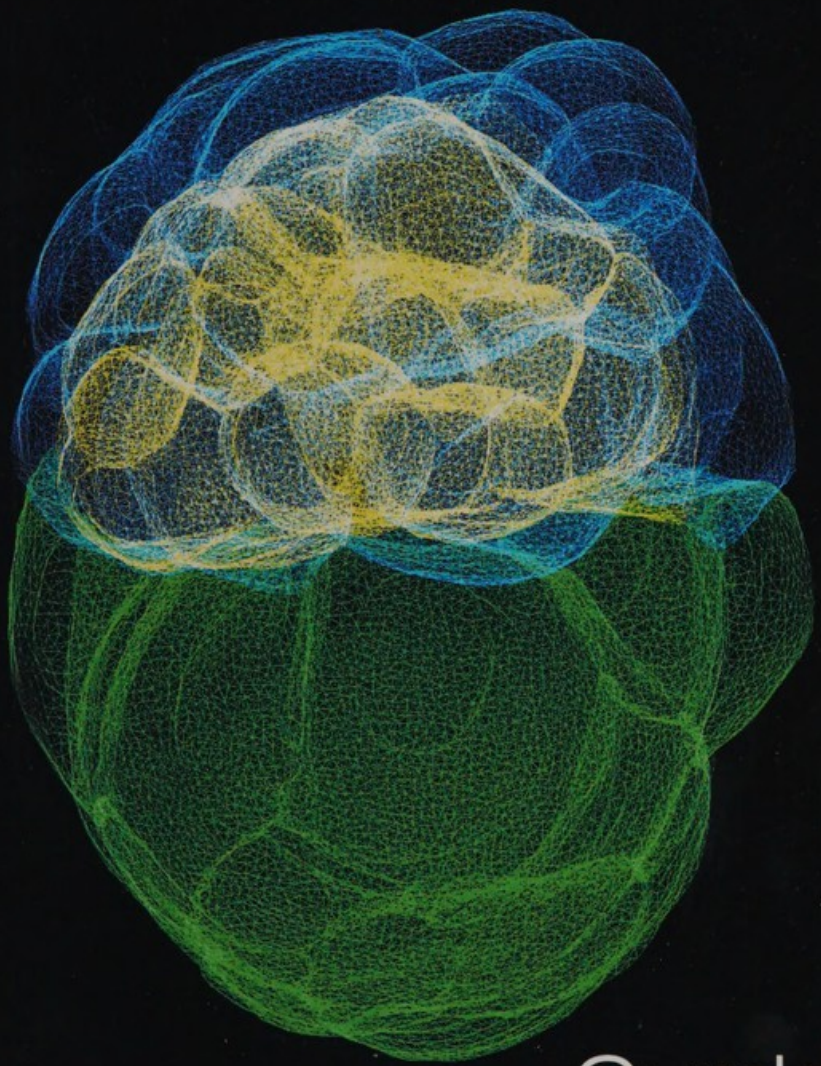
Annual report : 2006/2007 / The Wellcome Trust, Cancer Research UK Gurdon Institute of Cancer and Developmental Biology.

The Wellcome Trust and Cancer Research UK Gurdon Institute

2007 PROSPECTUS / ANNUAL REPORT 2006



Gurdon
INSTITUTE

wellcome trust

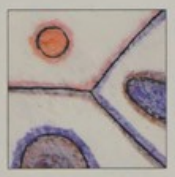
CANCER RESEARCH UK

UNIVERSITY OF CAMBRIDGE

PROSPECTUS 2007

ANNUAL REPORT 2006

Gurdon INSTITUTE

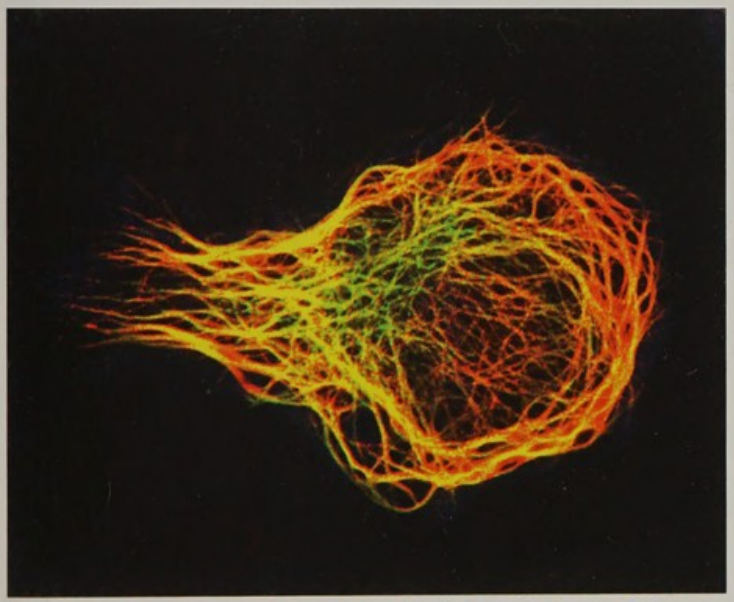


http://www.gurdon.cam.ac.uk

CONTENTS

CHAIRMAN'S INTRODUCTION

After the events of 2005, when we settled into our new building and held a Symposium to celebrate the move and to mark our re-naming, this has been a quieter year for the Gurdon Institute. The good news is that the teething troubles that accompanied our move (such as the temperature in the building, and problems with the lifts) have now been sorted out, and we are enjoying working in our new environment and concentrating on our science.



Drosophila S2 cells expressing a microtubule-binding protein fused to GFP in green and stained for tubulin in red. (Isabel Torres, St Johnston lab, 2006)

Amongst the Institute's scientific activities, we were pleased that our International Scientific Advisory Board visited the Institute in November of 2006, and as always we are grateful to them for their wisdom and advice; we look forward to welcoming them back in 2007. The year also saw Andrea Brand being presented with the Royal Society's Rosalind Franklin Award, which recognises an individual for an outstanding contribution to any area of natural science, engineering or technology, and we were also very proud that Daniel St Johnston renewed his Wellcome Trust Principal Research Fellowship. Finally, we heard recently that Anne McLaren is to receive the 2007 March of Dimes Prize in Developmental Biology (jointly with Janet Rossant from Toronto), and we offer her our congratulations too.

During 2006 we also said farewell to Enrique Amaya and Nancy Papalopulu, who have moved to the University of Manchester. Enrique is Professor of Tissue Regeneration, and is heading a £10 million partnership between Manchester University and the Healing Foundation. Nancy has taken her Wellcome Trust Senior Research Fellowship to Manchester, where she is Professor of Developmental Neuroscience. Nancy and Enrique will be greatly missed at the Institute, and we wish them well for the future. We are, of course, now recruiting new Group Leaders to replace Nancy and Enrique, and I look forward to writing about these new members of the Institute in next year's annual report.

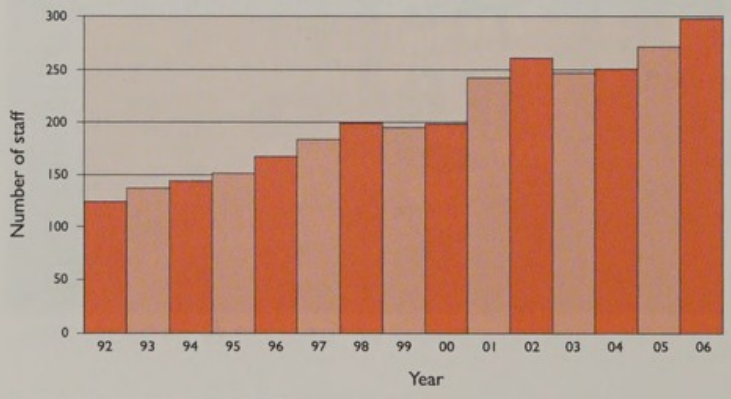
The new year will see the next Group Leaders' retreat, when we spend two days away from Cambridge to discuss our science and our plans for the future. This year will also see the Institute increase its 'outreach' activities, in the course of which we hope to explain our work to members of the Cambridge community, including teachers, school children and indeed anyone interested in cancer and developmental biology. Many of these activities are outlined on our web site, where Group Leaders have recently provided a 'lay' summary of their work that we hope will be accessible to, and understood by, anyone with an interest in science.

The Wellcome Trust/Cancer Research UK Gurdon Institute (Al Downie, 2005)

Finally, this annual report, as always, lists the people who have left the Gurdon Institute over the last year, all of whom we wish well. Of these, I should like to pay particular tribute to Caroline Webb, who joined the Institute as a secretary in 1991 and became secretary to our former Chairman, John Gurdon, in 1998. Caroline was an extraordinarily valuable and respected member of the Institute, and she retires with our very best wishes.

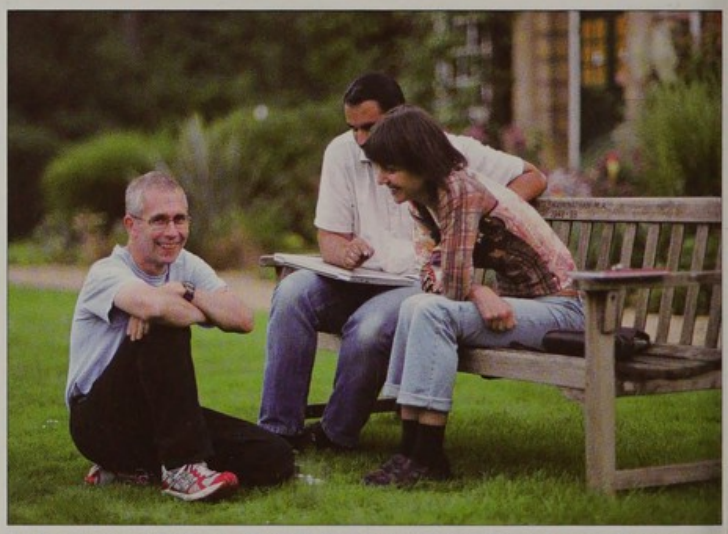
HISTORICAL BACKGROUND

The Institute continues to be situated in the middle of the area containing the science departments of the University of Cambridge and within a short distance from the centre of the historic city. Founded in 1989 to promote research in the areas of developmental biology and cancer biology, the Institute is an assemblage of independent research groups located in one building designed to promote as much interaction as possible. Developmental and cancer biology are complementary since developmental biology is concerned 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 cellular and molecular levels. These research areas are complementary 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 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.



Total staff numbers 1992 - 2006

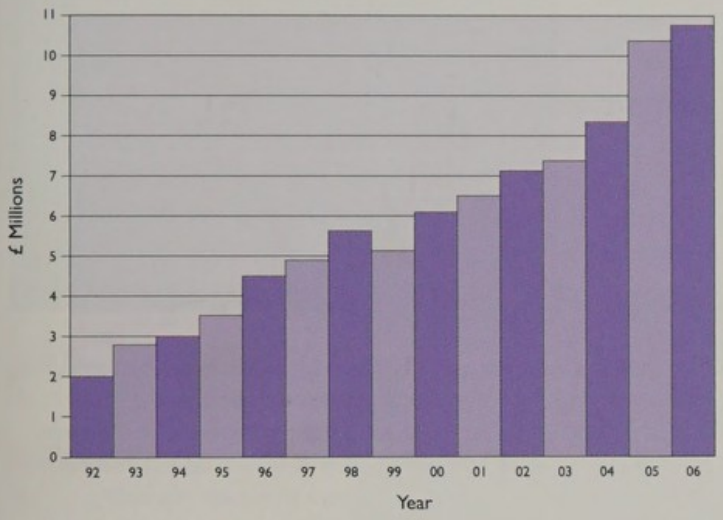
The Institute is an integrated part of Cambridge University, and all Group Leaders are members of a University Department and contribute to teaching and graduate student supervision.



Jim Smith, Amer Rana and Clara Collart at the Annual Retreat, Lady Margaret Hall, Oxford (John Overton, Brown lab, 2006)

CENTRAL SUPPORT SERVICES

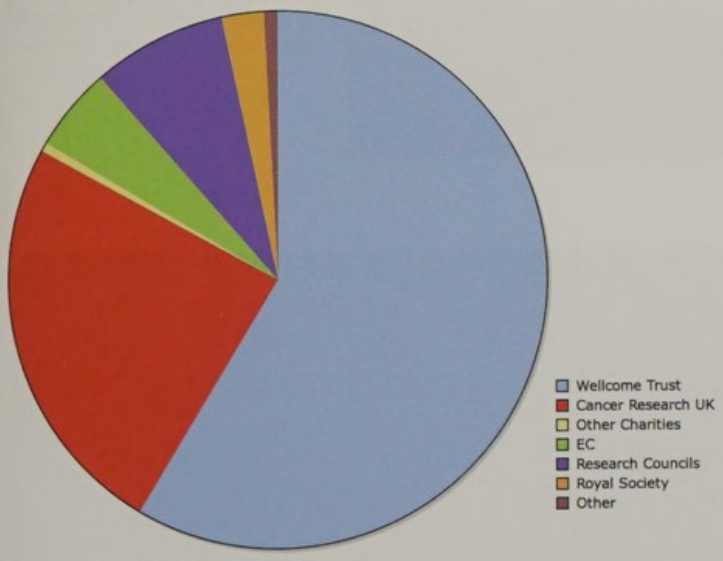
The Institute's 'core staff' provides essential administrative, technical and computing support to our scientists, so that the scientists can spend as much time as possible on their research. The amount of time devoted to getting our new building up-and-running decreased during 2006, but time still had to be devoted to various snags and breakdowns during this period, and the Institute is grateful to members of the core team for their efforts. We are also grateful for their flexible, helpful and positive attitude to their work, which has contributed in no small part to the smooth running of the Institute.



Total grant income 1992 - 2006

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 project grants, and programme and equipment grants, in addition to our invaluable core funding.



Grant sources (August 2005 - July 2006)

Other sources of financial support, both direct and indirect, include the European Community, BBSRC, the MRC, EPSRC, the Royal Society, the Lister Institute, the Isaac Newton Trust, the Leverhulme Trust, Beit Memorial Fellowships, the Association for International Cancer Research, NIH, the European Molecular Biology Organisation, Autism Speaks, and the March of Dimes. We are extremely grateful to all these organisations for their continuing support.

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

RETREAT

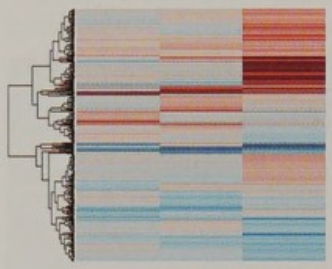
(John Overton, Brown lab, 2006)

Our Annual Retreat was held again at Lady Margaret Hall, Oxford on 21st and 22nd September 2006; this provided an ideal venue, allowing members of the Institute every opportunity to interact both scientifically and socially. As always there was a strong attendance and we are grateful to the administrative team and to Jon Pines and Magdalena Zernicka-Goetz for organising it.

Julie Ahringer

Developmental roles of chromatin regulatory complexes and the control of cell polarity

Co-workers: Yan Dong, Bruno Fievet, Paulina Kolasinska-Zwierz, Taejoon Kwon, Isabel Latorre, Neeraj Mandhana, Costanza Panbianco, Gino Poulin, David Rivers, Josana Rodriguez, Christine Turner, Shane Woods



Our research is focused on two different biological questions: First, how is cell polarity established in the embryo and this information then transduced within the cell? Second, what are the functions of chromatin regulatory complexes in a developmental context? For both of these studies, we are taking advantage of a genome-wide RNAi library that we have constructed.

Cell polarity is an essential feature of most animal cells. For example, it is critical for epithelial formation and function and for correct partitioning of fate-determining molecules. In *C elegans*, cell polarity is established during the first cell cycle and results in an asymmetric first division. Embryos are large and transparent, making these events easily visualised. Using genome-wide RNAi screening coupled with videomicroscopy of live embryos, we identified many new conserved cell polarity genes, which we study using genetics, biochemistry, and real-time fluorescent cell imaging.

Transcriptional control is mediated through multiprotein chromatin regulatory complexes. However, little is known about the developmental roles and regulation of these complexes. In *C elegans*, "synMuv" genes, which function together in several developmental contexts, encode components of different chromatin regulatory complexes, including the histone deacetylase complex NuRD, the Retinoblastoma containing complex Myb-MuvB and a TIP60 histone acetyltransferase complex. We are studying the function of these proteins in transcriptional control and development, and their relationships to each other using microarray expression profiling, chromatin immunoprecipitation and other techniques.

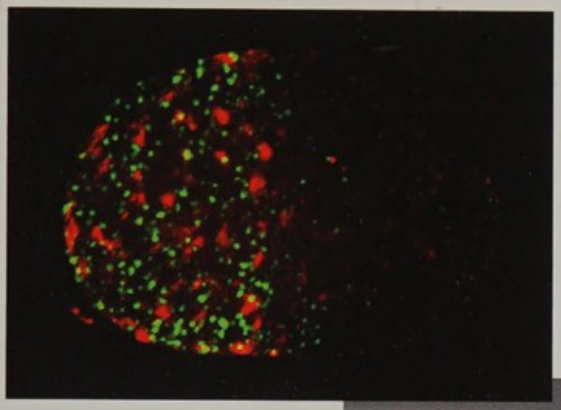
(Inset left): Expression profiling of synMuv mutants using microarrays shows widespread gene expression changes compared to wild-type (dark red and dark blue colour in last row).

Ahringer J ed (2006) Reverse genetics, WormBook, ed. The *C. elegans* Research Community, **WormBook**, doi/10.1895/wormbook.1.47.1, **http://www.wormbook.org**

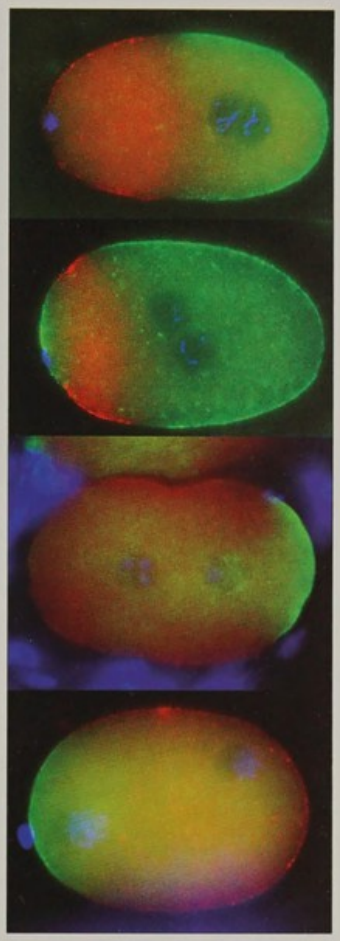
Poulin G, Dong Y, Fraser AG, Hopper N and Ahringer J (2005) Chromatin regulation and sumoylation in the inhibition of Ras-induced vulval development in *C. elegans*. **EMBO Journal** 24, 2613–2623

Gotta M, Dong Y, Peterson YK, Lanier SM and Ahringer J (2003) Asymmetrically distributed *C. elegans* homologues of AGS3/PINS control spindle position in the early embryo. **Current Biology** 13, 1029-37

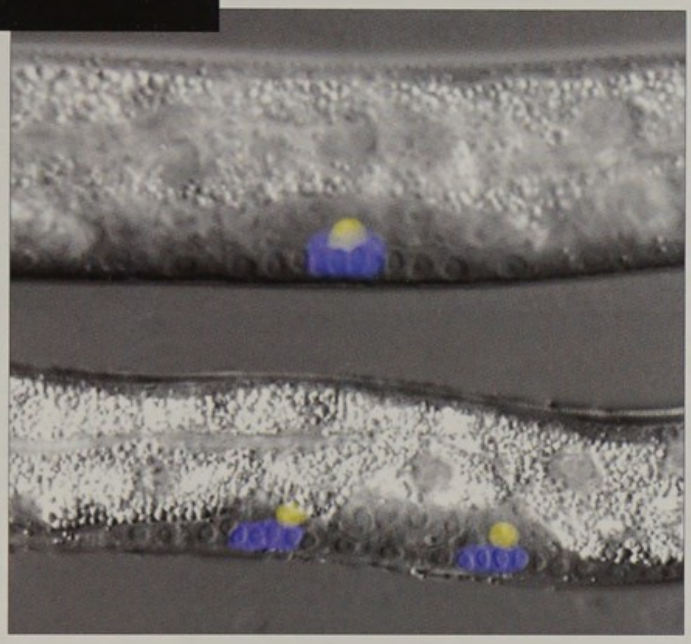
Kamath RS, Fraser AG, Dong Y, Poulin G, Durbin R, Gotta M, Kanapin A, Le Bot N, Moreno S, Sohrmann M, Welchman D, Zipperlen P and Ahringer J (2003) Systematic functional analysis of the *C. elegans* genome using RNAi. **Nature** 421, 231-237



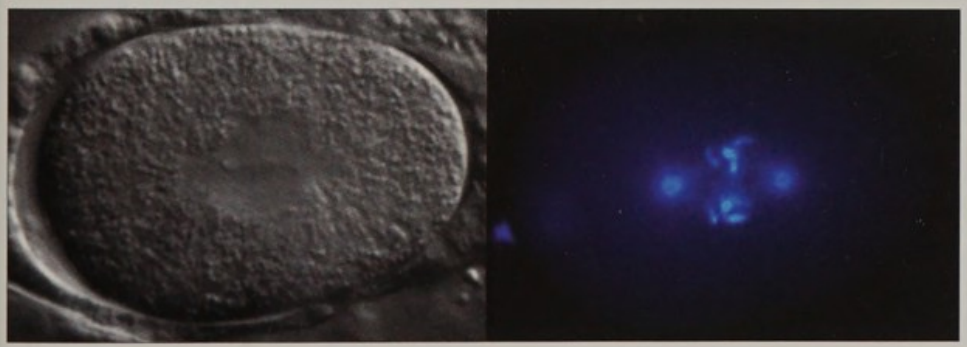
Early endosomes (green) are asymmetrically distributed in the one-celled embryo and are coincident with the domain of non-muscle myosin NMY-2 (red).



Abnormal distributions of polarity proteins PAR-3 (red) and PAR-2 (green) after RNAi of genes involved in establishing embryonic polarity. Top, wild-type, mutants below.



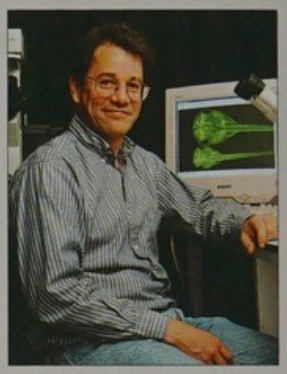
RNAi of the small G protein cdc-42 (bottom) or components of the PAR-3 complex (not shown) causes widespread defects in polarised cell growth and cell migrations; one consequence is anchor cell duplication (yellow) which induces extra vulval cells (blue); wild-type, top



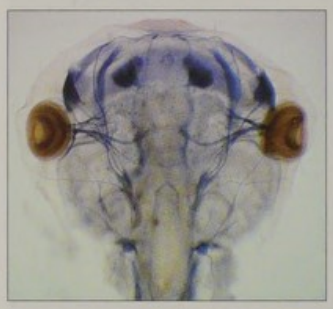
Live imaging of embryos carrying flurorescent reporters; simultaneous collection of DIC image (left) and GFP labelled histone and tubulin (right, blue) to mark the mitotic spindle

Enrique Amaya

Growth factor signal interpretation in *Xenopus*



Enrique and staff have transferred to the Healing Foundation, University of Manchester



One of the main interests of our group is understanding the molecular events responsible for mesoderm formation and patterning. In particular we are investigating the role of fibroblast growth factor (FGF) signalling during mesoderm formation in the frog, *Xenopus*. We have shown that inhibiting FGF signalling during gastrulation disrupts mesoderm specification and morphogenesis. In order to understand these processes better, we have begun to isolate downstream targets of FGF signalling. We have identified Xsprouty2 as an important target gene. This protein and the related proteins, Xsprouty1, Xspred1 and Xspred2 are both targets and modulators of FGF signalling. We have recently shown that the Sprouty and Spred proteins play an important role in FGF signal interpretation, allowing mesoderm specification and morphogenesis to occur in a coordinated fashion.

In order to identify additional genes involved in mesoderm specification and morphogenesis, we are using bioinformatics tools in combination with functional screens to identify additional genes involved in these processes. As part of this project we have identified around 7000 full-length clones from *Xenopus tropicalis* and have screened nearly 2000 of these clones for genes affecting mesoderm formation and/or morphogenesis. Of those tested, we have isolated 82 genes, which alter or inhibit mesoderm formation and/or gastrulation movements.

In addition we are investigating the role of a novel D-type cyclin during the specification and maintenance of the motor neuron and interneuron precursors within the spinal chord of *Xenopus*. We are also studying the development of primitive myeloid cells, which give rise to the embryonic macrophages. Furthermore we are investigating their migratory behaviour, especially their recruitment to embryonic wound sites. Finally, we have begun to investigate the genes involved in the development and regeneration of the vasculature in *Xenopus*.

Inset left: Cranial nerves revealed in a transgenic stage-47 tadpole expressing placental alkaline phosphatase (PLAP) from the neural specific beta-tubulin promoter.

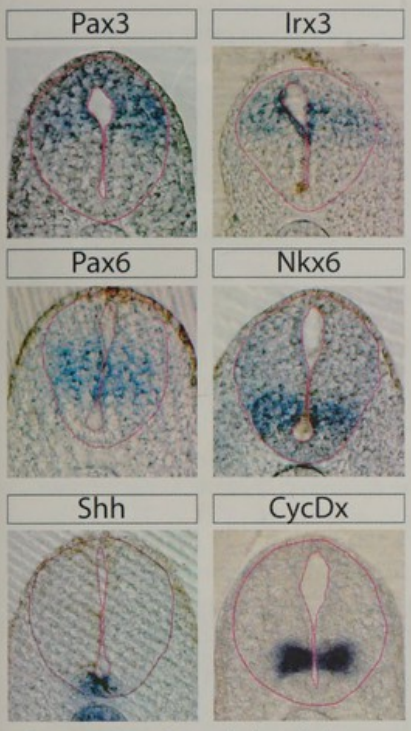
Amaya E (2005) Xenomics. **Genome Research** 15:1683–1691.

Sivak JM, Petersen L and Amaya E (2005) FGF signal interpretation is directed by Sprouty and Spred proteins during mesoderm formation. **Developmental Cell** 8, 689-701

Chen J-A, Voigt J, Gilchrist M, Papalopulu N and Amaya E (2005) Identification of novel genes affecting mesoderm formation and morphogenesis through an enhanced large-scale functional screen in *Xenopus*. **Mechanisms of Development** 122, 307-331

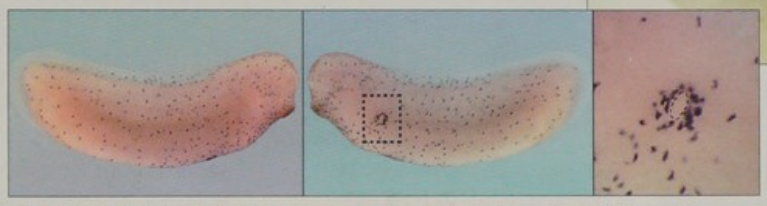
Gilchrist M, Zorn AM, Smith JC, Voigt J, Papalopulu N and Amaya E (2004) Defining a large set of full length clones from a *Xenopus tropicalis* EST project. **Dev Biol** 271, 498-516

Voigt J, Chen J-A, Gilchrist M, Amaya E and Papalopulu N (2005) Expression cloning screening of a unique and full-length set of cDNA clones is an efficient method for identifying genes involved in *Xenopus* neurogenesis. **Mechanisms of Development** 122, 289-306



Cross sections of the spinal cord of *Xenopus* tadpoles stained for the expression of different markers along the dorso-ventral axis.

Trigeminal nerve in a transgenic stage-28 tadpole expressing placental alkaline phosphatase (PLAP) from the neural specific beta-tubulin promoter.



