Institution: Institute of Cancer Research

Unit of Assessment: UoA5 Biological Sciences

a. Overview

The Institute of Cancer Research (ICR) is a postgraduate college of the University of London. In pursuit of its mission to make the discoveries that defeat cancer, the ICR deploys a comprehensive range of research disciplines to achieve a better understanding of the causes of cancer and to translate this knowledge into improvements in diagnosis and treatment. The range combines **fundamental research** into the genetics and biology of cancer (submitted to UoA5: Biological Sciences) and **translational and clinical research** conducted through close collaboration with our partner hospital, The Royal Marsden NHS Foundation Trust (RM) (submitted to UoA1: Clinical Medicine). The ICR has over 1,000 staff and a total annual research expenditure of £75.4M; RM has over 3,850 staff and R&D expenditure of £25M; together the institutions form the largest comprehensive cancer centre in Europe. We share two London sites, in Chelsea and Sutton, which provide an outstanding environment for research and training. In 2006, and again in 2011, we were designated as one of six NIHR Specialist Biomedical Research Centres, and the only one dedicated to cancer.

The ICR is organised into eight Divisions and, to enable scientific interaction, many Faculty (academic staff) hold joint appointments across Divisions. Some Divisions are grouped around a discipline and others cover the whole spectrum of research, focusing on a tumour type. Our REF submissions therefore do not strictly adhere to organisational groupings. This return incorporates the Divisions of Cancer Biology and Structural Biology and the biological science teams in the Divisions of Genetics and Epidemiology, Molecular Pathology and Breast Cancer Research.

b. Research strategy (Note: numbered references in brackets refer to published outputs in REF2)

Over the period, the ICR Scientific Strategy has focused on the three connected themes of genetics, molecular pathology and therapeutics, underpinned by fundamental research into the biological basis of cancer. Research in this UoA focuses on the genetic and molecular basis of cancer, the identification and characterisation of cellular components that may serve as molecular targets against which new cancer treatments and diagnostics might be directed, and on understanding the mechanisms of resistance to targeted therapeutics. Structural biology studies prioritise investigations of the molecular structure of these key target proteins and the elucidation of how the structures relate to biological functions. Scientific achievements over the period include:

Genetics and Functional Genomics

In the assessment period we have (i) identified over 1,000 genetic mutations associated with 17 major cancer types (Garcia-Closas1-3; Kote-Jarai1-4; Orr1,2; Rahman1-4); (ii) demonstrated that cancer stem cells in the most common childhood leukaemia have complex and diverse combinations of mutations, even within individual patients, which may help explain why advanced cancers remain so difficult to eradicate (Greaves1,3); (iii) using pooled next generation sequencing of 507 genes in 1,150 blood samples, discovered mutations in the *PPM1D* gene that are linked to a two-fold and ten-fold risk of breast and ovarian cancer, respectively. The *PPM1D* mutations display a mosaic pattern of expression, being found only in blood cells, not in the tumour cells or the normal breast or ovarian cells, suggesting a newly identified mechanism of cancer development (Rahman1); (iv) demonstrated that constitutional 11p15 abnormalities, including heritable imprinting centre mutations, cause nonsyndromic Wilms tumour (Rahman4).

Cell Biology – the mechanisms of tumour progression and metastasis

In the assessment period we have (i) used a systematic siRNA screen of Rho family GAPs and GEFs to identify key components that regulate the switch between mesenchymal and amoeboid modes of tumour cell migration (Marshall1) and further identified tumour:stroma crosstalk pathways that modulate different modes of tumour cell invasion (Marshall2); (ii) developed high-throughput imaging and computational methods to interrogate the morphological complexity of cells and demonstrated that loss of the tumour suppressor gene *PTEN* in melanoma cells results in the stabilisation of a pro-metastatic mesenchymal morphology (Bakal3); (iii) revealed that in the progression and metastasis of lung cancers, the non-histone high-mobility group family member *Hmga2* acts in a dual manner, both as protein-coding gene and as a non-coding ceRNA

(Downward3); (iv) used phosphoproteomics approaches and subsequent biochemical validation to discover a key SHP2-mediated signalling node downstream of the collagen receptor DDR2, which may have therapeutic implications in a subset of lung squamous cell carcinomas with *DDR2* mutations (Huang1); (v) identified a large 2MDa cell death-inducing platform, the ripoptosome, and demonstrated its role in converting chemotherapeutic stimulated proinflammatory cytokines into prodeath signals (Meier2).

