Medicine

Kenyon JC, Tanner SJ, Legiewicz M, Phillip PS, Rizvi TA, Le Grice SFJ, Lever AM. SHAPE analysis of the FIV leader RNA reveals a structural switch potentially controlling viral packaging and genome dimerization. Nucleic Acids Res. 2011; in press.

Harris SR, Feil EJ, Holden MT, Quail MA, Nickerson EK, Chantratita N, Gardete S, Tavares A, Day N, Lindsay JA, Edgeworth JD, de Lencastre H, Parkhill J, Peacotyttck SJ, Bentley SD. Evolution of MRSA during hospital transmission and intercontinental spread. Science 2010; 327:469–474.

Metabolic Medicine

Professor Cox's group studies the molecular pathogenesis of lysosomal diseases with particular emphasis on the development of effective treatments – he gave the inaugural lecture at the first Gordon Conference on Lysosomal Diseases in 2011. With Dr Deegan, Clinical Director of the National Centre for the Treatment and Diagnosis of Lysosomal diseases, several clinical trials of substrate reducing drugs, pharmacological chaperones and innovative enzyme therapies are underway, particularly for Gaucher's disease and Fabry disease. Dr Stein, in collaboration with Professor Read, has been analysing the 3-dimensional structure of mutant and therapeutic-lysosomal proteins to understand the consequences of the disease-related changes and their susceptibility to therapeutic molecular manipulation – pharmacological chaperones. Dr Marchesan conducts studies of the molecular targeting and delivery of lysosomal proteins to their sites of action. With Dr Pavlova, there are studies to investigate the predictive role of cytokine biomarkers for the development of the much-feared bone complications in Gaucher disease; in a cross-sectional collaborative in more than 100 patients with Gaucher disease, we have found that those with a history of sporadic infarction events have higher serum cytokine biomarkers, which respond to enzymatic therapy. With other investigators in a European Framework Package 7 (FP7) award 'EUCLYD' Dr Pavlova is investigating novel inhibitors of sphingolipid in a tissue–specific and inducible experimental model of Gaucher disease. These studies should reveal much about the molecular pathogenesis of the osseous complications and further define the relationship between defined cytokines and disease manifestations. Dr Cachón-González and Dr Sargeant study the molecular pathogenesis of the emblematic neurodegenerative storage disorder, Tay-Sachs disease. Overall the group has been central to the formation of an International Tay-Sachs disease Gene Therapy Consortium to translate successful gene therapy conducted in murine models into a viable therapeutic agent for use in man. These studies can be applied clinically and offer the opportunity for a unique understanding of the molecular pathogenesis of disorders affecting the metabolism of complex glycosphingolipids.

Selected references

Jeyakumar M, Williams I, Smith DA, Cox TM, Platt FM. Critical role of iron in the pathogenesis of the murine gangliosidoses. Neurobiol Dis 2009; 34:406–16.

Griffiths WJH, Mayr R, McFarlane I, Hermann H, Halsall DJ, Zoller H, Cox TM. Clinical presentation and molecular pathophysiology of autosomal dominant hemochromatosis caused by a novel ferroportin mutation. Hepatology 2010; 51:788–95.

Cox TM. Eliglustat tartrate, an orally active glucocerebroside synthase inhibitor for the potential treatment of Gaucher disease and other lysosomal storage diseases. Curr Opin Invest Drugs 2010; 11:1169–81.

Roos HI, Roos JCP, Cox TM. Orphan drug pricing may merit a competition law investigation. Brit Med J 2010; 341:1084–6.

Pavlova EV, Deegan, PB, Tindall J, McFarlane I, Mehta A, Hughes D, Wraith JE, Cox TM. Potential Biomarkers of Osteonecrosis in Gaucher Disease. Blood Cells Mol and Dis 2011; 46:27–33.

Deegan PB, Pavlova EV, Tindall J, Stein P, Bearcroft P, Mehta A, Hughes D, Wraith JE, Cox TM. Osseous Manifestations of Adult Gaucher Disease in the Era of Enzyme Replacement Therapy. Medicine (Baltimore) 2011; 90:52–60.

Renal Medicine

1. Professor Smith's group is based in the CIMR, and works on immune regulation and autoimmune and inflammatory disease. This has focused on how naturally occurring variants in immune molecules such as FcγRIIB alter immune function and predispose to autoimmunity. The accumulation of these risk variants in the population has been shown to be, at least in part, due to their ability to protect against infections such as malaria. With Dr Lyons and in collaboration with Addenbrooke's Vasculitis & SLE Clinic and the Division of Gastroenterology, Smith runs a translational programme studying the pathogenesis of human disease at the same time as looking for biomarkers. A CD8T cell transcriptional signature has been found which predicts prognosis in autoimmune disease. The European Vasculitis Genetics Consortium is also led from the laboratory.
2. Dr Clatworthy studies immunological mechanisms of renal injury, in particular in areas of acute tubular necrosis and transplantation, using cutting-edge imaging technology.
3. Dr Jayne runs the Vasculitis & Lupus clinic, and coordinates multi-centre trials in vasculitis and SLE. These are focused on the evaluation of new agents and the optimization of conventional therapies. His group recently coordinated a study contributing to the DFA approval of Rituximab for use in the therapy of vasculitis. He coordinates the European Vasculitis Study Group which forms clinical trials and long term evaluation of vasculitis patients.
4. Dr Bradley's group has been studying the pathways involved in signaling by TNF-alpha family members in endothelial cells and their relevance to renal inflammation and transplant rejection. He coordinates the Yale-Cambridge Cardiovascular Research Initiative, and is the Director of the NIHR Cambridge Biomedical Research Centre.

Selected references

Al-Lamki RS, Sadler TJ, Wang J, Reid MJ, Warren AY, Movassagh M, Lu W, Mills IG, Neal DE, Burge J, Vandenebeele P, Pober JS, Bradley JR. Tumor necrosis factor receptor expression and signaling in renal cell carcinoma. Am J Pathol 2010; 177:943–54.

Jones RB, Tervaert JW, Hauser T, Luqmani R, Morgan MD, Peh CA, Savage CO, Segelmark M, Tesar V, van Paassen P, Walsh D, Walsh M, Westman K, Jayne DRW. European Vasculitis Study Group. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis. N Engl J Med 2010; 363:211–20.

Linterman MA, Pierson W, Lee SK, Kallies A, Kawamoto S, Rayner TF, Srivastava M, Divekar DP, Beaton L, Hogan JJ, Fagarasan S, Liston A, Smith KGC*, Vinuesa CG* (equal senior authors). Foxp3(+) follicular regulatory T cells control the germinal center response. Nature Med. 2011;17:975–82.

McKinney EF, Lyons PA, Carr EJ, Hollis JL, Jayne DRW, Willcocks LC, Koukoulaki M, Brazma A, Jovanovic V, Kemeny DM, Pollard AJ, Macary PA, Chaudhry AN, Smith KGC. A CD8+ T cell transcription signature predicts prognosis in autoimmune disease. Nature Med 2010; 16:586–591.

Willcocks LC, Carr EJ, Niederer HA, Rayner TF, Williams TN, Yang W, Scott JA, Urban BC, Peshu N, Vyse TJ, Lau YL, Lyons PA, Smith KG. A defunctioning polymorphism in FCGR2B is associated with protection against malaria but susceptibility to systemic lupus erythematosus. Proc Natl Acad Sci USA 2010; 107:7881–5.

Clatworthy MR, Watson CJ, Plotnek G, Bardsley V, Chaudhry AN, Bradley JA, Smith KGC. B-cell-depleting induction therapy and acute cellular rejection. N Engl J Med 2009; 360:2683–5.

Respiratory Medicine

The Respiratory Medicine Division has six main areas of research: granulocyte cell biology and trafficking, the structure and function of alpha1-antitrypsin and related serpins, the genetic and molecular basis of pulmonary hypertension, the immunopathology of allergic diseases, the control of antigen processing by dendritic cells and the molecular mechanisms of ER stress.

1 Professor Chilvers', Dr Condliffe's and Dr Parfrey's interests relate to granulocyte cell biology, in particular, mechanisms underlying neutrophil priming, activation and apoptosis. The group also has an interest in TNFα and hypoxia signaling and neutrophil and eosinophil trafficking in vivo.

2 Professor Lomas' group works on the pathobiology of alpha-1-antitrypsin deficiency and the serpinopathies. They are also interested in the identification of genetic factors and protein biomarkers that relate to components of the COPD phenotype.

3 Professor Morrell's group is studying the molecular mechanisms leading to the development of idiopathic pulmonary arterial hypertension (PAH). In particular, his laboratory has elucidated the ways in which mutations in the bone morphogenetic protein type II receptor (BMPR-II), which underlie the majority of cases of familial PAH, disrupt intracellular signaling and proliferation of pulmonary vascular cells.

4 Dr Ewan's, Dr Clark's and Dr Nasser's research interests are in the clinical and immunological aspects of food allergy, anaphylaxis and asthma and novel approaches to desensitization with particular reference to nut allergy.

5 Dr Floto's group works on the molecular basis of antigen processing by dendritic cells and macrophages and how this influences the host responses to bacterial and mycobacterial infection.

6 Dr Marciniak's group studies the role of endoplasmic reticulum stress in human disease, including malignant mesothelioma, using both tissue culture and Drosophila model systems.

Selected references

McGovern NN, Cowburn AS, Walmsley SR, Thompson R, Summers C, Willcocks LC, Whyte MKB, Condliffe AM, Chilvers ER. Hypoxia inhibits respiratory burst activity and killing of staphylococcus aureus in human neutrophils. J Immunol 2011; in press.

Walmsley SR, Chilvers ER, Vaughan K, Marriott H, Thompson R, McGrath E, Shaw G, Pugh CW, Ratcliffe PJ, Taylor C, Sabroe I, Dockrell D, Johnson RS, Maxwell PH, Carmeliet P, Whyte M. Prolyl hydroxylase PHD3 is essential for hypoxic regulation of neutrophilic inflammation. J Clin Invest 2011; in press.

Miranda E, Pérez J, Ekeowa UI, Hadzic D, Kalsheker N, Gooptu B, Portmann B, Belorgey D, Hill M, Chambers S, Teckman J, Alexander GJ, Marciniak SJ, Lomas DA. A novel monoclonal antibody to characterize pathogenic polymers in liver disease associated with a1-antitrypsin deficiency. Hepatology 2010; 52:1078–88.

Ekeowa UI, Freeke J, Miranda E, Gooptu B, Bush MF, Pérez J, Teckman J, Robinson CV, Lomas DA. Defining the mechanism of polymerization in the serpinopathies. Proc Natl Acad Sci 2010; 107:17146–51.

Yang J, Li X, Al-Lamki RS, Southwood M, Zhao J, Lever AM, Grimminger F, Schermuly RT, Morrell NW. Smad-dependent and smad-independent induction of id1 by prostacyclin analogues inhibits proliferation of pulmonary artery smooth muscle cells in vitro and in vivo. Circ Res 2010; 107:252–62.