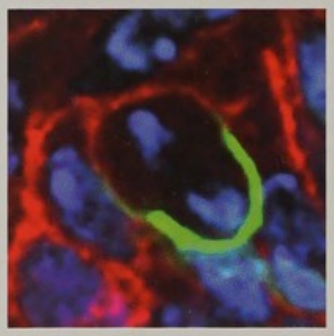
Primitive myeloid cells (dark spots) are present throughout the tailbud stage embryo. These three images are of the same embryo; the one on the left shows the right side of the embryo, the middle image shows the left side of the embryo, and the image on the right is a magnification of the area outlined in the middle image, where the primitive myeloid cells have congregated around an embryonic wound.

A montage of embryos showing the expression pattern of a select group of genes isolated in a large-scale gain of function screen aimed at identifying genes able to alter the specification and/or morphogenesis of the mesoderm. The top row shows embryos at the gastrula stages, the next two rows show embryos at the neurula stages and the bottom four rows show embryos at the tailbud stages.

Andrea Brand

Embryonic nervous system development: stem cells to synapses

Co-workers: Torsten Bossing, Adrian Carr, James Chell, Melanie Cranston, Catherine Davidson, James Dods, Karin Edoff, Boris Egger, David Elliott, Liz Gavis, Ugo Mayor, Tony Southall, Christine Turner, Jakob von Trotha, Pao-Shu (Paul) Wu



Stem cells have the remarkable ability to give rise to both self-renewing and differentiating daughter cells. *Drosophila* neural stem cells segregate cell fate determinants from the self-renewing stem cell to the differentiating daughter at each division. We have shown that one such determinant, the homeodomain transcription factor Prospero, regulates the choice between self-renewal and differentiation. We identified the *in vivo* binding sites of Prospero throughout the genome and demonstrated, by expression profiling on DNA microarrays, that Prospero represses genes required for self-renewal and, surprisingly, is also required to activate genes for terminal differentiation. We have shown that Prospero acts as a binary switch between self-renewal and differentiation. In the absence of Prospero differentiating daughters revert to a stem-cell-like fate: they express markers of self-renewal, proliferate, fail to differentiate and form small tumours. By identifying neural stem-cell-specific genes, and genes specific for differentiating daughters, we can begin to assess the potential for redirecting post-mitotic cells to divide in a regenerative manner, or to induce stem cells to differentiate.

In vertebrates, adult neural stem cells can proliferate in response to injury. We have discovered that *Drosophila* ventral midline cells, which normally divide only once, can undergo an extra cell division if a sibling midline cell is destroyed. Remarkably, the regenerated midline cell differentiates appropriately to replace the damaged cell. We aim to uncover the molecules that enable, or inhibit, neural regeneration. These molecules will be key targets for mutagenesis and targeted misexpression, as well as potential drug targets.

Further information is available on the Brand Lab website:
http://www.gurdon.cam.ac.uk/~brandlab

Inset left: A neural stem cell in the optic lobe, dividing asymmetrically (Partner of Numb-GFP, green; DAPI, blue Discs large, red).

Choksi SP, Southall T, Bossing T, Edoff K, de Wit E, van Steensel B, Micklem G and Brand AH (2006) Prospero acts as a binary switch between self-renewal and differentiation in *Drosophila* neural stem cells. **Developmental Cell** 11, 775-789

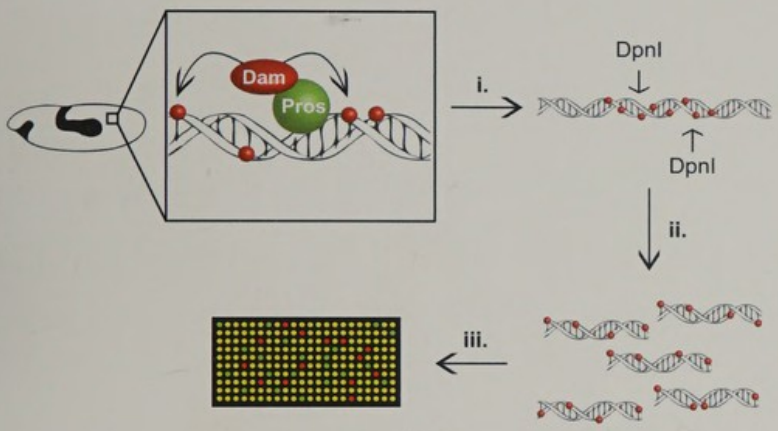
Bossing T and Brand AH (2006) Determination of cell fate along the antero-posterior axis of the *Drosophila* ventral midline. **Development** 133, 1001-1012

Pym ECG, Southall TD, Mee CJ, Brand AH and Baines RA (2006) The homeobox transcription factor Even-Skipped regulates acquisition of electrical properties in *Drosophila* neurons. **Neural Development** 1, 3

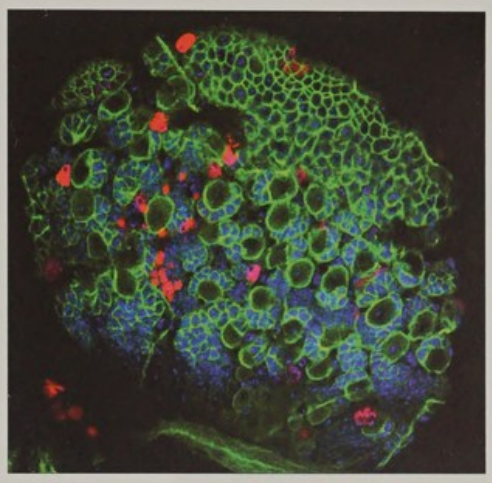
van Roessel PJ, Elliott DA, Robinson IM, Prokop A and Brand AH (2004) Independent regulation of synaptic size and activity by the anaphase-promoting complex. **Cell** 119, 707-718.

Barros CS, Phelps CB and Brand AH (2003) *Drosophila* non-muscle myosin II promotes the asymmetric segregation of cell fate determinants by cortical exclusion rather than active transport. **Developmental Cell** 5, 829-840

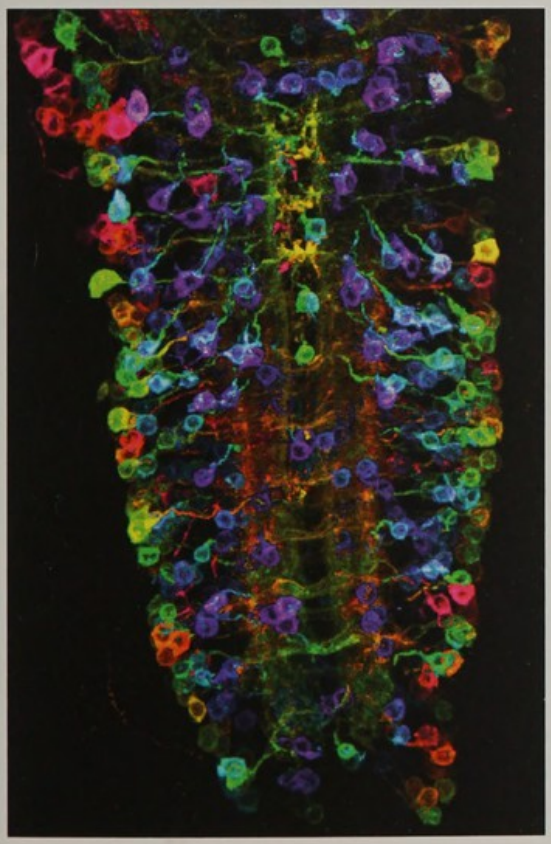
For complete list of this lab's publications since the last report, see numbers 6, 7, 14, 15, 16 & 36 on pp 56-61



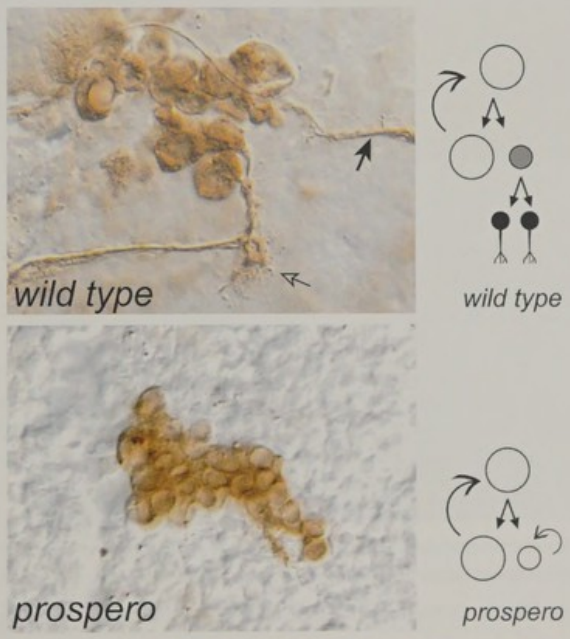
Genome-wide mapping of Prospero binding sites using the DamID technique



Neural stem cells in a larval brain lobe (Discs large, green; DAPI, blue; histone RFP, red)



The *Drosophila* embryonic nerve cord

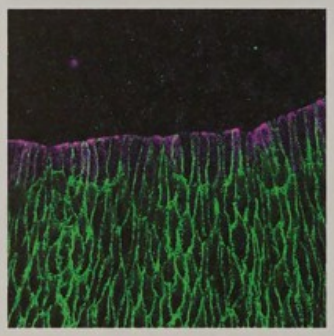


Prospero mutant GMCs are transformed into self-renewing neural stem cells; single neuroblast clones labelled with DiI in wild type (top) and *Prospero* mutant embryos (bottom)

Nick Brown

Molecular analysis of morphogenesis

Co-workers: Isabelle Delon, Samantha Herbert, Sven Huelsmann, Yoshiko Inoue, John Overton, Dora Sabino, Xiao Tan



Cellular adhesion and communication are vital during the development of multicellular organisms. These processes use proteins on the surface of cells, which stick cells together or transmit signals from outside the cell to the interior, so that the cell can respond to its environment. Members of one family of cell surface receptors, called integrins, can perform both of these activities, and therefore provide a molecular link between cell adhesion and signalling. Our research is focused on determining how proteins inside and outside the cell assist the integrins in their developmental roles: mediating cell migration, adhesion between cell layers, and cell differentiation.

We use the genetics of the fruit fly *Drosophila* to elucidate integrin function within the developing animal, and to identify the proteins that work with integrins. The isolation of mutations in genes encoding proteins required for integrin function, using forward and reverse-genetic approaches, has revealed how much they are required for integrin function. Removing talin causes the same defects as removing integrins, demonstrating it is needed for all integrin functions, while tensin is just required for integrin function in the adult. One region of talin is needed for strong adhesion of integrins to their extracellular matrix ligands, while a second region connects integrins to the cytoskeleton. Integrins not only attach to the cytoskeleton, but also organise its structure within the cell (Fig 1). New integrin-associated proteins we are characterising have novel properties. One is restricted to just a few of the cells in which integrins are active (Fig 2). A second is recruited to the plasma membrane independent of its connection with integrins (Fig 3).

Inset left: A novel integrin-associated protein (purple) is expressed in the leading edge cells of the embryonic dorsal epidermis.

Narasimha M and Brown NH (2005) Integrins and associated proteins in *Drosophila* development. In "**Integrins and development**" Danen E, editor. Landes Bioscience

Tanentzapf G, Martin-Bermudo MD, Hicks MS and Brown NH (2006) Multiple factors contribute to integrin-talin interactions *in vivo*. **J. Cell Sci.** 119, 1632-1644

Tanentzapf G and Brown NH (2006) An interaction between integrin and the talin FERM domain mediates integrin activation but not linkage to the cytoskeleton. **Nat. Cell Biol.** 8, 601-606

Bökel C and Brown NH (2002) Integrins in development: moving on, responding to, and sticking to the extracellular matrix. **Dev Cell** 3, 311-321

For complete list of this lab's publications since the last report, see numbers 46, 60 & 61 on pp 56-61

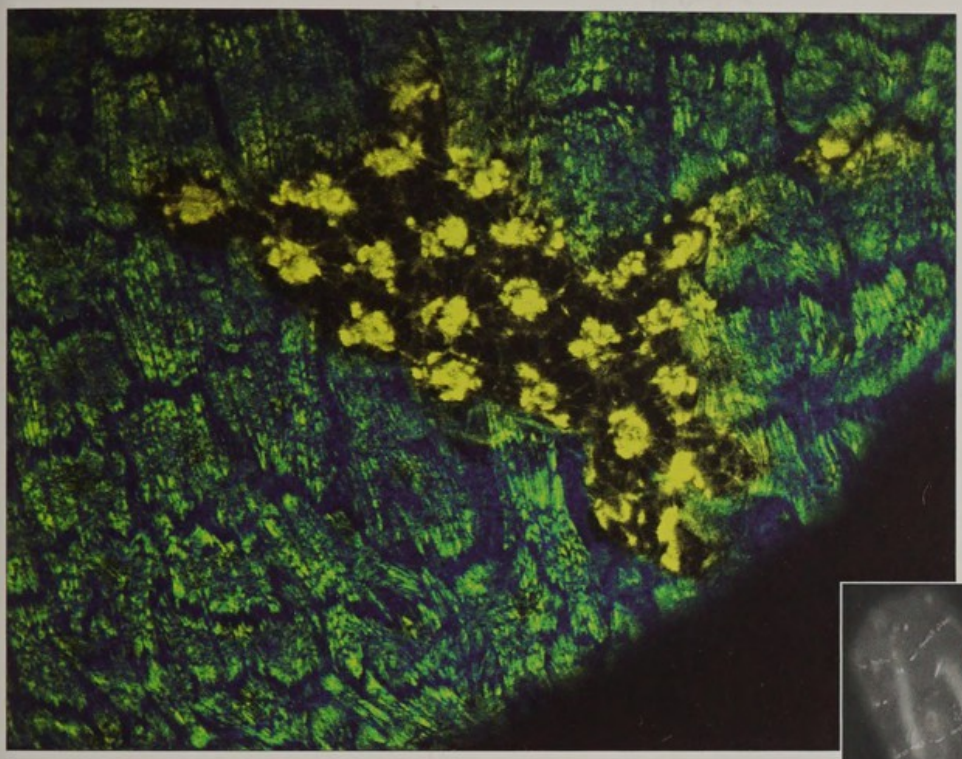


Fig 1 Cells that lack integrins (marked by the absence of the blue cytoplasmic protein) do not assemble actin cytoskeletal filaments (yellow/green) properly on the basal surface of the follicular epithelium.

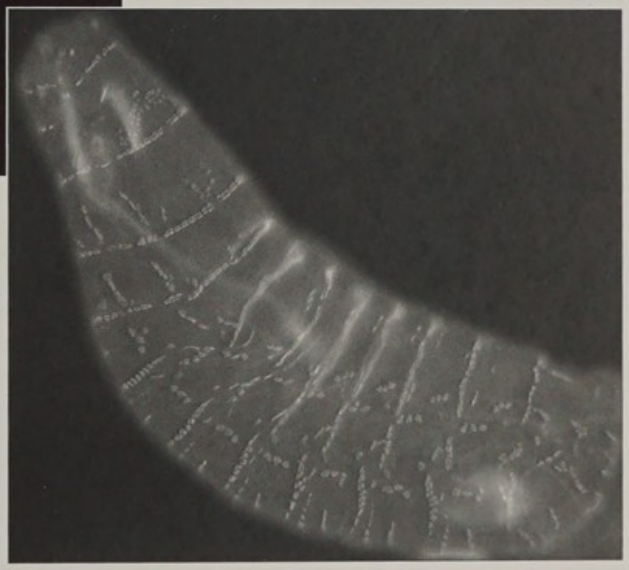


Fig 2 Expression of the novel integrin-associated protein Bloated (white) is restricted to the tendon cells: epidermal cells that attach to the muscles.

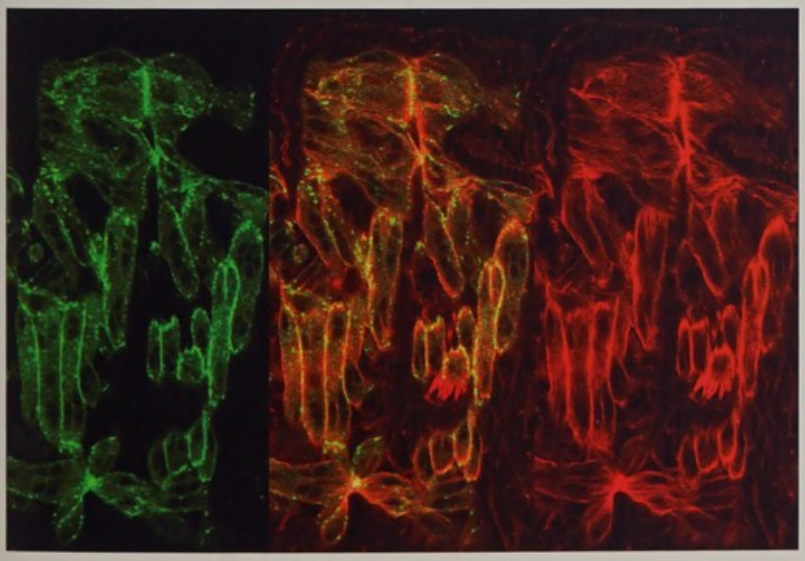
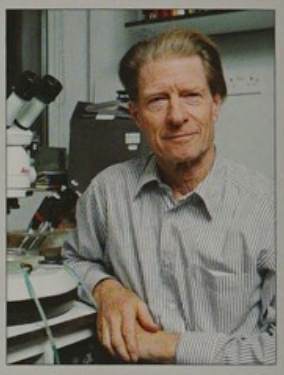


Fig 3 The pleckstrin homology domain of another novel integrin-associated protein is sufficient to target green fluorescent protein to the plasma membrane of embryonic muscles (green, yellow in middle panel). Actin is stained in red.

John Gurdon

Reprogramming of gene expression by nuclear transfer



Co-workers: Adrian Biddle, Nigel Garrett, Jerome Jullien, Magda Koziol, Yen-Hsi Kuo, Nichole Lant, Kazutaka Murata, Ilenia Simeoni, Henrietta Standley

When the nuclei of differentiated cells are transplanted to enucleated eggs, multipotential embryonic cells can be obtained. These can be made to differentiate into a range of cell types unrelated to the original cells from which the nuclei were taken. This is the basis of a cell replacement strategy by which rejuvenated cells can be derived from an adult cell. These newly-generated cells are of the same genetic constitution as the donor cell, and are therefore suitable for cell replacement therapy without the need for immunosuppression. We aim to identify the molecules and to understand the mechanisms by which the reprogramming of gene expression takes place. The same experiments give valuable information about the mechanisms that stabilise cell differentiation during normal development, and that therefore need to be reversed for cell rejuvenation.

Our principal method of analysis involves transplanting multiple nuclei from adult tissues such as the mouse thymus into the growing oocytes of *Xenopus*. Within 2 days, or within a few hours for the nuclei of less specialised cells, the transplanted nuclei express genes such as Oct4 and Nanog, which are diagnostic of embryo or stem cells. We analyse the reprogramming of gene expression at several levels. We have found that oocytes have a DNA demethylating activity that reverses differentiation by acting on the promoter of Oct4. We use extracts of oocytes to identify, and test the function of, oocyte components that bind to the promoter region of Oct4. We use confocal microscopy to view in real time the binding of defined proteins to somatic cell nuclei as they undergo gene reprogramming.

In related work, we are analysing the epigenetic memory of an active gene state in certain examples of somatic cell nuclear transfer. We are also analysing the mechanisms by which cells can memorise an extracellular concentration of morphogen long after the morphogen has been removed.

Inset left: a partially cleaved *Xenopus* embryo resulting from the transplantation of a somatic cell nucleus. Such embryos often show epigenetic memory.

Gurdon JB (2006) From nuclear transfer to nuclear reprogramming: the reversal of cell differentiation. **Annual Review of Cell and Developmental Biology** 22, 1-22

Ng RK, and Gurdon JB (2005). Epigenetic memory of active gene transcription is inherited through somatic cell nuclear transfer. **Proc Natl Acad Sci USA** 102, 1957-1962

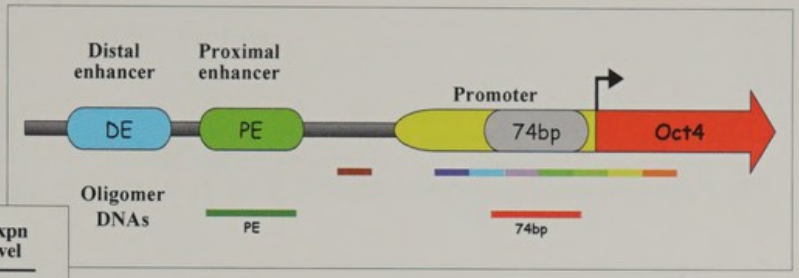
Jullien J, and Gurdon JB (2005). Morphogen gradient interpretation by a regulated trafficking step during ligand-receptor transduction. **Genes Dev** 19, 2682-2694

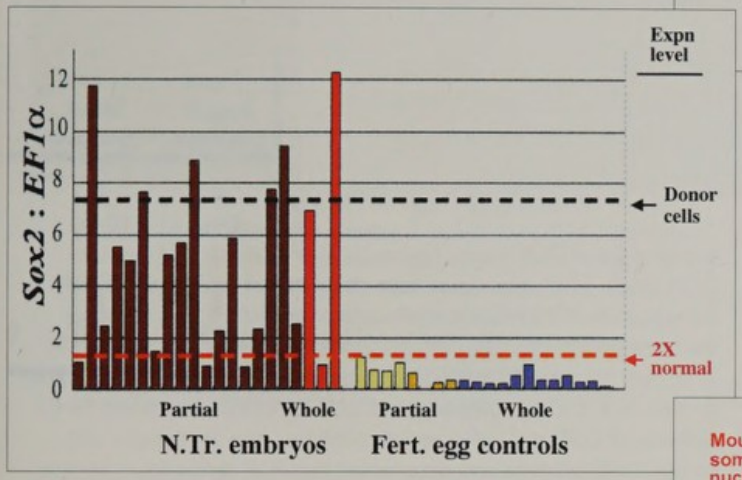
Simonsson S, and Gurdon JB (2004). DNA demethylation is necessary for the epigenetic reprogramming of somatic cell nuclei. **Nature Cell Biology** 6, 984-990

Gurdon JB, Byrne JA, and Simonsson S (2003). Nuclear reprogramming and stem cell creation. **Proc Natl Acad Sci USA** 100, 11819-11822

For complete list of this lab's publications since the last report, see number 19 on pp 56-61

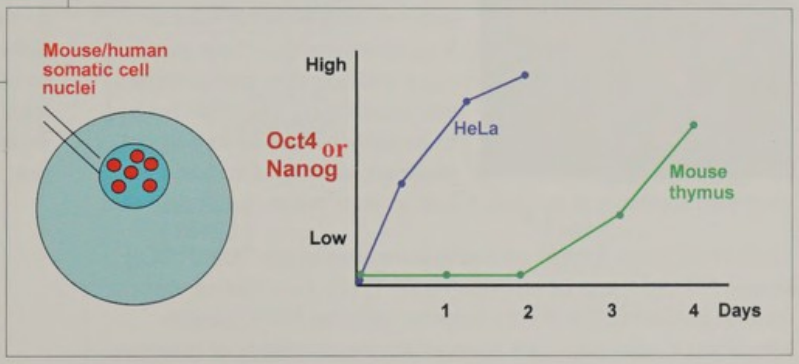
The mouse Oct4 promoter and corresponding DNA oligos used to identify Oct4-binding proteins in extracts of *Xenopus* oocytes.

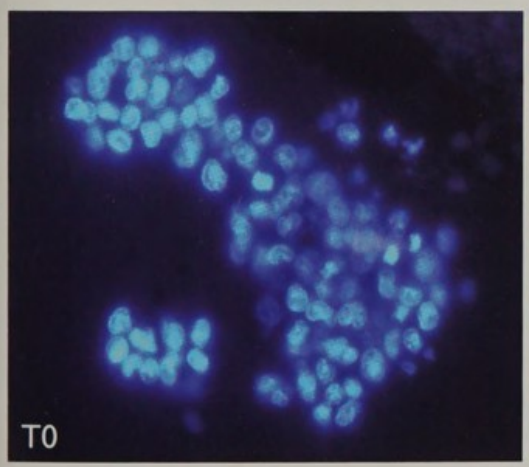


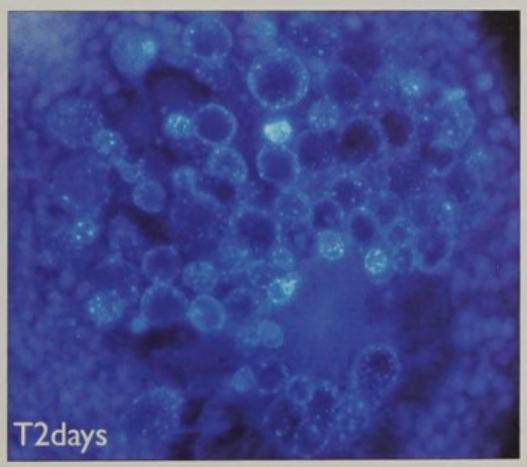


Epigenetic memory of an active gene state. Transcript levels of donor-specific gene expression in single nuclear transplant embryos and controls.

Some mammalian stem cell genes are rapidly activated in mammalian nuclei in *Xenopus* oocytes.





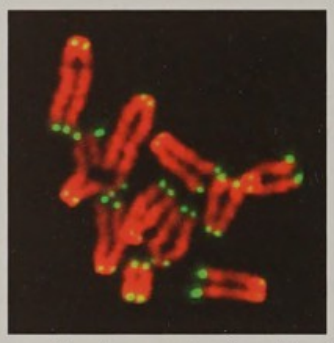


Human HeLa cell nuclei immediately and 2 days after injection into the germinal vesicle of a *Xenopus* oocyte. The nuclei are reprogrammed to re-express stem cell marker genes including Oct4 and Nanog.

Steve Jackson

Maintenance of genome stability in eukaryotic cells

Co-workers: Rimma Belotserkovskaya, Richard Chahwan, Ross Chapman, Julia Coates, Robert Driscoll, Kate Dry, Yaron Galanty, Sabrina Giavara, Simona Giunta, Serge Gravel, Jeanine Harrigan, Pablo Huertas, Christine Magill, Andreas Meier, Kyle Miller, Sophie Polo, Helen Reed, Alex Sartori, Philippa Smith, Jorrit Tjeertes



Our work focuses on the DNA damage response (DDR): the programmed set of events that optimises cell survival by detecting DNA damage, signalling its presence and mediating its repair. Our aim is to determine how these events occur and how they are controlled and coordinated. The DDR has been highly conserved throughout evolution, allowing us to take the combined approach of studying it both in yeast and in mammalian cells.

Much of our work focuses on events controlled by the "apical" DDR kinases ATM, ATR and DNA-PKcs (Figure 1) [1]. For instance, we recently discovered that ATM – together with the MRN complex with which it associates – are required for the processing of radiation-induced DNA double-strand breaks (DSBs) into structures that activate ATR [2]. Furthermore, we established that these events are restricted to the S and G2 phases of the cell cycle, indicating how ATM- and ATR-dependent signalling are coordinated and intimately connected to pathways of DSB repair (Figure 2) [2]. We also found that the DDR kinase Chk1 dissociates from chromatin in response to DNA damage in an ATM/ATR-dependent manner, and that this facilitates the transmission of DNA damage signals to downstream targets [3]. Finally, we recently discovered that a previously uncharacterised human protein, XLF, is a key component of the DNA-PKcs-dependent NHEJ pathway of DSB repair (Figure 3), established how it interacts with known NHEJ proteins and determined that XLF deficiency in people leads to radiosensitivity and immune deficiency [4]. These and other exciting areas of investigation will be further pursued over the coming year.