Mechanisms of drug resistance
We have advanced our understanding of the mechanisms underlying *de novo* and acquired resistance to targeted drug therapies. For example, we have (i) identified EGFR signalling as a resistance mechanism against FGFR inhibition in FGFR3-mutant breast cancers (Turner4); (ii) discovered that intragenic deletion of *BRCA2* leads to restoration of homologous recombination in *BRCA2* mutant cells and resistance to poly(ADP-ribose) polymerase (PARP) inhibition (Ashworth1); (iii) demonstrated a potential means of reversing breast cancer cells' resistance to aromatase inhibitors by chemically reducing the activity of the receptor tyrosine kinase RET (Isacke4) and identified the cyclin-dependent kinase CDK10 as a modulator of response to tamoxifen (Ashworth2); (iv) demonstrated that *Ras*-oncogene driven non-small cell lung cancers (NSCLCs) depend on the presence of the transcription factor GATA2, and that combined suppression of GATA2-regulated pathways improves tumour clearance in a *Kras*-mutant mouse model of NSCLC (Downward1).

Structural Biology
We have solved the molecular structures of a number of proteins involved in protein folding, protein degradation and cell division that have implications for cancer treatment. For example, (i) superfamily 1B (SF1B) helicases translocate in a ′5 -3′ direction and are required for a range of cellular activities including telomere maintenance and DNA repair. Crystal structures of the complex between the SF1B helicase RecD2 and ssDNA in the presence and absence of an ATP analogue provide both a model of a step size for translocation of one base per ATP hydrolysed and reveal that SF1B nucleic acid translocation in the 5′-3′ direction is surprisingly different from that of 3′-5′ translocation by SF1A enzymes (Wigley1, Wigley3); (ii) we have developed a recombinant expression system allowing reconstitution of the large multimeric anaphase-promoting complex (APC/C) that controls sister chromatid segregation and exit from mitosis. Combined with electron microscopy, mass spectrometry and docking of crystallographic and homology-derived coordinates, this has allowed the precise definition of organisation and structure of all essential APC/C subunits and a structural framework for understanding APC/C substrate specificity and catalysis (Barford1, Morris2). The same experimental approach has been successfully used to analyse the structure of (iii) the mitotic checkpoint complex responsible for imposing the spindle assembly checkpoint in mitosis (Barford2) and (iv) the human 26S proteasome (Morris1) and Cop9 signalosome (CSN):Skp1-Cul1-Fbox (SCF) complexes (Morris3).

Other significant developments during the assessment period are: (i) in 2011, Professor Alan Ashworth FRS succeeded Professor Peter Rigby FRS as Chief Executive of the ICR; (ii) 3 new Professors (Downward FRS, Garcia-Closas, Wigley FRS) and 15 new Faculty, Career Development Faculty and Fellows with active research programmes have been recruited to support our new strategy; (iii) the recent appointment of Professor Andrew Tutt as the new Head of the ICR Division of Breast Cancer Research and as Breakthrough Centre Director, whilst retaining his responsibility to lead the Breakthrough Unit at King's Health Partners, has created an opportunity to stimulate a wider "Breakthrough London" research programme.

Future Strategy:
The central research theme for the next period will be the exploitation of advances in genetics, molecular pathology, cancer biology and therapeutic development to deliver precision treatment, thereby improving patient outcomes. Research activity falling outside the central themes has been closed down to allow for re-investment. Newly recruited faculty are indicated below against relevant research areas.

