

Supervisor	Dept.	Rotation Project Description	Rotations offered:
<p><b>Dr Richard Adams</b>  <a href="mailto:rja46@cam.ac.uk">rja46@cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.pdn.cam.ac.uk/groups/adamslab/">http://www.pdn.cam.ac.uk/groups/adamslab/</a></p>	PDN	<p><b>Development of epithelial morphologies</b></p> <p>It is classically described that the bending of sheets of cells during developmental processes such as invagination and neurulation involves cells adopting a wedge-shaped configuration. On theoretical grounds we believe that this is an incomplete description of tissue morphogenesis. This project will use 3D imaging and computer analysis of cell and tissue shapes to investigate this problem.</p>	2 & 3
<p><b>Dr Boris Adryan</b>  <a href="mailto:ba255@cam.ac.uk">ba255@cam.ac.uk</a></p> <p>Lab website:  <a href="http://logic.sysbiol.cam.ac.uk/Adryan_Lab.html">http://logic.sysbiol.cam.ac.uk/Adryan_Lab.html</a></p>	Genetics	<p><b>Computational and genomics approaches to transcriptional regulation</b></p> <p>Our group is primarily interested in the transcriptional regulation of various aspects of <i>Drosophila</i> development. We address these questions using a combination of bioinformatics, computational biology and genomics.</p> <p><u>Transcriptional regulatory networks in <i>Drosophila</i> tracheal development</u></p> <p>The <i>Drosophila</i> tracheal system is a model system for branching morphogenesis. Most transcription factors (TFs) involved in the formation of the trachea are only characterised on the level of their mutant morphology, but not much is known about their actual target genes. We would like to understand how these TFs combine their regulatory signals in order to facilitate the different cellular responses necessary for tracheal development. The rotation project aims to use chromatin immunoprecipitation (ChIP) on a selected TF, and if successful, interpret genome-wide data in the light of the regulatory network.</p> <p><u>Isolation of RNA from purified nuclei</u></p> <p>As part of our efforts to generate tissue-specific ChIP, we have established a protocol to generate highly purified populations of nuclei from <i>Drosophila</i> embryos. We are now asking the question whether we can combine this methodology with RNA extraction to generate tissue-specific RNA profiles. The rotation project aims to test commercially available kits for nuclear RNA extraction (typically used on cell culture) on sorted nuclear populations from <i>Drosophila</i> embryos. If successful, this could be combined with genomic detection methods to survey the transcriptome of the <i>Drosophila</i> tracheal system.</p> <p><u>Computational integration of large-scale datasets: Concepts and coding</u></p> <p>We are currently developing a database on the basis of the InterMine framework which aims to provide a convenient search tool for the community of tracheal system researchers to address their questions about genomic aspects of tracheal development. The rotation project aims to support a computational biologist with a strong background in the technical aspects of this work and develop the concept of this database. What are relevant queries? What sort of information should be integrated? How should this information be provided to the biologist? Students with previous programming experience may also become involved in some genome bioinformatics to assist this project.</p>	All

<p><b>Dr Julie Ahringer</b>  <a href="mailto:jaa@mole.bio.cam.ac.uk">jaa@mole.bio.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gurdon.cam.ac.uk/~ahringerlab/">http://www.gurdon.cam.ac.uk/~ahringerlab/</a></p>	<p>Gurdon Institute</p>	<p><b>Chromatin regulation in gene expression</b>  Chromatin is the substrate upon which DNA is regulated for events such as transcription, replication, and mRNA post-transcriptional events. Hundreds of chromatin-associated proteins are known, many of which have activities such as modification or binding to histone tails, or nucleosome movement, and these are thought to alter local and/or higher order chromatin structure. However how most chromatin proteins regulate chromatin structure and function is poorly understood.</p> <p>To provide a framework for chromatin studies in <i>C. elegans</i>, we generated a genome-wide map of three histones and 15 histone modifications, which revealed broad domains of chromatin organization and differential marking of autosomes and the dosage compensated X chromosome. We also discovered that exon sequences in chromatin are preferentially marked with H3K36me3 relative to intron sequences, and we found that such marking also occurs in humans and mice.</p> <p>We are applying the histone modification map to the study of chromatin complexes linked to human disease and pluripotency, including the Retinoblastoma/DRM complex, the TIP60 acetyltransferase complex, and the NuRD chromatin remodelling complex. We have mapped the genome-wide locations of all eight members of the DRM complex and identified chromatin alterations in mutants lacking DRM function.</p> <p>Projects in the lab focus on the function of chromatin complexes relevant to human disease, the formation and regulation of different types of chromatin domains, and on links between chromatin and mRNA splicing.</p>	<p>All</p>
<p><b>Professor Michael Akam</b>  <a href="mailto:akam@mole.bio.cam.ac.uk">akam@mole.bio.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.zoo.cam.ac.uk/zoostaff/akam/index.html">http://www.zoo.cam.ac.uk/zoostaff/akam/index.html</a></p>	<p>Zoology</p>	<p><b>Comparative analysis of development in arthropods.</b>  Projects in our lab use a range of different species to investigate the diversity of patterning mechanisms across the arthropods, particular in the context of axial patterning, segmentation and mesoderm formation. We are part of a consortium sequencing the genome of a centipede, which is well placed to provide an outgroup for comparison with insect and crustacean model systems. Projects may involve participation in the annotation and mining of this genome for data on gene loss, gene duplication, synteny and other aspects of comparative and evolutionary genomics.</p>	<p>All</p>
<p><b>Dr Clare Baker</b>  <a href="mailto:cvhb1@cam.ac.uk">cvhb1@cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.pdn.cam.ac.uk/staff/baker/">http://www.pdn.cam.ac.uk/staff/baker/</a></p>	<p>PDN</p>	<p><b>Vertebrate PNS development from the neural crest and cranial neurogenic placodes</b>  Neurogenic placodes (paired patches of thickened cranial ectoderm) and the neural crest are two distinct embryonic cell populations that are crucial for the development of the vertebrate head. Together, they give rise to the whole peripheral nervous system, i.e., all the sensory receptor cells, neurons and glial cells located outside the brain and spinal cord. (Neural crest cells also build much of the craniofacial skeleton.) We are investigating a broad range of questions relating to the development of neurogenic placodes and the neural crest.</p> <p>Current projects include:</p> <ul style="list-style-type: none"> <li>- the development of olfactory ensheathing glia (clinically important cells that can promote spinal cord repair after grafting to injury sites) from the neural crest;</li> <li>- the development of oxygen-sensing and other sensory cells from the neural crest;</li> <li>- the role of Pax genes in neurogenic placode development;</li> </ul>	<p>2 &amp; 3</p>

		- the development of electroreceptors from lateral line placodes. Specific rotation projects will depend on student interest, whether in trying out chicken embryo techniques such as <i>in ovo</i> electroporation and/or transgenic GFP:chick-chick grafting, or in evo-devo projects such as electroreceptor development in shark, axolotl, paddlefish and/or catfish (opportunities for experimental approaches in these species are limited for a rotation project but could be discussed).	
