Institution: Institute of Cancer Research (ICR)

Unit of Assessment: UOA1 Clinical Medicine

1. Unit context and structure, research and impact strategy

The ICR's Clinical Medicine submission incorporates the integrated translational and clinical research taking place in the Divisions of Genetics and Epidemiology, Molecular Pathology, Breast Cancer Research, Radiotherapy and Imaging, Cancer Therapeutics (which includes the Cancer Research UK (CRUK) Cancer Therapeutics Unit (CTU)) and Clinical Studies (which includes the CRUK Clinical Trials and Statistics Unit (ICR-CTSU)) and Drug Development Unit (DDU).

On the REF census date, the UOA consisted of 76 independent researchers and their associated research teams totalling 611 staff, including 98 postdoctoral researchers, 43 analytical scientists, 196 Scientific Officers/specialist technical staff and 138 postgraduate research students (including 30 clinical research fellows). UOA1 research is critically dependent on the co-location and longstanding partnership with the Royal Marsden NHS Foundation Trust (RM). 21 ICR Team Leaders, including 14 Professors, hold honorary consultant posts at RM and over 70 RM consultants hold ICR Honorary Faculty positions.

Research strategy

Our joint ICR/RM research strategy for the period 2016–2021 was published following organisation-wide consultation. Our long-term aim is to increase cure rates and improve survival with smarter, kinder treatments significantly reducing immediate and long-term side effects and enabling patients to live well with, and beyond, cancer.

The research returned to UOA1, predominantly aligns with Pillars 2 (innovative approaches) and 3 (smarter, kinder treatments) of our research strategy and includes:

- Discovering new treatments; including those designed to tackle drug resistance and cancer's ability to evolve.
- Designing clinical trials that will help anticipate cancer evolution and adapt treatments as drug resistance emerges.
- Developing more effective, convenient and cost-effective forms of radiotherapy with fewer side effects.
- Conducting trials to accelerate the development of innovative combination treatments, such as the use of targeted drugs together with immunotherapy or radiotherapy.
- Identifying genetic markers that predict how cancer will develop and how it will respond to treatment.
- Utilising predictions of treatment response to select optimal therapeutic approach for patients.
- Developing new imaging technologies to assess a tumour's behaviour and metabolism, and monitor response to treatment.

Pillar 1, our fundamental biological research investigating the genetic and cellular mechanisms that underlie and drive cancer development and progression, and the response and resistance to cancer treatment, is predominantly returned to UOA5. However, interdisciplinary research is integral to our approach to creating impact and there are numerous collaborations between UOA5 and UOA1 to translate discoveries into patient benefit (see Impact Case Studies). Our appraisal systems recognise and reward those contributing to our collaborative and team science values.

Achievement of strategic aims stated in REF 2014

In our REF 2014 UOA1 submission we said:

- *We would continue to focus on cancer genetics to identify people most at risk and epidemiology to increase understanding of how genetics, environmental and lifestyle factors interact.*

Achievements: We led international Genome-Wide Association Studies (GWAS) consortia identifying common variants influencing risk in various cancers, identified cancer susceptibility genes for prostate, colorectal, testicular and paediatric cancers (Eeles, Houlston, Turnbull, Kote-Jarai). In the Breast Cancer Now Generations Study, an ICR cohort study of over 100,000 women to investigate breast cancer aetiology (Swerdlow, M. Jones, Schoemaker), we quantified the raised risk in relation to recent childbirth and, reassuringly, found no raised risk of breast cancer in relation to night shift work—a highly prevalent exposure in the population that had been suggested as a serious public health concern. We (1) developed the CanGene-CanVar initiative, which will centralise data and create an interface between the NHS and research groups to underpin future expansions in genetic testing; (2) established BRCA-DIRECT, to streamline genetic testing services (Turnbull); (3) using capture Hi-C identified putative target genes at 33 breast cancer risk loci (Fletcher); and (4) carried out the first UK study to assess genetic screening for prostate cancer in the general population, paving the way for a much larger study, with 5,000 participants recruited from 70 general practices (Eeles).

- *We would expand our capacity in Molecular Pathology and open the National Institute for Health Research (NIHR) Centre for Molecular Pathology. Our immediate aim was to introduce targeted sequencing to introduce genome level tumour analyses into the clinic as rapidly as possible and at scale.*

Achievements: We opened the NIHR Centre for Molecular Pathology (see infrastructure). We established the Department of Data Science which works across all ICR Divisions to apply computational approaches, machine learning and artificial intelligence to address key questions in translational and clinical cancer research.

We developed a next-generation sequencing (NGS) panel for genetic testing in paediatric cancers to guide treatment decisions and this test is now integrated into standard NHS practice (Chesler). We also (1) defined gene signatures of translational relevance for risk stratification (Sadanandam, Kaiser); (2) designed and validated a molecular risk classifier for predicting response to tyrosine kinase inhibitors in sarcoma (Huang); (3) defined the frequency of genetic aberrations and their prognostic significance in paediatric sarcomas (Shipley); and (4) led on the genomic and epigenomic profiling of over 1,000 paediatric high-grade glioma and diffuse intrinsic pontine gliomas (DIPG) leading to the identification of new therapeutic targets (C. Jones).

- *Increase our emphasis on the discovery and development of biomarkers, including imaging biomarkers. We aimed to improve our capability to carryout pre-clinical imaging research by building the Centre for Cancer Imaging.*

Achievements: We discovered and developed biomarkers, for implementation in clinical practice: (1) the plasmaMATCH trial, which used liquid biopsy and circulating tumour DNA (ctDNA) to rapidly genotype patients with advanced breast cancer for therapeutic stratification and showed sufficient clinical validity for adoption into routine clinical practice (Bliss, Turner); (2) the TO-PARP phase II trial showed the clinical benefit of olaparib in homologous recombination-mutated prostate cancer (Hall, de Bono) leading to a practice-changing phase III trial, led by de Bono (see Impact Case Study); (3) the TNT phase III trial demonstrated an increased response to platinum chemotherapy in *BRCA*-mutated breast cancer (Bliss, Tutt (UOA5)); (4) we showed that mutation tracking in circulating tumour DNA provided early prediction of relapse in breast cancer (Turner).

We opened the £20M Centre for Cancer Imaging (see Infrastructure). We (1) evaluated and quantified magnetic resonance imaging (MRI) biomarkers in brain tumours and paediatric neuroblastomas (Robinson, Boult); (2) assessed treatment response using a novel semi-automatic technique from whole body diffusion-weighted MRI (DW-MRI) data (Blackledge); (3)

demonstrated that whole-body DW-MRI can be used for assessment of treatment response in myeloma (deSouza); (4) provided evidence to support the use of MR elastography in diagnosing and staging brain malignancies (Jamin, Robinson, Bamber, Boult); and (5) delivered the world's first treatment with acoustic cluster therapy, a technology in which microscopic clusters of bubbles and liquid droplets are used to enhance the delivery of chemotherapy drugs to tumours (Bamber, Banerji).

- *Our strategy for radiotherapy is to increasingly take account of developments in tumour biology and the incorporation of targeted systemic therapeutics as well as the underpinning physics. We aimed to focus on the: (1) management of intra-fraction organ motion; (2) development of MR-guided Therapeutic Ultrasound and Radiotherapy; and (3) advanced treatment planning.*

Achievements: A Magnetic Resonance Linear Accelerator (MR Linac) was funded by a £10M Medical Research Council (MRC) award from the Clinical Research Capabilities and Technology Initiative (Harrington, Oelfke, Dearnaley, Leach, Nutting (RM)). It combines an MRI scanner and a linear accelerator to precisely locate tumours, tailor the shape of X-ray beams in real-time, and accurately deliver doses of radiation to moving tumours—important for treating cancers which change position through breathing, bladder filling or bowel movement. This has the potential to reduce debilitating and distressing side effects due to normal tissue damage. The introduction of the MR Linac technology has been underpinned by advances in physics, engineering and computer science (Oelfke, Wetscherek, Blackledge).