We plan an expansion of programmes in cancer heterogeneity and evolution, since this has a

major impact on treatment resistance and outcomes; most advanced cancers remain difficult, if not impossible, to eradicate. The basic principles of evolutionary biology can be applied to three distinct areas of cancer medicine: (i) causation or vulnerability; (ii) the time ordered biological development of cancer (over years) in the body; and (iii) the emergence of drug resistance. Under the leadership of the founding Scientific Director, Greaves FRS, we are developing a new Centre for Evolution and Cancer by assembling a critical mass of researchers with the required mix of skill sets and interests, e.g. computational biologists, geneticists, cell biologists and clinical scientists including individuals trained in evolutionary ecology and the first new team leaders have been recruited (Sottoriva, Gerlinger).

The analysis and exploitation of our understanding of cell signalling pathways in cancer has been one of our major strengths in the last two decades and will continue to be an important area, particularly with the advent of new techniques for pathway and biological network analysis in tumours via proteomics and imaging (Bakal, Downward, Jørgensen, Huang, Whittaker, Yuan)

It is clear that an important component of tumour behaviour is the interplay between cancer cells and their microenvironment; an area of research which is key to understanding tumours at a systems level (Calvo). The alterations in metabolism that are evident and increasingly understood at the molecular level in many cancers provide new molecular diagnostic and therapeutic opportunities. In 2012, we established a major new collaboration with Imperial College (IC), initially focusing on metabonomics, epigenomics and bioinformatics (Centre for Systems Oncology and Cancer Innovation (CSOCCI)). The aim is to stimulate collaborative activity in these areas through the development of joint research initiatives, funding opportunities and training programmes. Both the ICR (Poulogiannis) and Imperial are recruiting new team leaders in this field, and each year, 4 research studentships will be available for projects jointly supervised between ICR and IC.

The structural analysis of molecules, and increasingly molecular complexes, relevant to cancer, will continue to be very important to our strategy, both in providing insights into the molecular mechanisms of key cellular components and guiding therapeutic design (Guettler, Vannini, Wigley).

In breast cancer biology, we will continue our work to understand the causes and mechanism of primary breast cancers but will have a renewed focus on advanced disease and on the translational and clinical studies (Garcia-Closas, Natrajan, Orr, Reynolds, Turner), increasingly working collaboratively across the London Cancer Alliance (see section d).

c. People, including:

i. Staffing strategy and staff development

New team leaders are recruited to reflect developing research priorities and to maintain existing strengths. All posts which become available are reviewed in detail and filled in accordance with our current strategy so as to promote a coherent research programme and, in particular, to promote interdisciplinary research across Divisions (see section b). During the period of assessment, the ICR reviewed its research strategy. To allow for further investment in the fields of molecular pathology and therapeutic development (in UoA1) and the new Centres for Evolution and Cancer and Systems Oncology and Innovation described above, activity that fell outside of the central themes was identified, and a number of teams were supported to move to other HEIs. Further, as part of their career progression, some staff have moved to senior positions elsewhere (Pearl, Head of the School of Life Sciences, University of Sussex; Marais, Director of the Cancer Research UK Manchester Institute; So, Chair in Leukaemia Biology, King's College London). We have therefore been able to make a significant number of recruitments.

Research career levels within the ICR are:

- Postgraduate students: complete programme and move to post-doctoral experience elsewhere;
- Postdoctoral training fellows: 3-4 year post, maximum extension to 7 years, move elsewhere after training period;
- ICR Fellows: researchers on independent fellowships and recipients of pathway to

independence scheme funding starting to pursue their own research programmes;
- Career Development Faculty; independent investigators, lead their own research, acquire grants and studentships, 5 year review for transfer to non-time-limited post;
- Non-time-limited Faculty; established investigators with international reputations, entry via promotion from career development posts or external recruitment.

Externally-funded fellows are appointed either as post-doctoral training fellows, ICR Fellows or as CDF, depending upon the level of the fellowship and their prior research experience. The ICR provides a comprehensive support framework for all early career researchers through mentoring by senior research staff.

On appointment, Faculty and CDF receive a package comprising: own salary, salaries for a Postdoctoral Fellow and Scientific Officer, and access to PhD studentships and clinical training fellowships, together with laboratory start-up costs, including essential equipment and consumables. CDFs are mentored by the Head of Division and have a mid-term review at 3 years involving external advisers. The CDF association has regular meetings with the research leadership of the ICR. External coaches are available to research leaders at all levels. Team leader performance is monitored annually by an ICR Career Development Review group of senior staff in addition to the annual appraisal by their Head of Division.

