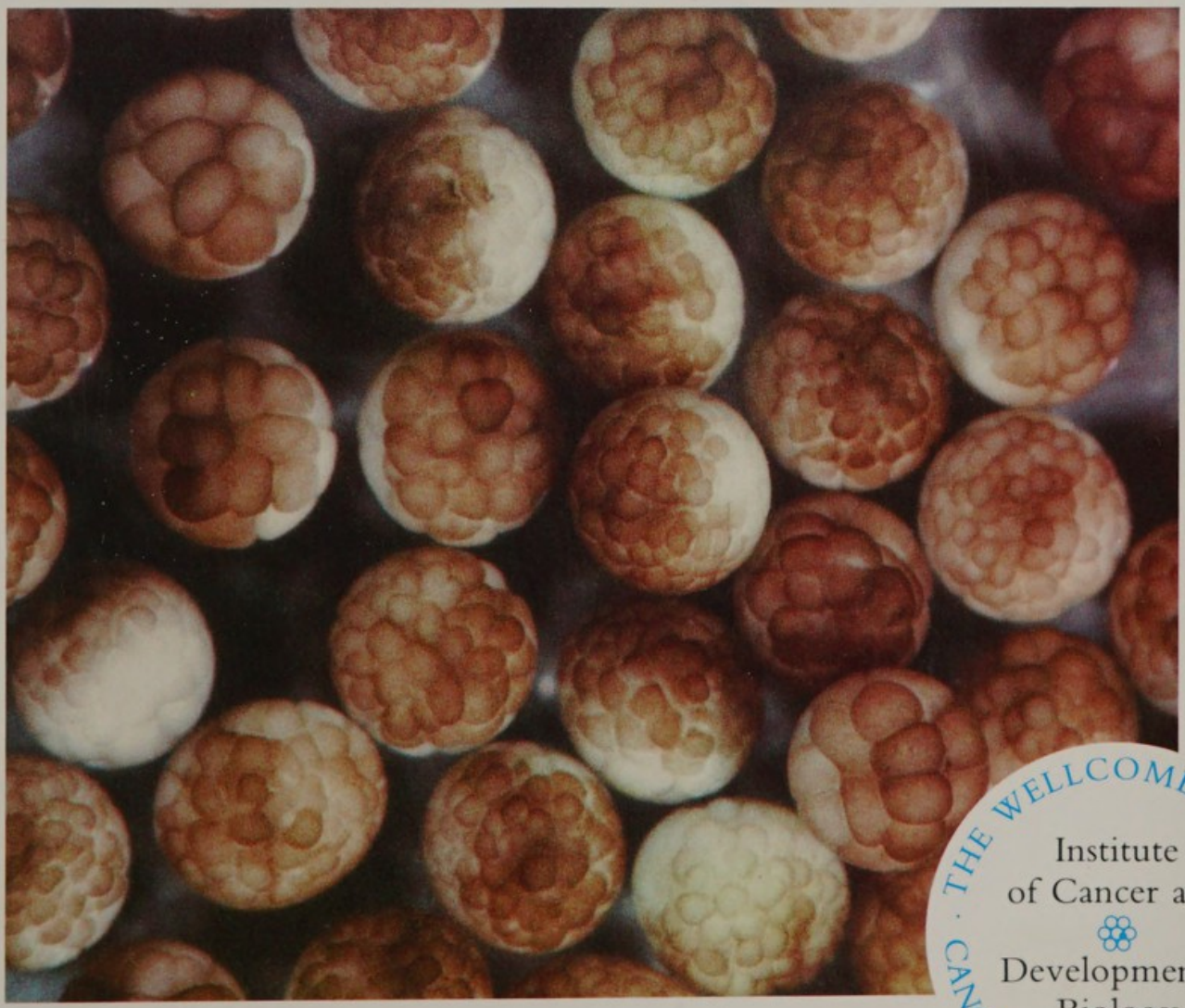
Annual report : 1991/1992 / The Wellcome Trust, Cancer Research UK Gurdon Institute of Cancer and Developmental Biology.

WELLCOME · CRC INSTITUTE CAMBRIDGE 1991



THE WELLCOME TRUST · CANCER RESEARCH CAMPAIGN ·

Institute of Cancer and Developmental Biology

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Institute of Cancer and Developmental Biology

ANNUAL REPORT

1991

AND 1992 PROSPECTUS

University of Cambridge

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Front Cover Photograph:
Early frog embryos at blastula stage
Photograph by Nick Torpey

INTRODUCTION

The Wellcome/CRC Institute of Cancer and Developmental Biology was formally opened by the Chancellor, the Duke of Edinburgh, on 13th June 1991. He was accompanied by Mr. R.G. Gibbs, Chairman of Wellcome Trustees, Lady Elizabeth Cavendish, Chairman of Council of the Cancer Research Campaign, and Lord Adrian, representing the Vice Chancellor. The Duke of Edinburgh and senior representatives from the Wellcome Trust and the Cancer Research Campaign were shown around the building and saw examples of the work being carried out by the

eleven research groups at present in the Institute. In July, we marked our opening with a 1½ day scientific meeting, at which 9 distinguished senior scientists from various parts of the world lectured in the areas of cell and cancer biology, to a large audience in the Babbage Theatre. The move into the new premises took place during February, 1991, and most of the research groups were fully functional soon after that.

The Institute represents a new type of research support within British Universities. Its key features are that it is an assemblage of independent research groups with closely complementary interests; all research groups are located in one building designed to promote as much interaction as possible. The building, located on land owned by the University, was funded by two charities, the Wellcome Trust (WT) and the Cancer Research Campaign (CRC), who also provide most of the continuing support for the research groups in the ratio of 2:1 (WT:CRC). The University maintains the building and administers the Institute, whose members are also affiliated to various University Departments to which they contribute teaching. These Departmental affiliations are worked out in the most appropriate way according to members' research interests.

The Institute was founded to promote research in the areas of Developmental Biology (WT) and Cancer Biology (CRC). These two areas of biology are complementary since developmental

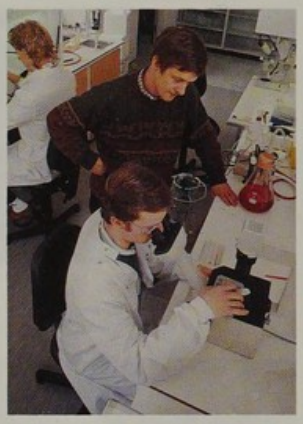
biology is concerned with how cells come to acquire and maintain their normal function; cancer is a result of a cell breaking loose from its correct controls and becoming abnormal. Both areas require a detailed knowledge of intracellular processes, which need to be analyzed at the cellular and molecular levels. These research areas are complementary at the scientific and technical levels. To understand what goes wrong when a cell becomes cancerous requires a knowledge of the processes which ensure correct cell function in normal development. And at the technical level, the analysis of cellular and molecular processes requires familiarity with techniques which no one person can master, such as gene cloning, antibody preparation, cell culture, and embryological manipulation. There is, therefore, a major benefit in having scientists with different but complementary knowledge and technical skills working in close proximity to each other.

This is a brief background to the formation of this Institute. We will have space for new members in the forthcoming years, since we are now at only two thirds of our full capacity. We will in future wish to concentrate our activities in the areas of vertebrate development and cancer biology. Our primary aim is to provide an excellent scientific environment for the best younger independent scientists within the areas of our interest.