In 2018, we treated the first patient in the UK using the MR Linac and since then over 1,000 treatments have been completed for more than 80 patients with prostate, bladder, rectal, gynaecological, breast, and head and neck cancers, and oligometastatic tumours in the pelvis and abdomen, as part of clinical research trials. We are a founding member (one of seven) of the international Elekta MR Linac Consortium and provide global leadership for three (prostate, breast, cervix cancer) of the nine tumour site groups that are initially being evaluated by the Consortium.

We led practice-changing radiotherapy trials including IMPORT LOW, CHHiP and FAST-Forward (Bliss, Yarnold, Dearnaley, Hall, Haviland; see Impact Case Studies). IMPORT LOW demonstrated clinical utility of partial breast radiotherapy in women with early breast cancer at low risk of local recurrence. CHHiP showed that, when treating prostate cancer, having a higher dose of radiation per fraction, across fewer sessions is as effective as conventional fractionation and reduced the level of side effects. FAST-Forward showed that for women with early stage breast cancer a one-week course of radiotherapy was as effective as the standard 3-week treatment schedule.

- *The pursuit of new and more effective therapies for cancer would continue to be a major aim with a focus on expansion of programmes in cancer heterogeneity and evolution with researchers in UOA5.*

Achievements: We developed innovative approaches to tackle difficult-to-drug targets by exploiting cereblon-mediated protein degradation (Collins); and developed computational drug discovery tools, canSAR and Probe Miner (Al-Lazikani, Antolin, Workman, see Open research environment). In collaboration with researchers in the Centre for Evolution and Cancer (UOA5) we exploited evolutionary steering to induce collateral drug sensitivity in cancer (Valeri, Banerji), and modelled clonal evolution to forecast time to treatment failure (Valeri, Cunningham (RM), Hubank (RM)).

During the REF 2021 period, the CTU discovered three new drug candidates and six ICR-discovered drugs entered clinical trials (target shown in brackets): CT900 (alpha folate receptor), CYC065 (CDK2/9), BAL3833 (panRAF), SRA737 (CHK1), BOS172722 (MPS1) and EP0042 (FLT3/Aurora). In total, since 2005 the CTU discovered 20 drug candidates with 11 entering clinical trials and one approved (abiraterone). We also discovered chemical probes and drug

candidates for CDK8/19 and the HSF1 pathway (Workman, Clarke); designed chemical probe targeting the bromodomains of BAZ2A and BAZ2B (Hoelder, Raynaud); and in collaboration with the Structural Genomics Consortium, discovered a series of potent KDM4 (JMJD2) and KDM5 (JARID1) histone lysine demethylase inhibitors (Bavetsias, van Montfort, Raynaud, Shipley).

The DDU led the first-in-human trial of capivasertib (AZD5363, AKT inhibitor) and showed that it was well-tolerated and achieved plasma levels and robust target modulation in tumours (Banerji). Capivasertib is based on a chemical series discovered jointly by the ICR (Collins, Workman) and Astex Pharmaceuticals and has now entered phase III trials in three therapeutic indications. We also showed proof-of-concept for both single-agent activity, and in multiple combinations, of capivasertib in breast and prostate cancers (Banerji, Turner, de Bono). We evaluated multiple immunoconjugates in clinical trials, targeting novel and more established targets but with agents carrying new payloads (Banerji, de Bono). We contributed to the practice-changing development of the first-in-class oncolytic viral immunotherapy leading to international regulatory approvals (talimogene laherparepvec (T-VEC), Harrington, see Impact Case Studies). As a result of the PALOMA-3 study palbociclib combined with fulvestrant is being used internationally to treat advanced oestrogen-receptor positive (ER+) breast cancer patients who had progression or relapse during previous endocrine therapy (Turner).

Research plans for the next period:
We are developing new cross-cutting Centres to provide a platform for interdisciplinary and team science collaboration between investigators, both internal and external to ICR/RM, to address key areas of the scientific strategy, without changing our Divisional structure:

- **Centre for Paediatric Oncology Experimental Medicine** (Chesler, Marshall (RM), Lancaster (RM), Hubank (RM)) aims to deliver novel treatments, diagnostic tests and clinical practice change to children with cancer within the context of hypothesis-driven and biomarker-enriched clinical trials, e.g. fadraciclib (CYC065) a drug discovery by ICR CTU in collaboration with Cyclacel.
- **Sarcoma Research Centre** (Huang, Robin Jones (RM), Shipley) combines the ICR and RM's significant strengths in sarcoma research and treatment. The centre connects these various teams to ensure a unified research strategy, promote interdisciplinary team science and facilitate the training of a new generation of clinicians and scientists skilled in translational sarcoma research.
- **Centre for Translational Immunotherapy** (Melcher) aims to enhance links between UOA1 and UOA5 teams working on the immunotherapeutic aspects of cancer research and expand the crosstalk between clinicians and scientists at the ICR and RM.
- **Radiation Research Centre of Excellence (RRC)** at ICR/RM (Harrington, Oelfke, Van As (RM)) is a programme of interlinked preclinical and clinical research themes with the direct aim of delivering translational clinical studies over the course of the next five years. The three major themes are: (1) molecular responses to radiation-induced DNA damage; (2) modulation of radiation-induced innate and adaptive immune responses; and (3) translational and clinical research.
- **Integrated Pathology Unit** (Salto-Tellez) at the ICR and RM aims to build the infrastructure and support for an integrated research laboratory that cuts across technologies and cancer types. Using digital pathology, morpho-molecular diagnostic approaches and artificial intelligence, this will enable key research questions to be addressed taking the clinical and diagnostic needs as the primary research focus.
- **Joint ICR/Imperial College London (Imperial) Cancer Epidemiology and Prevention Research Unit** (see Interdisciplinary research and responsiveness to national and international priorities).
- In the **Centre for Cancer Drug Discovery** (CCDD, see Infrastructure for supporting research and impact), the Centre for Evolution and Cancer (UOA5 researchers) and CTU will harness our understanding of tumour evolution to develop more effective treatment strategies for cancer therapeutics. The CTU will focus on four themes: (1) non-oncogene

addiction; (2) genomic instability; (3) tumour host-interaction, including immuno-oncology; and (4) cellular state and plasticity.

