Annual report : 2011/2012 / The Wellcome Trust, Cancer Research UK Gurdon Institute of Cancer and Developmental Biology.

Contributors

Wellcome Trust (London, England)
Cancer Research UK. Gurdon Institute of Cancer and Developmental Biology
Cancer Research Campaign (Great Britain)
Gurdon Institute of Cancer and Developmental Biology (Great Britain)

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The Wellcome Trust/Cancer Research UK Gurdon Institute

2012 PROSPECTUS / ANNUAL REPORT 2011

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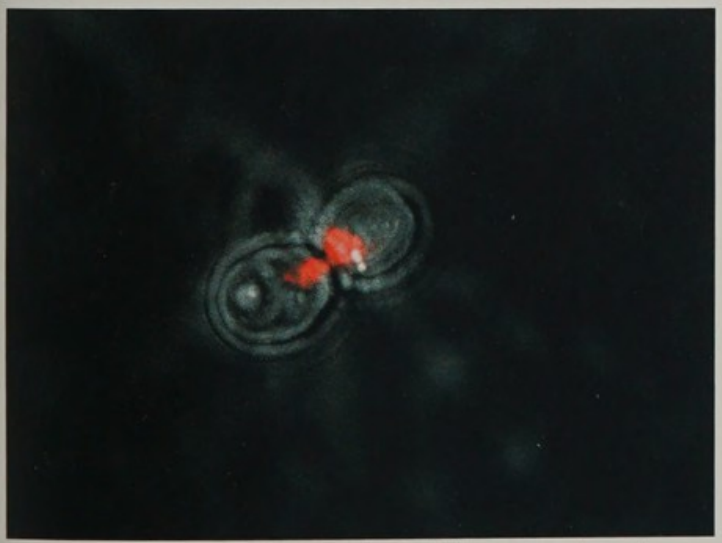
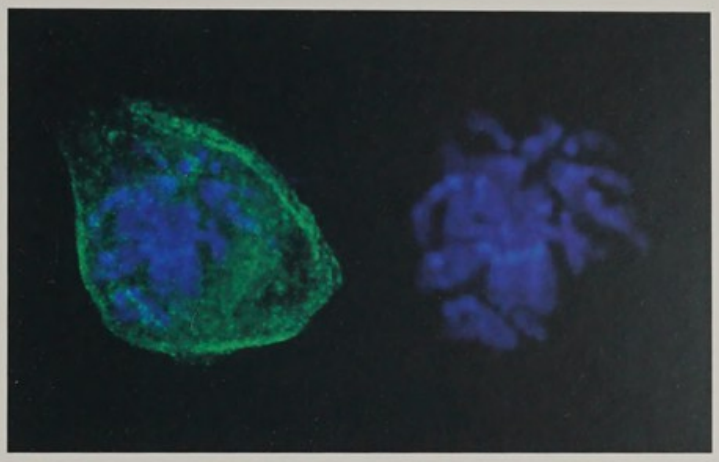
INTRODUCTION

As the reports from the individual research groups on the following pages demonstrate, 2011 has been another productive year for the Institute. The most notable changes have been the arrival of Dr Jenny Gallop as a new group leader, and the departure of Dr Masanori Mishima. Jenny joins us from Marc Kirschner's group at Harvard Medical School, where she developed an *in vitro* model for the formation of cellular protrusions, such as filopodia. She has been awarded a Wellcome Trust Research Career Development Fellowship and a European Research Council starting grant to study how membranes and actin regulators interact to control the assembly of various actin structures. Masanori is leaving us after six years in the Institute to become a Professor at the Centre for Mechanochemical Cell Biology that has just opened at the University of Warwick. We shall all miss him and his group very much, and wish them every success in their exciting new venture. We also said farewell to the staff of Mission Therapeutics, who had been provided space in the Institute for a year, while they set up their own laboratories. Mission Therapeutics is a new biotechnology company founded by Professor Steve Jackson to develop new anticancer treatments based on the work on DNA damage pathways coming out of his lab.

As usual, the outstanding research of my colleagues has been recognised by various prizes and awards. Steve Jackson was awarded



Separation of DNA (stained red with propidium iodide) between mother and daughter yeast cells. (Davide Mantiero & Vincent Gaggioli, Zegerman Group, 2011)



OMX photomicrograph of A dividing Primordial Germ cell (100x). GOF reporter, green; DAPI, blue. (Roopsha Sengupta, Surani Group, 2011)

the Royal Society's Buchanan Medal " in recognition of his distinguished contribution to medical sciences", as well as a European Research Council Advanced Investigator award to support his research into DNA damage responses. Tony Kouzarides has also been awarded a European Research Council Advanced Investigator grant to study the role of non-coding RNAs in transcription, and Azim Surani has won a Wellcome Trust Senior Investigator Award to study the principles and programming of the mammalian germline. Phil Zegerman was awarded the Cancer Research UK Hardiman Redon prize 2010. Many other groups in the Institute have also secured new research funding, bringing our annual income from grants to over £12 million this year.

Advanced imaging has always been one of the strengths of the Institute and 2011 has seen several important developments that will significantly improve our facilities in this area. For many years, the resolution of light microscopy was limited by diffraction, making it impossible to distinguish structures that are less than 200nm apart. A number of recent advances have now made it possible to resolve much smaller structures and the Institute has been awarded funding to invest in several systems that break the diffraction limit in different ways. Firstly, we have been awarded a Wellcome Trust equipment grant with other groups in Cambridge to purchase an OMX microscope that uses structured illumination to give twice the resolution of a standard light microscope. Secondly, Jenny Gallop has secured funding for a dSTORM (direct stochastic optical reconstruction microscopy) system that can resolve structures as small as 20nm, although it cannot image quickly. Finally, my group has been awarded a Wellcome Trust Strategic Award to collaborate with groups at Yale and Oxford Universities and the

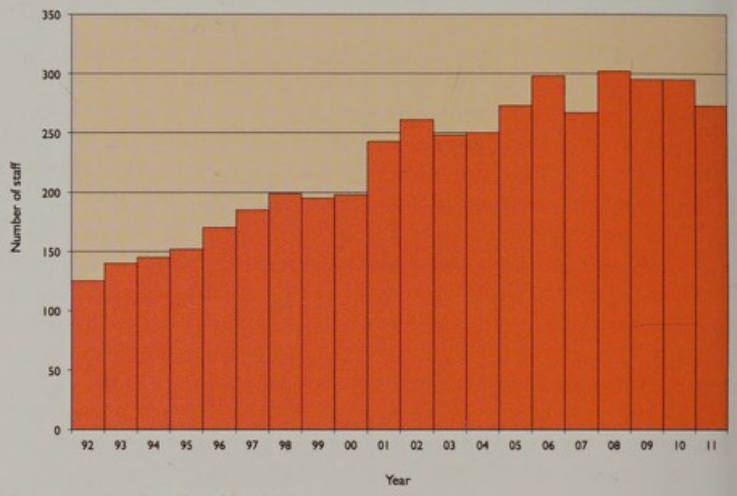
MRC Laboratory of Molecular Biology to develop the next generation of super-resolution microscopes that can image deep inside cells in real-time. Thus, the researchers in the Gurdon will be able to observe the behaviour of molecules in living tissues with unprecedented resolution, keeping us at the forefront of this rapidly moving field.

Much of the success of the Institute depends on its friendly and cooperative atmosphere, and I would like to highlight the role played by Gurdon Institute Postdoc Association in enhancing the scientific and social life of the Institute. This year, the postdocs hosted research seminars from Titia de Lange (Rockefeller University), Marco Foiani (IFOM-IEO. Milan) and Anne Ridley (King's College, London), as well as career talks by Jonathon Milner, a former Gurdon postdoc, now founder and CEO of Abcam, Pamela Feliciano, an associate editor of Nature Genetics, and Alison Schuldt who did her PhD in the Institute and is now chief editor of Nature Reviews Molecular Cell Biology. They also held a one day postdoc retreat that included a collaboration networking event, a session on how to supervise students and a barbecue. Most recently, the postdocs invited all of the core staff to a special beer and pizza 'Happy Hour' to thank them for all their work ensuring the smooth running of the Institute. I am therefore delighted to announce that the President of the Postdoc Association, Benjamin Klapholz, has been awarded this year's Martin Evans Memorial Cup, which is given annually to the person who has made the greatest contribution to the social life of the Institute.

Next year marks the 21st anniversary of the founding of the Gurdon Institute (although we only adopted this name in 2004), and we are busy preparing for a special symposium and celebration to mark our coming of age. We have lined up a distinguished list of participants, including three Nobel laureates, and half of the speakers will be former students and postdocs in the Institute who have gone on to become very successful group leaders elsewhere. If you are interested in joining us for what I am sure will be a very exciting meeting, details for how to register can be found at www.gurdon.cam.ac.uk/symposium/.

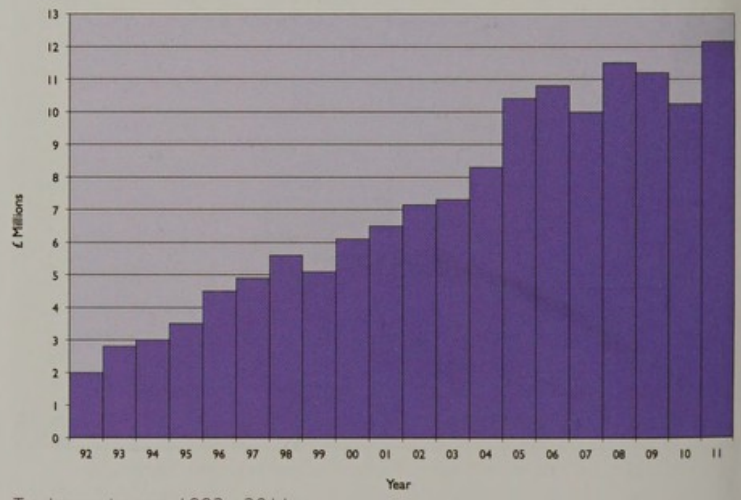
HISTORICAL BACKGROUND

The Institute was founded in 1989 to promote research in the areas of developmental biology and cancer biology, and is situated in the middle of the area containing the biological science departments of the University of Cambridge, close to the newly-established Wellcome Trust Institute for Stem Cell Research. The Institute hosts a number of independent research groups in a purpose-built building designed to promote as much interaction as possible. Developmental and cancer biology are complementary since developmental biology is concerned



Total number of staff 1992 - 2011

with how cells, including stem cells, acquire and maintain their normal function, whereas cancer is a result of a cell breaking loose from its correct controls and becoming abnormal. Both areas require a detailed knowledge of intra- and intercellular processes, which need to be analysed at the scientific and technical levels. To understand what goes wrong when a cell becomes cancerous requires knowledge of the processes that ensure correct function in normal development. At the technical level, the analysis of cellular and molecular processes requires familiarity with techniques that no single person can master, including



Total grant income 1992 - 2011

molecular biology, biochemistry, microarray technology, bioinformatics, cell culture, imaging and embryonic manipulations. There is, therefore, a major benefit in having scientists with different but complementary knowledge and technical skills working in close proximity to one another as is the case in the Institute.

The Institute is an integrated part of Cambridge University, and all group leaders are also members of another University department within the School of Biological Sciences, and contribute to both undergraduate and graduate student teaching.

CENTRAL SUPPORT SERVICES

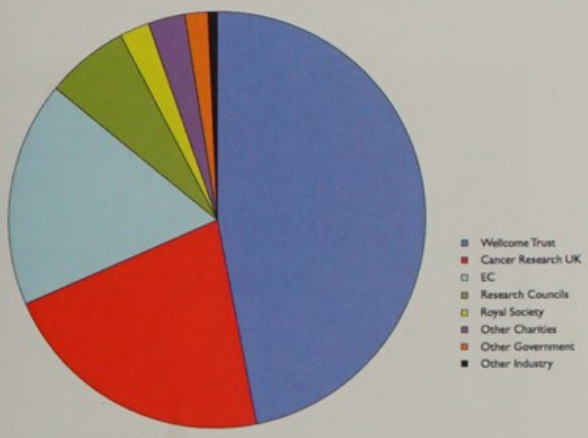
The Institute's 'core staff' provides essential administrative, technical and computing support to our scientists so that the scientists can spend as much time as possible on their research.

FUNDING

Our two major funding bodies, the Wellcome Trust and Cancer Research UK continue to offer the Institute vital backing in the form of Fellowships, individual programme, project and equipment grants, in addition to our invaluable core funding.

Other sources of funding, both direct and indirect, include The European Commission, BBSRC, MRC, the Royal Society, NIH, the European Molecular Biology Organization, HFSP, the Isaac Newton Trust, the Association for International Cancer Research, the Alzheimer's Research Trust, the Federation of European Biochemical Societies, the Japan Society for the Promotion of Science, the Sankyo Foundation of Life Science, the Swiss National Science Foundation, the Wenner-Gren Foundation, the Wiener-Anspach Foundation, the Cambridge Overseas Trust, Gates Cambridge Scholarships, DAAD, the Thai Government, the Liechstenstein Government, the Ramon Areces Foundation, Fundacao para a Gerência e Tecnologica, KAUST, March of Dimes, GSK and the Darwin Trust.

The University has also been very generous in its support of the Institute, particularly in funding equipment.



Grant sources (July 2010 - July 2011)

RETREAT

Our Annual Retreat this year was held at the Five Lakes Hotel, Maldon, Essex on 29th and 30th September 2011. The event was highly successful. Many Institute members attended and all gained from the experience both scientifically and socially.

The Institute on retreat, October 2011 (image by John Overton, Brown Group)

Professor Daniel St Johnston

Julie Ahringer

Chromatin regulation in transcription and splicing, and cell polarity establishment and transduction

Co-workers: Alex Appert, Dasha Ausiannikava, Ron Chen, Mike Chesney, Yan Dong, Bruno Fievet, Moritz Herrmann, Josana Rodriguez, Mariana Ruiz Velasco, Przemyslaw Stempor, Christine Turner, Eva Zeiser

Regulation of chromatin structure plays a central role in transcriptional control and also impacts mRNA post-transcriptional events. The small well-annotated genome, powerful RNAi technology, and rich resource of chromatin mutants of *C elegans* make it an excellent system for studies of chromatin function. Through generation of a genome-wide map of 18 histone modifications in *C elegans*, we found that many modifications are organised into broad chromosomal domains that differently mark the more recombinagenic distal arm regions and the central regions. We also found that exon and intron sequences are differentially marked by H3K36me3, and that H4K20me1 is enriched on the X chromosome and has a role in dosage compensation. We are studying the functions of different histone modifications in transcription and post-transcriptional processes such as mRNA splicing. We are also investigating the functions of *C elegans* counterparts of major chromatin regulatory complexes that are implicated in human disease including the histone deacetylase complex NuRD, the Retinoblastoma complex DRM, and a TIP60 histone acetyltransferase complex. We study the function of these proteins in transcriptional control and development using chromatin immunoprecipitation followed by deep sequencing, global mRNA expression analyses and other genetic and genomic methods.

Cell polarity is crucial for many of the functions of animal cells, such as migration, axis formation, and asymmetric cell division. Many of the known molecules involved in cell polarity are conserved across animals, however, the mechanisms by which these function are not well understood. We use the one-celled *C elegans* embryo to investigate the polarity cue, its reception, and how polarisation leads to downstream events such as asymmetric spindle positioning. We have completed a large number of genetic interaction RNAi screens that have identified many new cell polarity genes. We have generated a large cell polarity network and are probing the functions of the new genes using a range of techniques, including live cell imaging, genetics, and biochemistry.

Selected publications:

• Cheung M-S, **Down TA**, Latorre I and **Ahringer J** (2011) Systematic bias in deep sequencing data and its correction by BEADS. Nucleic Acids Research 39(15):e103

• Zeiser E, Frøkjær-Jensen C, Jorgensen E and **Ahringer J** (2011) MosSCI and Gateway compatible plasmid toolkit for constitutive and inducible expression of transgenes in the *C. elegans* germline. PlosOne 6(5):e20082

• Liu T, **Ahringer J** et al (2011) Broad chromosomal domains of histone modification patterns in *C. elegans*. Genome Research 21: 227-236

• Gerstein MB, **Ahringer J** et al (2010) Integrative Analysis of the *Caenorhabditis elegans* Genome by the mod ENCODE Project. Science 330, 1775-87

• Kolasinska-Zwierz P, **Down T**, Latorre I, Liu T, Liu XS and **Ahringer J** (2009) Differential chromatin marking of introns and expressed exons by H3K36me3. Nature Genetics 41, 376-381

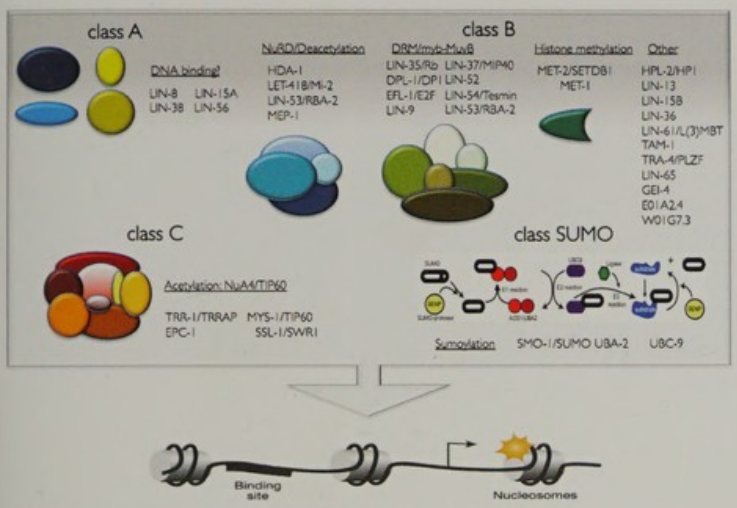


Figure 1 Many chromatin regulators under study are counterparts of proteins implicated in human disease.

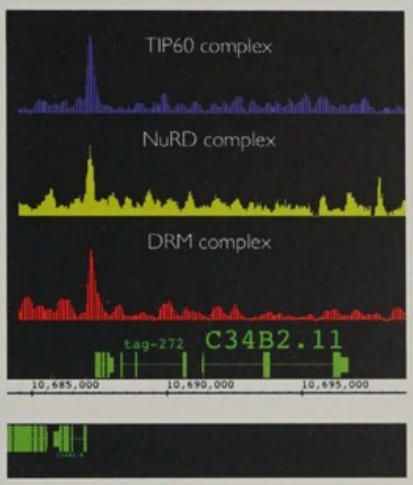


Figure 2 Chromatin immunoprecipitation followed by high-throughput sequencing reveals common sites occupied by different chromatin regulatory complexes

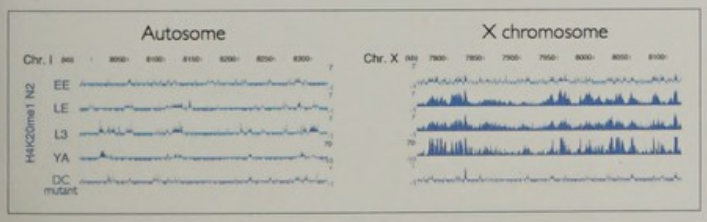


Figure 3 H4K20me1 has a role in X chromosome dosage compensation. ChIP tracks show enrichment on the X chromosome that is dependent on dosage compensation.

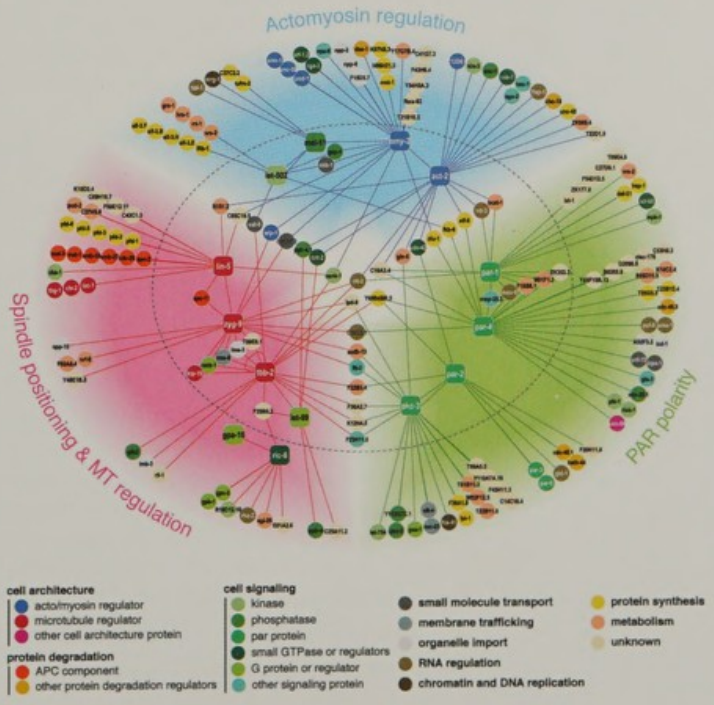


Figure 4 Interconnected cell polarity network derived from genetic interaction RNAi screening

Andrea Brand

Stem cells to synapses: regulation of self-renewal and differentiation in the nervous system

Co-workers: Janina Ander, Elizabeth Caygill, Esteban Contreras-Sepulveda, Melanie Cranston, Catherine Davidson, David Doupé, Jack Etheredge, Barret Pfeiffer, Katrina Gold, Jun Liu, Tony Southall, Pauline Spéder, Christine Turner

Discovering how stem cells are maintained in a multipotent state and how their progeny differentiate into distinct cellular fates is a key step in the therapeutic use of stem cells to repair tissues after damage or disease. We are investigating the genetic networks that regulate neural stem cells in *Drosophila*. Stem cells can divide symmetrically to expand the stem cell pool, or asymmetrically to self-renew and generate a daughter cell destined for differentiation. Symmetrically dividing stem cells exist in the optic lobe of the brain, where they convert to asymmetrically dividing neuroblasts. By comparing the transcriptional profiles of symmetrically and asymmetrically dividing stem cells, we identified Notch as a key regulator of the switch from symmetric to asymmetric division. The balance between symmetric and asymmetric division is critical for the generation and repair of tissues, as unregulated stem cell division results in tumourous overgrowth.

During asymmetric division cell fate determinants, such as the transcription factor Prospero, are partitioned from the neural stem cell to its daughter. We showed that Prospero acts as a binary switch between self-renewal and differentiation. By identifying Prospero's targets throughout the genome we showed that Prospero represses genes for self-renewal and activates differentiation genes. In Prospero mutants, differentiating daughters revert to a stem-cell-like fate: they express markers of self-renewal, continue to proliferate, fail to differentiate and generate tumours.

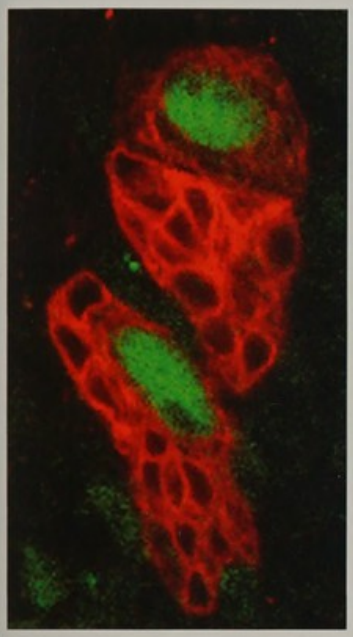
Neural stem cells transit through a period of quiescence at the end of embryogenesis. We showed that insulin signalling is necessary for these stem cells to exit quiescence and reinitiate cell proliferation, we identified nutrition-responsive glial cells as the source of the insulin-like peptides that reactivate neural stem cells *in vivo*.

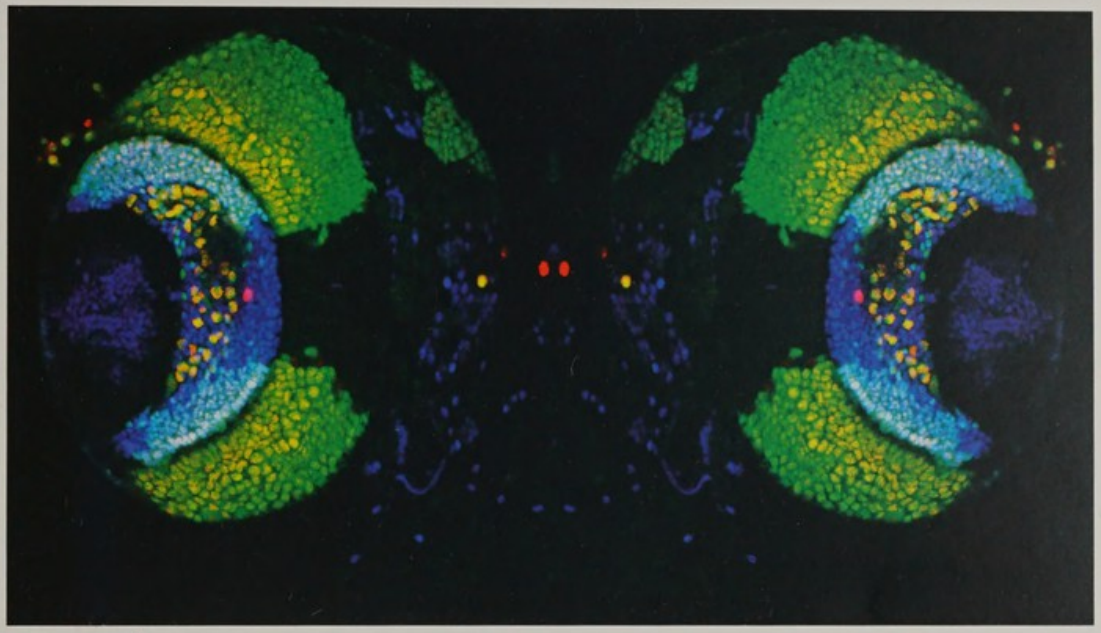
For more information, see the Brand lab home page:

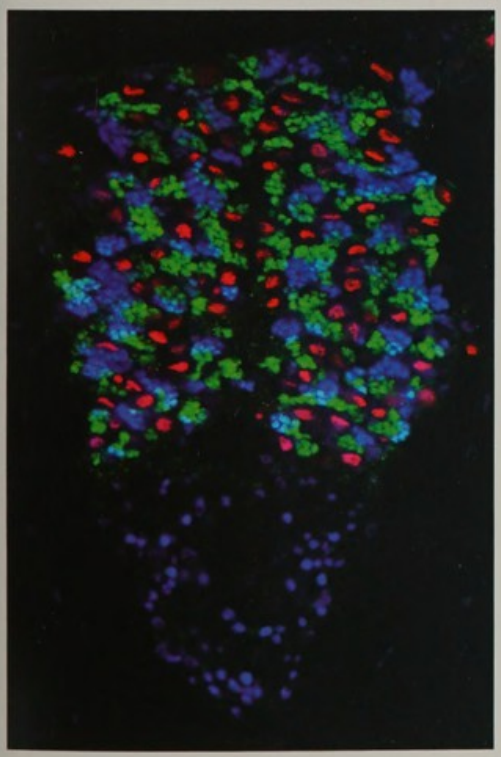
http://www.gurdon.cam.ac.uk/~brandlab/

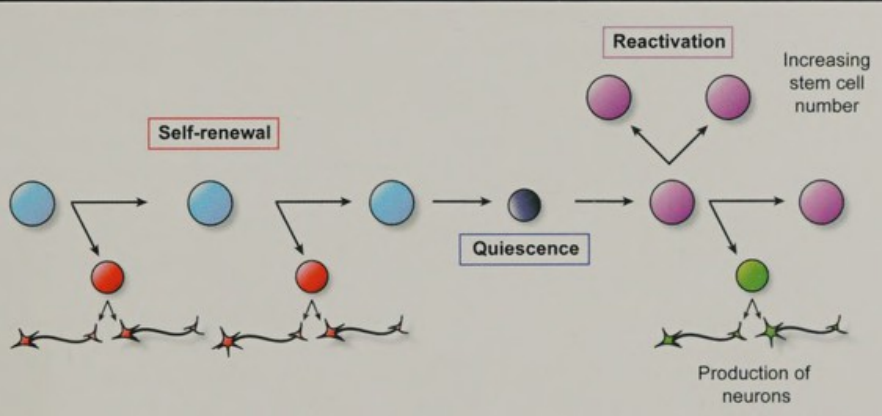
Selected publications:

- Chell JM and **Brand AH** (2010) Nutrition-responsive glia control exit of neural stem cells from quiescence. Cell 143(7), 1161-1173
- Egger B, Gold KS and **Brand AH** (2010) Notch regulates the switch between symmetric and asymmetric neural stem cell division in the *Drosophila* optic lobe. Development, 137, 2981-2987
- Bardin AJ, Perdigoto CN, Southall TD, **Brand AH** and Schweisguth F (2010) Transcriptional control of stem cell maintenance in the *Drosophila* intestine. Development 137, 705-714
- Monier B, Pelissier A, **Brand AH** and Sanson B (2010) An actomyosin-based barrier inhibits cell mixing at compartmental boundaries in *Drosophila* embryos. Nature Cell Biology 12, 60-65
- Southall TD and **Brand AH** (2009) Multiple transcription factor binding identifies neural stem cell gene regulatory networks. EMBO J. 28, 3799-807









Top left: two neural stem cell clones in the larval brain, labelled in red. Neuroblast nuclei are green.

Top right: Lineage tracing in the Drosophila optic lobes of the Drosophila brain, using the Gtrace system. Cells currently expressing the transcription factor Optix express RFP (red); cells descended from Optix-expressing cells express GFP (green). The transcription factor Dachshund (blue) marks the lamina region of the developing visual system.

Left: Expression of temporal transcription factors Castor (green) and Chinmo (blue) in the larval ventral nerve cord. Neuroblasts in red.

Above: Drosophila neural stem cells (blue) divide asymmetrically during embryogenesis, to self-renew and generate differentiating daughter cells (red). Neural stem cells then enter a period of quiescence (grey) from which they are reactivated to expand the stem cell pool (purple) and generate the neurons of the adult nervous system (green).

Nick Brown

Molecular analysis of morphogenesis

Co-workers: Natalia Bulgakova, Jonathan Friedlander, Anabel Griffiths, Sven Huelsmann, Yoshiko Inoue, Benjamin Klapholz, John Overton, Nikki Parsons, Peerapat Thongnuek

Cellular adhesion and communication are vital during the development of multicellular organisms. These processes use proteins on the surface of cells, receptors, which stick cells together (adhesion) and/or transmit signals from outside the cell to the interior, so that the cell can respond to its environment. Our research is currently focused on how adhesion receptors are linked with the cytoskeleton to specify cell shape and movement within the developing animal. This linkage between the adhesion receptors and the major cytoskeletal filaments contains many components, giving it the ability to grow or shrink in response to numerous signals. For example, as the cytoskeleton becomes contractile and exerts stronger force on the adhesion sites, additional linker proteins are recruited in to strengthen adhesion.