The ICR's Learning and Development team works closely with the ICR's four researcher associations (Student, Postdoc, Scientific Officer and CDF) to implement the Researcher Concordat, and achieved EU HR Excellence in Research reaccreditation in 2013. The Researcher Associations manage their own budgets and promote a range of activities including away-days, scientific conferences, training courses and careers conferences. They also inform, prioritise and help to deliver 150 individual training and career development activities at the ICR, open to all research staff including visiting researchers (http://training.icr.ac.uk/).

There is an active exchange of course places between the ICR, other HEIs, and research institutes to ensure our researchers have access to the widest possible range of training and career development opportunities. These collaborations include "The Pathway to Independence; Developing Future Scientific Leaders", an innovative residential programme developed through collaboration between the ICR, the BBSRC and the Wellcome Trust Sanger Institute. The project was led by the ICR's Researcher Development Advisor and funded by a grant from the Leadership Foundation for Higher Education. Partners include the CRUK London Research Institute (LRI), the Cancer Research UK Manchester Institute and the European Bioinformatics Institute (EBI). The programme aims to support outstanding postdocs with a proven track record of academic achievement at the point in their career when they are seeking their first independent research position and the sessions aim to prepare delegates for the challenges associated with becoming a scientific leader (see http://training.icr.ac.uk/pathway/). Further, we have now established a Dean's Pathway to Independence Award and ICR's successful applicants to the programme have been awarded grants to pilot some of the research ideas they submitted as part of the application process.

Evidence of how the submitting unit supports equalities and diversity
The ICR's Athena SWAN Charter Bronze Award was successfully renewed in April 2013 and half the research divisions are currently working towards Silver Awards. The ICR has committed to achieving an organisational Silver Award by 2016. Diversity training is mandatory for all new staff and students, and briefings for new team leaders utilise the 'every researcher counts' materials. The published annual equality report details key initiatives eg a review of promotion processes, improved support for parents.
(http://www.icr.ac.uk/about_us/strategic_plan/equality_and_diversity/index.shtml)

ii. Research students

Postgraduate research training is an essential activity in all areas of this submission. The environment provides a unique training experience because of the widespread use of integrated multidisciplinary teams in our translational research. We invest heavily in training activity and

attract excellent graduates and Postdoctoral Fellows not only from the top UK Universities but also from Europe, the USA and worldwide.

Support for research students is organised on an ICR-wide basis. The Dean's team (postgraduate tutors) make regular checks on progress and resolve problems as and when they arise. There is an active student society and the students have themselves organised a buddy system for international students, help for new students in finding accommodation, and a student confidant system.

The Institute has experience of, and a strong track record in, supporting research students from a wide variety of subject and educational backgrounds, and key to this is that they are provided with two e-learning resources to develop the knowledge and skills that are necessary to excel in cancer research. "Perspectives in Oncology" is a modular e-learning website providing a basic grounding in cancer science covering subject matter such as cancer epidemiology, cancer genetics, cell biology, bioinformatics, medical physics, structural biology, cancer treatment and drug development. "Skills" is a blog-style resource giving advice in transferable skills at appropriate times throughout the four years. Themes covered include – Year 1: effective team work, time and workload management, and critical reading, as well as the broader implications of work at the ICR. Year 2: communicating research to a wider audience, scientific writing skills and referencing guidance. Year 3: thesis and viva preparation, writing style and avoiding scientific fraud.

Between 2008 and 2013, competitively won studentships were obtained from research councils (6) and UK-based medical charities including CRUK (22). The ICR also won funding for a prestigious and innovative combined clinical/science Wellcome Trust PhD programme in Mechanism-Based Drug Discovery to which 34 students in total have been recruited during the period, 3 based in this UoA. The ICR self-funds studentships (21 in the period) and has taken strategic decisions to (i) fund all science students for four years to allow sufficient time to complete high-quality research projects and skills training; and (ii) to match stipends to those awarded by major cancer charities to ensure we attract the brightest applicants. The ICR therefore supplements external awards where necessary. In January 2012 the QAA conducted an institutional review of the ICR, which found that the ICR meets UK expectations in all areas. The QAA review team also identified the following features of good practice: (i) the monitoring of, and support for, research students' progress; (ii) the quality of the research environment for research students; and (iii) the contribution students make to quality assurance.