Strategy for impact

The ICR's aim is to ensure appropriate and effective exploitation and dissemination of research findings to maximise speed to patient benefit. Our key principle is to make an assessment of which route to impact would provide the maximum benefit to patients. Routes taken are as follows:

- In some instances, we decide patients will be better served by **making the discovery/technology widely available through publication** rather than commercialisation.
- **Develop our discoveries ourselves**. Our approach is to systematically take the findings of fundamental discovery research through the translational steps of preclinical validation, phase I proof-of-concept studies, liquid biopsy and molecular imaging-supported tumour-specific phase II trials, leading to large-scale network-adopted clinical trials.
- Set up commercial agreements that maximise ICR researchers' **freedom to operate** and ability to help multiple companies in the same field to increase the chances of success.
- **Work with the pharmaceutical industry** to take promising lead compounds through the various stages of development, approval and launch on to the market.
    - We aim to sign a **collaborative licence agreement** rather than simply "selling off" the programme. We find the most effective way of accelerating progress is for the ICR to continue laboratory research to identify markers of response, possible mechanisms of resistance and other indications where the drug might be effective —this research can be critical to the overall success of the drug programme.
    - **Monitor progress** even after the formal collaboration period ended to ensure that the impact is being realised. If the commercial partner discontinues development, we ensure that the results are returned to us so that we can seek other opportunities to exploit them.
    - Where the lead on commercialisation is being taken by another organisation, the above principles are enshrined in our agreement with them and they are obliged to ensure relevant terms are included in the commercial contracts.
- **License directly to a commercial partner** where this is likely to lead to faster product development, for greater patient benefit, and produces a greater commercial return to the ICR.
- Create a **spin-out company** where this is a better route, for example to commercialise a technology or to develop the concept further before commercial partners are willing to invest.
    - We founded Monte Rosa Therapeutics which specialises in targeted protein degradation. The company was formed in 2018 by Versant Ventures, the ICR and CRUK (Collins, Professor Raj Chopra, formerly the Director of CTU). An initial $32.5M of funding was announced when Monte Rosa Therapeutics launched publicly in 2020. Monte Rosa announced Series B financing in September 2020 ($96M) and Series C financing in March 2021 ($95M).

We also influence policy (see Engagement with stakeholders to develop impact).

Relationship to UOA1 Impact Case Studies

<u>Developing our discoveries ourselves, systematically taking the findings of discovery research through translational steps</u>

Biology researchers (Ashworth, Lord, Tutt (UOA5)) expanded the understanding of BRCA function and provided evidence of sensitisation to PARP inhibition in *BRCA*-mutated cells. This led to first phase I trial of olaparib (de Bono, UOA1) and demonstration of activity in breast, ovarian and prostate cancer patients. Olaparib is now being used to treat these and also pancreatic cancer patients across the world.

Developing our discoveries ourselves, through large-scale network-adopted clinical trials
Our clinical radiotherapy fractionation research in breast and prostate cancer resulted in shorter standard curative radiotherapy regimens being adopted internationally. This resulted in reduced side effects, less time off work, savings in travel time and costs and reduced treatment costs for healthcare systems—while maintaining very high levels of cancer control.

Working with the pharmaceutical industry and monitoring progress
ICR synthesised and clinically developed abiraterone and collaborated with industry to gain regulatory approval. The original commercial partner discontinued development, but abiraterone was returned to ICR allowing a new partner to be identified and this drug is now transforming the lives of men with prostate cancer worldwide.

Open research environment
We are committed to making our research available for the largest possible audience for the benefit of patients and provide significant institutional support to ensure a high level of open access publishing. We are working towards compliance with the Concordat on Open Research Data. We provide public access to many of our unique tools and resources. Specific UOA1 examples are:

- canSAR, the ICR "knowledgebase", which brings together and integrates data across biology, chemistry, pharmacology, structural biology, cellular networks, clinical annotations and more (Al-Lazikani, Workman, Antolin).
- Open source drug discovery project, collaborating with researchers at Universities of North Carolina and Oxford, and the Chordoma and Mark Foundations, to discover compounds targeting brachyury in chordoma (Workman).
- Making available a new series of compounds that could form the basis for drugs that target the childhood brain cancer DIPG through M4K pharma, an open access consortium of researchers dedicated to finding new treatments for rare diseases (Hoelder, C. Jones with the Structural Genomics Consortium).
- As a member of the European Paediatric Soft tissue sarcoma Study Group (EpSSG), we are establishing a database containing information from clinical trials on children with rhabdomyosarcoma from around the world and making that clinical data available to investigators for data mining studies (Shipley).
- Contributing mouse models of paediatric cancers to a European consortium, Innovative Therapies for Children with Cancer Paediatric Preclinical Proof-of-concept Platform (ITCC-P4), which aims to establish fully characterised patient-derived preclinical models of high-risk paediatric solid tumours and to build a sustainable comprehensive platform to use these models for drug testing (Chesler, Shipley).
- Locus Explorer, open source GWAS data plotting tool, which produces an interactive graphical illustration of genetic associations and their biological context (Eeles).

Research integrity
We are committed to maintaining the highest standards of research ethics and integrity. In 2017, we conducted a full review and update of the ICR's **Good Research Practice Guidelines**. Three open discussion sessions were held, each led by a senior academic, on (1) publication and authorship; (2) robustness and reproducibility; and (3) openness. All three sessions featured substantial research-integrity content and their outcomes fed into revision of the Guidelines, which were approved and disseminated in early 2018.

We completed the implementation of **FreezerPro, a Human Tissue Act compliant system**, adopted by the ICR/RM as the centralised database for sample and tissue information management in a joint project to ensure data quality and traceability of human samples.

A significant barrier to biomedical research and drug discovery is the widespread use of poorly selective, or otherwise flawed, chemical probes. The Chemical Probes Portal (£1.5M Wellcome Trust Biomedical Resources grant, Workman, Al-Lazikani, Antolin) is a public online resource created to provide biomedical researchers with an expert-curated resource to identify the most

appropriate chemical probes for their experiments. Together the **Chemical Probes Portal** and **Probe Miner** (Antolin, Al-Lazikani, Workman) aim to reduce the use of poor quality probes, promote best practice and increase the quality and reproducibility of scientific research.

2. People

Staffing strategy

There is no fixed number of teams in Scientific Divisions; Team Leaders are recruited to support the aims of the research strategy. Where we wish to cement collaborative working we make joint appointments. We offer fractional contracts to grow expertise in particular areas or support clinical academic career development. A key part of our strategy to create impact is to recruit Team Leaders who have experience of working in industry (10 Team Leaders in this UOA).

We maintain a healthy and sustainable demographic: in July 2020 our REF-eligible staff fell into the following age bands: 26–40 (14.5%), 40–50 (39.5%), 50–60 (27.6%), >60 (18.4%). 100% of eligible staff totalling 70.2 FTE have been submitted. This comprises 69.8% on Team Leader contracts and 30.2% on research-only contracts.

We have a bespoke pay policy which enabled the recruitment of senior scientists from the UK and abroad and to attract the most promising early career researchers (ECRs). We have a strong track record of "growing our own" clinician scientists, identifying talented clinicians in training and supporting them successively through NIHR Academic Clinical Fellowships (ACF), Clinical Training Fellowships, NIHR Academic Clinical Lecturer (ACL) posts and into Clinician Scientists Fellowships or Clinical Career Development Faculty (CDF) positions. ICR funded ACL posts in addition to those provided by our NIHR allocation so that more clinicians can stay research active after their PhD.

Those involved in the review of outputs had training covering overview of the REF, responsible use of citation analysis, unconscious bias in the assessment of research outputs, and other relevant equality issues. Choices of outputs for submission will not be used in relation to the promotion or career progression of individuals.

Recruitment and career progression of Team Leaders

Over the period of assessment we recruited six tenure track Team Leaders and 11 Team Leaders at the tenured, Reader or Professorial level from external organisations.

Name	Recruited from	Research area
Cancer Therapeutics		
Dr Gurdip Bhalay	Charles River Early Discovery	Design and synthesis of safe and effective drugs for the treatment of cancer.
Dr Astero Klampatsa	University of Pennsylvania	Cellular mechanisms of T cell immune response; development of novel CAR T cell therapies.
Dr Gary Newton	Domainex	Covalent and allosteric medicinal chemistry approaches for chemical probes and generating lead compounds.
Professor Terry Rabbitts FRS	MRC Weatherall Institute of Molecular Medicine, University of Oxford	Impact of chromosomal translocations on proliferation and differentiation of cancer initiating cells; establishing technologies to target intracelluar proteins, particularly protein-protein interactions, using antibody fragments.
Dr Olivia Rossanese	Vanderbilt University (previously GSK)	Developing assays to support the drug discovery process and investigating the underlying biology of cancer targets and the response to targeted therapeutics.