We use the fruit fly *Drosophila* as our model organism to discover how the complex machinery linking cell adhesion to the cytoskeleton works, and contributes to morphogenesis. We are seeking to discover how adhesion receptors form contacts of differing strength and longevity, at one point mediating dynamic attachments as the cell moves, and at another point stable connections essential for the functional architecture of the body. At these stable sites of adhesion, such as the integrin-dependent attachments of the muscles, we can see that the different components have unique properties and distribution (Fig 1). By combining quantitative imaging with genetics we are discovering the rules that govern the assembly of the integrin adhesion complex. To combine biophysical approaches with genetics, we are establishing muscle attachments in culture (Fig 2). We find that the other major cytoskeletal element, microtubules, regulates both integin and cadherin adhesion (Fig 3). Another important question is how a variety of actin-membrane linkages are formed in the same cell, which can be addressed particularly well in the developing egg chamber. There is a rapid change in the actin structures in nurse cells, with new synthesis of cytoplasmic actin cables from the plasma membrane, extending inwards to connect to an actin network surrounding the nucleus (Fig 4). We are currently addressing how the different actin structures in the cell are coordinated by actin-binding proteins, such as adducin and spectraplakin.

Selected publications:

- **Brown NH** (2011) Extracellular matrix in development: insights from mechanisms conserved between invertebrates and vertebrates. Cold Spring Harb Perspect Biol E-pub ahead of print
- Zervas CG, Psarra E, Williams V, Solomon E, Vakaloglou KM and **Brown NH** (2011) Central multifunctional role of Integrin-Linked Kinase at muscle attachment sites J Cell Sci 124, 1316-1327
- Delon I and **Brown NH** (2009) The integrin adhesion complex changes its composition and function during morphogenesis of an epithelium. J Cell Sci 122, 4363-4374
- Delon I and **Brown NH** (2007) Integrins and the actin cytoskeleton. Curr Opin Cell Biol 19, 43-50

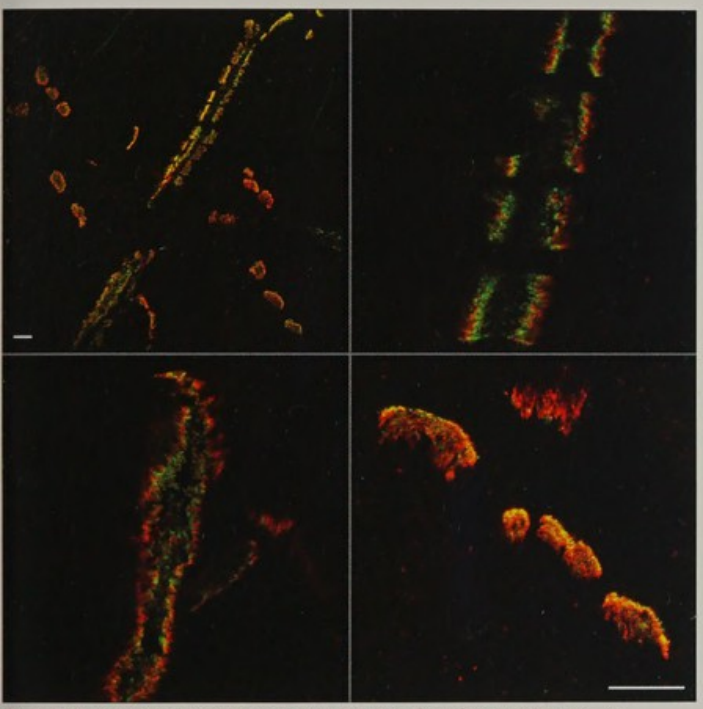


Fig 1: Different views of muscle attachment sites from Drosophila embryos, showing the distribution of two proteins that link integrin extracellular matrix receptors to the cytoskeleton (Git in green and integrin-linked-kinase in red). Note that they are in distinct regions of the attachment structure, suggesting that the two proteins have different roles.

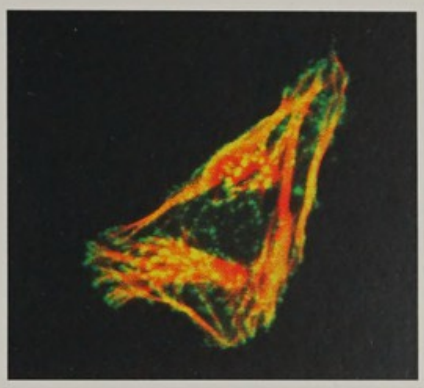


Fig 2: Primary cell culture of embryonic muscles, showing integrin adhesions (green) connected to actin filaments (red).

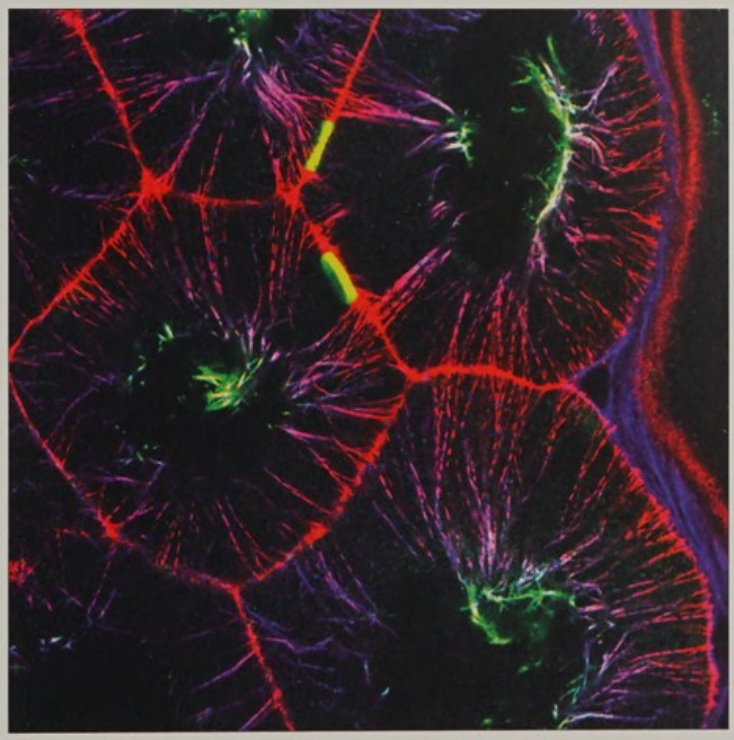


Fig 4: Actin cables (red) extending from the plasma membrane to the nucleus (visible as black area in the centre of each cell) in nurse cells hold the nucleus in place during dumping. The spectraplakin Short stop (blue) is enriched on the parts of the actin cables close to the nucleus (red and blue = magenta), where they connect to an actin meshwork surrounding the nucleus, containing the actin-networking protein adducin (green).

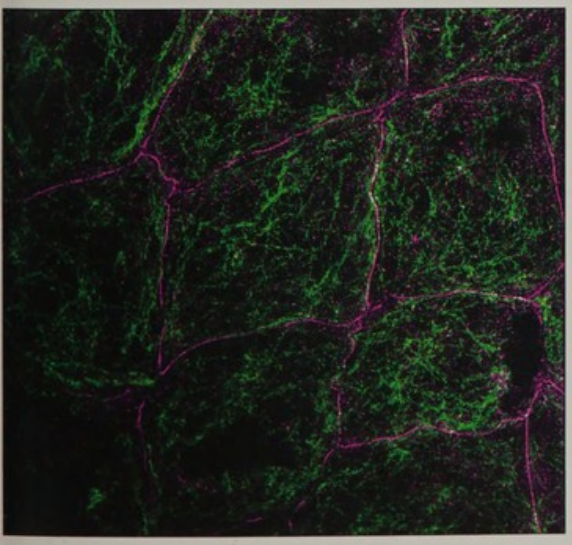
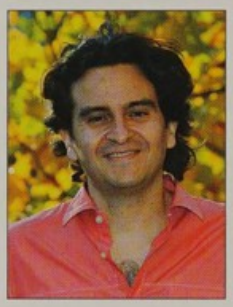


Fig 3: Arrays of microtubules (green) in the amnioserosa cells regulate the cell-cell adhesion molecule cadherin (magenta)

Rafael Carazo Salas

Functional genomics of cell morphogenesis

Co-workers: Juan Francisco Abenza Martinez, Anatole Chessel, James Dodgson, Marco Geymonat, Veronika Graml, Jonathan Lawson, Yung-Chin Oei, Kathy Oswald, Claudia Stocker, Xenia Studera



An extraordinary capacity of cells is their ability to modulate their shape, polarity and intracellular cytoskeletal organisation, according to the functions they need to perform. Our work seeks to identify the gene and protein networks that regulate these three processes and overall cell morphogenesis, in space and time. To that end we adopt a multi-disciplinary approach combining high-content and quantitative microscopy, genetics, biochemistry and computational methods. We use fission yeast as our primary model organism and plan to extend our scope to mammalian cells in the future.

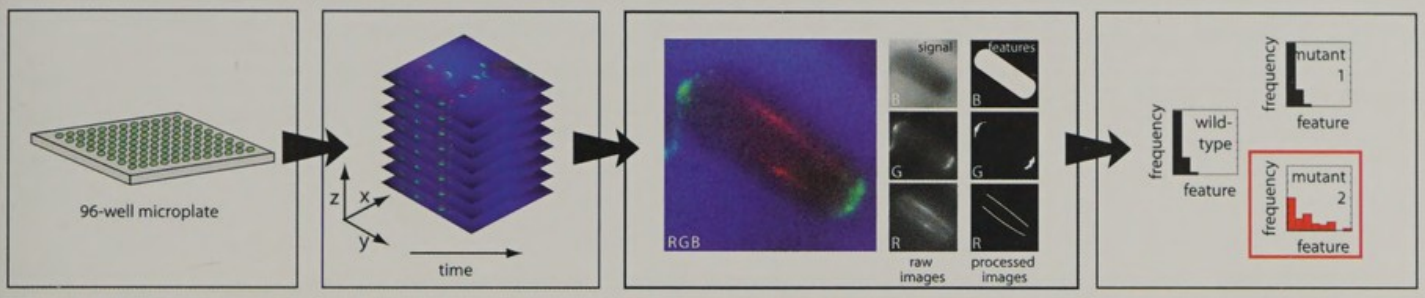
We recently established a high-throughput/high-content microscopy platform for yeast-based functional genomics studies. Using that platform and systematic gene knock-outs, we recently completed the first comprehensive live cell-based screen for microtubule and cell shape regulators and discovered tens of potential novel regulators that we are in the course of validating. With that screen, we hope to obtain the most exhaustive genomic map and spatiotemporal annotation of such regulators to date. Various other microscopy-based functional genomics projects are also ongoing in our group.

We have also developed, in collaboration with theoreticians, computational methods to simulate the collective interaction of microtubules and microtubule regulator recipes in 3D over time, in order to clarify the mechanisms that precisely pattern microtubules in cells. We find that, together with regulator abundance, cell geometry is a strong determinant of microtubule pattern, something we are actively investigating experimentally.

Lastly, we have begun characterising the dynamics and structure of the polarity machinery at high spatiotemporal resolution. Using live super-resolution microscopy and custom-made image analysis tools, we find that components of the machinery previously thought to regulate polarity by physically interacting at the cell cortex actually localise to separate, distinct complexes. This suggests novel layers of polarity regulation we are seeking to unravel.

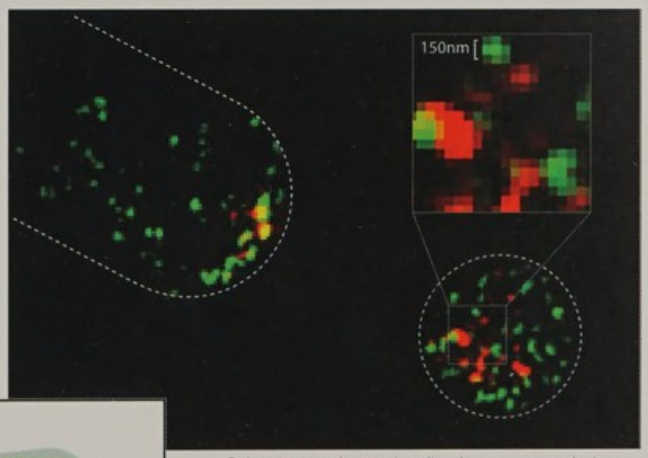
Selected publications:

- **Carazo-Salas RE**, and Nurse P (2007). Sorting out interphase microtubules. Mol Syst Biol 3:95-6.
- Salinas S, **Carazo-Salas RE**, Proukakis C, Schiavo G, Warner TT (2007). Spastin and microtubules: Functions in health and disease. J Neurosci Res 85(12):2778-82.
- **Carazo-Salas RE**, and Nurse P (2006). Self-organization of interphase microtubule arrays in fission yeast. Nat Cell Biol 8(10):1102-7.
- Salinas S, **Carazo-Salas RE**, Proukakis C, Cooper JM, Weston AE, Schiavo G, Warner TT (2005). Human spastin has multiple microtubule-related functions. J Neurochem 95(5):1411-20.
- **Carazo-Salas RE**, Antony C, Nurse P (2005). The kinesin Klp2 mediates polarization of interphase microtubules in fission yeast. Science 309(5732):297-300.



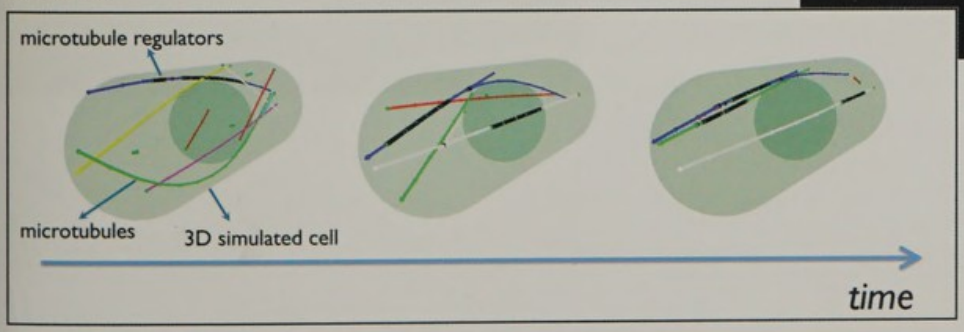
A high-throughput/high-content microscopy workflow used to systematically screen through the genome for novel regulators of cell morphogenesis.

High-resolution image of cells expressing GFP-tubulin, generated with an automated high-throughput spinning disc confocal microscope.



Polarity complexes visualised at superresolution. Live cells expressing two fluorescently-labelled (green:GFP, red: mCherry) polarity factors. Superresolution reveals that both factors, thought to regulate polarity by physically interacting, belong to separate 150nm-sized complexes. Left: cell visualised 'sideways'. Right: cell visualised 'head on'. Dotted lines: cell contours.

Snapshots from a computer simulation of microtubule organisation in a virtual cell.



Thomas Down

Epigenomics and transcription informatics

Co-workers: Paulina Chilarska, Kenneth Evans, Jing Su

We study the mechanisms by which programs of gene expression are selected and perpetuated during the development of multicellular organisms. Regulatory sequence elements contain clusters of binding sites for transcription factors, most of which interact with some specific DNA sequence motif. By discovering the repertoire of transcription factor binding sites, we can uncover an important part of the cell's regulatory network. We are addressing this question using a new computational motif discovery tool, NestedMICA, to find DNA sequence motifs that are over-represented in larger sets of regulatory sequences from across the genomes of a panel of multicellular organisms.

It has become increasingly clear that the function of regulatory elements depends on their context in terms of nuclear location and chromatin structre. To this end, we are keen to understand the landscape and functions of stable epigenetic modifications - particularly DNA cytosine methylation. High-throughput sequencing technologies allow epigenetic marks to be studied on a genome-wide basis, and we have used a combination of deep sequencing and a new analytical technique to generate the first map of DNA methylation across a complete vertebrate genome. We are now combining this technology with other analysis and data visualisation methods in order to study how DNA methylation interacts with other regulatory and epigenetic mechanisms. We are also investigating how human DNA methylation changes are associated with ageing and complex diseases.

Selected publications:

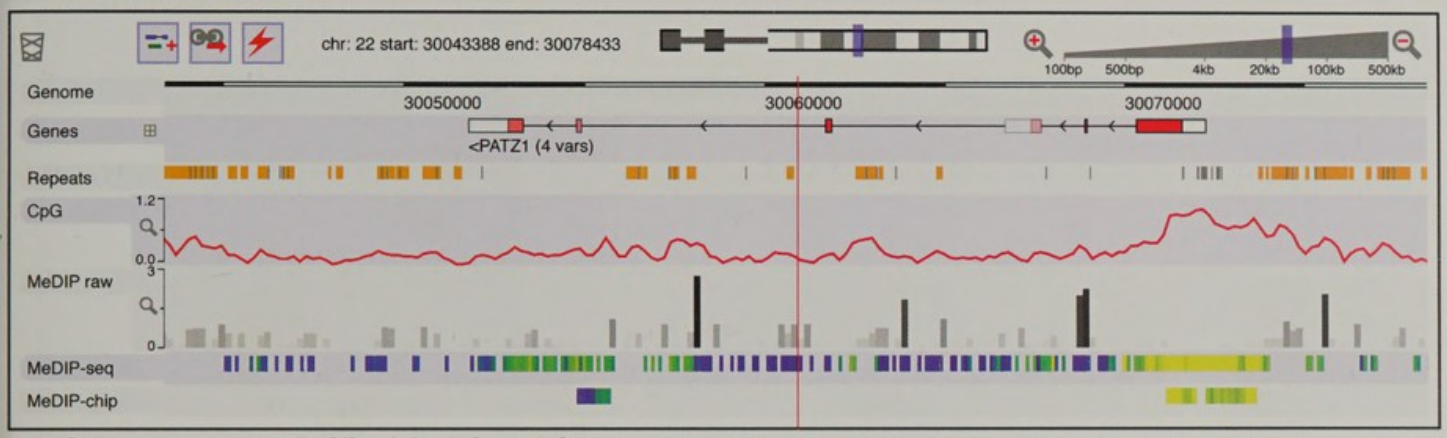
• Rakyan VK, **Down TA**, Maslau S, Andrew T, Yang T-P, Beyan H, Whittaker P, McCann OT, Finer S, Valdes AM, Leslie RD, Deloukas P, and Spector TD (2010) Human aging-associated DNA hypermethylation occurs preferentially at bivalent chromatin domains. Genome Res 20:434-439

• Kolasinska-Zwierz P, **Down T**, Latorre I, Liu T, Liu XS and **Ahringer J** (2009) Differential chromatin marking of introns and expressed exons by H3K36me3. Nature Genetics 41:376-381

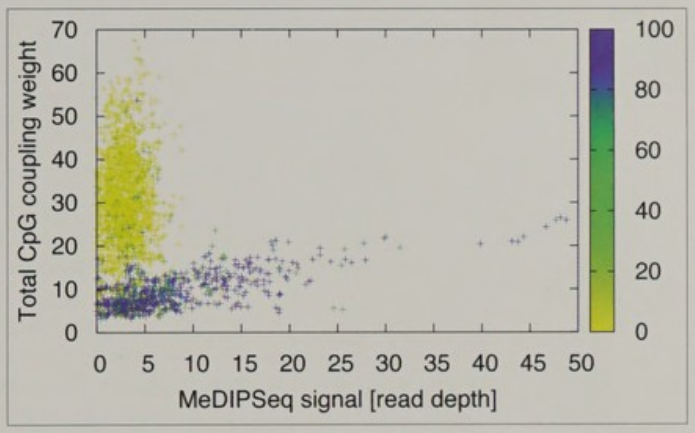
• **Down TA**, Rakyan VK, Turner DJ, Flicek P, Li J, Kulesha E, Graf S, Johnson N, Herrero J, Tomazou EM, Thorne NP, Backdahl L, Herberth M, Howe KL, Jackson DK, Miretti MM, Marioni JC, Birney E, Hubbard TJP, Durbin R, Tavare S and Beck S (2008) A Bayesian deconvolution strategy for immunoprecipitation-based DNA methylome analysis. Nature Biotech 26:779-785

• **Down TA**, Bergman CM, Su J and Hubbard TJP (2007) Large scale discovery of promoter motifs in *Drosophila* melanogaster. PLoS Comput Biol 3:e7

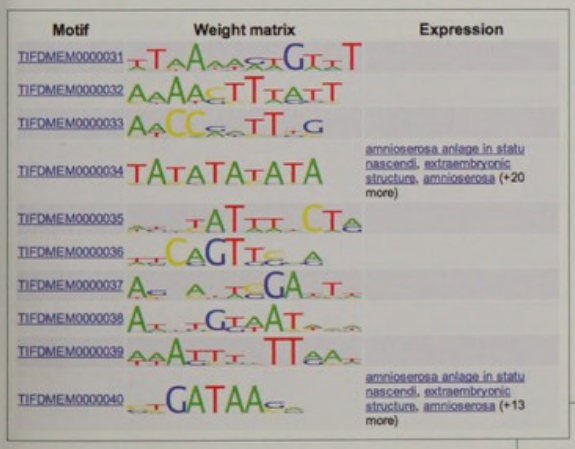
• **Down TA** and Hubbard TJP (2005) NestedMICA: sensitive inference of over-represented motifs in nucleic acid sequences. Nucleic Acids Res 33, 1445-1453



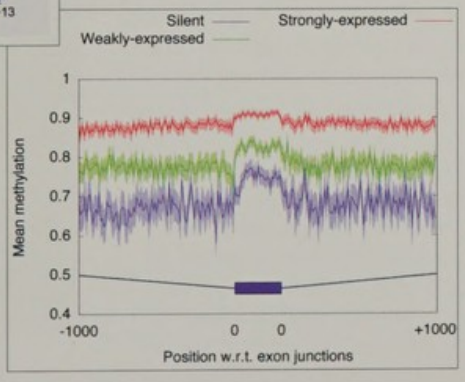
Methyl-DNA immuonprecipitation (MeDIP-seq) data before and after normalisation using the Batman method. Viewed in the Dalliance genome visualisation tool (http://www.biodalliance.org/)



The Methyl DNA Immunoprecipitation (MeDIP) technique can be used to quantify the methylation state of genomic DNA on a large scale. In methylated regions (coloured blue), signal correlates with the density of CpG dinucleotides.



The BioTIFFIN interface for browsing regulatory sequence motifs.



Multiple epigenetic marks "paint" exons in the genome. In the case of DNA methylation (shown here) the marking of exon boundaries is remarkably sharp, and appears to be independent of transcription. (single-base methylation data from Lister et al, Nature AOP 14th October 2009).

Jenny Gallop

Membranes, actin and morphogenesis

Co-workers: Lynn Froggett, Julia Mason

Understanding the molecular basis of cell shape and the changes that occur when cells move is vital for understanding the different cell rearrangements that underlie morphogenesis. The actin cytoskeleton is of key importance. The actin cytoskeleton is remodelled in response to changes in the cellular environment, which are transduced through signalling at the plasma membrane. Many actin regulators are recruited to membranes and my lab will study how the organisation of proteins at membranes prompts the formation of distinct actin structures that influence cell shape and movement. We hope to gain a better understanding of how the changes in cell shape lead to morphogenesis in the whole organism.

We will particularly concentrate on how actin is polymerised during filopodia formation and endocytosis. Filopodia are finger-like actin-rich protrusions that are thought to be sensory structures. In previous work I established an *in vitro* reconstitution system using supported lipid bilayers and *Xenopus* egg extracts that recapitulates the formation of actin structures resembling filopodia (Fig 1), and proposed a model for how filopodia form in cells (Fig 2). The role of actin in endocytosis is somewhat unclear, but there are many molecular links that suggest it is important. Endocytic actin structures can also be recapitulated using reconstitution systems and key actin regulator, toca, found using this approach, appears to be involved in endocytosis and gastrulation in *Xenopus* (Fig 3).

Specifically we will ask: how are filopodia formed? How are endocytic actin structures generated at the membrane and in what ways is this different from filopodia formation? How are the proteins that regulate actin structures used during morphogenesis? To answer these questions we will take a two-pronged approach: (1) reconstitution of actin polymerisation *in vitro* using artificial membranes and *Xenopus* egg extracts combined with advanced microscopy and (2) investigation of how actin regulators are used by cells *in vivo* during early development in the frog, *Xenopus laevis*. This interdisciplinary approach has two main strengths: (1) The possibility of attaining a complete molecular understanding using the *in vitro* systems and (2) study of cell biological events within the natural complement of physiological signals provided by the whole organism.

Selected publications:

• Lee K*, **Gallop JL***, Rambani K and Kirschner MW (2010) Self-assembly of filopodia-like structures on supported lipid bilayers. Science 329: 1341-1345

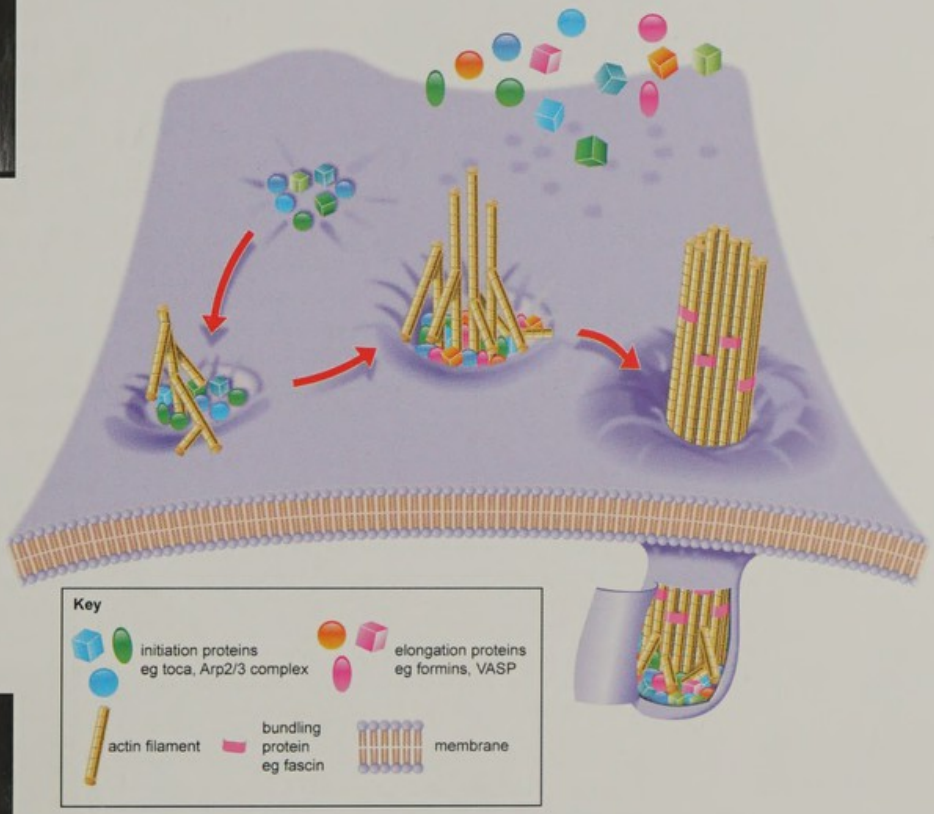
• **Gallop JL***, Jao CC*, Kent HM, Butler PJ, Evans PR, Langen R and McMahon HT (2006) Mechanism of endophilin N-BAR domain-mediated membrane curvature EMBO J 25: 2898-2910

• **Gallop JL**, Butler PJ and McMahon HT (2005) Endophilin and CtBP/BARS are not acyl transferases in endocytosis or Golgi fission. Nature 438: 675-678

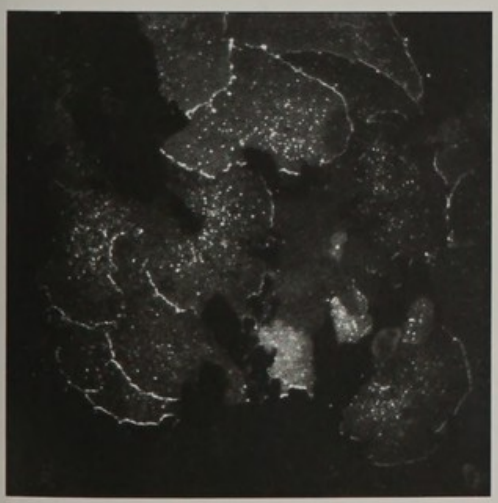
• McMahon HT and **Gallop JL** (2005) Membrane curvature and mechanisms of dynamic cell membrane remodelling. Nature 438: 590-596

(* joint first authors)

(1) Filopodia-like structures made of fluorescently-labelled actin which grow from supported lipid bilayers (at the base of the picture).



(2) Model for filopodia formation from the study of filopodia-like structures, with an initial clustering step followed by actin polymerisation at the membrane surface then elongation of actin filaments to cause outgrowth of the filopodium.

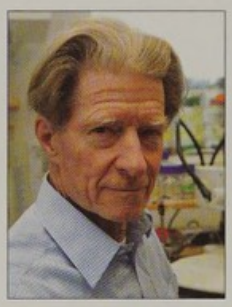


(3) Toca localisation to lamellipodial edges, filopodia tips and endocytic vesicles in cells within a Keller explant from a Xenopus gastrula.

John Gurdon

Nuclear reprogramming by oocytes and eggs

Co-workers: Dilly Bradford, Richard Halley-Stott, Jo-Anne Johnson, Jerome Jullien, Kei Miyamoto, Patrick Narbonne, Vincent Pasque, Marta Teperek-Tkacz, Stan Wang



The differentiated state of adult cells is remarkably stable, and ensures the normal function of our body tissues and organs. Hardly ever does a cell of one kind change into a different kind of cell. However, there are certain experimental procedures by which gene expression of a specialised adult cell can be reversed to that of an embryonic cell. This opens the way to provide therapeutically useful replacement cells of any kind from other readily available cells of another kind, such as skin.

One procedure for reversing the differentiated state of a cell is by transplanting its nucleus to an egg or oocyte. Our aim is to understand how eggs or oocytes achieve this, so as to identify the reprogramming molecules involved, and thus, eventually, to improve the efficiency of this route towards cell replacement without immunosuppression.

We use the growing eggs ("oocytes") of amphibia to activate embryo-expressing genes in the transplanted nuclei of adult mammalian cells. We have recently identified polymerised actin and its cofactors as a significant component of this oocyte transcriptional apparatus for reprogramming somatic nuclei. A question of at least as much importance is how the differentiated state of a cell makes its nucleus resistant to the reprogramming activities of an oocyte. Genes that become transcriptionally repressed in normal development are of this kind. Such genes show an epigenetic memory of their quiescent state. We have identified macroH2A as one chromatin protein that helps to confer an inactive state of genes on the inactive X chromosome of female mammals. We have recently developed a procedure by which chromosomal proteins can be progressively removed from somatic cell nuclei to improve embryonic gene reactivation. This can lead to the identification of chromosomal components that resist reprogramming by oocytes. The removal of these could greatly improve the efficiency of nuclear reprogramming.