<b>Dr Howard Baylis</b> <a href="mailto:hab@mole.bio.cam.ac.uk">hab@mole.bio.cam.ac.uk</a>  Lab website: <a href="http://www.zoo.cam.ac.uk/zoostaff/baylis/homepage.html">http://www.zoo.cam.ac.uk/zoostaff/baylis/homepage.html</a>	Zoology	<b>IP3 signalling in development, using <i>C. elegans</i> as a model</b>	2 & 3
<b>Professor Andrea Brand</b> <a href="mailto:ahb@mole.bio.cam.ac.uk">ahb@mole.bio.cam.ac.uk</a>  Lab website: <a href="http://www.gurdon.cam.ac.uk/~brandlab/">http://www.gurdon.cam.ac.uk/~brandlab/</a>	Gurdon Institute	<b>Stem cells to synapses: regulation of self-renewal and differentiation in the nervous system</b>	2 & 3
<b>Professor Paul Brakefield</b> <a href="mailto:pb499@cam.ac.uk">pb499@cam.ac.uk</a>  Lab website: <a href="http://www.zoo.cam.ac.uk/zoostaff/Brakefield/paul.html">http://www.zoo.cam.ac.uk/zoostaff/Brakefield/paul.html</a>	Zoology	<b>Evo-devo in ladybird beetles and butterflies</b> Please contact me directly in 2012 for details of potential rotation projects.  <u>Selected recent publications:</u> Brakefield, P.M. (2011) Evo devo and accounting for Darwin's endless forms. <i>Phil. Trans. R. Soc. B.</i> (in press) <a href="http://rstb.royalsocietypublishing.org/content/366/1574/2069">http://rstb.royalsocietypublishing.org/content/366/1574/2069</a>  Saenko, S.V., Brakefield, P.M., and Beldade, P. (2010) Single locus affects embryonic segment polarity and multiple aspects of an adult evolutionary novelty. <i>BMC Biology</i> 8: 111  Lommen, S.T.E., Saenko, S.V., Tomoyasu, Y., and Brakefield, P.M. (2009) Development of a wingless morph in the ladybird beetle, <i>Adalia bipunctata</i> . <i>Evol. Dev.</i> 11: 278-289.  Beldade P, French V., and Brakefield P.M. (2008) Developmental and genetic mechanisms for evolutionary diversification of serial repeats: eyespot size in <i>Bicyclus anynana</i> butterflies. <i>J. Exp. Zool. Part B: Mol. Dev. Evol.</i> 310B, 191-201	3
<b>Professor Sarah Bray</b> <a href="mailto:sjb32@cam.ac.uk">sjb32@cam.ac.uk</a>  Lab website: <a href="http://www.pdn.cam.ac.uk/staff/bray_s/">http://www.pdn.cam.ac.uk/staff/bray_s/</a>	PDN	<b>Decoding the Notch signal</b> The Notch pathway is one of a small handful of cell signalling pathways that coordinate development, regulating the types and numbers of cells formed in many developmental contexts.. Working with the <i>Drosophila</i> model, because of its simplicity, we have most recently been taking a genome-wide approach to identify direct targets of Notch pathway activation. Our analysis uncovers many novel targets, with a high degree of conservation with human genes. Current projects are focussed on investigating the regulation and function of these targets or on further exploiting genomic approaches to discover more about the outputs from the Notch pathway in different contexts.	All

<p><b>Dr Nick Brown</b>  <a href="mailto:n.brown@gurdon.cam.ac.uk">n.brown@gurdon.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gurdon.cam.ac.uk/brown.html">http://www.gurdon.cam.ac.uk/brown.html</a></p>	<p>Gurdon Institute</p>	<p><b>Mechanisms of integrin adhesion in morphogenesis and mechanotransduction</b></p> <p>Integrins are transmembrane receptors that maintain the cohesion between cell layers and enable cell migration, making them crucial in development and disease. When activated and clustered, integrins nucleate a cytoplasmic complex of proteins that links the cytoskeleton to the extracellular matrix. We are using the powerful genetics tools of <i>Drosophila</i> to discover new components of this complex and discover how they contribute to diverse developmental processes. Possible projects include the analysis of the critical components fermitins/kindlins, or a newly discovered putative mechanosensitive channel.</p>	<p>3</p>
<p><b>Professor Graham Burton:</b>  <a href="mailto:gjb2@cam.ac.uk">gjb2@cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.pdn.cam.ac.uk/staff/burton/index.html">http://www.pdn.cam.ac.uk/staff/burton/index.html</a></p>	<p>PDN</p>	<p><b>Placental development and function</b></p> <p>My focus is on human early placental development, and the involvement of the placenta in complications of pregnancy such as miscarriage, intrauterine growth restriction and pre-eclampsia. In particular, we are interested in the effects of oxygen, hypoxia, and oxidative and endoplasmic reticulum stress on trophoblast differentiation and function at the molecular and cellular levels. By understanding these at the basic science level, we aim to develop novel therapeutic interventions to improve outcome in complicated pregnancies. We recently identified a transcriptional network that may define a trophoblast stem cell population within the placenta. Please contact me directly for details of potential rotation projects.</p> <p><u>Recent papers:</u>  Hemberger, M., Udayashankar, R., Tesar, P., Moore, H. and Burton, G.J. (2010) ELF5-enforced transcriptional networks define an epigenetically regulated trophoblast stem cell compartment in the human placenta. <i>Hum Mol Genetics</i>, 19, 2456-2467.  Burton, G.J., Jauniaux, E. and Charnock-Jones, D.S. (2010) The influence of the intrauterine environment on human placental development. <i>Int J Dev Biol</i>, 54, 303-312.  Burton, G.J. (2009) Oxygen the Janus gas; its effects on human placental development and function. <i>J Anat</i>, 215, 27-35.</p>	<p>3</p>