Durrington HJ, Upton PD, Hoer S, Boname J, Dunmore BJ, Yang J, Crilley TK, Butler LM, Blackbourn DJ, Nash GB, Lehner PJ, Morrell NW. Identification of a lysosomal pathway regulating degradation of the bone morphogenetic protein receptor type II. J Biol Chem 2010; 285:37641–9.

Clark AT, Islam S, King Y, Deighton J, Anagnostou K, Ewan PW. Successful oral tolerance induction in severe peanut allergy. Allergy 2009; 64:1218–20.

Renna M, Schaffner C, Winslow AR, Menzies FM, Peden AA, Floto RA, Rubinsztein DC. Autophagic substrate clearance requires activity of the syntaxin-5 SNARE complex. J Cell Sci 2011; 124:469–82.

Renna M, Schaffner C, Brown K, Shang S, Henao Tamayo M, Hegyi K, Grimsey N, Cusens D, Coulter S, Cooper J, Bowden A R, Newton S, Kampmannm B, Helm J, Jones A, Haworth H, Basaraba, RJ, DeGroote M, Ordway DJ, Rubinsztein DC, Floto RA. Azithromycin blocks autophagy and may predispose to mycobacterial infection. J Clin Invest 2011 in press.

Hopkins TG, Maher E, Reid E, Marciniak SJ. Recurrent pneumothorax. Lancet 2011; in press.

Malzer E, Daly ML, Moloney A, Sendall TJ, Thomas SL, Ryder E, Ryoo HD, Crowther DC, Lomas DA, Marciniak SJ. Impaired tissue growth is mediated by checkpoint kinase 1 (CHK1) in the integrated stress response. J Cell Sci 2010; 123:2892–900.

Medicine

Rheumatology

Research in this division covers the basic mechanisms underlying inflammatory arthritis and metabolic bone disease, together with development and validation of novel biomarkers which can be used to predict clinical outcomes.

1 Prof Gaston and Dr Goodall study the immunologic basis of inflammatory arthritis, and the factors which influence differentiation of pro-inflammatory T lymphocytes, particularly the role of dendritic cells in integrating signals from pathogens and cellular stress to alter cytokine production.

2 Dr Hall is investigating biomarkers in connective tissue diseases, including lymphocyte phenotype, novel measures of hand ischaemia, and assessment of the micro-circulation using haemoglobin video microscopy.

3 Dr Busch's group studies the biochemical mechanisms that link genetic variants of antigen-presenting MHC molecules to autoimmune pathogenesis, focusing on the characterisation of allelic differences in MHC protein turnover, their mechanistic basis and immunological consequences.

4 Prof Compston's laboratory combines clinical and laboratory studies in osteoporosis. Recent work includes bone histomorphometric study of age-related changes, the relationship between regional skeletal blood flow and osteoblast activity in postmenopausal osteoporosis or renal bone disease, and study of the incidence, skeletal location and underlying risk factors for fragility fracture in the obese population.

5 Dr Poole's group applies novel imaging techniques to investigate human bone diseases. With the Engineering for Clinical Practice team of Graham Treece and Andrew Gee, they have studied focal thinning as a cause of femoral neck fracture and have discovered that bone building drugs have targeted effects at key sites within the osteoporotic femur.

Selected references

Shen H, Goodall J, Gaston JSH. Frequency and phenotype of peripheral blood Th17 cells in ankylosing spondylitis and rheumatoid arthritis. Arthritis Rheum 2009; 60:1647–56.

Goodall JC, Wu C, Zhang Y, Ellis L, O'Brien L, Saudek V, Gaston JSH. ER stress signals are integrated by dendritic cells to enhance IL-23 responses to Toll-like receptor. Proc Natl Acad Sci USA 2010; 107:17698–703.

De Riva A, Deery MJ, McDonald S, Lund T, Busch R. Measurement of protein synthesis using heavy water labeling and peptide MS: discrimination between MHC allotypes. Anal Biochem 2010; 403:1–12.

Poole KES, Treece GM, Ridgway GR, Mayhew PM, Borggrefe J, Gee AH. Targeted Regeneration of Bone in the Osteoporotic Human Femur. PLoS ONE 2011; 6:e1619.

Poole KES, Mayhew PM, Rose CM, Brown JK, Bearcroft PJ, Loveridge N, Reeve J. Changing structure of the femoral neck across the adult female lifespan. J Bone Miner Res 2010; 25:482–91.

Vedi S, Kaptoge S, Compston JE. Age-related changes in iliac crest cortical width and porosity: a histomorphometric study. J Anat 2011; 218:510–6.

Premaor MO, Pilbrow L, Tonkin C, Parker RA, Compston JE. Obesity and fractures in postmenopausal women. J Bone Miner Res 2010; 25:292–7.

Obstetrics and Gynaecology

Head of Department and Professor of Obstetrics and Gynaecology

Professor GCS Smith
Tel 01223 336871
Fax 01223 215327
Email gcss2@cam.ac.uk

Staff list

University Readers

DS Charnock-Jones, Reader in Reproductive Biology
F Colucci, Reader in Immunology

University Lecturers

M Constancia
A Prentice

NHS Consultants/Associate Lecturers

P Baldwin	R Kearney	C Patient
P Bose	J Latimer	C Prasannan-Nair
J Brocklesby	C Lees	M Shafi
RAF Crawford	J MacDougall	M Slack
GA Hackett	R Mathur	A Wilson
F Hoveyda	H Missfelder-Lobos	

Research synopsis

The Department of Obstetrics and Gynaecology has programmes of basic, translational and clinical research addressing the determinants of pregnancy complications. Dr Charnock-Jones, Dr Constancia and Dr Colucci use transgenic mouse models to identify key genes involved in murine placentation with the aim of better understanding normal reproductive function. Dr Charnock-Jones studies the effect of oxygen on endothelial cells and trophoblast in the placenta. Dr Constancia has a major interest in placental epigenetics, in particular genomic imprinting (ie. selective epigenetic silencing of genes according to parent of origin). Dr Colucci aims at understanding how immune cells impact on reproduction, cancer and transplantation.

Other basic work in the department addresses preparative changes in gene expression in the fetus for post-natal life. The major focus of translational research in the Department is a prospective cohort study of women in their first pregnancy, which will have recruited 3500–4000 women by the end of 2011 and is funded by the NIHR Cambridge Comprehensive Biomedical Research Centre. The project has created a central resource of data, blood samples taken throughout pregnancy, and samples of placenta obtained at birth. The resource will be used to understand better the role of the placenta in determining adverse pregnancy outcome and, it is hoped, to identify novel biomarkers which may be clinically useful. A major focus of this research will involve the application of next generation sequencing to these samples, with a particular focus on the epigenetic regulation (methylation, histone modification and non-coding RNA) of placental gene expression. These studies involve close collaboration with the University's Centre for Trophoblast Research (www.trophoblast.cam.ac.uk). Finally, clinical research in the Department uses secondary analysis of diverse data sources to study determinants and predictors pregnancy outcome.

Selected references

Smith GCS. First trimester determination of complications of late pregnancy. JAMA 2010;303:561–562.

Pasupathy D, Wood AM, Pell JP, Fleming M, Smith GCS. Rates of and factors associated with delivery-related perinatal death among term infants in Scotland. JAMA 2009;302:660–668.

Dilworth MR, Kusinski LC, Cowley E, Ward BS, Husain SM, Constancia M, Sibley CF, Glazier JD. Placental-specific Igf2 knock-out mice exhibit hypocalcemia and adaptive changes in placental calcium transport. Proc Natl Acad Sci USA 2010;107:3894–3899

Li P, Burke S, Wang J, Chen X, Ortiz M, Lee S, Lu D, Campos L, Goulding D, Ling Ng B, Dougan G, Huntly B, Gottgens B, Jenkins NA, Copeland NG, Colucci F, Liu P. Reprogramming of T Cells to Natural Killer–like Cells upon Bcl11b Deletion. Science 2010;329(5987):85–9.

Colucci F, Cilio CM. Taming killer cells may halt diabetes progression. Nat Immunol 2010;11:111–2

Lakshmikanth T, Burke S, Ali TH, Kimpfler S, Ursini F, Ruggeri L, Capanni M, Umansky V, Paschen A, Sucker A, Pende D, Groh V, Biassoni R, Höglund P, Kato M, Shibuya K, Schadendorf D, Anichini A, Ferrone S, Velardi A, Kärre K, Shibuya A, Carbone E, Colucci F. NCRs and DNAM-1 mediate NK cell recognition and lysis of human and mouse melanoma cell lines in vitro and in vivo. J Clin Invest 2009;119:1251–63

Saudemont A, Garçon F, Yadi H, Roche-Molina M, Segonds-Pichon A, Martín-Fontecha A, Okkenhaug K, Colucci F. The p110gamma and p110delta isoforms of phosphoinositide 3-kinase differentially regulate natural killer cell migration in health and disease. PNAS 2009;106:5795–800

Mokhtar NM, Cheng CW, Cook E, Bielby H, Smith SK, Charnock-Jones DS. Progestin regulates chemokine (C-X-C motif) ligand 14 transcript level in human endometrium. Mol Hum Reprod 2010; 16: 170–177.

Oncology

Head of Department and Li Ka Shing Professor of Oncology and Director of Cancer Research UK Cambridge Research Institute

Professor Sir Bruce Ponder, FRCP, FRCPath, FMedSci, FRS
Tel 01223 404124
Fax 01223 404128
Email bruce.ponder@cancer.org.uk

Staff list

Professors

C Caldas, Professor of Clinical Oncology
T Eisen, Professor of Medical Oncology
J Griffiths, Professor of Molecular Imaging
D Jodrell, Professor of Cancer Therapeutics
G Murphy, Professor of Cancer Cell Biology
D Neal, Professor of Surgical Oncology
S Tavaré, Professor of Bioinformatics
AR Venkitaraman, Ursula Zoellner Professor of Cancer Research

University Readers

NG Burnet, Reader in Radiation Oncology
HM Earl, Reader in Clinical Cancer Medicine
P Pharoah, Reader in Cancer Epidemiology
A Philpott, Reader in Cancer and Developmental Biology

Senior Research staff

J Brenton	F Gergely	K Jensen
A M Dunning	E Gherardi	A Murrell
R Fitzgerald	H Hatcher	
V Gnanapragasam	R Jena	

NHS Consultants/Associate Lecturers

A Ahmed	D Gilligan	C Palmer
R Benson	S Harden	S Russell
S Booth	G Horan	LT Tan
R Bulusu	SJ Jefferies	RJ Thomas
C Coles	CR Jepthcott	D Traue
PG Corrie	D Mazhar	K Waite
MM Daly	KF McAdam	MV Williams
K Fife	AM Moody	C Wilson
H Ford	H Patterson	C Woodward

Clinical Lecturer

C Parkinson F Skoulidis

Research synopsis

Since 1998, we have developed a new Centre for cancer research in Cambridge. Our aim is to provide a nucleus of clinical and laboratory research that can interface with research across the University and science parks, and bring the combined expertise of Cambridge to practical application within the hospital. The Cancer Centre is a virtual organisation which provides a framework (and pump priming funds) to encourage cancer-related collaborations across disciplines, especially between biology, medicine and the physical sciences.