Selected publications:

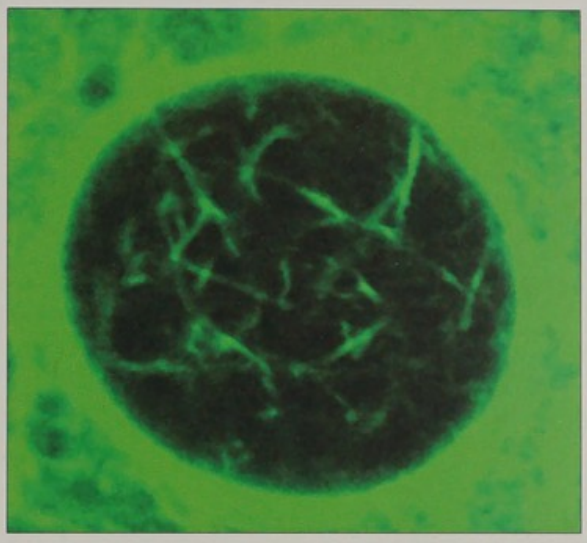
• Miyamoto K, Pasque V, Jullien J and **Gurdon JB** (2011) Nuclear actin polymerization is required for transcriptional reprogramming of Oct4 by oocytes. Genes & Development 25(9):946-958

• Pasque V, Gillich A, Garrett N and **Gurdon JB** (2011) Histone variant macroH2A confers resistance to nuclear reprogramming. EMBO J 6;30(12):2373-87

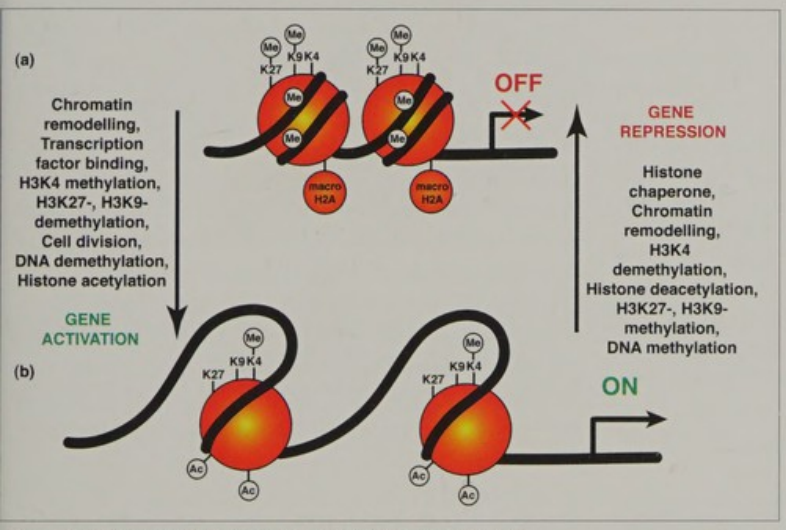
• Jullien J, Halley-Stott RP, Miyamoto K, Pasque V and **Gurdon JB** (2011) Mechanisms of nuclear reprogramming by eggs and oocytes: a deterministic process? Nature Reviews Molecular & Cell Biology, 12, 453-459

• Narbonne P, Simpson DE and **Gurdon JB** (2011) Deficient induction response in a *Xenopus* nucleocytoplasmic hybrid. PLoS Biology 9(11):e101197

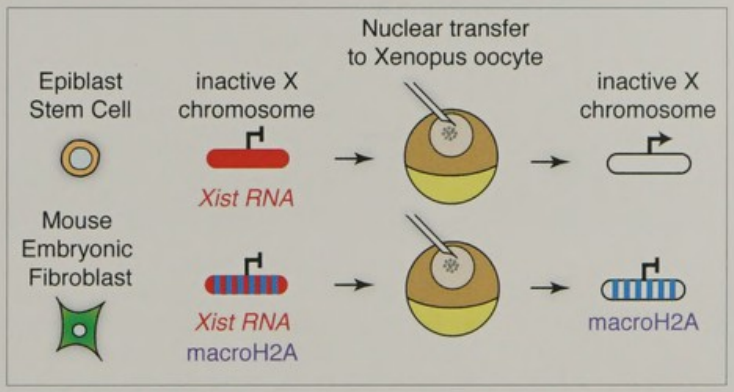
• Pasque V, Jullien J, Miyamoto K, Halley-Stott RP and **Gurdon JB** (2011) Genetic and epigenetic factors affecting nuclear reprogramming efficiency. Trends in Genetics 27(12)516-525



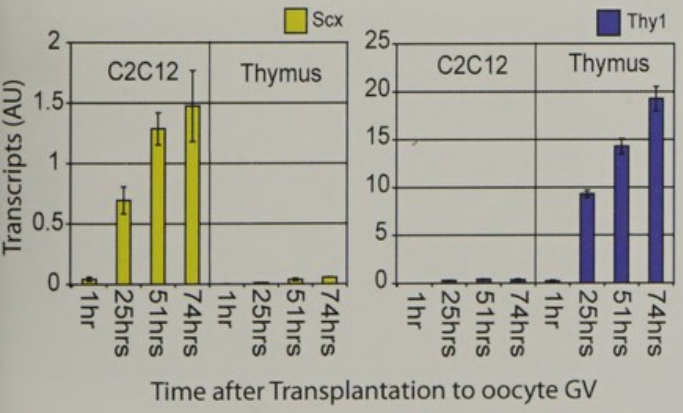
Polymerised nuclear actin enhances nuclear reprogramming.



A model of changes in chromatin state during reprogramming.



Transcription of an inactive X chromosome of mice is inhibited in part by macroH2A.



A dramatic difference exists in the ability of an oocyte to activate Scleraxis (Scx) or Thy1 genes in different cell types.

Steve Jackson

Maintenance of genome stability

Co-workers: Linda Baskcomb, Rimma Belotserkovskaya, Melanie Blasius, Sebastien Britton, Jessica Brown, Julia Coates, Kate Dry, Josep Forment, Yaron Galanty, Ilaria Guerini, Jeanine Harrigan, Abderrahmane Kaidi, Delphine Larrieu, Carlos Le Sage, Natalia Lukashchuk, Ryotaro Nishi, Tobias Oelschlägel, Helen Reed, Christine Schmidt, Matylda Sczaniecka-Clift, Neha Thakkar, Jorrit Tjeertes, Jon Travers, Paul Wijnhoven

Our work focuses on the DNA-damage response (DDR): the set of events that optimises cell survival and genomic integrity by detecting DNA damage, signalling its presence and mediating its repair. The importance of the DDR is underscored by defects in it being associated with various pathologies, including neurodegenerative disease, immunodeficiency, developmental defects, premature ageing, infertility and cancer. Indeed, we recently identified mutations in the DDR protein CtIP that cause Seckel syndrome, a recessively inherited dwarfism disorder characterised by microcephaly, and a related disease called Jawad syndrome (1).

For many years, we have been studying how protein phosphorylation controls the DDR. We have now carried out phospho-proteomic screens in collaboration with Dr. Chunaram Choudhary (Copenhagen, Denmark), enabling us to identify novel substrates of the cell-cycle checkpoint kinase Chk1 (2). In addition, we identified a DNA-damage dependent phosphorylation site on the key homologous recombination protein Rad51 that controls Rad51 function (3). Furthermore, we have studied how DNA damage arises in the absence of Chk1 activity, showing that this is mediated by the endonuclease Mus81/Eme1 (4). Another recent highlight has been our data showing how DNA replication stress leads to the formation of chromosomal fragile sites in G1 phase of the next cell cycle (5). This work has thus helped our understanding of how fragile sites arise and contribute to cancer and other diseases.

In addition, our studies have led to new therapeutic opportunities. To exploit these, with the assistance of Cancer Research Technology and Cambridge University, Steve Jackson founded *MISSION* Therapeutics whose aim is to translate new molecular understandings of human cell biology into drugs that will markedly improve the management of life-threatening diseases, particularly cancer (http://www.missiontherapeutics.com/).

Selected publications:

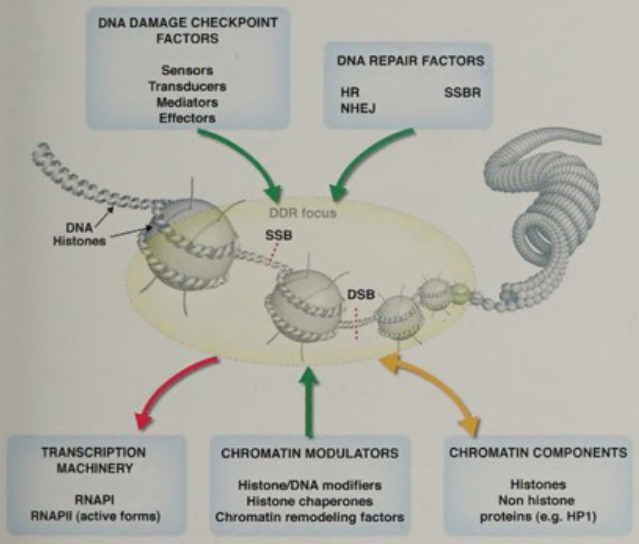
1) Qvist P, Huertas P, Jimeno S, Nyegaard M, Hassan MJ, **Jackson SP** and Børglum AD (2011) CtIP mutations caus Seckel and Jawad syndromes. PLoS Genetics 7, e100231

2) Blasius M, Forment JV, Thakkar N, Wagner SA, Choudhary C and **Jackson SP** (2011) A phospho-proteomic screen identifies substrates of the checkpoint kinase Chk1. Genome Biol 12(8), R78

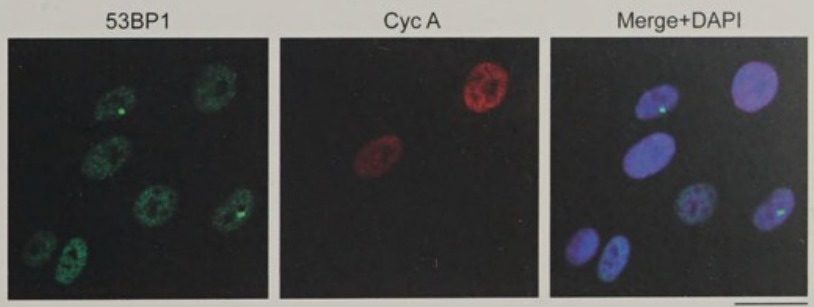
3) Flott S, Kwon Y, Pigli YZ, Rice PA, Sung P and **Jackson S** (2011) Regulation of Rad51 function by phosphorylation EMBO Rep 12, 833-9

4) Forment JV, Blasius M, Guerini I and **Jackson SP** (2011) Structure-Specific DNA Endonuclease Mus81/Eme1 Generates DNA Damage Caused by Chk1 Inactivation. PLoS ONE 6, e23517

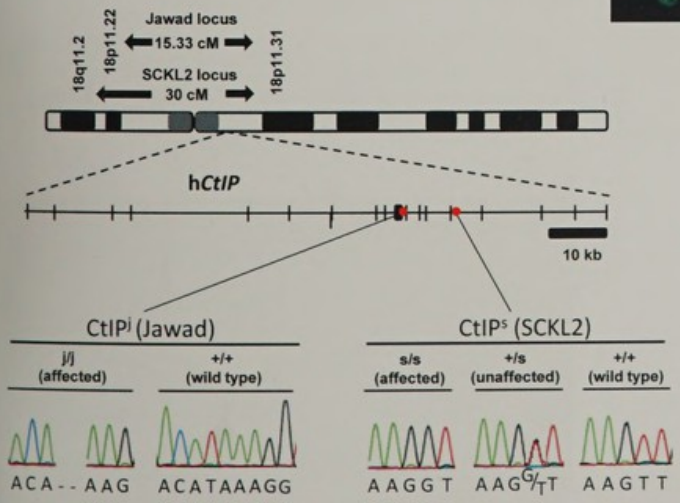
5) Harrigan JA, Belotserkovskaya R, Coates J, Dimitrova DS, Polo SE, Bradshaw CR, Fraser P and **Jackson SP** (201 Replication stress induces 53BP1-containing OPT domain in G1 cells. J Cell Biol 193, 97-108



Protein dynamics to and from sites of DNA breaks. DNA damage checkpoint and repair factors and modulators of chromatin organization are recruited (green arrows) to DNA breaks (SSB and DSB), while transcription machineries are excluded (red arrows), and the dynamics of structural chromatin components operate in both directions (orange arrows). HR, homologous recombination; NHEJ, non-homologous end joining. Taken from Polo SE and Jackson SP (2011) Dynamics of DNA damage response proteins at DNA breaks: A focus on protein modifications. **Genes Dev** *25, 409-433*



53BP1 (green) accumulates in nuclear bodies in a subset of G1 cells. Cyclin A positive cells (red) are in S/G2 phase of the cell cycle. Scale bar, 30 μm.



Schematic genetic map of chromosome 18 with the SCKL2 and Jawad loci, defined by homozygous chromosomal segments in affected consanguineous families. The CtIP gene spans 93 kb of genomic sequence covering 19 exons (vertical bars), of which 18 are coding. Red dots indicate positions of mutations and point to sequence electropherograms of homo- and heterozygous carriers and corresponding wild-type sequence.

Tony Kouzarides

Function of chromatin modifications and their role in cancer

Co-workers: Paulo Amaral, Andrew Bannister, Isaia Barbieri, Gonçalo Castelo-Branco, Maria Christophorou, Alistair Cook, Mark Dawson, Sri Lestari, Nikki Parsons, Sam Robson, Helena Santos Rosa, Marc Schneider, Peter Tessarz, Emma Viré, Beata Wyspianska

Our group is interested in defining the mechanisms by which chromatin modifications function to regulate cellular processes. Our attention is focussed on a set of enzymes (acetylases, deacetylases, methylases and kinases), which regulate transcription by covalently modifying histories. We would like to understand what biological processes these enzymes control and the precise role of each modification on chromatin dynamics. In addition we are dissecting as far as possible, how modification pathways are mis-regulated in cancer cells.

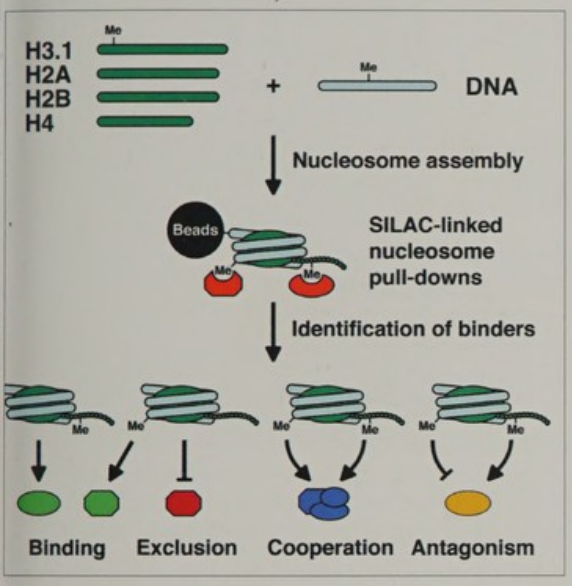
Histones are very highly modified. This complexity is necessary because histones integrate many signalling pathways regulating DNA function. We are taking a number of complementary approaches to characterise the role of chromatin modifications. We are using yeast as a model system whenever possible to define new pathways and we are using human cells to characterise their function in higher organisms and probe connections to cancer.

Modifications work by the recruitment of proteins. We have developed an assay for capturing proteins that recognise differentially modified nucleosomes, called SNAP (Silac Nucleosome Affinity Purification). This approach has been successfully used to identify proteins that are sensitive to nucleosomes methylated on histones and DNA, thus defining categories of 'cross talk' between these two distinct classes of modification.

Recently we have shown that a set of bromodomain proteins called BET are involved in activating a set of genes regulated by MLL-fusions, the gene products responsible for MLL-leukaemias. A small molecule inhibitor of BETs, called I-BET which prevents them from binding to acetylated histones, is able to suppress this gene program in primary human leukaemias and halts the process of leukaemia in model systems. Together these data give hope for the development of a therapeutic agent against MLL-leukaemias.

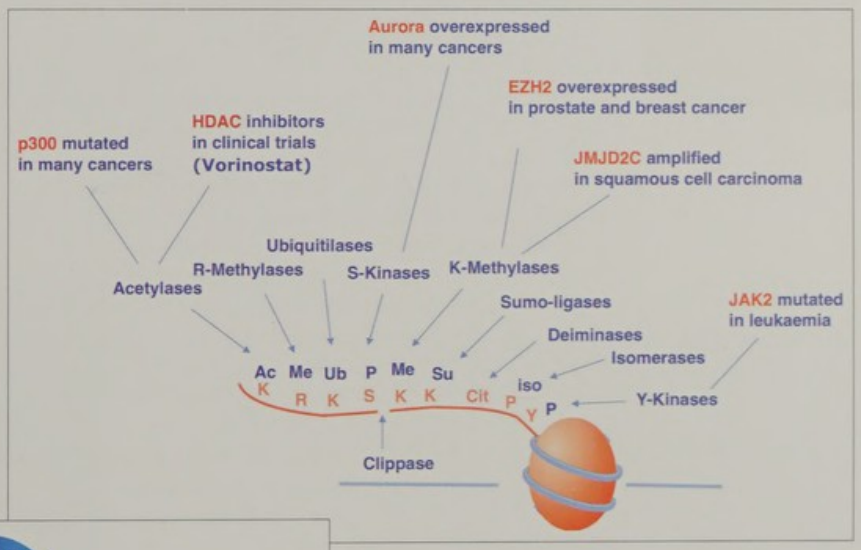
Selected publications:

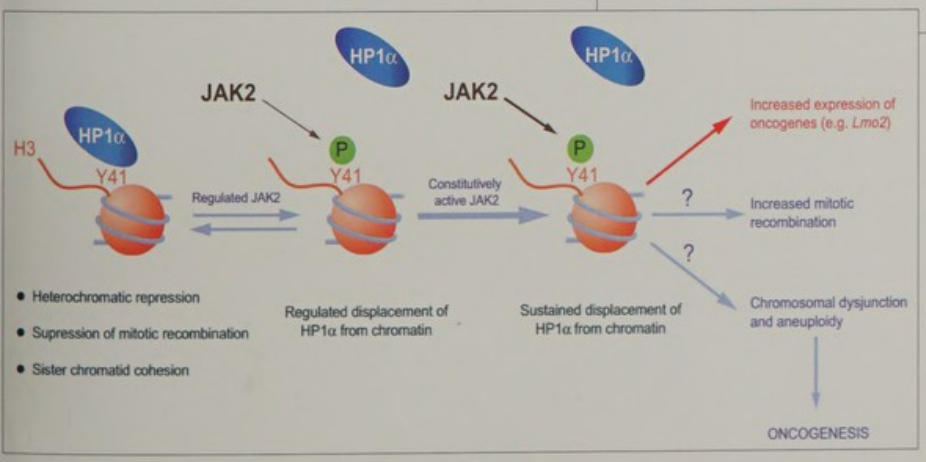
- Dawson MA, Prinjha RK, Dittmann A, Giotopoulos G, Bantscheff M, Chan WI, Robson SC, Chung CW, Hopf C, Savitski MM, Huthmacher C, Gudgin E, Lugo D, Beinke S, Chapman TD, Roberts EJ, Soden PE, Auger KR, Mirguet O, Doehner K, Delwel R, Burnett AK, Jeffrey P, Drewes G, Lee K, Huntly BJ and **Kouzarides T** (2011) Inhibition of BET recruitment to chromatin as an effective treatment for MLL-fusion leukaemia. Nature 478(7370), 529-533
- Bartke T, Vermeulen M, Xhemalce B, Robson SC, Mann M and **Kouzarides T** (2010). Nucleosome-interacting Proteins Regulated by DNA and Histone Methylation. Cell 143: 470 – 84
- Xhemalce B and **Kouzarides T** (2010) A chromodomain switch mediated by histone H3 Lys 4 acetylation regulates heterochromatin assembly. Genes Dev 24(7), 647-652
- Dawson MA, Bannister AJ, Göttgens B, Foster SD, Bartke T, Green AR and **Kouzarides T** (2009) JAK2 phosphorylates histone H3Y41 and excludes HP1alpha from chromatin. Nature 461(7265), 819-822
- Santos-Rosa H, Kirmizis A, Nelson C, Bartke T, Saksouk N, Cote J and **Kouzarides T** (2009) Histone H3 tail clipping regulates gene expression. Nat Struct Mol Biol 16(1), 17-22



The SNAP approach identifies 'cross-talk' between modifications in nucleosomes.

Model for the nuclear role of JAK2 in normal cells and in leukaemias containing JAK2 mutations.





Chromatin-modifying enzymes are deregulated in cancer.

Rick Livesey

Mammalian neural stem cell biology, fundamental and applied

Co-workers: Jessica Alsiö, Therese Andersson, Chibawanye Ene, Peter Kirwan, João Pereira, Nathalie Saurat, Yichen Shi, James Smith, Anthony Walsh

The cerebral cortex, which makes up three quarters of the human brain, is the part of the nervous system that integrates sensations, executes decisions and is responsible for cognition and perception. Given its functional importance, it is not surprising that diseases of the cerebral cortex are major causes of morbidity and mortality. Understanding the biology of cortical neural stem cells is essential for understanding human evolution, the pathogenesis of human neurodevelopmental disorders and the rational design of neural repair strategies in adults. During embryonic development, all of the neurons in the cortex are generated from a complex population of multipotent stem and progenitor cells. Much of the research in the lab centres on the cell and molecular biology of cortical stem cells. We are particularly interested in the molecular mechanisms controlling multipotency, self-renewal and neurogenesis, and how these are coordinated to generate complex lineages in a fixed temporal order. A number of ongoing projects in the group address the functional importance of transcriptional and epigenetic mechanisms in this system.

In the other major strand of research in the group, we have developed methods for directing differentiation of human pluripotent stem cells to cortical neurons, via a cortical stem cell stage. Human stem cell-derived cortical neurons form functional networks of excitatory synapses in culture. We are using this system for studies of human neural stem cell biology and to generate models of cortical diseases. Our initial focus has been on dementia, where we have used stem cells from people with Down syndrome and from patients with familial Alzheimer's disease to create cell culture models of Alzheimer's disease pathogenesis in cortical neurons. We are using those models to study Alzheimer's disease pathogenesis and the efficacy of current therapeutic strategies.

Selected publications:

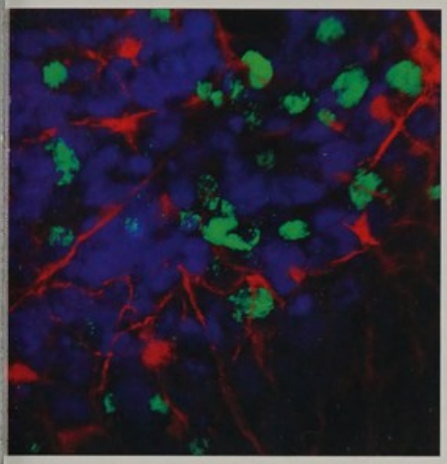
• Pereira JD, Sansom SN, Smith J, Dobenecker MW, Tarakhovsky A and **Livesey FJ** (2010) Ezh2, the histone methyltransferase of PRC2, regulates the balance between self-renewal and differentiation in the cerebral cortex. Proc Natl Acad Sci USA 107, 15957-15962.

• Andersson T, Rahman S, Sansom SN, Alsio JM, Kaneda M, Smith J, O'Carroll D, Tarakhovsky A and **Livesey FJ** (2010) Reversible block of mouse neural stem cell differentiation in the absence of dicer and microRNAs. PLoS ONE 5, e13453

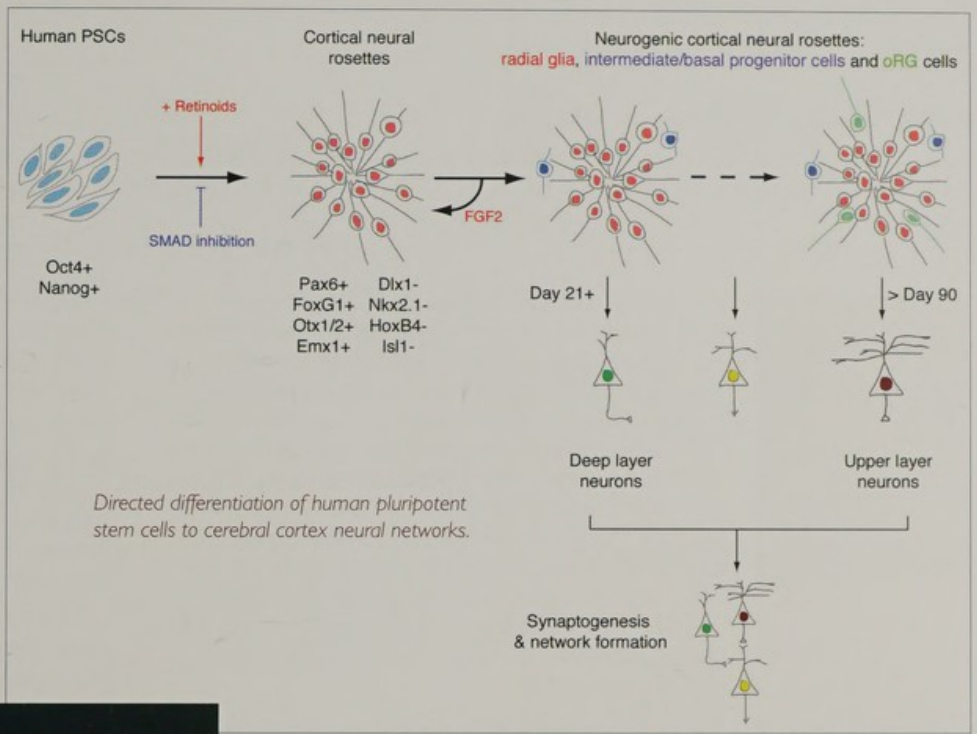
• Subkhankulova T, Yano K, Robinson HP and **Livesey FJ** (2010) Grouping and classifying electrophysiologically-defined classes of neocortical neurons by single cell, whole-genome expression profiling. Front Mol Neurosci 3, 10

• Sansom SN, Griffiths DS, Faedo A, Kleinjan DJ, Ruan Y, Smith J, van Heyningen V, Rubenstein JL and **Livesey FJ** (2009) The level of the transcription factor Pax6 is essential for controlling the balance between neural stem cell self-renewal and neurogenesis. PLoS Genetics 5, e1000511

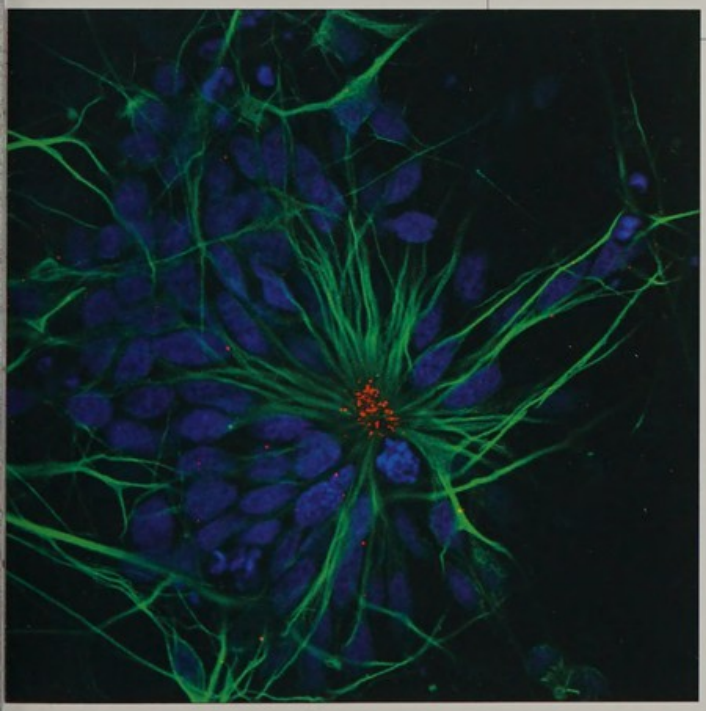
• Sansom SN and **Livesey FJ** (2009) Gradients in the brain: the control of the development of form and function in the cerebral cortex. Cold Spring Harb Perspect Biol 1:a002519



Extracellular aggregates (green) of the Alzheimer's disease pathogenic peptide Aβ42 in cultures of human cortical neurons generated from Down syndrome iPS cells.

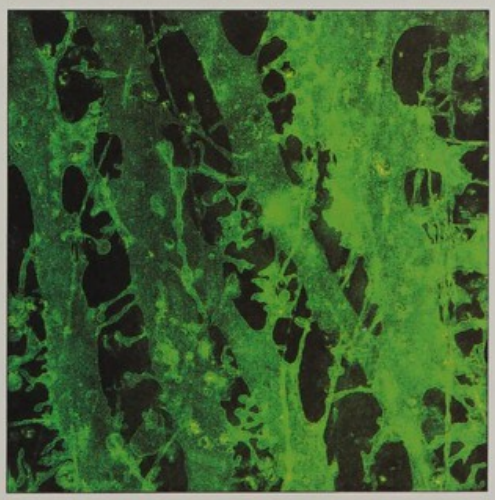


Directed differentiation of human pluripotent stem cells to cerebral cortex neural networks.



Human cortical stem cells formed polarised neuroepithelial rosettes in culture, with centrosomes (red) located apically at the centre of the rosette.

Super-resolution microscopy image of DiO-labelled human iPS cell-derived cortical neurons



Eric Miska

Small regulatory RNA

Co-workers: Javier Armisen Garrido, Alyson Ashe, Alejandra Clark, Leonard Goldstein, Ethan Kaufman, Miranda Landgraf, Nic Lehrbach, Jeremie Le Pen, Helen Lightfoot, Sylvianne Moss, Kenneth Murfitt, Greta Pintacuda, Amie Regan, Alexandra Sapetschnig, Peter Sarkies, Eva-Maria Weick, Julie Woolford

microRNAs (miRNAs), a large class of short non-coding RNAs found in many plants and animals, often act to inhibit gene expression post-transcriptionally. Approximately 3% of all known human genes encode miRNAs. Important functions for miRNAs in animal development and physiology are emerging. A number of miRNAs have been directly implicated in human disease. We have generated loss-of-function mutations in almost all of the 112 known miRNA genes in the nematode *Caenorhabditis elegans*. This collection provides the only comprehensive resource for the genetic analysis of individual miRNAs to date. Our main goal is to understand the genetic networks underlying miRNA-dependent control of development.

We are also studying other short RNA (sRNA) species, their biology and mechanism of action. For example, we recently identified the piRNAs of *C elegans*. piRNAs are required for germline development and maintenance in worms, flies and mammals. Neither the biogenesis nor the mechanism of action is understood for this class of small RNAs. We are using genetic screens, biochemical and molecular biology approaches to address basic questions about sRNA biology. Of particular interest is how small RNA regulatory networks interact with the genome and the environment.

In addition, we have developed tools for the analysis of miRNA expression in human disease and have discovered miRNAs that have potential as molecular markers for diagnosis and prognosis.