<p><b>Dr Rafael Carazo Salas</b>  <a href="mailto:r.carazosalas@gurdon.cam.ac.uk">r.carazosalas@gurdon.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gurdon.cam.ac.uk/carazosalas.html">http://www.gurdon.cam.ac.uk/carazosalas.html</a></p>	<p>Gurdon Institute</p>	<p><b>Please note this lab is unavailable for a PhD place: rotations offered only.</b></p> <p>Our lab's overall goal is to understand how the gene and protein networks that regulate cellular morphogenesis operate in space and in time, and how different cell shapes and growth patterns can arise from a single genome.</p> <p><b>Microtubule regulation during cell growth</b></p> <p>Despite the fundamental biological importance of microtubules, to this day we do not possess a genomic catalogue of factors that regulate microtubules, even for the simplest cell types. We are currently carrying out the most detailed genome-wide screen for microtubule regulators to date, using systematic gene knock-outs, high-throughput/high-content (HT/HC) microscopy and automated image analysis. A rotation project in our lab could focus on characterizing candidate regulators from our screen using genetics and microscopy, or on statistical/bioinformatics data mining of our screen results.</p> <p><b>Regulation of cell polarity through the cell cycle</b></p> <p>Cell polarity is key to many aspects of cell function and its perturbation has been implicated in countless cellular pathologies. Work in our lab seeks to clarify how polarity is regulated through the cell cycle. This rotation project would use microscopy and quantitative image analysis to design 'live' reporters of cell cycle and polarity suited for designing a HT/HC microscopy screen for genes involved in coordinating both processes.</p>	<p>All</p>

		<p><b>Cell shape establishment and maintenance</b> Cell shape and plasticity are regulated not only by genes/proteins but also by physical constraints. We are interested in understanding the role of existing cell shape on future cell shape and proliferation. Therefore, a project in our lab could use a novel live microscopy assay that we have recently established and (automated) quantitative image analysis to: (i) study the vectorial expansion of the cellular cortex at the areas of cell growth and (ii) investigate how cortical forces feed back into the cellular growth process.</p>	
<p><b>Dr Mark Carrington</b> <a href="mailto:mc115@mole.bio.cam.ac.uk">mc115@mole.bio.cam.ac.uk</a></p> <p>Lab website: <a href="http://www.bioc.cam.ac.uk/uto/carrington.html">http://www.bioc.cam.ac.uk/uto/carrington.html</a></p>	Biochemistry	<p><b>How the external environment alters the subcellular localisation of an mRNA</b> Trypanosomes are protozoans that diverged from plants, fungi and animals early in the eukaryotic lineage. This ancient divergence is reflected in the predominance of molecular mechanisms that are often minor in other eukaryotes and an example is the almost exclusive use of post-transcriptional mechanisms for regulated gene expression. The cytoplasmic metabolism of mRNAs is intimately linked to their movement between polysomes and other RNP particles in the cytoplasm. The aim of this project is to determine the effect of various external stimuli on the subcellular localisation of a GFP-tagged mRNA in live cells as a means of gaining evidence for the function of different RNP granules.</p>	All
<p><b>Professor Anne Ferguson-Smith</b> <a href="mailto:afsmith@mole.bio.cam.ac.uk">afsmith@mole.bio.cam.ac.uk</a></p> <p>Lab website: <a href="http://www.pdn.cam.ac.uk/staff/ferguson/">http://www.pdn.cam.ac.uk/staff/ferguson/</a> Also see: <a href="http://www.trophoblast.cam.ac.uk/people/afsmith.shtml">http://www.trophoblast.cam.ac.uk/people/afsmith.shtml</a></p>	PDN	<p><b>Genomic imprinting and the epigenetic control of genome function during mammalian development.</b></p> <p>Imprinting and non-imprinting specific projects are available.</p> <p>Topics fall into three main categories - stem cells and programming; functional epigenomics; epigenetics and the environment in development and disease</p>	All
<p><b>Professor Abby Fowden</b> <a href="mailto:alf1000@cam.ac.uk">alf1000@cam.ac.uk</a></p> <p>Lab website: <a href="http://www.pdn.cam.ac.uk/staff/fowden/">http://www.pdn.cam.ac.uk/staff/fowden/</a></p>	PDN	<p><b>The role of the placenta in developmental programming</b></p>	2 & 3
<p><b>Dr Jenny Gallop</b> <a href="mailto:j.gallop@gurdon.cam.ac.uk">j.gallop@gurdon.cam.ac.uk</a></p> <p>Lab website: <a href="http://www.gurdon.cam.ac.uk/gallop.html">http://www.gurdon.cam.ac.uk/gallop.html</a></p>	Gurdon Institute	<p><b>Signalling pathways important for gastrulation movements</b> How the changes in cell shape and movement that give rise to wider the morphogenetic events of embryonic development are generated by developmental programs is poorly understood. This project will explore hits from a screen of known bioactive small molecules on <i>Xenopus</i> gastrulation. A number of compounds have been identified, with known targets, that cause defects in blastopore closure and later stage phenotypes consistent with gastrulation defects. The contribution of new signaling pathways not previously implicated in control of gastrulation movements to changes in cell shape and cytoskeletal organization will be investigated using application of the inhibitors, morpholino-mediated knockdown of their targets and visualization of the actin cytoskeleton using advanced microscopy. The goal is to find out how signaling pathways important during gastrulation cause the changes in actin organization that underlie morphogenetic movements.</p>	All

<p><b>Professor David Glover</b>  <a href="mailto:d.glover@gen.cam.ac.uk">d.glover@gen.cam.ac.uk</a></p> <p>Lab website:  <a href="http://dmgweb.gen.cam.ac.uk/">http://dmgweb.gen.cam.ac.uk/</a></p>	<p>Genetics</p>	<p><b>Roles of Protein Phosphatases in kinetochore assembly</b>  Our laboratory is studying how the kinetochore is assembled for its mitotic functions in <i>Drosophila</i>. We make use of particular developmental stages such as the syncytial embryo that have rapid cell division cycles in which we can study the natural progression of synchronised mitoses. While much is known about the roles of mitotic kinases in such cycles, little attention has been paid to protein phosphatases. The rotation student would participate in a project to study how specific protein phosphatases associate with the protein complexes at the kinetochore to regulate its assembly and function.