J.B. GURDON
CHAIRMAN

INSTITUTE FACILITIES

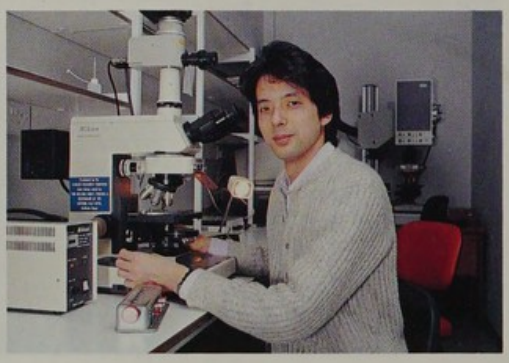
The Institute benefits from its position within the central science area of the University, allowing easy contact with biology departments.



Internal seminars are now a regular feature and sponsorship enables us to invite both national and international speakers to attend open meetings. The Institute has two seminar rooms and also a meeting room; not only does this latter room permit somewhat more formal conferences, but it also houses our growing collection of journals.

In addition to the equipment of individual groups, the Institute possesses core equipment facilities. These include, in central rooms on each floor, ultracentrifuges, –70°C storage, gel drying, incubator space etc. All are easily accessible from the laboratories.

Self service histology laboratory, a photography suite with black-and-white/colour processing and slide-making facilities, and light or fluorescent microscopy rooms are also available. Darkrooms house X-ray film processing, UV gel photography and confocal microscopes.



The Institute has a growing computer network comprising mostly Macintosh PCs. Additional facilities are currently being planned to enable, for example, on-line ordering, grant management and further fax facilities.

Support services include laboratory administration, secretaries, accounts, equipment and computer maintenance, stores and, in the future, a new building to handle

site deliveries and further solvent, gas and refuse storage.

The Institute staff, scientific and technical, are keen to see the continued provision of new technologies and efficient working practices which support first class research. To this end a lively, democratic atmosphere has been cultivated within which the members of the Institute contribute to policy matters at all levels.

AND THE SOCIAL SIDE ...

Interaction, scientific and social, has a high priority in the Institute. Although the laboratories are close to each other, many of them interconnecting with access routes to other rooms and areas of the building, it is an advantage to have a central area in which to meet. This is provided by a light and spacious coffee room, which is both a social and a scientific point of contact at morning coffee, lunch and afternoon tea, all vitally important to the British way of life! It also provides an ideal venue for out-of-hours social gatherings and doubles as a large seminar room.

As most staff are also associated with individual departments of the University they can participate in both work-related and social events organised by the department to which they are affiliated.

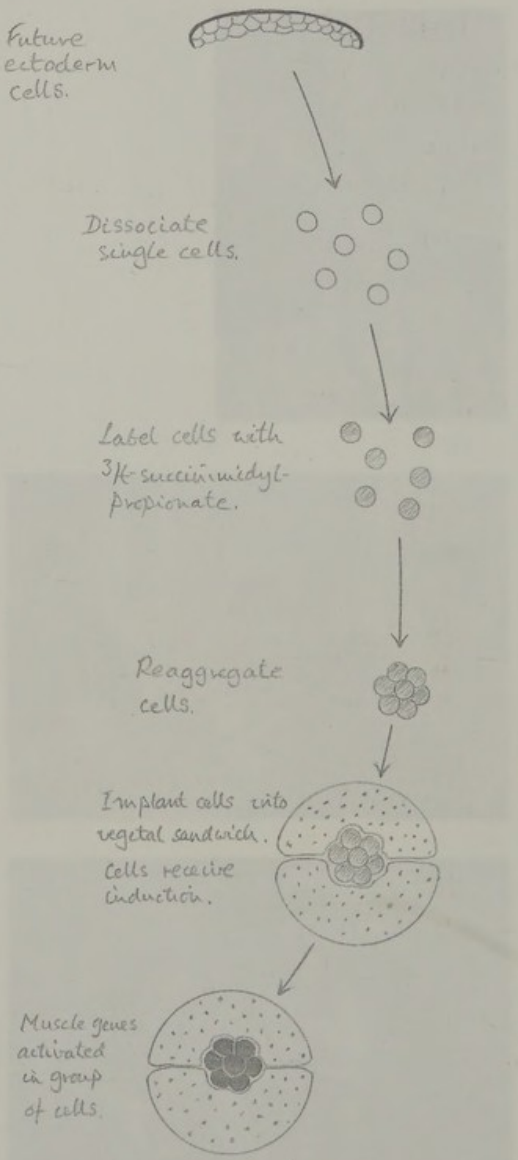
The Institute has recently fielded a football squad, successfully competing in its first two friendly matches, and table tennis and squash tournaments are planned.

MECHANISMS OF CELL DIFFERENTIATION IN EARLY AMPHIBIAN DEVELOPMENT

How do differences between cells first arise in early embryos? In the Vertebrates, much the most important mechanism leading to cell differences is interactions between cells. We are analysing this process in Amphibia: a few hours after fertilization, cells at one end of the embryo induce those at the other to become muscle, which is one of the first differentiated cell-types to be formed in embryos.

Using a muscle-specific actin gene as an early marker of muscle differentiation, we have identified two regulatory myogenic genes, XMyoD and XMyf5, whose products bind to the actin gene promoter. Furthermore, these regulatory genes can activate muscle genes when overexpressed in embryonic cells of non-muscle type.

We are using subtractive hybridization of cDNA libraries to find new genes which have an essential role in gene activation and cell interactions. We are analysing the mode of action of regulatory genes by injecting their messenger RNA together with actin promoter DNA constructs into an oocyte nucleus where they interact under the conditions that exist in living cells. Lastly, we are transplanting single muscle precursor cells into whole embryos, or into cultured tissues, to determine the time and nature of cell interactions required to initiate and maintain muscle gene expression.



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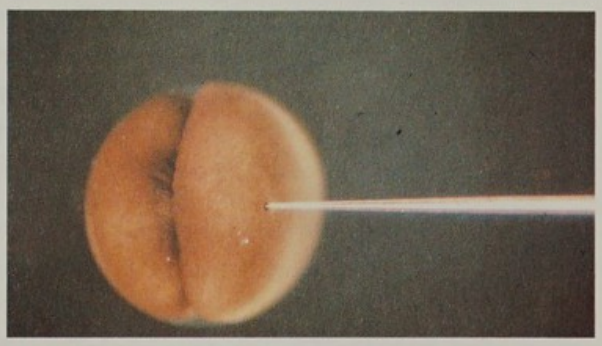


Microinjection of a 2-cell embryo

Expression of muscle actin (red) and XMyoD (black), from head (left) to tail (right)

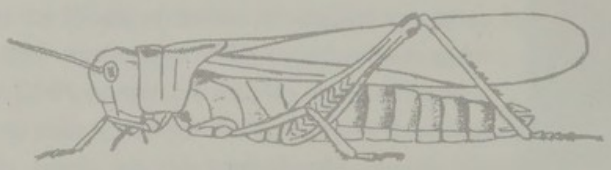
HOPWOOD, N.D., PLUCK, A. and GURDON, J.B. 1991. *Xenopus* Myf-5 marks early muscle cells and can activate muscle genes ectopically in early embryos. **Development 111**, 551-560.
GURDON, J.B. 1992. The generation of diversity and pattern in animal development. **Cell 68**, 1-15.
See also nos. 14,17,20,37,38, page 34 ff.

HOMEOTIC GENES AND SEGMENT PATTERNING IN INSECTS AND CRUSTACEA

Our studies focus on the Antennapedia-like family of homeobox genes. One aspect of this work is a comparison of the role of these genes in *Drosophila* and *Schistocerca*, two insect species that have very different modes of early development. We find that the segmental limits of expression of the homeotic genes are largely conserved, although the timing of their expression relative to segmentation and cellularization is not. In marked contrast, the role in early development of one segmentation gene, *ftz* appears not to be shared by the two species.

Comparison of homeotic gene expression between insects and crustacea may allow homologies between different body regions to be established by molecular markers. We have isolated homeobox containing clones from two crustacean species, *Daphnia* and *Artemia*. Preliminary results suggest that gene duplications may have amplified different members of the ancestral Hox gene cluster in these two groups of arthropods.