Dr Igor Vivanco	Memorial Sloan Kettering Cancer Centre, New York	Interplay between metabolism and cancer cell signalling and identifying therapies that target these interactions.
Dr Anderson Wang	AstraZeneca	Functional characterisation of DNA damage response deficiencies in cancer cells.
Clinical Studies		
Dr Maggie Cheang	University of North Carolina	Development of genomics classifiers for tumour subtypes for clinical utility.
Professor Christina Yap	University of Birmingham	Design and development of innovative and efficient clinical trial designs and analysis.
Genetics and Epidemiology		
Professor Clare Turnbull	Genomics England (Queen Mary, University of London)	Application of molecular, statistical and epidemiologic approaches to identify and characterise genomic factors related to cancer susceptibility.
Molecular Pathology		
Dr Alejandra Bruna	CRUK Cambridge Institute	Modelling cancer evolutionary processes in paediatric brain cancers, with a focus on epigenetic dynamics.
Professor Manuel Salto-Tellez	Queen's University Belfast	Molecular and digital pathology, and cancer biomarker development.
Radiotherapy and Imaging		
Professor Nick James	University of Birmingham	Evaluating new treatment approaches in bladder and prostate cancers via large multi-centre clinical trials.
Professor Alan Melcher	University of Leeds	Activation of the immune system to recognise and attack cancer using therapeutic viruses.
Professor James O'Connor	University of Manchester	Oxygen-enhanced MRI biomarkers to guide precision medicine strategies in early phase clinical trials.
Dr Erik Wennerberg	Weill Cornell Medicine New York	Development of mouse models that accurately mimic the molecular events triggered by radiotherapy in humans; and leveraging these models to identify the molecular mechanisms involved.
Dr Andreas Wetscherek	German Cancer Research Centre (DKFZ, Heidelberg)	Development of new magnetic resonance imaging techniques for radiotherapy.

We have supported researcher career development internally through ACLs and through external fellowships. **Dr Magnus Dillon** gained a PhD from the ICR in 2018 and went on to undertake an ICR ACL. **Dr Julia Cockle** is completing an ACL in paediatric cancers. **Dr Adam Sharp** joined ICR as an ACL and then won a MRC Clinical Research Training Fellowship. He was awarded a Wellcome Trust Clinician Scientist Fellowship starting in September 2020 to study translational biology in prostate cancer. **Dr Amit Sud** completed a CRUK-funded PhD at ICR and is now an ACL. Sud's main research interest is in genetic susceptibility to haematological malignancy and the long-term side effects of cancer therapies. **Dr Charlotte Pawlyn** completed a PhD and ACL at ICR; she now holds a CRUK Clinician Scientist Fellowship to identify and target the mechanism of acquired resistance in multiple myeloma. **Dr Martin Kaiser** was awarded a Jacquelin Forbes-Nixon Research Fellowship in 2018. Under the fellowship, he will undertake a programme of work to identify and characterise the genetic changes responsible for the progression of myeloma and why it becomes resistant to treatment.

Departures
During the assessment period the following CDFs moved to more senior roles at other research organisations: **Dr Gerhardt Attard,** John Black Charitable Foundation Endowed Chair in Urological Cancer Research, University College London (UCL) Cancer Institute,; **Dr Bronwyen Shaw**, Scientific Director and Professor of Medicine, Medical College of Wisconsin; and **Dr Tim Yap**, Medical Director, The Institute for Applied Cancer Sciences and Associate Professor, University of Texas MD Anderson Cancer Centre.

Senior researchers recruited to leadership positions elsewhere include: **Professor Julian Blagg**, VP Drug Discovery, Azeria Therapeutics; **Dr Faith Davies**, Director of the Clinical Myeloma Program, Perlmutter Cancer Center, New York University; **Professor Gareth Morgan**, Director of the Myeloma Institute, Deputy Director of the Winthrop P. Rockefeller Cancer Institute, and Professor of Hematology at the University of Arkansas for Medical Sciences; **Dr Michelle Garrett**, Professor of Cancer Therapeutics, University of Kent; **Professor Caroline Springer**, Director of the Drug Discovery Unit, Manchester Cancer Centre; and **Dr Arthur Zelent**, Sylvester Comprehensive Cancer Center, University of Miami School of Medicine.

Staff development
The ICR has been awarded the HR Excellence in Research award from the European Commission since 2010 for its ongoing work in supporting researcher career development is defined by the Researcher Development Concordat. The ICR provides a comprehensive framework to support the development of researchers of all levels including Team Leaders, postdoctoral researchers, scientific officers and students.

We have a particular focus on the following areas:

<u>Supporting transition from PhD to postdoctoral researcher and postdoctoral researcher to independent researcher</u>
The Pathway to Independence; Developing Future Scientific Leaders, an innovative residential programme, was developed through collaboration between the ICR, the Biotechnology and Biological Sciences Research Council (BBSRC) and the Wellcome Trust Sanger Institute. The programme supports outstanding postdoctoral researchers at the point in their career when they are seeking their first independent research position.

We surveyed our postdoctoral researchers who left ICR between 2009–2018: 93% of these alumni are in research, science or education-related roles with over 15% achieving independent academic roles including: Birgit Wilding (Boehringer Ingelheim, Austria); Zoe Walters (University of Southampton); Cihan Yandim (İzmir University of Economics, Turkey); Maria Vinci (Bambino Gesù Children's Hospital, Italy); Stephanie Myers (University of Sunderland); Mark McLaughlin (Manchester Metropolian University); Mark Honey (University of Wolverhampton); and Alan Jones (University of Birmingham).

<u>Supporting clinical academics and building capacity locally and nationally</u>
- The ICR and RM partnership is the UK's largest training centre for oncology, with 30% of all consultant medical oncologists in the UK receiving training from the RM and/or the ICR at registrar, doctoral or post-doctoral level.
- Pre-PhD, our MSc in Oncology trains medically qualified candidates from across the UK and approximately 50% of the UK's clinical oncologists.
- We established a Molecular Pathology Starter Programme, a six-month out-of-programme research experience for UK histopathology trainees. To date, nine histopathologists have been trained with two progressing to ICR PhD studentships. One of these students, Dr Matt Clarke, won a Gold Medal in the Royal College of Pathologists Trainee Research Medal Awards for his PhD research.
- We are part of the Pan London Collaborative Research Fellowship Programme which is aimed at clinicians, allied health professionals (AHPs) and clinical research practitioners wishing to obtain pre-doctoral research experience. Since its inception in 2016, ICR/RM