It is based on the University Department of Oncology, whose activities are reported here, but contains other substantial components: (1) the Cancer Research UK Cambridge Research Institute, opened in 2007, which when complete will contain over 30 research groups; (2) the MRC Cancer Cell Unit opened in 2001, which shares the Hutchison/MRC Research Centre building with the Department of Oncology; (3) the Strangeways Research Laboratories for Genetic Epidemiology, which involve close collaboration between Oncology and Public Health in studies of cancer susceptibility; (4) a new Clinical Trials Centre within the hospital.

Our aim is to create an environment in which individual research ideas can flourish, supported by the necessary clinical infrastructure. Nevertheless, to build the Centre, we have had to specify some focus. Within Oncology, we have set up programmes around selected cancer sites, that will span from basic biology to clinical application and which will act as a framework with which science across the Clinical School and University can interact. Currently, these cancer sites are breast, prostate, pancreas and ovary, with additional programmes under development in lung cancer. Infrastructure and interactions are shared with established programmes in haematological cancers (within the Cambridge Institute for Medical Research) and in oesophageal cancer (within the MRC Cancer Cell Unit). Laboratory research themes include epithelial cell biology, gene regulation, DNA repair and checkpoint function, and there are strong programmes in molecular imaging, genomics, computational biology, drug discovery, and animal models of cancer. These biological and technological resources underpin a further major clinical programme in experimental cancer therapeutics.

In the past two years research in the Department of Oncology and the CRUK Cambridge Research Institute has contributed significantly in several fields. For example, in breast cancer we have identified proteins that are required for the oestrogen receptor to bind the DNA and induce transcription. One such protein is FoxA1; inhibitors of FoxA1 binding may provide a therapeutic approach to breast cancer which is resistant to endocrine deprivation. In a separate collaborative study of 1000 women from whom we have frozen breast tumour material and clinical data with a median 10 year follow-up, we have completed a genome-wide analysis of copy number variation and of gene expression, which has provided a far more detailed molecular subclassification of breast cancer than was previously available, with new insights into personalised approaches to treatment. In pancreatic cancer, we have shown using transgenic mouse models that resistance to the commonly used drug gemcitabine may result from poor penetration of the drug into the tumour because of the dense surrounding stroma. Experimental data suggest that combined use of a drug targeted at the stroma may improve treatment outcome: an idea that is now being tested in the clinic. In prostate cancer, our 100,000-strong cohort of men who have had PSA testing as part of a study of the management of the early disease, has provided low-PSA controls for successful genome-wide association studies, which have identified a majority of the prostate

cancer susceptibility loci so far identified. Further investigation of one of these loci has yielded a protein biomarker, MSMB, which may provide a better, and urine-based, marker for detection of significant early disease than PSA. Details of these and of many other research studies can be found at www.cambridgecancer.org.uk, www.cancer.cam.ac.uk, www.oncology.cam.ac.uk.

Selected references

Ahmed AA, Etemadmoghadam D, Temple J, Lynch AG, Riad M, Sharma R, Stewart C, Fereday S, Caldas C, Defazio A, Bowtell D, Brenton JD. Driver mutations in TP53 are ubiquitous in high grade serous carcinoma of the ovary. J Pathol. 2010 May;221(1):49– 56. PMID: 20229506

Barnett GC, Wilkinson JS, Moody AM, Wilson CB, Twyman N, Wishart GC, Burnet NG, Coles CE. Randomized Controlled Trial of Forward-Planned Intensity-Modulated Radiotherapy for Early Breast Cancer: Interim Results at 2 Years. Int J Radiat Oncol Biol Phys. 2011 Feb [Epub ahead of print] PMID: 21345620

Holland DG, Burleigh A, Git A, Goldgraben MA, Perez-Mancera PA, Chin SF, Hurtado A, Bruna A, Ali HR, Greenwood W, Dunning MJ, Samarajiwa S, Menon S, Rueda OM, Lynch AG, McKinney S, Ellis IO, Eaves CJ, Carroll JS, Curtis C, Aparicio S, Caldas C. ZNF703 is a common Luminal B breast cancer oncogene that differentially regulates luminal and basal progenitors in human mammary epithelium. EMBO Mol Med. 2011 Mar;3(3):167–80. doi: 10.1002/emmm.201100122. Epub 2011 Feb 18. PMID: 21337521

Fitzgerald RC, Hardwick R, Huntsman D, Carneiro F, Guilford P, Blair V, Chung DC, Norton J, Ragunath K, Van Krieken JH, Dwerryhouse S, Caldas C; Hereditary diffuse gastric cancer: updated consensus guidelines for clinical management and directions for future research. International Gastric Cancer Linkage Consortium. J Med Genet. 2010 Jul;47(7):436–44. Erratum in: J Med Genet. 2011 Mar;48(3):216. Van Krieken, Nicola [corrected to Van Grieken, Nicola C]. PMID: 20591882

Blows FM, Driver KE, Schmidt MK, Broeks A, van Leeuwen FE, Wesseling J, Cheang MC, Gelmon K, Nielsen TO, Blomqvist C, Heikkilä P, Heikkinen T, Nevanlinna H, Akslen LA, Bégin LR, Foulkes WD, Couch FJ, Wang X, Cafourek V, Olson JE, Baglietto L, Giles GG, Severi G, McLean CA, Southey MC, Rakha E, Green AR, Ellis IO, Sherman ME, Lissowska J, Anderson WF, Cox A, Cross SS, Reed MW, Provenzano E, Dawson SJ, Dunning AM, Humphreys M, Easton DF, García-Closas M, Caldas C, Pharoah PD, Huntsman D. Subtyping of breast cancer by immunohistochemistry to investigate a relationship between subtype and short and long term survival: a collaborative analysis of data for 10,159 cases from 12 studies. PLoS Med. 2010 May 25;7(5):e1000279.PMID: 20520800

Tutt A, Robson M, Garber JE, Domchek SM, Audeh MW, Weitzel JN, Friedlander M, Arun B, Loman N, Schmutzler RK, Wardley A, Mitchell G, Earl H, Wickens M, Carmichael J. Lancet. Oral poly (ADP-ribose) polymerase inhibitor olaparib in patients with BRCA1 or BRCA2 mutations and advanced breast cancer: a proof-of-concept trial. 2010 Jul 24;376(9737):235–44. Epub 2010 Jul 6. PMID: 20609467

Bartlett JM, Munro AF, Dunn JA, McConkey C, Jordan S, Twelves CJ, Cameron DA, Thomas J, Campbell FM, Rea DW, Provenzano E, Caldas C, Pharoah P, Hiller L, Earl H, Poole CJ. Predictive markers of anthracycline benefit: a prospectively planned analysis of the UK National Epirubicin Adjuvant Trial (NEAT/BR9601). Lancet Oncol. 2010 Mar;11(3):266–74. Epub 2010 Jan 13.PMID: 20079691

Kadri SR, Lao-Sirieix P, O'Donovan M, Debiram I, Das M, Blazeby JM, Emery J, Boussioutas A, Morris H, Walter FM, Pharoah P, Hardwick RH, Fitzgerald RC. Acceptability and accuracy of a non-endoscopic screening test for Barrett's oesophagus in primary care: cohort study. BMJ. 2010 Sep 10;341:c4372. doi: 10.1136/bmj.c4372. PMID: 20833740

Bapiro TE, Richards FM, Goldgraben MA, Olive KP, Madhu B, Frese KK, Cook N, Jacobetz MA, Smith DM, Tuveson DA, Griffiths JR, Jodrell DI. A novel method for quantification of gemcitabine and its metabolites 2',2'-difluorodeoxyuridine and gemcitabine triphosphate in tumour tissue by LC-MS/MS: comparison with (19)F NMR spectroscopy. Cancer Chemother Pharmacol. 2011 Mar 23. [Epub ahead of print]

Massie CE, Lynch A, Ramos-Montoya A, Boren J, Stark R, Fazli L, Warren AY, Scott H, Madhu B, Sharma N, Bon H, Zecchini V, Smith DM, DeNicola GM, Mathews N, Osborne M, Hadfield J, MacArthur S, Adryan B, Lyons SK, Brindle KM, Griffiths J, Gleave ME, Rennie PS, Neal DE* and Mills IG*. * These authors contributed equally to the research. The androgen receptor fuels prostate cancer by regulating central metabolism and biosynthesis. EMBO J. 2011. In press.

Gudmundsson J, Besenbacher S, Sulem P, Gudbjartsson DF, Olafsson I, *et al.* Genetic correction of PSA values using sequence variants associated with PSA levels. Sci Transl Med. 2010 Dec 15;2(62):62ra92. PMID: 21160077

Gudmundsson J, Besenbacher S, Sulem P, Gudbjartsson DF, Olafsson I, Arinbjarnarson S, Agnarsson BA, Benediktsdottir KR, Isaksson HJ, Kostic JP, Gudjonsson SA, Stacey SN, Gylfason A, Sigurdsson A, Holm H, Bjornsdottir US, Eyjolfsson GI, Navarrete S, Fuertes F, Garcia-Prats MD, Polo E, Checherita IA, Jinga M, Badea P, Aben KK, Schalken JA, van Oort IM, Sweep FC, Helfand BT, Davis M, Donovan JL, Hamdy FC, Kristjansson K, Gulcher JR, Masson G, Kong A, Catalona WJ, Mayordomo JI, Geirsson G, Einarsson GV, Barkardottir RB, Jonsson E, Jinga V, Mates D, Kiemeney LA, Neal DE, **Thorsteinsdottir U, Rafnar T, Stefansson K.**

Goode EL, Chenevix-Trench G, Song H, Ramus SJ, Notaridou M, *et al.* A genome-wide association study identifies susceptibility loci for ovarian cancer at 2q31 and 8q24. Nat. Genet. 2010;42(10):874-879.

Goode EL, Chenevix-Trench G, Song H, Ramus SJ, Notaridou M, Lawrenson K, Widschwendter M, Vierkant RA, Larson MC, Kjaer SK, Birrer MJ, Berchuck A, Schildkraut J, Tomlinson I, Kiemeney LA, Cook LS, Gronwald J, Garcia-Closas M, Gore ME, Campbell I, Whittemore AS, Sutphen R, Phelan C, Anton-Culver H, Pearce CL, Lambrechts D, Rossing MA, Chang-Claude J, Moysich KB, Goodman MT, Dork T, Nevanlinna H, Ness RB, Rafnar T, Hogdall C, Hogdall E, Fridley BL, Cunningham JM, Sieh W, McGuire V, Godwin AK, Cramer DW, Hernandez D, Levine D, Lu K, Iversen ES, Palmieri RT, Houlston R, van Altena AM, Aben KK, Massuger LF, Brooks-Wilson A, Kelemen LE, Le ND, Jakubowska A, Lubinski J, Medrek K, Stafford A, Easton DF, **Tyrer J, Bolton KL, Harrington P, Eccles D, Chen A, Molina AN, Davila BN, Arango H, Tsai YY, Chen Z, Risch HA, McLaughlin J, Narod SA, Ziogas A, Brewster W, Gentry-Maharaj A, Menon U, Wu AH, Stram DO, Pike MC, Beesley J, Webb PM, Chen X, Ekici AB, Thiel FC, Beckmann MW, Yang H, Wentzensen N, Lissowska J, Fasching PA, Despierre E, Amant F, Vergote I, Doherty J, Hein R, Wang-Gohrke S, Lurie G, Carney ME, Thompson PJ, Runnebaum I, Hillemanns P, Durst M, Antonenkova N, Bogdanova N, Leminen A, Butzow R, Heikkinen T, Stefansson K, Sulem P, Besenbacher S, Sellers TA, Gayther SA,** Pharoah PD.