</p> <p><u>References:</u>  Venkei, Z., Przewloka, M. R., and Glover, D.M. (2011) <i>Drosophila</i> Mis12 complex acts as a single functional unit essential for anaphase chromosome movement and a robust spindle assembly checkpoint <i>Genetics</i> 187: 131-140  Przewloka, M.R., Venkei, Z., Bolanos-Garcia, V.M., Debski, J., Dadlez, M., and Glover, D.M. (2011) CENP-C is a structural platform for kinetochore assembly <i>Current Biology</i> 21: 399-405</p> <p><b>Centriole – basal body duality in <i>Drosophila</i></b>  We are using a combination of genetic and proteomic approaches to tease apart the network of proteins that regulate the de novo formation and duplication of the centriole. We study these events in cultured cells, and in the syncytial embryos and male meiotic divisions of <i>Drosophila</i>. The rotation student would participate in projects to examine the functional importance of protein-protein interactions in centriole assembly, function in cultured cells and in mitosis in the embryo and meiosis and spermatogenesis in the male fly.  Dzhinzhev, N., Yu, Q.D., Weiskopf, K., Cunha-Ferreira, I., Riparbelli, M., Rodrigues-Martins, A., Bettencourt-Dias, M., Callaini, G., and Glover, D.M. (2010) Asterless provides a molecular platform for centriole assembly – <i>Nature</i> 467, 714-8</p> <p><b>Genesis of the centrosome in mouse embryos</b>  Centrioles are eliminated in oogenesis in many species. However, the mouse is an unusual organism in that the sperm does not contribute a basal body to provide the first centriole for mitosis. Centrioles are made de novo at the blastocyst stage. The microtubule organising centres (MTOCs) of the first mitoses therefore lack centrioles. Nevertheless many of the molecules required for centriole function are present from the zygote onwards and we are studying their function. The project student would characterise protein-protein interactions between mouse centriolar and centrosomal proteins and study their functions in the early embryo. Some of the technical approaches we use can be seen in the following reference:  Sharif, B., Na, J., Lykke-Hartmann, K., McLaughlin, S.H., Laue, E., Glover, D.M. and Zernicka-Goetz, M. (2010) The chromosome passenger complex is required for fidelity of chromosome transmission and cytokinesis in meiosis of mouse oocytes. <i>J. Cell Sci.</i> 123: 4292-4300</p>	<p>All</p>
<p><b>Professor John Gurdon</b>  <a href="mailto:j.gurdon@gurdon.cam.ac.uk">j.gurdon@gurdon.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gurdon.cam.ac.uk/gurdon.html">http://www.gurdon.cam.ac.uk/gurdon.html</a></p>	<p>Gurdon Institute</p>	<p><b>Reprogramming of somatic cells by nuclear transfer to eggs or oocytes</b>  The differentiated state of somatic cells is very stable but can be experimentally reversed by nuclear transfer to eggs or oocytes. We try to understand the mechanisms of pluripotency gene activation by normal components of eggs and oocytes. We use a combination of mammalian somatic cell nuclei and amphibian eggs or oocytes. We use the overexpression of dominant negative proteins to determine the role of remodelling complex and other proteins. A project would involve using dominant negative proteins to inhibit remodelling complex proteins.</p>	<p>2 &amp; 3</p>

<p><b>Professor Bill Harris</b>  <a href="mailto:harris@mole.bio.cam.ac.uk">harris@mole.bio.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.pdn.cam.ac.uk/staff/harris/index.html">http://www.pdn.cam.ac.uk/staff/harris/index.html</a></p>	<p>PDN</p>	<p><b>Development of vertebrate retina</b></p> <p>Our lab uses zebrafish and <i>Xenopus</i> embryos to explore basic issues in neural development. We focus primarily in the retina because it exemplifies the features of any part of the developing brain, yet is much more approachable than most parts experimentally. Two key issues that we are currently studying are: How is the right number of neurons generated, and how are the correct proportions of each type of neuron made? To investigate these issues we are using 3D time-lapse imaging to look at how clones form from retinal progenitors in combination with knocking down or out key genes that effect the the size of the retina or the composition of cells within the retina. These studies are helping us understand the logic of neural development and to pinpoint the autonomous and non-autonomous aspects of this programme. We are also keenly interested in the early circuitry of the retina as a model for how the brain wires up. Who connects to whom first and are the first connections necessary for the next ones and so forth. Finally we are interested in the sustained growth of the retina in these lower vertebrates as a model for neural stem cell behaviour in vivo. A project in this lab would therefore be in one of these areas depending on availability and student interest.</p>	<p>All</p>
<p><b>Dr Chris Jiggins</b>  <a href="mailto:c.jiggins@zoo.cam.ac.uk">c.jiggins@zoo.cam.ac.uk</a></p> <p>Lab website:  <a href="http://heliconius.zoo.cam.ac.uk/">http://heliconius.zoo.cam.ac.uk/</a></p>	<p>Zoology</p>	<p><b>Gene expression in butterfly wing development</b></p> <p><i>Heliconius</i> butterflies offer an opportunity to understand how divergent morphologies are encoded in the genome. We have recently published evidence that the <i>optix</i> transcription factor acts a switch between different red patterns (Reed et al., 2011, <i>Science</i> 333: 1137-41). This project would involve studying the spatial patterns of expression of another candidate gene (<i>fzy</i>) expressed during wing development in <i>Heliconius</i> butterflies, with the goal of identifying the gene responsible for the adaptive radiation of yellow wing pattern elements. The project would offer insight into how the evolution of gene regulation can control divergent phenotypes. Alternatively, genome resequence data and transcriptome data are available for multiple <i>Heliconius</i> species, and an alternative project would annotate candidate signalling pathways that show expression differences between different wing pattern forms, and study their patterns of molecular evolution.</p> <p>Reed et al. (2011) <i>Optix</i> drives the repeated convergent evolution of butterfly wing pattern mimicry. <i>Science</i> 333: 1137-41</p>	<p>All</p>