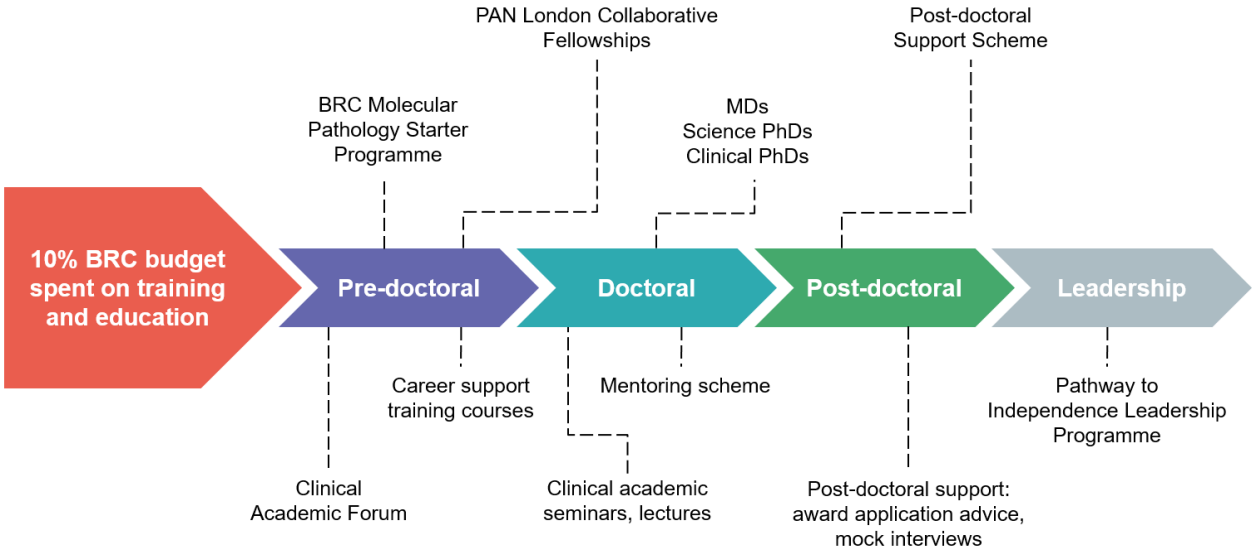
has hosted nine fellows and been a collaborator in seven other projects. One of these fellows was awarded an ICR PhD studentship in radiomics.

10% of the RM and ICR NIHR Biomedical Research Centre (BRC) budget is spent on training with the aim of supporting clinicians and AHPs at key transition points along their academic career (see Figure 1). We have a strong development programme for clinical researchers, which is significantly shaped by their input.

Activities include:

- Delivered every other autumn, the "Meet the Funders" programme provides clinical researchers with an understanding of the funding landscape and the fellowship opportunities available to them.
- The Clinical Academic Forum—a network for ICR/RM clinical academics of all career stages promoting discussion on current challenges and career ambitions.
- Bridge funding to help make the transition from research degree to clinician scientist. Since the scheme began in 2017, we have funded six fellows e.g. Dr Anna Wilkins, ICR PhD 2019, was awarded a competitive one-year postdoctoral clinical fellowship at the Francis Crick Institute (Crick) followed by BRC bridge-funding. She is now a CRUK RadNet Clinician Scientist at ICR and co-PI on a CRUK-funded clinical trial (£1.5M).
- Mentoring from senior clinical academics to support the transitions between clinical training and research.
- Post-PhD, the ICR/RM lead the competitive residential programme: "Pathway to Independence: clinical academics in cancer research". This biennial programme provides intensive coaching to prepare for academic independence and applications for clinician scientist awards. It has been attended by 52 participants nationally since its launch in 2016. 50% of all 2016 participants now hold clinician scientist fellowships, clinical lectureships or principal investigator awards.

Figure 1: BRC career support and interventions across the clinical academic career pathway



Research students

Over the REF period, 196 research students were awarded their research doctorate degree within UOA1. This includes MD(Res) students as well clinically-qualified and science PhD students. Between 2013 and 2020, competitively won studentships were obtained from European Commission, Research Councils, including an MRC industrial CASE (iCASE) programme in Enabling Integrated Drug Discovery and UK-based medical charities including CRUK and Sarcoma UK. The ICR self-funds studentships and has taken strategic decisions to fund all science students for four years to allow sufficient time to complete high-quality research projects and skills training, and 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. The ICR won funding for a Clinical PhD Programme in Cancer Research from the Wellcome Trust (2017, five intake years) and a joint CRUK Clinical Academic Training Programme with Imperial College London (2019, five intake years) which includes funding for both clinical training fellowships and an intercalated MBPhD programme.

The Academic Dean's Team, under the leadership of the Academic Dean (Professor Clare Isacke FMedSci) is responsible for the management of all education and training activities and ensuring that all students receive appropriate supervision, have adequate resources at their disposal during their time at the ICR and keeping a regular check on student welfare. All supervisors undertake training in Effective Research Degree Supervision and attend refresher training every five years. The ICR Registry supports all aspects of the ICR's research degree programmes. Student progression is tracked via a bespoke online iProgress platform and the supervisory team have access to this. After one year, PhD students submit transfer reports detailing their progress and outlining future plans. An internal assessor, who is outside of the project, provides feedback on work achieved so far and plans for the future, and evaluates training needs. All students submit a report after two and half years highlighting progress and project risks, which is also independently assessed internally.

Research students, who come from a wide variety of subject and educational backgrounds, 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 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.

All students participate in mandatory Research Integrity training, which examines the issues and practicalities involved in ensuring their research meets the highest ethical standards.

In the Postgraduate Research Experience Survey (PRES) 2019, Advance HE's sector-wide survey, the ICR came top nationally (out of 103) for overall student satisfaction rates for research degree experience and research culture, with a score of 92% (55% response rate). The ICR also performed strongly in other categories including professional development, research skills, supervision and resources. The ICR uses this survey to work with the Student Committee to continue to enhance the learning experience and student support at the ICR.

Our goal is to develop future research leaders and to support their careers after their PhD. ICR offers a "Succeeding in Academia" programme, delivered by ICR Team Leaders and including support for fellowship applications, panel interviews and leadership skills.

Our student alumni can access career support for up to three years after graduating, and we hold regular career development workshops and events as well as alumni networking events, to maintain engagement of the community with ICR.

Over the full REF period, 88% of non-clinical students moved into science-based roles in academia or industry as a first destination post-graduation, and 65% of students stayed in science-based roles three years post-graduation.

A 2018 survey of ICR clinical alumni (PhD and MD(Res)) who completed their studies between 1983 and 2017 showed that 98% of clinicians who studied at the ICR were research active in their first role following speciality training with 38% of PhD respondents involved in laboratory-based biomedical research in their current roles. For example, Joaquin Mateo completed his MRC and Prostate Cancer UK supported PhD in 2016 and received a Prostate Cancer Foundation Young Investigator Award to support postdoctoral work. In 2017, he joined the Vall d'Hebron Institute of Oncology (VHIO), Barcelona as Principal Investigator of their newly established Prostate Cancer Translational Research Group.

Equality and diversity
Ensuring an equal, diverse and inclusive culture is of institutional importance for the ICR.

The Equality Steering Group oversees all our equality programmes and ensures that they are integrated, and aligned with the ICR's other strategies:

- Athena Swan Steering Group (co-chaired by the Chief Executive Officer, Professor Paul Workman FRS and Professor Christina Yap). The ICR renewed its Athena Swan Charter Silver Award in 2019; we apply as a Research Institute and do not hold separate departmental-level awards.
- BAME: Beyond the Statements Project Board.

We have three equality networks, all run in collaboration with the RM, to strengthen links between the two institutions: The BAME Forum, The LGBT+ Network and the Network for staff and students with disabilities and health conditions. These groups work with the ICR and RM to develop a welcoming and inclusive culture for all.

The Women in Science Network supports women to reach their potential and to help address the inequality in the number of women in the most senior research leadership roles. Topics explored include supporting high-performance teams, influencing skills, personal brand, leadership, and mentoring. We take career breaks/other circumstances into account in recruitment and promotion and "stopping the tenure clock" for those who take career breaks.