[1] Falck J, Coates J and Jackson SP (2005) Conserved modes of recruitment of ATM, ATR and DNA-PKcs to sites of DNA damage. **Nature** 434, 605-611

[2] Jazayeri A, Falck J, Lukas C, Bartek J, Lukas J, Smith GCM and Jackson SP (2006) ATM- and cell cycle-dependent regulation of ATR in response to DNA double-strand breaks. **Nat Cell Biol**. 8, 37-45

[3] Smits VAJ, Reaper PM and Jackson SP (2006) Rapid PIKK-dependent release of Chk1 from chromatin promotes the DNA-damage checkpoint response. **Current Biology** 16, 150-159

[4] Ahnesorg P, Smith P and Jackson SP (2006) XLF interacts with the XRCC4-DNA ligase IV complex to promote DNA nonhomologous end-joining. **Cell** 124, 301-313

For complete list of this lab's publications since the last report, see numbers 2, 3, 11, 18, 22, 23, 30, 49, 52, 55 & 67 on pp 56-61

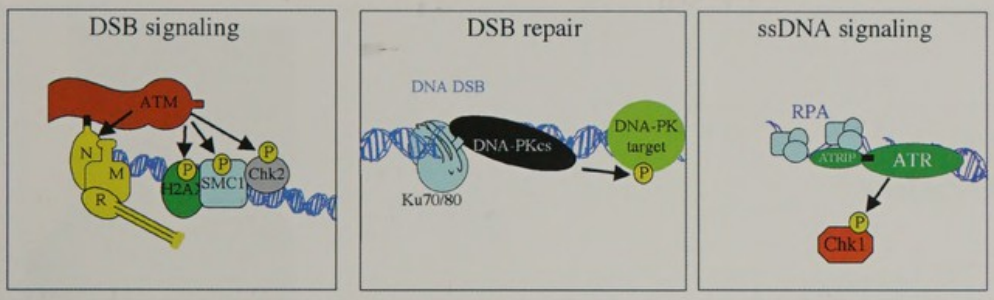


Fig 1: Model for common DNA-damage recruitment and activation mechanisms for the apical DDR kinases. ATM, DNA-PKcs and ATR are recruited and activated at sites of damage through interactions with their partner proteins – NBS1 (part of the MRN complex), Ku80 and ATRIP, respectively – in order to bring about DDR signalling or repair, as indicated.

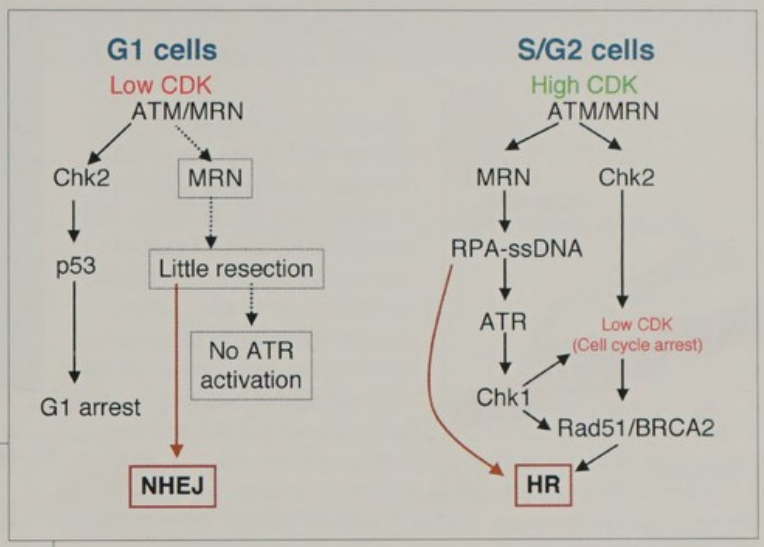


Fig 2: Cell-cycle coordination of DSB signalling and repair. In G1, cells carry out little DSB resection, leading to activation of ATM-dependent signalling and DSB repair by non-homologous end-joining (NHEJ). In S and G2 cells, ATM signalling also occurs but in these circumstances, DSBs are then resected to produce single-stranded DNA which triggers activation of ATR and leads to DSB repair by homologous recombination (HR).

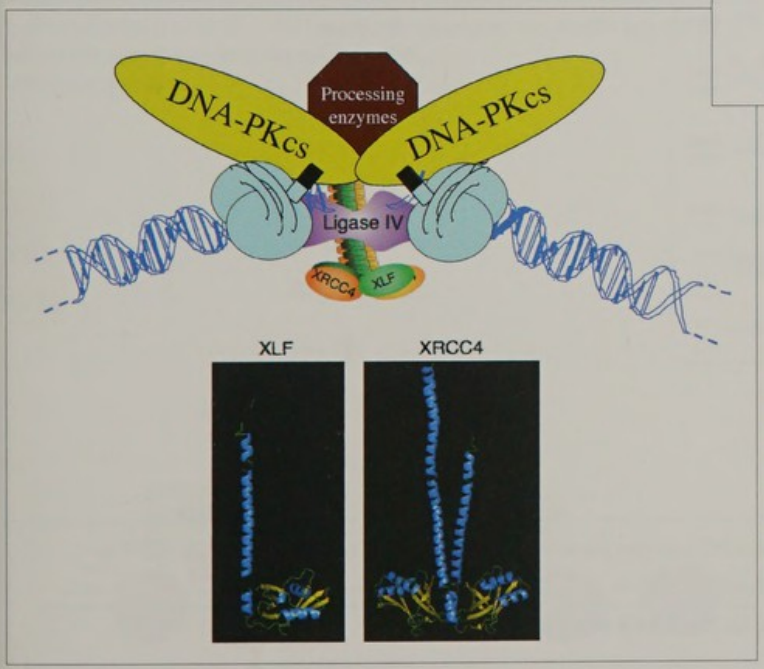


Fig 3: Top: Assembly of NHEJ proteins at the site of a DSB. Shown are Ku and DNA-PKcs, processing enzymes that are required to "clean up" DNA ends, and the DNA ligase IV-XRCC4-XLF complex. Bottom: XLF is predicted to display similarity to the structure of XRCC4 that has been determined experimentally (Sibanda BL et al (2001) Crystal structure of an Xrcc4-DNA ligase IV complex. **Nat. Struct. Biol.** 8, 1015-1020).

Tony Kouzarides

Function of Chromatin Modifications

Co-workers: Hatice Akarsu, Andrew Bannister, Till Bartke, Maria Christophorou, Alistair Cook, Silvia Dambacher, Sophie Deltour, Karen Halls, Paul Hurd, Antonis Kirmizis, David Lando, Susana Lopes, Chris Nelson, Nikki Oliver, Claire Pike, Helena Santos Rosa, Blerta Xhemalce

Our group is interested in defining the mechanisms by which chromatin modifications function to regulate cellular processes. Our attention is focused on a set of enzymes (acetylases, deacetylases, methylases and kinases), which regulate transcription by covalently modifying histones. We would like to understand what biological processes these enzymes control and the precise role of each modification on chromatin dynamics. In addition, a number of chromatin modifying enzymes have been implicated in the genesis of cancer, so we are dissecting as far as possible the pathways misregulated in cancer cells.

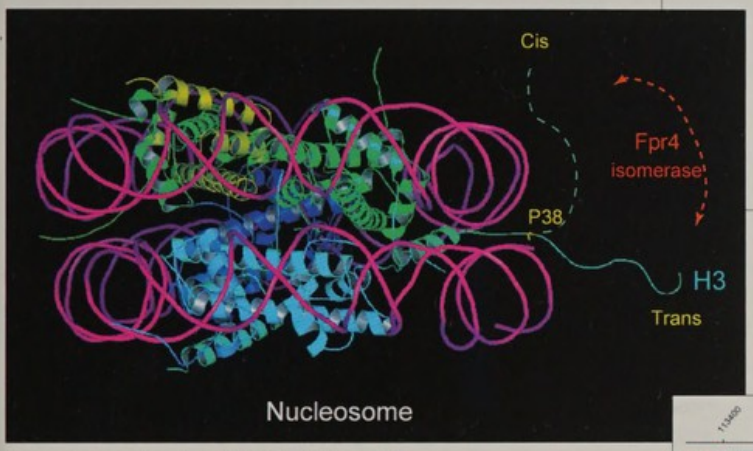
We are taking a number of complimentary approaches to characterise chromatin modifications. We use yeast as a model system whenever possible, since it has a much simpler modification pattern. We are using Chromatin Immunoprecipiation experiments on a genome-wide yeast and human arrays to map the position of all known and some novel modifications. We are also reconstituting recombinantly, nucleosomes carrying specific combinations of modifications, in order to understand how they affect transcription, how they affect compaction of chromatin and to identify specific proteins that recognise them.

Histones are very highly modified. Despite their abundance, we believe that more modifications are likely to exist on histones. This complexity is probably necessary because histones integrate many signalling pathways with biological processes involving DNA metabolism and function. A major drive at the moment is to identify new histone modifications, as the pathways that control them may well be deregulated in cancer. Recently we have characterised a novel non-covalent modification, Proline Isomerisation. We have identified an enzyme in yeast that can isomerise prolines in the tail of histone H3 and regulate transcription of a specific subset of genes. This new modification has the potential to bend the tail and therefore may have profound effects on chromatin structure.

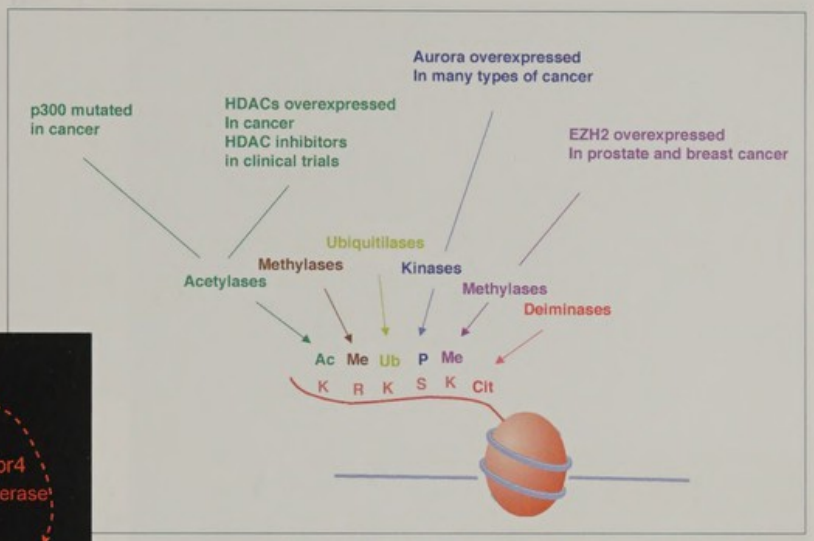
Nelson CJ, Santos-Rosa H and Kouzarides T (2006) Proline isomerisation of histone H3 regulates lysine methylation and gene expression. **Cell** 126, 905-916

Bannister AJ, and Kouzarides T (2005) Reversing histone methylation. **Nature** 436, 1103-1106.

For complete list of this lab's publications since the last report, see numbers 4, 25, 39, 41, 64 & 66 on pp 56-61

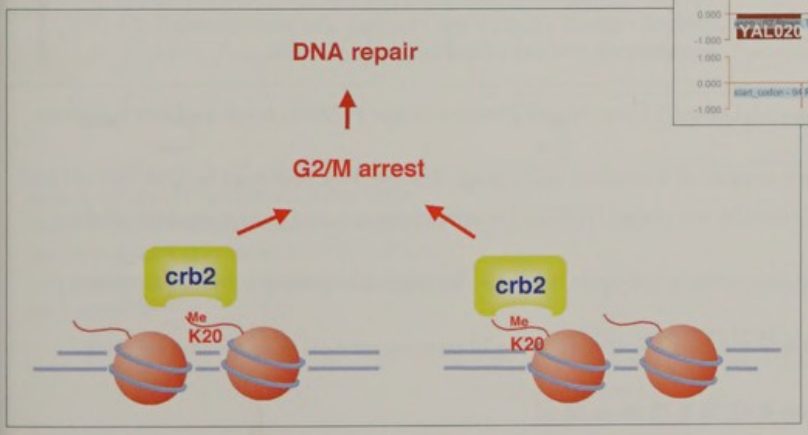


Isomerisation of proline 38 in the histone H3 tail has the potential to bend the tail and affect chromatin structure.



Chromatin modifying enzymes are deregulated in cancer.

Genomic pattern of methylation at all currently known methylation sites in yeast (part of chromosome I shown).

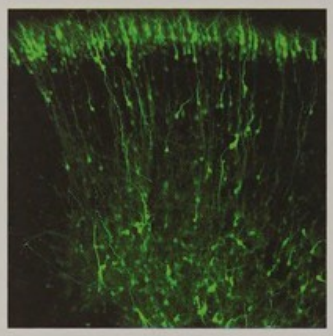


Methylation of H4K20 recruits the CrB2 protein to mediate G/2M arrests and allows cells to repair damaged DNA.

Rick Livesey

Neocortical stem and progenitor cell biology

Co-workers: Juliet Barrows, Dean Griffiths, Grace Nisbet, Stephen Sansom, James Smith, Tatiana Subkhankoulova, Uruporn Thammongkol



The neocortex is the part of the brain that integrates sensations, executes decisions and is responsible for cognition and perception. Neurons in the cortex are organised in two ways: they belong to one of six layers of neurons, each of which is generated in a stereotyped order, and they belong to a discrete piece or area of the cortex that is dedicated to a single function such as visual processing or motor control.

All of the neurons in the cortex are generated from a population of multipotent neocortical stem and progenitor cells. The majority of the research in the lab centres on the biology of neocortical stem cells and in particular how neocortical stem cells produce layer-specific neurons in order (the timing problem) and for the correct area (the patterning problem).

Our current work on the patterning problem is focused on how a transcription factor-based map that controls spatial identity is set up in neocortical stem cells and subsequently used to produce spatially discrete populations of neurons. To do so, we combine *in vivo* location analysis by chromatin-IP (ChIP-on-chip) to identify the target genes of each transcription factor with expression profiling following gain and loss of function analyses of each factor and bioinformatics to produce predictive models of stem and progenitor cell decision making.

How neurons for specific layers are generated in order is a timing problem, in that it is controlled by a poorly understood cellular mechanism intrinsic to neocortical stem cells. Our work in this area concentrates on testing candidate genes and mechanisms for controlling developmental timing in neocortical stem cells *in vivo*. Finally, the lab is also studying some of the clinical consequences of our research, particularly in the aetiology and pathogenesis of autistic spectrum conditions.

Inset left: Differentiating neocortical neurons (green, GFP expressing): live confocal image of a cortical slice four days after electroporation of a GFP-expressing plasmid into neocortical progenitor cells

Cobb BS, Hertweck A, Smith J, O'Connor E, Graf D, Cook T, Smale ST, Sakaguchi S, Livesey FJ, Fisher AG and Merkenschalager M (2006) A role for Dicer in immune regulation. **J Exp Med** 203, 2519-27

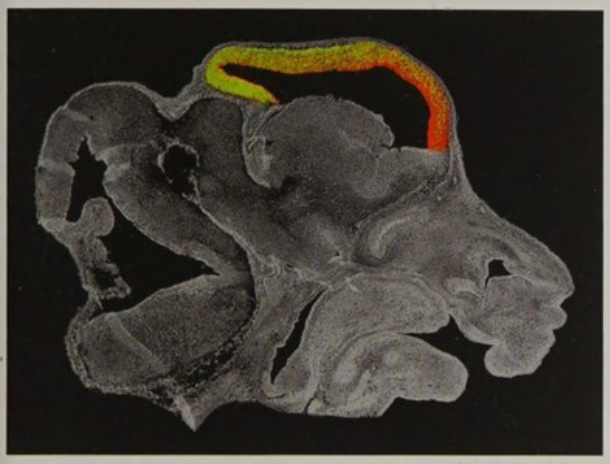
Livesey FJ, Young TL and Cepko CL (2004) An analysis of the gene expression program of mammalian neural progenitor cells. **Proc Natl Acad Sci USA** 101, 1374-9

Sansom SN, Hebert JM, Thammongkol U, Smith J, Nisbet G, Surani MA, McConnell SK and Livesey FJ (2005) Genomic characterisation of a Fgf-regulated gradient-based neocortical protomap. **Development** 132, 3947-61.

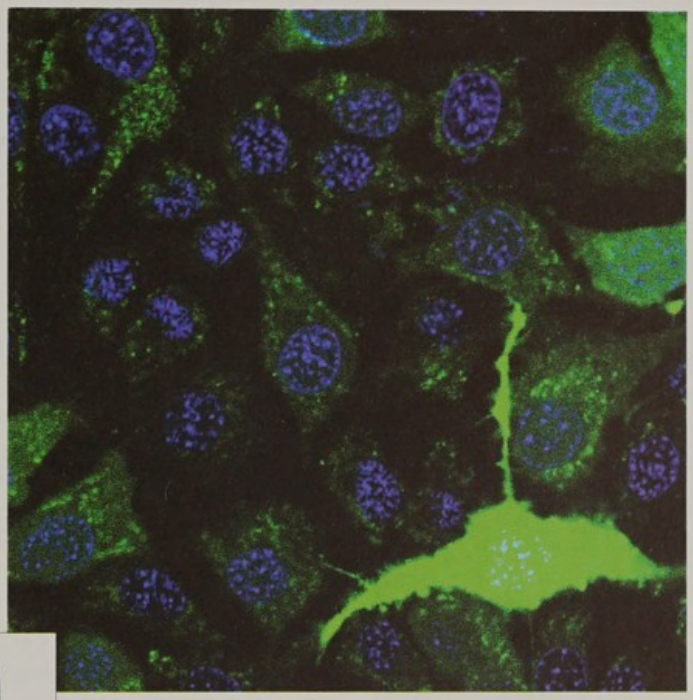
Subkhankulova T and Livesey FJ (2006) Comparative evaluation of linear and exponential amplification techniques for expression profiling at the single cell level. **Genome Biol** 7, R18

Yano K, Subkhankulova T, Livesey FJ and Robinson HP (2006) Electrophysiological and gene expression profiling of neuronal cell types in mammalian neocortex. **J Physiol** 575, 361-5

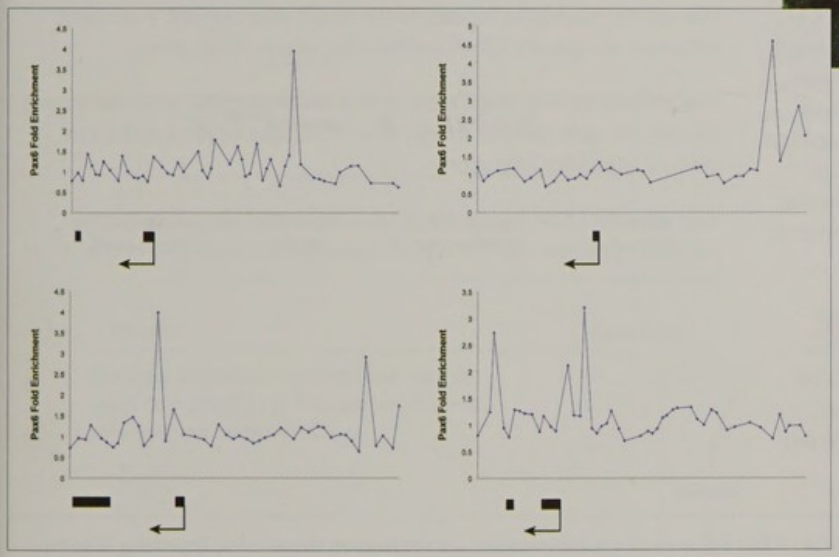
For complete list of this lab's publications since the last report, see numbers 8, 42, 56 & 72 on pp 56-61



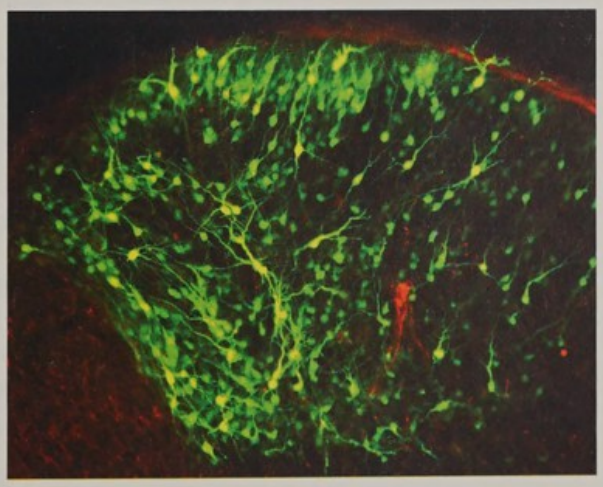
A readout of neocortical patterning is front-to-back (red) and back-to-front (green) gradients of expression of transcription factors across the developing neocortex, as shown by two-colour fluorescent *in situ* hybridisation.



Subcellular distribution of a GFP-tagged form of a novel FGF signalling inhibitor, expressed in fibroblasts.



Binding curves of a neocortical transcription factor to the promoters of four target genes in neocortical stem cells, as detected in ChIP-on-chip experiments. Peaks indicate bound regions of each promoter.

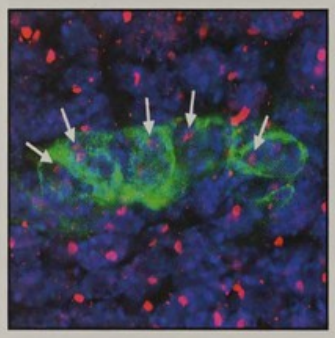


Migrating neurons (green, GFP-expressing) in a neocortical slice culture.

Anne McLaren

The development of mouse primordial germ cells (PGCs) and the pluripotent embryonic germ (EG) cells derived from them.

Co-workers: Dilly Bradford, Cristina Eguizabal, Tanya Shovlin



Our research focuses on the epigenetic changes that PGCs undergo both during their normal *in vivo* development, and also when they are cultured with growth factors appropriate for reprogramming into pluripotent EG cells. We are particularly interested in the X chromosome inactivation and reactivation effects shown by female (XX) PGCs and their epiblast precursors, and by the entry of female PGCs into meiotic prophase before birth. Our studies aim to distinguish between cell-autonomous effects programmed into the germ cells themselves, and those induced by signals from the surrounding somatic environment.

Genes subject to genomic imprinting erase their sex-specific DNA methylation during or shortly after their migration to the site of the future gonads. EG cell lines derived from male (XY) or female (XX) PGCs exhibit the appropriate sex-specific methylation pattern on imprinted genes, but studies on EG cell lines made from sex-reversed embryos (XX male, XY female) show that the methylation pattern, at least for H19, depends on the sex-chromosome constitution (XX versus XY) rather than on the sex of the embryo from which they were derived. For the germ cells, the effect of the sex-chromosome constitution is much less marked, perhaps because of the countervailing influence of the tissue environment in which they are developing. We aim to investigate aspects of the tissue environment that might influence sex-specific DNA methylation of imprinted genes.

We are also looking at differences and developmental potential among ES cells, EG cells derived shortly after PGC specification, and those derived later, after migration.

Inset left: Blimp1/GFP—positive PGC precursors, each positive (as are the surrounding epiblast cells) for H3K27me (red spot), indicating an inactive X chromosome.

Durcova-Hills G, Hajkova P, Sullivan S, Barton SC, Surani MA and McLaren A (2006) Influence of sex chromosome constitution on the genomic imprinting of germ cells. **PNAS USA** 103, 11184-8

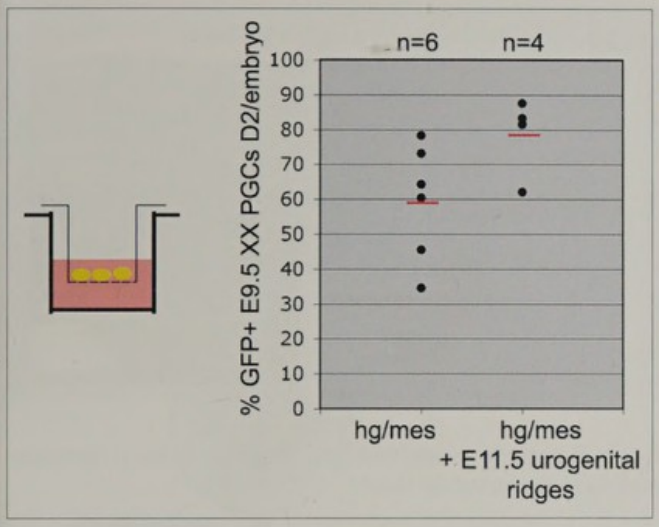
Durcova-Hills G, Adams IR, Barton SC, Surani MA and McLaren A (2006) The role of exogenous fibroblast growth factor-2 on the reprogramming of primordial germ cells into pluripotent stem cells. **Stem Cells** 24, 1441-1449

Moffett A, Loke C and McLaren A (Eds) (2006) **Biology & Pathology of Trophoblast**, Camb Univ Press

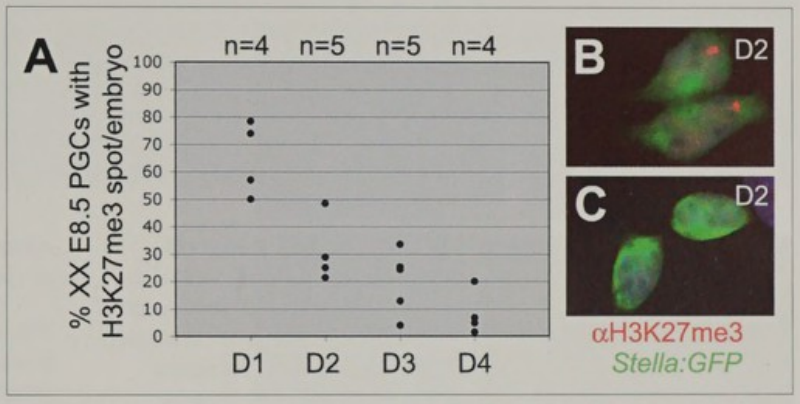
Ko MS and McLaren A (2006) Epigenetics of germ cells, stem cells, and early embryos. **Dev Cell** 10, 161-166

Surani MA and McLaren A (2006) Stem cells: a new route to rejuvenation. **Nature** [News & Views] 443, 284-5

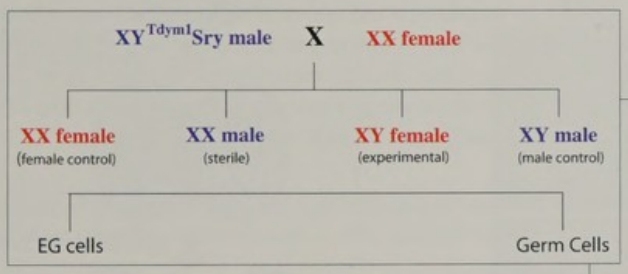
For complete list of this lab's publications since the last report, see numbers 12, 13, 34 & 59 on pp 56-61



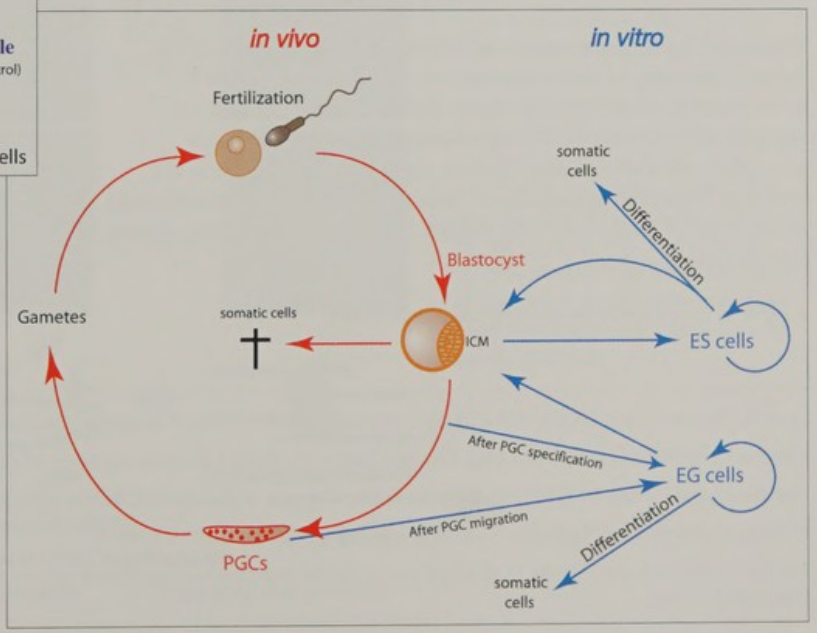
Migrating PGCs isolated from the hind gut, cultured in TransWells for 48 hrs, show significantly more reactivation of the silent X chromosome when genital ridge tissue is added to the culture medium than with hind gut tissue alone. The presence of genital ridge tissue appears sufficient to induce reactivation precociously in the 9.5 dpc PGCs. (Chuva de Sousa Lopes S and McLaren A, unpublished)



When PGCs are reprogrammed into pluripotent EG cells in culture, one of the first changes seen (A) is the loss of H3K27me3 (red spot, B), the histone modification indicative of an inactive X chromosome. After 48 hrs, most of the PGCs have lost the spot (C). (Chuva de Sousa Lopes S and McLaren A, unpublished)



We have studied sex-reversed and control germ cells, and EG cell lines derived from sex-reversed and control PGCs.