<p><b>Dr Matthias Landgraf</b>  <a href="mailto:ml10006@cam.ac.uk">ml10006@cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.zoo.cam.ac.uk/zoostaff/landgraf.htm">http://www.zoo.cam.ac.uk/zoostaff/landgraf.htm</a></p>	<p>Zoology</p>	<p><b>Identification of genes required for dendrite development in <i>Drosophila</i></b></p> <p>The development of postsynaptic terminals in the central nervous system is much less well understood than of presynaptic axon terminals. We have modified the so-called 'MARCM' system so as to make individual motoneurons mutant for specific genes or defined deficiencies that remove up to 200 genes at a time, thus facilitating relatively rapid screening of the genome for regions important for dendrite development.</p> <p><b>Neuron - glia interactions and synapse development</b></p> <p>We recently identified Jelly Belly as a putative glia-derived secreted regulator of dendritic growth. We also find that the longitudinal glia invade the neuropil extensively, as astrocytes do in vertebrates. Gene expression profiling by others suggest a fair degree of diversity among longitudinal glia. Our preliminary experiments suggest that different longitudinal glia may invade different neuropil territories - is this indeed the case? What are the underlying mechanisms for targeting glial</p>	<p>2 &amp; 3</p>

		<p>processes? Do glia regulate dendritic growth by affecting synapse formation?</p> <p><b>Developmental logic of a motor system</b>  Is there an underlying developmental logic to motor systems? Working with the <i>Drosophila</i> embryonic motor system we have shown that at the output side motorneurons distribute their dendrites into distinct regions, so that their dendritic trees form a neural map of the musculature in the periphery. We are now seeking to understand how this network is organised at the next level, of pre-motor interneurons. On the issue of transmitter type, preliminary evidence suggests that neurons of different transmitter types arise from distinct locations. Are transmitter types linked to specific (sub-)lineages and/or projection patterns?</p>	
<p><b>Dr Rick Livesey</b>  <a href="mailto:rick@gurdon.cam.ac.uk">rick@gurdon.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gurdon.cam.ac.uk/~liveseylab/fjlhome/index.html">http://www.gurdon.cam.ac.uk/~liveseylab/fjlhome/index.html</a></p>	Gurdon Institute	<p><b>Human stem cell models of cerebral cortex development and disease</b>  Projects will be offered this year in the following areas that all make use of a robust and efficient system that recapitulates key stages in human cortical development from pluripotent stem cells:  -The cell biology of asymmetric cell division in human neurogenesis;  -Engineering human neural circuits in vitro from pluripotent stem cells;  Functional analysis of the pathogenesis of familial Alzheimer's disease, using patient-specific stem cells</p>	All
<p><b>Professor Alfonso Martinez Arias</b>  <a href="mailto:a.martinezarias@gen.cam.ac.uk">a.martinezarias@gen.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gen.cam.ac.uk/Research/AMA/martinezarias.htm">http://www.gen.cam.ac.uk/Research/AMA/martinezarias.htm</a></p>	Genetics	<p><b>Quantitative analysis of the interactions between signal and gene regulatory networks in cell fate assignments.</b>  We use quantitative image analysis to find principles underlying the response of gene regulatory networks to signals. The work is done with mouse embryonic stem cells and also <i>Drosophila</i> stem cells from the midgut.</p>	All
<p><b>Dr Juan Mata</b>  <a href="mailto:jm593@cam.ac.uk">jm593@cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.bioc.cam.ac.uk/uto/mata.html">http://www.bioc.cam.ac.uk/uto/mata.html</a></p>	Biochemistry	<p><b>Genome-wide RNA-protein networks:</b>  We are interested in how multiple posttranscriptional processes are coordinated. Our main approach is the use of genomic methods for the systematic analysis of the interaction networks between proteins and RNAs. Our model system is the fission yeast <i>Schizosaccharomyces pombe</i>. Projects are possible in two areas:</p> <ol style="list-style-type: none"> <li>1. Genome-wide role of RNA-binding proteins (RBPs). Although posttranscriptional regulation has been extensively studied using specific transcripts, little is known about the genome-wide aspects of this control. We are using fission yeast cellular differentiation to study how transcriptional and posttranscriptional mechanisms are integrated to implement dynamic programs of gene expression.</li> <li>2. Role of metabolic enzymes in posttranscriptional control. Several metabolic enzymes that do not contain canonical RNA-binding domains are known to bind RNA, but little is known about the extent or function of this phenomenon. The project would involve the identification of metabolic enzymes that bind RNA and the identification of their targets.</li> </ol> <p>Amorim M, Cotobal C, Duncan C and Mata J (2010) Global coordination of transcriptional control and mRNA decay during cellular differentiation. <i>Molecular Systems Biology</i> 6: 380  Hentze M and Preiss T (2010) The REM phase of gene regulation. <i>Trends in Biochemical Sciences</i> (10.1016/j.tibs.2010.05.009)</p>	All

<p><b>Dr Irene Miguel-Aliaga</b>  <a href="mailto:im307@cam.ac.uk">im307@cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.zoo.cam.ac.uk/zoostaff/miguel-aliaga.html">http://www.zoo.cam.ac.uk/zoostaff/miguel-aliaga.html</a></p>	<p>Zoology</p>	<p><b>Developmental interaction between the nervous and digestive systems in <i>Drosophila</i></b></p> <p>Recent work in the lab has revealed the existence of extensive crosstalk between the nervous and digestive systems, both during development and in the maintenance of homeostasis. Ongoing work suggests that intestinal neurons utilize novel innervation mechanisms, and that they play unexpected roles in the modulation of appetite and internal metabolism.</p> <p><i>1) Identification of the genetic programmes involved in the apoptosis and differentiation of visceral neurons</i>  Many visceral neurons differentiate after making a "life or death" decision. The project will involve investigating the mechanisms that control this choice, as well as those that guide their axons to visceral targets.</p> <p><i>2) Identification of the signals mediating the crosstalk between the nervous system and the intestine</i>  You will investigate the nature and roles of the intestinal neurons and/or systemic signals that mediate the developmental and homeostatic crosstalk between the nervous system and the gut.</p> <p><i>3) Function of insulin-producing neurons</i>  We have recently identified two groups of intestinal neurons that secrete insulin-like peptides. The project will involve investigating what these insulins do and how they do it.</p>	<p>1 &amp; 3</p>