To study the effects of homeotic gene products on cell behaviour, we have built gene constructs (utilizing GAL4 regulatory elements from yeast) that should allow us to alter their expression in precisely controlled ways. We are now inserting these genes into fly strains to study their effects on pattern formation.



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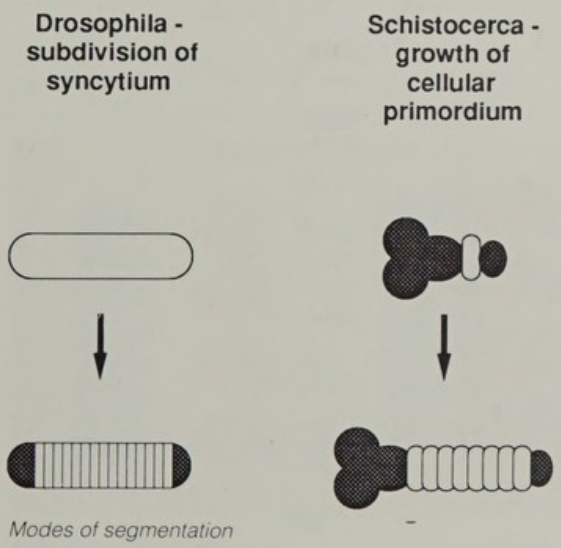
SILVIA FRENK
HANS GEORG FRÖHNHOFER
STEPHEN GREIG
ROBERT KELSH
MIGUEL MANZANARES
SANDRA RYLANCE

The developing nervous system of a locust embryo, stained to show those cells that express a Schistocerca ftz-like gene

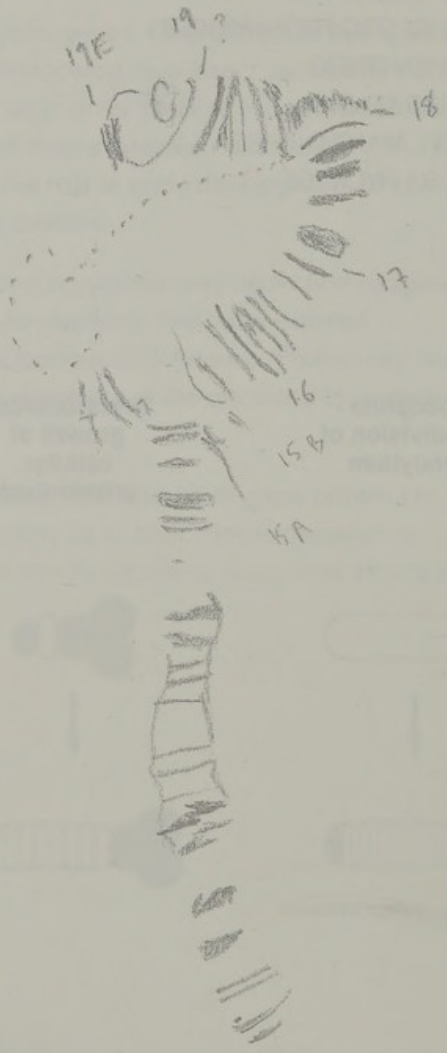


Modes of segmentation

AKAM, M. 1989. Hox and HOM: homologous gene clusters in insects and vertebrates. **Cell 57**, 347- 349.
TEAR, G., AKAM, M. and MARTINEZ-ARIAS, A. 1990. Isolation of an *abdominal-A* gene from the locust *Schistocerca gregaria* and its expression during early embryogenesis. **Development 110**, 915-925.
See also nos. 1,2,3,4, page 34 ff.

MOLECULAR ANALYSIS OF CELL ADHESION

The major interest of our group is to comprehend how an organism is formed through cell interactions during embryogenesis. Cells adhere to each other during embryogenesis to form coherent masses (tissues), and these tissues adhere to each other to form the recognizable organism. We are pursuing studies on the structure and function of cell surface proteins that mediate these events, in particular a family of proteins called the integrins. These proteins are involved in a variety of essential adhesive events in humans, including the migration of leukocytes to sites of inflammation and the formation of blood clots. In the fruit fly, *Drosophila melanogaster*, the particular integrins that we have identified and characterised appear to mediate adhesion between tissues (e.g. the adhesion of muscles to the epidermis), judging from the failure of this adhesion to occur in embryos that are mutant for the integrin genes. One avenue that we are currently investigating is the examination of the role of specific regions of the α_{PS2} integrin by replacing the wild type gene with copies that have been specifically altered by *in vitro* mutagenesis. By studying the effect of these changes on the development of the embryo we hope to relate the structure of the protein to its role in orchestrating the adhesion of cell layers to produce a functional organism.

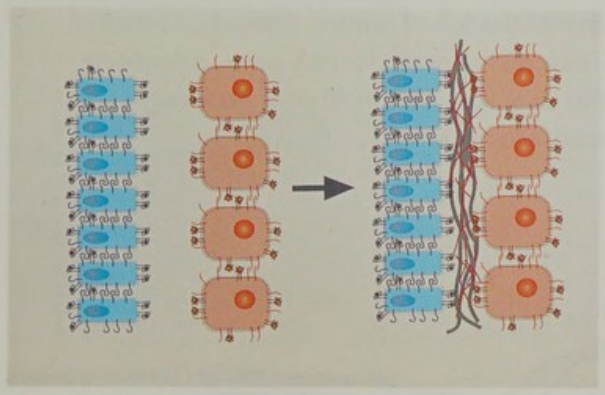


Polytene chromosome showing aberration at the PS2α/inflated locus

NICHOLAS BROWN

JAMES BLOOR
HOLLY DUNCAN
OLGA DUNIN-BORKOWSKI

Expression of the PS2α integrin on the surface of embryonic mesodermal cells



Adhesion of cell layers via the extracellular matrix

BROWN, N.H., KING, D.L., WILCOX, M. and KAFATOS, F.C. 1989. Developmentally regulated alternative splicing of *Drosophila* integrin PS2α transcripts. **Cell 59**, 185-195.

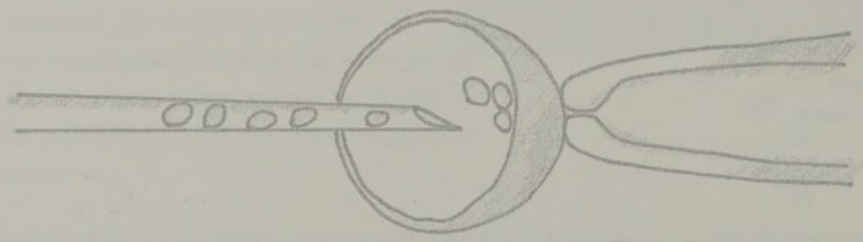
BOGAERT, T., BROWN, N. and WILCOX, M. 1987. The *Drosophila* PS2 antigen is an invertebrate integrin that, like the fibronectin receptor, becomes localized to muscle attachments. **Cell 51**, 929-940.

MAMMALIAN DEVELOPMENTAL BIOLOGY AND GENETICS THROUGH THE CULTURE OF EMBRYONIC STEM CELLS

The use of embryonic stem (ES) cells of mice as a route to somatic and germ line transgenesis has allowed several new approaches to experimental mammalian genetics. Because these cells provide a bridge between the whole animal and tissue culture, specific genetic modification which may be induced, screened or selected in culture, can be tested and recombined within the context of the physiology and genetics of the whole animal.

Injection of ES cells into 2.5 day host blastocysts results in chimaeric mice with the ES cells having the ability to contribute to all organs. Germline transmission of the ES cell clone results in multiple transgenic mice which can be analysed to determine the function of transgenes in the development of the mouse.