The relatively small size of the student cohort fosters awareness of potential links with research elsewhere in the ICR and gives all third year students the opportunity to present their research at the ICR's annual conference. The learning and development opportunities offered to ICR staff, described above, are also open to all research students, who also benefit from careers advice provided in partnership with the University of London Careers Service.

d. Income, infrastructure and facilities

All laboratory space is either new or has been refurbished since 2001, and throughout the period, the ICR has continued to make substantial investment in 'state-of-the-art' facilities. All research areas receive long-term competitive research support (in the form of Centre, Unit and programme grants) from major funders. The Cancer Research UK Centre awarded to the ICR and RM (£12.28M, 2012-2014 and renewed) provides core infrastructure support across the ICR.

Research in Genetics, Cell and Molecular Biology is supported by CRUK funding to the CRUK Cell Signalling Unit, secured by Marshall (£13.25M, 2008-2013), and by the Breakthrough Breast Cancer Research Centre (£17.3M, 2011-2014; rated Outstanding). Marshall also secured a programme grant from CRUK (£2.02M, 2013-2018; rated Forefront/Outstanding) and Ashworth successfully renewed CRUK programme funding (£2.07M, 2007-2012, £2.36M, 2012-17; rated Outstanding). Rahman won two programme grants from the Wellcome Trust (£2.67M, 2012-2015; £2.18M, 2013-2018) and renewed CRUK programme funding (£3M 2012-2015; rated Forefront/ Outstanding).

Four separate programme grants support research in Structural Biology: Barford successfully

renewed programmatic funding from CRUK (£1.95M, 2007-2012; £3.23M, 2012-2017; rated Outstanding); Wigley secured new programme awards from CRUK (£2.32M, 2011-2016) and the Wellcome Trust (£2.21; 2011-2016); Morris won a new programme grant from CRUK (£1.19M, 2013-2018).

Genetics

All research groups have access to a range of standard, costs effective genetic analyses provided by the Genetics Core Facility. Using a 96-capillary 3730xl DNA Analyser, the facility performs Sanger DNA sequencing as well as DNA fragment analysis applications including MLPA and microsatellites. A Sequenom mass array analyser is also available for SNP genotyping, methylation detection and quantitative gene expression analysis. More bespoke applications, such as targeted re-sequencing from sub-microgram DNA amounts and shRNA screen deconvolution, can also be provided.

Studies of cancer evolution and drug resistance will be supported by the Tumour Profiling Unit (TPU), which has been established to facilitate the 'horizontal' analysis of patient biopsies from diagnosis throughout treatment. ICR investment of £1.7M has enabled laboratory refurbishment and equipment purchases to support genomic capabilities and development of patient-derived xenografts. The Genomics Facility within the TPU is a state-of-the-art facility working under GCLP guidelines to provide Next Generation Sequencing. It currently houses two Illumina HiSeq2500 instruments and acquired the first Ion Proton in Europe from Life Technologies, which is able to sequence two whole exomes in as little as 4 hours. The Tumour Transplantation Facility (TTF) within the TPU was set up to generate, archive and analyse patient-derived xenografts (PDXs).These animals will be housed in The Biological Services Unit, which has had investment of £1.9M over the assessment period to upgrade facilities.