Selected publications:

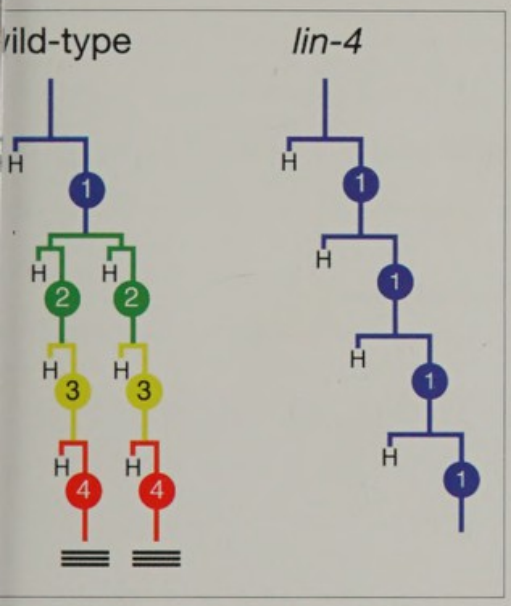
• Lehrbach N, Armisen J, Lightfoot H, Murfitt K, Bugaut A, Balasubramanian S, **Miska EA** (2009) LIN-28 and the poly(U) polymerase PUP-2 regulate let-7 microRNA processing in *Caenorhabditis elegans*. Nature Struct Mol Biol 16, 1016-1022

• Armisen J, Gilchrist MJ, Wilczynska A, Standart N and **Miska EA** (2009) Abundant and dynamically expressed miRNAs, endo-siRNAs and piRNAs in the African clawed frog *Xenopus tropicalis*. Genome Research 19, 1766-1755

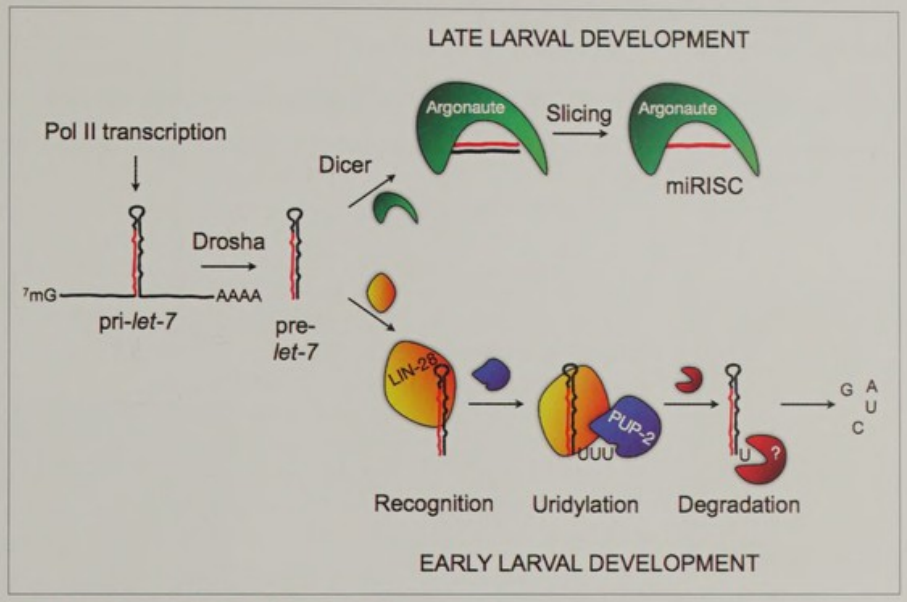
• Das PP, Bagijn MP, Goldstein LD, Woolford JR, Lehrbach NJ, Sapetschnig A, Buhecha HR, Gilchrist MJ, Howe KJ, Stark R, Berezikov E, Ketting RF, Tavaré S, **Miska EA** (2008) Piwi and piRNAs act upstream of an endogenous siRNA pathway to suppress Tc3 transposon mobility in the *Caenorhabditis elegans* germline. Mol Cell 31, 79-90

• **Miska EA**, Alvarez-Saavedra E, Abbott AL, Lau NC, Hellman AB, Bartel DP, Ambros VR, Horvitz HR (2007) Most *Caenorhabditis elegans* microRNAs are individually not essential for development or viability. PLoS Genet 3, e215

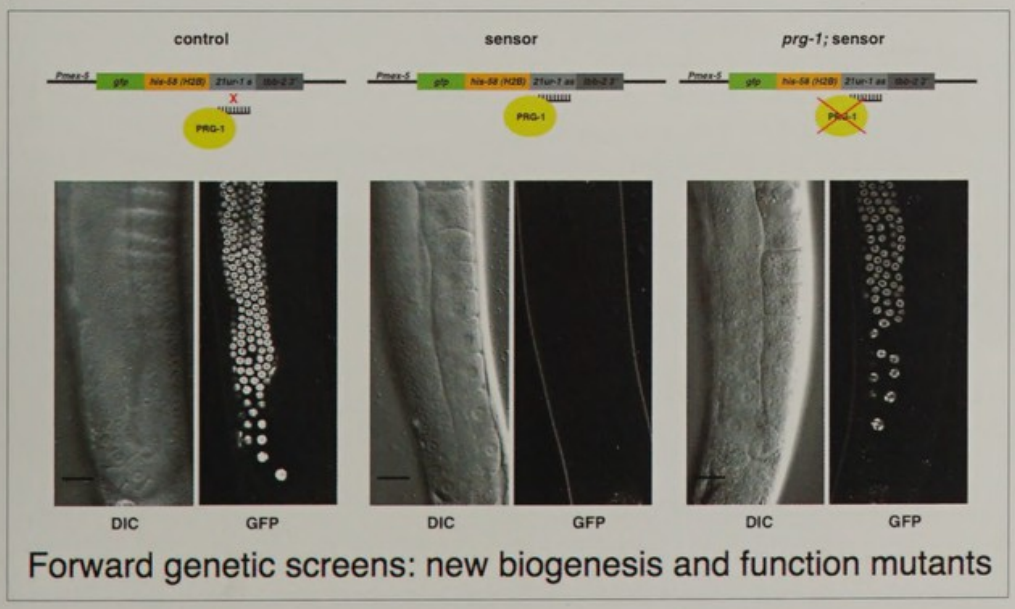
• Clark AM, Goldstein LD, Tevlin M, Tavaré S, Shaham S, **Miska EA** (2010) The microRNA miR-124 controls gene expression in the sensory nervous system of *Caenorhabditis elegans*. Nucleic Acids Res 38(11):3780-93, Epub 2010 Feb 21



first miRNA to be identified was the product of
C elegans gene lin-4. Loss of function of **lin-4** leads
ne failure of a stem cell lineage to differentiate.



We have discovered that let-7, LIN-28 and the poly(U) polymerase form an ultraconserved switch that regulates stem cell decisions in C elegans



An in-vivo assay for piRNA function in the germline. piRNAs and Piwi proteins protect the germline. We are using molecular genetics, cell biology and high-throughput sequencing to discover miRNA biogenesis and mechanisms.

Eugenia Piddini

Competitive cell interactions in normal physiology and cancer

Co-workers: Laura Blackie, Alexis Braun, Maja Goschorska, Golnar Kolahgar, Carolina Mendoza-Topaz, Kathy Oswald, Enzo Poirier, Benjamin Smith, Silvia Vivarelli, Laura Wagstaff

Cell interactions are at the basis of all multi-cellular life. They allow cells to coordinate decisions such as whether to proliferate, differentiate or die and are therefore essential to generate and maintain healthy tissues and organs. Our lab studies the mechanisms and the physiological role of competitive cell interactions. These interactions were first discovered in *Drosophila* when it was found that, within tissues, cells compete for survival and less fit cells are induced to die.

We have recently found that, in *Drosophila*, cells with different signalling levels of the growth factor Wingless (the *Drosophila* homolog of the mammalian Wnt family oncogene Wnt-1) engage in cell competition and, in particular, that cells with abnormally high signalling levels induce the death of neighbouring wild-type cells. Since Wnt signalling is overactivated in a variety of cancers, Wnt-induced cell competition could allow cancer cells to kill surrounding normal cells during early tissue colonisation.

Based on these observations, our current work is expanding in two main directions. First, we want to understand at the molecular level how this newly-discovered type of competition is brought about. To this end, we are using the power of *Drosophila* genetics to investigate how cells sense differential Wingless signalling levels among them, and what molecules they exchange that lead to the selective elimination of low Wingless signalling cells. Secondly, we want to investigate the relevance of this phenomenon in Wnt-induced cancers. For that purpose, we are working towards reconstituting Wnt-induced cell competition between normal cells and Wnt-induced tumour cells in culture. This will allow us to translate our findings from *Drosophila* to mammals and to identify novel mediators of cell competition of potential therapeutic relevance.

Selected publications:

• Vincent JP*, Kolahgar G, Gagliardi M and **Piddini E***. Steep differences in Wingless signalling trigger Myc-independent competitive cell interactions. Dev Cell 2011 21, 366-374. * Corresponding authors

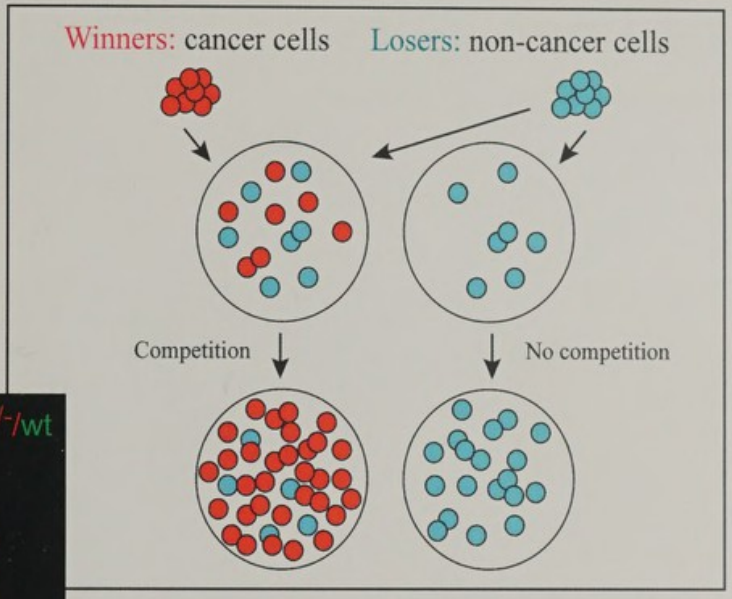
• Hogan C, Dupré-Crochet S, Norman M, Kajita M, Zimmermann C, Pelling AE, **Piddini E**, Baena-López LA, Vincent JP, Itoh Y, Hosoya H, Pichaud F, Fujita Y (2009) Characterisation of the interface between normal and transformed epithelial cells. Nat Cell Biol Apr;11(4):460-7

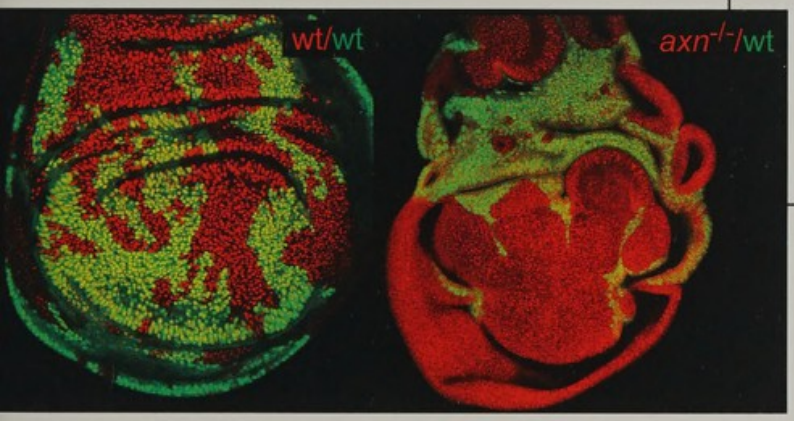
• **Piddini E** and Vincent JP (2009) Interpretation of the Wingless gradient requires signalling-induced self-inhibition. Cell Jan 136, 296-307

• **Piddini E***, Marshall F*, Dubois L, Hirst E, Vincent JP (2005) Arrow (LRP6) and Frizzled2 cooperate to degrade Wingless in *Drosophila* imaginal discs. Development Dec;132(24):5479-89. * equal contribution

• Franch-Marro X, Marchand O, **Piddini E**, Ricardo S, Alexandre C, Vincent JP (2005) Glypicans shunt the Wingless signal between local signalling and further transport. Development Feb;132(4):659-66

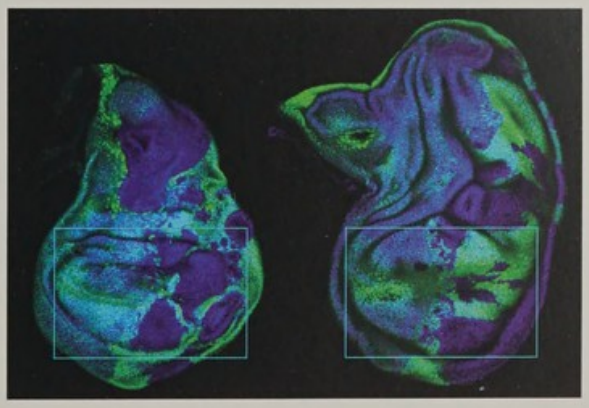
We are working towards reconstituting cell competition among tumour cells and normal cells in vitro. We do so by mixing them in culture and analysing how this affects the proliferation and survival of normal cells.

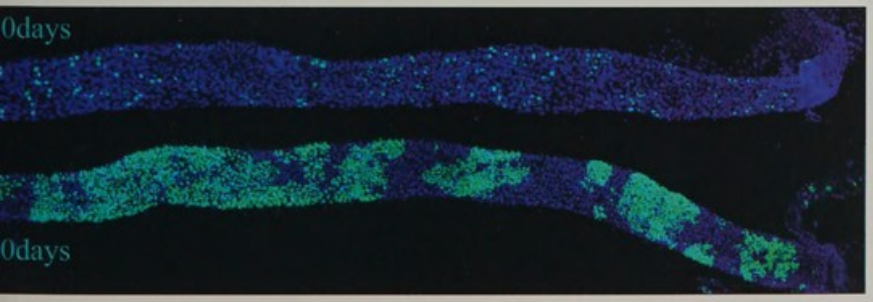




a control disc, where both GFP-positive d GFP-negative cells are wild-type, they lonise the tissue equally (left panel). owever when GFP-negative cells have gh-Wnt signalling they outcompete wild- pe GFP-positive cells (right panel).

Left panel: High Wnt signaling cells (GFP-negative) generated in the Posterior compartment of a wing pouch (boxed area) colonise the tissue at the expense of wild-type cells. Right panel: By contrast, in a notum mutant background outcompetition by high Wnt signaling cells is inhibited.



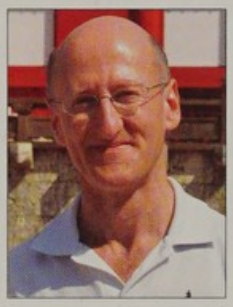


Like in the mammalian colon, overactivation of Wnt signaling leads to adenomas in the Drosophila gut. High-Wnt cells (green) overproliferate and form extensive adenomas 20 days after induction. The top gut was fixed 10 days after high-Wnt cells generation. The bottom gut was fixed 20 days after high-Wnt cells generation.

Jonathon Pines

How do cells control mitosis?

Co-workers: Philippe Collin, Barbara Di Fiore, Anja Hagting, Daisuke Izawa, Mark Jackman, Agata Lichawska, Jörg Mansfeld, Paola Marco, Takahiro Matsusaka, Oxana Nashchekina, Bernhard Strauss, Samuel Wieser



How do cells regulate entry to mitosis? And, once in mitosis, how do cells coordinate chromosome segregation with cell division (cytokinesis) to ensure that the two daughter cells receive an equal and identical copy of the genome? The answer lies in the interplay between protein kinases, protein phosphatases, and APC/C-mediated proteolysis, and this is the focus of our research. Because mitosis is a highly dynamic process we study living cells by time-lapse fluorescence microscopy but to complement this with biochemical analyses we are using somatic cell recombination to knock-out and mutate specific mitotic regulators. This has given us remarkably accurate and precise *in vivo* kinetics for protein degradation.

To understand how cells initiate mitosis we are analysing the behaviour of the key mitotic kinases, the Cyclin A- and B-dependent kinases, and their regulation by phosphorylation and dephosphorylation. We recently developed a FRET biosensor to assay Cyclin B1-Cdk1 activity *in vivo* and are using this to define the pathways that regulate the timing of mitosis. To identify the proteins responsible for regulating the Cyclin-Cdks, and provide insights into Cyclin-Cdk substrates, we have analysed protein complexes through the cell cycle by SILAC mass spectrometry and are following up some of the exciting results from this screen.

To understand how proteolysis regulates progress through mitosis we complement the analysis of APC/C-dependent degradation in living cells with biochemical analyses of protein complexes and ubiquitination activity. These studies are revealing how the APC/C is activated and how it is able to select a particular protein for destruction at a specific time. Our research is also providing insights into how APC/C activity is regulated by the spindle assembly checkpoint that is essential to the control of chromosome segregation and cytokinesis. In particular, we are beginning to elucidate the key events in the checkpoint pathway and their antagonism by the APC/C itself.

Selected publications:

• Mansfeld J, Collin P, Collins MO, Choudhary J and **Pines J** (2011) APC15 drives the turnover of MCC-Cdc20 to make the spindle assembly checkpoint responsive to kinetochore attachment. Nat Cell Biol 13, 1234-1244.

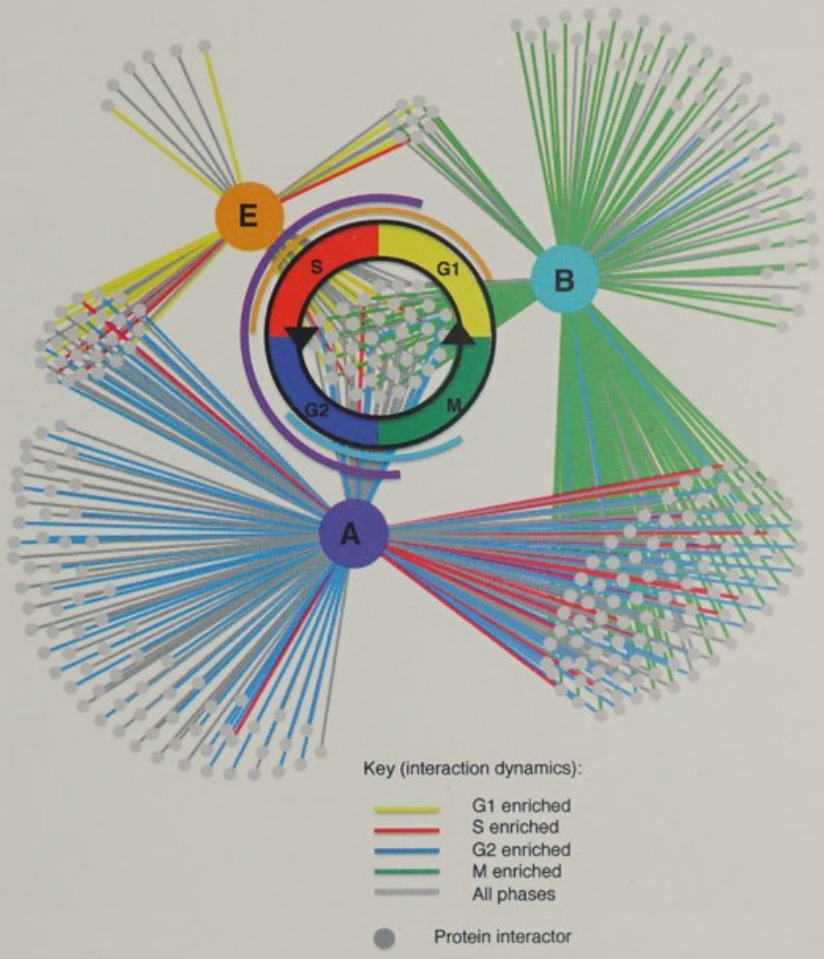
• Pagliuca F, Collins MO, Lichawska A, **Zegerman P**, Choudhary JS and **Pines J** (2011) Quantitative proteomics reveals the basis for the biochemical specificity of the cell cycle machinery. Mol Cell 43, 406-417.

• Gavet O and **Pines J** (2010) Progressive activation of Cyclin B1-Cdk1 coordinates entry to mitosis. Dev Cell 18, 533-543.

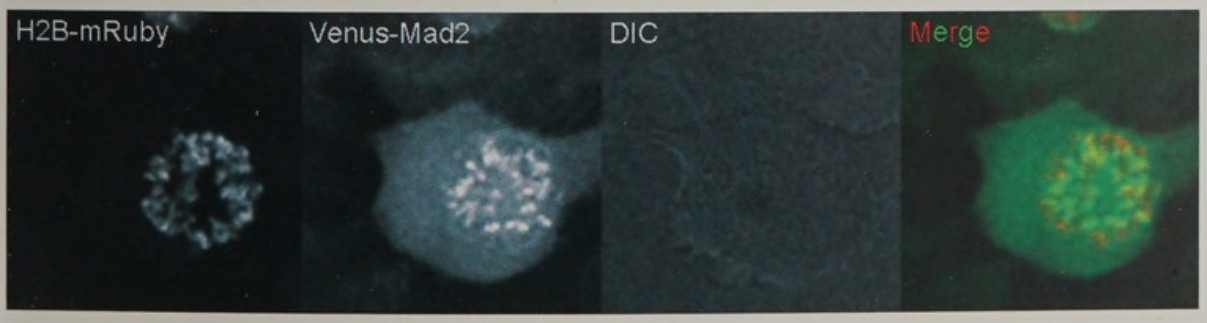
• Nilsson J, Yekezare M, Minshull J and **Pines J** (2008) The APC/C maintains the spindle assembly checkpoint by targeting Cdc20 for destruction. Nat Cell Biol 10, 1411-1420

• Wolthuis R, Clay-Farrace L, van Zon W, Yekezare M, Ogink J, Medema R and **Pines J** (2008) Cdc20 and Cks direct the spindle checkpoint-independent destruction of Cyclin A. Mol Cell 30, 290-302

Mass spectroscopy analysis reveals the dynamic interactions of the different cyclins through the cell cycle.
Credit: Felicia Walton-Pagliuca & Mark Collins (Sanger Institute)



Montage of a prometaphase cell in which the Venus fluorescent protein has been knocked into the Mad2 locus. Mad2 binds to unattached kinetochores. The chromosomes are labelled with ectopically expressed Histone H2B-mRuby. (Philippe Collin, 2010)



Emma Rawlins

Stem and progenitor cells in the mammalian lung

Co-workers: Gayan Balasooriya, Christoph Budjan, Simon Gerber, Usua Laresgoiti, Rachel Seear

Our lungs have a complex three-dimensional structure which facilitates respiration and host defence. Building this structure requires that lung embryonic progenitor cells produce the correct types and numbers of cells in the correct sequence. How is this controlled? And how is the final structure maintained in the adult? Our lab investigates the cellular and molecular mechanisms which control stem and progenitor cell fate decisions in the developing and adult lungs. Key unanswered questions include what mechanisms control the decision of lung progenitors to self-renew or to differentiate? Which pathways are required for cell lineage specification in the lung? Our approach is to use the power of mouse genetics to understand the control of lung progenitor cell behaviour at the single cell level. This allows individual cells to be analysed quantitatively *in vivo*, or by live-imaging in organ culture systems.

We have previously shown that in the embryonic lung there is a population of Id2+ multipotent epithelial progenitor cells located at the distal tips of the budding epithelium. The developmental potential, or competence, of these cells changes during embryogenesis. At the same time the cells undergo a change in gene expression pattern. We are currently exploring the cellular and molecular basis of this change in competence.

The identity of the epithelial stem and progenitor cells in the postnatal lung remains controversial. Our previous work has shown that each anatomical region (trachea, bronchioles, alveoli) has its own progenitor cell population and that the behaviour of these progenitors can change in response to local conditions. Our current postnatal work focuses on:

• Better characterising the adult lung progenitor cells. This includes testing whether progenitor cell behaviour is widespread or there are stem cells.

• Understanding the genetic regulation of the progenitors under several different physiologically-relevant conditions. In particular, we are focusing on genes that are hypothesised to control the decision to self-renew or differentiate.

Our long-term vision is to combine the developmental and homeostatic aspects of our work to develop new approaches to ameliorate human pulmonary disease. In particular, we are working towards being able specifically to direct endogenous lung stem cells to generate any lung epithelial cell type.

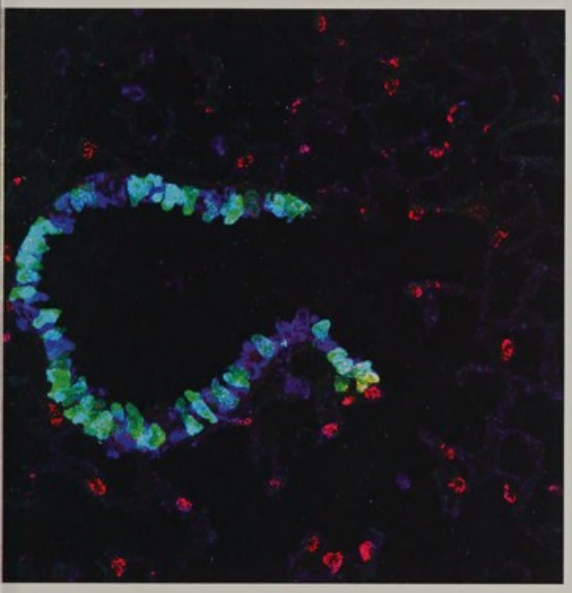
Selected publications:

• **Rawlins EL**, Okubo T, Xue Y, Brass DM, Auten RL, Hasegawa H, Wang F and Hogan BLM (2009) The role of Scgb1a1+ Clara cells in the long-term maintenance and repair of lung airway, but not alveolar, epithelium. **Cell Stem Cell** 4 525-534

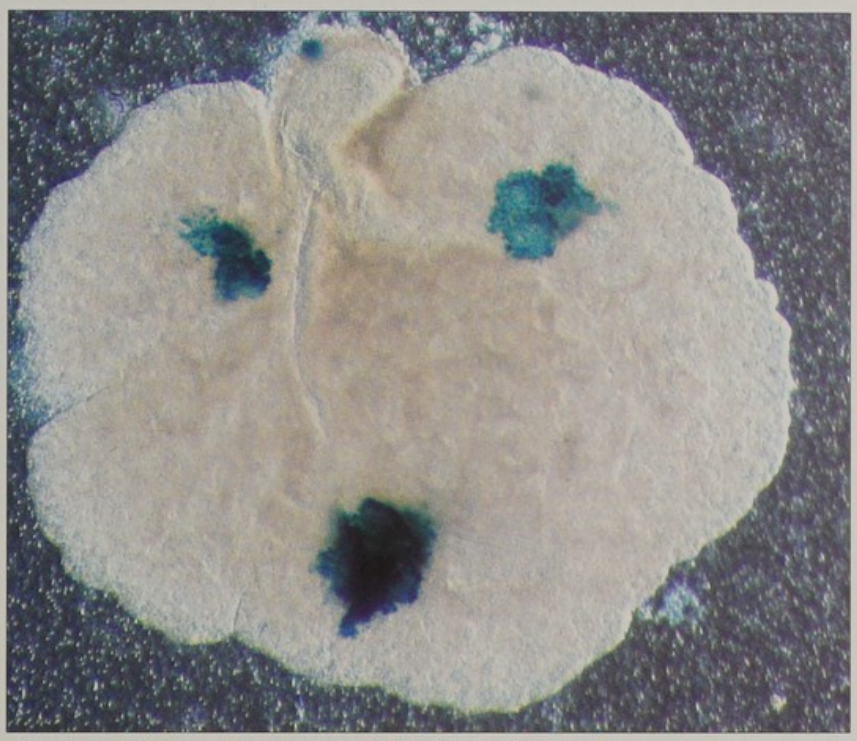
• **Rawlins EL**, Clark CP, Xue Y and Hogan BLM (2009) The Id2 distal tip lung epithelium contains individual multipotent embryonic progenitor cells. **Development** 136 3741-3745

• **Rawlins EL** (2011) The building blocks of mammalian lung development. **Developmental Dynamics** 240 463-76

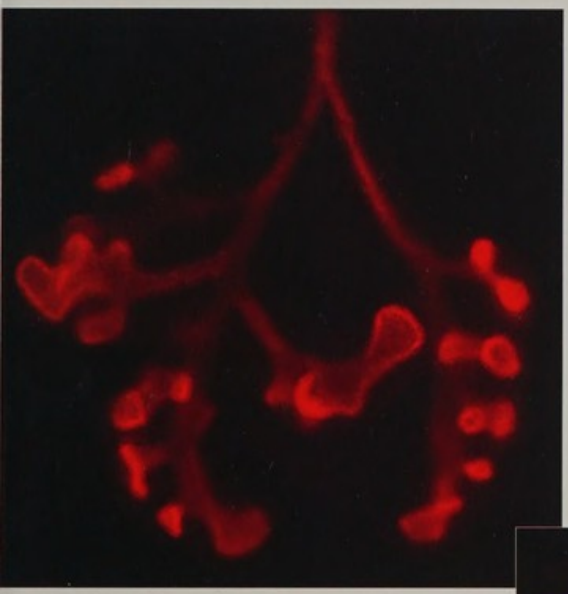
• Onaitis M, D'Amico TA, Clark C, Guinney J, Harpole DH and **Rawlins EL** (2011) A 10-gene progenitor cell signature predicts prognosis in lung adenocarcinoma. **Annals of Thoracic Surgery** 91 1046-50



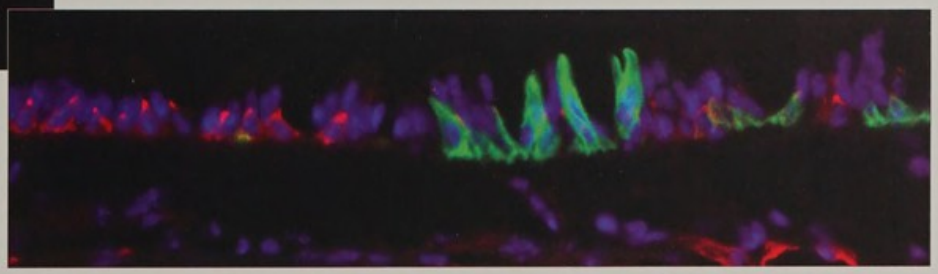
Adult mouse lung section showing lineage-labelled secretory cells (green) in the conducting airways.



Mouse embryonic lung growing in culture. Blue (X-gal staining) shows grafted stem cells which have been incorporated into the lung structure.



Mouse embryonic lung undergoing branching morphogenesis, stained to show the epithelium (E-cadherin).



A clone of mutant tracheal epithelial cells labelled with GFP (green).

Ben Simons

Patterns of stem cell fate in adult and developing tissues

Co-workers: John Biggins (Harvard), Allon Klein (Harvard), Gen Zhang

Theories of tissue maintenance place stem cells at the apex of proliferative hierarchies, possessing the lifetime property of self-renewal. In homeostasis the number of stem cells remains fixed imposing an absolute requirement for fate asymmetry in the daughters of dividing stem cells, such that only half are retained as stem cells. Fate asymmetry can be achieved either by being the invariant result of every division or by being orchestrated from the whole population, where cell fate following stem cell division is specified only up to some probability. These alternative models suggest different mechanisms of fate regulation, yet their identification in most tissues remains elusive.

In recent years, much emphasis has been placed on resolving the extrinsic factors controlling stem cell fate and the spatial organisation associated with the stem cell niche. Guided by the paradigm of invariant asymmetry, many studies have sought to identify factors that provide proliferative control, and ensure stem cell longevity. However, by addressing long-term lineage tracing studies involving several adult tissue types, from interfollicular epidermis and intestine to germ line, we have found that stem cell loss, leading to population asymmetric renewal, is central to homeostasis.