Oncology

Ahmed S, Thomas G, Ghoussaini M, Healey CS, Humphreys MK, *et al.* Newly discovered breast cancer susceptibility loci on 3p24 and 17q23.2. Nat Genet. 2009 May;41(5):585–90. Epub 2009 Mar 29. PMID: 19330027

Ahmed S, Thomas G, Ghoussaini M, Healey CS, Humphreys MK, Platte R, Morrison J, Maranian M, Pooley KA, Luben R, Eccles D, Evans DG, Fletcher O, Johnson N, dos Santos Silva I, Peto J, Stratton MR, Rahman N, Jacobs K, Prentice R, Anderson GL, Rajkovic A, Curb JD, Ziegler RG, Berg CD, Buys SS, McCarty CA, Feigelson HS, Calle EE, Thun MJ, Diver WR, Bojesen S, Nordestgaard BG, Flyger H, Dörk T, Schürmann P, Hillemanns P, Karstens JH, Bogdanova NV, Antonenkova NN, Zalutsky IV, Bermisheva M, Fedorova S, Khusnutdinova E; SEARCH, Kang D, Yoo KY, Noh DY, Ahn SH, Devilee P, van Asperen CJ, Tollenaar RA, Seynaeve C, Garcia-Closas M, Lissowska J, Brinton L, Peplonska B, Nevanlinna H, Heikkinen T, Aittomäki K, Blomqvist C, Hopper JL, Southey MC, Smith L, Spurdle AB, Schmidt MK, Broeks A, van Hien RR, Cornelissen S, Milne RL, Ribas G, González-Neira A, Benitez J, Schmutzler RK, Burwinkel B, Bartram CR, Meindl A, Brauch H, Justenhoven C, Hamann U; GENICA Consortium, Chang-Claude J, Hein R, Wang-Gohrke S, Lindblom A, Margolin S, Mannermaa A, Kosma VM, Kataja V, Olson JE, Wang X, Fredericksen Z, Giles GG, Severi G, Baglietto L, English DR, Hankinson SE, Cox DG, Kraft P, Vatten LJ, Hveem K, Kumle M, Sigurdson A, Doody M, Bhatti P, Alexander BH, Hooning MJ, van den Ouweland AM, Oldenburg RA, Schutte M, Hall P, Czene K, Liu J, Li Y, Cox A, Elliott G, Brock I, Reed MW, Shen CY, Yu JC, Hsu GC, Chen ST, Anton-Culver H, Ziogas A, Andrulis IL, Knight JA; kConFab; Australian Ovarian Cancer Study Group, Beesley J, Goode EL, Couch F, Chenevix-Trench G, Hoover RN, Ponder BA, Hunter DJ, Pharoah PD, Dunning AM, Chanock SJ, Easton DF.

Narita M, Young AR, Arakawa S, Samarajiwa SA, Nakashima T, Yoshida S, Hong S, Berry LS, Reichelt S, Ferreira M, Tavaré S, Inoki K, Shimizu S, Narita M. Spatial Coupling of mTOR and Autophagy Augments Secretory Phenotypes. Science. 2011 Apr 21. [Epub ahead of print] PMID: 21512002

Barbosa-Morais NL, Dunning MJ, Samarajiwa SA, Darot JF, Ritchie ME, Lynch AG, Tavaré S. A re-annotation pipeline for Illumina BeadArrays: improving the interpretation of gene expression data. Nucleic Acids Res. 2010 Jan;38(3):e17. Epub 2009 Nov 18. PMID: 19923232

Garnett MJ, Mansfeld J, Godwin C, Matsusaka T, Wu J, Russell P, Pines J, Venkitaraman AR. UBE2S elongates ubiquitin chains on APC/C substrates to promote mitotic exit. Nat Cell Biol. 2009 Nov;11(11):1363–9. Epub 2009 Oct 11. PMID: 19820702

Carreira A, Hilario J, Amitani I, Baskin RJ, Shivji MK, Venkitaraman AR, Kowalczykowski SC. The BRC repeats of BRCA2 modulate the DNA-binding selectivity of RAD51. Cell. 2009 Mar 20;136(6):1032–43. PMID: 19303847

Kraman M, Bambrough PJ, Arnold JN, Roberts EW, Magiera L, Jones JO, Gopinathan A, Tuveson DA, Fearon DT. Suppression of antitumor immunity by stromal cells expressing fibroblast activation protein-alpha. Science. 2010 Nov 5;330(6005):827–30. PMID: t21051638

Olive KP, Jacobetz MA, Davidson CJ, Gopinathan A, McIntyre D, Honess D, Madhu B, Goldgraben MA, Caldwell ME, Allard D, Frese KK, Denicola G, Feig C, Combs C, Winter SP, Ireland-Zecchini H, Reichelt S, Howat WJ, Chang A, Dhara M, Wang L, Rückert F, Grützmann R, Pilarsky C, Izeradjene K, Hingorani SR, Huang P, Davies SE, Plunkett W, Egorin M, Hruban RH, Whitebread N, McGovern K, Adams J, Iacobuzio-Donahue C, Griffiths J, Tuveson DA. Inhibition of Hedgehog signaling enhances delivery of chemotherapy in a mouse model of pancreatic cancer. Science. 2009 Jun 12;324(5933):1457–61. Epub 2009 May 21. PMID: 19460966

Karreth FA, DeNicola GM, Winter SP, Tuveson DA. C-Raf inhibits MAPK activation and transformation by B-Raf(V600E). Mol Cell. 2009 Nov 13;36(3):477–86. PMID: 19917255

Paediatrics

Head of Department and Professor of Paediatrics

Professor D Dunger (Acting until October, 2012)
Tel 01223 336886
Fax 01223 336996
Email dbd25@cam.ac.uk

Staff list

Professor
IA Hughes, Foundation Chair

University Senior Lecturer
C Acerini

University Lecturer
K Beardsall

Principal Research Associate
R Hovorka

Senior Research Staff
C Petry

Clinical Lecturers
R Williams
M Zilbauer

Affiliated Lecturer
K Ong

Associate Lecturers/NHS Consultants

N Abdullah	P Heinz	A Parker
J Ahluwalia	R Heuschkel	L Preston
A Aslam	R Iles	U Ramaswami
T Austin	C Jackson	A Rehm
J Brain	F Janjua	R Ross-Russell
S Broster	W Kelsall	C Salvestrini
A Burke	A Khan	A Sansome
D Carroll	D Krishnakumar	F Torrente
A Clarke	E Lewis	C Verity
D Conlan	D McShane	D Vickers
A Curley	S Morley	D Williams
D D'Amore	J Nicholson	M Williams
K Farrer	D O'Donnell	
M Gattens	A Ogilvy-Stuart	

Research synopsis

The Department's research is in four main areas: genetic and hormonal control of human sex development; genetics and pathophysiology of diabetes; the determinants of birth size and infant growth; critical illness endocrine physiology.

Studies on mammalian sex development are applied to the management of infants with disorders of sex development (DSD), including the effects of environmental chemicals, which may disrupt endocrine control of fetal development. Polymorphic variants in genes controlling androgen production and action appear to affect normal development, including growth at puberty. Much of this research is underpinned by the Cambridge Baby Growth Study (CGGS) established by Professor Hughes in 2001 and now celebrating its 10th Anniversary, with over 2000 families recruited. A major component of CBGS studies, directed by Dr Ken Ong at the MRC Epidemiology Unit, is now focusing on nutrition and how early feeding practices influence risks of obesity and age of onset of puberty. This unique resource is spawning collaborative studies across several specialties in the Cambridge Biomedical Campus. In 2008 Professor Dunger and his team launched the first international study of the use of ACE inhibitors and statins in adolescents with Type 1 diabetes (T1D). Ongoing studies on T1D include the role of the growth hormone – IGF1 axis in insulin resistance, and the place of growth hormone inhibitors in preventing diabetic complications.

Clinical testing of closed-loop insulin delivery in T1D developed by Dr Hovorka is showing promising results. Under supervised conditions, overnight closed-loop reduced the risk of nocturnal hypoglycaemia and improved glucose control. First ever home testing will adopt an in-house prototype system which has received regulatory approval. The physiology of survival and late morbidity as a consequence of acute life-threatening or critical illness is being studied by examining the effects of stress endocrinology and hyperglycaemia. The successful Neonatal Insulin Replacement Therapy in Europe (NIRTURE) study is being extended to early childhood to determine the role of insulin and glucose control on long term risk of glucose intolerance in later life.

Selected references

Miles HL, Gidlöf S, Nordenström A, Ong KK, Hughes IA. (2010) The role of androgens in fetal growth: observational study in two genetic models of disordered androgen signalling. Arch Dis Child Fetal Neonatal Ed 2010; 95:F435–438.

Ong KK, Elks CE, Li S, Zhao JH *et al.* Genetic variation in LIN28B is associated with the timing of puberty. Nat Genet 2009; 41:729–733.

Acerini CL, Miles HL, Dunger DB, Ong KK, Hughes IA. The descriptive epidemiology of congenital and acquired cryptorchidism in a UK infant cohort. Dis Child. 2009;94:868–72.

Hovorka R, Allen JM, Elleri D, Chassin LJ *et al.* Manual closed-loop insulin delivery in children and adolescents with type 1 diabetes: a phase 2 randomised crossover trial. Lancet 2010; 375:743–51.

Regan FM, Williams RM, McDonald A, Umpleby AM *et al.* Treatment with Recombinant Human Insulin-like Growth Factor (rhIGF)-1/rhIGF Binding Protein-3 Complex Improves Metabolic Control in Subjects with Severe Insulin Resistance. J Clin Endocrinol Metab 2010;95:2113–22.

Beardsall K, Vanhaesebrouck S, Ogilvy-Stuart AL, et al. Prevalence and determinants of hyperglycaemia in very low birth weight infants: cohort analyses of the NIRTURE study. J Pediatr 2010; 157: 715–9.