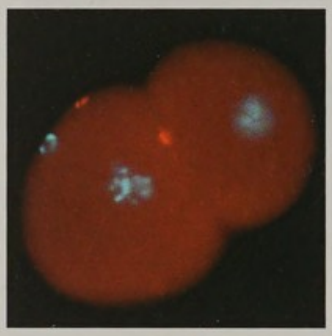


Pluripotent stem cell lines can be derived from early peri-implantation embryos (ES cell lines), and also from germ cells soon after PGC specification or later in the germ cell lineage after PGC migration.

Masanori Mishima

Molecular mechanism of cytokinesis

Co-workers: Juliet Barrows, Max Douglas, Andrea Hutterer, Julia Mason .



Cytokinesis is essential for cell proliferation. Failure of cytokinesis leads to aneuploidy or chromosomal instability, which has been associated with human cancers. Successful cytokinesis relies on a dynamic interplay between microtubules, the actin cytoskeleton, and membrane compartments under the control of the cell cycle machinery. In spite of its importance, the molecular mechanism of cytokinesis in animal cells has not yet been fully clarified.

We would like to understand cytokinesis more fully, in terms of the dynamic assembly of molecular machinery. The central spindle is a microtubule-based molecular assembly that forms between the segregating chromosomes during anaphase. During telophase, it associates with the ingressing cleavage furrow and matures into the midbody. These microtubule-based structures have crucial roles through all the steps of cytokinesis from initiation to completion. We will address the following questions:

- How is the central spindle/midbody assembled?
- How does the central spindle/midbody contribute to the progression of cytokinesis at the molecular level?

We will focus on centralspindlin, a stable protein complex of a mitotic kinesin-like protein and a Rho-family GTPase-activating protein (RhoGAP), which is crucial for assembly of the central spindle and the midbody. We will characterise the dynamic behaviour of centralspindlin and investigate centralspindlin-interacting proteins by using mammalian cultured cells and *Caenorhabditis elegans* embryos as model systems. In addition to biochemical and genetical analyses, live imaging both at single molecule level *in vitro* and at subcellular level *in vivo* will be performed. We will also develop experimental strategies to (in)activate molecules of interest *in vivo* in a reasonable time resolution to dissect the molecular mechanism of cytokinesis

Inset left: A *C. elegans* embryo finishing cytokinesis. Centralspindlin (red) is highly concentrated to the midbody when chromosomes are reforming nuclei (cyan).

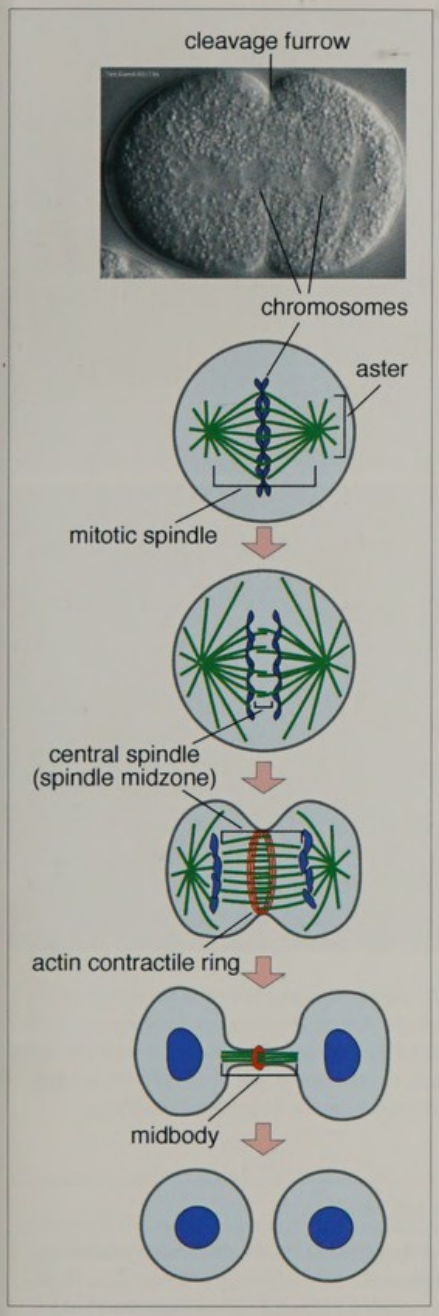
Guse A, Mishima M and Glotzer MA (2005) Conserved role for Aurora B phosphorylation of ZEN-4/MKLP1 in completion of cytokinesis. **Curr Biol** 15, 778-86

Mishima M, Pavicic V, Grüneberg U, Nigg EA, and Glotzer M (2004) Cell cycle regulation of central spindle assembly. **Nature** 430, 908-13

Mishima M, and Glotzer M (2004) Cytokinesis. In **Encyclopedia of Biological Chemistry** (WJ Lennarz & MD Lane eds), Elsevier, Oxford, vol 1, pp. 556-62

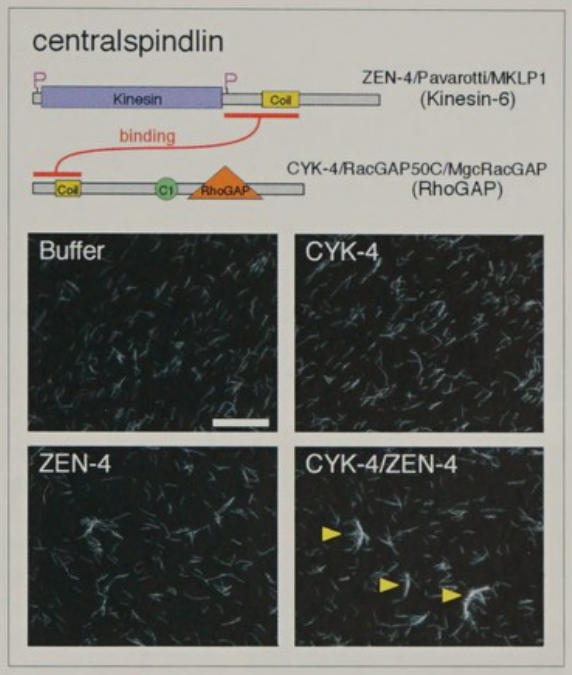
Mishima M and Glotzer M (2003) Cytokinesis: a logical GAP. **Curr Biol** 13, R589-91

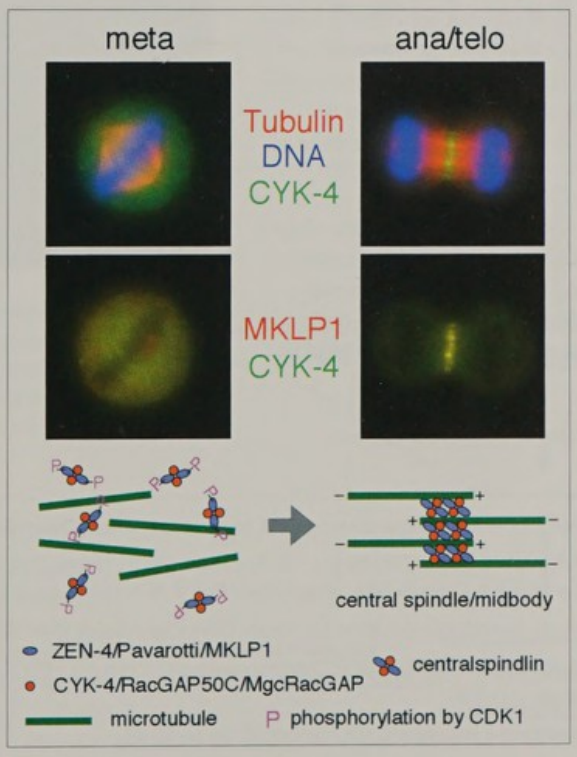
Mishima M, Kaitna S and Glotzer M (2002) Central spindle assembly and cytokinesis require a kinesin-like protein/RhoGAP complex with microtubule bundling activity. **Dev Cell** 2, 41-54



Cytokinesis

Centralspindlin is an evolutionarily conserved protein complex of a mitotic kinesin and a RhoGAP critical for the assembly of the central spindle. Being in a complex is essential both for the formation of the central spindle and for the *in vitro* microtubule-bundling activity. When incubated with microtubules, the complex causes the strong bundling of microtubules (arrowheads), while neither the kinesin subunit alone nor the RhoGAP subunit alone does.



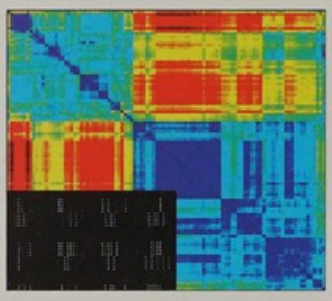


Centralspindlin dramatically changes its localisation at metaphase/anaphase transition under the control of a master cell-cycle regulating protein kinase, CDK1. The kinesin subunit is phosphorylated by CDK1 at the sites flanking its catalytic core (P). This phosphorylation reduces the affinity for microtubules and contributes to the prevention of premature formation of the central spindle before anaphase onset, ensuring proper segregation of genetic materials.

Eric Miska

Control of gene expression through non-coding RNA

Co-workers: Marloes Bagijn, Cheri Blenkiron, Heeran Buhecha, Alejandra Clark, Partha Pratim Das, Ethan Kaufman, Nic Lehrbach, Funda Sar, Stefanie Sassen, Robert Shaw



The recent discovery of microRNAs has added a completely new dimension to the control of eukaryotic gene expression. MicroRNAs are a large class of 18-26 nucleotide short regulatory RNAs. Approximately 1% of all known human genes encode microRNAs, but very little is known about their biological roles. Our laboratory is interested in understanding how microRNAs contribute to the determination of cell fate, ie the decision to divide, die or differentiate, and how deregulation of microRNAs may contribute to disease, in particular to cancer.

We use the powerful genetics of the nematode *Caenorhabditis elegans* to study the function of microRNAs. Our starting point is a collection of microRNA knockout strains covering the majority of all known microRNA genes in this organism. To place microRNAs into biological pathways we combine phenotypic analysis, expression studies, genetic screens and bioinformatics.

We are also interested in the mechanism of microRNA action.

Currently we are focusing on the Argonaute family of RNA-binding proteins, which have been implicated in both the mechanism of RNAi and microRNA pathways. Of particular interest to us are the orthologues of two *Drosophila Argonaute* family members, Aubergine and Piwi that define germ line identity in the fly. We use a combination of biochemical and genetic approaches to understand their function.

In invertebrates microRNAs have been implicated as regulators of developmental timing (eg *lin-4*), neuronal differentiation, cell proliferation, programmed cell death and fat metabolism. In contrast, no *in vivo* function for any microRNA has been established in mammals. To help uncover the biological roles of microRNAs in mammals we first ask the question where and when microRNAs are expressed using microarray profiling. One focus is the analysis of microRNA expression in primary human tumours. This work is being carried out as a collaboration with the Cancer Genomics Group at the Broad Institute of MIT, and Harvard.

Inset left: We have developed microRNA microarrays to profile microRNA expression in *C elegans* and mammals (insert). We compare the expression of microRNAs in different tissues, at different stages during development and under a variety of physiological conditions to understand where microRNAs act and how their expression is regulated. Shown here is a correlation heat map.

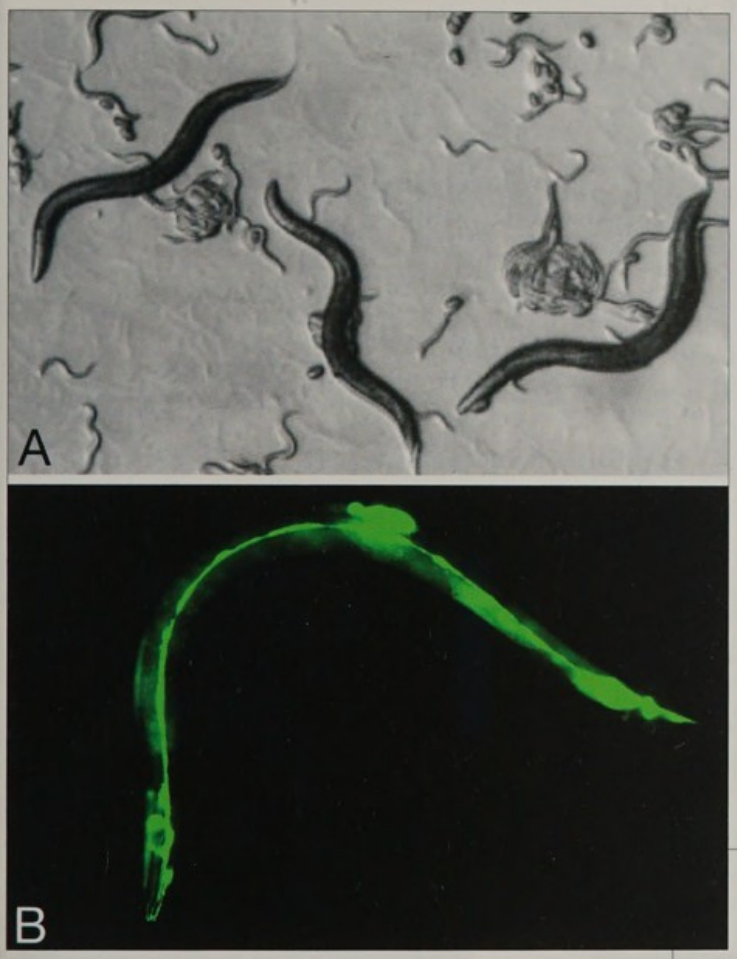
Alvarez-Garcia I, Miska EA (2005) MicroRNA functions in animal development and human disease. **Development** 132, 4653-4662

Abbott AL*, Alvarez-Saavedra E*, Miska EA*, Lau NC, Bartel DP, Horvitz HR, Ambros V (2005) The let-7 MicroRNA family members mir-48, mir-84, and mir-241 function together to regulate developmental timing in *Caenorhabditis elegans*. **Dev Cell** 9, 403-414 (* equal contribution)

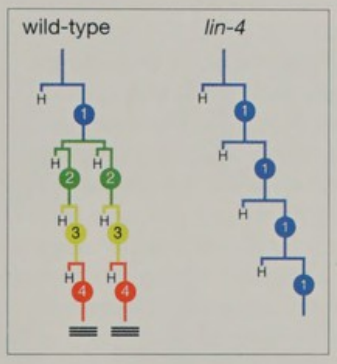
Miska EA (2005) How microRNAs control cell division, differentiation and death. **Curr Opin Genet Dev** 15, 563-568

Miska EA, Alvarez-Saavedra A, Townsend M, Yoshii A, Sestan N, Rakic P, Constantine-Paton M, Horvitz HR (2004) Microarray analysis of microRNA expression in the developing mammalian brain. **Genome Biology** 5(2), R60

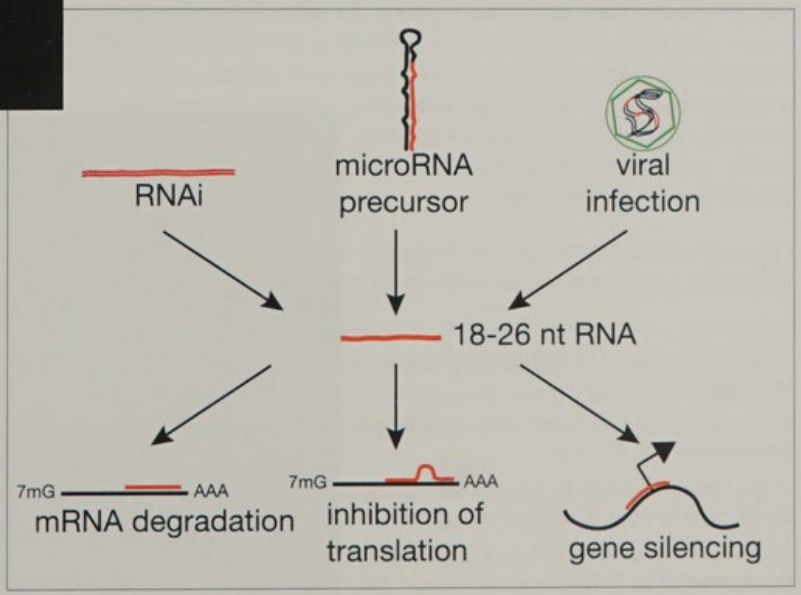
For complete list of this lab's publications since the last report, see number 41 on pp 56-61



A: we are using a functional genomics approach in *Caenorhabditis elegans* to study microRNA function. B: the microRNA miR-84 is expressed in a number of cell types including the seam cells, as assayed by a GFP reporter in the living animal.



The first microRNA to be identified was the product of the *C elegans* gene *lin-4*. Loss of function of *lin-4* leads to an over-proliferation defect of the seam cells, which are part of the outer epithelial covering of the worm. The cell divisions of the first larval stage (1) are reiterated in these mutants: 1, 1, 1, 1, ...

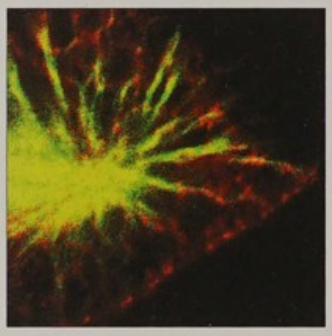


Short RNAs as key players of gene regulation: Primary microRNA gene transcripts contain stem-loop structures that are processed by RNAse type III enzymes such as Dicer to give rise to the mature microRNA. Dicer is also required for the processing of double-stranded viral RNA and for generating siRNAs in RNAi. microRNAs can act through the inhibition of translation, mRNA degradation and possibly transcriptional gene silencing.

Nancy Papalopulu

Molecular control of neurogenesis in vertebrate embryos

Nancy and staff have transferred to the Faculty of Life Sciences, University of Manchester



During embryonic development neuroectodermal cells exit the cell cycle and differentiate in a stereotypical spatial and temporal pattern. Other cells remain undifferentiated and serve as stem cells for growth and later waves of neurogenesis. We aim to understand how the balance of differentiation and progenitor maintenance is achieved and we use the frogs *Xenopus laevis* and *Xenopus tropicalis* as model systems.

We are studying the function and regulation of localised transcription factors, such as FoxG1, a master gene controlling neurogenesis and cell division in the forebrain. Our current emphasis is on the role of protein modifications that serve to integrate signalling pathways in controlling the activity of FoxG1. In parallel, we are using *Xenopus* microarrays to identify target genes in order to decipher the gene networks controlling differentiation in the forebrain.

Neuronal differentiation is also controlled by the intrinsic competence of the cells to differentiate. This is the result of asymmetric cell divisions of polarised cells that generate outer polar and inner apolar cells on the neural plate. We have found that only inner apolar cells are competent to participate in early neurogenesis while outer polar cells have a propensity to remain as undifferentiated progenitor cells to the end of embryogenesis. In these cells, aPKC is located on the apical membrane and Lgl-2 on the basolateral side. By gain and loss of function experiments we have shown that an antagonistic interaction between aPKC and Lgl-2 defines the proportion of specialised apical and basolateral membrane in these cells. We are now investigating whether these membrane asymmetries influence the transcriptional program of the neuroepithelial cells. By microarray analysis, we have identified several genes that are specific for polarised or apolar cells of the neural plate and their function is now investigated.

Finally, gain and loss of function screens based on a *X tropicalis* EST project, has uncovered novel genes that affect many aspects of neural development.

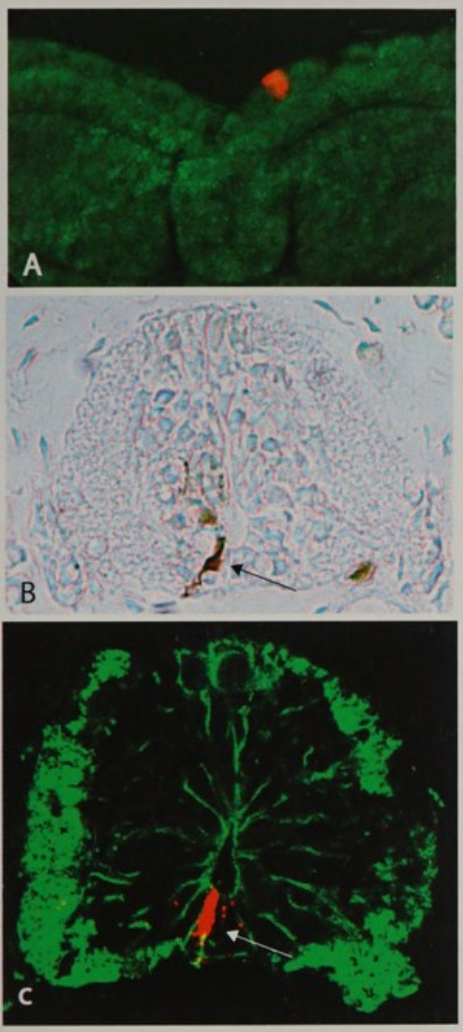
Inset left: Dynein-decorated (red) astral microtubules (green) of *Xenopus* blastula cells. (Bernhard Strauss).

Voigt J and Papalopulu N (2006) A dominant negative Cullin-1, an E3 ubiquitin ligase, disrupts the correct allocation of cell fate in the neural crest lineage. **Development** [in press]

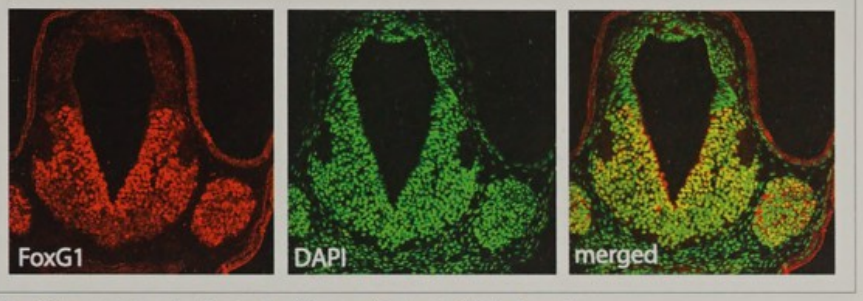
Chalmers A, Pambos M, Lang S, Wylie C and Papalopulu N (2005) aPKC, crumbs3 and Lgl –2 control apical/basal polarity in early vertebrate development, **Development** 132, 977-986

Voigt J, Chen JA, Gilchrist M, Amaya E and Papalopulu N (2005) Expression cloning screening of a unique and full-length set of cDNA clones is an efficient method to identify gene function in *Xenopus* neurogenesis, **Mech Dev** 122, 289-306

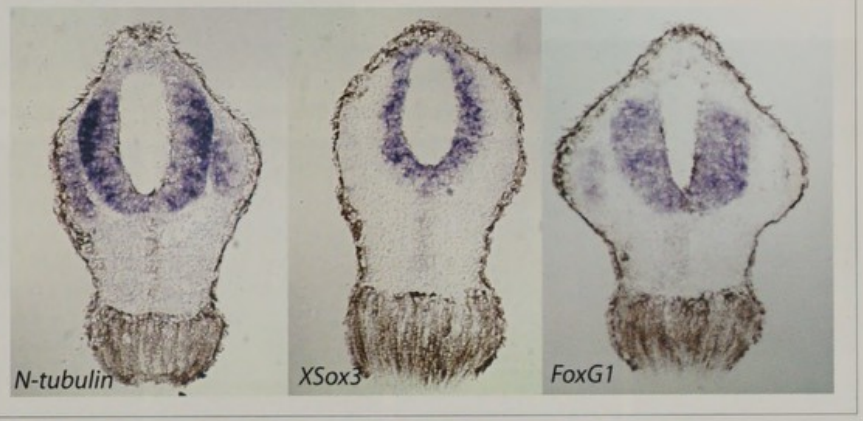
Chalmers AD, Strauss B and Papalopulu N (2003) Oriented cell divisions asymmetrically segregate aPKC and generate cell fate diversity in the early *Xenopus* embryo. **Development** 130, 2657-68



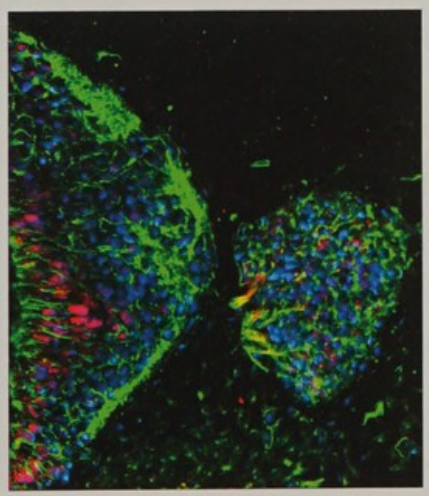
Single cell injections of superficial cells at the neural plate stage with a lineage label (A) reveals that they are fated to become radial glia cells at the feeding tadpole stage, based on their morphology (B) or antibody staining with GFAP (C) (Eva Asscher)



FoxG1 protein localisation in the *Xenopus* forebrain (Tarik Regad)



FoxG1 RNA is present in differentiating neurons (*N-tubulin* positive) as well as proliferating progenitors (*XSox3* positive) (Martin Roth)



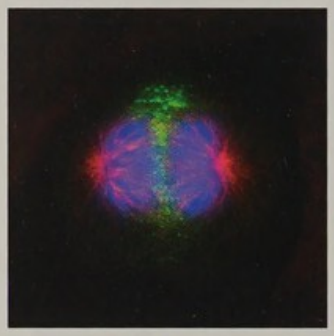
Olfactory axons (yellow) emerging from the olfactory placode and directed towards the olfactory bulb (Tarik Regad)

Jonathon Pines

How do cells control mitosis?

Co-workers: Caroline Broad, Fay Cooke, Barbara Di Fiore, Suzanne Floyd* Olivier Gavet, Anja Hagting, Daisuke Izawa, Mark Jackman, Lars Koop, Catherine Lindon*, Takahiro Matsusaka, Bernhard Strauss, Jakob Nilsson, Mona Yekezare

* Suzanne is working with Catherine Lindon (independent MRC Fellow).



How do cells regulate entry to mitosis? And, once in mitosis, how do cells coordinate the remarkable events of chromosome alignment and segregation with cell division itself (cytokinesis) to ensure that the two daughter cells receive an equal and identical copy of the genome? The answer seems to be the interplay between protein kinases, phosphatases and ubiquitin-mediated proteolysis, in particular ubiquitination mediated by the Anaphase Promoting Complex/Cyclosome (APC/C), and this is the focus of our research. Because mitosis is a highly dynamic process we are studying events in living cells by time-lapse fluorescence microscopy. We use FRAP and photo-activation to gain a better understanding of the kinetics of protein behaviour, deconvolution to improve the spatial resolution and FRET to assay protein-protein interaction and kinase activity.

To understand how cells first initiate mitosis we are analysing the behaviour of the mitotic cyclin-CDKs, cyclins A and B1, and their regulation by phosphorylation and subcellular localisation. We use GFP-fusion proteins to reveal the dynamics of protein localisation through the cell cycle, and to define how proteins are targeted to specific subcellular structures. To identify the proteins responsible for targeting the cyclins, and to provide insights into Cdk substrates, we are analysing protein complexes by mass spectrometry. Recently, we have developed biosensors to assay mitotic kinase activities *in vivo*.

To understand how proteolysis is used to regulate progress through mitosis we assay the degradation of the GFP-fusion proteins in living cells. These studies are beginning to reveal how the APC/C is first activated and, most importantly, how it is able to select a particular protein for destruction at a specific time in mitosis to coordinate events such as chromosome segregation and cytokinesis. We have strong evidence that the ubiquitination machinery is spatially regulated in mitosis and we are investigating whether this is responsible for the exquisite control of protein degradation by the spindle assembly checkpoint. We hope that these studies will increase our understanding of how cells control their division to prevent improper chromosome segregation (aneuploidy) that is the hallmark of many cancers.