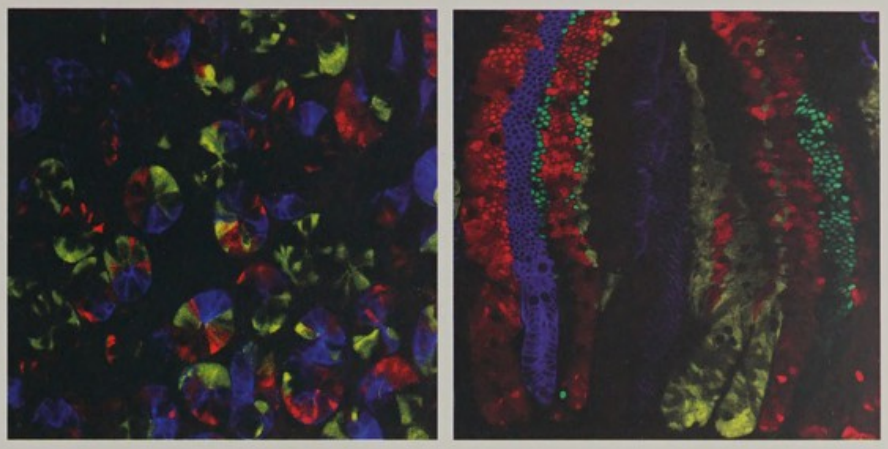
By drawing upon concepts from the statistical physics and mathematical literature, we have shown that tissue homeostasis permits just three classes of stem cell behaviour, discriminated by universal patterns of long-term clonal evolution. As well as achieving a functional classification of tissue stem cell types, this identification provides a general framework that we are using to interpret lineage tracing and mosaic-chimera studies, and to explore mechanisms of dysregulation. Current collaborators include Hans Clevers, Phil Jones, Alfonso Martinez-Arias, Michael Shen, Colin Watts, Doug Winton, and Shosei Yoshida.

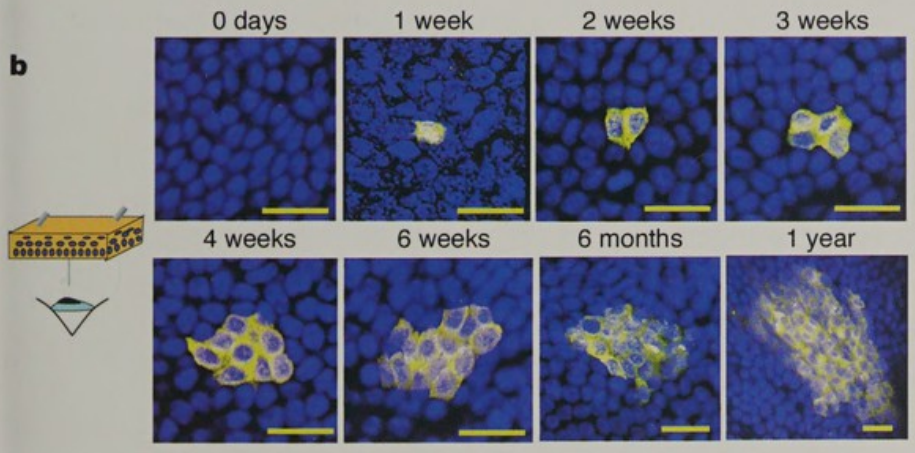
In a separate but related programme of research we are also using these general concepts and lineage tracing methodologies to elucidate patterns of progenitor cell fate in the late stage development of retina and spinal cord. Current collaborators include James Briscoe, Bill Harris, and Michel Cayouette.

Selected publications:

- Snippert H J, van der Flier L G, Sato T, van Es J H, van den Born M, Kroon-Veenboer C, Barker N, Klein A M, van Rheenen J, **Simons BD** and Clevers H (2010) Intestinal crypt homeostasis results from neutral competition between symmetrically dividing Lgr5 stem cells. Cell 143, 134-144
- Lopez-Garcia C, Klein AM, **Simons BD**, and Winton DJ (2010) Intestinal stem cell replacement follows a pattern of neutral drift. Science 330, 822-825
- Klein AM, Nakagawa T, Ichikawa R, Yoshida S, and **Simons BD** (2010) Mouse germ line stem cells undergo rapid and stochastic turnover. Cell Stem Cell 7, 214-224
- Klein AM, Brash DE, Jones PH, and **Simons BD** (2010) Stochastic fate of p53-mutant epidermal progenitor cells is tilted toward proliferation by UV B during preneoplasia. Proceedings of the National Academy of Sciences 107, 270-275
- Clayton E, Doupe DP, Klein AM, Winton D, **Simons BD**, and Jones PH (2007) A single type of progenitor cell maintains the epidermis. Nature 446, 185-189

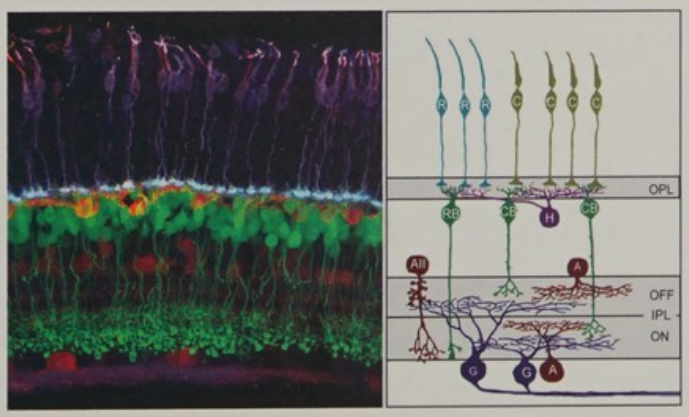
Studies of clonal fate using a multi-colour inducible genetic labelling system provide a vivid demonstration of neutral drift dynamics and the progession towards monoclonality in crypt. The left-hand image shows a section through the base of the crypt showing the clonal progeny of the stem/paneth cell compartment at 7 days post-induction. The right-hand image shows the migration streams of differentiated cells moving up (fully-clonal crypts) and onto villi.





The confocal sections through the basal layer of interfollicular epidermis show the clonal progression of a set of progenitor cells induced at a sequence of timepoints. The data show the continual expansion of clones from an ever-diminishing clone population. A detailed analysis of the lineage-tracing data show that tissue is maintained by a single progenitor cell population following a pattern of balanced stochastic fate in which stem cell loss is compensated by self-renewal.

Lineage-tracing studies show that mechanisms of stochastic stem cell fate play a central role in the homeostasis of adult tissues. However, it remains unclear whether such patterns of fate play a role in the development of tissue. Currently, we are working with experimentalists to resolve the pattern of progenitor cell fate in retina, where retinal precursors must coordinate to give rise to multiple differentiated cell types.



Daniel St Johnston

Cell polarity, the cytoskeleton and mRNA localisation

Co-workers: Rebecca Bastock, Dan Bergstralh, Hélène Doerflinger, Weronika Fic, Alejandra Gardiol, Timm Haack, Jackie Hall, Holly Lovegrove, Ni Lowe, Dmitry Nashchekin, Ross Nieuwburg, Artur Ribiero Fernandes, Aram Sayadian, Vanessa Stefanak, Vitor Trovisco, Tongtong Zhao

Cell polarity is essential both for cell function and for several key developmental processes, such as cell migration, axis determination and asymmetric cell division, whereas loss of polarity is a critical step in the formation of tumours. We use *Drosophila* and mammalian tissue culture cells to analyse how polarity is established, taking a combination of cell-biological, genetic and molecular approaches.

Much of our work focuses on how epithelial cells become polarised along their apical-basal axis, using the follicle cells as a typical secretory epithelium and the adult midgut as model absorptive epithelium. We have recently discovered that the tumour suppressor, LKB1, and the energy sensor, AMPK, are required for epithelial polarity under conditions of energetic stress, revealing the existence of a distinct low energy polarity pathway. We have identified several other components of this pathway in *Drosophila* and mammals, all of which have been implicated in cancer. We are currently analysing the functions of these factors and are performing genetic screens for new genes required for epithelial polarity under either high or low energy conditions.

In parallel, we are examining how the *Drosophila* oocyte is polarised, since the localisation of *bicoid* and *oskar* mRNAs to opposite ends of this very large cell defines the anterior-posterior axis of the embryo. We are using proteomic and biochemical approaches to elucidate how conserved polarity proteins regulate the organisation of the microtubule cytoskeleton in the oocyte, and we are investigating the mechanisms of mRNA transport by making time-lapse films of moving mRNA particles in wildtype and mutant oocytes. In addition, we are performing genetic screens for mutants that affect the localisations of *bicoid* and *oskar* mRNAs, and are analysing the novel polarity and mRNA localisation factors that these identify.

Selected publications:

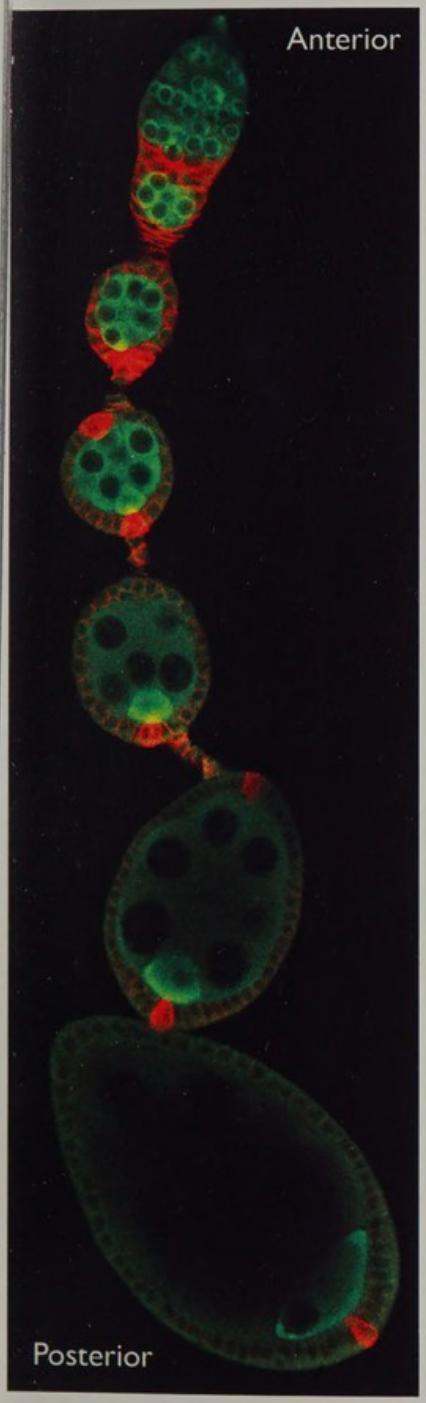
• Doerflinger H, Vogt N, Torres IL, Mirouse V, Koch I, Nusslein-Volhard C and **St Johnston D** (2010) Bazooka is required for polarisation of the *Drosophila* anterior-posterior axis. **Development** 137, 1765-73

• Morais-de-Sa E, Mirouse V and **St Johnston D** (2010) aPKC phosphorylation of Bazooka defines the apical/later border in *Drosophila* epithelial cells. **Cell** 141, 509-23

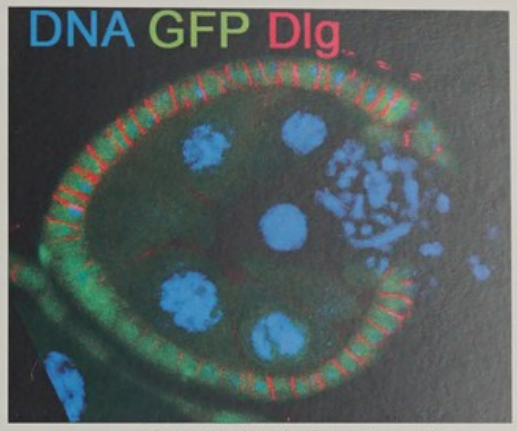
• **St Johnston D** and **Ahringer J** (2010) Cell polarity in eggs and epithelia: parallels and diversity. **Cell** 141, 757-774

• Mirouse V, Christoforou CP, Fritsch C, **St Johnston D** an Ray R (2009) Dystroglycan and Perlecan provide a basal cue that is required for epithelial polarity during energetic stress. **Dev Cell** 16, 83-92

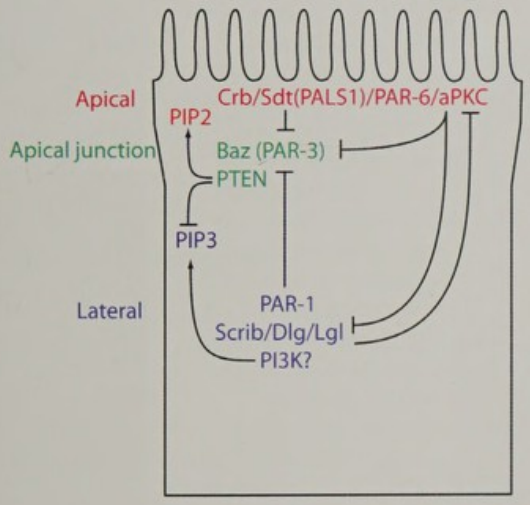
• Zimaynin VL, Belaya K, Pecreaux J, Gilchrist MJ, Clark A, Davis I and **St Johnston D** (2008) *In vivo* imaging of *oskar* mRNA transport reveals the mechanism of posterior localization. **Cell** 134, 843-853



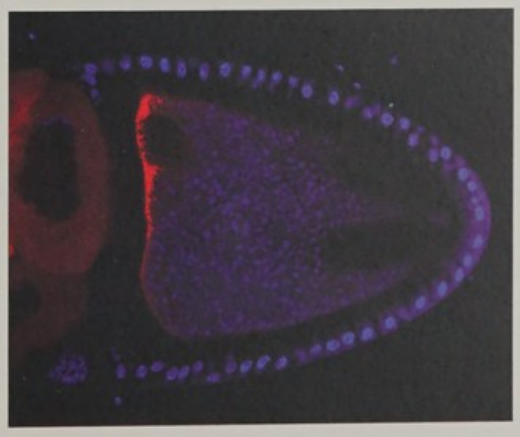
A Drosophila ovariole containing a series of germline cysts that progress through oogenesis as they move posteriorly. The cysts are born at the anterior of the ovariole, and become surrounded by somatic follicle cells (red, FasIII). Each cyst contains 16 germ cells, one of which becomes the oocyte and accumulates higher levels of BicD protein (green).



Removal of the AMP-dependent protein kinase from clones of follicle cells (marked by the absence of GFP; green) causes the cells to lose their polarity and over-proliferate, resulting in small tumours.



A model showing the polarity factors that mark different cortical domains in epithelial cells and the inhibitory interactions between them.

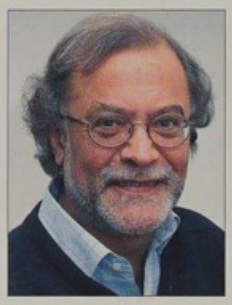


A stage 10 egg chamber expressing a marker for the microtubule minus ends fused to Cherry fluorescent protein (red), counterstained for DNA (blue). The minus ends of the microtubules are anchored to the anterior cortex of the oocyte and direct the localisation of bicoid mRNA.

Azim Surani

Principles and programming of the mammalian germ line

Co-workers: Delphine Cougot, Lynn Froggett, Astrid Gillich, Nils Grabole, Ufuk Gunesdogan, Jamie Hackett, Naoko Irie, Shinseog Kim, Caroline Lee, Harry Leitch, Erna Magnusdottir, Kazuhiro Murakami, Roopsha Sengupta, Qin Si, Julia Tischler, Katarzyna Wilczynska, Jan Zylicz



The primary objective of our research is to elucidate the mechanism of primordial germ cell (PGC) specification, and to investigate the mechanism of extensive epigenetic reprogramming in early germ cells, and by the maternally inherited factors in oocytes. Building on our previous work on germ cell determinants, we aim to resolve comprehensively the molecular foundations of specification of the mammalian germ cell lineage. Specification of PGCs is accompanied by the repression of the somatic programme, and epigenetic modifications that erase the epigenetic memory of their trajectory towards the somatic fate, while restoring an underlying pluripotency. Whereas a repressive complex maintains unipotency of germ cells, dedifferentiation of unipotent PGCs to pluripotent stem cells *in vitro* is accompanied by the reversal of the PGC specification process. Early germ cells also exhibit unprecedented epigenetic reprogramming, genome-wide DNA demethylation and chromatin remodelling, which are essential towards the establishment of totipotency. These events together with the maternal inheritances of genetic and epigenetic regulators in oocyte are critical towards the establishment of the pluripotent state. We are gathering insight into the mechanisms involved, and continuing to identify the key factors that are crucial at these times. We are interested in exploiting the knowledge gained from studies on germ cells by creating *in vitro* models for induced epigenetic reprogramming, and using these models towards attempts at rejuvenation of somatic cells.

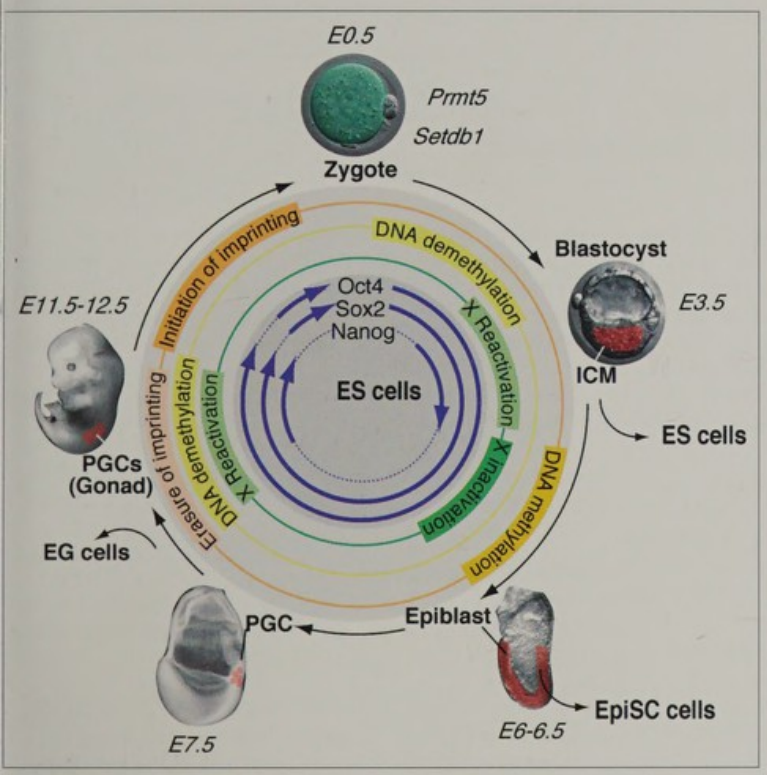
Selected publications:

• **Surani MA** and Hajkova P (2010) Epigenetic reprogramming of mouse germ cells towards totipotency. **Cold Spring Harbor Symposium on Nuclear Organisation and Function**, Volume LXXV

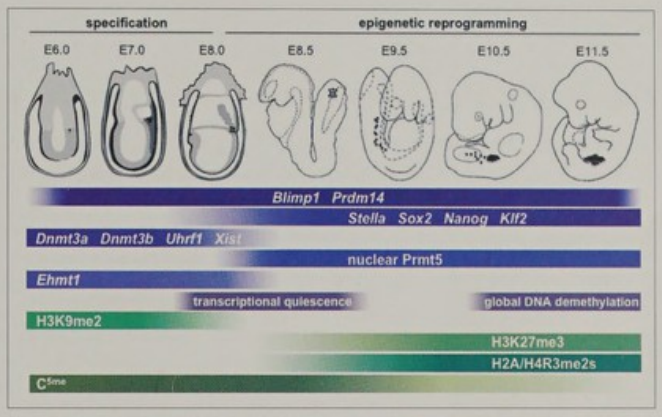
• Hajkova P, Jeffries SJ, Lee C, Miller N, **Jackson SP**, **Surani MA** (2010) Genome-wide reprogramming in the mouse germ line entails the base excision repair pathway **Science** 329, 78-82

• Tang F, Barbacioru C, Bao S, Lee C, Nordman E, Wang X, Lao K, **Surani MA** (2010) Tracing the derivation of embryonic stem cells from the inner cell mass by single cell RNA-Seq analysis. **Cell Stem Cell** 6, 468-478

• Bao S, Tang F, Li X, Hayashi K, Gillich A, Lao K, **Surani MA** (2009) Epigenetic reversion of postimplantation epiblast to pluripotent embryonic stem cells. **Nature** 461, 1292-1295



Mouse germ line cycle with the origin of primordial germ cells and pluripotent stem cells. PGC specification is accompanied by unprecedented genome-wide epigenetic program, including DNA demethylation and chromatin modifications. Maternal inheritance of epigenetic modifiers in the zygote is critical for the establishment of the pluripotent state



Overview of epigenetic reprogramming in early germ cells following PGC specification.

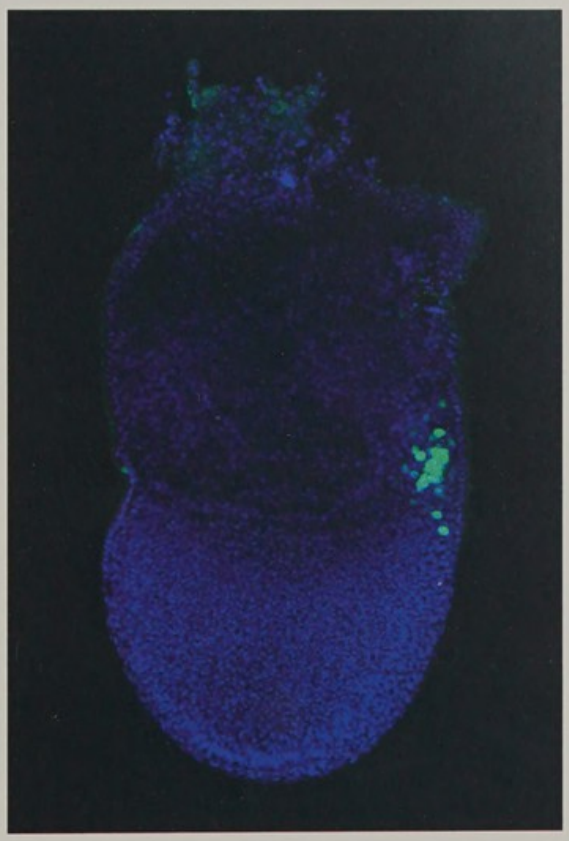
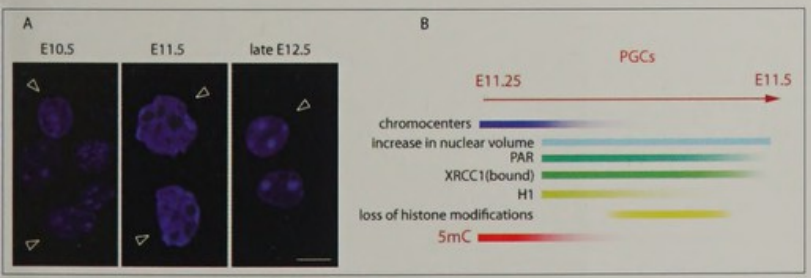


Figure 2. Mouse E7.5 embryo with founder PGCs detected by Stella-GFP reporter Surani, 2010)



A) Changes in nuclear morphology and loss of chromocenteres in gonadal PGCs.
B) Genome-wide DNA demethylation is accompanied by base excision repair.

Philip Zegerman

The regulation of DNA replication initiation in eukaryotes

Co-workers: Davide Mantiero, Vincent Gaggioli, Oleg Kovalevskiy, Christine Hänni, Barbara Schöpf

To successfully pass on its genetic information, every cell must make a perfect duplicate of the genome in every cell cycle. Failure to copy every chromosome faithfully leads to genomic instability, which is the cause of cancer. As a result, replication initiation is strictly regulated, both within the normal cell cycle and after DNA damage. We are interested in how this regulation of DNA replication is achieved in eukaryotes during the cell cycle and when replication forks stall.

Unlike prokaryotes, eukaryotes replicate their genomes from multiple origins. This has the advantage of facilitating the evolution of much larger and more complex genomes, but it does create a problem: If there are multiple origins in the genome, how is origin firing coordinated to make sure that no origin fires more than once?

The assembly of the eukaryotic replication apparatus at origins is tightly regulated in two critical steps. The first step, pre-replicative complex (pre-RC) formation, involves the loading of the replicative helicase Mcm2-7 in an inactive form at origins. This complex can only form in G1 phase of the cell cycle when the APC/C is active and CDK activity is low. This is because CDKs and other APC/C targets such as Geminin are potent inhibitors of pre-RC formation. Once cells enter S-phase, the APC/C is inactivated, CDK activity (and also Geminin) rises and any further pre-RC formation is blocked.

In addition to its role as an inhibitor of pre-RC formation, CDK, together with a second kinase - DDK (Cdc7/Dbf4), are essential for the second step in replication initiation, which involves the activation of the Mcm2-7 helicase and the recruitment of DNA polymerases to origins. We have previously shown that CDK phosphorylates the two essential initiation factors Sld2 and Sld3, which in turn allows binding to another essential initiation factor called Dpb11. How CDK phosphorylation of these targets facilitates replication initiation is not known, but the transient association of these factors at origins has been termed the pre-initiation complex (pre-IC). Since CDK activity both inhibits pre-RC formation and is essential to initiate replication, this produces a switch that only allows replication initiation in S-phase.

Our research is focused on the pre-initiation complex step in the replication reaction. This step is the key CDK regulatory step, but the function of this intermediate is not known. Furthermore, the pre-IC also integrates information from other kinases, such as the DNA damage checkpoint and may be responsible for regulating how efficiently and when an origin fires during S-phase. Much of our understanding of the pre-IC in eukaryotes comes from studies in budding yeast, but how replication initiation is regulated in other eukaryotes is largely unknown. Our aim is to take advantage of the expertise in the wide variety of organisms within the institute and extend these budding yeast studies to the nematode *C elegans* and to mammalian cells.

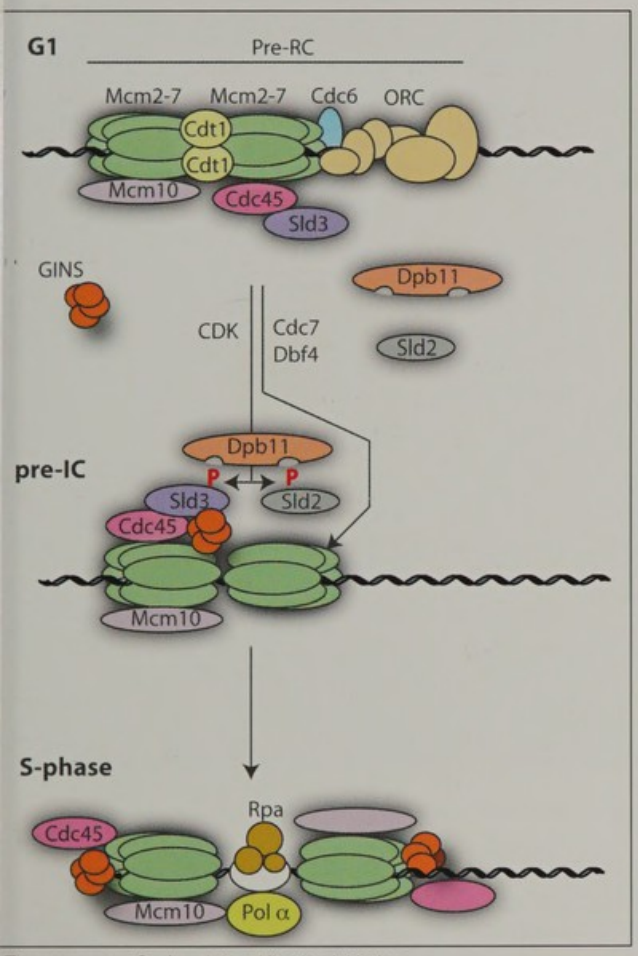
Selected publications:

• Mantiero D, Mackenzie A, Donaldson A and **Zegerman P** (2011) Limiting factors execute the temporal programme of origin firing in budding yeast. **EMBO J** 23, 4805-4814

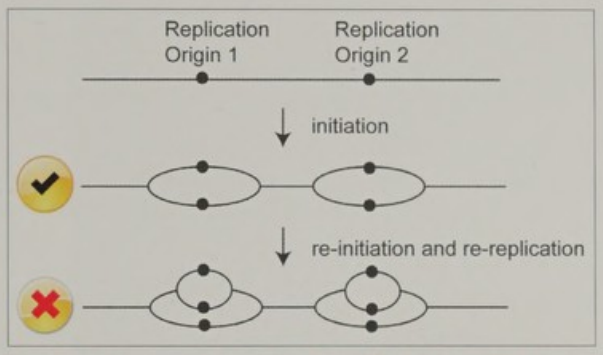
• Walton-Pagliuca F, Collins M, **Zegerman P**, Choudhary J and **Pines J** (2011) Quantitative proteomics reveals the basis for the biochemical specificity of the cell cycle machinery. **Mol Cell** 43, 406-417

• **Zegerman P** and Diffley JF (2010) Checkpoint dependent inhibition of DNA replication initiation via phosphorylation of Sld3 and Dbf4. **Nature** 467, 474-478

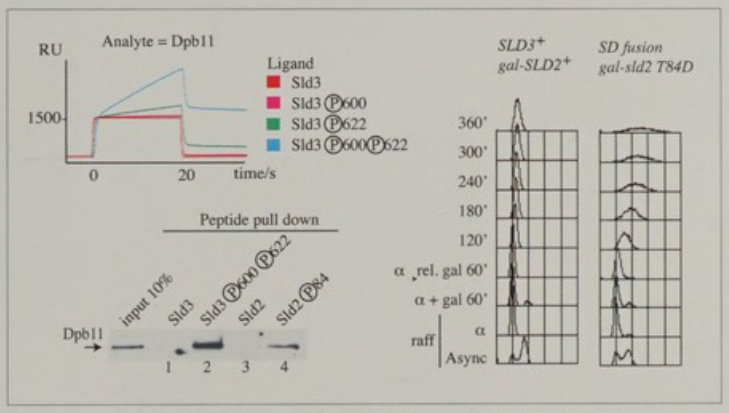
• **Zegerman P** and Diffley JF (2007) Phosphorylation of Sld2 and Sld3 by cyclin-dependent kinases promotes DNA replication in budding yeast. **Nature** 445, 281-285



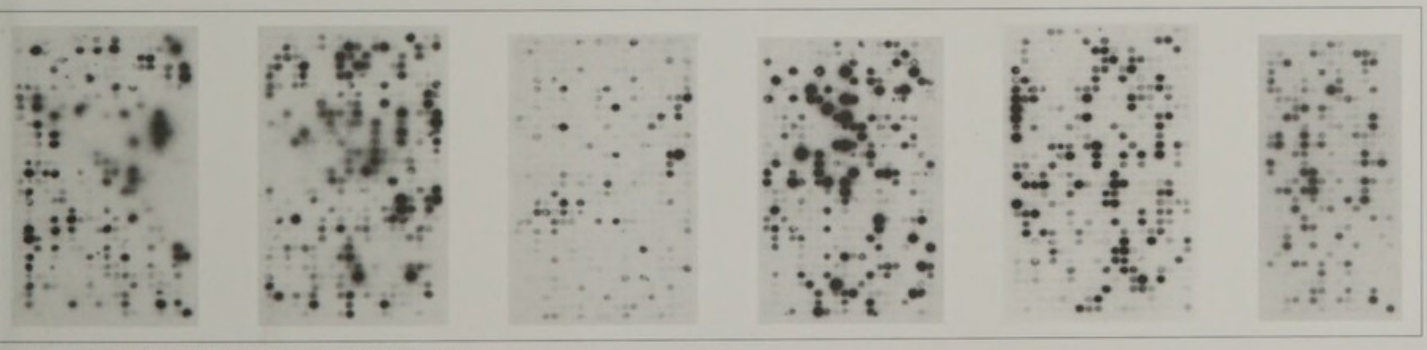
The sequence of eukaryotic replication initiation



Replication initiation must be strictly controlled to occur once, and only once, in every cell cycle.