We are analysing mouse mutants resulting from random integration of viral DNA into the genome, and are using homologous recombination to introduce specific mutations into ES cells to study the results of such gene targeting *in vivo* and generate animal models of human diseases. Genes of interest in the laboratory, which have been targeted, include the cystic fibrosis gene, adenosine deaminase, mos and the oestrogen receptor, and after selection and analysis of homologous recombination events these clones are being introduced into mice.



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SIU-YUEN CHAN
BILL COLLEDGE
JOANNE DORAN
DIANE FOSTER
DARREN GILMOUR
DIPA NATARAJAN
ROSEMARY RATCLIFF
JUDITH SKINNER
GARRY UDY

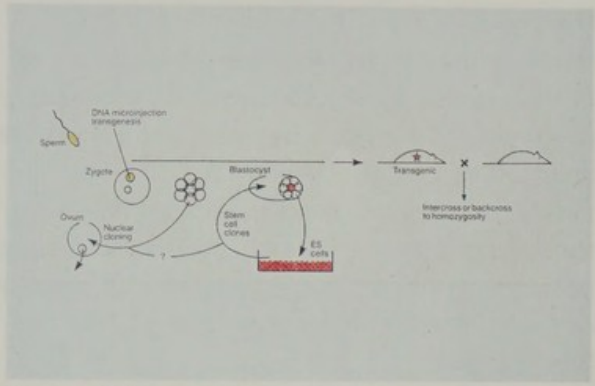
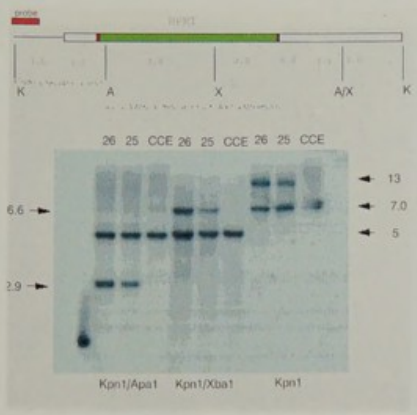


Diagram of the route to transgenic mice



Targeting an HPRT cassette into exon 10 of the mouse cystic fibrosis locus

EVANS, M.J. 1991. Embryonic stem cells as a route to an experimental mammalian genetics. *In:* **Genome Analysis 2: Gene expression and its control.** pp 1-12.

NOTORIANNI, E., LAURIE, S., GALLI, C., MOOR, R.M. and EVANS, M.J. 1991. Derivation of pluripotent, embryonic cell lines from pig and sheep. **J. Reprod. Fert. 43**, 255-260.

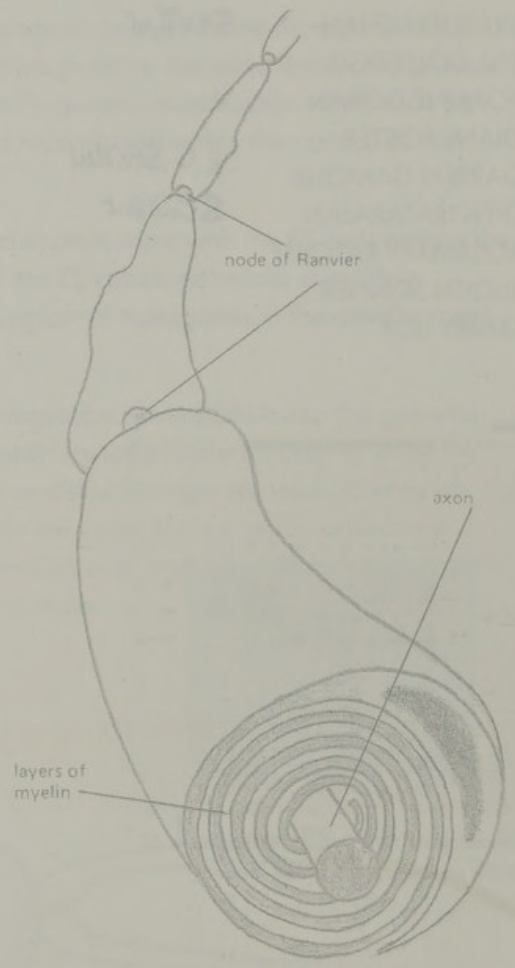
See also no. 6, page 34 ff.

DEVELOPMENT AND REPAIR OF THE VERTEBRATE CENTRAL NERVOUS SYSTEM

The goal of our research is to understand the development and repair of the vertebrate central nervous system (CNS). Our work is focused on myelination, the process by which nerve fibres are enclosed in a series of sheaths produced by a specialised glial cell, the oligodendrocyte. These sheaths are essential for rapid conduction of action potentials and this process represents an important example of cell-cell interaction during CNS development.

Our current interest is the mechanisms by which the distribution of myelin is regulated. Not all regions of the CNS contain myelinated axons and in at least one example, the retina, we have shown previously that this results from a restriction of the migration of the oligodendrocyte progenitor cell within the developing CNS.

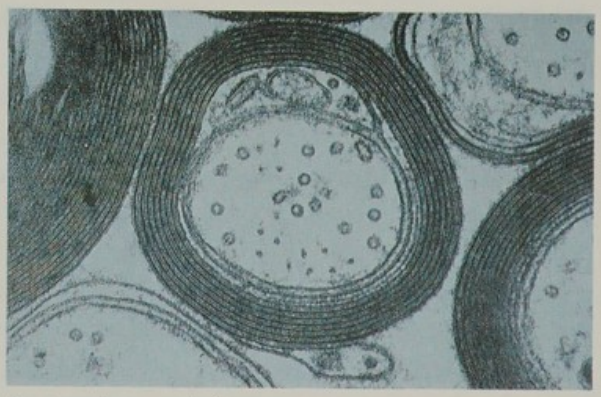
In order to elucidate these mechanisms, we are examining the extracellular matrix molecules present within the CNS, as these molecules and their cell-surface receptors play a central role in the control of migration elsewhere in the developing embryo. Initially we have focused on two molecules, thrombospondin and tenascin, and are using the techniques of cell culture to determine their effects on the migration, proliferation and differentiation of oligodendrocytes and their precursors. These studies should allow the development of hypotheses that can be tested in intact animals, either by antibody perturbation experiments or by using transgenic animals.



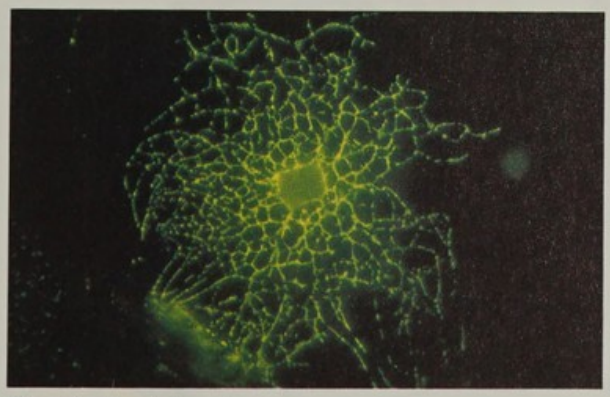
Structure of a myelinated axon

CHARLES FFRENCH-CONSTANT

BRENT KIERNAN R.C. Student
RICHARD MILNER Student
SUZANNA SCOTT-DREW



Electron micrograph of a myelinated axon



Oligodendrocyte in cell culture

FFRENCH-CONSTANT, C. and RAFF, M. 1986. The oligodendrocyte-type-2 cell lineage is specialized for myelination. **Nature 323**, 335-338.