Psychiatry

Head of Department and Professor of Psychiatry

Professor PB Jones
Tel 01223 336961
Fax 02223 336581
Email pbj21@cam.ac.uk

Staff list

Professors

S Baron-Cohen, Developmental Psychopathology
GE Berrios, Epistemology of Psychiatry (Emeritus)
ET Bullmore, Psychiatry
S Gathercole, Cognitive Psychology (faculty board appointment)
IM Goodyer, Child & Adolescent Psychiatry
AJ Holland, Learning Disability (Healthcare Foundation Professorship)
FA Huppert, Psychology
ES Paykel, Psychiatry (Emeritus)
B Sahakian, Cognitive Neuropsychology
P Fletcher, Health Neuroscience (Bernard Wolfe Professorship)

University Senior Lecturer

T Croudace

University Lecturers

B Lennox
HA Ring
U Muller
P Wilkinson

Director of Research

J Suckling

Senior Research Associates

K Ersche
J Murray
M Spencer
E Fernandez-Egea
M Redley
V Voon
G Murray

Clinical Lecturer

R Cardinal
V Dobler
J Deakin
R Dudas

Affiliated Lecturers

A Bateman
P Emson
ICH Clare
A Humphrey

Visiting Research Staff

M Aguis
E Fernandez-Egea
J Semple
J Akiste
N Fineberg
A Stringaris
J Barnett
M Kar-Ray
D Tantam
A Blackwell
N Martin
G Todd
S Chamberlain
M O'Riordan
R Zaman
F Chen
J Perez Sancho-Toledo
S Zaman
G Gomez de la Curesta
W Riedel
J Zimbron
J Eccles

NHS Consultants/Associate Lecturers

R Chipperfield
AJ Jaffa
J Shapleske
T Denning
CA Lawton
M Stefan
FMC Denman
A Michael
E Vithayathil
DM Girling
J Perez
C Walsh (Clinical sub-Dean)
E Hegazi
R Ramana
NJ Hunt
S Robling

Research synopsis

The Department boasts the highest quality psychiatry research in the UK, with 80% of research rated as being 4* or 3* (world-leading or internationally excellent) in the Research Assessment Exercise 2008.

Research in the Department is focused on major disease areas using a range of investigative techniques. Developmental paradigms are central in much of the Department's work from the point of view of pathological states, life course models of adult health and the application of novel statistical techniques.

Contemporary neurobiological techniques such as structural and functional MRI, neuro-endocrinology, cognitive psychology and molecular genetics are used to characterize large, epidemiologically principled or longitudinal samples as well as to elucidate drug models of disorders and their treatments in smaller scale, more mechanistic studies. There are cognate methodological strengths in many of these techniques, especially epidemiology neuroimaging, cognitive psychology and psychopharmacology. The full gamut of translational clinical research is an increasing focus. Research activity in the Department benefits from a wide range of national and international collaborations including leadership roles in the MRC/Wellcome Trust Behavioural & Clinical Neurosciences Institute, the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) for Cambridgeshire and Peterborough, a Wellcome Trust Strategic Award for Neurosciences and Mental Health and the GSK Clinical Unit.

Selected references

Bassett DS, Greenfield DL, Meyer-Lindenberg A, Weinberger DR, Moore SW, Bullmore ET (2010). Efficient physical embedding of topologically complex information processing networks in brains and computer circuits. PLoS Computational Biology. 6(4):e1000748.

Chen CH, Suckling J, Ooi C, Jacob R, Lupson V, Bullmore ET, Lennox BR (2010). A longitudinal fMRI study of the manic and euthymic states of bipolar disorder. Bipolar Disorders. 12: 344–347.

Colman I, Murray J, Abbott RA, Maughan B, Kuh D, Croudace TJ, Jones PB (2009). Outcomes of conduct problems in adolescence: 40 year follow-up of national cohort. BMJ; 338:a2981.

Fairchild G, Stobbe Y, van Goozen SH, Calder AJ, Goodyer IM (2010). Facial expression recognition, fear conditioning, and startle modulation in female subjects with conduct disorder. Biological Psychiatry; 68(3):272–9.

Fletcher PC, Napolitano A, Skeggs A, Miller SR, Delafont B, Cambridge VC, de Wit S, Nathan PJ, Brooke A, O'Rahilly S, Farooqi IS, Bullmore ET (2010). Distinct modulatory effects of satiety and sibutramine on brain responses to food images in humans: a double dissociation across hypothalamus, amygdala, and ventral striatum. Journal of Neuroscience; 30(43):14346–55.

Lai MC, Lombardo MV, Chakrabarti B, Sadek SA, Pasco G, Wheelwright SJ, Bullmore ET, Baron-Cohen S, Suckling J (2010). A Shift to Randomness of Brain Oscillations in People with Autism. Biological Psychiatry. 68: 1092–1099.

The Oxford Handbook of Neuroethics. Eds. J Illes & BJ Sahakian (Oxford University Press, 2011).

Scoriels L, Barnett JH, Murray GK, Cherukuru S, Fielding M, Cheng F, Lennox BR, Sahakian BJ, Jones PB (2011) Effects of modafinil on emotional processing in first episode psychosis. Biological Psychiatry; 69(5): 457–464.

Public Health and Primary Care

Head of Department and Professor of Epidemiology and Medicine

Professor JN Danesh
Tel 01223 741302
Fax 01223 741339
Email john.danesh@phpc.cam.ac.uk

Staff list

Professors

C Brayne, Professor of Public Health Medicine (Director, Institute of Public Health)
DF Easton, Professor of Genetic Epidemiology
KT Khaw, Professor of Clinical Gerontology
AL Kinmonth, Professor of General Practice
JW Mant, Professor of Primary Care Research
T Marteau, Professor of Health Psychology (KCL) (Director, Policy Research Unit)
M Roland, Professor of Heath Services Research
SR Sutton, Professor of Behavioural Science
SG Thompson, Professor and Director of Research in Biostatistics
NJ Wareham, Honorary Professor of Epidemiology (Director, MRC Epidemiology Unit)

Reader

P Pharoah, Reader in Cancer Epidemiology

University Senior Lecturers

JA Benson, S Cohn, JW Powles, P Monsivais

University Lecturers

E Di Angelantonio, D Saleheen (unestablished), MS Sandhu, AM Wood

Clinical Lecturers

O Franco, R Payne, J Yip, N Mavaddat, FM Walter

Affiliated Lecturers

P Badrinath, A Hibble, P Treasure, R Fordham, MH Reacher

Senior Research Staff

AC Antoniou, T Minett, CR Palmer, SIG Barclay, HC Morris, B Stephan, M Farquhar, R Mullis, N Wainwright, W Hardeman, D Nunn, M Walker, S Kaptoge, C Paddison, KM Williams

Senior Visiting Fellows

P Cosford, C Jagger, P Surtees, N Day, M Kelly, H Thomas, J Emery, T Ling, I White, J Grant, E Nolte, D Williams, V Gudnason, DC Pencheon, R Himsworth, TC Prevost

Clinical Research Fellows/Associates

JP Graffy, G Lyratzopoulos, V Keevil, J Usher-Smith

NHS Consultants/Associate Lecturers

TS Alderson, E Fistein, R O'Donnell, LK Atkinson, S Forrest, J Sargent, RG Davies, SJ Gillam, J Schram, J Ferdinand, RJ Morris, RL Zimmern

Research synopsis

The Department of Public Health and Primary Care at the University of Cambridge is one of the UK's leading university departments of population health sciences, top-ranked in Epidemiology and Public Health in the Research Assessment Exercise 2008.

The department has been led since 2001 by Professor John Danesh and consists of over 330 staff and postgraduate students. The overall research mission is to generate scientific evidence that will inform the prevention of premature death and disability, particularly in relation to common chronic conditions such as cardiovascular disease, common cancers, dementia, diseases of ageing, osteoporosis, and metabolic diseases. The goal is to translate this evidence into the development and evaluation of preventative interventions.

Key strategies involve investigations of the separate and combined influences of genetic and environmental factors in chronic diseases by studies of several in-house epidemiological collections and of large-scale collections established through national and international collaborations. In several of these studies, aetiological investigations and patho-physiological natural history studies are integrated with molecular biology and clinical medicine. Understanding of the determinants of disease and behaviour change are then utilised in the development and evaluation of interventions at individual and population levels. There is also research into methods of study design, development of interventions and biostatistical analyses.

The Department has recently made senior appointments, including Professor Theresa Marteau (Director, Policy Research Unit, 2010) and Professor Simon Thompson (Director of Research in Biostatistics, 2011). Further examples of major developments in recent years include:

1. establishment of major research initiatives in developing countries, especially in South Asia, such as the Pakistan Risk of Myocardial Infarction Study and partnership in the Public Health Foundation of India-UK Consortium from 2008
2. establishment of the MPhil course in Public Health in 2006, and co-direction of a new four-year inter-disciplinary PhD programme in cardiovascular research supported by the British Heart Foundation from 2009
3. establishment of a new Department of Health funded Policy Research Unit in 2010
4. leadership of international customised gene array consortia in cancer ('iCOGs') and in vascular disease ('metabochip+').

Public Health and Primary Care

Selected examples of population collections
(Study name/sample size/major focus of study)

1 EPIC-Norfolk / 30,000 / nutrition and cancer
2 Emerging Risk Factor Collaboration / 1,800,000 / evaluation of novel coronary biomarkers
3 EPIC-CVD / 25,000 incident CVD cases, 520,000 participants / gene-lifestyle interplay
4 Breast Cancer Association Consortium / >90,000 / genetics of breast cancer
5 Cognitive Function and Ageing / 18,000 / cognitive decline
6 SEARCH / >20,000 / genetics of breast, ovarian, and other cancers
7 Ely / 2,000 / determinants of metabolic disease
8 Pakistan Risk of Myocardial Infarction Study / >30,000 / genetics of MI and stroke

Teaching and training

The Department continues to train and provide teaching to a wide range of constituencies. These main areas are teaching within the medical student curriculum, training for public health careers, and research training (as a recognised MRC training location in epidemiology and public health and NIHR training centre for ACFs and Clinical Lectureships). Key events and achievements are noted below:

Postgraduate

1 Appointment of University Lecturer, Dr Emanuele Di Angelantonio (UL in Medical Screening, 2010) and Clinical Lecturers Dr Oscar Franco (Clinical Lecturer in Public Health, 2010), Dr Rupert Payne (NIHR Clinical Lecturer in General Practice, 2010) and Dr Jennifer Yip (Clinical Lecturer in Public Health, 2011).
2 The MPhil in Epidemiology is a one-year full-time course, which in 2009/10 had 18 students and has been running for 19 years. The course has had over 200 students graduate to date. The Nick Day Prize in Epidemiology for the top student was established in 2006.
3 The MPhil in Public Health is a one-year full-time course, which in 2009/10 had 16 students and has been running for 6 years. The course has had about 50 students graduate to date. The Tom Davies Prize in Public Health for the top student was established in 2007.
4 Together, the MPhil programmes are supported by a total of five annual studentships from the MRC. There are about 44 doctoral students studying a range of topics.
5 Academic supervision has been provided to around 40 public health trainees.
6 Postgraduate students and honorary fellows are supported by a range of competitive awards including

MRC studentships and fellowships from the BHF, Cancer Research UK, Wellcome Trust, NIHR, ESRC and Macmillan Cancer Support.

Selected references

N Engl J Med. The Emerging Risk Factors Collaboration. Diabetes mellitus, fasting glucose, and risk of cause-specific death. 2011;364:829–841.