Interactions between Dpb11 and phospho-Sld2/Sld3 in vitro (left panel) are confirmed to be essential for replication initiation in vivo (right panel).



Phospho-peptide array analysis of replication initiation factors.

Magdalena Zernicka-Goetz

Regulation and dynamics of cell fate transitions and morphogenesis during development of the early mouse embryo

Co-workers: Anna Ajduk, Stoyana Alexandrova, Paula Almeida Coelho, Florencia Barrios, Helen Bolton, John Crang, Sarah Graham, Agnieszka Jedrusik, Manuela Monti, Maryna Panamarova, Maria Skamagki, Clara Slade, Bernhard Strauss, Krzysztof Wicher, Chuen Yan Leung

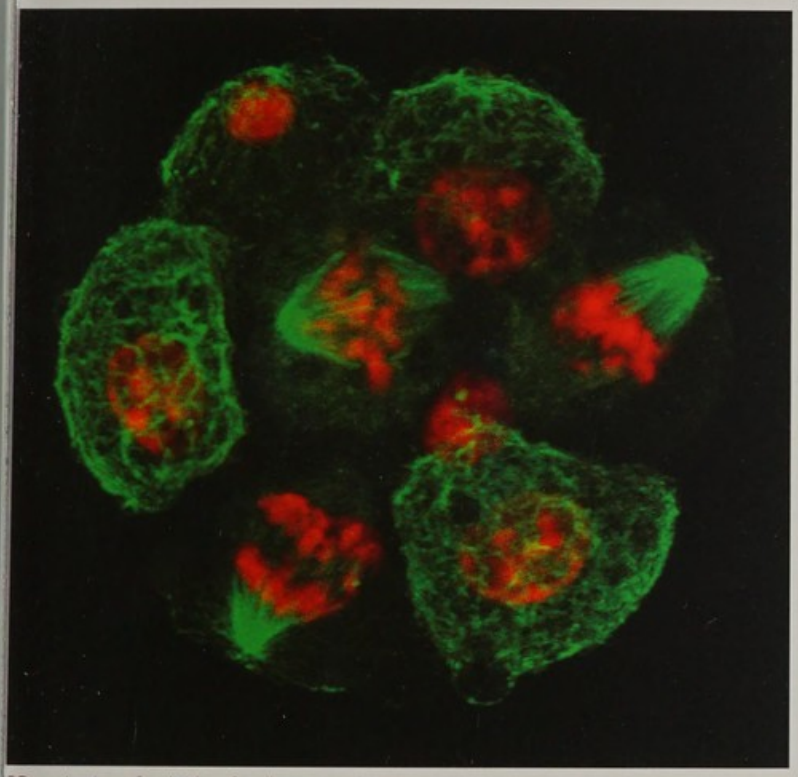
Setting aside the pluripotent cells that give rise to the future body from the extra-embryonic tissues is key to early mammalian development. It requires that some blastomeres divide asymmetrically to direct cells to the inside of the embryo, where they retain pluripotency. Is this regulated or does it occur at random and then what makes inside and outside cells different from each other? To address these questions, we have traced the origins and followed the division orientations and fates of every single cell in three-dimensional space throughout the first four days of development of mouse embryos. This revealed a spatial and temporal pattern of symmetric versus asymmetric cell divisions that depends on a cell's history and defines the orientation of the embryonic-abembryonic axis of the embryo. Our findings suggest that the first cell fate decision of the mouse embryo is a result of the generation of heterogeneity among blastomeres and this affects whether blastomeres undertake symmetric or asymmetric divisions. Our recent studies show that second fate decision that leads to the formation of the second extra-embryonic tissue is bound up with the later asymmetric divisions. Currently we are addressing:

- The role of epigenetic modifications at very early stages, specifically histone H3 arginine 26 methylation that we found affects the extent of cell pluripotency.
- The cellular mechanisms regulating asymmetric divisions.
- The contributions of cell polarity and cell position in determining specific patterns of gene expression in both fate decisions.
- How the first signalling centres arise in the two extra-embryonic tissues and function immediately after implantation.

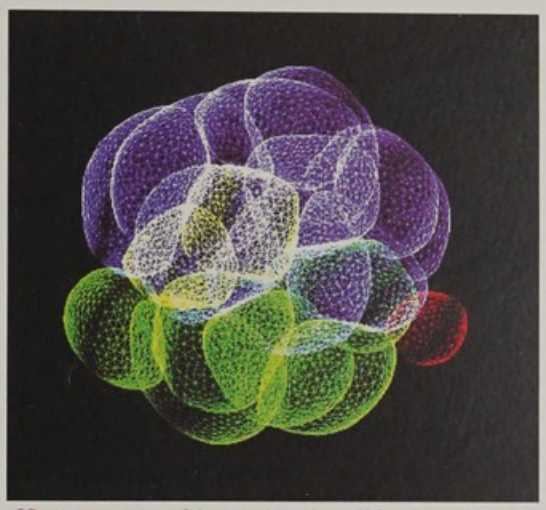
To address these questions we combine methods of classical experimental embryology with modern 4D time-lapse microscopy and molecular cell biology techniques that we have previously developed or optimised in the lab.

Selected publications:

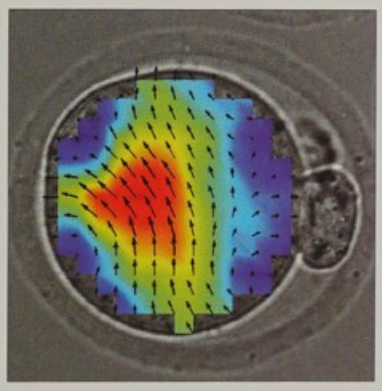
- Ajduk A, Ilozue T, Windsor S, Yu Y, Seres KB, Bomphrey RJ, Tom BD, Swann K, Thomas A, Graham C and **Zernicka-Goetz M** (2011) Rhythmic actomyosin-driven contractions induced by sperm entry predict mammalian embryo viability **Nature Communications** 2, Article number: 417 doi:10.1038/ncomms1424
- Morris SA, Teo RT, Li H, Robson P, Glover DM, and **Zernicka-Goetz M** (2010) Origin and formation of the first two distinct cell types of the inner cell mass in the mouse embryo. **Proc Natl Acad Sci USA** 6;107(14):6364-9
- **Zernicka-Goetz M**, Morris S and Bruce A (2009) Making a firm decision: layers of regulation in early mouse embryo. **Nature Rev Genet** 10, 467-77
- Jedrusik A, Parfitt DE, Guo G, Skamagki M, Grabarek JB, Johnson MH, Robson P and **Zernicka-Goetz M** (2008) Role of Cdx2 and cell polarity in cell allocation and specification of trophectoderm and inner cell mass in the mouse embryo. **Genes Dev** 22, 2692-706



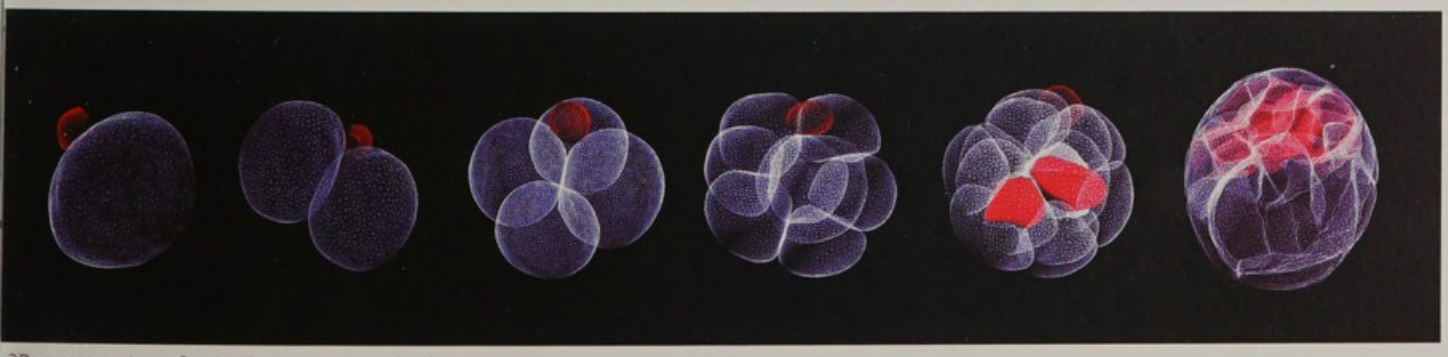
3D projection of a dividing 8 cell stage embryo (DNA, in red and α-tubulin, in green).



3D reconstruction of the mouse embryo (16-cell stage).



The cytoplasmic flows in a fertilised mouse egg



3D reconstructions of preimplantation mouse development.

CATEGORIES OF APPOINTMENT

SENIOR GROUP LEADER
Professor, Reader or Director of Research

GROUP LEADER
5-year grant-funded appointment (maximum 10 years)

CAREER DEVELOPMENT FELLOW
4-year grant-funded appointment

INDEPENDENT SENIOR RESEARCH ASSOCIATE
3-year grant-funded appointment within individual groups

RESEARCH ASSOCIATE/FELLOW
Postdoctoral Fellow within individual groups, appointed by group leader

RESEARCH ASSISTANT
Postgraduate within individual groups, mainly grant-funded

GRADUATE STUDENT
3 or 4 year studentship within individual groups, mainly grant-funded

RESEARCH TECHNICIAN
Within individual groups, mainly grant-funded

LABORATORY ASSISTANT / TECHNICIAN
Within individual groups or part of core support, grant-funded

ITALICS: LEAVERS DURING THE LAST YEAR

POSTGRADUATE OPPORTUNITIES

As part of the University of Cambridge, the Institute welcomes enquiries from prospective graduate students. We have a thriving population of graduates who contribute greatly, not only to the stimulating research environment, but also to the life of the Institute as a whole. Additionally, graduates become members of the biological or medical sciences department to which their group is affiliated. Graduate studentships are supported mainly by the Wellcome Trust or Cancer Research UK but additional sponsorship may be solicited from a variety of sources, including government research councils. Applicants should write, in the first instance, to the leader of the group they wish to join.

DANIEL ST JOHNSTON PhD FRS FMedSci, Chairman

Wellcome Trust Principal Research Fellow
Professor of Developmental Genetics
Member, European Molecular Biology Organization
Director, Company of Biologists
(Member of the Department of Genetics)

HERVE ALEGOT
Visiting Student from Université Blaise Pascal, Clermont-Ferrand

REBECCA BASTOCK PhD
Wellcome Trust Research Associate

DAN BERGSTRALH PhD
Marie Curie Research Fellow/Wellcome Trust Research Associate

HÉLÈNE DOERFLINGER PhD
Wellcome Trust Research Associate

CELIA FARIA BSc
PhD Student

WERONIKA FIC PhD
Wellcome Trust Research Associate

ALEJANDRA GARDIOL PhD
Wellcome Trust Research Associate

TIMM HAACK BSc
Wellcome Trust PhD Student

JACKIE HALL MSc
Wellcome Trust Senior Research Technician

HOLLY LOVEGROVE MSc
Herchel Smith PhD Student

NICK LOWE PhD
Wellcome Trust Research Associate

DMITRY NASHCHEKIN PhD
Wellcome Trust Research Associate

ROSS NIEUWBURG BSc
PhD Student

JOHANNA REES PhD
Wellcome Trust Research Associate

HANNA REUTER
DAAD Erasmus Student

ANNE SAPIRO
Visiting Student from University of Wisconsin-Madison (SCORE Program)

ARAM SAYADIAN BSc
Wellcome Trust PhD Student

VANESSA STEFANAK BA MA
PA

VITOR TROVISCO PhD
Marie Curie Intra-European Fellow

ANTONIO VEGA RIOJA PhD
FEBS Fellow

LUCY WHEATLEY BSc
Wellcome Trust Research Assistant

TONGTONG ZHAO BSc
PhD Student

JULIE AHRINGER PhD FMedSci

Wellcome Trust Senior Research Fellow
Member, European Molecular Biology Organization
Director of Research in Genetics and Genomics
(Member of the Department of Genetics)

ALEX APPERT PhD
NIH/Wellcome Trust Research Associate

DARYA AUSIANNIKAVA BSc
Darwin Trust PhD Student

RON CHEN PhD
Wellcome Trust Research Associate

MIKE CHESNEY PhD
Wellcome Trust Reseach Associate

YAN DONG MSc
Wellcome Trust Research Assistant

SKY FEUER MPhil
Gates Scholarship Graduate Student

BRUNO FIEVET PhD
Wellcome Trust Research Associate

MORITZ HERRMANN BSc
BBSRC PhD Student

JOSANA RODRIGUEZ PhD
Herchel Smith Research Fellow

MARIANA DEL ROSARIO RUIZ VELASCO LEYVA
Visiting Student from UNAM, Mexico

PRZEMYSLAW STEMPOR MSc
NIH/Wellcome Trust Bioinformatics Research Associate

CHRISTINE TURNER
PA/Secretary

ANNE VIELLE MSc
NIH Research Assistant

EVA ZEISER MSc
Wellcome Trust Research Assistant

ANDREA BRAND PhD FRS FMedSci

Herchel Smith Professor of Molecular Biology
Member, European Molecular Biology Organization
(Member of the Department of Physiology, Development and Neuroscience)

JANINA ANDER BSc
DAAD Visiting Student from University of Heidelberg

ELIZABETH CAYGILL PhD
Herchel Smith Research Fellow

ESTEBAN CONTRERAS SEPULVEDA MPhil
Wellcome Trust PhD Student

MELANIE CRANSTON BA
Wellcome Trust Research Assistant

CATHERINE DAVIDSON BSc
Wellcome Trust Research Associate

DAVID DOUPE PhD
Sidney Sussex College Junior Research Fellow

BORIS EGGER PhD
Wellcome Trust Research Associate

JACK ETHEREDGE BS
Janelia Farm/Cambridge University PhD Student

KATRINA GOLD MPhil
Wellcome Trust PhD Student

HARRY HAN
CD Broad Rice Exchange Fellow

CLARE HOWARD BSc
Gates Scholarship MPhil Student

JUN LIU BA
Dr Herchel Smith Graduate Fellow

BARRET PFEIFFER BS MS
Janelia Farm/Cambridge University PhD Student

TONY SOUTHALL PhD
Wellcome Trust Research Associate

PAULINE SPÉDER PhD
Sir Henry Wellcome Postdoctoral Fellow

ALYSON THOMPSON BSc
MRC PhD Student

CHRISTINE TURNER
PA/Secretary

PAO-SHU (PAUL) WU MA MD
Cambridge Overseas Trust PhD Student

NICK BROWN PhD

Reader in Cell Biology
Member, European Molecular Biology Organization
(Member of the Department of Physiology, Development and Neuroscience)

NATALIA BULGAKOVA PhD
HFSP Research Associate

JONATHAN FRIEDLANDER MA
Gates Scholarship and BBSRC PhD Student

ANNABEL GRIFFITHS BA
MRC PhD Student

SVEN HUELSMANN PhD
Wellcome Trust Research Associate

ELEANOR HULLIS
Vacation Student

YOSHIKO INOUE PhD
Wellcome Trust Research Associate

BENJAMIN KLAPHOLZ PhD
Wellcome Trust Research Associate

MATT NEWTON
Volunteer Researcher

JOHN OVERTON HNC
Wellcome Trust Chief Research Technician

PEERAPAT THONGNUEK
MRes in Regenerative Medicine Thai Government PhD Student

JUTTA WELLMANN MPhil
Herchel Smith and BBSRC PhD Student

JARI YLANNE PhD
Sabbatical Visitor from the University of Jyväskylä, Finland

JOHN GURDON Kt DPhil DSc FRS

Distinguished Group Leader
Foreign Associate, US National Academy of Sciences
Foreign Associate, US National Academy of Sciences Institute of Medicine
Foreign Associate, French National Academy of Sciences
Member, European Molecular Biology Organization
Member, Academia Europaea
Honorary Member of American Anatomical Society
Honorary Member of Anatomical Society of Great Britain
Chairman, Company of Biologists (up to mid 2011)
Honorary Fellow UK Academy of Medical Sciences
(Member of the Department of Zoology)

DILLY BRADFORD
PA/Secretary

NIGEL GARRETT MIBiol
Isaac Newton Trust Research Associate

RICHARD HALLEY-STOTT PhD
PhD Student/MRC Research Associate

JO-ANNE JOHNSON MB ChB MRCPCH
Wellcome Trust Clinical Research Fellow

JEROME JULLIEN PhD
Wellcome Trust Research Associate

KEI MIYAMOTO PhD
Japan Society for the Promotion of Science Research Fellow

PATRICK NARBONNE PhD
HSFP Research Fellow

VINCENT PASQUE MPhil
PhD Student

MARTA TEPEREK-TKACZ MSc
Wellcome Trust PhD Student

STAN WANG BS
NIH/Gates MD-PhD Student

SENIOR GROUP LEADERS

STEVE JACKSON PhD FRS FMedSci
Frederick James Quick Professor of Biology
Head of Cancer Research UK Labs
Member, European Molecular Biology Organization
(Member of the Department of Biochemistry)

LINDA BASKCOMB MSc
Cancer Research UK Chief Research Laboratory Technician

RIMMA BELOTSERKOVSKAYA PhD
Cancer Research UK Research Associate

MELANIE BLASIUS PhD
EU Research Associate

INGER BRANDSMA BSc
Visiting MSc Student from Utrecht University

SEBASTIEN BRITTON PhD
EMBO Research Fellow

JESSICA BROWN MB BChir
Wellcome Trust Clinical Fellow/PhD Student

JULIA COATES MA
Cancer Research UK Research Assistant

KATE DRY PhD
Cancer Research UK Information Specialist

JOSEP FORMENT PhD
Cancer Research UK Research Associate

YARON GALANTY PhD
ERC Senior Research Associate

MARCOS GALLEGO LLORENTE
Wellcome Trust Biomedical Vacation Student

ILARIA GUERINI PhD
EU Research Associate

JEANINE HARRIGAN PhD
Cancer Research UK Research Associate

XAVIER JACQ PhD
Research Associate

LOUISE JONES BSc
Research Assistant

KAMILA JOZWIK BSc
Graduate Student (part funded by the Corbridge Trust)

ABDERRAHMANE KAIDI PhD
Herchel Smith Research Fellow

CHARLOTTE KNIGHTS BSc
Research Assistant

DELPHINE LARRIEU PhD
Cancer Research UK Research Associate

CARLOS LE SAGE PhD
EMBO Research Fellow

NATALIA LUKASHCHUK PhD
Cancer Research UK Research Associate

KYLE MILLER PhD
Wellcome Trust Research Associate

RYOTARO NISHI PhD
Sankyo Foundation of Life Science Research Fellow

TOBIAS OELSCHLÄGEL PhD
Cancer Research UK Research Associate

HELEN REED
PA/Secretary

MAXIE ROCKSTROH
Visiting Graduate Student from the Helmholtz Centre for Environmental Research in Leipzig

CHRISTINE SCHMIDT PhD
FEBS Research Fellow

MATYLDA SCZANIECKA-CLIFT PhD
ERC Research Associate

LISA SMITH PhD
Research Assistant

NEHA THAKKAR MSc
Cancer Research UK Senior Research Laboratory Technician

JORRIT TJEERTES PhD
PhD Student/Research Associate

JON TRAVERS PhD
Wellcome Trust Research Associate

PAUL WIJNHOVEN BSc
Cancer Research UK Research Assistant/MPhil Student

TONY KOUZARIDES PhD FMedSci
Deputy Director
Royal Society Napier Professor
Member, European Molecular Biology Organization
(Member of the Department of Pathology)

HATICE AKARSU PhD
EU Research Associate

PAULO AMARAL PhD
Royal Society Newton International Fellow

ANDREW BANNISTER PhD
Cancer Research UK Senior Research Associate

ISAIA BARBIERI BSc
Visiting Graduate Student from the University of Turin

TILL BARTKE PhD
Cancer Research UK Research Associate

GONÇALO CASTELO-BRANCO PhD
Marie Curie Research Fellow

MARIA CHRISTOPHOROU PhD
Cancer Research UK Research Associate

ALISTAIR COOK GIBiol
EU Chief Research Technician

MARK DAWSON MBBS (Hons) BMEDSci FRACP FRCPA PhD
Wellcome-Beit Intermediate Clinical Fellow

SRI LESTARI MSc
Cancer Research UK Senior Research Laboratory Technician

NIKKI PARSONS BA
PA/Secretary

SAM ROBSON PhD
ERC Research Associate (Bioinformatics)

HELENA SANTOS ROSA PhD
Cancer Research UK Senior Research Associate

MARC SCHNEIDER PhD
Leopoldina Research Fellow

PETER TESSARZ PhD
EU/Cancer Research UK Research Associate

EMMANUELLE VIRÉ PhD
Wiener-Anspach Foundation/ERC Research Associate

BEATA WYSPIANSKA MSc
BBSRC Case PhD Student

BLERTA XHEMALCE PhD
EU Research Associate

JONATHON PINES PhD FMedSci
Director of Research in Cell Division
Cancer Research UK Senior Research Fellow
Member, European Molecular Biology Organization
(Member of the Department of Zoology)

PHILIPPE COLLIN PhD
BBSRC Research Associate

BARBARA DI FIORE PhD
Cancer Research UK Research Associate

CHIARA GALLONI
Visiting Researcher

ANJA HAGTING PhD
Cancer Research UK Research Associate

DAISUKE IZAWA PhD
AICR/MRC Research Associate

MARK JACKMAN PhD
Cancer Research UK Research Associate

AGATA LICHAWSKA MSc
Herchel Smith PhD Student

JÖRG MANSFELD PhD
FEBS Research Fellow/MRC Research Associate

PAOLA MARCO BSc
BBSRC CASE PhD Student/MRC Research Assistant/ Associate

TAKAHIRO MATSUSAKA PhD
Cancer Research UK Research Associate

OXANA NASHCHEKINA MSc
Cancer Research UK Chief Research Technician

EMILIE HAINE BA
PA/Secretary

BERNHARD STRAUSS PhD
MRC Research Associate (joint with Prof Magdalena Zernicka-Goetz)

ELIANA TACCONI BA
Volunteer Researcher

SAMUEL WIESER MSc
Liechtenstein Government PhD Student

AZIM SURANI PhD CBE FRS FMedSci

Mary Marshall & Arthur Walton Professor of Physiology and Reproduction
Head of Wellcome Trust Labs
Member, European Molecular Biology Organization
Member Academia Europaea
Associate Fellow, Third World Academy of Sciences
(Member of the Department of Physiology, Development and Neuroscience)

SUZAN BER PhD
Wellcome Trust Research Associate

DELPHINE COUGOT PhD
Wellcome Trust Research Associate

LYNN FROGGETT
PA/Secretary

ASTRID GILLICH MSc
Wellcome Trust PhD Student

NILS GRABOLE BSc
Wellcome Trust PhD Student

UFÜK GÜNESDOGAN PhD
Wellcome Trust Research Associate

JAMIE HACKETT PhD
Wellcome Trust Research Associate

NAOKO IRIE PhD
JSPS/University of Keio Visiting Research Fellow

SHINSEOG KIM PhD
Wellcome Trust Research Associate

CAROLINE LEE ONC
Wellcome Trust Chief Research Technician

HARRY LEITCH MA
MB/PhD Graduate Student

ERNA MAGNÚSDÓTTIR PhD
Marie Curie Research Fellow/Wellcome Trust Research Associate

KAZUHIRO MURAKAMI PhD
Riken/JSPS Visiting Research Fellow

ROOPSHA SENGUPTA PhD
Wellcome Trust Research Associate

QIN SI PhD
Wellcome Trust Research Associate

JULIA TISCHLER PhD
KAUST Research Fellow

KATARZYNA WILCZYNSKA PhD
EMBO Research Fellow

JAN ZYLICZ BSc
Wellcome Trust PhD Student

GROUP LEADERS

RAFAEL CARAZO SALAS PhD
ERC Starting Independent Researcher
(Member of the Department of Genetics)

JUAN FRANCISCO ABENZA MARTINEZ PhD
Ramón Areces Foundation Research Fellow

ANATOLE CHESSEL PhD
HFSP Research Associate

JAMES DODGSON PhD
HFSP Research Associate

MARCO GEYMONAT PhD
ERC Research Associate

VERONIKA GRAML MSc
SystemsX.ch PhD Student

JONATHAN LAWSON BA MSci
Wellcome Trust PhD Student

YUNG-CHIN OEI MSc
Cancer Research UK PhD Student

KATHY OSWALD MA
PA/Secretary

XENIA STUDERA MSc
ERC Research Assistant/PhD Student

THOMAS DOWN PhD
Wellcome Trust Career Development Fellow
(Bioinformatics)
(Member of the Department of Genetics)

PAULINA CHILARSKA BSc
Wellcome Trust PhD Student

KENNETH EVANS PhD
Wellcome Trust Bioinformatics Research Associate

JING SU
Visiting Researcher/PhD student from LMB

JENNIFER GALLOP PhD
Wellcome Trust Career Development Fellow
(Member of the Department of Biochemistry)

LYNN FROGGETT
PA/Secretary

JULIA MASON BSc
Wellcome Trust Research Assistant

RICK LIVESEY MB BChir PhD
Wellcome Trust Group Leader
(University Senior Lecturer in Biochemistry)

JESSICA ALSIÖ BSc
Wellcome Trust PhD Student/MRC Research Assistant/Associate

THERESE ANDERSSON PhD
Wenner-Gren Foundation Research Fellow

JULIET BARROWS BA
PA/Secretary

MARTIN BINDER
Vacation Student

CHIBAWANYE ENE BSc
NIH-Cambridge PhD Student

PETER KIRWAN BSc
Wellcome Trust PhD Student

MOYRA LAWRENCE BSc
WT/MRC Stem Cell Biology Graduate Student (The Livesey Lab is a member of the Cambridge Stem Cell Initiative)

JOÃO PEREIRA BSc
Fundação para a Ciência e Tecnologia PhD Student

STEPHEN SANSOM PhD
Wellcome Trust Research Associate

NATHALIE SAURAT BSc
Woolf Fisher PhD Student

YICHEN SHI BSc
Cambridge Trusts PhD Student

JAMES SMITH BSc
Wellcome Trust/MRC Research Assistant

URUPORN THAMMONGKOL BSc
PhD Student

ANTHONY WALSH PhD
ARUK Research Associate

MASANORI MISHIMA PhD
Cancer Research UK Group Leader
(Member of the Department of Biochemistry)

TIM DAVIES BSc
BBSRC PhD Student

NIMESH JOSEPH PhD
Cancer Research UK Research Associate

KIAN-YONG LEE BSc
Cancer Research UK PhD Student

JULIA MASON BSc
Cancer Research UK Research Assistant

EVA PABLO-HERNANDO PhD
Isaac Newton Trust Research Associate

ERIC MISKA PhD
Cancer Research UK Group Leader
(Member of the Department of Biochemistry)

JAVIER ARMISEN GARRIDO PhD
EU/Cancer Research UK Research Associate

ALYSON ASHE PhD
Herchel Smith Research Fellow

MARLOES BAGIJN MSc
PhD Student

ALEJANDRA CLARK PhD
Cancer Research UK Research Associate

LEONARD GOLDSTEIN PhD
Cancer Research UK Research Associate

ETHAN KAUFMAN BSc
PhD Student

MIRANDA LANDGRAF MA
PA

NIC LEHRBACH PhD
ERC Research Associate

HELEN LIGHTFOOT BSc
Cancer Research UK PhD Student (joint with Dept of Chemistry)

KAI LUDWIG
Visiting Student from University of Wisconsin-Madison (SCORE Program)

NGOC-SUNG LY MLA
ERC Research Assistant

SYLVIANE MOSS PhD
Cancer Research UK Lab Manager

KENNETH MURFITT BSc
Wellcome Trust PhD Student

GRETA PINTACUDA
Scuola Normale Superiore Pisa Visiting Graduate Student

AMIE REGAN
Visiting Student

ALEXANDRA SAPETSCHNIG PhD
Herchel Smith Research Fellow

FUNDA SAR PhD
Cancer Research UK Research Associate

EVA-MARIA WEICK BSc
Herchel Smith/BBSRC PhD Student

JULIE WOOLFORD MPhil
Cancer Research UK PhD Student

EUGENIA PIDDINI PhD

Royal Society Research Fellow
(Member of the Department of Zoology)

ALEXIS BRAUN MSc
PhD Student

MARIA JESUS GOMEZ LAMARCA MSc
Visiting PhD Student from CABD, Seville

MAJA GOSCHORSKA BSc
MPhil Student

GOLNAR KOLAHGAR PhD
Cancer Research UK Research Associate

CAROLINA MENDOZA TOPAZ PhD
Cancer Research UK Research Assistant

SARAH MANSOUR MSc
Visiting MSc Student from Technische Universität, Dresden

KATHY OSWALD MA
PA/Secretary

ENZO POIRIER BSc
Visiting Graduate Student from Ecole Normale Supérieure, Paris

SILVIA VIVARELLI PhD
MRC Research Associate

LAURA WAGSTAFF PhD
MRC Research Associate

EMMA RAWLINS PhD

MRC Research Fellow
(Member of the Department of Pathology)

GAYAN BALASOORIYA MSc
MRC Research Technician/PhD Student

JULIET BARROWS BA
PA/Secretary

CHRISTOPH BUDJAN MSc
Wellcome Trust PhD Student

SIMON GERBER PhD
SNF Research Fellow

USUA LARESGOITI GARAY PhD
Basque Government Visiting Research Fellow

RACHEL SEEAR MPhil
Wellcome Trust Chief Research Laboratory Technician

PHILIP ZEGERMAN PhD

AICR Research Fellow
(Member of the Department of Zoology)

JULIET BARROWS BA
PA/Secretary

VINCENT GAGGIOLI PhD
AICR Research Associate

CHRISTINE HANNI MSc
CCC PhD Student

OLEG KOVALEVSKIY PhD
Cancer Research UK Research Associate

DAVIDE MANTIERO PhD
EMBO Research Fellow

BARBARA SCHÖPF PhD
EMBO Research Fellow

MAGDALENA ZERNICKA-GOETZ PhD

Wellcome Trust Senior Research Fellow
Professor of Developmental Biology
Member, European Molecular Biology Organization
Reader in Developmental Biology
(Member of the Department of Physiology, Development and Neuroscience)

ANNA AJDUK PhD
Wellcome Trust Research Associate

STOYANA ALEXANDROVA BA
MRC PhD Student

PAULA ALMEIDA COELHO PhD
Visiting Academic

SOURIMA B SHIVHARE MSc
Visiting Graduate Student from Oxford

FLORENCIA BARRIOS PhD
Royal Society Newton International Fellow

HELEN BOLTON BSc MB BS MRCOG
Wellcome Trust Clinical Fellow/PhD Student

JOHN CRANG DPhil
PA

SARAH GRAHAM MSc
PhD Student

AGNIESZKA JEDRUSIK PhD
Wellcome Trust Research Associate

CHUEN YAN LEUNG BSc
Graduate Student

MACIEJ MEGLICKI MSc
Lister Vacation Student from University of Warsaw

SAMANTHA MORRIS PhD
Wellcome Trust Research Associate

CLARA SLADE OLIVEIRA MVB
Visiting Graduate Student from FAPESP, Brazil

MARYNA PANAMAROVA BSc
Darwin Trust PhD Student

MATTHIAS ROMAUCH Dr med univ
Visiting Student from University of Graz

BEDRA SHARIF BSc
Gates PhD Student

MARIA SKAMAGKI PhD
Wellcome Trust Research Associate

BERNHARD STRAUSS PhD
MRC Research Associate (joint with Dr J Pines)

MARIA SUCIU
Visiting MSc Student from UCL

ROY (TANG YI) TEO
A PhD Student*

KRZYSZTOF WICHER PhD
Wellcome Trust Research Associate

SABBATICAL VISITORS

BEN SIMONS
Academic Visitor (Professor of Theoretical Condensed Matter Physics at the Cavendish Laboratory)

MARVIN WICKENS PhD
Sabbatical Visitor (Max Perutz Professor of Molecular Biology and Biochemistry, University of Wisconsin-Madison)

ADMINISTRATION

ANN CARTWRIGHT MPhil
Institute Administrator

GEORGE BROWN
Accounts Manager

SUZANNE CAMPBELL BSc
HR/Grants Manager

MAISIE CATTELL
Receptionist

JANE COURSE
Accounts/Admin Assistant

SUE CROYSDALE
Receptionist

DIANE FOSTER
Deputy Administrator

EMILIE HAINE BA
Receptionist

KATHY HILTON DipMgm
CBSG Manager

LYNDA LOCKEY
Office Manager

NIKKI PARSONS BA
Receptionist

JACKIE SIMCOX
Receptionist

COMPUTING

ALASTAIR DOWNIE
Computer Systems Manager

RICHARD BUTLER PhD
Computer Imaging Associate

NICOLA LAWRENCE PhD
Computer Imaging Associate

NIGEL SMITH
Computer Associate

ALEX SOSSICK BSc
Computer Imaging Manager

PETER WILLIAMSON BSc
Computer Associate

BIOINFORMATICS

CHARLES BRADSHAW PhD
Computer Associate (Bioinformatics)

ACCOUNTS/PURCHASING/STORES

IAN FLEMING
Stores/Purchasing Manager

SIMON ALDIS
Purchasing/Accounts Assistant

DAVID COOPER
Stores Technician

RICHARD ETTERIDGE MA
Purchasing/Accounts Assistant

ANDY VINCENT
Stores Technician

MICK WOODROOFE
Purchasing/Accounts Assistant

TECHNICAL SUPPORT

KEITH SAVILL
Senior Technical Officer

RYAN ASBY
NIGEL BARNETT
SOPHIE BROUGHTON
DANIEL DUDMAN
GARY GARNER
RICHARD HARPER
GILLIAN HYNES
SHANE JOHNSON
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ROBERT BRETT
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LISA WRIGHT
DAVID SIMPSON
JO WATSON

COMBINED BUILDING SERVICES GROUP (CBSG)

CLIVE BENNETT
MIGUEL GONÇALVES
STEPHEN SALT
STUART TURNER
KATHERINE BENNETT
ALAN RIX
JAMES SMITH (JT)
PAUL TURRELL

MEDIA/GLASS WASHING

JUANITA BAKER-HAY
Media/Glass Washing Manager

JANIS ABBOTT
LISA BAKER
VINCE DAMS
MARK JOHNS
AGNES ASSELIN LE FOLL
KAZUKO COLLINS
SANDRA HUMAN
TRACY MITCHELL

ZEST CATERING

AMANDA HARRIS
MELISSA PLOWDEN ROBERTS

The following is a list of articles by members of the Institute that were either published or accepted for publication, since the date of publication of the last Annual Report.

