxcl8 zebrafish line using a CRISPR-Cas9 knock-in strategy

Jerome Bohere

Identifying how Integrins promote intestinal stem cell proliferation in Drosophila

Connor Ross

Bananas about hypoblast - The derivation and functional characterisation of marmoset hypoblast stem cells.

Sophie Bergmann

Unravelling the implanting primate embryo: SHOT-seq allows spatial transcriptome and methylome analysis

Ana López Ramírez

Felodipine induces autophagy and clears neurotoxic proteins in mice and fish with pharmacokinetics amenable to repurposing in humans.

Christos Kyprianou

Epithelial rosettes orchestrate tissue remodelling and lumenogenesis in the implanting mouse embryo

Nathan Hervieux

Epithelial apical vertices are important for morphogenesis

Thomas Sharrock

Sarah Holt

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Thank you !