The Emerging Risk Factors Collaboration. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. Lancet 2011;377:1085–95.

Spurdle AB, Thompson DJ, Ahmed S, Ferguson K, Healey CS, O'Mara T *et al.* Genome-wide association study identifies a common variant associated with risk of endometrial cancer. Nat Genet 2011; 43:451–454.

The Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet 2010;375:2215–2222.

The Triglyceride Coronary Disease Genetics Consortium and The Emerging Risk Factors Collaboration. Triglyceride-mediated pathways and coronary disease: collaborative analysis of 101 studies. Lancet 2010;375:1634–9.

McManus RJ, Mant J, Bray EP, Holder R, Jones MI, Greenfield S *et al.* Telemonitoring and self-management in the control of hypertension (TASMINH2): a randomised controlled trial. Lancet 2010;375:163–72.

Turnbull C, Rapley EA, Seal S, Pernet D, Renwick A, Hughes D *et al.* Variants near DMRT1, TERT and ATF7IP are associated with testicular germ cell cancer. Nat Genet 2010;42:604–607.

Turnbull C, Ahmed S, Morrison J, Pernet D, Renwick A, Maranian M et al. Genome-wide association study identifies five new breast cancer susceptibility loci. Nat Genet 2010;42:504–7.

Rodondi N, den Elzen WP, Bauer DC, Cappola AR, Razvi S, Walsh JP *et al.* Subclinical hypothyroidism and the risk of coronary heart disease and mortality. JAMA 2010;304:1365–74.

Eeles RA, Kote-Jarai J, Al Olama AA, Giles GG, Guy M, Severi G *et al.* Identification of seven new prostate cancer susceptibility loci through a genome-wide association study. Nat Genet 2009;41:1116–1121.

Savva GM, Wharton SB, Ince PG, Forster G, Matthews F, Brayne C. Age, neuropathology, and dementia. N Engl J Med 2009;360:2302–2309.

Campbell SM, Reeves D, Kontopantelis E, Sibbald B, Roland M. Effects of pay-for-performance on the quality of primary care in England. N Engl J Med 2009;361:368–78.

Paddison CAM, Eborall H, Sutton S, French DO, Vasconcelos J, Prevost AT *et al.* Are people with negative screening tests for diabetes falsely reassured? A parallel group cohort study embedded in the ADDITION (Cambridge) randomised controlled trial. BMJ 2009;339: b4535. (Acting) Head of Department and Professor of Clinical MRI

Radiology

Head of Department and Professor of Radiology

Professor F Gilbert
Tel 01223 336890
Fax 01223 330915
Email: fjg28@cam.ac.uk

Staff list

Professors

AK Dixon, Emeritus Professor of Radiology
DJ Lomas, Professor of Clinical MRI
JH Gillard, Professor of Neuroradiology
JR Griffiths, Hon Prof in Magnetic Resonance applied to Cancer

University Lecturers

LH Berman TF Massoud E Sala

Senior Research Staff

F Gallagher

NHS Consultants/Associate Lecturers

N Antoun	J Cross	N Screaton
J Babar	J Dutton	T See
A Balan	A Freeman	P Set
K Balan	S Freeman	A Shaw
S Barter	M Gaskarth	R Sinnatamby
P Bearcroft	A Gomez	A Tasker
A Booth	D Gopalan	S Uppon
P Britton	B Khoo	M Wallis
J Buscombe	N Higgins	S Whitley
N Carroll	M Hopper	A Winterbottom
HK Cheow	J Hughes	
C Cousins	D Scoffings	

Clinical Lecturers

O Arthurs O Thomas

Affiliated Lecturer

MJ Graves

Research synopsis

The research activity of the department spans a wide range from molecular imaging developments at a 'bench' level, through novel imaging technique development to clinical studies of new imaging applications. These activities involve numerous multi-disciplinary collaborations across the Campus and the wider University, including links with Engineering, Physics, Medical Physics, the CRUK Cambridge Research Institute and the major themes of the NIHR Cambridge Biomedical Research Centre of which Imaging forms a key cross-cutting theme.

The department benefits from access to an extensive portfolio of modern imaging equipment including advanced colour Doppler Ultrasound, 1.5T and 3T MRI and MRS, 16, 64 and 128 detector and dual energy CT as well as PET-CT and advanced radiochemistry. There are close research links with the Neurosciences utilising CT, MR and PET techniques in studies involving stroke and carotid disease in particular. Multiple new clinical trials in Oncology have been established, investigating both new imaging based biomarkers and the evaluation of new therapeutic agents in early phase 1 trials. A particular focus of current and future work has been molecular imaging with the development of gene reporter techniques as well as hyperpolarised 13C agents and related imaging applications in collaboration with the CRI and Biochemistry.

Individual groups have undertaken research in the identification and characterization of vulnerable plaque, the improved definition and characterization of brain tumours, the development of new interactive real-time techniques for paediatric and neonatal MRI, the development of non-contrast enhanced 3D vascular imaging techniques, the clinical applications of ultrasound and MR based elastography for malignant lymph node detection and focal liver lesion characterisation. Our previous work on the impact of imaging techniques on clinical decision making continues to be cited in national guidelines, notably involving breast cancer and chest disease management.

High spatial resolution 3D arteriograms of the lower legs generated using a novel non-invasive MR technique that removes the need for any injected contrast medium.

Selected references

1 **Barrett T, Bowden DJ, Greenberg DC, Brown CH, Wishart GC, Britton PD.** 2009. Radiological staging in breast cancer: which asymptomatic patients to image and how. Br J Cancer, 101(9), Nov 3, 1522–8.

2 **Sadat U, Weerakkody RA, Bowden DJ, Young VE, Graves MJ, Li ZY, Tang TY, Gaunt ME, Hayes PD, Gillard JH.** 2009. Utility of high resolution MR imaging to assess carotid plaque morphology: a comparison of acute symptomatic, recently symptomatic and asymptomatic patients with carotid artery disease. Atherosclerosis, 207(2), Dec, 434–9.

3 **Graves MJ, Black RT, Lomas DJ.** 2009. Constrained surface controllers for three-dimensional image data reformatting. Radiology, 252(1), Jul, 218–24.

4 **Gallagher FA, Kettunen MI, Hu DE, Jensen PR, Zandt RI, Karlsson M, Gisselsson A, Nelson SK, Witney TH, Bohndiek SE, Hansson G, Peitersen T, Lerche MH, Brindle KM.** 2009. Production of hyperpolarized [1,4-13C2] malate from [1,4-13C2] fumarate is a marker of cell necrosis and treatment response in tumors. Proc Natl Acad Sci U S A, 106(47), Nov 24, 19801–06.

5 **Massoud TF, Paulmurugan R, Gambhir SS.** 2010. A molecularly engineered split reporter for imaging protein-protein interactions with positron emission tomography. Nat Med. Aug;16(8):921–6.

6 **Priest AN, Gill AB, Kataoka M, McLean MA, Joubert I, Graves MJ, Griffiths JR, Crawford RA, Earl H, Brenton JD, Lomas DJ, Sala E.** Dynamic contrast-enhanced MRI in ovarian cancer: Initial experience at 3 tesla in primary and metastatic disease. Magn Reson Med, 2010. 63(4): p. 1044–9.

Surgery

Head of Department and Professor of Surgery

Professor JA Bradley
Tel 01223 336976
Fax 01223 762523
Email jab52@cam.ac.uk

Staff list

Professors
DE Neal, Professor of Surgical Oncology
RAL Pedersen, Professor of Regenerative Medicine
N Rushton, Professor of Orthopaedic Surgery
J Wallwork, Honorary Professor of Cardiothoracic Surgery
CJE Watson, Professor of Transplantation

University Senior Lecturer
P Gibbs

University Lecturers
A Butler, VJ Gnanapragasam, GJ Pettigrew

Assistant Director of Research
EM Bolton

Senior Research Staff
RA Brooks, L Vallier (Principal Research Associate)

Clinical Lecturers
CJ Callaghan, SS Liau, G Shaw
S Harper, K Saeb-Parsy, MGB Tran
MRV Kosmoliaptsis

NHS Consultants/AssociateLecturers

DM Adlam	PH Gillespie	R Miller
TF Aho	I Grant	DA Moffat
T Ahmed	RF Gray	CN Morrison
A Aslam	NR Hall	AM Nashef
P Axon	PN Hall	A Norrish
AM Baxter	RH Hardwick	PJ Owen
JR Benson	PD Hayes	M Pereira
SL Benyon	E Huguet	R Praseedom
D Bister	J Hopkinson-Woolley	RD Price
A Boyle	MS Irwin	A Rehm
JR Boyle	C Jackson	J Rimes
AJL Brain	A Jah	AHN Robinson
JA Bavisha	NV Jamieson	SM Robinson
MG Cameron	P Jani	PM Safranek
D Carroll	D Jenkins	NC Shah
C Collins	P Johnstone	NP Smith
DP Conlon	AR Kahn	N Thiruchelvam
GC Cormack	C Kastner	MK Thomson
RJ Davies	V Khanduja	S Tsui
A Doble	GS Keene	WH Turner
N Donnolly	RJ Kendall	G Tytherleigh-Strong
AJ Durrani	MG Kerr-Muir	L Van-Rensburg
DJ Edwards	SR Large	K Varty
NS Fearnhead	CM Malata	AS Vince
BM Fish	K Madavan	FC Wells
P Forouhi	DJ McAuley	MPL Williams
ME Gaunt	DC McKiernan	OJ Wiseman

Research synopsis

The Department of Surgery has a strong clinical emphasis and the overall research strategy is to improve the surgical management of disease through developments in both basic and translational research. There is a major focus on applied clinical research and a key feature of the department is the close integration of University and NHS surgeons. University surgeons in parallel with directing programmes of research play an important role in the development and delivery of specialist surgical services. Similarly, many NHS surgeons are, in addition to their clinical responsibilities, undertaking high quality clinical research supported through close collaboration with University colleagues. In contrast with the trend in many other UK universities, academic surgery in Cambridge is flourishing and the department continues to expand. The principal research interests are transplantation, stem cell medicine, surgical oncology and orthopaedic surgery. In addition, clinical research of international importance is being led by NHS surgical colleagues across a range of surgical disciplines, including ear, nose and throat surgery, ophthalmic surgery, gastrointestinal surgery and vascular surgery.

Transplantation

The Division of Transplantation, directed by Professor Bradley, has been at the international forefront of clinical developments in organ transplantation for many years and the world-renowned clinical programmes in abdominal organ transplantation based at Addenbrooke's, and thoracic organ transplantation based at Papworth Hospital NHS Foundation Trust, are each underpinned by well-established multidisciplinary research programmes. Research ranges from basic molecular and cellular immunology to translational research and evaluation of new technologies. The Division includes the Transplantation and Regenerative Medicine Theme of the NIHR Biomedical Research Centre. There are strong programmes of basic research into the molecular basis of allograft rejection, with a particular focus on the role of B cells and alloantibody in acute and chronic rejection, interactions between endothelial and immune cells in allograft vasculopathy, molecular mechanisms underlying the induction and maintenance of immunological tolerance, and analysis of physicochemical properties determining the immunogenicity of HLA molecules. The division is undertaking, a number of investigator led single and multi-centre clinical research programmes aimed at evaluating novel immunosuppressive agents, extending donor organ use and minimising organ injury prior to transplantation. Senior investigators in the department are also working closely with scientists and statisticians in the Division of Organ Donation and Transplantation at NHS Blood and Transplant to maximise the outcome of organ transplantation in the UK.