Since REF 2014, we initiated a range of actions including extensive career development training, leadership programmes for all staff groups, mentoring programmes, flexible working options and improved support for new parents and those with families. Since 2016, we recognise NHS service when calculating maternity, adoption and shared parental leave entitlement to support clinical academics. Maternity return rates improved from 76% (2012–2015) to 94% in 2015/16–2017/18, reflecting the impact of our expanded support for parents. However, as with other institutions nationally and internationally, there is a loss of female clinical academics post-PhD.

In a 2018 ICR survey of clinical alumni, female respondents reported greater difficulties in remaining research active. Whilst both female and male respondents stated that greater job security in academic roles would enable them to be research active, female respondents also prioritised greater support for career breaks and flexible working, and greater visibility of senior clinical academic role models.

We subsequently put support mechanisms in place to address these issues such as the post-PhD funding options, and mentoring and support for career transitions (see above). Prior to 2015, women comprised 33–40% of ICR clinical postdoctoral researchers, compared to 60% of clinical PhD students. Following the implementation of our action plan, the gender balance of clinical postdoctoral researchers is now in line with the clinical PhD cohort—67% female in 2018, 60% female in 2020—and two females and two males have progressed to become Team Leaders.

3. Income, infrastructure and facilities

Income
UOA1 received £352.1M of external research income over the REF period (£50.3M mean average p.a.), including £190.6M from UK-based charities, £17.1M from Research Councils, £63.8M from UK Government and Health Research funding bodies, £34.8M from UK industry and other UK sources, £20.8M from EU sources and £25.0M from non-EU sources.

Strategies for generating research income
Our research is predominantly funded by the cancer-focussed charities, NIHR and industry.

In addition to our major infrastructure awards (see below), there is very significant funding from CRUK for the CRUK CTU (>£42M over five years) and the CRUK ICR-CTSU (£8M over five years), from Breast Cancer Now for the Generations Study (five-year renewal in 2014 for

£5.47M and four-year renewal in 2019 for £2.38M), from the Prostate Cancer UK and Movember charities for our UK Centre of Excellence (£5.2M) and from Myeloma UK (renewed in 2015 £5.4M, and 2020 for £2M).

Many Team Leaders have had programmatic funding in the REF period: ERC Advanced Grant (Eeles), CRUK programmatic funding (Al-Lazikani, Chesler, Eeles, Hall, Harris, Harrington, Houlston, Huang, Melcher, C. Jones, Oelfke, Robinson, Turner, Turnbull, Valeri, Vivanco), Wellcome Trust Collaborative Award in Science (Houlston), and NIHR Professorship (Banerji).

For details of funding to support collaborative working, see collaborations, networks and partnerships below.

Major benefits in-kind
Substantial research income in-kind (£77.93M total, £11.13M p.a. mean average) has been received from the NIHR over the review period. This comprises £72.41M associated with the NIHR BRC at the RM, £3.89M associated with the NIHR Clinical Research Facility and £1.62M associated with the ICR/RM Experimental Cancer Medicine Centre (ECMC).

The Structural Biology Division is awarded data collection time for macromolecular crystallography and small-angle X-ray scattering experiments at the Diamond Light Source in Didcot, UK, and the European Synchrotron Radiation Facility (ESRF) in Grenoble, France. These facilities provide state-of-the art X-ray beam lines specific for the investigation of macromolecular complexes. Moreover, the Division is awarded electron microscopy data collection time at the Electron Bio-Imaging Centre (eBIC) at the Diamond Light Source, equipped with four Titan Krios microscopes. Researchers in UOA1, led by van Montfort, received access time equivalent to £1.04M at Diamond and £79k at the ESRF.

Through close partnership working with industry on translational research, the ICR has received, in addition to direct collaborative research funding, further in-kind income over the review period (reported to HESA via the HEBCI survey). Examples include specialist software from Elekta for use on the MR Linac platform (£100k) and provision of a diagnostic ultrasound system from Canon (£128k), associated with an MRC Developmental Pathway Funding Scheme (DPFS) award.

We close the gap between the dual support of peer-reviewed charity funding for direct research costs and the Research England funding streams on the one hand and the full economic costs on the other through fundraising/development activities and intellectual property (IP) income. In our ICR Operational Strategy we have four programmes to increase income, through fundraising, IP, commercial activities and improved cost recovery.

Infrastructure for supporting research and impact
The ICR and RM are co-located on two sites, Chelsea and Sutton. The NIHR competitively-awarded BRC, was successfully renewed for a third time in 2017 (£43M). This major benefit in-kind, together with that derived from being a CRUK Centre (renewed 2016, £16.1M) and an Experimental Cancer Medicine Centre, (renewed following quinquennial review in 2017 for £2.56M), enables us to support an infrastructure in which we systematically take the findings of fundamental cancer research, cancer drug discovery and radiotherapy and physics through translational steps of tumour profiling, molecular pathology diagnostics, predictive and pharmacodynamics biomarkers into phase I proof-of-concept studies and molecular imaging supported tumour specific phase II clinical trials. Transition into large-scale network-adopted clinical trials is facilitated by the CRUK-funded, National Cancer Research Institute (NCRI)-accredited, ICR-CTSU, which has particular expertise in radiotherapy, breast, and urology trials. The CTU is equipped with compound libraries and high-throughput compound screening facilities to support our drug discovery research.

We have opened **two new buildings** since 2013:

The joint ICR and RM **NIHR Centre for Molecular Pathology** (CMP) is an example of collaborative use of infrastructure (£18.2M). The CMP co-locates clinicians, pathologists, geneticists and other scientists, a Clinical Genomics Research and Diagnostics laboratory, a translational immuno-oncology laboratory and a dedicated biobanking facility:

- The BRC Generic Biobank is a stand-alone, ethically approved sample resource which includes plasma collected for ctDNA analysis; it has been pivotal to the delivery of a number of key national programmes, e.g. 100,000 Genomes Project, and is available to researchers for both discovery and translational studies.
- The CMP Clinical Genomics laboratory (Hubank (RM)) is accelerating the implementation of research into routine clinical practice by accurate profiling of solid tumours and haematological malignancies to direct treatment strategies and is the first NHS laboratory to introduce NovaSeq 6000 for high-throughput sequencing.

The **Centre for Cancer Imaging building** (CCI) has enabled us to co-locate pre-clinical and clinical imaging research and provide totally new animal facilities for the Sutton site (£20M).

- The CCI utilises multi-modality imaging, combining different imaging techniques such as MRI and ultrasound.
- An institutional capital funding award from the Engineering and Physical Sciences Research Council (£622k, Bamber, Oelfke) supported the purchase of multispectral optoacoustic tomography (MSOT) equipment for 3D mouse spectral imaging and a small animal radiation research platform (SARRP) for delivering clinically-equivalent, conformal radiotherapy to mice for the CCI. This technology enabled MSOT images to be registered to various types of conventional ultrasound images, and researchers have shown that level of blood oxygenation determined by MSOT imaging immediately before and shortly after treatment is a good predictor of tumour response to radiotherapy.

NIHR Imaging Clinical Research Facility (CRF)

The RM/ICR CRF (£2.5M) facilitates around 1,000 patient visits for MRI or PET/CT imaging across approximately 150 clinical trials in a wide range of cancer types. The facility currently has three 1.5T and two 3.0T MRI scanners, four dual-energy multi-channel CTs and four PET-CT scanners with on-site cyclotron. Over the next year, capability and capacity will be increased with the introduction of two additional MRI scanners. The imaging research team has already installed XNAT, a platform that serves as the core data hub for radiomics and machine learning pipelines, in addition to enabling safe data sharing and hosts imaging data from more than 40 clinical trials within a robust governance framework. The development programme includes harmonisation of anonymisation methodology across sites, a web-based image viewer, integration of advanced segmentation tools, support for new data formats, digital pathology viewing capabilities, as well as future data integration to support analytics.