Cell and molecular biology

Infrastructure for molecular biology includes extensive facilities for tissue culture, cell histopathology, microinjection, time-lapse microscopy and confocal imaging, cell sorting and cell analysis. Ariol scanning systems which combine an automated scanning microscope and image analysis system have been provided at each site. We have made significant investment in mass spectrometry, high content imaging (2 Perkin Elmer Operas, 1 PE Operetta) and capacity for computational biology. We are about to acquire a two-photon microscope, which will allow intravital imaging. We have established a Proteomics mass spectrometry facility including pre- and post-analysis support. The Velos LTQ Orbitrap platform allows for high-resolution mass analyses. Current services focus on high sensitivity protein identification and characterisation. Common applications include the identification of protein or drug binding partners, identification of phosphorylation, acetylation, methylation and ubiquitination sites, and comparative sequence mapping of truncated protein domains. To support two new CDF we purchased further specialist mass spectrometry instruments. Of these the LTQ Orbitrap Velos and the Vantage Mass Spectrometer are still in use and two other two instruments have been replaced recently with an AB SCIEX TripleTOF 5600+ System Mass Spectrometer, ordered in September 2013.

Structural biology

Infrastructure for structural biology includes two X-ray crystallography units, a Rigaku RU800 generator and an Ultimate HomeLab (with Pilatus 300k), Complete PILATUS 300K Pixel Detector system, AFC11 Partial-c, 4-axis goniometer FR-X generator, which at the time of purchase (2013) was the most advanced in-house crystallography system outside of a Synchrotron. This was funded by equipment grants from the Wellcome Trust and CRUK with the balance from the ICR.

Incorporation of a CCD detector and automated crystal sampler facilitated high-throughput screening as part of an initiative with Cancer Therapeutics (submission to UoA1 in Structure Based Drug Design, led by van Montfort). Crystallisation is supported by crystallisation robots, temperature-controlled incubators, and automated visualisation 'plate-hotel' systems. Recombinant protein production is performed in bacterial, yeast and insect cell systems, the latter in a dedicated facility supported by CRUK and ICR funding. As insect cell-expressed proteins are a major aspect of structural work, this facility is important for addressing eukaryotic multi-protein systems and

studying structural implications of post-translational modifications. A 60L fermentor for isolating native protein complexes from yeast has been installed. The cryoelectron microscopy facility (Tecnai T12/F20 cryoelectron microscopes, Vitrobot robot, headed by Morris) has significantly enhanced existing studies on supra-molecular complexes. All groups have access to multiple semi-automated systems for protein purification and to a wide range of biochemical/biophysical systems for the analysis of protein composition and interactions, including dynamic light-scattering, absorption and fluorescence polarisation spectrophotometry, isothermal titration calorimetry, dynamic light scattering and mass spectrometry.

High Performance Computing
Key activities at the ICR demand high-end computation and extremely large amounts of data storage. Recognising requirements, the ICR has invested £1.7M to establish a High Performance Computing core facility. The three platforms initially acquired provided a total of 896 usable processors and around 400TB of high performance storage. A further £0.5M has been invested to increase capacity, with three new platforms providing an additional 992 high performance processing cores and 550TB of additional high performance storage.

Collaborative use of research infrastructure: Imperial College (IC) and the ICR have established a joint Centre for Systems Oncology and Cancer Innovation (CSOCI) which will build on the complementary expertise in the institutions; metabolomics and biomarkers at IC and cancer biology, drug discovery and development at the ICR, as well as areas of common interest in bioinformatics, "poly-omics" and clinical trials. This will provide ICR researchers with access to state of the art instrumentation and expertise in mass spectrometry and computational medicine at IC, and to facilitate this initiative, we are establishing an in-house metabolomics facility, which will be housed alongside the mass spectrometry facility.

Major benefits-in-kind: The Division of Structural Biology is awarded data collection time for macromolecular crystallography and small-angle X-ray scattering (SAXS) experiments at the European Synchrotron Radiation Facility (ESRF) in Grenoble, France, and the Diamond Light Source, Oxford UK, and coordinates a Block Allocation Group consortium (BAG) comprising the ICR, the Cancer Research UK London Research Institute and the University of Sussex. This BAG is allocated beam time at the Diamond MX (Macromolecular Crystallography) Village which comprises five state-of-the art X-ray beam lines specific for investigation of macromolecular crystals including microcrystals of large macromolecular complexes. At the ESRF, the BAG is allocated beam time at the Structural Biology (MX and SAXS) eight beam lines. During the period from October 2010 to March 2013, the BAG was awarded 1,296 hours at the MX Village DIAMOND, of which the ICR used approximately 640 hours. In the same period, the BAG was awarded 824 hours at the ESRF, of which the ICR used 360 hours. The ICR principal investigators were Barford, whose projects included the Anaphase Promoting Complex (APC/C) and its co-activators, a 1.2 MDa (megadalton) protein machine which functions to regulate progression through the mitotic phase of the cell cycle and controls entry into S phase; Wigley, whose projects included large macromolecular protein/DNA complexes controlling DNA double-strand break repair and chromatin remodelling complexes; and Vannini, whose experiments target the architecture of the RNA polymerase III pre-initiation complex and its regulation by oncogenes, tumour suppressors and additional kinases.