<p><b>Dr Eric Miska</b>  <a href="mailto:e.miska@gurdon.cam.ac.uk">e.miska@gurdon.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gurdon.cam.ac.uk/%7Emiskalab/">http://www.gurdon.cam.ac.uk/%7Emiskalab/</a></p>	<p>Gurdon Institute</p>	<p><b>Please note this lab is unavailable for a PhD place: rotations offered only.</b></p> <p><b>Small Regulatory RNA</b></p> <ol style="list-style-type: none"> <li>1. Mechanism of miRNA function</li> <li>2. Transgenerational epigenetic inheritance</li> <li>3. PIWI/piRNAs in germ stem cell genome integrity</li> <li>4. Host virus interactions and RNAi</li> </ol>	<p>All</p>
<p><b>Dr Cahir O’Kane</b>  <a href="mailto:c.okane@gen.cam.ac.uk">c.okane@gen.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gen.cam.ac.uk/Research/okane.htm">http://www.gen.cam.ac.uk/Research/okane.htm</a></p>	<p>Genetics</p>	<p><b><i>Drosophila</i> neuronal cell biology and degeneration</b></p> <p>Summary: Genetic approaches to dissecting learning circuits in <i>Drosophila</i>; neuronal membrane traffic and autophagy and their roles in neurodegeneration</p>	<p>All</p>

<p><b>Dr Isabel Palacios</b>  <a href="mailto:mip22@hermes.cam.ac.uk">mip22@hermes.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.zoo.cam.ac.uk/zoostaff/palacios/index.html">http://www.zoo.cam.ac.uk/zoostaff/palacios/index.html</a></p>	<p>Zoology</p>	<p>Our research group focuses on understanding the genetic, cell biological and biophysical bases of cell differentiation/proliferation and cell polarity in multicellular organisms:</p> <p><i>1. The SWH tumor suppressor pathway and cell growth</i>  1.1. We aim to understand how cell growth and tissue architecture are regulated. We have found that the maturation/architecture of the <i>Drosophila</i> follicular epithelium requires the action of the conserved Hippo tumor suppressor pathway: differentiation, epithelium integrity and cessation of division are all affected in follicle cells that are mutant for this pathway. We plan to decipher further how Hippo modulates the genetic and morphological changes required for tissue maturation.  1.2. We are also investigating the role of this tumor suppressor pathway in regulating stem cell fate, proliferation and differentiation in the adult testis.</p> <p><i>2. Motor proteins and cell polarity</i>  We are also interested in decoding how cell asymmetries are generated during development. More specifically, we study the function of motor proteins in setting up these asymmetries. A large family of kinesins is known to exist; our goal is to understand how they function and how their activity is regulated in order to perform their particular tasks, with special emphasis in their actions in the germline and the brain.</p>	<p>All</p>
<p><b>Dr Eugenia Piddini</b>  <a href="mailto:e.piddini@gurdon.cam.ac.uk">e.piddini@gurdon.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gurdon.cam.ac.uk/piddini.html">http://www.gurdon.cam.ac.uk/piddini.html</a></p>	<p>Gurdon Institute</p>	<p><b>Mechanisms and function of cell competition</b></p> <p>Our lab investigates the molecular mechanisms and the physiological role of cell competition, as well as its consequences in cancer. Cell competition is a type of cell interaction whereby fitter cells eliminate weaker cells from a tissue by inducing, depending on the tissue, their death, senescence or differentiation. We use <i>Drosophila</i> and mammalian cultured cells as model systems to investigate this phenomenon.</p> <p><b>Rotation Project 1: testing the involvement of stress-related genes in competition.</b>  Our recent findings suggest that some stress-related pathways may be involved in cell competition. This rotation project will explore a small collection of stress-related genes for their involvement in cell competition. We will use RNAi or genetic mutations of these genes to test whether they are necessary or sufficient for cell competition in <i>Drosophila</i> wing imaginal discs.</p> <p><b>Rotation Project 2: cell competition during adult tissue homeostasis.</b>  We are interested in understanding whether cell competition influences the rate of cellular turnover as well as cell fate and proliferative decisions of stem cells during adult tissue homeostasis. To this end we exploit the adult <i>Drosophila</i> midgut as a system to study tissue homeostasis. This project will probe the behaviour of adult intestinal stem cells during cell competition.</p>	<p>2 &amp; 3</p>

<p><b>Dr Benedicte Sanson</b>  <a href="mailto:bs251@cam.ac.uk">bs251@cam.ac.uk</a></p> <p><b>Lab website:</b>  <a href="http://www.pdn.cam.ac.uk/staff/sanson/">http://www.pdn.cam.ac.uk/staff/sanson/</a></p>	<p>PDN</p>	<p><b>Morphogenesis of early embryos: <i>in vivo</i> mechanisms for cell sorting and collective cell movements</b></p> <p>Below are two of many possible projects in the lab; please come and discuss if interested:</p> <p>1) Cell sorting: functional analysis of putative Myosin II regulators  We have recently demonstrated using Chromophore-Assisted Laser Inactivation (CALI) in live <i>Drosophila</i> embryos, that a pool of Myosin II which forms cables at compartmental boundaries, is required for cell sorting at these boundaries (Monier et al, 2010, Nature Cell Biology, vol 12: 60-5). Using live imaging, we showed that this supracellular cable of Myosin II is required to stop dividing cells in one compartment from invading the adjacent compartment. To understand how actomyosin barriers form and function, we have performed a screen to find YFP-tagged proteins localising at these barriers. We need now to test the role of these proteins in compartmental cell sorting and in actomyosin barrier formation.</p> <p>2) Collective cell movements: whole volume imaging of gastrulation in live embryos  We have mapped the collective cell movements during <i>Drosophila</i> embryo gastrulation and found that an axial force deforms the ectodermal cells (Butler et al, 2009, Nature Cell Biology, vol 11: 859-64). This gives us an unprecedented opportunity to analyse how active cell behaviours and extrinsic forces mechanistically interact to shape embryos. We have evidence that mesoderm invagination might provide the axial force that propels ectoderm convergence and extension. Analysing the relationship between these two morphogenetic movements will require imaging cell shapes in 3D (using cell membrane labelling and spinning disc and multiphoton microscopy) and mapping their positions in the whole embryo volume, as a function of developmental time (in collaboration with Richard Adams' group, PDN).</p>	<p>All</p>