Inset left: A deconvolved image of a HeLa cell stained for Aurora B (green), tubulin (red) and DNA (blue). (Suzanne Floyd)

Pines J (2005) Mitosis: a matter of getting rid of the right protein at the right time. **Trends in Cell Biology**, 16, 55-63

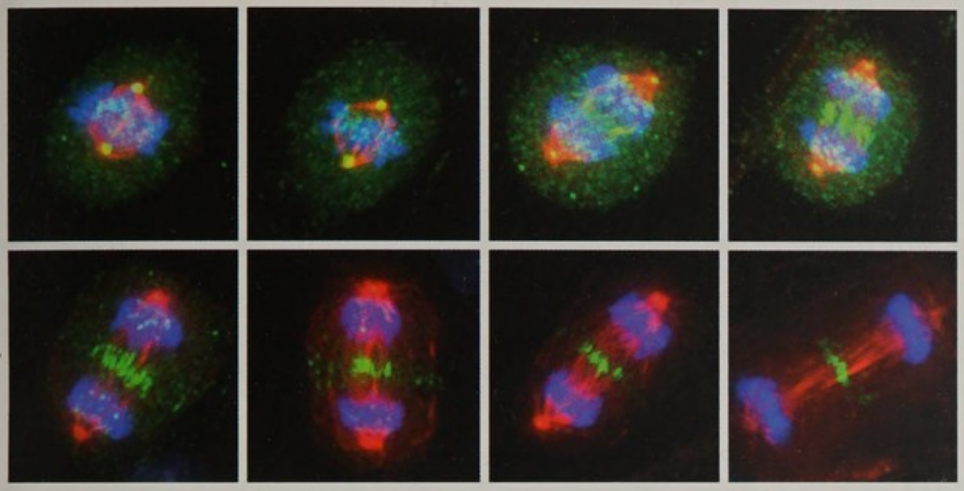
Acquaviva C, Herzog F, Kraft C and Pines J (2004) The Anaphase Promoting Complex/Cyclosome is recruited to centromeres by the spindle assembly checkpoint. **Nature Cell Biology** 6, 892-898

Matsusaka T, and Pines J (2004) Chfr acts with the p38 stress kinase to block entry to mitosis in mammalian cells. **J Cell Biol.** 166, 507-516

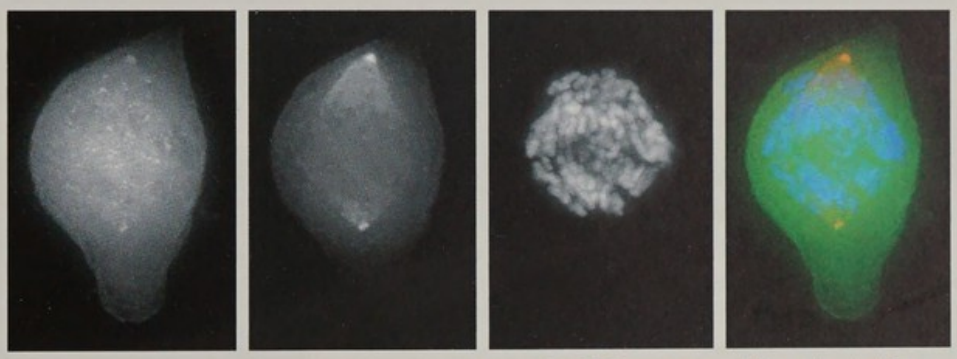
Lindon C and Pines J (2004) Ordered proteolysis in anaphase inactivates Plk1 to contribute to proper mitotic exit in human cells **J Cell Biol.** 164, 233-241.

Jackman M, Lindon C, Nigg EA and Pines J (2003) Active cyclin B1-Cdk1 first appears on centrosomes at the end of prophase. **Nature Cell Biol.** 5, 143-148

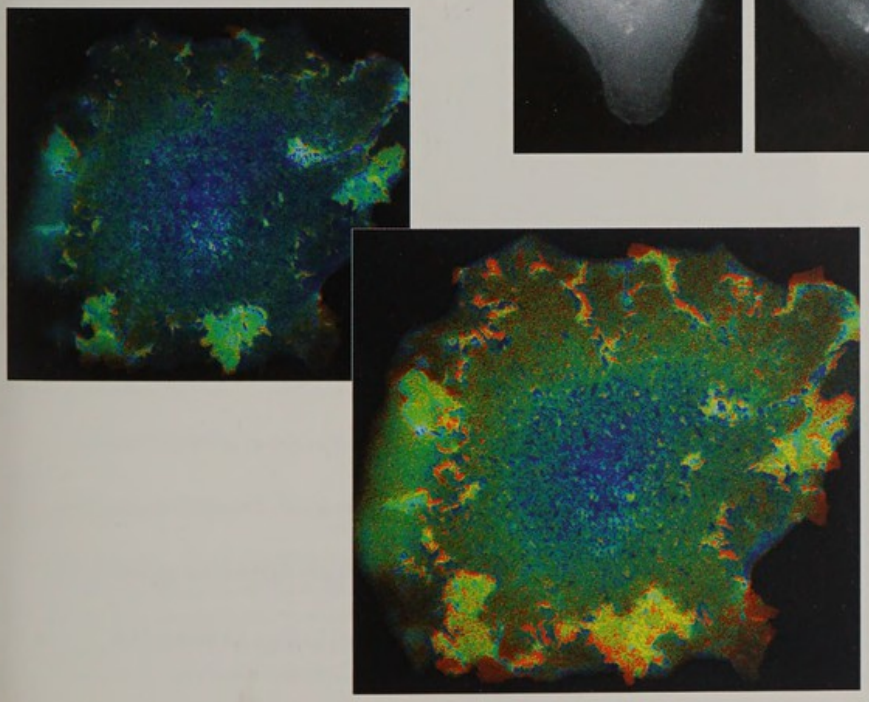
For a complete list of this lab's publications since the last report, see numbers 1, 21, 44 & 45 on pp 56-61



Plk: Deconvolved images of Hela cells progressing through mitosis stained for Polo-like kinase 1 (green), tubulin (red) and DNA (blue). (Catherine Lindon).



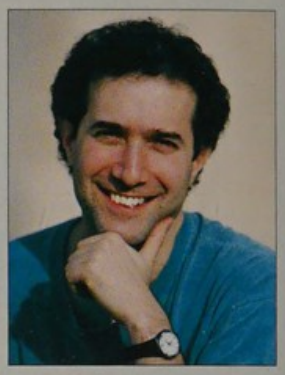
Aurora_Cdc20: Pro-metaphase Hela cell stained for (Cdc20, left and green; Aurora A, middle and red; DNA, right and blue) (Lorena Clay).



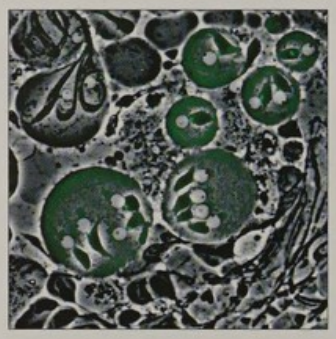
A COS cell expressing a FRET reporter for ras activation before (left) and after EGF stimulation (right). Colour shift represents the level of activation from blue (low) to green to yellow to red (high). (Olivier Gavet)

Jordan Raff

Molecular analysis of the centrosome



Co-workers: Renata Basto, Paul Conduit, Sue Croysdale, Carly Dix, Jeroen Dobbelaere, Joyce Lau, Eliana Lucas, Nina Peel, Naomi Stevens



The centrosome is the main microtubule organising centre in animal cells, and it is thought to play an important role in organising many cell processes. We have shown DSas-4 is essential for centriole replication in flies, and that centrioles are rapidly lost from DSas-4 mutant cells during development (Figure 1). Amazingly, we find that morphologically normal mutant flies are born with near normal timing at near normal rates (Figure 2), even though these flies completely lack centrioles, centrosomes, cilia and flagella. The flies die shortly after birth, however, as they lack cilia in their sensory neurons, and so are uncoordinated.

How do flies survive without centrosomes? We find that about 30% of the asymmetric divisions of acentrosomal neuroblasts are abnormal, but flies can somehow compensate for these defects and neurogenesis is not dramatically perturbed. We are currently studying how processes such as oogenesis, spermatogenesis, stem cell divisions and cell migrations occur in mutant flies.

These studies suggest that the primary function of centrosomes in mitosis is not to organise cell division, but rather to ensure the efficient segregation of the centrioles. We are now examining how the centrioles organise the pericentriolar material (PCM) around themselves. Live cell imaging of centrosomin (cnn) mutant embryos has revealed that this protein is required to maintain the proper connection between the centrioles and the PCM (Figure 3 and 4). We are currently performing a genome-wide RNAi screen to search for other proteins that are required for the recruitment of the PCM around the centrioles.

Inset left: Centrioles are essential for cilia and flagella formation. Phase contrast image showing the localisation of a centriolar marker GFP-PACT (green) during spermatid elongation.

Basto R, Lau J, Vinogradova T, Gardiol A, Wood G, Khodhjakov A, and Raff JW (2006) Flies without centrioles. **Cell** 125, 1375-1386

Barros T, Kinoshita K, Hyman AA and Raff JW (2005) Aurora-A activates D-TACC/Msps complexes exclusively at centrosomes to stabilise centrosomal MTs. **J Cell. Biol.** 170, 1039-1046

Kinoshita K, Noetzel TL, Pelletier L, Mechtler K, Drechsel DN, Schwater A, Lee M, Raff JW and Hyman AA (2005) Aurora A phosphorylation of TACC3/Maskin is required for centrosome dependent microtubule assembly in mitosis. **J Cell Biol.** 170, 1047-1055

Chodagam S, Royou A, Whitfield W, Karess R and Raff JW (2005) The centrosomal protein CP190 regulates myosin function during early *Drosophila* development. **Curr Biol.** 15, 1308-1313

Martinez-Campos M, Basto R, Baker J, Kernan M and Raff JW (2004) The *Drosophila* pericentrin-like protein is essential for cilia/flagella function but appears to be dispensable for mitosis. **J Cell Biol.** 165, 673-683

Raff JW (2004) Centrosomes in a developing organism: lessons from *Drosophila*. In: "**Centrosomes in Development and Disease**". Ed Nigg, EA Wiley-VCH.

For complete list of this lab's publications since the last report, see number 5 on pp 56-61

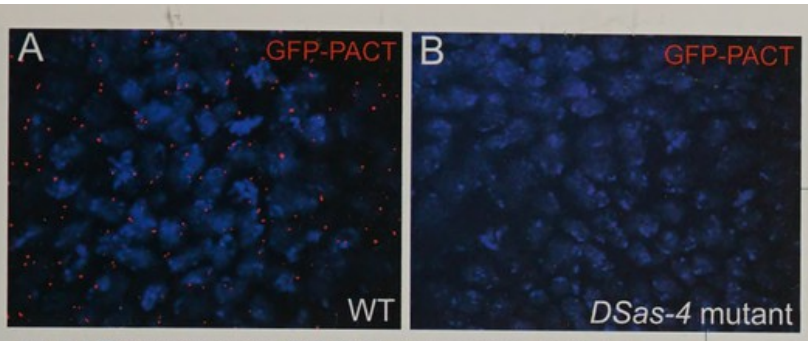


Figure 1: The centriole marker GFP-PACT stains centrioles in WT 3rd instar larval brains (A), but centrioles are not detectable in DSas-4 mutant brains (B).

Figure 2: A wild type (WT) fly (top) and a DSas-4 mutant fly (bottom). The DSas-4 mutant fly lacks proprioception (as its sensory neurons are non-funtional due to the lack of cilia), and so it cannot hold its wings or legs in their normal position. In every other respect, however, the mutant fly appears to be morphologically normal.

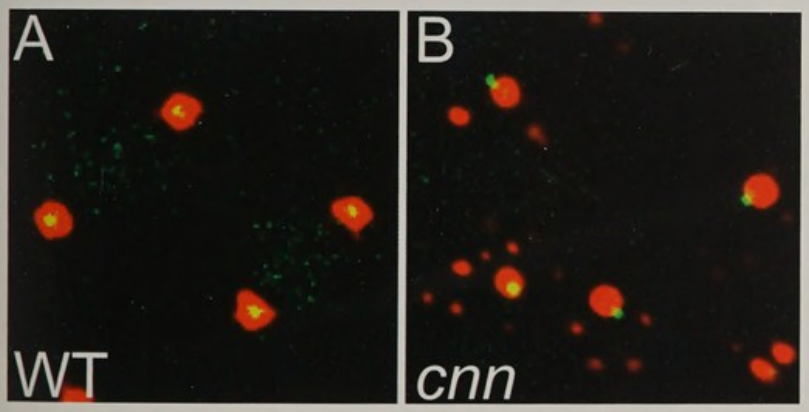


Figure 3: The centrioles (green) are always centrally positioned within the PCM of WT centrosomes (A), but are usually positioned at the edge of the PCM in centrosomes that lack Cnn (B).

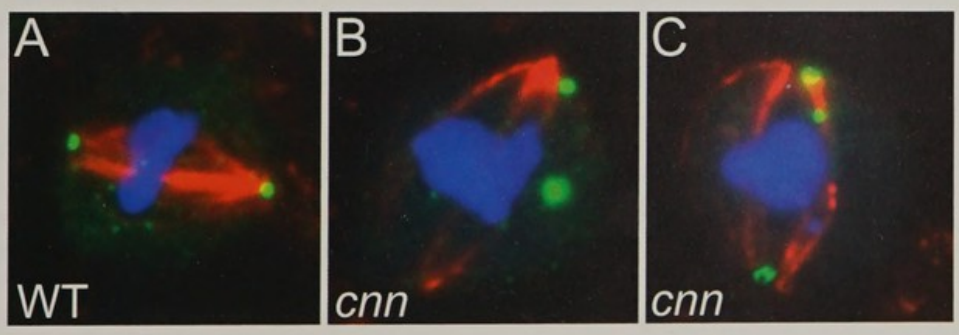
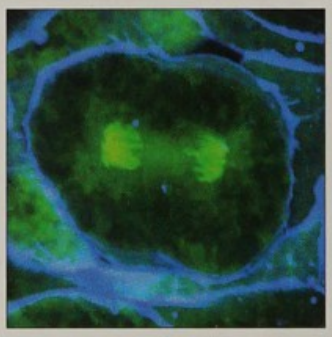


Figure 4: In WT cells, the centrioles are always well positioned at the poles of the mitotic spindle (A). The failure of the centrioles to maintain their proper connection to the PCM results in defects in centriole segregation in cnn mutant cells (B,C).

Jim Smith

Molecular basis of mesoderm formation

Co-workers: Joanna Argasinska, Julia Bate, Clifford Bogue, Liz Callery, Clara Collart, Kevin Dingwell, Amanda Evans, Anja Hagemann, Steve Harvey, Kim Lachani, Nigel Messenger, Oliver Nentwich, Amer Rana, Stefan Tümpel, Fiona Wardle, Xin Xu



Work in our laboratory is aimed at understanding the molecular basis of mesoderm formation. We hope to identify the signals that cause mesoderm to form, to understand how they can exert their effects at long range and in a concentration-dependent manner, to identify the genes that are activated by the mesoderm-inducing signals, and to determine how these genes contribute to the regulatory network that underlies mesodermal differentiation. We hope that our work will assist in efforts to direct embryonic stem cells down particular developmental pathways and that it might even allow us to make differentiated cells move backwards in developmental time, so that they can then be re-programmed as the experimenter desires.

Our work makes use of *Xenopus* species (both *X. laevis* and *X. tropicalis*) and, more recently, the zebrafish. We are using genomic resources in both fish and frog to help us isolate new genes involved in mesoderm formation, and to identify their partners and transcriptional targets. We have also carried out an antisense morpholino oligonucleotide screen to study the functions of large numbers of genes in *Xenopus tropicalis*, and as in some of our other projects, we plan to ask to what extent our results obtained in this species will apply to mammalian embryos.

One particular interest concerns the mechanisms by which inducing factors exert long-range effects in the early embryo, and we are studying this by means of tagged forms of inducing factors such as Xnr2 and by using novel approaches to identify, in real time, cells that are responding to such signals. In common with other members of the transforming growth factor type β family, Xnr2 exerts its effects by causing Smad proteins to form heteromeric complexes, and another aspect of our work has been to identify and characterise Smad-interacting proteins such as SmicI.

Additional experiments address morphogenetic processes in the early embryo, including gastrulation and neurulation, and we continue to study the regulation and function of members of the T box family of proteins, the founder member of which is Brachyury.

Inset left: Bimolecular fluorescence complementation allows one to visualise interactions between Smad2 and Smad4, components of the TGF-β signal transduction pathway, *in vivo* and in real time. This image shows that Smad2 and Smad4 interact on mitotic chromosomes.

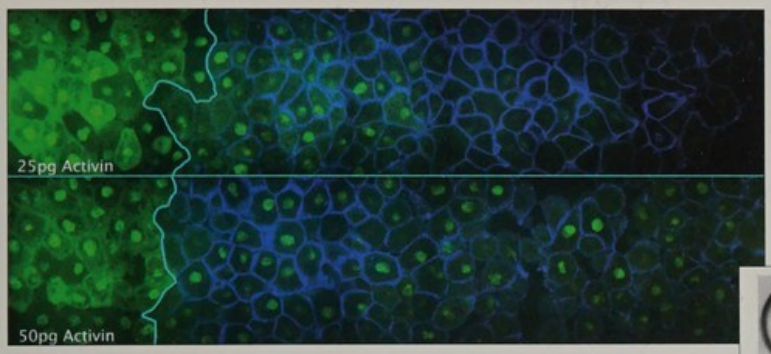
Rana AA, Collart C, Gilchrist MJ and Smith JC (2006) Defining synphenotype groups in *Xenopus* tropicalis by use of antisense morpholino oligonucleotides. **PLoS Genetics** (doi:10.1371/journal.pgen.0020193.eor)

Wardle FC, Odom DT, Bell GW, Yuan B, Wiellette EL, Herbolsheimer E, Sive HL, Young RA, Smith JC (2006) Zebrafish promoter microarrays identify actively transcribed embryonic genes. **Genome Biology**, 7:R71 (doi:10.1186/gb-2006-7-8-r71)

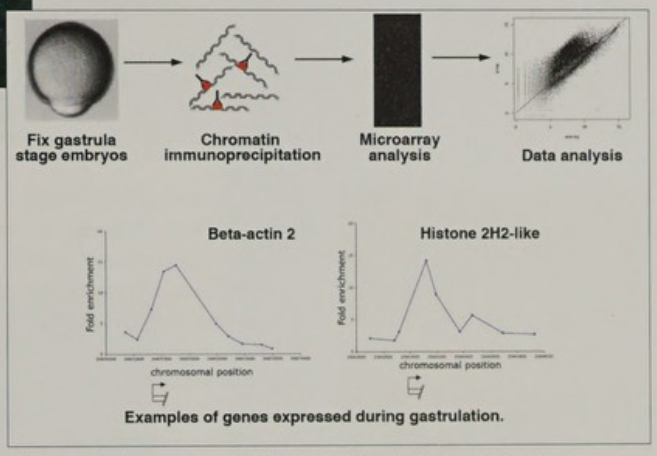
Dingwell KS and Smith JC (2006). Tes regulates neural crest migration and axial elongation in *Xenopus*. **Dev Biol** 293, 252-267

Knapp D, Messenger N, Rana AA and Smith JC (2006) Neurotrophin Receptor Homolog (NRH1) proteins regulate mesoderm formation and apoptosis during early *Xenopus* development. **Dev Biol** 300, 554-569

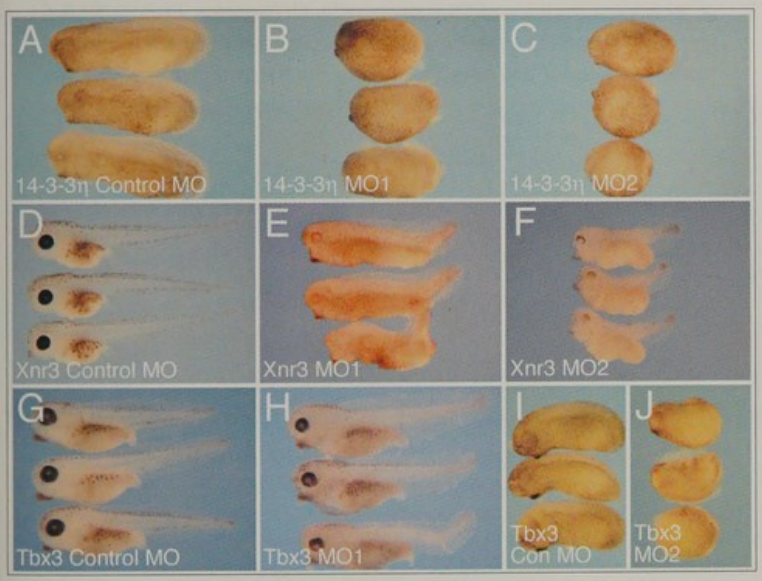
For complete list of this lab's publications since the last report, see numbers 9, 27, 47, 50, 51, 54, 69, 70 & 71 on pp 56-61



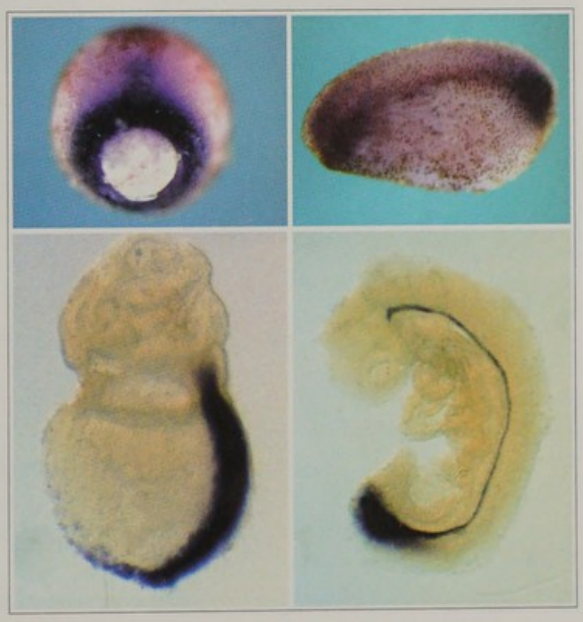
Higher concentrations of activin signal over a longer distance. Activin is expressed in cells on the left-hand-side of each image, and activation of Smad signalling is visualised in cells with blue membranes on the right-hand-sides.



Chromatin immunoprecipitation combined with genomic microarrays identifies actively transcribed genes in the zebrafish gastrula embryo.



As part of a large-scale antisense morpholino oligonucleotide (MO) screen, we have tested the specificities of various MOs by designing a second MO (MO2) which is targeted against a different region of the target mRNA than is MO1. Usually, the phenotypes are the same or similar (top two rows), but sometimes, as in the case of Tbx3, they differ (bottom row).



Comparison of the expression patterns of *Brachyury* in *Xenopus tropicalis* (top) and the mouse (bottom). Much of our work is aimed at asking whether similar genetic regulatory networks are employed in different vertebrate species.

Daniel St Johnston

mRNA localisation and the origin of polarity in *Drosophila*

Co-workers: Rebecca Bastock, Katsiaryna Belaya, Chin-Wen Chang, Sue Croysdale, Katja Dahlgaard, Eurico De Sa, Helene Doerflinger, Celia Faria, Alejandra Gardiol, Jacqueline Hall, Nick Lowe, Vincent Mirouse, Dmitry Nashchekin, Alexandre Raposo, Isabel Torres, Lucy Wheatley

The localisation of *bicoid* and *oskar* mRNAs to the anterior and posterior poles of the *Drosophila* oocyte defines AP axis of the embryo, and provides an excellent model for analysing the molecular mechanisms that underlie cell polarity and mRNA localisation. We are taking a combination of cell-biological, genetic and molecular approaches to investigate these mechanisms:

1) Since many proteins involved in mRNA transport or cell polarity are required throughout development, they were not identified in the classical screens for mutations that disrupt axis formation. To overcome this problem, we are performing screens in germline clones for mutants that affect the localisation of GFP-labelled *bicoid* mRNA and RFP-labelled *oskar* mRNA in living oocytes. We have identified many novel genes required for cell polarity or mRNA localisation, and are now examining their functions.

2) We have shown that the anterior-posterior polarity of the oocyte and the apical-basal polarity of epithelial cells depend on the formation of reciprocal domains of PAR proteins, with Bazooka (PAR-3), PAR-6 and aPKC marking anterior and apical cortical domains, and PAR-1 marking posterior and lateral domains. Furthermore, these domains are maintained by mutual inhibitory interactions, in which PAR-1 phosphorylates and disrupts the Bazooka complex, whereas aPKC phosphorylates PAR-1 to remove it from the cortex. We are now analysing how this asymmetry is established, and how the PAR proteins polarise the cytoskeleton.

3) We are making time-lapse films of mRNA movement *in vivo* to determine how *bicoid* and *oskar* mRNAs are transported to opposite poles of the same cell. We are also attempting to purify mRNA localisation complexes and to reconstitute mRNA transport *in vitro*.

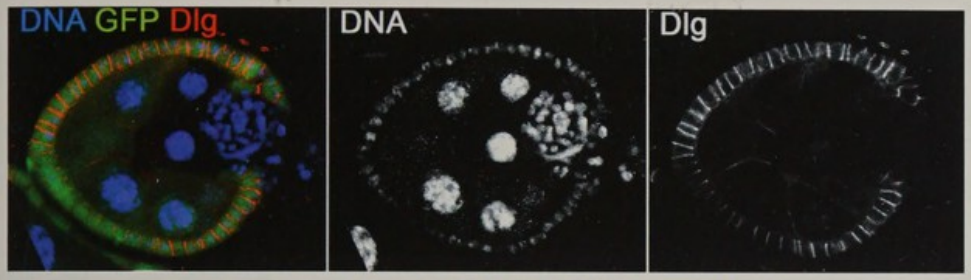
Inset left: The localisation of *bicoid* mRNA (green) and *oskar* mRNA (red) to the anterior and posterior poles of the stage 10 oocyte. *bicoid* mRNA has been labelled with MS2-GFP and *oskar* mRNA with RFP-Staufen.

Doerflinger H, Benton R, Torres IL, Zwart MF and St Johnston D (2006) *Drosophila* anterior-posterior polarity requires actin-dependent PAR-1 recruitment to the oocyte posterior. **Curr Biol** 16, 1090-1095

Munro TP, Kwon S, Schnapp B and St Johnston D (2006) A repeated IMP-binding motif controls *oskar* mRNA translation and anchoring independently of *Drosophila* IMP. **J Cell Biol.** 172, 577-588

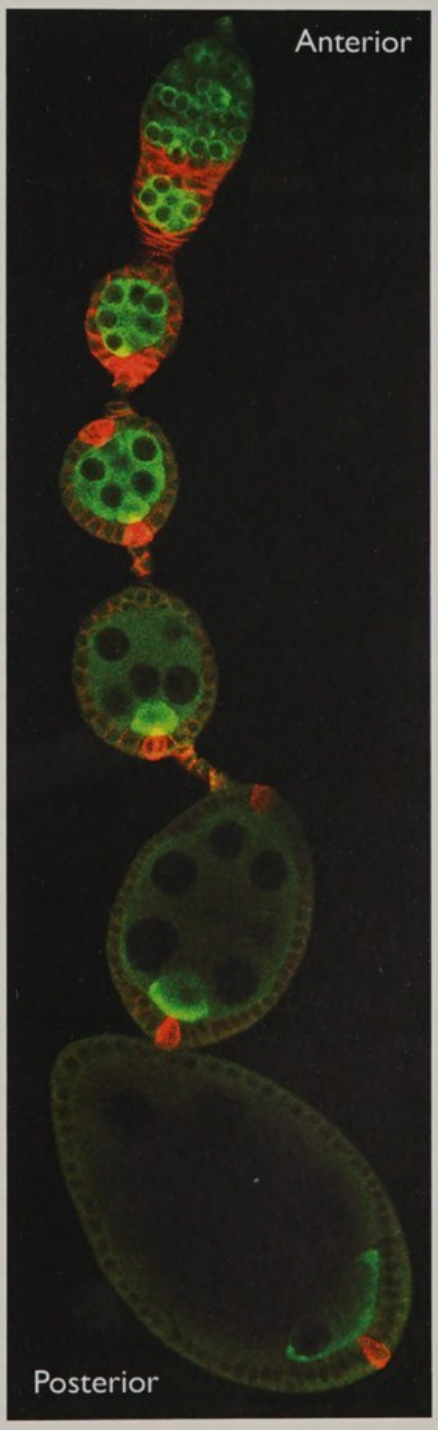
Irion U, Adams J, Chan C-W and St Johnston D (2006) Miranda couples *oskar* mRNA/Staufen complexes to the *bicoid* mRNA localization pathway. **Dev Biol.** 297, 522-533.