Selected references

Reid AW, Harper S, Jackson CH, Wells AC, Summers DM, Gjorgjimajkoska O, Sharples LD, Bradley JA, Pettigrew GJ. Expansion of the kidney donor pool by using cardiac death donors with prolonged time to cardiorespiratory arrest. Am J Transplant. 2011; 11: 995–1005.

Kosmoliaptsis V, Sharples LD, Chaudhry AN, Halsall DJ, Bradley JA, Taylor CJ. Predicting HLA class II alloantigen immunogenicity from the number and physiochemical properties of amino acid polymorphisms. Transplantation. 2011; 91: 183–90.

Watson CJ, Wells AC, Roberts RJ, Akoh JA, Friend PJ, Akyol M, Calder FR, Allen JE, Jones MN, Collett D, Bradley JA. Cold machine perfusion versus static cold storage of kidneys donated after cardiac death: a UK multicenter randomized controlled trial. Am J Transplant. 2010; 10: 1991–9.

Summers DM, Johnson RJ, Allen J, Fuggle SV, Collett D, Watson CJ, Bradley JA. Analysis of factors that affect outcome after transplantation of kidneys donated after cardiac death in the UK: a cohort study. Lancet. 2010; 376: 1303–11.

Kosmoliaptsis V, Chaudhry AN, Sharples LD, Halsall DJ, Dafforn TR, Bradley JA, Taylor CJ. Predicting HLA class I alloantigen immunogenicity from the number and physiochemical properties of amino acid polymorphisms. Transplantation. 2009; 88: 791–8.

Win TS, Rehakova S, Negus MC, Saeb-Parsy K, Goddard M, Conlon TM, Bolton EM, Bradley JA, Pettigrew GJ. Donor CD4 T cells contribute to cardiac allograft vasculopathy by providing help for autoantibody production. Circ Heart Fail. 2009; 2: 361–9.

Stem Cell Medicine

Prof Roger Pedersen's and Dr Ludovic Vallier's groups are conducting research into the early stages of embryonic stem cell differentiation and the genetic mechanisms responsible for these processes. Both mouse and human embryonic stem (hES) cells are being studied, and interfering (si)RNAs are being used to modify gene function and examine the role of specific genes, with the aim of ultimately controlling differentiation into specialised cell types for potential therapeutic use. Research is also being undertaken into the mechanisms responsible for the maintenance of pluripotency in hES cells and the formation of mesodermal and endodermal cell lineages, as well as the epigenetic stability of pluripotent stem cell lines. Both groups interact extensively with other leading investigators within and outwith the University; both are key contributors to the Cambridge Stem Cell Initiative, which aims at biomedical translation of stem cell and regenerative medicine research. Both Prof Pedersen and Dr. Vallier are founding members of the School of Clinical Medicine's Anne McLaren Laboratory for Regenerative Medicine (LRM). The LRM has played a key role in the Cambridge Stem Cell Initiative by serving as the Clinical School host for the MRC Centre Centre for Stem Cell Biology and Regenerative Medicine, which together with the Wellcome Trust Centre for Stem Cell Research on Tennis Court Road constitute the hubs of the Cambridge Stem Cell Initiative. In 2009, Dr Vallier established the human induced pluripotent stem cell Core Resource, with support from the National Institute for Health Research Cambridge University Hospitals NHS Trust Biomedical Research Centre. During the past two years, the hIPSC Core Facility has derived more the 400 hIPSC lines from 60 patients suffering from neurodegenerative diseases, cardiovascular syndromes, metabolic and blood disorders. In parallel, the hIPSC Core Facility has become a major training centre by accommodating more than 20 visiting scientists and by supporting the development of similar platforms in several European countries.

Selected references

Yusa K*, Rashid ST*, Strick-Marchand H, Varela I, Liu PQ, Paschon DE, Miranda E, Ordóñez A, Hannan N, Rouhani FJ, Darche S, Alexander G, Marciniak SJ, Fusaki N, Hasegawa M, Holmes MC, Di Santo JP, Lomas DA*, Bradley A* and Vallier L* (2011). Targeted gene correction of α1-antitrypsin deficiency in induced pluripotent stem cells. Nature, 12;478(7368):191–5 (*joint authorship).

Teo AKK, Arnold SJ, Trotter MWB, Brown S, Ang LT, Chng, Z, Robertson EJ, Dunn NR, Vallier L (2011). Pluripotency factors regulate definitive endoderm specification through eomesodermin. Genes & Development, 25: 238–250.

Brown S, Teo A, Pauklin S, Hannan N, Cho CH-H, Lim B, Vardy L, Dunn NR, Trotter M, Pedersen R, Vallier L. (2011). Activin/Nodal Signalling Controls Divergent Transcriptional Networks in Human Embryonic Stem Cells and in Endoderm Progenitors. Stem Cells 29:1176–85.

Bernardo AS, Faial T, Gardner L, Niakan KK, Ortmann D, Senner CE, Callery EM, et al. (2011). BRACHYURY and CDX2 Mediate BMP-Induced Differentiation of Human and Mouse Pluripotent Stem Cells into Embryonic and Extraembryonic Lineages. Cell Stem Cell, 9(2), 144–55.

Patani R, Hollins AJ, Wishart TM, Puddifoot CA, Álvarez S, de Lera AR, Wyllie DJA, Compston DAS, Pedersen RA, Gillingwater TH, Hardingham GE, Allen ND and Chandran S. Retinoid independent generation of motor neurons from human embryonic stem cells reveals a medial columnar ground state. In press, Nature Communications.

Rashid ST, Corbineau S, Hannan N, Marciniak SJ, Miranda E, Alexander G, Huang-Doran I, Ahrlund-Richter L, Skepper J, Griffin J, Semple R, Weber A, Lomas DA, Vallier L. (2010) Modelling inherited metabolic disorders of the liver with human induced pluripotent stem cells. Journal of Clinical Investigations. J Clin Invest. 2010 Sep 1;120(9):3127–36.

Touboul T, Hannan N, Corbineau S, Martinez A, Martinet C, Branchereau S, Mainot S, Strick-Marchand H, Pedersen R, Di Santo J, Weber A and Vallier L. (2010). Generation of functional hepatocytes from human embryonic stem cells under chemically defined conditions which recapitulate liver development. Hepatology. 51(5):1754–65.

Chng ZZ, Teo A, Pedersen R*, Vallier L* (2010) SIP1 mediates cell fate decisions between neuroectoderm and mesendoderm in human embryonic pluripotent stem cells. Cell Stem Cell. 6(1). 59–70 * joint authorship.

Vallier L, Touboul T, Brown, Cho C, Bilican B, Alexander M, Cedervall J, Chandran S, Ährlund-Richter L, Weber A, Pedersen RA. (2009). Signalling pathways controlling pluripotency and early cell fate decisions of human induced pluripotent stem cells. Stem Cells. 27(11):2655–2666.

Vallier L, Touboul T, Chng Z, Brimpari M, Hannan N, Millan E, Smithers LE, Trotter M, Rugg-Gunn P, Weber A, Pedersen RA (2009). Early cell fate decisions of human embryonic stem cells and mouse epiblast stem cells are controlled by the same signalling pathways. Plos One. June 30;4(6):e6082.

Vallier L, Mendjan S, Brown S, Chng Z, Teo A, Smithers LE, Trotter MW, Cho CH, Martinez A, Rugg-Gunn P, Brons G, Pedersen RA. (2009) Activin/Nodal signalling maintains pluripotency by controlling Nanog expression Development. Apr;136(8):1339–49.

Surgery

Orthopaedics (Department of Surgery)

The Orthopaedic Research Unit, directed by Professor Neil Rushton, has a novel programme of fundamental and translational research in bone and joint repair using in vitro and in vivo approaches.

The basic science programme is designed to elucidate the developmental cascade of the osteoblast and chondrocyte lineages, both from known precursors and novel sources, and to understand their interaction with normal and newly developed matrices. Understanding how local niches impinge on the developmental cascade is a new theme. In addition to investigations on the developmental cascade there is an ongoing programme investigating the damage /repair response of the osteochondral unit.

In collaboration with the Departments of Materials Science and Engineering we are evaluating the interactions of human cells and in particular mesenchymal stem cells with collagen-based materials for the regeneration of cartilage, meniscus and tendon. With the Department of Chemistry we are using nuclear magnetic resonance spectroscopy to investigate chemical signatures within bone matrix and between the matrix and mineral phases of bone.

Translational research has resulted in the CE marking and first in man trials of an osteochondral repair product following development work carried out in the Unit. The clinical use of bone substitute materials in impaction grafting has been supported by research on the mechanical properties of mixtures of bioactive ceramic and bone.

Selected references

Enea D, Henson F, Kew S, Wardale J, Getgood A, Brooks R, Rushton N. Extruded collagen fibres for tissue engineering applications: effect of crosslinking method on mechanical and biological properties. J. Mater. Sci: Mater Med. 2011; 22(6):1569–78.

Getgood A, Henson F, Brooks R, Fortier LA, Rushton N. Platelet-rich plasma activation in combination with biphasic osteochondral scaffolds-conditions for maximal growth factor production. Knee Surg Sports Traumatol Arthrosc. 2011; 19 (11):1942–7.

Kew SJ, Gwynne JH, Enea D, Abu-Rub M, Pandit A, Zeugolis D, Brooks RA, Rushton N, Best SM, Cameron RE. Regeneration and repair of tendon and ligament tissue using collagen fibre biomaterials. Acta Biomaterialia 7 (9): 3237–3247

Cristofolini L, Juszczyk M, Taddei F, Field R, Rushton N, Viceconti M. Assessment of femoral neck fracture risk for a novel proximal epiphyseal hip prosthesis. Clinical Biomechanics 2011; 26 (6): 585–91.

Mullen LM, Best SM, Brooks RA, Ghose S, Gwynne JH, Wardale J, Rushton N, Cameron RE. Binding and Release Characteristics of Insulin-Like Growth Factor-1 from a Collagen-Glycosaminoglycan Scaffold. Tissue Engineering Part C. 2010; 16 (6):1439–48.

Brooks RA, Field RE, Jones E, Sood A, Rushton N. A histological study of retrieved Cambridge acetabular components. Hip Int. 2010; 20 (1):56–63.

Spence G, Patel N, Brooks R, Bonfield W, Rushton N. Osteoclastogenesis on hydroxyapatite ceramics: the effect of carbonate substitution. J Biomed Mater Res A. 2010; 92(4): 1292–300.