The RM and ICR Biomedical Research Centre (BRC) was established in 2007, following the award of a competitive grant from the NIHR. In 2012 this grant was renewed for a further 5 years. The BRC provides crucial support for our translational and clinical research submitted in UoA1, but of relevance here, we plan to facilitate our studies of cancer evolution by setting up a "warm" autopsy programme to enable the study of clonal evolution of cancer within individual patients.

Institutional Research Management and Governance
The ICR has an effective governance structure for prioritising research as a core institutional academic activity. Its Board of Trustees oversees scientific strategy and monitors the associated objectives against defined outcome measures. The ICR and RM have joint structures for research management and clinical research governance. The Joint Research Committee reviews the

progress of research programmes that implement the strategy, and advises upon and prioritises new initiatives and their resource implications.

The ICR/RM joint Clinical Research Directorate (CRD), chaired by the Director of Clinical R&D (Professor David Cunningham, also the Director of the NIHR Biomedical Research Centre) with a membership constituted from senior management (including both Chief Executives) and researchers of both institutions, advises Boards of both organisations on all issues and resources relevant to clinical research. All research involving patients, clinical staff, tissues, samples and/or data at the ICR and RM (or tissues, samples or data) must be approved by the joint RM/ICR Committee for Clinical Research (CCR), which also provides the mechanism for sponsorship approval. Committee members assigned to review a research proposal include a clinical or scientific peer reviewer, a statistician, a GCP compliance specialist, and a pharmacist, under the direction of the CCR Chair. CCR reviews research for scientific quality, research governance arrangements, compliance with the EU Directive, resource implications and insurance arrangements, and conducts a formal risk assessment to ensure that studies are not approved until all scientific and regulatory requirements have been met and that areas of risk to the institution have been identified and addressed. Sponsorship arrangements are assessed on a case by case basis by the CCR.

The Clinical R&D Office, located at RM and under the direction of the Director of Clinical Research, is the sponsor office for both the ICR and RM, and is responsible for servicing the joint RM/ICR CCR; for developing and managing RM/ICR systems for good governance and management of clinical research; facilitating inspections carried out by the regulatory authorities; providing Good Clinical Practice and pharmacovigilance training to RM/ICR clinical research personnel; and for providing support for monitoring and auditing of clinical research.

e. Collaboration or contribution to the discipline or research base

During the period of assessment, Ashworth was elected to the ***Fellowship of the Royal Society*** (2008), bringing the total number of Royal Society Fellows in this UoA to 6 (Ashworth, Barford, Downward, Greaves, Marshall, Wigley). Downward (2009) and Rahman (2010) were elected to the ***Fellowship of the Academy of Medical Sciences***, bringing the total number of FMedSci in this UoA to 6 (Ashworth, Barford, Downward, Greaves, Marshall, Rahman).

Other senior awards: The Royal Society Buchanan Medal (Marshall, 2008); Royal Society Wolfson Research Merit Awards (Barford, Meier, 2012); Lifetime Achievement Awards: European Society for Medical Oncology (Ashworth, 2009), Leukaemia and Lymphoma Research (UK) (Greaves, 2010), CRUK Lifetime Achievement Award (Marshall, 2011), Basser Global Prize (Ashworth, 2013), David Workman Memorial Award (Ashworth, 2010), NIH Merit Award (Garcia-Closas, 2008).