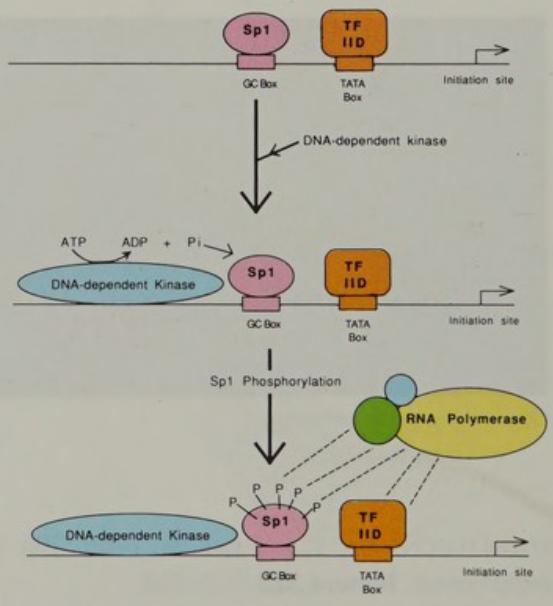
FFRENCH-CONSTANT, C., MILLER, R.H., BURNE, J.F. and RAFF, M.C. 1988. Evidence that migratory oligodendrocyte-type-2 astrocyte (O-2A) progenitor cells are kept out of the rat retina by barrier at the eye-end of the optic nerve. **J. Neurocytology 17**, 13-15.

See also nos. 10,11,42, page 34ff.

MECHANISMS AND REGULATION OF MAMMALIAN GENE TRANSCRIPTION

The aim of our work is to determine the mechanism of gene transcription at the molecular level and to understand how transcriptional initiation is regulated. One approach we have taken has been to analyse the general transcriptional machinery. We have made the surprising discovery that the general RNA polymerase II transcription factor, TFIID, is also a general factor for RNA polymerase III, even though most RNA polymerase III promoters do not contain TATA box elements.

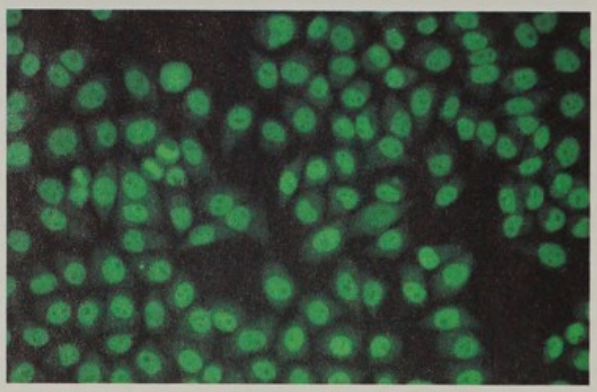
Another approach has been to study how the activity of the gene-specific RNA polymerase II factor, Sp1, is regulated. We have shown that this occurs both by modulating Sp1 levels (for example, during mouse development and upon infection by the SV40 virus), and by post-translational modification. In particular, we have focused on the DNA-dependent protein kinase (DNA-PK) that phosphorylates Sp1 and a variety of other transcription factors. This kinase is unusual in that it is a DNA binding protein that actually needs to be bound to DNA in order to function. We are employing biochemical techniques to determine the role(s) of the DNA-PK in transcription, and are investigating its physiological function by studying its regulation. Finally, we have cloned the DNA-PK cDNA. Characterisation of this clone will tell us the primary sequence of the DNA-PK protein and will allow us to map the functional domains of this intriguing molecule.



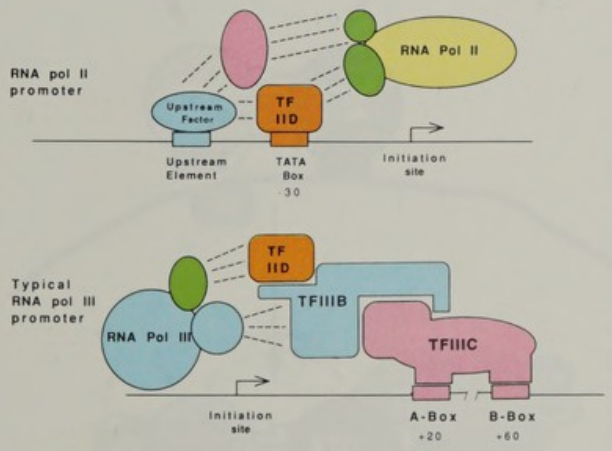
DNA-dependent kinase phosphorylates promoter-bound Sp1

STEPHEN JACKSON

TANYA GOTTLIEB Student
KATHARINE HARTLEY
ROBERT WHITE



Nuclear localisation of transcription factor Sp1



General factors involved in RNA pol II and RNA pol III transcription

JACKSON, S.P., MACDONALD, J.J., LEES-MILLER, S. and TIJAN, R. 1990. GC box binding induces phosphorylation of Sp1 by a DNA-dependent protein kinase. **Cell 63**, 155-165.

WHITE, R.J., JACKSON, S.P. and RIGBY, P.W.J. 1992. A role for the TATA-binding protein component of the TFIID complex as a general RNA polymerase III transcription factor. **Proc. Natl. Acad. Sci. USA 89**, in press.

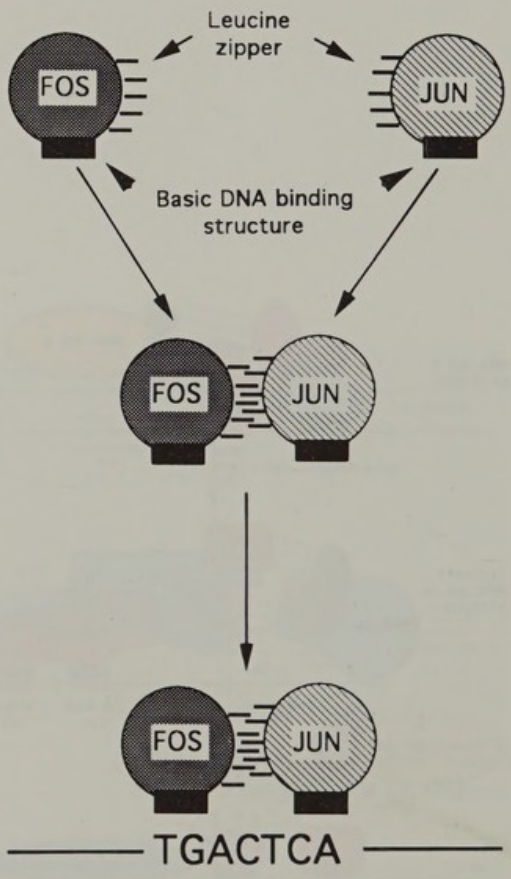
See also nos. 26,27,31,36, page 34ff.

TRANSCRIPTIONAL REGULATION IN EUKARYOTES

Our group is interested in the mechanisms by which 'regulatory' transcription factors activate gene expression. Regulatory factors bound to the promoter of genes are thought to activate transcription by contacting and stabilising the 'general' factor/RNA polymerase II complex assembled at the initiation site. In order to establish the points of interaction between 'regulatory' and 'general' transcription factors we are characterizing regulatory factors, such as Fos and Jun, and general factors, such as the TATA box binding protein TFIID.

Our previous work has shown that the Fos and Jun proteins can form a complex, via a leucine zipper and together bind to a specific DNA sequence, TGACTCA. We are now characterizing the domains of Fos and Jun which mediate transcriptional activation. We have identified an activation domain which is structurally and functionally homologous in Fos and Jun. This domain has two conserved motifs, it is phosphorylated by MAP kinase and its activity is modulated by the Ras oncoprotein. Our efforts are now concentrated towards identifying any protein(s) that bind to this domain and mediate the activation process.

Our work on general factors has led to the identification of several regulatory factors which directly contact the TFIID protein *in vitro*. Transient transfection assays show that the domains involved in contacting TFIID have intrinsic transactivating ability *in vivo*.