<p><b>Dr Marisa Segal</b>  <a href="mailto:m.segal@gen.cam.ac.uk">m.segal@gen.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gen.cam.ac.uk/Research/segal.htm">http://www.gen.cam.ac.uk/Research/segal.htm</a></p>	<p>Genetics</p>	<p><b>Cyclin-dependent kinase - mediated control of spindle pole asymmetry in budding yeast</b></p> <p>The orientation of the yeast mitotic spindle is achieved by targeting each spindle pole to opposite cortical compartments - the mother and the bud. This asymmetric fate is controlled by cyclin-dependent kinase (CDK), which delays the organisation of astral microtubules by the new spindle pole body (SPB). Thus, the old SPB inherited from the preceding cell cycle is the only one competent to establish astral microtubule-based contacts with the emerging bud. By contrast, the new SPB acquires astral microtubules after spindle assembly has begun and is effectively confined to the mother cell. This is an excellent model to understand the mechanisms underlying spindle polarity and orientation in an asymmetric cell division. Having identified a molecular target responsible for asymmetric control by CDK, the aim of this project is to explore the mechanism by which phosphorylation controls microtubule organisation. The work entails the use of genetics, biochemical analysis and live-imaging microscopy.</p>	<p>2 &amp; 3</p>

<p><b>Professor Daniel St Johnston</b>  <a href="mailto:d.stjohnston@gurdon.cam.ac.uk">d.stjohnston@gurdon.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gurdon.cam.ac.uk/%7Estjohnstonlab/">http://www.gurdon.cam.ac.uk/%7Estjohnstonlab/</a></p>	<p>Gurdon Institute</p>	<p><b>A structure/function analysis of the roles of Shot domains in microtubule organization in epithelial cells</b>  Dima Nashchekin &amp; Daniel St Johnston  Our recent results suggest that the large microtubule /actin crosslinking protein spectropilakin Short stop (Shot) functions downstream of polarity cues to polarise the microtubule cytoskeleton in the <i>Drosophila</i> oocyte and follicle cell epithelium. However, the precise mechanism of how Shot is involved in the organisation of microtubules is very unclear. The current project will focus on deciphering the function/requirement of various Shot domains in follicle cell polarity. Various truncations of Shot will be expressed in wild type cells and in a range of <i>shot</i> mutant backgrounds, and their localisation and their effects on cell polarity and microtubule organisation will be studied.</p> <p><b>The role of the depolymerising kinesin KLP59D in microtubule dynamics and cell polarity in the <i>Drosophila</i> oocyte.</b>  Rebecca Bastock &amp; Daniel St Johnston  The formation of stable polarised arrays of microtubules is critical for the morphology and function of a wide variety of cells during development and adult life. However most studies of microtubule regulation and behaviour have been performed in dividing, unpolarised cultured cells. In this project we propose to investigate the function of a new depolymerising kinesin in the establishment and maintenance of cell polarity <i>in vivo</i>. We will be using the <i>Drosophila</i> oocyte and follicular epithelium as a genetically tractable and easily imaged model system. The project will involve genetics, immunofluorescence and live imaging.</p> <p><b>Regulation of female germline development by Bicardal-C-dependent translational control</b>  Vitor Trovisco &amp; Daniel St Johnston  Bicardal-C plays a dosage sensitive role in female germline development (Bic-C mutations are dominant female sterile) by controlling the translation of several key transcripts, including <i>oskar</i> mRNA. The project will be to characterise two mutations that we have recently identified that completely suppress all aspects of the Bic-C/+ and Bic-C homozygous phenotypes, which are likely to affect other key factors in translational control.</p>	<p>All</p>
<p><b>Dr Octavian Voiculescu</b>  <a href="mailto:ogv20@cam.ac.uk">ogv20@cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.pdn.cam.ac.uk/groups/voiculesculab/index.html">http://www.pdn.cam.ac.uk/groups/voiculesculab/index.html</a></p>	<p>PDN</p>	<p><b>Building and shaping the central nervous system in higher vertebrates</b>  The generation and morphogenesis of the neural plate is of tremendous fundamental and clinical importance (neural tube defects occur in humans at about 1 per 1000 pregnancies). The main focus in my laboratory is on deciphering the mechanisms of this process in higher vertebrates. In particular, we aim at understanding the following key aspects:</p> <ol style="list-style-type: none"> <li>1) What are the individual cell behaviours underlying the morphogenesis of the early neural plate, and how are they controlled and orchestrated in terms of tissue interactions and molecular control?</li> <li>2) How do the naturally occurring stem cells function to build the main embryonic axis, including the neural plate? What are their modes of renewal, lineage relationships, and how are they established?</li> </ol>	<p>All</p>

		Our experimental approaches combine multi-photon, high-resolution imaging in intact embryos ( <i>Nature</i> 449: 1049) with precisely controlled gene-targeting methods ( <i>Nat Protoc</i> 3: 410) and embryological manipulations in the chick embryo. We are also using computer simulations to integrate the data from these reductionist approaches into a complete model. Ultimately, we aim to understand the shaping of the neural tissue and of the entire embryo.	