Fellowships: Wellcome Trust Senior Investigator Awards (Wigley, 2011, Rahman, 2012); ERC Advanced Investigator Award (Downward, 2013); Wellcome Trust Intermediate Fellowship (Bakal, 2010), CRUK Career Establishment Award (Jorgensen, 2011, Guettler, 2013); BBSRC New Investigator Award (Vannini, 2013); Breast Cancer Campaign Career Development Fellowship (Natrajan, 2011); Sir Henry Wellcome Postdoctoral Fellowships (Huang, 2009, Stengel, 2011, Tape, 2012).

Membership of External Committees:

Ashworth: Scientific Advisory Board Member for Susan G. Komen for the Cure, USA; Centre for Cancer Research & Cell Biology, Queen's University Belfast; Horizon Discovery, UK; AC Carmago Hospital, Brazil; Basser Research Centre, Penn University, USA; Netherlands Cancer Institute.

Barford: Council of the Royal Society.

Garcia-Closas: External Scientific Committee for the Multicenter Case-Control Study in Spain; Centre for Research in Environmental Epidemiology (CREAL); Etiology and Early Marker Studies (EEMS) Review Panel for PLCO Studies, National Cancer Institute, USA.

Greaves: Chair, Royal Society Section Committee 10.

Isacke: Deputy Board Chair, Molecular and Cellular Medicine Board (MCMB) MRC; CRUK

Programme Review Panel; Academy of Finland Grant Committee.
Marshall: Chair, CRUK Science Committee; Scientific Advisory Boards (i) King's College London BHF Centre of Research Excellence; (ii) Gray Institute for Radiation Oncology and Biology, Oxford; (iii) IRCC, University of Torino.
Rahman: Scientific Programme Committee, American Association for Cancer Research; Wellcome Trust Case Control Consortium Management Committee; Chair WTCCC Exon Resequencing Committee.
Turner: NCRI Breast Cancer Clinical Studies Group Member.
Wigley: Royal Society Wolfson Merit Award Committee; EMBL Grenoble site review committee EMBO Fellowships committee Member; Wellcome Trust/ Royal Society Henry Dale Fellowships committee; Wellcome Trust Senior Fellowships committee.

There were 11 staff members in UoA5 on editorial boards in the period: (Ashworth, Barford, Greaves, Howard, Huang, Isacke, Marshall, Meier, Swain, Turner, Wigley)

Partnership and collaboration
Within the ICR's research strategy, key strategic objectives are:

- To form strategic alliances and collaborations which enhance opportunities to conduct research aimed at improving outcomes for cancer patients
- To ensure appropriate and effective exploitation of the ICR's intellectual property and research outputs to maximise patient benefit

At the core, the ICR will continue its partnership with the RM and ensure we have the most appropriate research and governance structures in place to translate our findings in basic research to the clinical setting. However, we will also forge broader alliances and collaborations where these will enhance our research:

- We have jointly established a Centre for Systems Oncology and Cancer Innovation (CSOCI) with Imperial College.
- Our partnership with the RM has been extended to include an academic and research partnership with Mount Vernon Hospital.
- We have established The London Lung Cancer Alliance which aims to deliver dramatic benefits for patients through collaboration, coordination and an ambition to give every patient access to a trial suitable for them.
- The ICR/RM is participating in the national effort to deliver precision medicine as part of the CRUK Stratified Medicines programme. We are one of the three institutions to be selected as both a Clinical and Technology Hub for this programme.

During the assessment period, ICR/RM international collaboration has increased in both volume, and in relative terms as a percentage of our research output, as evidenced by internationally co-authored publications. In descending order, our most frequent collaborating partners are from the USA, Germany, France, the Netherlands and Italy. Research collaboration has also increased notably with Spain and Canada.

Our primary objective for the ICR's discoveries is that they are developed first and foremost for patient benefit. In addition, we seek to achieve a fair financial return as an outcome for any exploitation by commercial organisations of ICR discoveries. If a discovery such as a diagnostic or bio-marker can be used widely with little or no further development, it is made available freely or through non-exclusive licensing; exclusive licensing is limited to those discoveries, primarily new therapeutics, which require substantial further investment from an industrial partner to realise patient benefit.