For an additional publication since the last report, see numbers 5, 10, 24, 26, 31, 32 & 35 on pp 56-61



Starvation-dependent tumour formation. 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. This phenotype is only observed under starvation conditions. Collaboration with Jay Brenman (University of North Carolina).

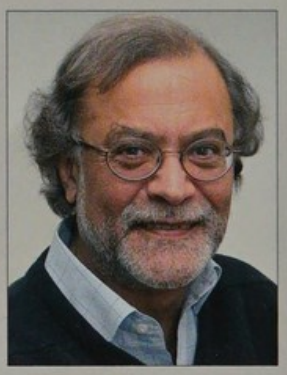
Miranda targets Staufen and oskar mRNA to the anterior of the oocyte. Staufen (green) and oskar mRNA localise to the posterior of wildtype oocytes, where Oskar protein defines the abdomen (bottom). Ectopic expression of Miranda targets some Staufen and oskar mRNA to the anterior of the oocyte, resulting in bicaudal embryos. In mago nashi mutants, which disrupt posterior localisation, Miranda directs all Staufen and oskar mRNA to the anterior, leading to reversed embryos with an anterior abdomen and no head.



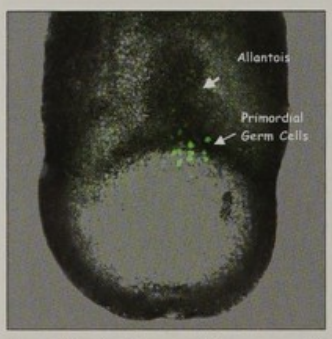
Drosophila oogenesis. A Drosophila ovariole, containing a series of germline cysts (green, BicD) that progress through oogenesis as they move posteriorly. The cysts are born at the anterior of the ovariole, and become surrounded by somatic follicle cells (red, FasIII) as they exit the germarium. Each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

Azim Surani

Germ cells: a genetic programme regulating epigenetic modification



Co-workers: Sheila Barton, Francesca Cesari Weimar, Gabriela Durcova-Hills, Lynn Froggett, Petra Hajkova, Sophie Hanina, Katsuhiko Hayashi, Sean Jeffries, Masahiro Kaneda, Ulrike Lange, Caroline Lee, William Mifsud, Fuchou Tang, Wee Wei Tee, Leng Siew Yeap



Germs cells are the source of totipotency, a unique state that links all generations. We are investigating the genetic programme, which regulates specification of founder primordial germ cells (PGCs), and the epigenetic programming of the lineage, which underlie the distinctive properties of mouse germ cell lineage.

A particular focus of our work has been to elucidate the mechanism of PGC specification by using molecular analysis of single founder germ cells and their nearest somatic neighbours. This has led to the identification of Blimp1, (amongst other genes), a transcriptional regulator as the key determinant of the mouse germ cell lineage. Blimp1 is first detected in a few pluripotent epiblast cells at E6.25, which marks the beginning PGC precursors that give rise to the founder about 40 founder PGCs at E7.25. A specific role of Blimp1 is to repress the somatic programme represented by region-specific Hox genes in founder PGCs. PGCs are highly specialised cells, but it is possible to derive pluripotent stem cells from PGCs in culture.

Extensive epigenetic programming of the genome in PGCs follows their specification, which is an essential first step towards eventual totipotency. In particular, when PGCs migrate into developing gonads at E11.5, they undergo substantial epigenetic modifications, including genome-wide DNA demethylation, erasure of imprints and reactivation of the X chromosome. We are investigating the mechanism and identity of the intrinsic factors involved in this event, together with the nature of the external signals that trigger it.

Our broader objectives are to use our comprehensive knowledge of the mechanism of germ cell specification and properties, to elucidate mechanisms of cell fate determination generally, for example, during differentiation of pluripotent embryonic stem cells. Mechanisms that govern erasure of epigenetic information in PGCs could be extended to investigate genomic reprogramming and dedifferentiation of somatic cells when they acquire pluripotency.

Inset left: Expression of stella-GFP at E 7.8. PGCs are detected at the base of the allantois. Stella is located within a cluster of pluripotency genes, including nanog and Gdf3 that are expressed in ES and EG cells.

Surani MA, Ancelin K, Hajkova P, Lange UC, Payer B, Western P and Saitou M (2004) Mechanism of germ cell specification: A genetic programme regulating epigenetic reprogramming. **Cold Spring Harbor Symposium** 69 (Epigenetics), 1-9

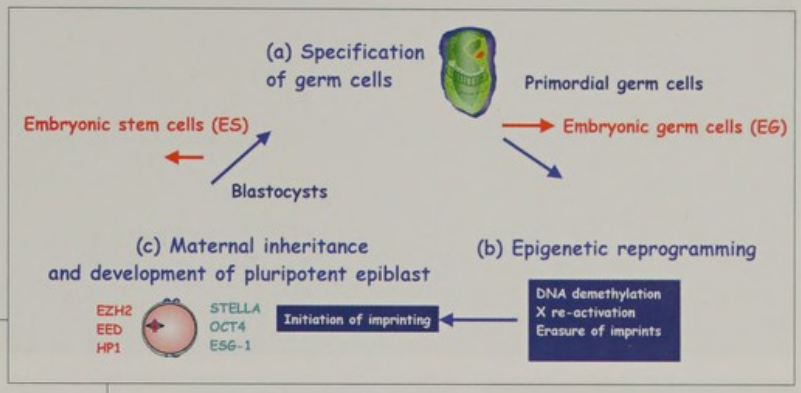
Ohinata Y, Payer B, O'Carroll D, Ancelin K, Ono Y, Sano M, Barton SC, Obukhanych T, Nussenzweig M, Tarakhovsky A, Saitou M, and Surani MA (2005) Blimp1 is a critical determinant of the germ cell lineage in mice. **Nature** 436, 207-213

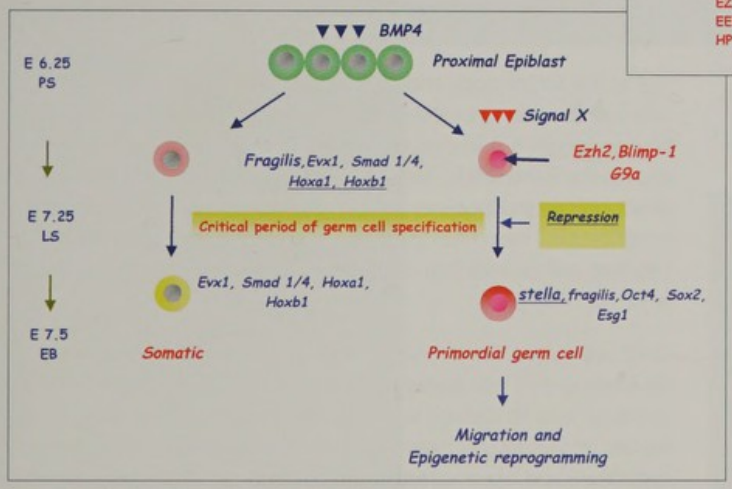
Ancelin K, Lange UC, Hajkova P, Schneider R, Bannister AJ, Kouzarides T, Surani MA (2006) Blimp 1 associates with Prm5 and directs histone arginine methylation in mouse germ cells. **Nature Cell Biology** 8, 623-630

Surani MA, McLaren A (2006) Stem cells: A new route to rejuvenation. **Nature** 443, 284-285

For complete list of this lab's publications since the last report, see numbers 4, 12, 13, 20, 28, 29, 33, 40, 43, 57, 58, 59, 62, 63 & 68 on pp 56-61

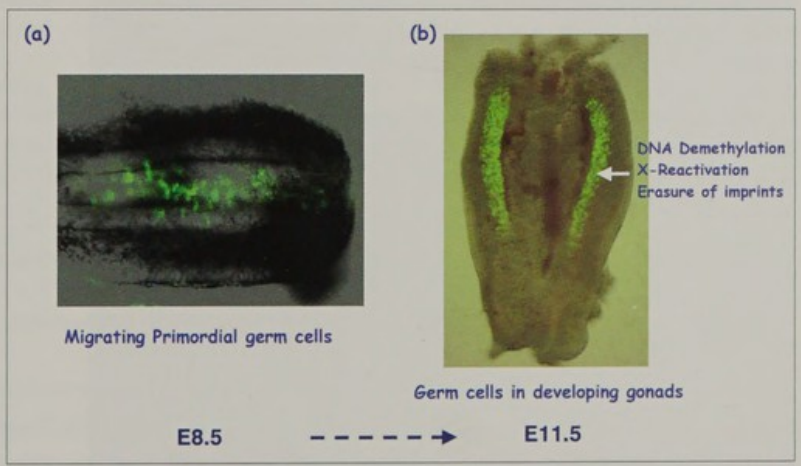
Mouse germ line cycle. (a) Founder population of primordial germ cells are detected at E7.5 consisting of about 45 cells. (b) They proliferate and migrate into the developing gonads at E10.5, when a major epigenetic reprogramming event commences, and continues during gametogenesis. (c) There is also maternal inheritance of key epigenetic and totipotency factors in oocytes, which are essential for early development.





Mechanism of PGC specification. The proximal epiblast cells acquire germ cell competence in response to signalling molecules, including BMP4. Some of these cells acquire PGC fate subsequently, which is associated with transcriptional repression of genes that are expressed in the neighbouring cells, including Hox genes. Several epigenetic modifiers including Ezh2, G9a and Blimp-1 probably have a critical role in this process. PGCs continue to express pluripotent-specific genes such as Oct4, and the germ cell specific gene, Stella, which is the definitive marker of nascent PGCs.

Epigenetic reprogramming in PGCs. (a) PGCs expressing Stella-GFP are seen migrating into the developing gonads. (b) When PGCs enter into the developing gonads, they undergo extensive epigenetic reprogramming of the genome that includes genome-wide DNA demethylation and reactivation of the inactive X-chromosome.



Magdalena Zernicka-Goetz

Development of cell fate and polarity in the regulative mammalian embryo

Co-workers: Dilly Bradford, Tagbo Ilozue, Agnieszka Jedrusik, Emlyn Parfitt, Lucy Richardson, Bedra Sharif, Maria Skamagki, Bernhard Strauss, Qiang Wu

We are interested in origins of patterning and cell fate determination in the mouse embryo focusing on three major questions.

First, how is the polarity of the egg first established to permit the drastically asymmetric, meiotic divisions and then re-organised following fertilisation to allow apparently symmetric, embryonic divisions? We are addressing this question by a combination of experimental embryology and molecular techniques to disturb egg polarity. Time-lapse fluorescent imaging of spindle positioning and cell division allows us to follow dynamics of these processes in live embryos and the ectopic expression of GFP-fusion proteins enables us to perturb these processes.

Second, how are the decisions made to allow early embryonic cells to shift their division patterns from being initially symmetric to asymmetric. This is instrumental in generating pluripotent, inside cells that will give rise to the future body and outside cells which differentiate into the extra-embryonic tissues. We have found that we can direct these cell fate decisions by down-regulating the function of cell polarity proteins such as Par3 and aPKC. We have also recently discovered that we can direct cells to pluripotency by manipulating a very specific chromatin modification. These findings together lead us to study the interplay between cell polarity and cell potency in directing cell fate in the mouse embryo.

Third, we would like to understand how this early patterning influences development of first signalling centres that establish the anterior-posterior axis. To address when and how such signalling centres develop, we are undertaking expression profiling and lineage tracing combined with RNAi and overexpression of signalling genes. We have carried out screens that revealed novel genes asymmetrically expressed at these early stages and are currently characterising their function.

Inset left: Over-expression of Carm1 in a single 2-cell stage blastomere directs cells to the pluripotency at the blastocyst stage. Daughters of cells in which Carm1 was overexpressed are in red. (Image from Maria-Elena Torres-Padilla and Emlyn Parfitt).

Torres-Padilla ME, Parfitt DE, Kouzarides T and Zernicka-Goetz M (2006) Histone arginine methylation directs cells to pluripotency in the early mouse embryo. **Nature** [in press]

Na J and Zernicka-Goetz M (2006) Asymmetric positioning and organisation of the meiotic spindle of mouse oocytes requires CDC42 function. **Curr Biol** 16(12)1249-54

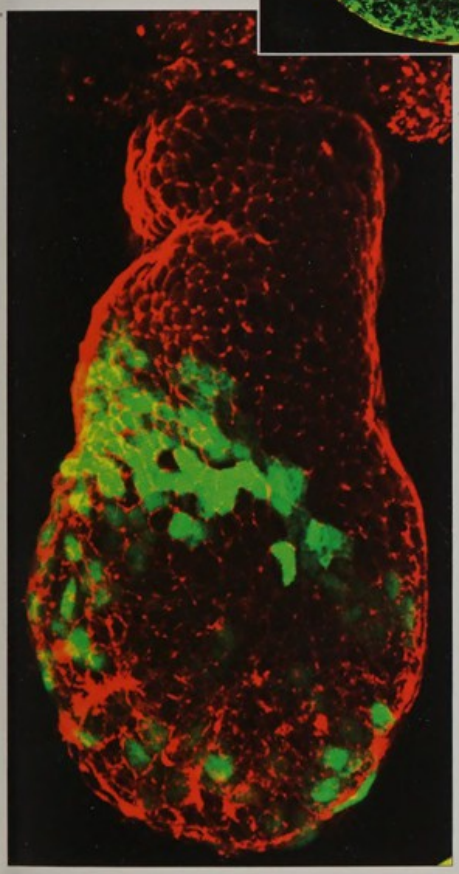
Torres-Padilla ME and Zernicka-Goetz M (2006) Role of TIF1a as a modulator of embryonic transcription in the mouse zygote. **J Cell Biol** 174(3):329-38

Plusa B, Hadjantonakis AK, Gray D, Piotrowska-Nitsche K, Jedrusik A, Papaioannou VE, Glover DM and Zernicka-Goetz M (2005) The first cleavage of the mouse zygote predicts the blastocyst axis. **Nature** 434:391-5.

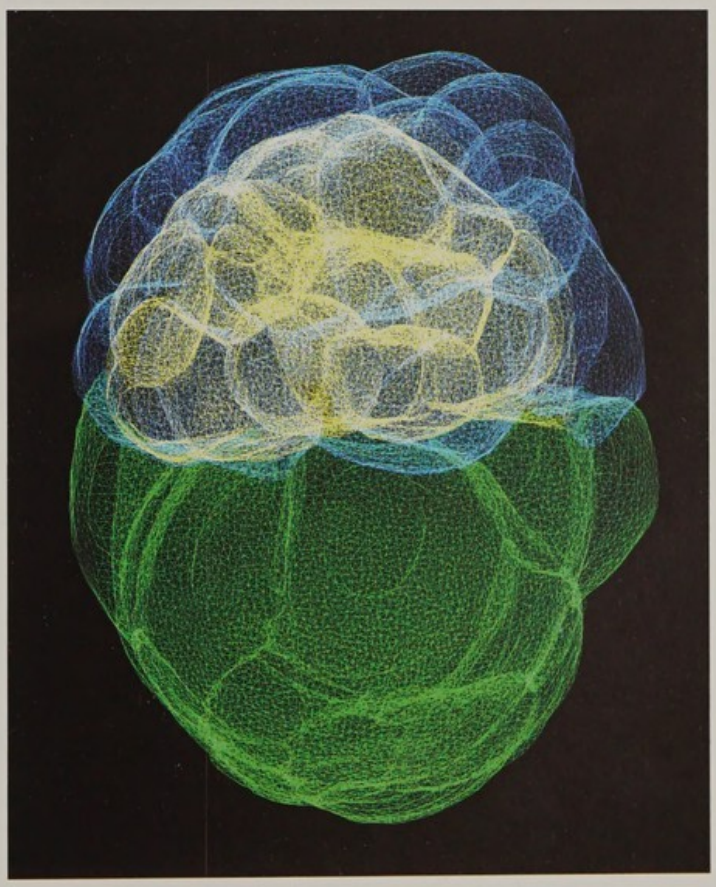
Zernicka-Goetz M (2005) Cleavage pattern and emerging asymmetry of the mouse embryo. **Nature Reviews** 6(12):919-28

For complete list of this lab's publications since the last report, see numbers 17, 37, 38, 48, 53, 64, 65, 66 & 73 on pp 56-61

First cleavage division of the mouse zygote in relation to the animal-vegetal axis of the egg (marked by the attached second polar body). Chromatin in blue, microtubules in green. (Image from Berenika Plusa).



Post-implantation mouse embryo with migrating anterior visceral endoderm cells expressing Cerl (in green). Boundaries between cells shown in red. (Image from Lucy Richardson)



3D reconstruction of the mouse blasotcyst showing how the first set of pluripotent cells that will give rise to the future body (yellow) is cradled by the outside cells of the embryo (blue). (Image from Emlyn Parfitt and Magdalena Zernicka-Goetz).

CATEGORIES OF APPOINTMENT

SENIOR GROUP LEADER
Professor, Reader or equivalent

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

CAREER DEVELOPMENT FELLOW
4-year grant-funded appointment, within individual groups

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
Within individual groups or part of core support, grant-funded

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.

JIM SMITH PhD FRS FMedSci, Chairman

John Humphrey Plummer Professor of Developmental Biology, Member European Molecular Biology Organization, Member Academia Europaea (Member of the Department of Zoology)

JOANNA ARGASINSKA PhD
BBSRC Research Associate

JULIA BATE
Personal Assistant

CLIFFORD BOGUE
Sabbatical Visitor

LIZ CALLERY PhD
Wellcome Trust Research Associate

CLARA COLLART PhD
Wellcome Trust Research Associate

KEVIN DINGWELL PhD
Wellcome Trust Research Associate

AMANDA EVANS HNC
Wellcome Trust Research Assistant

ANJA HAGEMANN
Gulbenkian Graduate Student

STEVE HARVEY PhD
VolkswagenStiftung Research Associate

KIM LACHANI
BBSRC Chief Research Technician

NIGEL MESSENGER
Wellcome Trust Research Associate

OLIVER NENTWICH PhD
Wellcome Trust Research Associate

JOANA RAMIS MOREY PhD
Marie Curie Fellow

AMER RANA PhD
Wellcome Trust Research Associate

YASUSHI SAKA PhD
Wellcome Trust Research Associate

STEFAN TÜMPEL PhD
EU Research Associate

FIONA WARDLE PhD
Wellcome Trust Senior Research Associate

XIN XU
Graduate Student

ANDREA BRAND PhD FMedSci

Director of Research in Developmental Neurobiology,
Member, European Molecular Biology Organization
(Member of the Department of Physiology, Development and Neuroscience)

TORSTEN BOSSING PhD
Wellcome Trust Research Associate

ADRIAN CARR MPhil
Wellcome Trust Graduate Student

JAMES CHELL MPhil
Wellcome Trust Graduate Student

SEMIL CHOKSI BSc
Gates Cambridge Scholar

MELANIE CRANSTON BA
Wellcome Trust Research Assistant

CATHERINE DAVIDSON BSc
Wellcome Trust Research Associate

JAMES DODS BSc
Wellcome Trust Graduate Student

KARIN EDOFF PhD
Stem Cell Career Development Fellow

BORIS EGGER PhD
Wellcome Trust Research Associate

DAVID ELLIOTT PhD
Wellcome Trust Research Associate

LIZ GAVIS PhD
Sabbatical Visitor from Princeton University

UGO MAYOR PhD
Royal Society Dorothy Hodgkin Fellow

JOHN SOLLY BSc
BBSRC Graduate Student

TONY SOUTHALL PhD
MRC Research Associate

CHRISTINE TURNER
Secretary

JAKOB VON TROTHA BSc
Graduate Student

PAO-SHU (PAUL) WU MD
Graduate Student

SENIOR GROUP LEADERS

NICK BROWN PhD

Wellcome Trust Research Fellow
(Member of the Department of Physiology, Development and Neuroscience)

ISABELLE DELON PhD
BBSRC Research Associate

SAMANTHA HERBERT BSc
Wellcome Trust Research Assistant

SVEN HUELSMANN BSc
Wellcome Trust Research Associate

YOSHIKO INOUE PhD
Wellcome Trust Research Associate

BOBBY JOHNSON
Work Experience Student

VANESSA MAYBECK BSc
Research Assistant

MAITHREYI NARASIMHA PhD
Wellcome Trust Research Associate

JOHN OVERTON HNC
Wellcome Trust Senior Research Technician

MARY PINES BSc
Graduate Student

KATJA RÖPER PhD
David Phillips Research Fellow

DORA SABINO BSc
Graduate Student

ESTHER SOLOMON
Wellcome Trust Research Assistant

XIAO TAN BSc
Graduate Student

GUY TANENTZAPF PhD
HFSP Fellow

JOHN GURDON Kt DPhil DSc FRS

Distinguished Group Leader
Foreign Associate, US National Academy of Sciences
Foreign Associate, US Institute of Medicine of the National Academies
Member European Molecular Biology Organization
Member Academia Europaea
(Member of the Department of Zoology)

ADRIAN BIDDLE BSc
Graduate Student

NIGEL GARRETT MIBiol
Wellcome Trust Research Assistant

JEROME JULLIEN PhD
Wellcome Trust Research Associate

MAGDA KOZIOL BSc
Wellcome Trust Graduate Student

YEN-HSI KUO BSc
Wellcome Trust Graduate Student

NICHOLE LANT
Personal Assistant

KAZUTAKA MURATA BSc
Graduate Student

RAY NG BSc
Graduate Student

ILENIA SIMEONI PhD
EU Research Associate

HENRIETTA STANDLEY PhD
BBSRC Research Associate

CAROLINE WEBB
Personal Assistant

STEVE JACKSON PhD FMedSci

Frederick James Quick Professor of Biology
Member European Molecular Biology Organization
(Member of the Department of Zoology)

PETER AHNESORG BSc
Cancer Research UK Graduate Student

RIMMA BELOTSERKOVSKAYA PhD
Cancer Research UK Research Associate

RICHARD CHAHWAN BSc
Cancer Research UK Graduate Student

ROSS CHAPMAN BSc
EU Graduate Student

JULIA COATES MA
Cancer Research UK Senior Research Technician

ROBERT DRISCOLL BSc
BBSRC Graduate Student

KATE DRY PhD
Cancer Research UK Senior Research Associate

YARON GALANTY PhD
EU Research Associate

SABRINA GIAVARA PhD
EU Research Associate

SIMONA GIUNTA BSc
BBSRC Graduate Student

SERGE GRAVEL PhD
Cancer Research UK Research Associate

JEANINE HARRIGAN PhD
Cancer Research UK Research Associate

PABLO HUERTAS PhD
EMBO Fellow

ALICIA LEE BSc
NIH-Cambridge University Graduate Student

CHRISTINE MAGILL BSc
Cancer Research UK Research Assistant

ANDREAS MEIER PhD
Swiss National Science Foundation Fellow

KYLE MILLER PhD
EU Research Associate

ABDEL MOUMEN PhD
AICR Research Associate

VENKAT PISUPATI PhD
Cancer Research UK Research Associate

SOPHIE POLO PhD
Cancer Research UK Research Associate

HELEN REED
Secretary

SENIOR GROUP LEADERS

ALEX SARTORI PhD
Swiss National Science Foundation Fellow

PHILIPPA SMITH BSc
Cancer Research UK Lab Manager

JORRIT TJEERTES
Visiting Student

TONY KOUZARIDES PhD FMedSci, Deputy Chairman

Royal Society Napier Professor
Member European Molecular Biology Organization
(Member of the Department of Pathology)

HATICE AKARSU PhD
EU Research Associate

ANDREW BANNISTER PhD
Cancer Research UK Senior Research Associate

TILL BARTKE PhD
HFSP Research Fellow

MARIA CHRISTOPHOROU PhD
Cancer Research UK Research Associate

ALISTAIR COOK GI Biol
Cancer Research UK Chief Research Technician

SILVIA DAMBACHER
Visiting Student

SOPHIE DELTOUR PhD
Cancer Research UK Research Associate

KAREN HALLS BSc
Royal Society Research Assistant

PAUL HURD PhD
Cancer Research UK Research Associate

ANTONIS KIRMIZIS PhD
Marie Curie Research Fellow

DAVID LANDO PhD
Cancer Research UK Research Associate

SUSANA LOPES PhD
Cancer Research UK Research Associate

CHRIS NELSON PhD
CIHR Research Fellow

NIKKI OLIVER
Secretary

CLAIRE PIKE BSc
Cancer Research UK Graduate Student

HELENA SANTOS ROSA PhD
Cancer Research UK Senior Research Associate

BLERTA XHEMALCE PhD
EU Research Associate

ANNE MCLAREN DPhil FRS

BBSRC Distinguished Group Leader
Member European Molecular Biology Organization
(Member of the Department of Zoology)

DILLY BRADFORD
Secretary

SUSANA CHUVA de SOUSA LOPES PhD
Isaac Newton Trust Research Associate

CRISTINA EGUIZABAL PhD
BBSRC Research Associate

TANYA SHOVLIN PhD
BBSRC Research Associate

JONATHON PINES PhD FMedSci

Director of Research in Cell Division
Member European Molecular Biology Organization; Fellow, Academy of Medical Sciences
(Member of the Department of Zoology)

CLAIRE ACQUAVIVA PhD
Cancer Research UK Research Associate

CAROLINE BROAD
Cancer Research UK Lab Manager

LORENA CLAY
Cancer Research UK Graduate Student

FAY COOKE
MRC Graduate Student

BARBARA DI FIORE PhD
Cancer Research UK Research Associate

ALEX DOMIN
Gates Trust Graduate Student

SUZANNE FLOYD PhD
MRC Research Associate

OLIVIER GAVET PhD
Marie Curie Fellow

ANJA HAGTING PhD
Cancer Research UK Research Associate

DAISUKE IZAWA PhD
JSPS Fellow

MARK JACKMAN PhD
Cancer Research UK Research Associate

LARS KOOP
BBSRC Graduate Student

RYOKO KURIYAMA PhD
Sabbatical Visitor

CATHERINE LINDON PhD
MRC Career Development Fellow

TAKAHIRO MATSUSAKA PhD
Cancer Research UK Research Associate

ESTHER SON
Vacation Student

BERNHARD STRAUSS
Cancer Research UK Research Associate

JAKOB NILSSON PhD
Danish Cancer Society Fellow

MONA YEKEZARE
Yousef Jameel Graduate Student

JORDAN RAFF PhD

Cancer Research UK Senior Research Fellow
(Member of the Department of Genetics)

RENATA BASTO PhD
Royal Society Dorothy Hodgkin Fellow

PAUL CONDUIT BSc
Graduate Student

SUE CROYSDALE
Secretary

BEN DAVID
Vacation Student

CARLY DIX MPhil
Wellcome Trust Graduate Student

JEROEN DOBBELAERE PhD
HFSP Fellow

JOYCE LAU MPhil
Cancer Research UK Senior Research Technician

ELIANA LUCAS MSc
Graduate Student

TERESA PEREIRA de BARROS PhD
Graduate Student

NINA PEEL MPhil
Wellcome Trust Graduate Student

NAOMI STEVENS MPhil
Wellcome Trust Graduate Student

SASKIA SUIJKERBUIJK
Visiting Student

DANIEL ST JOHNSTON PhD FRS FMedSci

Professor of Developmental Genetics
Member, European Molecular Biology Organization
(Member of the Department of Genetics)