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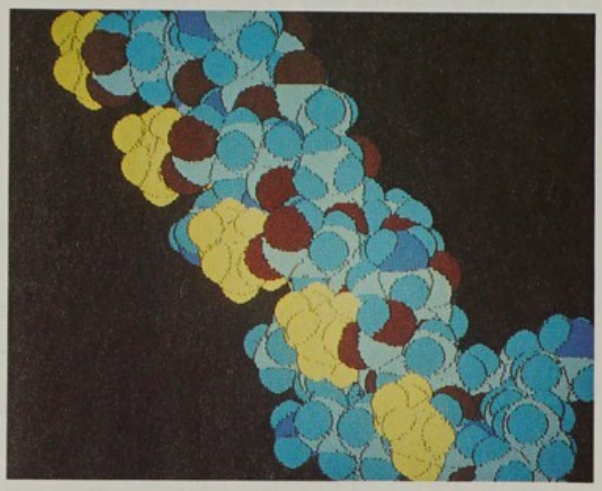
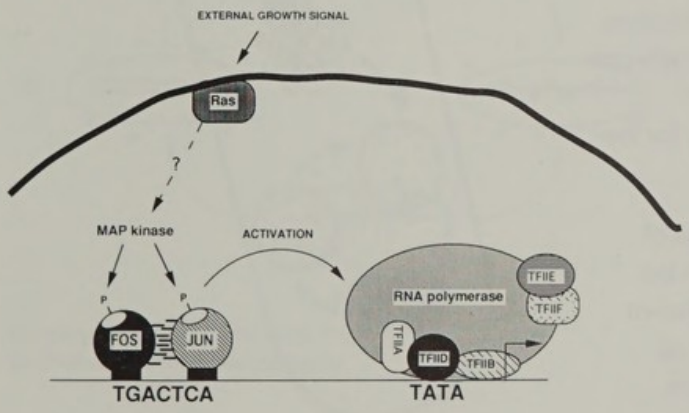
JACQUI SUTHERLAND



Graphics model of the Fos leucine zipper domain



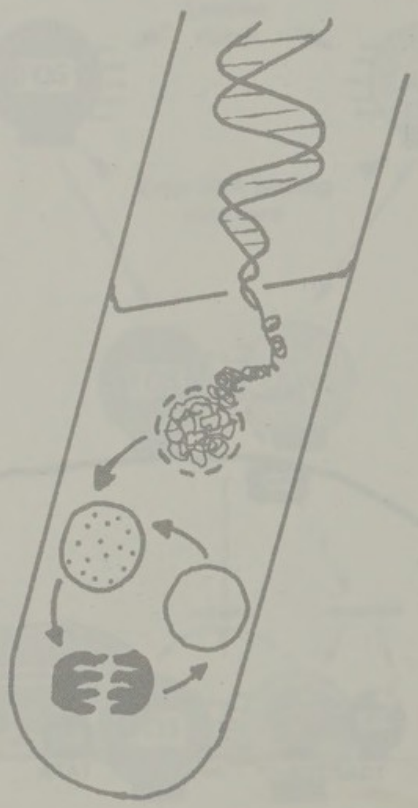
KOUZARIDES, T. and ZIFF, E.B. 1988. The role of the leucine zipper in the Fos-Jun interaction. **Nature 336**, 646-651.

KOUZARIDES, T. and ZIFF, E.B. 1989. Leucine zippers of Fos, Jun and GCN4 dictate dimerisation specificity and thereby control DNA binding. **Nature 340**, 568-571.

See also nos. 5,21, page 34ff.

CONTROL OF EUKARYOTIC CHROMOSOME REPLICATION

We have analysed the control of eukaryotic chromosome replication using a cell-free system derived from eggs of *Xenopus laevis*. Replication forks are clustered into groups of several hundred and this pattern has been reconstructed in pseudonuclei assembled *in vitro* from bacteriophage DNA as shown opposite.



Replication is coupled to the cell cycle so that DNA replicates only once between consecutive divisions. Disrupting the nuclear membrane overcomes this mechanism allowing a further cycle of complete replication. This observation can be explained by the licensing factor model of Blow and Laskey also shown opposite. We have found that the replication capacity of nuclei from synchronised human cells can be accounted for by a similar model. These experiments have produced a possible assay for the hypothetical licensing factor.

In addition we have identified a bipartite class of nuclear targeting sequence which appears to be common in nuclear proteins. We have also shown that *Xenopus* sperm nuclei are decondensed at fertilization by the acidic protein nucleoplasmin.

We have cloned and characterized the proto-oncogenes ski and A myb from *Xenopus* and found that A myb is expressed in ovary and testis in a manner which suggests it may be specific for proliferating germ cells.

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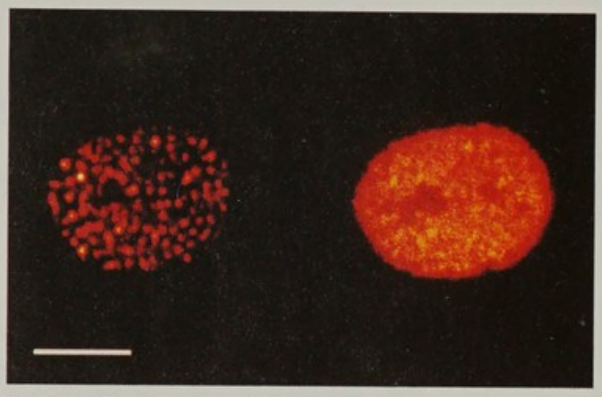
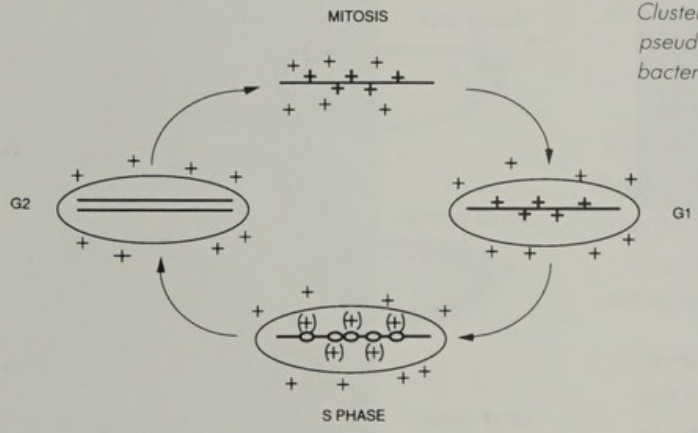
PAUL FISHER
CHONG YEE KHOO
GREG LENO
JOE MAKKERH
TONY MILLS
JACKIE ROBBINS



Clusters of replication forks in pseudonuclei assembled from bacteriophage DNA



Licensing factor model for the control of DNA replication in the cell cycle

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ROBBINS, J., DILWORTH, S.M., LASKEY, R.A. and DINGWALL, C. 1991. Two interdependent basic domains in nucleoplasmin nuclear targeting sequence: identification of a class of bipartite nuclear targeting sequence. **Cell 64**, 615-623.

See also nos. 8,22,23,24,25,29,33, page 34ff.