Clinical Trial Units

Our three clinical trial units combine to provide a complete infrastructure for the leadership and management of phase I-III trials in all tumour types.

The RM has wards dedicated to the treatment of patients in clinical trials. The Oak Ward provides inpatient facilities for patients participating in first-in-human trials and the West Wing provides outpatient treatment facilities for early to late phase trials.

(1) The ICR investigator initiated phase I trials team within the joint DDU specialises in first-in-human trials with a portfolio of over 75 trials open at any one time. They review approximately 600 patients and recruit over 300 patients to these trials each year, making it one of the largest of its kind in the world. The DDU takes three to four novel drugs forward to later stage trials every year, including those discovered at the ICR. We have on-site laboratories for drug metabolism and pharmacokinetics, clinical pharmacodynamic biomarkers and cancer biomarkers.
(2) The UK Clinical Research Collaboration-accredited RM Clinical Trials Unit (RM-CTU) provides oncology specialist trial managers, statisticians and data programmers to

manage investigator initiated trials in all aspects of cancer treatment and diagnosis, across all tumour types within the RM. There is a particular emphasis on early phase studies including radiotherapy/immunotherapy combination studies and cancers of unmet need.

(3) The NCRI-accredited CRUK-funded ICR-CTSU provides national leadership of phase II and phase III trials of new treatments and technologies (including radiotherapy), particularly in breast, urological and head and neck cancers. The ICR-CTSU enables the advancement of research into clinical practice by pulling through early phase trials to later phase trials.

Core Research Facilities

There has been a major shift, since REF 2014, to maximise investment in equipment and staff to provide high-quality facilities and technical support through the formation of a new Core Research Facilities unit operating across both sites. ICR invested over £10M in addition to funding from the CRUK Centre Core Grant and Major Centre grants in microscopy, proteomics, metabolomics, structural biology, genomics and bioinformatics and £5M in equipment for the CCDD. We are developing a comprehensive inventory to promote sharing of equipment, reagents and services. We have committed £4M for a major upgrade of animal facilities in Chelsea and £1.6M for lab refurbishment over the next 12 months.

- The **Genomics Core Facility** (formerly the Tumour Profiling Unit) provides access to a range of cutting-edge techniques for genomic, transcriptomic and epigenomic analysis. It was the first in the UK to deploy the NovaSeq 6000 sequencer, through a collaboration with Illumina.
- The **Core Bioinformatics Facility** is an experienced group of bioinformaticians who support teams that do not have their own bioinformatics capability. They ensure quality and consistency in data analysis, maximising the value of profiling data and ensuring they can be easily integrated through the Knowledge Hub, the ICR's Big Data platform.
- Secure data storage, which is provided by our resilient and rapid access six-petabyte **Research Data Storage** infrastructure. This is managed by the Scientific Computing team who further enable research through the High-Performance Computing (HPC) cluster, and through scientific software support and training. Over the REF period, the ICR invested in its HPC and Research Data Storage (RDS) services, including the recent completion of a full infrastructure refresh (£500k capital investment for HPC, £3M for RDS). This recognises the increased demand for machine learning infrastructure supports new research capabilities in areas such as digital pathology and provides a new hybrid on premise/cloud capability as part of ICR's Unlimited Computing strategy.
- The newly established **translational immuno-oncology laboratory** uses advanced imaging techniques and artificial intelligence to determine the impact of the immune system on patient outcomes and identify new biomarkers for optimal treatment.
- Our **microscopy facilities** have the instrumentation and expert staff to support a wide range of applications, including time-lapse and super-resolution microscopy. In addition to widefield and confocal microscopy, the facility offers access and training on cutting edge spinning disk and lattice light sheet microscopes in collaboration with the manufacturer 3i.
- The **flow cytometry facilities** benefitted from recent investment to enhance state-of-the-art multiparameter flow analysis for our growing cancer immunology community on both sites. Cell sorting is offered as a service and covers a wide range of needs in both fundamental and clinical research.
- The **joint ICR/RM Mechanical Workshop** provides design and manufacture of both clinical and research from intricate, high precision items to medium-heavy engineering projects. Staff are skilled in electro-mechanical instrumentation, computer design software, medical gas, pneumatic, hydraulic and high vacuum systems, with access to a wide range of precision equipment and 3D printing.
- **Laboratory Support Services** provide first-line support to scientists including the collection of dirty glassware, wash up and sterilisation, biohazard waste collection,

sterilisation and disposal, specialist sterilisation, pure water supply and media preparations.

The **ICR Library** provides access to over 12,500 journals, with the majority online and the remainder through inter-library loan and publisher downloads. It also provides access to information, guidance on research data management and expertise to assist and train users in making use of the most suitable information available. The Academic Systems team manage the ICR's publication management system, Symplectic, which maintains a record of ICR-authored publications, and the ICR's outputs repository, which provides free public open access to a range of ICR-authored outputs.

Future infrastructure plans

The ICR secured a £30M grant from the UK Research Partnership Investment Fund (UKRPIF) scheme towards the costs of building a drug discovery facility, the **£70M Centre for Cancer Drug Discovery**. The CCDD, opened in November 2020, brings together over 300 biologists, medicinal chemists, pharmacologists, clinicians, data scientists and evolutionary scientists under one roof. The 7,325m^2 facility includes cutting-edge biology, chemistry and computational laboratories, meeting rooms and collaboration hubs to foster cross-disciplinary working and creativity.

RM Oak Cancer Centre will be a new **£70M facility bringing together over 400 researchers** currently dispersed across the Sutton site, with spaces designed to encourage communication across different tumour specialties to help speed up the development of new treatments. The new facility will include a Rapid Diagnostics Centre and is expected to open in 2022.

The CCDD and Oak Cancer Centre form the cornerstone of the plans for the **London Cancer Hub, a world-class cancer research campus** and a major boost to the UK's life-science industry and economy as a whole. The Hub can provide up to 100,000m^2 of new space for private enterprises to share the Sutton site and could ultimately create 13,000 jobs and contribute £1.2B to the UK economy annually.

The joint ICR and Imperial Convergence Science Centre is an example of **collaborative use of infrastructure.** There is dedicated space on the Imperial campus to support joint working both through meeting and laboratory space.

4. Collaboration and contribution to the research base, economy and society

RM Partnership

The ICR and RM have worked together in partnership for more than a century, and our bench-to-bedside-and-back relationship is crucial to conducting research for patient benefit. During the REF period, we reviewed the ways in which we work together and signed a new Joint Working Arrangement.

We revised our **Honorary Faculty appointment** process through which RM staff have a formal academic affiliation with the ICR. Full Honorary Faculty status is equivalent to ICR non-time limited (NTL) Faculty. In 2015, we introduced a new level of appointment: Associate Honorary Faculty to better support those at the early stages of developing their research. As of the 31st July 2020 there are over 70 Honorary Faculty and Associate Honorary Faculty, all playing a key role in our vibrant research ecosystem and in the majority aligned with our translational and clinical research. There are 12 full Professors (Cunningham, Dowsett, Johnston, Robin Jones, Koh, Larkin, Nicol, Nutting, Padhani, Paleri, Parker, Popat) and 17 Readers (Banerjee, Bhide, Brown, Chau, Fotiadis, Hayes, Hubank, Khoo, McNair, Messiou, O'Brien, Ring, Rusby, Starling, Thway, Turajlic, Van As).