REBECCA BASTOCK PhD
Wellcome Trust Research Associate

KATSIARYNA BELAYA BSc
Darwin Trust Graduate Student

CHIN-WEN CHANG
Graduate Student

SUE CROYSDALE
Secretary

KATJA DAHLGAARD
Wellcome Trust Graduate Student

EURICO DE SA
Portuguese Foundation of Science and Technology Graduate Student

HELENE DOERFLINGER PhD
Wellcome Trust Research Associate

CELIA FARIA
Wellcome Trust Graduate Student

ALEJANDRA GARDIOL PhD
Wellcome Trust Research Associate

JACQUELINE HALL MSc
Wellcome Trust Senior Research Technician

UWE IRION PhD
Wellcome Trust Research Associate

NICK LOWE PhD
Wellcome Trust Research Associate

VINCENT MIROUSE PhD
EMBO Fellow

ANTOINE MOLARO
Vacation Student

TRENT MUNRO PhD
Wellcome Trust Research Associate

DMITRY NASHCHEKIN PhD
Wellcome Trust Research Associate

ALEXANDRE RAPOSO
Graduate Student

ISABEL TORRES
Wellcome Trust Graduate Student

LUCY WHEATLEY
Wellcome Trust Research Assistant

VITALY ZIMYANIN PhD
Graduate Student/Wellcome Trust Research Associate

AZIM SURANI PhD FRS FMedSci

Mary Marshall & Arthur Walton Professor of Physiology and Reproduction
Member, European Molecular Biology Organization
(Member of the Department of Physiology)

SHEILA BARTON
Wellcome Trust Senior Research Associate

FRANCESCA CESARI WEIMAR PhD
Marie Curie Fellow

SUSANA CHUVA de SOUSA LOPES PhD
Netherlands Organisation for Scientific Research Fellow/Collaborator

GABRIELA DURCOVA-HILLS PhD
MRC Fellow

LYNN FROGGETT
Secretary

PETRA HAJKOVA PhD
Wellcome Trust Research Associate

SOPHIE HANINA
MRC Graduate Student

KATSUHIKO HAYASHI PhD
JSPS Fellow

SEAN JEFFRIES
NIH Graduate Student

MASAHIRO KANEDA PhD
JSPS Fellow

ULRIKE LANGE
Graduate Student

CAROLINE LEE
Wellcome Trust Senior Research Technician

WILLIAM MIFSUD
Wellcome Trust Graduate Student

BERNHARD PAYER
Graduate Student

FUCHOU TANG PhD
BBSRC Research Associate

WEE WEI TEE
Wellcome Trust Graduate Student

LENG SIEW YEAP
BBSRC Dorothy Hodgkin Graduate Student

JULIE AHRINGER PhD

Wellcome Trust Senior Research Fellow
Member European Molecular Biology Organization
(Member of the Department of Genetics)

ROB ANDREWS MPhil
Graduate Student

CAN CENIK
Visiting Student

YAN DONG MSc
Wellcome Trust Research Assistant

BRUNO FIEVET PhD
HFSP Fellow

PAULINA KOLASINSKA-ZWIERZ
Graduate Student

TAEJOON KWON MSc
Wellcome Trust Research Assistant

ISABEL LATORRE PhD
Wellcome Trust Research Associate

NATALIE LEBOT PhD
Royal Society Dorothy Hodgkin Fellow

NEERAJ MANDHANA BSc
Wellcome Trust Graduate Student

COSTANZA PANBIANCO BSc
Graduate Student/Research Assistant

GINO POULIN PhD
Wellcome Trust Research Associate

DAVID RIVERS PhD
Wellcome Trust Research Associate

JOSANA RODRIGUEZ PhD
HFSP Fellow

FRAN STEDHAM BSc
Wellcome Trust Research Assistant

MIAO-CHIH TSAI BSc
Graduate Student

CHRISTINE TURNER
Secretary

DAVID WELCHMAN BSc
Graduate Student

SHANE WOODS BSc
Gates Graduate Student

ENRIQUE AMAYA PhD

Wellcome Trust Senior Research Fellow
(Member of the Department of Zoology)

JULIET BARROWS
Secretary

JUN-AN CHEN
Taiwanese Government Graduate Student

RICARDO COSTA Phd
Wellcome Trust Research Associate

KAREL DOREY
Wellcome Trust Research Associate

ROSALIND FRIDAY
Wellcome Trust Research Assistant

KATHY HARTLEY
Wellcome Trust Research Associate

XIAO HUANG PhD
Wellcome Trust Research Associate

SHOKO ISHIBASHI PhD
Wellcome Trust Research Associate

NICHOLAS LOVE
Churchill Graduate Student

ROBERT PAREDES PhD
Wellcome Trust Research Associate

XIMENA SOTO RODRIGUEZ PhD
Wellcome Trust Research Associate

RICK LIVESEY MB BChir PhD

Wellcome Trust Group Leader
(Senior Lecturer in Department of Biochemistry)

JULIET BARROWS BA
Secretary

PAOLO CODEGA
Visiting Student

NILS GRABOLE
Visiting Student

DEAN GRIFFITHS PhD
MRC Research Associate

ALAN KERSHAW
Vacation Student

GRACE NISBET BSc
Jean Shanks Graduate Student

SABHI RAHMAN BSc
Graduate Student

STEPHEN SANSOM BSc
Graduate Student

JAMES SMITH BSc
March of Dimes Research Assistant

TATIANA SOUBKHANKOULOVA PhD
EU Research Associate

URUPORN THAMMONGKOL BSc
Graduate Student

MASANORI MISHIMA PhD

Cancer Research UK Senior Research Fellow
(Member of the Department of Biochemistry)

GROUP LEADERS

JULIET BARROWS BA
Secretary

MAX DOUGLAS BSc
BBSRC Graduate Student

ANDREA HUTTERER PhD
Cancer Research UK Research Associate

JULIA MASON BSc
Cancer Research UK Research Assistant

ERIC MISKA PhD

Cancer Research UK Senior Research Fellow
(Member of the Department of Biochemistry)

MARLOES BAGIJN BSc
Graduate Student

CHERI BLENKIRON PhD
Academic Visitor

HEERAN BUHECHA BSc
Cancer Research UK Graduate Student

ALEJANDRA CLARK PhD
Cancer Research UK Research Associate

PARTHA PRATIM DAS BSc
Cancer Research UK Chief Research Technician

ETHAN KAUFMAN BSc
Gates Graduate Student

NIC LEHRBACH BSc
Wellcome Trust Graduate Student

FUNDA SAR PhD
Cancer Research UK Research Associate

STEFANIE SASSEN
Visiting Academic

ROBERT SHAW BSc
Wellcome Trust Graduate Student

NANCY PAPALOPULU PhD

Wellcome Trust Senior Research Fellow
(Member of the Department of Physiology, Development and Neuroscience)

EVA ASSCHER
Wellcome Trust Graduate Student

JULIET BARROWS
Secretary

JULIA MASON
Wellcome Trust Research Assistant

TARIK REGAD PhD
Wellcome Trust Research Associate

MARTIN ROTH PhD
Wellcome Trust Research Associate

NITIN SABHERWAL PhD
Wellcome Trust Research Associate

BERNHARD STRAUSS
Wellcome Trust Research Associate

MAGDALENA ZERNICKA-GOETZ PhD

Wellcome Trust Senior Research Fellow
(Member of the Department of Genetics)

DILLY BRADFORD
Secretary

JOANNA GRABAREK PhD
BBSRC Research Associate

SEIKI HARAGUCHI PhD
Wellcome Trust Research Associate

TAGBO ILOZUE
AstraZeneca Graduate Student

AGNIESZKA JEDRUSIK
Graduate Student

KARIN LYKKE-ANDERSEN PhD
Research Associate

ZOFIA MADEJA PhD
BBSRC Research Associate

SIGOLENE MEILHAC PhD
Marie Curie Fellow

EMLYN PARFITT
MRC Graduate Student

LUCY RICHARDSON
Graduate Student

BEDRA SHARIF
Visiting Academic

MARIA SKAMAGKI
Graduate Student

BERNHARD STRAUSS PhD
Cancer Research UK Research Associate

MARIA ELENA TORRES PADILLA PhD
Wellcome Trust Research Associate

QIANG WU PhD
Wellcome Trust Research Associate

ADMINISTRATION

ANN CARTWRIGHT MPhil
Institute Administrator

GEORGE BROWN
Accounts Manager

JILL BULLMAN
Accounts Manager

SUZANNE CAMPBELL BSc
Administration Assistant

JANE COURSE
Accounts/Admin Assistant

DIANE FOSTER
Principal Technician

KATHY HILTON Dip Mgmt
Senior Chief Technician

LYNDA LOCKEY
Office Manager

NIKKI OLIVER
Receptionist

JACKIE SIMCOX
Receptionist

COMPUTING

ALASTAIR DOWNIE
Computer Associate

NICOLA LAWRENCE PhD
Computer Associate

NIGEL SMITH
Computer Associate

ALEX SOSSICK HNC
Computer Imaging Associate

PETER WILLIAMSON BSc
Computer Associate

BIOINFORMATICS

MIKE GILCHRIST PhD
Computer Associate

JIA TIAN BSc
Bioinformatics Assistant

ACCOUNTS/PURCHASING/STORES

SIMON ALDIS
Purchasing/Accounts Assistant

RAY BOREHAM
Stores Technician

RICHARD ETTERIDGE
Stores Technician

LEN SYMONDS
Senior Stores Technician

ANDY VINCENT
Stores Technician

MICK WOODROOFE
Purchasing/Accounts Assistant

CUSTODIANS

CLIVE BENNETT
Senior Custodian

CHRISTIAN GUZMAN-QUEIROLO
Assistant Custodian

PAUL TURRELL
Assistant Custodian

MEDIA/GLASSWASHING

JUANITA PEACOCK
Glass Washing/Media Manager

JANIS ABBOTT
LISA BAKER
BEVERLEY CORNELL
SANDRA HUMAN
MARIAN SARGEANT
LINDA ADAMS
BETTINA CASHIN
BETTY HUDSON
JOAN MENDHAM

TECHNICAL SUPPORT

GARY DOYLE
Building Services Manager

CHRIS HAYLOCK
Senior Building Services Technician

STEPHEN SALT
Senior Equipment Technician

KEITH SAVILL
Senior Technical Officer

POLLY ATTLESEY
JOHN HALE
CAROL HENDERSON
SHANE JOHNSON
URSZULA KOKOT
JENNIE PIDGEN
JASON RISEBOROUGH
PAULINE WHITING
PAUL BROCK
KATARZYNA GACEK
GILLIAN HYNES
RUE JONES
KARIN MULLENGER
ROBIN PLUMRIDGE
DAVID SIMPSON

CATERING

DARIA SKRODZKA
AGNIESZKA SURLES

INSTITUTE PUBLICATIONS

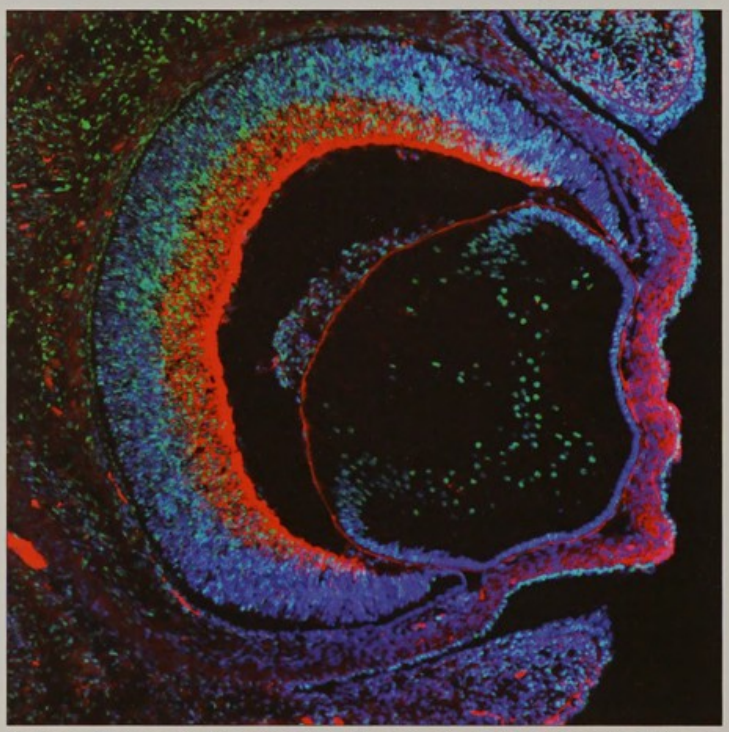
The following is a list of articles by members of the Institute that were either published or accepted for publication, since the date of publication of the last Annual Report. (note: refs no 24 and 45 were published prior to 2005, but previously unlisted in Institute reports).

* Indicates equal priority.

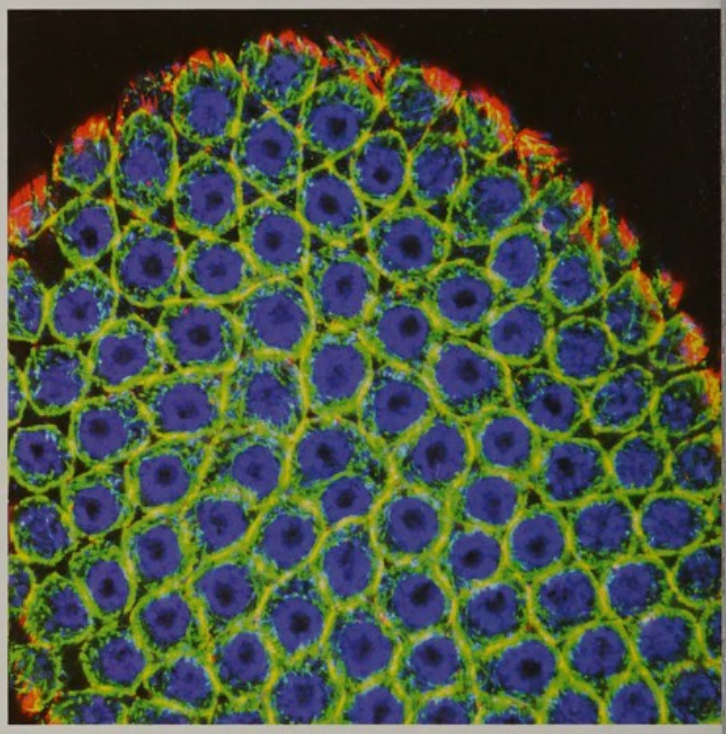
1 Acquaviva C and Pines J (2006) The anaphase promoting complex/ cyclosome: APC/C. **Journal of Cell Science** 119, 2401-2404

2 Ahnesorg P, Smith P and Jackson SP (2006) XLF interacts with the XRCC4-DNA ligase IV complex to promote DNA nonhomologous end-joining. **Cell** 124, 301-313

3 Ahnesorg P and Jackson SP (2006) The non-homologous end-joining protein Nej1p is a target of the DNA damage checkpoint. **DNA Repair** [in press]



Neurons (Tuj1 red) in the developing eye appear to have lower levels of histone 3 lysine 4 tri-methylation (green) than neural progenitors. Nuclei stained with DapI (blue) (Dean Griffiths, Livesey lab, 2006)



Drosophila follicle cells stained for tubulin in green, actin in red and a nuclear marker in blue. (Isabel Torres, St Johnston lab, 2006)

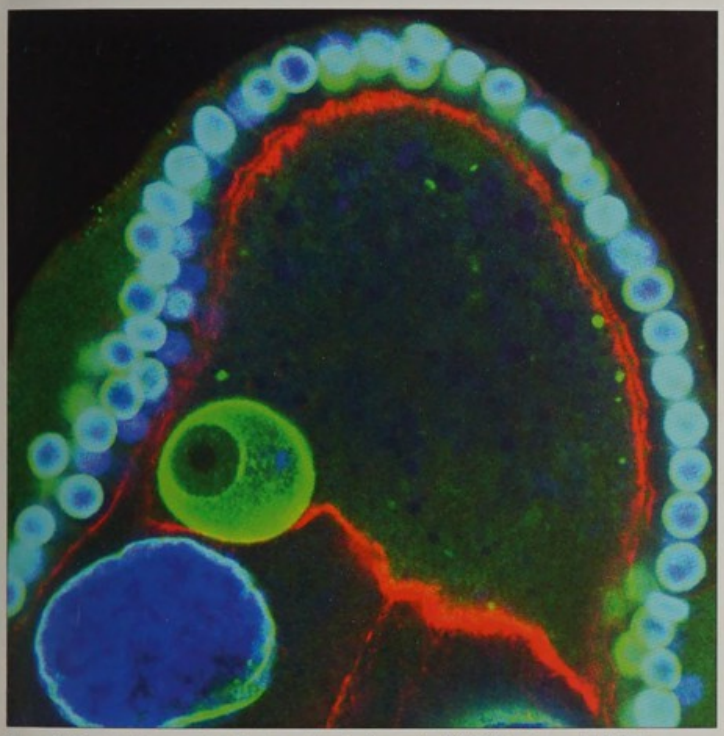
4 Ancelin K, Lange UC, Hajkova P, Schneider R, Bannister AJ, Kouzarides T and Surani MA (2006) Blimp1 associates with Prmt5 and directs histone arginine methylation in mouse germ cells. **Nat Cell Biol** 8, 623-630

5 Basto R, Lau J, Vinogradova I, Gardiol A, Woods CJ, Khodjakov A and Raff JW (2006) Flies without centrioles. **Cell** 125, 1–12

6 Bossing T, Brand AH (2006) Determination of cell fate along the anteroposterior axis of the *Drosophila* ventral midline. **Development** 133 (6), 1001-12

7 Choksi SP, Southall T, Bossing T, Edoff K, de Wit E, van Steensel B, Micklem G and Brand AH Prospero acts as a binary switch between self-renewal and differentiation in *Drosophila* neural stem cells. **Developmental Cell** [in press]

8 Cobb BS, Hertweck A, Smith J, O'Connor E, Graf D, Cook T, Smale ST, Sakaguchi S, Livesey FJ, Fisher AG and Merkenschlager M (2006) A role for Dicer in immune regulation. **J Exp Med** 203, 2519-2527



Stage 9 *Drosophila* oocyte. Nuclear lamin (green), DAPI (blue) and TRICT-Phalloidin (red) (Alexandre Raposo, St Johnston lab, 2006)

9 Dingwell KS and Smith JC (2006) Tes regulates neural crest migration and axial elongation in *Xenopus*. **Developmental Biology** 293, 252 – 267

10 Doerflinger H, Benton R, Torres IL, Zwart MF and St Johnston D (2006) *Drosophila* anterior-posterior polarity requires actin-dependant PAR-1 recruitment to the oocyte posterior. **Current Biology** 16, 1090-1095

11 Dore AS, Furnham N, Davies OR, Sibanda BL, Chirgadze DY, Jackson SP, Pellegrini L and Blundell TL (2006) Structure of an Xrcc4-DNA ligase IV yeast ortholog complex reveals a novel BRCT interaction mode. **DNA Repair** (Amst) 5, 362-8

12 Durcova-Hills G, Adams IR, Barton SC, Surani MA, McLaren A (2006) The role of exogenous fibroblast growth factor-2 on the reprogramming of primordial germ cells into pluripotent stem cells. **Stem Cells** 24, 1441-1449

13 Durcova-Hills G, Hajkova P, Sullivan S, Barton S, Surani MA and McLaren A (2006) Influence of sex chromosome constitution on the genomic imprinting of germ cells. **PNAS** 103 (30) 11184-11188

14 Edoff K, Dods JS and Brand AH (2006) Detection of GFP during nervous system development in *Drosophila melanogaster*. In: Reporter genes for eukaryotic systems. **Methods in Molecular Biology**, Ed. D Anson, Humana Press [in press]

15 Egger B, Chell JM and Brand AH (2006) Insights into neural stem cell biology from flies. In: **Stem Cells and Brain Repair**. Eds. Theo Palmer (Stanford), Nick Allen (Cardiff), Maeve Caldwell (Cambridge) Philosophical Transactions B: Biological Sciences [in press]

16 Elliott DA, Solloway MJ, Wise N, Biben C, Costa MW, Furtado MB, Lange M, Dunwoodie S, Harvey RP (2006) A tyrosine-rich domain within homeodomain transcription factor Nkx2-5 is an essential element in the early cardiac transcriptional regulatory machinery. **Development** 133 (7), 1311-22

17 Firtel R and Zernicka-Goetz M (2006) Pattern formation and developmental mechanisms. Editorial overview. **Current Opinion in Genetics and Development** 16, 331-332

18 Grenon M, Magill C, Lowndes N and Jackson SP (2006) Double-strand breaks trigger MRX- and Mec1-dependent, but Tel1 independent, checkpoint activation. **FEMS Yeast Research** 6, 836-847

19 Gurdon JB (2006) From nuclear transfer to nuclear reprogramming: the reversal of cell differentiation. **Annual Review of Cell and Developmental Biology** 22, 1-22

20 Hagege H, Nasser R, Weber M, Milligan L, Aptel N, Jacquet C, Drewell RA, Dandolo L, Surani MA, Cathala G, Forne T (2006) The 3' portion of the mouse H19 Imprinting-Control Region is required for proper tissue-specific expression of the Igf2 gene. **Cytogenetic and Genome Research** 113, 230-237

21 Hayes MJ, Kimata Y, Wattam SL, Lindon C, Mao G, Yamano H, Fry AM (2006) Early mitotic degradation of Nek2A depends on Cdc20-independent interaction with the APC/C. **Nat Cell Biol** 8, 607-614

22 Henderson MJ, Munoz MA, Saunders DN, Clancy JL, Russell AJ, Williams B, Pappin D, Khanna KK, Jackson SP, Sutherland RL and Watts CKW (2006) EDD mediate DNA damage-induced activation of CHK2. **J Biol Chem** 281, 39990-40000

23 Hentges P, Ahnesorg P, Pitcher RS, Bruce CK, Kysela B, Green AJ, Bianchi J, Wilson TE, Jackson SP and Doherty AJ (2006) Evolutionary and functional conservation of the DNA non homologous end joining protein, XLF/Cernunnos. **J Biol Chem** 281, 37517-37526

24 Irion U, Adams J, Chang C and St Johnston D (2006) Miranda couples oskar mRNA/Staufen complexes to the bicoid mRNA localization pathway. **Dev Biol** 297, 522-533

25 Iyer NG, Xian J, Chin SF, Bannister AJ, Daigo Y, Aparicio S, Kouzarides T and Caldas C (2006) p300 is required for orderly G1/S transition in human cancer cells. **Oncogene** [Epub ahead of print]

26 Jenny A, Hachet O, Závorszk P, Cyrklaf A, Weston MDJ, St Johnston D, Erdélyi M and Ephrussi A (2006) A translation-independent role of oskar RNA in early *Drosophila* oogenesis. **Development** 133, 2827-2833

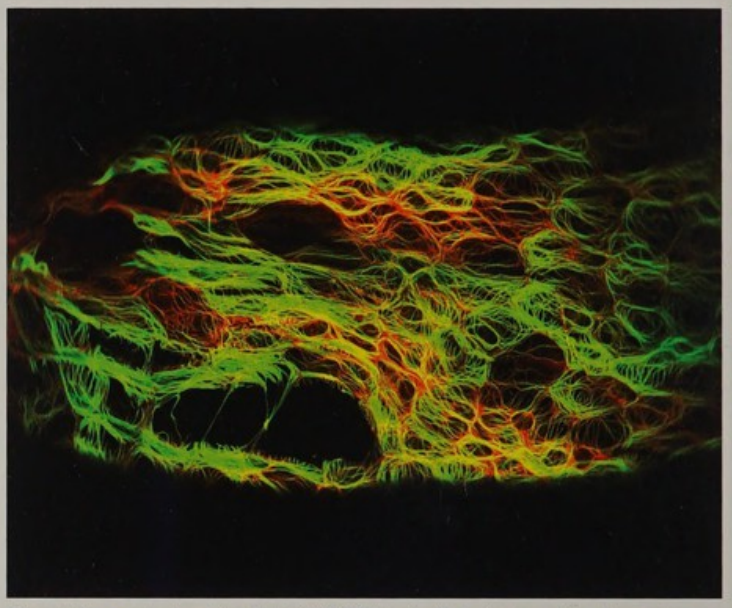
27 Knapp D, Messenger N, Rana AA and Smith JC (2006) Neurotrophin Receptor Homolog (NRH1) proteins regulate mesoderm formation and apoptosis during early *Xenopus* development. **Dev Biol** 300, 554-569

28 Maldonado-Saldivia J, van den Bergen J, Kruskos M, Gilchrist M, Ruili L, Sinclair AH, Surani MA and Western P (2006) Dppa3 and Dppa4 are closely linked SAP motif genes restricted to pluripotent cells and the germ line. **Stem Cells** 10, 1634

29 Matsumura H, Tada M, Otsuji T, Yasuchika K, Nakatsuji N, Surani MA, Tada T (2006) Targeted chromosome elimination from ES-somatic hybrid cell nuclei. **Nature Methods** [in press]

30 McCabe N, Turner NC, Lord CJ, Kluzek K, Bialkowska A, Swift S, Giavara S, O'Connor MJ, Tutt AN, Zdzienicka MZ, Smith GC and Ashworth A (2006) Deficiency in the repair of DNA damage by homologous recombination and sensitivity to poly(ADP-Ribose) polymerase Inhibition. **Cancer Res** 66, 8109-15

31 McCaffrey R, St Johnston D, González-Reyes A (2005) A novel mutant phenotype implicates dicephalic in cyst formation in the *Drosophila* ovary. **Developmental Dynamics** 235, 908 – 917



Drosophila oocyte shedding its 'skin' (GFP labelled) during transition to embryo. (Mary Pines, Brown lab, 2006)

32 McCaffrey R, St Johnston D, Gonzalez-Reyes A (2006) *Drosophila* mus301/spindle-C encodes a helicase with an essential role in dsDNA break repair and meiotic progression. **Genetics** 174, 1273-1285

33 Miyoshi N, Barton SC, Kaneda M, Hajkova P, Surani MA (2006) The continuing quest to comprehend genomic imprinting. **Cytogenet Genome Research** 113, 6-11

34 Moffett A, Loke C and McLaren A (2006) Eds. **Biology & Pathology of Trophoblast**. Camb Univ Press

35 Munro TP, Kwon S, Schnapp BJ, St Johnston D (2006) A repeated IMP-binding motif controls oskar mRNA translation and anchoring independently of *Drosophila melanogaster* IMP. **J Cell Biol** 172(4), 577-88

36 Murray MJ, Davidson CM, Hayward NM and Brand AH (2006) The Fes/Fer non-receptor tyrosine kinase cooperates with Src42A to regulate dorsal closure in *Drosophila*. **Development** 101242/dev.02467

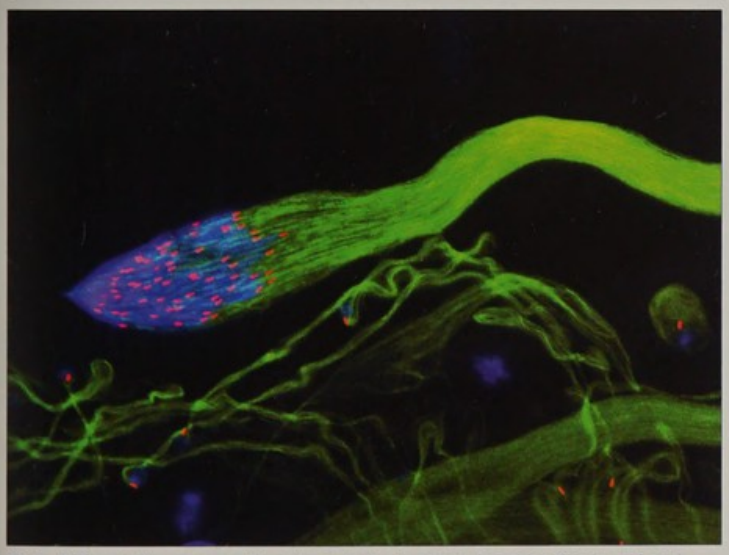
37 Na J & Zernicka-Goetz M (2006) Asymmetric positioning and organization of the meiotic spindle of mouse oocytes requires CDC42 function. **Current Biology** 16, 1249-1254