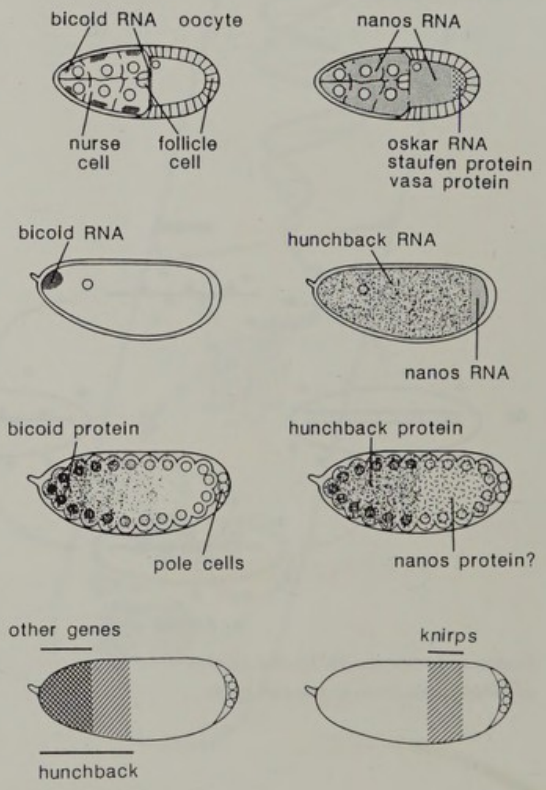
THE LOCALISATION OF MATERNAL DETERMINANTS IN THE *DROSOPHILA* EGG

In many organisms, the formation of one of the primary body axes is controlled by cytoplasmic determinants which are synthesized during oogenesis and are localised in the unfertilised egg. These signals have been best characterized in *Drosophila*, where the pattern of the anterior-posterior axis of the embryo is determined by the products of two localised maternal mRNAs: *bicoid* RNA which is localised to the anterior pole of the egg and *nanos* RNA which is found at the posterior pole. Our group is taking several different approaches to investigate how these RNAs are localised during oogenesis.

1) The maternal gene *staufen* is required for the localisation of both RNAs, and we have shown that staufen protein colocalises with each at the two ends of the egg. We are currently investigating whether or not staufen binds directly to RNA to mediate localisation to both the anterior and posterior poles.

2) We have recently identified mutations in several genes which cause *nanos* RNA to localise to the anterior as well as the posterior pole. In order to understand the normal functions of these genes, we are characterising two of them at a molecular level.

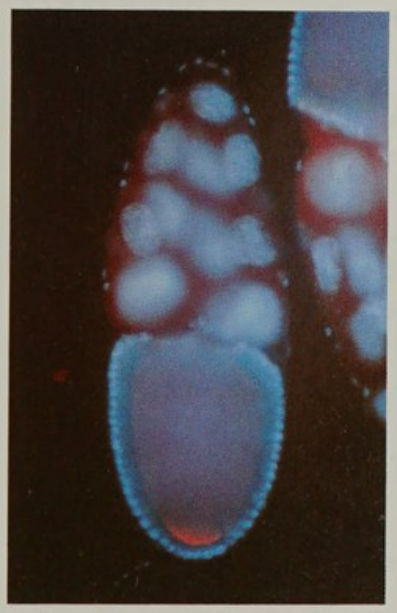
3) Localised *nanos* RNA is associated with large particles called polar granules, and we are beginning a biochemical analysis of these particles to discover how they are assembled, and what components they contain.



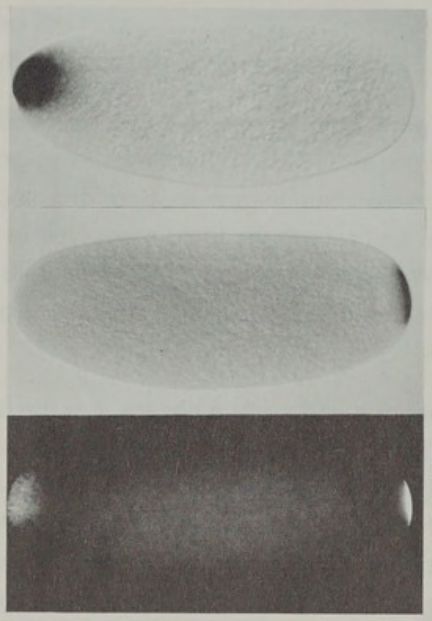
The determination of the anterior-posterior axis of the Drosophila *embryo*

DANIEL ST JOHNSTON

LISA ELPHICK
DAVID MICKLEM



The localisation of staufen protein (red) to the posterior pole of the oocyte



The colocalisation of staufen protein with maternal RNAs at both poles of the egg

ST JOHNSTON, D. and NÜSSLEIN-VOLHARD, C. 1992. The origin of pattern and polarity in the *Drosophila* embryo. **Cell 68**, in press.

ST JOHNSTON, D, BEUCHLE, D. and NÜSSLEIN-VOLHARD, C. 1991. *Staufen*, a gene required to localize maternal RNAs in the *Drosophila* egg. **Cell 66**, 51-63.

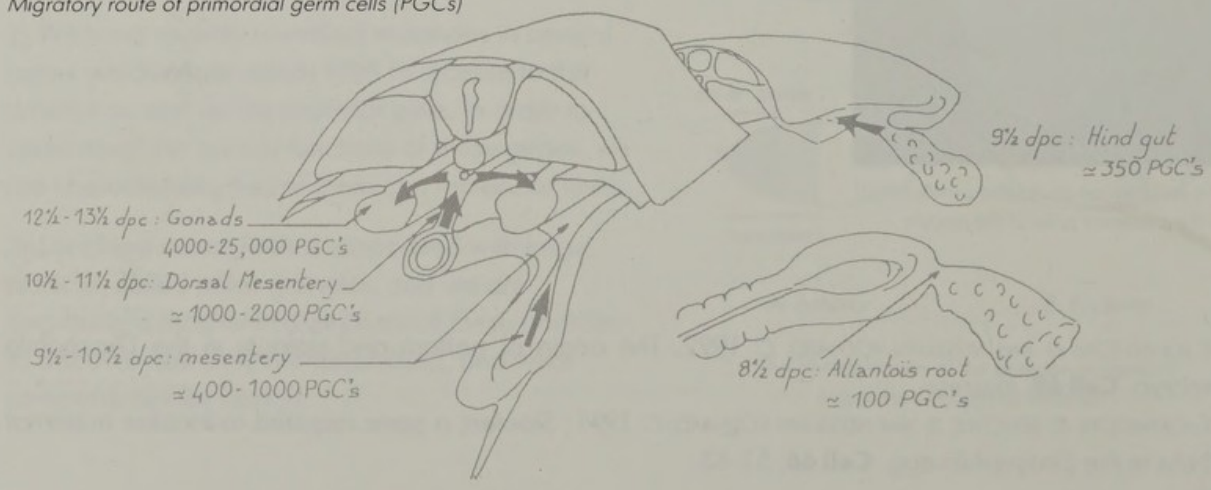
THE ESTABLISHMENT OF CELL BEHAVIOUR IN EARLY EMBRYOS

Morphogenesis is controlled by changes in cell behaviour. We study the molecules that underlie these changes, focusing on the cell surface and the cytoskeleton using two model systems.

1. **Primordial germ cells.** These give rise eventually to the functional gametes. In all vertebrates these cells migrate from elsewhere to the developing gonad. We are interested in the factors that control the survival, proliferation, migration, and targeting of these cells. Using an *in vitro* culture system we have identified several growth factors involved in their guidance (TGFβ), survival (Steel factor) and proliferation. We have also shown that germ cells modulate their adhesion to fibronectin during migration. These studies aim to show how the properties of a migratory cell population in the embryo are controlled.

2. ***Xenopus* oocytes and early embryos.** For the first 8 hours of *Xenopus* development there is no transcription. Nevertheless major changes occur at the cell surface and in the cytoskeleton during this time which must be dependent on maternal mRNAs and proteins. We have devised a technique to remove selectively from the oocyte specific mRNAs, and then to fertilise them to look for developmental abnormalities. We use this method to study the roles of intermediate filament proteins and cell surface proteins. We recently identified a novel cell surface molecule involved in cell adhesion during the first hours of development.