1 Ajduk A, Ilozue T, Windsor S, Yu Y, Seres KB, Bomphrey RJ, Tom BD, Swann K, Thomas A, Graham C and **Zernicka-Goetz M** (2011) Rhythmic actomyosin-driven contractions induced by sperm entry predict mammalian embryo viability. Nat Commun 2, 417

2 Akhtar A, Fuchs E, Mitchison T, Shaw RJ, **St Johnston D**, Strasser A, Taylor S, Walczak C and Zerial M (2011) A decade of molecular cell biology: achievements and challenges. Nat Rev Mol Cell Biol 12, 669-674

3 Bannister AJ and **Kouzarides T** (2011) Regulation of chromatin by histone modifications. Cell Res 21, 381-395

4 Bartke T and **Kouzarides T** (2011) Decoding the chromatin modification landscape. Cell Cycle 10, 182

5 Bastock R and **St Johnston D** (2011). Oogenesis: matrix revolutions. Curr Biology 21, R231-R233

6 Belaya K and **St Johnston D** (2011) Using the mRNA-MS2/MS2CP-FP system to study mRNA transport during *Drosophila* oogenesis. Methods Mol Biol 714, 265-283

7 Blasius M, Forment JV, Thakkar N, Wagner SA, Choudhary C and **Jackson SP** (2011) A phospho-proteomic screen identifies substrates of the checkpoint kinase Chk1. Genome Biol 12, R78

8 Bonadies N, Foster SD, Chan WI, Kvinlaug BT, Spensberger D, Dawson MA, Spooncer E, Whetton AD, Bannister AJ, Huntly BJ and Gattgens B (2011) Genome-wide analysis of transcriptional reprogramming in mouse models of acute myeloid leukaemia. PLoS One 6, e16330 [**Kouzarides** Group]

9 Bradshaw CR, Surendranath V, Henschel R, Mueller MS and Habermann BH (2011) HMMerThread: Detecting remote, functional conserved domains in entire genomes by combining relaxed sequence-database searches with fold recognition. PLoS One 6, e17568 [**Core Bioinformatics**]

10 **Brand AH** (2011) Stem cells to synapses: Regulation of self-renewal and differentiation in the nervous system. Developmental Biology 356, 104

11 **Brand AH** and **Livesey FJ** (2011) Neural stem cell biology in vertebrates and invertebrates: more alike than different? Neuron 70, 719-729

12 **Brown NH** (2011) Extracellular matrix in development: insights from mechanisms conserved between invertebrates and vertebrates. Cold Spring Harb Perspect Biol pii: cshperspect.a005082v1

13 Chang CW, Nashchekin D, Wheatley L, Irion U, Dahlgaard K, Montague TG, Hall J and **St Johnston D** (2011) Anterior-posterior axis specification in *Drosophila* oocytes: identification of novel bicoid and oskar mRNA localization factors. Genetics 188, 883-896

14 Chell JM and **Brand AH** (2010) Nutrition-responsive glia control exit of neural stem cells from quiescence. Cell 143, 1161-1173

15 Cheung MS, Down TA, Latorre I and **Ahringer J** (2011) Systematic bias in high-throughput sequencing data and its correction by BEADS. Nucleic Acids Res 39, e103

16 Chu LF, **Surani MA**, Jaenisch R and Zwaka TP (2011) Blimp1 expression predicts embryonic stem cell development *in vitro*. Curr Biology 21, 1759-1765

17 Daley GQ, **Surani MA**, Tanaka E and Plath K (2011) Reprogramming: What's unknown? Cell 145, 811-812

18 Dawson MA, Prinjha RK, Dittmann A, Giotopoulos G, Bantscheff M, Chan WI, Robson SC, Chung CW, Hopf C, Savitski MM, Huthmacher C, Gudgin E, Lugo D, Beinke S, Chapman TD, Roberts EJ, Soden PE, Auger KR, Mirguet O, Doehner K, Delwel R, Burnett AK, Jeffrey P, Drewes G, Lee K, Huntly BJ and **Kouzarides T** (2011) Inhibition of BET recruitment to chromatin as an effective treatment for MLL-fusion leukaemia. Nature 478, 529-533

19 Dawson MA and Bannister AJ (2011) JAK STAT Signaling from basics to disease [In Press] [**Kouzarides** Group]

20 **Down TA**, Piipari M and Hubbard TJ (2011) Dalliance: interactive genome viewing on the web. Bioinformatics 27, 889-890

21 Egger B, Gold KS and **Brand AH** (2011) Regulating the balance between symmetric and asymmetric stem cell division in the developing brain. Fly (Austin) 5, 237-241

22 Félix MA, Ashe A, Piffaretti J, Wu G, Nuez I, Bélicard T, Jiang Y, Zhao G, Franz CJ, Goldstein LD, Sanroman M, **Miska EA** and Wang D (2011) Natural and experimental infection of *Caenorhabditis* nematodes by novel viruses related to nodaviruses. PLoS Biol 9, e1000586

23 Feber A, Wilson GA, Zhang L, Presneau N, Idowu B, **Down TA**, Rakyan VK, Noon LA, Lloyd AC, Stupka E, Schiza V, Teschendorff AE, Schroth GP, Flanagan A and Beck S (2011) Comparative methylome analysis of benign and malignant peripheral nerve sheath tumors. Genome Res 21, 515-524

24 Flott S, Kwon Y, Pigli YZ, Rice PA, Sung P and **Jackson SP** (2011) Regulation of Rad51 function by phosphorylation. EMBO Rep 12, 833-839

25 Forment JV, Blasius M, Guerini I and **Jackson SP** (2011) Structure-specific DNA endonuclease Mus81/Eme1 generates DNA damage caused by Chk1 inactivation. PLoS One 6, e23517

26 Franco M, Seyfried NT, **Brand AH**, Peng JM and Mayor U (2010) A novel strategy to isolate neuronal ubiquitin conjugates reveals a wide role for ubiquitination in synaptogenesis. J Neurogenet 24, 38

27 Franco M, Seyfried NT, **Brand AH**, Peng JM and Mayor U (2011) A novel strategy to isolate ubiquitin conjugates reveals wide role for ubiquitination during neural development. Mol Cell Proteomics 10, M110.002188

28 Giunta S and **Jackson SP** (2011) Give me a break, but not in mitosis: The mitotic DNA damage response marks DNA double-strand breaks with early signaling events. Cell Cycle 10 1215-1221

29 Gu Y, Runyan C, Shoemaker A, **Surani MA** and Wylie C (2011) Membrane-bound steel factor maintains a high local concentration for mouse primordial germ cell motility, and defines the region of their migration. PLoS One 6,e25984

30 Harrigan JA, Belotserkovskaya R, Coates J, Dimitrova DS, Polo SE, Bradshaw CR, Fraser P and **Jackson SP** (2011) Replication stress induces 53BP1-containing OPT domains in G1 cells. J Cell Biol 193, 97-108

31 Izawa D and **Pines J** (2011) How APC/C-Cdc20 changes its substrate specificity in mitosis. Nat Cell Biol 13, 223-233

32 Jullien J and **Gurdon JB** (2011) Reprogramming of gene expression following nuclear transfer to the *Xenopus* oocyte. Biol Aujourdhui 205, 105-110

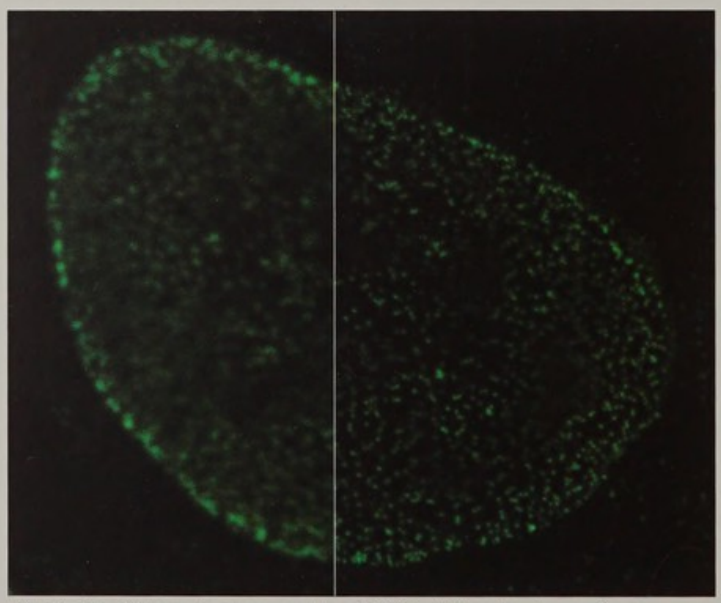
33 Jullien J, Pasque V, Halley-Stott RP, Miyamoto K and **Gurdon JB** (2011) Mechanisms of nuclear reprogramming by eggs and oocytes: A deterministic process? Nature Reviews Molecular Cell Biology 12, 453-459

34 Lehrbach NJ and **Miska EA** (2011) Regulation of pre-miRNA processing. Adv Exp Med Biol 700, 67-75

35 Lightfoot HL, Bugaut A, Armisen J, Lehrbach NJ, **Miska EA** and Balasubramanian S (2011) A LIN28-dependent structural change in pre-let-7g directly inhibits dicer processing. Biochemistry 50, 7514-7521

36 Llobet A, **Gallop JL**, Burden JJE, Camdere G, Chandra P, Vallis Y, Hopkins CR, Lagnado L and McMahon HT (2011) Endophilin drives the fast mode of vesicle retrieval in a ribbon synapse. J Neuroscience 31, 8512-8519

37 Mansfeld J, Collin P, Collins MO, Choudhary JS and **Pines J** (2011) APC15 drives the turnover of MCC-CDC20 to make the spindle assembly checkpoint responsive to kinetochore attachment. Nat Cell Biol 13, 1234-1243



Visualisation of the nuclear pore complex (NPC) in Hela cells using confocal microscopy (left) and with Stimulated Emission Depletion microscopy (STED), right. (Abderrahmane Kaidi, Jackson Group, 2011)

38 Mantiero D, Mackenzie A, Donaldson A and **Zegerman P** (2011) Limiting replication initiation factors execute the temporal programme of origin firing in budding yeast. EMBO J 30, 4805-14

39 Miyamoto K and **Gurdon JB** (2011) Nuclear actin and transcriptional activation. Commun Integr Biol 4 582-583

40 Miyamoto K, Pasque V and **Gurdon JB** (2011) Nuclear actin in transcriptional reprogramming by oocytes: Are actin nucleators key players? Cell Cycle 10 3040-3041

41 Miyamoto K, Pasque V, Jullien J and **Gurdon JB** (2011) Nuclear actin polymerization is required for transcriptional reprogramming of Oct4 by oocytes. Genes and Development 25, 946-958

42 Mladkova N, McHugh A, **Down TA**, Rakyan V, Proby C and Harwood C (2011) Identification of differentially methylated genes in cutaneous squamous cell carcinoma from *Epidermolysis Bullosa* patients and normal population. Journal of Investigative Dermatology 131, S24

43 Morris SA (2011) Cell fate in the early mouse embryo: Sorting out the influence of developmental history on lineage choice. Reprod Biomed Online 22, 521-424 [**Zernicka-Goetz** Group]

44 Morris SA (2011) Reply: Cell fate in the early mouse embryo: sorting out the influence of developmental history on lineage choice. Reprod Biomed Online 22, 528

45 Nanty L, Carbajosa G, Heap GA, Ratnieks F, van Heel DA, **Down TA** and Rakyan V (2011) Comparative methylomics reveals gene-body H3K36me3 in *Drosophila* predicts DNA methylation and CpG landscapes in other invertebrates. Genome Res 21 1841-1850

46 Ng HH and **Surani MA** (2011) The transcriptional and signalling networks of pluripotency. Nat Cell Biol 13, 490-496

47 Onaitis M, D'Amico TA, Clark CP, Guinney J, Harpole DH and **Rawlins EL** (2011) A 10-gene progenitor cell signature predicts poor prognosis in lung *Adenocarcinoma*. Annals of Thoracic Surgery 91, 1046-1050

48 Paez-Gonzalez P, Abdi K, Luciano D, Liu Y, Soriano-Navarro M, **Rawlins EL**, Bennett V, Garcia-Verdugo JM and Kuo CT (2011) Ank3-dependent SVZ niche assembly is required for the continued production of new neurons. Neuron 71, 61-75

49 Pagliuca FW, Collins MO, Lichawska A, **Zegerman P**, Choudhary JS and **Pines J** (2011) Quantitative proteomics reveals the basis for the biochemical specificity of the cell-cycle machinery. Mol Cell 43, 406-417

50 Pasque V, Gillich A, Garrett N and **Gurdon JB** (2011) Histone variant macroH2A confers resistance to nuclear reprogramming. EMBO Journal 30 2373-2387

51 Pasque V, Jullien J, Miyamoto K, Halley-Stott RP and **Gurdon JB** (2011) Epigenetic factors influencing resistance to nuclear reprogramming. Trends Genet 27, 516-525

52 **Pines J** (2011) Cubism and the cell cycle: the many faces of the APC/C. Nat Rev Mol Cell Biol 12, 427-438

53 Polo SE and **Jackson SP** (2011) Dynamics of DNA damage response proteins at DNA breaks: a focus on protein modifications. Genes Dev 25 409-433

54 Poulin GB and **Ahringer J** (2010) The *Caenorhabditis elegans* CDT-2 ubiquitin ligase is required for attenuation of EGFR signalling in vulva precursor cells. BMC Dev Biol 10, 109

55 Qvist P, Huertas P, Jimeno S, Nyegaard M, Hassan MJ, **Jackson SP** and Børglum AD (2011) CtIP mutations cause Seckel and Jawad syndromes. PLoS Genetics 7, e1002310

56 Rakyan VK, Beyan H, **Down TA**, Hawa MI, Maslau S, Aden D, Daunay A, Busato F, Mein CA, Manfras B, Dias KR, Bell CG, Tost J, Boehm BO, Beck S and Leslie RD (2011) Identification of type 1 diabetes-associated DNA methylation variable positions that precede disease diagnosis. PLoS Genetics 7, e1002300

57 Rakyan VK, **Down TA**, Balding DJ and Beck S (2011) Epigenome-wide association studies for common human diseases. Nat Rev Genet 12, 529-541

58 Rees JS, Lowe N, Armean IM, Roote J, Johnson G, Drummond E, Spriggs H, Ryder E, Russell S, **St Johnston D** and Lilley KS (2011) *In vivo* analysis of proteomes and interactomes using Parallel Affinity Capture (iPAC) coupled to mass spectrometry. Mol Cell Proteomics 10, M110.002386

59 Sabino D, **Brown NH** and Basto R (2011) *Drosophila* Ajuba is not an Aurora-A activator but is required to maintain Aurora-A at the centrosome. Journal of Cell Science 124, 1156-1166

60 Simeoni I, Gilchrist MJ, Garrett N, Armisen J and **Gurdon JB** (2011) Widespread transcription in an amphibian oocyte relates to its reprogramming activity on transplanted somatic nuclei. Stem Cells Dev [In Press].

61 Spéder P, Liu J and **Brand AH** (2011) Nutrient control of neural stem cells. Curr Opin Cell Biol [In Press].

62 **St Johnston D** and Sanson B (2011) Epithelial polarity and morphogenesis. Curr Opin Cell Biol 23, 540-546

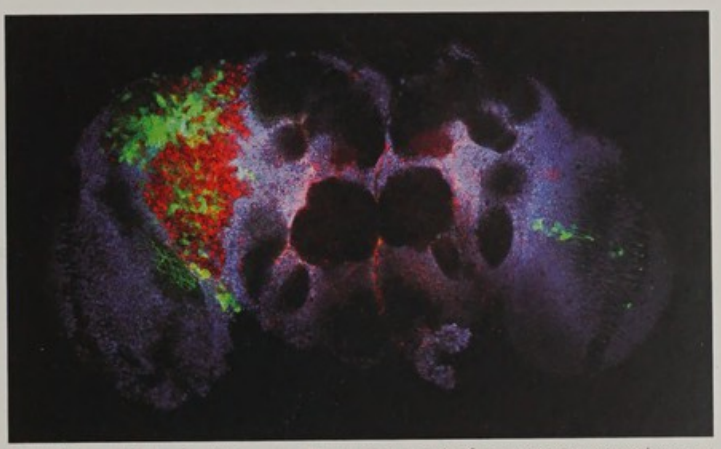
63 **Surani MA** and Hajkova P (2010) Epigenetic reprogramming of mouse germ cells toward totipotency. Cold Spring Harb Symp Quant Biol 75, 211-218

64 Tang F, Barbacioru C, Nordman E, Bao S, Lee C, Wang X, Tuch BB, Heard E, Lao K and **Surani MA** (2011) Deterministic and stochastic allele specific gene expression in single mouse blastomeres. PLoS One 6, e21208

65 Tang F, Lao K and **Surani MA** (2011) Development and applications of single-cell transcriptome analysis. Nat Methods 8, S6-11

66 Vincent JP, Kolahgar G, Gagliardi M and **Piddini E** (2011). Steep differences in wingless signaling trigger Myc-independent competitive cell interactions. Dev Cell 21, 366-374

67 Wolfram V, Southall T, **Brand AH** and Baines R (2010) Regulation of K+ channel expression in motoneurons. J Neurogenet 24, 11



Adult Drosophila brain with tumour. The tumour results from mutating a novel tumour suppressor during larval stages. Deadpan (a neural stem cell marker) is shown in red. Elav (neuronal marker) is shown in blue. (Tony Southall, Brand Group, 2011)

68 Xhemalce B, Dawson MA and Bannister AJ (2011) Histone modifications. In Encyclopedia of Molecular Cell Biology and Molecular Medicine: Epigenetic Regulation and Epigenomics (ed RA Meyers) 1-45 [**Kouzarides** Group]

69 Zeiser E, Frøkjær-Jensen C, Jorgensen E and **Ahringer J** (2011) MosSCI and gateway compatible plasmid toolkit for constitutive and inducible expression of transgenes in the *C elegans* germline. PLoS One 6, e20082

70 **Zernicka-Goetz M** (2011) Proclaiming fate in the early mouse embryo. Nat Cell Biol 13, 112-114

71 **Zernicka-Goetz M** and Huang S (2010) Stochasticity versus determinism in development: a false dichotomy? Nat Rev Genet 11 743-744

72 **Zernicka-Goetz M** (2010) The chromosome passenger complex is required for fidelity of chromosome transmission and cytokinesis in meiosis of mouse oocytes. J Cell Sci 123, 4292-4300

73 Zervas CG, Psarra E, Williams V, Solomon E, Vakaloglou KM and **Brown NH** (2011) A central multifunctional role of integrin-linked kinase at muscle attachment sites. J Cell Sci 124, 1316-1327

TALKS BY INSTITUTE RESEARCHERS

JANUARY

ANDY BANNISTER: Domainex, Cambridge, UK

ANDREA BRAND: Centre for Biological Sciences, TIFR Bangalore, India

PHILIPPE COLLIN: Paris (Orsay-Ville), Institut Curie, Orsay, Paris, France

BORIS EGGER: University BEFRI, Leysin, Switzerland

JOSEP FORMENT: UK Genome Stability Network, Robinson College, Cambridge,

JOHN GURDON: Science Society, Wolfson College, Cambridge

STEVE JACKSON: Keystone Symposium on Genetic Instability, Colorado, USA

RICK LIVESEY: Cambridge Stem Cell Initiative Seminar, CIMR, Cambridge

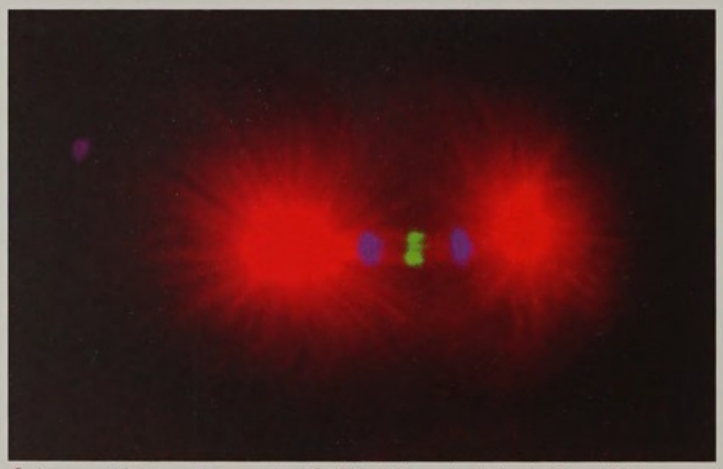
ERIC MISKA: TAU microRNA Consortium, Tel Aviv, Israel; University of Oxford, Oxford

EMMA RAWLINS: ECCPS Mini-Symposium MPI Bad Nauheim and University of Giessen, Germany

AZIM SURANI: Keystone Symposium, Utah, USA; Keystone Symposium, New Mexico, USA

EMMANELLE VIRÉ: Universite Paris Diderot Paris, France

MAGDALENA ZERNICKA-GOETZ: Stanford Stem Cell Institute, USA



C elegans wild-type embryo stained for SPD-1 (green), tubulin (red) and DNA (blue). At anaphase, SPD-1 accumulates to the central spindle. (Kian-Yong Lee, Mishima Group, 2011)

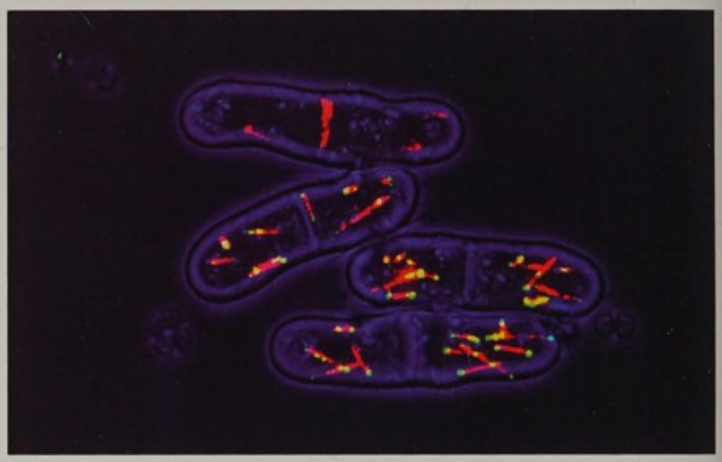
FEBRUARY

JULIE AHRINGER: Astra Zeneca Seminar, Manchester University

ANDY BANNISTER: Domainex, Cambridge

TILL BARTKE: Friedrich-Miescher Institute, Basel, Switzerland; CRUK London Research Institute, Clare Hall, London

ANDREA BRAND: MRC Centre for Regenerative Medicine, University of Edinburgh, Edinburgh



OMX imaging of S pombe microtubule organising motor protein (green) and cytoskeletal microtubules (red). Cell outlines are visualised using transmitted light (blue). (Jonathan Lawson, Carazo Salas Group, 2011)

STEVE JACKSON: Department of Biochemistry, Queens' College, University of Oxford

TONY KOUZARIDES: Epigenetics in Development & Disease, Miami, USA; Institute for Stem Cell Research, University of Edinburgh

RICK LIVESEY: Institute for Child Health, Great Ormond Street, London; WT Cambridge Stem Cell Initiative Retreat, Hinxton, Cambridge; Department of Neurology, Addenbrooke's Hospital, Cambridge

ERIC MISKA: EMBL/CIBB, Grenoble, France

EMMA RAWLINS: WT Cambridge Stem Cell Initiative Retreat, Hinxton, Cambridge; Division of Asthma, Allergy & Lung Biology, Kings College London

MARCH

JULIE AHRINGER: German Society for Cell Biology 34th Annual Meeting, Bonn, Germany

ANDY BANNISTER: Cellzome, Cambridge

TILL BARTKE: The Beatson Institute for Cancer Research, Glasgow

DELPHINE COUGOT, Department of Plant Sciences, University of Cambridge, Cambridge

JAMES DODGSON: British Yeast Group Meeting, Brighton

THOMAS DOWN: Institut Curie, Paris, France; European Bioinformatics Institute, Hinxton, Cambridge; Epigenetics and Developmental Programming Conference, Newcastle

STEVE JACKSON: Centro Andaluz de Biologia Molecular y Medicina Regenerativa (CABIMER) Spain; 50th Anniversary Meeting of the American Society of Toxicology, Washington, USA

TONY KOUZARIDES: Institute for Stem Cell Research, Edinburgh; Frontiers in Biology Symposium, CRG-Barcelona, Barcelona, Spain

RICK LIVESEY: Cambridge Spring School in Neurogenerative Disease, Cambridge

ERIC MISKA: Science Foundation Ireland, Trinity College, Dublin, Ireland; University of Lyon, France

ALEX SOSSICK: EMBO Optical Microscopy Course 2011, Plymouth

DANIEL ST JOHNSTON: Frontiers in Biology Symposium, CRG-Barcelona, Barcelona, Spain; Patterson Institute for Cancer Research, Manchester

AZIM SURANI: North American Testis Workshop, Montreal, Canada; Institut Curie, Paris, France

SILVIA VIVARELLI, National Institute for Medical Research, London

LAURA WAGSTAFF: National Institute for Medical Research, London

BLERTA XHEMALCE: UMR7216 Epigenetics and Cell Fate Institute, Paris, France

PHIL ZEGERMAN: Cancer Research UK, LRI Retreat, Oxford; British Yeast Group Meeting - British Society for Cell Biology Prize Lecture, Brighton

APRIL

JULIE AHRINGER: Abcam, Non-Coding RNA , Epigenetic Memory and the Environment Conference, RIBA, London

ALYSON ASHE: Abcam Non-Coding RNA Epigenetic Memory and the Environment Conference, London

TILL BARTKE: Max Delbrück Center for Molecular Medicine, Berlin, Germany

THOMAS DOWN: Science BarCamp, Cambridge

JOSEP FORMENT: CABIMER, Sevilla, Spain

JOHN GURDON: American Associations of Anatomists, Washington DC, USA; University of Massachusetts, Massachusetts, USA; 6th Annual Wisconsin Stem Cell Symposium, Madison USA

STEVE JACKSON: Responses to DNA damage: from molecular mechanism to human disease, Egmond aan Zee, The Netherlands

TONY KOUZARIDES: Center for Integrative Genomics, University of Lausanne, Switzerland; Department of Cell Biology, University of Geneva, Switzerland

RICK LIVESEY: University of Trieste, Neuroscience Seminar, Italy; British Society for Developmental Biology & British Society for Cell Biology Joint Spring Meeting, University of Kent, Canterbury; Wiring the Brain Conference, Co Wicklow, Ireland; British Neuroscience Association Annual Meeting, Harrogate, Yorkshire

JOERG MANSFELD: 6th UK-Japan Cell Cycle Workshop, Windermere, Cumbria

MASANORI MISHIMA: 6th UK-Japan Cell Cycle Workshop, Windermere, Cumbria

ERIC MISKA: Abcam Non-Coding RNA, Epigenetic Memory and the Environment Conference, London; Keystone Symposium, Colorado, USA

EUGENIA PIDDINI: 52nd Annual *Drosophila* Research Conference, San Diego, USA

JON PINES: PhD Symposium, University of Helsinki, Finland

EMMA RAWLINS: Universities of Giessen and Marburg Lung Center Regeneration Symposium, MPI Bad Nauheim and University of Giessen, Germany

MAGDALENA ZERNICKA-GOETZ: Stem Cell Institute, California Institute of Technology, USA

MAY

RAFAEL CARAZO-SALAS: Cambridge Institute for Medical Research Cambridge

JOHN GURDON: Young Embroyologists, King's College, London

STEVE JACKSON: Max Planck Institute, Germany; Liverpool Cancer Research Annual Meeting, Liverpool