38 Na J, Lykke-Andersen K, Torres-Padilla ME and Zernicka-Goetz M (2006) Dishevelled proteins regulate cell adhesion in mouse blastocyst and serve to monitor changes in Wnt signaling. **Dev Biol** [in press]

39 Nelson CJ, Santos-Rosa H and KouzaridesT (2006) Proline isomerization of histone H3 regulates lysine methylation and gene expression. **Cell** 126, 905-916

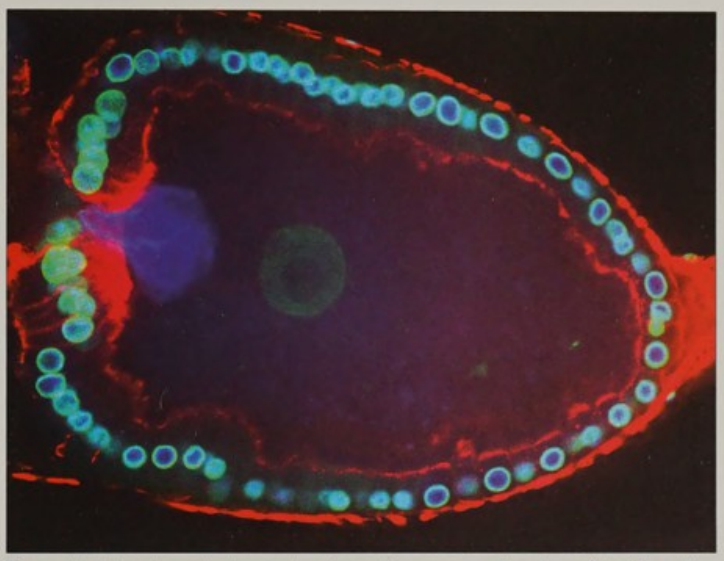
40 Ohinata Y, Seki Y, Payer B, O'Carroll D, Surani MA and Saitou M (2006) Germline recruitment in mice: a genetic program for epigenetic reprogramming. **Ernst Schering Res Found Workshop** (60) 143 74

41 Ozdag H, Teschendorff AE, Ahmed AA, Hyland SJ, Blenkiron C, Bobrow L, Veerakumarasivam A, Burtt G, Subkhankulova T, Arends MJ, Collins VP, Bowtell D, Kouzarides T, Brenton JD, Caldas C (2006) Differential expression of selected histone modifier genes in human solid cancers. **BMC Genomics** 7, 90



Cyst of *Drosophila* sperm with microtubules in green, basal bodies in red and DNA in blue. (Carly Dix, Raff lab, 2006)

42 Pance A, Livesey FJ and Jackson AP (2006) A role for the transcriptional repressor REST in maintaining the phenotype of neurosecretory-deficient PC12 cells. **J Neurochem** 25 October [Epub ahead of publication]



Stage 11 *chickadee* mutant egg chamber with a nurse cell nucleus (blue) invading the oocyte and displacing its nucleus (green). Nuclear lamin (green), DAPI (blue) and TRICT-Phalloidin (red) (Alexandre Raposo, St Johnston lab, 2006)

43 Payer B, Chuva de Sousa Lopes SM, Barton SC, Lee C, Saitou M, Surani MA (2006) Generation of stella-GFT transgenic mice, a novel tool to study germ cell development. **Genesis** 44(2) 75-83

44 Pines J (2006) New approaches to research on mitosis. Ed. **Methods** 38, 1-60

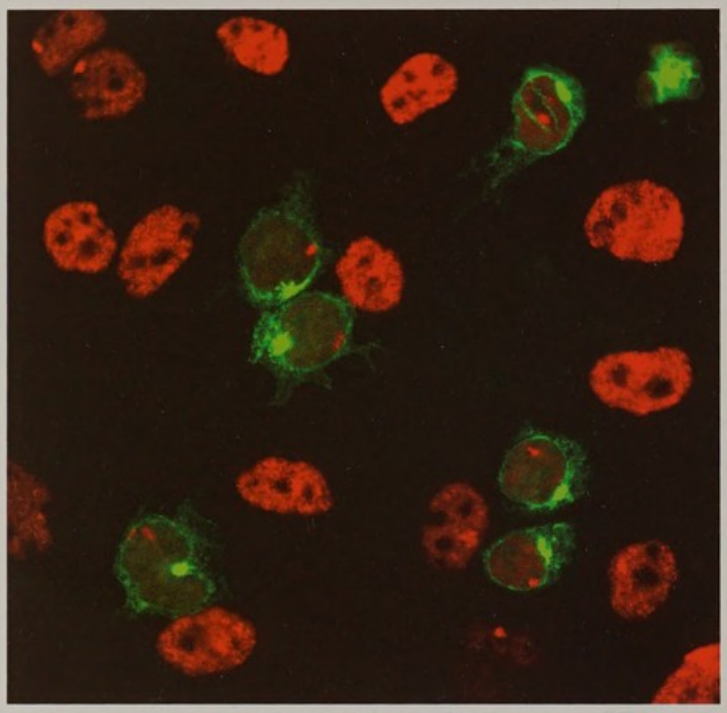
45 Pines J (2005) Mitosis: a matter of getting rid of the right protein at the right time. **Trends in Cell Biology** 16, 55-63

46 Polesello C, Huelsmann S, Brown NH and Tapon N (2006) The *Drosophila* RASSF homologue antagonises the Hippo pathway. **Curr Biol** 16, 2459-2465

47 Rana AA, Collart C, Gilchrist MJ and Smith JC (2006) Defining synphenotype groups in *Xenopus tropicalis* by use of antisense morpholino oligonucleotides. **PLoS Genetics** 101371/journalpgen0020193eor

48 Richardson L, Torres-Padilla ME, Zernicka-Goetz M (2006) Regionalised signalling within the extraembryonic ectoderm regulates anterior visceral endoderm positioning in the mouse embryo. **Mech Dev** 123, 288-296

49 Sartori A (2005) Networking in the framework. **Nature** 437, 292



E7.5 Blimp1:GFP female PGCs (green) after 2 days culture showing a distinct H3K27me3 nuclear spot (red) characteristic of the inactive X-chromosome. (Susana Chuva de Sousa Lopes, Surani lab, 2006)

50 Seitan VC, Laval S, Majid NA, Dorsett D, Rana A, Smith JC, Bateman A, Banks P, Newbury S, Krpic S, Hostert A, Rollins RA, Erdjument-Bromage H, Tempst P, Benard CY, Hekimi S and Strachan T (2006) Metazoan Scc4 homologues link sister chromatid cohesion to cell and axon migration guidance. **PLoS Biology** 4 e242

51 Smith JC and Alfred J (2006) Development: moving on in 2006. **Development** 133, 1-2

52 Smits VAJ, Reaper PM and Jackson SP (2006) Rapid PIKK-dependent release of Chk1 from chromatin promotes the DNA-damage checkpoint response. **Current Biology** 16, 150-159

53 Soares ML, Haraguchi S, Torres-Padilla ME, Kalmar T, Carpenter L, Bell G, Morrison A, Ring CJ, Clarke NJ, Glover DM, Zernicka-Goetz M (2005) Functional studies of signalling pathways in peri-implantation development of the mouse embryo by RNAi. **BMC Dev Biol** 5, 28

54 Stern CD, Charité J, Deschamps D, Duboule D, Durston AJ, Kmita M, Nicolas J-F, Palmeirim I, Smith JC and Wolpert L (2006) Head-tail patterning of the vertebrate embryo: one, two or many unresolved problems? **Int J Dev Biol** 50, 3-15

55 Stucki M and Jackson SP (2006) γH2AX and MDC1: anchoring the DNA-damage-response machinery to broken chromosomes. **DNA Repair** 5, 534-543

56 Subkhankulova T, Livesey FJ (2006) Comparative evaluation of linear and exponential amplification techniques for expression profiling at the single cell level. **Genome Biol** 7(3), R18

57 Surani MA (2006) Genomic reprogramming. In: **Essentials of Stem Cell Biology** Ed. R Lanza Elsevier Press, 349-454

58 Surani MA (2006) Germ cells. In: **Henry Stewart Talks on Epigenetics: Concepts, Theories, Paradigms and Mechanisms**. CD-ROM

59 Surani MA and McLaren A (2006) A new route to rejuvenation. **Nature** 443, 284-285

60 Tanentzapf G, Martin-Bermudo MD, Hicks MS and Brown NH (2006) Multiple factors contribute to integrin-talin interactions *in vivo*. **J Cell Sci** 119, 1632-1644

61 Tanentzapf G and Brown NH (2006) An interaction between integrin and the talin FERM domain mediates integrin activation but not linkage to the cytoskeleton. **Nat Cell Biol** 8, 601-606

62 Tang F, Hajkova P, Barton SC, Lao K, Surani MA (2006) MicroRNA expression profiling of single whole embryonic stem cells. **Nucleic Acids Research** 34, (2) e9

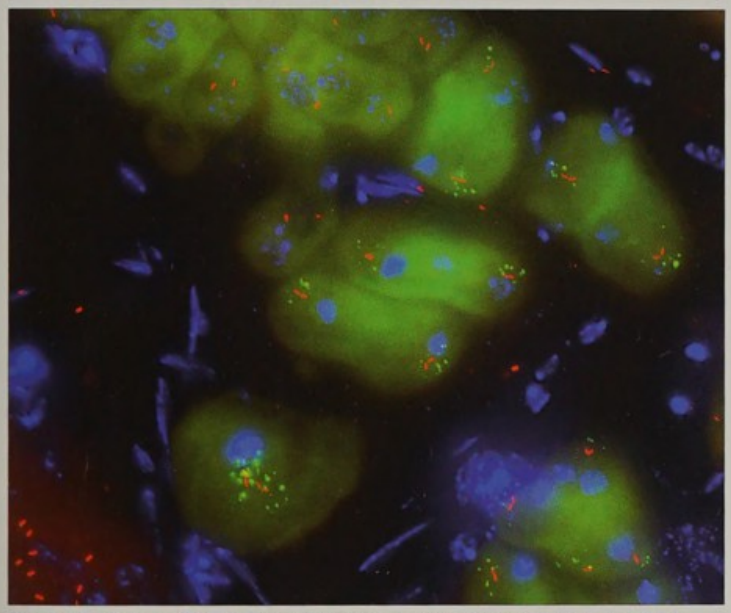
63 Tang F, Hajkova P, Barton SC, O'Carroll D, Lee C, Lao K, Surani MA (2006) 220-plex micro RNA expression profile of a single cell. **Nature Protocols** 1 (3) 1154 – 1159

64 Torres-Padilla ME, Bannister AJ, Hurd PJ, Kouzarides T and Zernicka-Goetz M (2006) Dynamic distribution of the replacement histone variant H3.3 in the mouse oocyte and preimplantation embryos. **Int J Dev Biol** 50, 455-61

65 Torres-Padilla ME and Zernicka-Goetz M (2006) Role of TIF1 as a modulator of embryonic transcription in the mouse zygote. **J Cell Biol** 174, 329-338

66 Torres-Padilla ME, Parfitt DE, Kouzarides T and Zernicka-Goetz M (2006) Histone arginine methylation directs cells towards pluripotency in the preimplantation mouse embryo. **Nature** [in press]

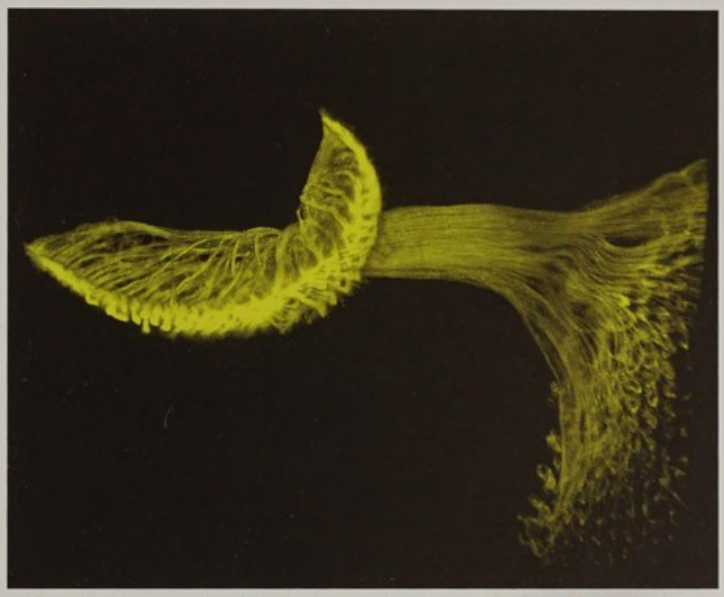
67 Tutt AN, Lord CJ, McCabe N, Farmer H, Turner N, Martin NM, Jackson SP, Smith GC and Ashworth A (2005) Exploiting the DNA repair defect in BRCA mutant cells in the design of new therapeutic strategies for cancer. **Cold Spring Harb Symp Quant Biol** 70, 139-48



Fixed preparation of adult *Drosophila* testis showing several stages of mutant spermatogenesis and stained with mRFP-centrioles (red), GFP-Pericentriolar material (green) and DNA (blue). (Eliana Lucas, Raff lab, 2006)

68 van der Weyden L, Arends MJ, Chausiaux OE, Ellis PJ, Lange UC, Surani MA, Affara N, Murakami U, Adams DJ, Bradley A (2006) Loss of TSLC1 causes male infertility due to a defect at the spermatid stage of spermatogenesis. **Molecular & Cellular Biology** 26, 9, 3595-3609

69 Wardle FC and Smith JC (2006) Transcriptional regulation of mesendoderm formation in *Xenopus*. **Seminars in Cell & Dev Biology** 17 99-109



Axons of the developing *Drosophila* visual system, stained with FasII-Alexa488. (James Chell, Brand lab, 2006)

70 Wardle FC, Odom DT, Bell GW, Yuan B, Wiellette EL, Herbolsheimer E, Sive HL, Young RA, Smith JC (2006) Zebrafish promoter microarrays identify actively transcribed embryonic genes. **Genome Biology** 7, R71 101186/gb-2006-7-8-r71

71 Wolpert L, Smith JC, Jessell T, Lawrence P, Robertson E and Meyerowitz E (2006) **Principles of Development**, 3rd edition, Oxford University Press

72 Yano K, Subkhankulova T, Livesey FJ and Robinson HP (2006) Electrophysiological and gene expression profiling of neuronal cell types in mammalian neocortex. **J Physiol** 575, 361-365

73 Zernicka-Goetz M (2006) The first cell-fate decisions in the mouse embryo: destiny is a matter of both chance and choice. **Current Opinion in Genetics and Development** 16, 406-412

STAFF AFFILIATIONS

JULIE AHRINGER is a member of the Scientific Advisory Board of Reactome.

ANDREA BRAND is a Founding Board Member of The Rosalind Franklin Society, a member of the Academy of Medical Sciences Academic Careers Committee, and the Institute representative to the Cambridge University Women in Science, Engineering and Technology Initiative (WiSETI).

JOHN GURDON is a member of the Conseil Scientifique of the Institut Curie, Paris, a member of the Scientific Advisory Board of the Max-Planck-Institut für Biophysikalische Chemie, Göttingen, and Chairman of the Company of Biologists, a member of the Board for Diagnostics of the Real World. He also sits on the Advisory Board of the new Harvard Stem Cell Institue, and is a Board member for the Daiwa Anglo-Japanese Foundation.

STEVE JACKSON is a member of the Radiation Oncology and Biology External Advisory Board, University of Oxford Steering Committee for the UK Research Network on the Biomedical Applications of High Energy Ion Beams, British Society for Cell Biology and is Chief Scientific Officer, KuDOS Pharmaceuticals Ltd.

TONY KOUZARIDES is a member of the Cancer Research UK Scientific Executive Board, a member of the Marie Curie Institute Scientific Committee, and non-executive director of AbCam Plc.

ANNE McLAREN is a member of the international Scientific Advisory Board (Fachbeirat) of The Max Planck Institute for Molecular Biomedicine in Munster, Germany and the Scientific Advisory Committee of the Institute for Molecular Bioscience in Brisbane, Australia, and is an Honorary Fellow of King's College, Cambridge.

JONATHON PINES is the Membership Secretary of the British Society for Cell Biology and a member of the HFSP Fellowship Committee.

JORDAN RAFF is a member of the Academy of Medical Sciences' working group on the Careers of Basic Scientists, a Non-Executive Director of the Company of Biologists, a life-long member of the Royal Institution, and a Committee Member and Honor Fell Travel Award Secretary of British Society for Cell Biology.

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.

JIM SMITH is a member of the Board of Directors of the Babraham Institute, Editor-in-Chief of Development, a member of the University of Cambridge Sub-Committee for Biological Sciences and Clinical Medicine (Senior Academic Promotions), and a member of the Cancer Research UK Scientific Promotions and Salaries Assessment Panel. He is also a member of the University of Cambridge School of Biological Sciences External Relations & Collaborations Group, the Royal Society B-Side Awards Committee and the University of Cambridge Consultative Committee for Safety. From 2007: Wellcome Trust Interview Committee for Sir Henry Wellcome Postdoctoral Fellowships.

AZIM SURANI is the Sir Dorabji Tata Professor, Tata Institute for Fundamental Research, NCBS, Bangalore, India (2005-2010), a member of the Royal Society Working Group on Stem Cells, a member of the German Stem Cells Initiative, and Founder and Consultant for CellCentric Ltd.

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

HONOURS AND AWARDS

ANDREA BRAND - The Royal Society Rosalind Franklin Award

ANNE McLAREN - Awarded March of Dimes prize for Developmental Biology, 2007.

AZIM SURANI - Rosenstiel Award for Distinguished Work in Basic Medical Research 2007

EDITORIAL BOARDS OF JOURNALS

JULIE AHRINGER – Public Library of Science Biology, Molecular Systems Biology, EMBO Journal, EMBO Reports, Phil. Transactions of the Royal Society B, Faculty of 1000.

ANDREA BRAND – Neural Development, BioEssays, 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, EMBO Reports, Nature Reviews, DNA Repair, Faculty of 1,000, Science, Genes and Development, Current Biology, The Scientist.

ANNE McLAREN – Gene Therapy, Current Opinion in Genetics and Development.

JON PINES – EMBO Journal, EMBO Reports.

DANIEL ST JOHNSTON – Development, EMBO Journal, EMBO Reports.

JIM SMITH – Trends in Genetics, EMBO Reports.

AZIM SURANI – Cell Stem Cell, Regenerative Medicine.

MAGDALENA ZERNICKA-GOETZ – Developmental Dynamics, BioMed Central, Developmental Biology, Reproduction, Development.

INTERNATIONAL ADVISORY BOARD

PROF KIM NASMYTH, University of Oxford, Oxford, UK (Chairman).

DR STEVE COHEN, European Molecular Biology Laboratory, Heidelberg, Germany.

DR TIM HUNT, Cancer Research UK, Potters Bar, UK.

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

DR JUDITH KIMBLE, Laboratory of Molecular Biology, University of Wisconsin, Madison, USA.

DR ROBB KRUMLAUF, Stowers Institute for Medical Research, Kansas City, USA.

PROF KAI SIMONS, Max-Planck-Institute of Molecular Cell Biology and Genetics, Dresden, Germany.

CHAIRMAN OF THE MANAGEMENT COMMITTEE

PROFESSOR SIR TOM BLUNDELL, Head, Department of Biochemistry and Chair of the School of Biological Sciences, University of Cambridge, UK

LEAVERS DURING 2006

CLAIRE ACQUAVIVA moved to Marseille, France to take up a postdoctoral position at the Inserm Cancer Institute.

PETER AHNESBORG completed his PhD and moved to Switzerland to take up a postdoctoral position in the lab of Josef Jiricny at the Institute of Molecular Cancer Research, University of Zurich.

ROBERT ANDREWS completed his PhD and is now a trainee patent attorney with Newburn Ellis.

EVA ASSCHER now works in the Faculty of Law at the Tilburg Institute for Law, Technology and Society, The Netherlands.

CAN CENIK was a visiting student in the Ahringer group who returned to full-time studies.

JUN-AN CHEN completed his PhD and moved to the USA to take up a postdoctoral position in the lab of Hynek Wichterle, Department of Pathology at Columbia University.

SEMIL CHOKSI completed his PhD and is now a Postdoctoral Fellow at the IMCB in Singapore.

SUSANA CHUVA DE SOUSA LOPES continues to participate in a collaboration with the Surani group funded by a Fellowship from the Netherlands.

LORENA CLAY completed her PhD and left to take up a postdoctoral position with Yves Barral at the ETH in Zurich.

PAOLO CODEGA was a visiting student in the Livesey group who returned to full-time studies.

ESTEBAN CONTRERAS was a visiting student from Chile who returned to full-time studies.

RICARDO COSTA moved to the University of Manchester with the Amaya group.

BEN DAVID returned to full-time studies after completing a Vacation Studentship at the Institute.

ALEX DOMIN completed his PhD and has joined Boston Management Consultants.

KAREL DOREY moved to the University of Manchester with the Amaya group.

ROSALIND DRUMMOND (aka **FRIDAY**) left following maternity leave.

JOANNA GRABAREK has transferred to the Core Technical Team.

NILS GRABOLE was a visiting student in the Livesey group who returned to Germany to continue his studies.

SEIKI HARAGUCHI left to establish a research group in Tokyo, Japan

KATHARINE HARTLEY left to take up the role of Cambridge Neuroscience Coordinator.

XIAO HUANG moved back to China to take up a faculty position at the College of Life Sciences, Zheijang University.

UWE IRION moved to Germany to establish a research group at the Max Planck Institute in Tübingen.

SHOKO ISHIBASHI moved to the University of Manchester with the Amaya group.

BOBBY JOHNSON started an undergraduate degree at Durham University.

ALAN KERSHAW returned to full-time studies after completing a Vacation Studentship at the Institute.

LEAVERS DURING 2006

RYOKO KURIYAMA completed her sabbatical and returned to the Department of Genetics, Cell Biology and Development at the University of Minnesota, USA.

NATALIE LE BOT took up the position of Editor of Nature Cell Biology.

ALICIA LEE completed her PhD and is currently in China teaching English to Chinese students.

NICHOLAS LOVE completed his MPhil and continues his studies in Japan.

KARIN LYKKE-ANDERSEN moved to Denmark to take up a Group Leader position at Aarhus University.

ZOFIA MADEJA left to take up a postdoctoral position at the Babraham Institute.

VANESSA MAYBECK moved with Katja Röper to the Department of Physiology, Development and Neuroscience, University of Cambridge.

SIGOLENE MEILHAC moved to Paris to take up a postdoctoral position at the Institut Pasteur.

ANTOINE MOLARO returned to full-time studies after completing a Vacation Studentship at the Institute.

ABDEL MOUMEN moved to St George's, University of London.

TRENT MUNRO moved to Brisbane, Australia to establish a research group at the Australian Institute for Bioengineering and Nanotechnology.

MAITHREYI NARASIMHA moved to take up a Group Leader position at the Tata Institute, Mumbai, India.

RAY NG completed his PhD and has taken up a postdoctoral position at the Babraham Institute.

NANCY PAPALOPULU moved to the University of Manchester to take up a chair in the Faculty of Life Sciences.

ROBERT PAREDES moved to the University of Manchester with the Amaya group.

BERNHARD PAYER completed his PhD and moved to Harvard, USA to take up a postdoctoral position.

TERESA PEREIRA-DE-BARROS completed her PhD and joined a drug discovery company in Cambridge.

MARY PINES moved with Katja Röper to the Department of Physiology, Development and Neuroscience, University of Cambridge.

VENKAT PISUPATI took up a new postdoctoral position at the Hutchison/MRC Research Centre in Cambridge.

SABHI RAHMAN completed his PhD, and is pursuing a career in Consultancy.

JOANA RAMIS MOREY returned to Mallorca, Spain to work for the island's Government Health Department in the Research and Information Section.

TARIK REGAD took up a new postdoctoral position in Leicester.

KATJA RÖPER established her own group as a David Phillips Fellow in the Department of Physiology, Development and Neuroscience, University of Cambridge.

MARTIN ROTH moved to the University of Manchester with the Papalopulu group.

NITIN SABHERWAL moved to the University of Manchester with the Papalopulu group.

YASUSHI SAKA moved to France to take up a Group Leader position at the Interdisciplinary Institute in Lille.

JOHN SOLLY completed his PhD and accepted a position at ZS Associates in London.

ESTHER SOLOMON has taken an administrative position in Israel.

ESTHER SON returned to full-time studies after completing a Vacation Studentship at the Institute.

XIMENA SOTO RODRIGUEZ moved to the University of Manchester with the Amaya group.

FRANCES STEDHAM took up a new position as a Research Assistant at the CIMR.

SASKIA SUIJKERBUIJK was a visiting student in the Raff Lab who returned to full-time studies.

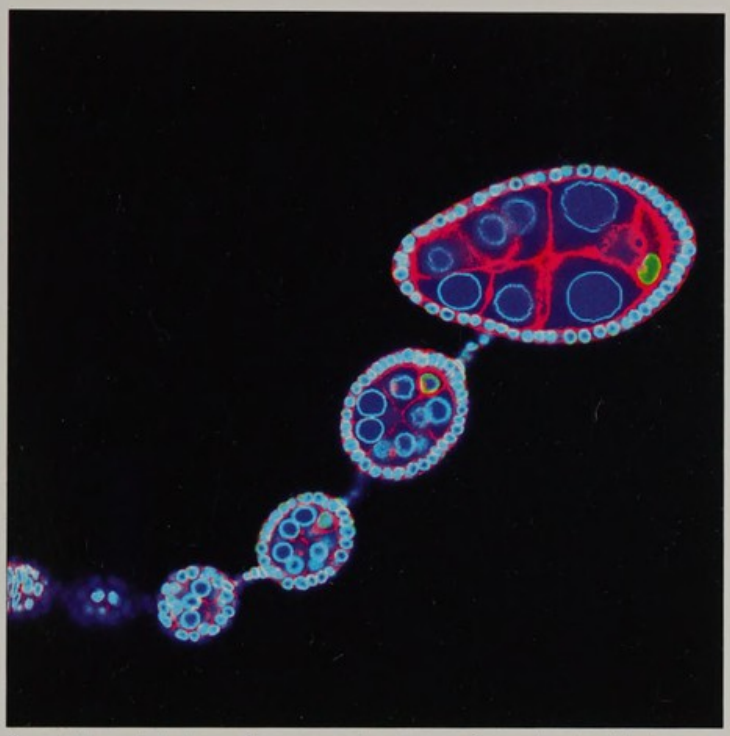
GUY TANENTZAPF moved to a second postdoctoral position in the University of Toronto.

MARIA-ELENA TORRES-PADILLA moved to Strasbourg to take up a postdoctoral position at the Institut de Genetique et de Biologie Moleculaire et Cellulaire.

MIAO-CHIH TSAI completed her PhD, and is preparing to study Medicine.

DAVID WELCHMAN completed his PhD and moved to the Department of Physiology, Development and Neuroscience, University of Cambridge as a Postdoctoral Fellow.

VITALY ZIMYANIN moved to Dresden to take up a postdoctoral position at the Max Planck Institute.



Drosophila ovariole shown from germarium to stage 8 egg chamber. Nuclear lamin (green), DAPI (blue) and TRICT-Phalloidin (red). (Alexandre Raposo, St Johnston lab, 2006)

ACKNOWLEDGEMENTS

Prospectus produced in the Wellcome Trust/Cancer Research UK Gurdon Institute. Edited by Ann Cartwright, production by Alastair Downie.

Group photographs by Chris Green (Dept of Biochemistry)

Printed by Cambridge University Press.

Front cover: 3D reconstruction of the mouse blasotcyst showing how the first set of pluripotent cells that will give rise to the future body (yellow) is cradled by the outside cells of the embryo (blue). (Emlyn Parfitt and Magdalena Zernicka-Goetz, 2006)

Back cover: Images from the Gurdon Institute Annual Retreat, Oxford 2006 (John Overton & Jim Smith)

Wellcome Trust and 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