<p><b>Dr Rob White</b>  <a href="mailto:rw108@mole.bio.cam.ac.uk">rw108@mole.bio.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.pdn.cam.ac.uk/staff/white/index.html">http://www.pdn.cam.ac.uk/staff/white/index.html</a></p>	PDN	<p><b>Genomic approaches to transcriptional regulation and chromatin organisation in <i>Drosophila</i></b></p> <p>Projects on transcriptional regulation in <i>Drosophila</i> and development using chromatin immunopurification together with genomic micro-arrays to identify the in vivo target sites of transcription factors and other DNA-binding proteins in <i>Drosophila</i>. Also projects on the nuclear organisation of transcription using the primary spermatocyte nucleus and the activation of the spermatogenesis transcription program as a model system.</p> <p><i>Recent publications:</i></p> <p>Holohan, E. E., Kwong, C., Adryan, B., Bartkuhn, M., Herold, M., Renkawitz, R., Russell, S. and White, R. (2007) CTCF Genomic Binding Sites in <i>Drosophila</i> and the Organisation of the Bithorax Complex. <i>PLoS Genet</i> 3:e112</p> <p>Adryan, B., Woerfel, G., Birch-Machin, I., Gao, S., Quick, M., Meadows, L., Russell, S. and White, R. (2007) Genomic mapping of Suppressor of Hairy-wing binding sites in <i>Drosophila</i>. <i>Genome Biol.</i> 8:R167</p> <p>Kwong C., Adryan, B., Bell, I., Meadows, L., Russell, S., Manak, J.R. and White, R. (2008) Stability and dynamics of Polycomb target sites in <i>Drosophila</i> development. <i>PLoS Genet</i> 4:e1000178.</p>	All
<p><b>Dr Phil Zegerman</b>  <a href="mailto:philip.zegerman@gurdon.cam.ac.uk">philip.zegerman@gurdon.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gurdon.cam.ac.uk/~zegermanlab/">http://www.gurdon.cam.ac.uk/~zegermanlab/</a></p>	Gurdon Institute	<p><b>Screen for factors that regulate the timing of the early embryonic divisions of <i>Caenorhabditis elegans</i></b></p> <p>In the early <i>Caenorhabditis elegans</i> embryo, asymmetric cell divisions produce descendants with asynchronous cell cycle times. The mechanism by which anterior-posterior (A-P) polarity controls differential timing of cell division in early <i>C.elegans</i> embryos remains to be found. As in other metazoa, such as flies and frogs, these early embryonic cell cycles lack G1 and G2 phases, so differences in the rate of DNA replication i.e S-phase are likely to account for the asynchrony in the early divisions<sup>1</sup>. Indeed mutations or knock downs of essential DNA replication factors lengthens S-phase and causes changes to the proper cell fate patterning in the early embryo<sup>2</sup>. It is possible therefore that AP polarity directly affects the rate of DNA replication in different cell types.</p> <p>The aim of this project is to understand how cell cycle length is regulated in the early divisions of the <i>C.elegans</i> embryo. This will involve developing novel assays to measure the timing and duration of S-phase. Subsequently these assays will form the basis of an RNAi screen for new genes involved in the regulation of cell cycle length in the early embryonic divisions of <i>C.elegans</i>.</p> <ol style="list-style-type: none"> <li>1. Edgar, L. G. and J. D. McGhee (1988). "DNA synthesis and the control of embryonic gene expression in <i>C. elegans</i>." <i>Cell</i> <b>53</b>(4): 589-99.</li> <li>2. Encalada, S. E., P. R. Martin, et al. (2000). "DNA replication defects delay cell division and disrupt cell polarity in early <i>Caenorhabditis elegans</i> embryos." <i>Dev Biol</i> <b>228</b>(2): 225-38.</li> </ol>	All

<p><b>Professor Magda Zernicka-Goetz</b>  <a href="mailto:mzg@mole.bio.cam.ac.uk">mzg@mole.bio.cam.ac.uk</a></p> <p>Lab website:  <a href="http://www.gurdon.cam.ac.uk/%7Ezernickagoetzlab/">http://www.gurdon.cam.ac.uk/%7Ezernickagoetzlab/</a></p>	<p>Gurdon Institute</p>	<p><b>The role of cell polarity and cell position in the first cell fate decisions in the early mouse embryo</b></p> <p>The first two cell fate decisions in the mammalian embryo are key to all subsequent development, because they set apart the embryo's population of stem cells for the whole body and surround these with tissues that signal vital developmental processes. The PhD project aims to identify the earliest molecular events leading to two alternative fates of inside cells: pluripotent progenitors of the future body (epiblast) and progenitors for one extra-embryonic tissue with crucial signalling properties (primitive endoderm). Deep sequencing analysis recently carried out in our group has identified a number of differentially expressed genes from several known signalling pathways between progenitors of epiblast and primitive endoderm. By the use of a combination of several approaches the project will assess whether the elimination of selected differentially expressed signaling pathways will change a cell's contribution to the epiblast or primitive endoderm and, if so, by which route.</p>	<p>All</p>
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If you are interested in their research, please contact Group Leaders directly to enquire.