Surgical Oncology

The uro-oncology division, directed by Professor Neal, is closely associated with the Departments of Oncology and Surgery. Cambridge has the largest robotic prostatectomy programme within the NHS and this, together with other clinical trials has allowed the development of a well-annotated bio-repository. Neal is one of the three PIs on a major NIHR funded trial (ProtecT) to determine the best treatment for men with early prostate cancer and is the largest ever surgical trial in prostate cancer. Collaborative genetic research continues with Strangeways and the ICR in London.

There is a large translational research programme involving Gnanapragasam and experimental medicine studies including imaging led from the Cambridge Research Institute where Neal is group leader. Following studies of SNPs in prostate cancer, novel biomarkers have been developed. The majority of the work in the CRI is focused on androgen receptor signalling where we have discovered novel binding sites and functionally important therapeutic targets.

Selected references

Al Olama AA, Kote-Jarai Z, Giles GG, Guy M, Morrison J, Severi G, *et al.* Multiple loci on 8q24 associated with prostate cancer susceptibility. Nat Genet. 2009 Oct;41(10):1058–60.

Eeles RA, Kote-Jarai Z, Al Olama AA, Giles GG, Guy M, Severi G, *et al.* Identification of seven new prostate cancer susceptibility loci through a genome-wide association study. Nat Genet. 2009 Oct;41(10):1116–21.

Murphy T, Darby S, Mathers ME, Gnanapragasam VJ. Evidence for distinct alterations in the FGF axis in prostate cancer progression to an aggressive clinical phenotype. J Pathol. 2010 Mar;220(4):452–60.

McLean MA, Barrett T, Gnanapragasam VJ, Priest AN, Joubert I, Lomas DJ, et al. Prostate cancer metabolite quantification relative to water in (1)H-MRSI in vivo at 3 Tesla. Magn Reson Med. 2010 Nov 16.

Whitaker HC, Kote-Jarai Z, Ross-Adams H, Warren AY, Burge J, George A, et al. The rs10993994 Risk Allele for Prostate Cancer Results in Clinically Relevant Changes in Microseminoprotein-Beta Expression in Tissue and Urine. PLoS One. 2010;5(10).

Massie CE, Lynch A, Ramos–Montoya A, Boren J, Stark R, Fazlil et al. The androgen receptor fuels prostate cancer by regulating central metabolism and biosynthsis EMBRO J 2011; 30(13): 2719–33

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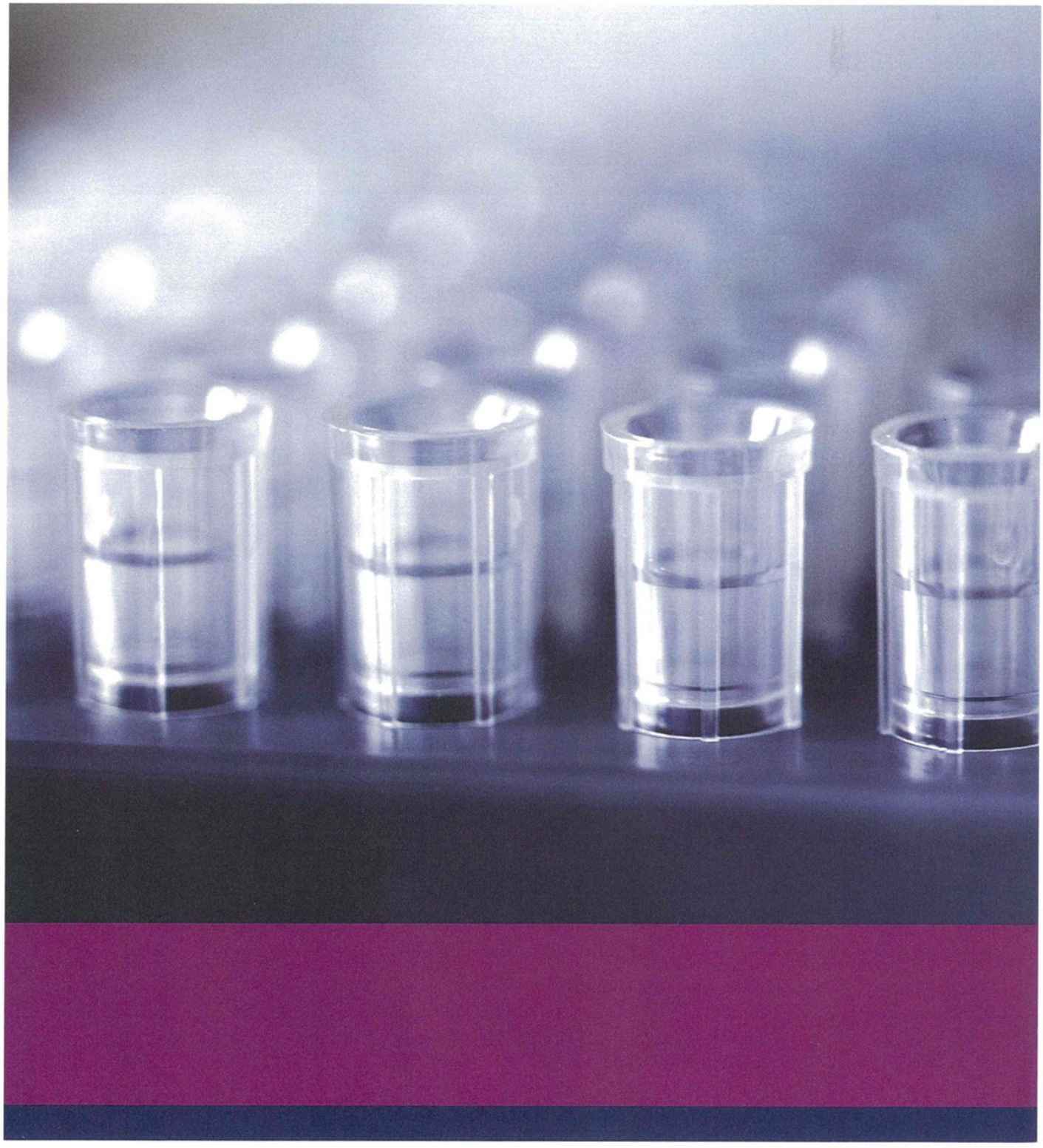

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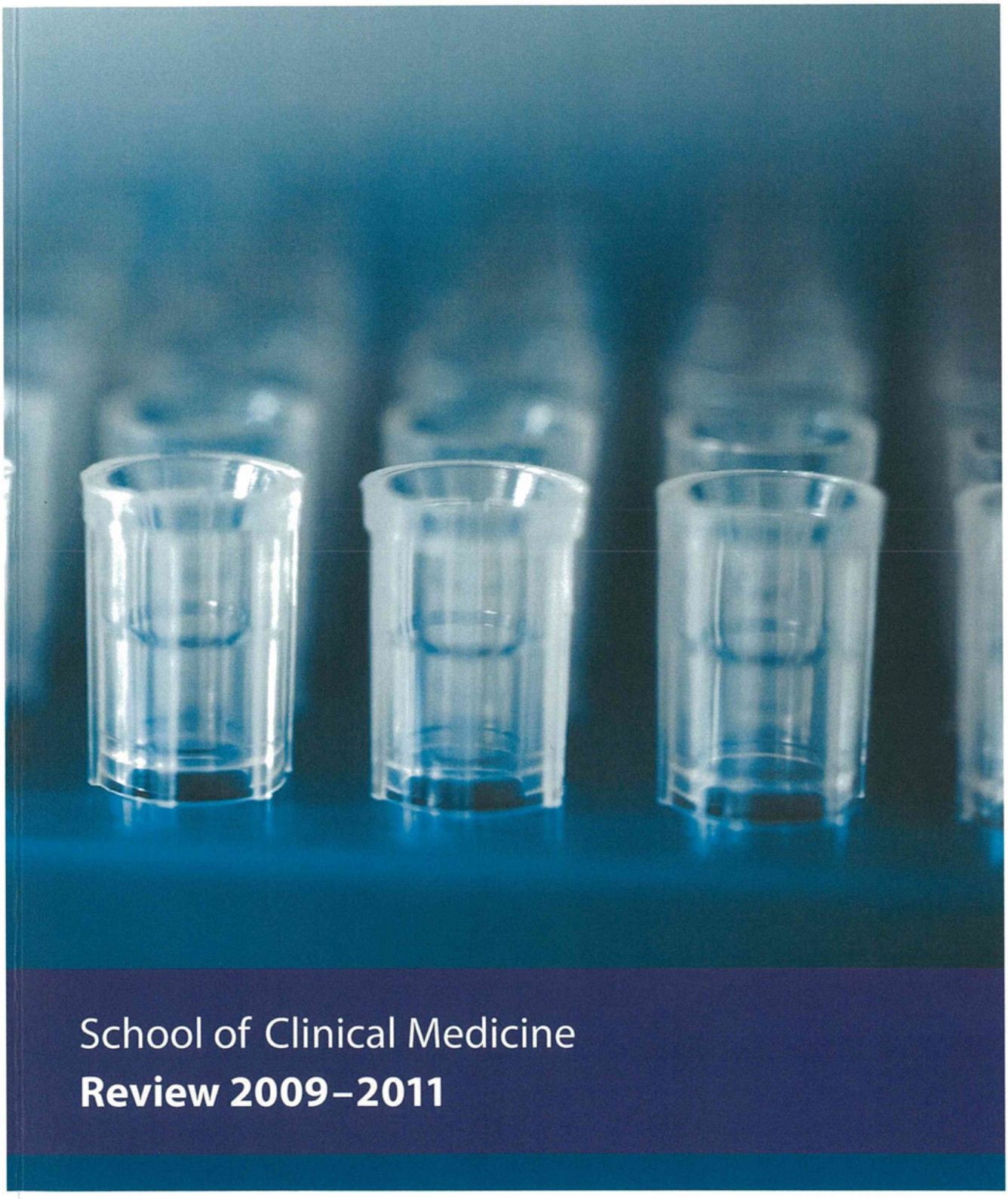

School of Clinical Medicine
Review 2009–2011

UNIVERSITY OF CAMBRIDGE

Contents

Introduction

Aerial view of campus

Regius Professor of Physic, Sir Patrick Sissons

Welcome to the Clinical School Review for 2009–2011. It tells a story of continuing progress in the development of the University's School of Clinical Medicine – progress, in all aspects of the 'tripartite mission' of education, research and clinical service.

This mission is enshrined in the constitution of Cambridge University Health Partners which brings together the University and its three principal NHS partners – Cambridge University Hospitals NHS Foundation Trust, Papworth Hospital NHS Foundation Trust and Cambridgeshire and Peterborough NHS Foundation Trust – in a new legal entity from 2009. It is one of five such partnerships formally designated as Academic Health Science Centres by the Department of Health in England. As I write, this is a time both of opportunity and challenge for all University/NHS partnerships. The opportunities lie in the translation of the outstanding research being pursued across the University and the partnership into advances in the treatment and management of disease. As this report shows, the vitality and success of our biomedical and translational research has never been greater. At the same time the challenge lies in the current major structural reorganisation within the NHS, and in the accompanying drive for efficiency savings across the whole service. This inevitably impacts on our NHS partners as it does throughout