TONY KOUZARIDES: CRG - Barcelona, Spain; Institute Pasteur, Paris France

RICK LIVESEY: Neuroscience and Mental Health Institute, University of Cardiff; Harvard Stem Cell Institute, USA

ERIC MISKA: MRC Prion Unit, London; IMBA, Vienna, Austria; University of Utrecht; EMBO Practical Course on Micro-RNA Profiling, National University of Ireland, Galway

JON PINES: Biocentrum, University of Basel, Switzerland; Doctoral School Symposium, University of Tartu and Konstanz, Estonia

AZIM SURANI: Wellcome Trust Sanger Institute, Cambridge

EMMANELLE VIRÉ: School of Biological Sciences, University of Portsmouth, UK

LAURA WAGSTAFF: Department of Zoology, University of Cambridge, Cambridge

JULIE WOOLFORD: Cambridge Resesarch Institute, Cambridge

MAGDALENA ZERNICKA-GOETZ: Stem Cell and Regenerative Biology, Harvard, USA

JUNE

PAOLO AMARAL: XI Genetics Workshop, Institute of Biosciences, UNESP, Sau Paolo, Brazil

RAFAEL CARAZO SALAS: MRC Laboratory for Molecular Cell Biology & Cell Biology Unit, London

JOHN GURDON: University of Cambridge; ISSCR Annual Meeting Toronto, Canada

STEVE JACKSON: School of Biological Sciences, University of Edinburgh; Cambridge Cancer Centre Symposium, Cambridge; University of Copenhagen, Denmark

RICK LIVESEY: Department of Physiology, Anatomy and Genetics Seminar Series, University of Oxford

MASANORI MISHIMA: University of San Diego, USA

ERIC MISKA: International *C elegans* Meeting, Los Angeles, USA; Russ Fernald Lab, Stanford University, USA

JON PINES: Global Centre of Excellence Program, Tokyo Institute of Technology, Japan; MEXT Priority Research Project Hakone, Japan

DANIEL ST JOHNSTON: Wellcome Trust Sanger Institute, Cambridge

ALEX SAPETSCHNIG: International *C elegans* Meeting, Genetics Society of America, Los Angeles, USA

AZIM SURANI: ISSCR Annual Meeting, Toronto, Canada

TALKS BY INSTITUTE RESEARCHERS

EMMANELLE VIRÉ: Laboratoire de Biochimie, Faculté de Médecine, Université d'Auvergne, France

JULIE WATSON: EuroSyStem Consortium, Prague, Czech Republic; U3A Cambridge Group, Cambridge

JULY

JULIE AHRINGER: 70th Annual Meeting of the Society for Developmental Biology, Chicago, USA;

MELANIE BLASIUS: Genetic Toxicology, Gordon Research Conferences, Barga, Italy

TILL BARTKE: Institute of Molecular Biology, Mainz, Germany

ANDREA BRAND: 70th Annual Meeting of the Society for Developmental Biology, Chicago USA

RAFAEL CARAZO SALAS: EMBL, Heidelberg, Germany

THOMAS DOWN: Advances in Medical Genomics, QMUL, London; BOSC, Vienna, Austria

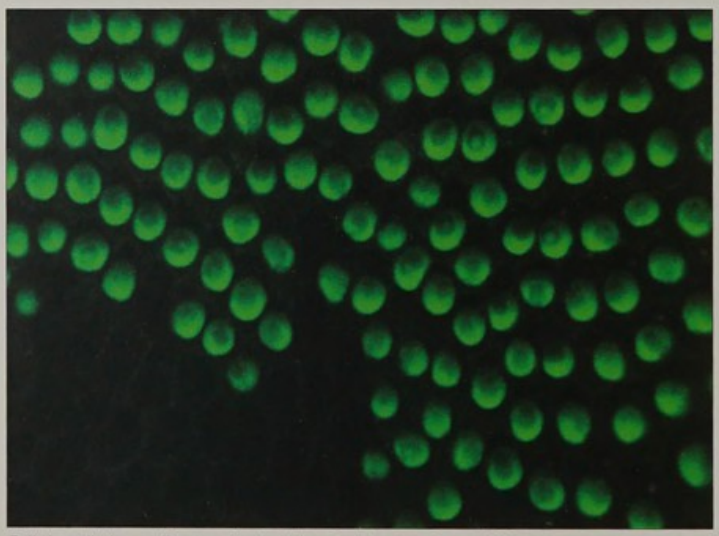
JOHN GURDON: Cambridge University Science Summer School, University of Cambridge

RICK LIVESEY: Institute of Neurology, London; Science Summer School, University of Cambridge; The Belgian Society for Cell and Developmental Biology, Summer Meeting, Rochehaut, Belgium

ERIC MISKA: MRC Clinical Centre, London; Sanger EBI, Hinxton, Cambridge; EMBO YIP Meeting, Heidelberg, Germany; Biochemical Society, Cambridge

EMMA RAWLINS: Stem Cells and Cell Therapies in Lung Biology and Lung Diseases, University of Vermont College of Medicine, USA

AZIM SURANI: Wellcome Trust Centre for Stem Cell Research, Cambridge; University of Oxford, Oxford



Follicle cell clones (Dmitry Nashchekin, St Johnston Group, 2011)

SILVIA VIVARELLI, National Institute for Medical Research, London

LAURA WAGSTAFF: National Institute for Medical Research, London

MAGDALENA ZERNICKA-GOETZ: European Society of Human Reproduction and Embryology Meeting, Barga, Italy

AUGUST

ANDREA BRAND: School of Biological Sciences, University of Sydney, Australia

STEVE JACKSON: Biochemical Society, Hinxton, Cambridge

NIMESH JOSEPH: Sphere Fluidics Talk, Cambridge

TONY KOUZARIDES FASEB Summer Research Conferences, Snowmass, Colorado, USA

MAGDALENA ZERNICKA-GOETZ: EMBO Intracellular RNA Localization and Localized Translation, Barga, Italy

SEPTEMBER

JULIE AHRINGER: European Science Foundation: From Phenotypes to Pathways, Cambridge; EMBO Nuclear Structure and Dynamics, Isle sur la Sorgue, France,

PAOLO AMARAL: Computational Biology Seminar Series, Institure for Molecular Bioscience, University of Queensland, Brisbane, Australia

ANDREA BRAND: Cambridge Neural Stem Cell Symposium, St Johns College, Cambridge; Howard Hughes Medical Institute, Ashburn Virginia, US; Cold Spring Harbor Laboratory Stem Cell Biology Meeting, Cold Spring Harbor, New York USA; SKMB Gene Regulation Workshop, Center for Integrative Genomics, Lausanne, Switzerland

RAFAEL CARAZO SALAS: 8th Bertinoro Computational Biology Meeting, Bertinoro, Italy; Physics of Living Matter Meeting, CMS, Cambridge

VINCENT GAGGIOLI: Cold Spring Harbor Laboratory Eukaryotic DNA Replication and Genome Maintenance, Cold Spring Harbour, New York, USA

JOHN GURDON: Athens Academy, Athens, Greece; Anne McLaren Laboratory for Regenerative Medicine, Leckhampton House, Cambridge; St Mary's School College, Ascot, Kent

STEVE JACKSON: EMBO-EMBL, Greece

TONY KOUZARIDES: Justus-Liebig-Universität Giessen, Germany

RICK LIVESEY: Wellcome/MRC Neurodegeneration Initiative Annual Meeting, Edinburgh; Cambridge Neural Stem Cell Symposium, St Johns College, Cambridge

JON PINES: University of Utrecht, The Netherlands; Paterson Institute Manchester; Norwegian Cancer Symposium, Oslo, Norway

EMMA RAWLINS: Cambridge Stem Cell Initiative Seminar; Cambridge Institute for Medical Research, Cambridge

DANIEL ST JOHNSTON: ERDC Conference, Lisbon, Portugal

ALEX SOSSICK: Friedrich-Miescher Institute for Biomedical Research, Basel, Switzerland

AZIM SURANI: Max Delbrück Center for Molecular Medicine, Berlin, Germany

PHIL ZEGERMAN: Cold Spring Harbor Laboratory Eukaryotic DNA Replication and Genome Maintenance, Cold Spring Harbour, New York, USA

OCTOBER

JUAN FRANCISCO ABENZA MARTINEZ: Nanoday Conference, Newnham College, Cambridge

JULIE AHRINGER: Max Planck Institute for Molecular Genetics, Berlin, Germany

ANDY BANNISTER: Domainex, Cambridge

RAFAEL CARAZO SALAS: Cancer Research UK, London

MARK DAWSON: Cambridge Haematopiesis Seminar Series, Cambridge Institute for Medical Research, Cambridge

JENNY GALLOP: Department of Biochemistry, University of Oxford; EMBO-FEBS Lecture Course/European Cytoskeletal Forum Meeting, Stresa, Italy

VERONIKA GRAML: First International System X.ch Conferences on Systems Biology, Basel, Switzerland

JOHN GURDON: EMBO Workshop, IGBMS Strasbourg, France

STEVE JACKSON: Queens University, Belfast; 39th Annual Meeting, Frontiers in Cell Biology, Copenhagen, Denmark; Babraham Institute, Cambridge; 5th Chemical Biology and Molecular Medicine Symposium, CRI, Cambridge

TONY KOUZARIDES: Cellzome/CellCentric/BioFocus, Chesterford Research Park, Chesterford; MRC Clinical Sciences Centre, London

RICK LIVESEY: Takeda UK Ltd, Cambridge

JOERG MANSFELD: Centre for Protein Research, Copenhagen, Denmark

JON PINES: Insititute for Research in Immunology and Cancer, Montreal, Canada; 5th International Workshop on Cell Regulation in Division and Arrest, Okinawa, Japan

DANIEL ST JOHNSTON: Institut Curie, Paris, France

NOVEMBER

PAOLO AMARAL: London Chromatin Club, University College London

ANATOLE CHESSEL: OMX Users' Meeting, Paris, France; Cancer Research UK, London Research Institute, London

MARK DAWSON: Australian Centre for Blood Diseases, Melbourne, Australia; Peter MacCullum Cancer Institute, Melbourne, Australia

JENNY GALLOP: Cambridge Cell Biology Seminar, CIMR, Cambridge; Department of Biochemistry, University of Bristol

JOHN GURDON: Academy of Medical Sciences Honorary Fellowship, London; Cardiff Scientific Society Cardiff, Wales; MRC/NIMR Mill Hill, London

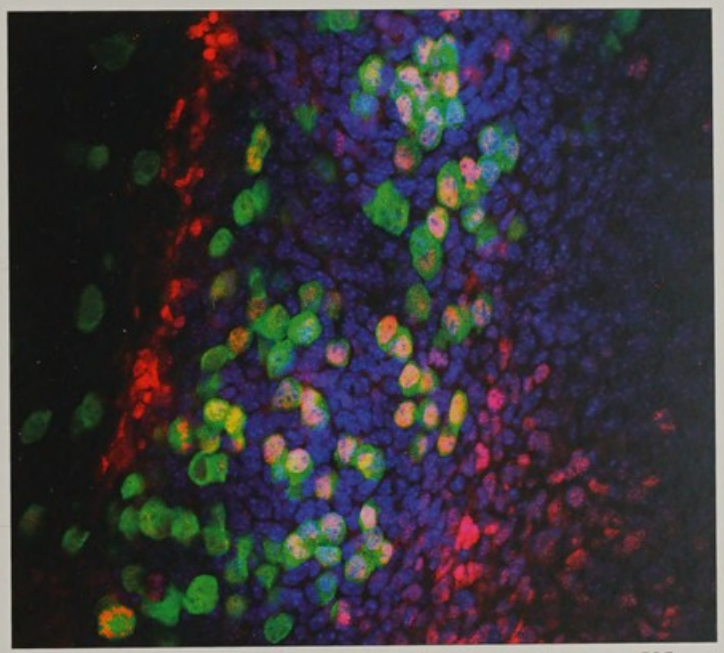
STEVE JACKSON: Universidad Internacional de Andalucia, Baeza, Spain; Health Research Board, Science Foundation Ireland and Molecular Medicine, Dublin, Ireland

RICK LIVESEY: Department of Cell and Developmental Biology, University College, London

ERIC MISKA: CSHL *C elegans* Course Organiser, Cold Spring Harbour, New York, USA; University of Wisconsin, Madison, USA

JON PINES: Cell Polarity in Health and Disease Workshop, Ottawa, Canada

DANIEL ST JOHNSTON: Cell Polarity in Health and Disease Workshop, Ludwig Institute for Cancer Research, Oxford



Primordial germ cells in a mouse gonad at e11.5". In blue is DAPI, green is GOF reporter, red is Histone H3 Lysine 27 trimethylation (H3K27me3). This is a whole mount staining. (Roopsha Sengupta, Surani Group, 2011)

AZIM SURANI: CNIO (Spanish National Cancer Centre) Conference, Madrid, Spain; Royal Society, London; Wellcome Trust, Hinxton, Cambridge

MAGDALENA ZERNICKA-GOETZ: Institute of Reproductive Science, Oxford; Cell Polarity in Health and Disease Workshop, Ludwig Institute for Cancer Research, Oxford

DECEMBER

JUAN FRANCISCO ABENZA MARTINEZ: Institut Curie, Paris, France

ANDREA BRAND: Rosalind Franklin Society, Washington DC, USA

MARK DAWSON: American Society of Haematology Annual Meeting, San Diego, USA

JENNY GALLOP: Tissue Systems Seminar Series, University of Manchester, Manchester

JOHN GURDON: Charterhouse School, Godalming; Cell Symposia: Stem Cell Programming and Reprogramming, Lisbon, Portugal

STEVE JACKSON: Genes and Cancer Symposium, Warwick

TONY KOUZARIDES: University of Leeds, Leeds; Abcam Chromatin: Structure and Function 2011, Aruba

JON PINES: Nordic Mitotic Network Meeting, Copenhagen, Denmark

AZIM SURANI: BIOTEC (Biotechnology Centre) Dresden, Germany

OTHER INFORMATION

STAFF AFFILIATIONS

JULIE AHRINGER is a member of the MRC Career Development Panel and a member of the Scientific Advisory Board of Reactome.

ANDREA BRAND is a Founding Board Member of The Rosalind Franklin Society (USA), member of Sectional Committee 7 of the Royal Society, member of the Royal Society Research Appointment Panel Bi, member of the EMBO Young Investigator Committee, member of the Review Panel of the Developmental Biology Unit, EMBL (Heidelberg, Germany) and external advisor to the Management Board of the National Centre for Biological Sciences (Bangalore, India). She is also a member of the steering group of the Cambridge Women in Science, Engineering and Technology Initiative, Patron of the Cambridge Science Festival, and member of Council, Jesus College.

JOHN GURDON is an honorary member of the Scientific Advisory Board of the Harvard Stem Cell Institute (USA) and the Rambam Medical Center (Israel), an honorary member of the British and American Anatomical Societies, Chairman of the Company of Biologists, a board member of Diagnostics for the Real World and a member of the Faculty of 1,000.

STEVE JACKSON is founding Scientist and Chief Scientific Officer of MISSION Therapeutics Ltd. He is also Chairman of the Board of the Scottish Centre for Cell Signalling (SCILLS), a member of the Cancer Research UK Drug Discovery Advisory Group, the Strategic Board of the Drug Discovery Program (IFOM-IEO, Milan, Italy), the Radiation Oncology and Biology External Advisory Board and the Scientific Advisory Board for the Beatson Institute. He is on the Steering Committee for the Cambridge Cancer Centre, and selection committee for Carcinogenesis Integrative Cancer Research Awards.

TONY KOUZARIDES is a member of the Cancer Research UK Science and Strategy Advisory Group, part of the Scientific Advisory Board for the Centre for Genomic Research (Spain), the Institute of Molecular Biology (Crete) and the Centre for Epigenetics and Biology (Spain). He is the founder and director of a Spanish cancer charity Vencer el Cancer (Conquer Cancer) and a founder of Chroma Therapeutics and Abcam Plc. He is a Director of Abcam Plc and on the Scientific Advisory Board of Glaxo Smith Kline and Cellzome

JONATHON PINES is a member of the Cancer Research UK Fellowship Committee, and a member of the Scientific Advisory Boards for the Institute of Biology, Paris Seine, and the Institute of Biochemistry, ETH, Zurich.

DANIEL ST JOHNSTON is a Director of the Wellcome Trust Four-Year PhD programme in Developmental Biology at the University of Cambridge, and is a non-executive Director of the Company of Biologists.

AZIM SURANI is Chairman of the Scientific Advisory Board of the Centre for Trophoblast Research, University of Cambridge; Member of the Steering Committee of the Cambridge Stem Cell Initiative, and Leader of the Pluripotency Programme; Member of the Cambridge India Partnership Advisory Group; Founder and Chief Scientific Advisor for CellCentric Ltd; Member of the Steering Committee for the UK Stem Cell Bank; Member of the Royal Society Nominations Committee; Visiting Professor, University of Kyoto, Japan

MAGDALENA ZERNICKA-GOETZ is a Stanley Elmore Senior Research Fellow at Sidney Sussex College and Board Member of the Cambridge Philosophical Society.

HONOURS AND AWARDS

STEVE JACKSON – Royal Society Buchanan Medal

PHIL ZEGERMAN – Cancer Research UK Hardiman Redon prize 2010

AZIM SURANI – Extraordinary Fellow, King's College, Cambridge

EDITORIAL BOARDS OF JOURNALS

JULIE AHRINGER – Public Library of Science Biology, Molecular Systems Biology

ANDREA BRAND – Neural Development, Fly, Biology Image Library

JOHN GURDON – Current Biology, Development, Growth and Differentiation, International Journal of Developmental Biology, Proceedings of the National Academy of Sciences of the USA

STEVE JACKSON – Carcinogenesis, EMBO Journal, DNA Repair, Ageing, Genes and Development, Current Biology.

RICK LIVESEY – BMC Developmental Biology, Molecular Autism

EMMA RAWLINS – Pediatric Research

JON PINES – EMBO Journal, EMBO Reports

DANIEL ST JOHNSTON – Development, Faculty of 1,000

AZIM SURANI – Cell, Nature Communications, Cell Stem Cell, BMC Epigentics and Chromatin, Epigenome, Epigenomics, Epigenetic Regulators, Regenerative Medicine, Differentiation, Stem Cell Research and Therapy, Faculty of 1,000

MAGDALENA ZERNICKA-GOETZ – Developmental Dynamics, BMC Developmental Biology, Reproduction, Development, Differentiation

INTERNATIONAL SCIENTIFIC ADVISORY BOARD

DR GENEVIEVE ALMOUZNI, Institut Curie, Paris, France

DR STEVE COHEN, Institute of Molecular and Cell Biology, Singapore

PROF NIC JONES, Paterson Institute for Cancer Research, Manchester, UK

DR JUDITH KIMBLE, Department of Biochemistry, University of Wisconsin-Madison, USA

DR ELISABETH KNUST, Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

DR ROBB KRUMLAUF (Chairman), Stowers Institute for Medical Research, Kansas City, USA

PROF ERICH NIGG, ETH, Zurich, Switzerland

CHAIRMAN OF THE MANAGEMENT COMMITTEE

PROFESSOR CHRIS GILLIGAN, Department of Plant Sciences and Chair of the School of Biological Sciences, University of Cambridge, UK

GROUP LEADERS

MASANORI MISHIMA: Associate Professor, Centre for Mechanochemical Cell Biology, Warwick University Medical School, Warwick, UK (Mishima Group)

SABBATICAL VISITORS

JARI YLANNE: Returned to NSC, University of Jyväskylä, Finland (Brown Group)

POSTDOCTORAL RESEARCHERS

ANNA AJDUK: Assistant Professor, Department of Embryology, University of Warsaw, Poland (Zernicka-Goetz Group)

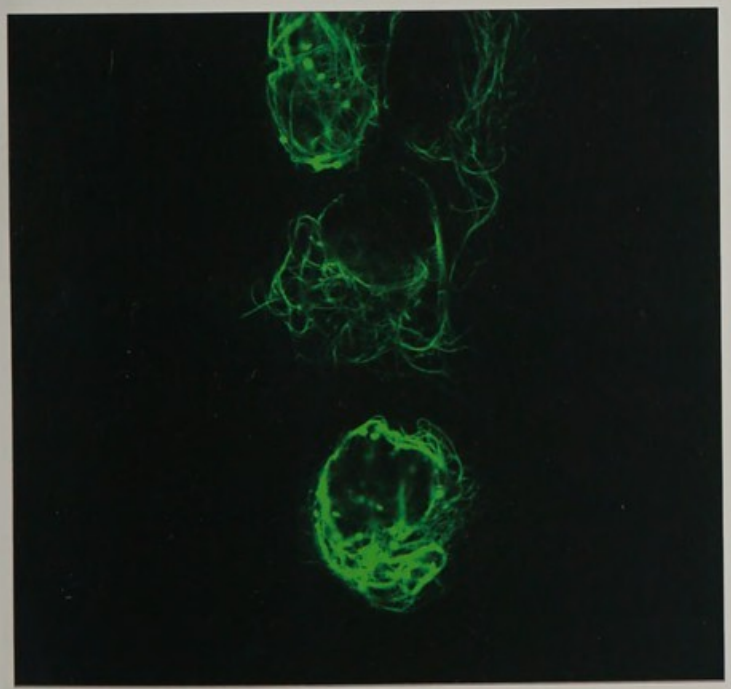
HATICE AKARSU: Cell Engineering Scientist, Horizon Discovery, Cambridge, UK (Kouzarides Group)

TILL BARTKE: Group Leader, MRC Clinical Sciences Centre, Imperial College Faculty of Medicine, London (Kouzarides Group)

SUZAN BER: Researcher, Brain Repair Centre, Addenbrooke's Hospital, Cambridge, UK (Surani Group)

BORIS EGGER: Lecturer, Department of Biology, University of Fribourg, Switzerland (Brand Group)

NIGEL GARRETT: Enforced career break (Gurdon Group)



GFP-RNF36 (Ring Finger 36 protein) live imaging in U2OS cells. RNF36 is an Ubiquitin E3-ligase. (Yaron Galanty, Jackson Group, 2011)

JEANINE HARRIGAN: Scientist at Mission Therapeutics, Cambridge, UK (Jackson Group)

XAVIER JACQ: Scientist at Mission Therapeutics, Cambridge, UK (Jackson Group)

NIMESH JOSEPH: Senior Scientific Officer, Cambridge Research Institute, Cambridge, UK (Mishima Group)

KYLE MILLER: Assistant Professor of Molecular Genetics and Microbiology, University of Texas at Austin, USA (Jackson Group)

SAMANTHA MORRIS: Postdoctoral position, Children's Hospital, Boston, US (Zernicka-Goetz Group)

EVA PABLO-HERNANDO: Travelling (Mishima Group)

JOHANNA REES: Biochemistry Department, University of Cambridge, Cambridge, UK (St Johnston Group)

FUNDA SAR: Assistant Professor, Koç University, Istanbul, Turkey (Miska Group)

ANTONIO VEGA RIOJA: Postdoctoral Researcher, Laboratorio de Inmunología y Alergia, Hospital Universitario Virgen Macarena, Seville (St Johnston Group)

BLERTA XHEMALCE: Independent Research Fellow, The Institute of Cellular and Molecular Biology, University of Texas, Austin, USA (Kouzarides Group)

RESEARCH ASSISTANTS/TECHNICIANS

LOUISE JONES: Scientist at Mission Therapeutics, Cambridge, UK (Jackson Group)

CHARLOTTE KNIGHTS: Scientist at Mission Therapeutics, Cambridge, UK (Jackson Group)

NGOC-SUNG LY: Department of Genetics, University of Cambridge, Cambridge, UK (Miska Group)

LISA SMITH: Scientist at Mission Therapeutics, Cambridge, UK (Jackson Group)

NEHA THAKKAR: Returned to India (Jackson Group)

ANNE VIELLE: Ingenieur, University of Sophia-Antipolis, Nice, France (Ahringer Group)

PHD STUDENTS

MARLOES BAGIJN: Consultant, PRMA Consulting (Miska Group)

TIM DAVIES: Postdoctoral Researcher, Centre for Mechanochemical Cell Biology, Warwick University Medical School, Warwick, UK (Mishima Group)

CELIA FARIA: Science Demonstrator, Bath, UK (St Johnston Group)

PAULINA KOLASINSKA-ZWIERZ: Completed PhD and left in 2010 (Ahringer Group)

KIAN-YONG LEE: Postdoctoral Researcher, Centre for Mechanochemical Cell Biology, Warwick University Medical School, Warwick, UK (Mishima Group)

STEPHEN SANSOM: Postdoctoral Researcher, CGAT, MRC Functional Genomics Unit, Oxford, UK (Livesey Group)

BEDRA SHARIF: Completed PhD and moved to Montreal, Canada (Zernicka-Goetz Group)

JING SU: Postdoctoral Researcher, Microarray group, EBI, Cambridge, UK (Collaborating PhD student Down Group)

DESTINATIONS OF LEAVERS DURING 2011

ROY (TANG YI) TEO: Returned to Singapore to complete his A*STAR PhD course (Zernicka-Goetz Group)

URUPORN THAMMONGKOL: Left to work in business in Thailand (Livesey Group)

ALYSON THOMPSON: Bain & Co, London, UK (Brand Group)

JORRIT TJEERTES: Presidential Postdoctoral Fellow, Novartis Institute for Biomedical Research, Switzerland (Jackson Group)

JUTTA WELLMAN: Deceased (Brown Group)

LUCY WHEATLEY: Field Application Specialist, Promega (St Johnston Group)

PAO-SHU (PAUL) WU: Clinical Resident, Department of Pathology, Taipei Veterans General Hospital, Taipei, Taiwan (Brand Group)

MPHIL STUDENTS

SKY FEUER: PhD student, UCSF, San Francisco, USA (Ahringer Group)

CLARE HOWARD: Fulbright Scholar, Ludwig Institute for Cancer Research, Karolinska Institute, Stockholm, Sweden (Brand Group)

KAMILA JOZWIK: PhD student, CRUK Cambridge Research Institute, Cambridge, UK (Jackson Group)

VISITING/VACATION STUDENTS/VISITING RESEARCHERS/VOLUNTEER RESEARCHERS

HERVÉ ALEGOT: (Visiting student) Université Blaise Pascal, France (St Johnston Group)

SOURIMA B SHIVHARE: (Visiting student) PhD student, University of Newcastle (Zernicka-Goetz Group)

MARTIN BINDER: Part III Maths student, University of Cambridge (Livesey Group)

INGER BRANDSMA: (Visiting student) Masters student, Utrecht University, The Netherlands (Jackson Group)

MARCOS GALLEGO LLORENTO: (Vacation student) Undergraduate student, Imperial College, London (Jackson Group)

CHIARA GALLONI: (Visiting student) Batchelors Student, Bologna University, Italy (Pines Group)

MARIA JESUS GOMEZ LAMARCA: (Visiting PhD student) PhD student, CABD, Seville (Piddini Group)

HARRY HAN: (Visiting student) Undergraduate student, Rice University, Texas, USA (Brand Group)

ELEANOR HULLIS: (Vacation student) Undergraduate student, Cambridge University (Brown Group)

KAI LUDWIG: (Visiting student) Undergraduate student, University of Wisconsin-Madison, USA (Miska Group)

MACIEJ MEGLICKI: (Vacation student), PhD student, University of Warsaw, Poland (Zernicka-Goetz Group)

SARAH MANSOUR: (Visiting Master's student) PhD student, Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany (Piddini Group)

MATT NEWTON: (Volunteer researcher) Completing A-Levels (Brown group)

HANNA REUTER: (Visiting student) PhD student, Ruprecht-Karls University in Heidelberg (St Johnston Group)

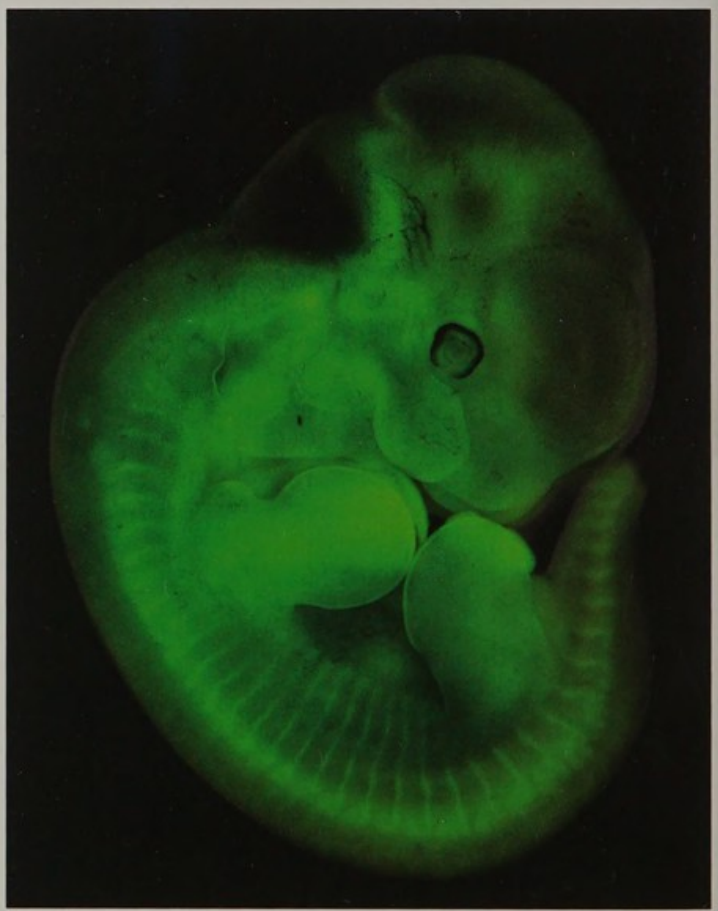
MAXIE ROCKSTROH: (Visiting student) PhD student, University of Leipzig (Jackson Group)

MATTHIAS ROMAUCH: (Visiting student) PhD student, Karl-Franzens University, Graz, Austria (Zernicka-Goetz group)

ANNE SAPIRO: (Visiting student) Undergraduate student, University of Wisconsin-Madison, USA (St Johnston group)

MARIA SUCIU: (Visiting student) Masters student, UCL, London, UK (Zernicka-Goetz group)

ELIANA TACCONI: (Volunteer researcher) PhD student, Gray Institute for Radiation Oncology and Biology, University of Oxford, UK (Pines group)



Mouse embryo expressing GFP. (Samantha Morris, Zernicka-Goetz Group, 2011)

Professor Sir John Gurdon investigates one of science's great unanswered questions: what does it actually *feel* like to be a frog? Hoppity-hop.... (photo by John Overton)

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Front cover: Super-resolution image of developing dendritic spines in human iPS derived cortical neurons. Green DiO, Blue DAPI. (Peter Kirwan, Livesey Group, 2011)

Back cover: Institute retreat, photos by Peter Williamson and John Overton.

Wellcome Trust/Cancer Research UK Gurdon Institute

The Henry Wellcome Building of Cancer and Developmental Biology
University of Cambridge, Tennis Court Road, Cambridge CB2 1QN, United Kingdom

Telephone: +44 (0)1223 334088
Fax: +44 (0)1223 334089
http://www.gurdon.cam.ac.uk
e-mail: info@gurdon.cam.ac.uk