Migratory route of primordial germ cells (PGCs)



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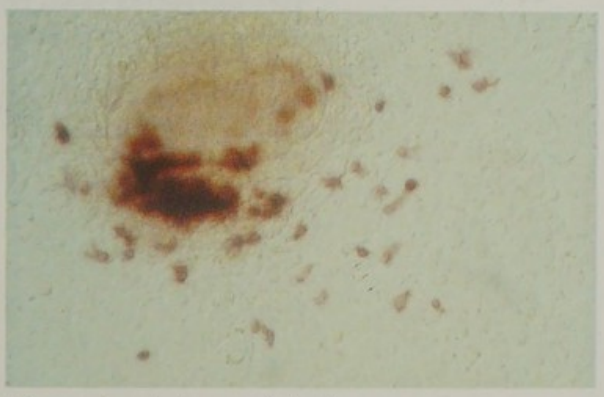
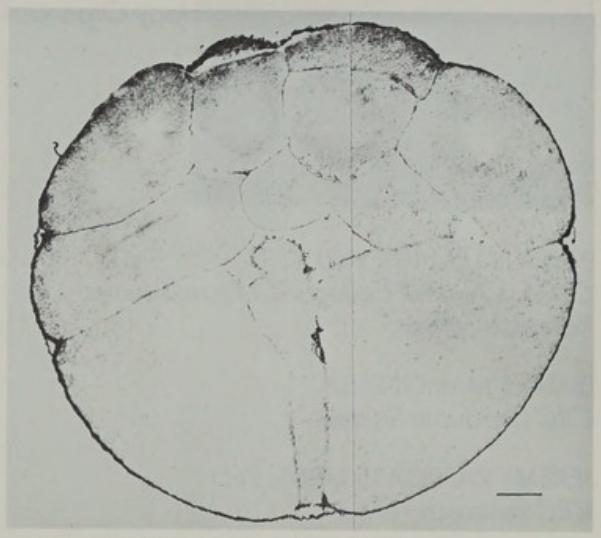


Mouse primordial germ cells (red) migrating out of an explant of gut from a 9½ day mouse embryo



a) Antibody M4B stains the surface of cells of early Xenopus blastula

b) A control cell-surface antibody does not prevent aggregation

c) Fab fragments of the antibody prevent aggregation of blastula cells

TORPEY, N.P., HEASMAN, J. and WYLIE, C.C. 1990. Identification of vimentin and novel vimentin-related proteins in *Xenopus* oocytes and early embryos. **Development 110**, 1185-1195.

GODIN, I., DEEDS, R., COOKE, J., ZSEVBO, K., DEXTER, M. and WYLIE, C.C. 1991. The effects of the *Steel* gene product on mouse primordial germ cells in culture. **Nature 352**, 807-809.

See also nos. 10,12,16,41, page 34ff.

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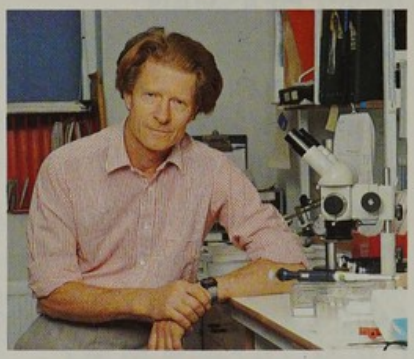

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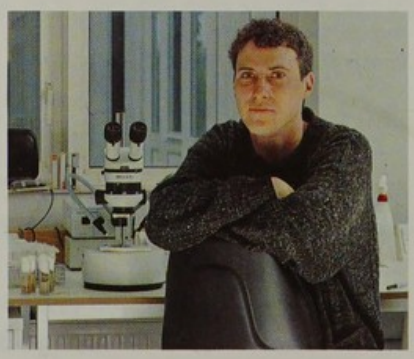

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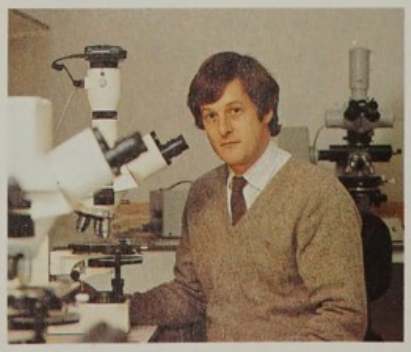

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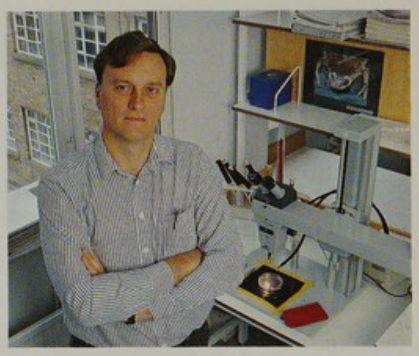

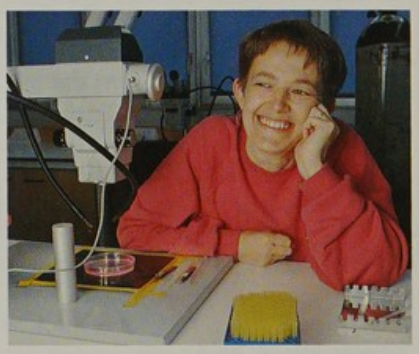

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INSTITUTE PUBLICATIONS

1. *AKAM, M.* 1991. Wondrous transformation. **Nature 349**, 282. (News & Views)

2. *AKAM, M., TEAR, G. and KELSH, R.* 1992. The evolution of segment patterning mechanisms in insects. **Proc. IV Int. Cong. Syst. Evol. Biol.**, Dioscorides Press, Portland, Oregon, in press.

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25. *LENO, G.H. and LASKEY. R.A.* 1991. The nuclear envelope determines the timing of DNA replication in *Xenopus* egg extracts. **J. Cell Biol. 112**, 557-566.

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27. *MASTRANGELO, I.A., COUREY, A.J., WALL, J.S., JACKSON, S.P. and HOUGH, P.V.C.* 1991. DNA looping and Sp1 multimer links: a mechanism for transcriptional synergism and enhancement. **Proc. Natl. Acad. Sci. USA 88**, 5670-5674.

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31. *SAFFER, J.D., JACKSON, S.P. and ANNARELLA, M.B.* 1991. Developmental expression of Sp1 in the mouse. **Mol. Cell. Biol.**, 2189-2199.

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34. *ST JOHNSTON, D. and NÜSSLEIN-VOLHARD, C.* 1992. The origin of pattern and polarity in the *Drosophila* embryo. **Cell, 68**, in press.

35. *ST JOHNSTON, D., BEUCHLE, D. and NÜSSLEIN-VOLHARD, C.* 1991. *Staufen*, a gene required to localize maternal RNAs in the *Drosophila* egg. **Cell 66**, 51-63.

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41. *TORPEY, N.P., HEASMAN, J. and WYLIE, C.C.* 1992. Distinct distribution of vimentin and cytokeratin in *Xenopus* oocytes and early embryos. **J. Cell Science**, in press.

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43. *WHITE, R.J., JACKSON, S.P. and RIGBY, P.W.J.* 1992. A role for the TATA-binding protein component of the TFIID complex as a general RNA polymerase III transcription factor. **Proc. Natl. Acad. Sci. USA 89**, in press.

OTHER ACTIVITIES

MICHAEL AKAM has been Chairman of the British Society for Developmental Biology since 1989.

JOHN GURDON was awarded the Jan Waldenström Lectureship and Medal from the Swedish Oncological Society.

RON LASKEY was awarded the Runnström Lectureship and Medal from the University of Stockholm.

CHRIS WYLIE has continued as Chief Editor of *Development.*

ACKNOWLEDGEMENTS

The figure on page 16 is based on a figure in Alberts et al. Molecular Biology of the Cell, *Garland Publishers, New York & London (Second edition 1989).*

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