We established:

- Joint Research Operational, Strategy and Executive Groups and a RM/ICR BRC Steering Committee to award project funding, and systematically review progress towards aims.
- BRC Theme Working Groups, combing basic, translational and clinical researchers to facilitate new internal (RM/ICR) and external collaborations. Each reports into the BRC Steering Committee and is supported by a senior operational manager.

National Partnerships
To deliver on our research strategy, we are also building upon many other existing research partnerships.

Our collaboration with the **UK ECMC Adult and Paediatric Network** is vital for conducting early phase trials in a multi-centre setting to inform and accelerate later phase studies and enable rapid recruitment of patients with rare cancers. This partnership is especially important in identifying promising novel agents already in use in the adult arena, which may be applicable to the paediatric setting, offering the teenage/young adult population the best options from both the adult and paediatric drug development programmes.

CRUK launched an **Accelerator Award** scheme in 2015 to enable a collaborative approach to develop tools and share resources. In 2017, CRUK formed a partnership with Associazione Italiana per la Ricerca sul Cancro (AIRC) and Fundación Científica de la Asociacion Española Contra el Cáncer (FC AECC), opening the scheme up to Italian and Spanish researchers in addition to the UK-based teams. To date 21 CRUK Accelerator projects received awards up to £5M, and the ICR is involved in the following 10.

We lead:
(1) The **Advanced Radiotherapy Network (ART-NET)** in collaboration with UCL, Oxford, Manchester and Leeds through which we are developing, assessing and implementing advanced radiotherapy technologies based on stereotactic ablative radiotherapy, magnetic-resonance image-guided radiotherapy (MR Linac) and proton-beam therapy.
(2) The **Improving Neoadjuvant Therapy in High-Risk Sarcoma network** in collaboration with Glasgow, Edinburgh, Birmingham, Milan and Seville, which aims to deliver datasets, data mining tools and patient-derived models that will drive the development of a stratified medicine approach for personalised therapy in sarcoma.

We are involved in:
(3) The Crick-led Accelerator funding for Clinical Research Training Fellows.
(4) The UCL-led Accelerator catalysing progress in cancer immunotherapy network.
(5) The Belfast-led national digital pathological and image analysis platform for solid tumours.
(6) The Leicester-led project to accelerate drug discovery through a networked structural biology resource.
(7) The Edinburgh-led project to accelerate functional studies in brain tumour research.
(8) The Milan-led Accelerator in single-cell cancer evolution in the clinic.
(9) The UCL-led NCITA: National Cancer Imaging Translational Accelerator.
(10) The Imperial-led project to accelerate the ability to understand and target complexity and heterogeneity in cancer through automated imaging of 3D cancer.

Following on from the success of ART-NET, we are now part of a **new national radiotherapy network RadNet** underpinned by a £56M programme from CRUK.

We lead (de Bono) one of two **UK multidisciplinary centres funded by Prostate Cancer UK and the Movember Foundation** charities. This London Centre of Excellence brings together leading researchers in a tri-partite collaboration between ICR, UCL, and Imperial and their respective BRCs across different scientific disciplines. The Centre aims to determine how men at high risk of prostate cancer can best be monitored to diagnose the disease early, how clinicians can tell which men with prostate cancer are likely to develop potentially lethal

disease that needs treatment, and how to use circulating biomarkers to personalise treatment and respond to early signs of drug resistance.

The **Children's Brain Tumour Centre of Excellence**, joint between the University of Cambridge and the ICR (Workman, Chesler, Collins), and with CRUK funding brings together world-leading experts to discover and develop new treatments to tackle brain tumours in children. By the end of the first four years of funding, the Centre aims to develop clinical trial designs for three new or repurposed drugs.

International collaborations
De Bono was a member of the transformative **Stand Up to Cancer (SU2C) International Prostate Cancer Dream team** ($10M), led by Professors Chinnaiyan (University of Michigan) and Sawyers (Memorial Sloan Kettering Cancer Centre) which delivered a comprehensive genetic map of the mutations in advanced prostate cancer. Eeles leads the **international IMPACT study** and **co-leads the Pan Prostate Cancer Group** which is part of the International Cancer Genome Consortium (ICGC). Our breast trials contribute to worldwide meta-analyses and our radiotherapy trials to international consortia investigating radiogenomic side effect predictors. We have strategic involvement in **international rare cancer initiatives** and maximise opportunities for integrated translational research as exemplified by CASPS, a trial for alveolar soft part sarcoma that demonstrated clinical activity of cediranib carried out in sites across the UK, Spain and Australia. The ICR is one of the founding members, alongside partners in Utrecht, Amsterdam, Texas, Wisconsin, Manchester, and Toronto, of the **international Elekta MR Linac Consortium**.

We participate in **internationally collaborative research projects funded by the European Commission** to develop new medical imaging technologies (Robinson, ter Haar); improve patient stratification (de Bono, Eeles, Sadanandam); and develop new cancer drugs for paediatric cancers (Chesler), with partners throughout Europe (Germany, Netherlands, France, Italy, Spain, Switzerland, Belgium, Sweden) but also in Australia, Israel and the USA. **Partnerships with American collaborators** are further promoted through US federal government funding to advance the understanding and treatment of brain and prostate cancers (de Bono, Eeles, Houlston, Huang, Kote-Jarai, Somaiah). Our networks also seek to respond to challenges faced by **Low and Middle-Income Countries** by developing new, adapted targeted interventions for cancers of particular unmet need through partnerships with researchers in Brazil, China, India, Lebanon and Nepal (Eeles, Huang, Sadanandam, Somaiah). Workman is Executive Director of the Chemical Probes Portal.

Interdisciplinary research and responsiveness to national and international priorities
We signed an institutional level strategic partnership with Imperial to increase the strength and breadth of interdisciplinary research we can leverage to tackle the key challenges of cancer.

The NHS Long Term Plan (LTP) includes the following cancer priorities:

- Diagnose cancer earlier.
- Faster diagnosis.
- Access to personalised care.
- More effective treatments.
- Better outcomes and faster recovery.
- Children and young people aged 5–14 years.

The LTP and other recent policy reports highlight the opportunities provided by interdisciplinary and collaborative research, with cancer identified as a particular area to benefit from interdisciplinary collaboration.

Cancer Research Centre of Excellence (CRCE): The CRCE is a strategic partnership between ICR and Imperial to drive forward advances in the detection, prevention, diagnosis and treatment of cancer. It was established in May 2016 and acts as the umbrella for joint ICR/Imperial activity.

CRUK Convergence Science Centre: The CRUK Convergence Science Centre (£13M) at ICR and Imperial is bringing together leading researchers in engineering, physical sciences, life sciences and medicine to develop innovative ways to address challenges in cancer.

The Cancer Epidemiology and Prevention Unit: This joint ICR/Imperial initiative is bringing together a critical mass of cancer epidemiologists, biostatisticians and population health scientists in Imperial's School of Public Health with the ICR's expertise in cancer epidemiology and genetics and its expert oncologists. The Unit's founding Director is Professor Elio Riboli.

Both ICR and RM joined the Imperial College Academic Health Science Centre (AHSC) and participated in the successful bid for re-designated by the DHSC as one of the six strategic University-NHS alliances that aim to accelerate the translation of scientific breakthroughs into innovative ways of providing patient care. The AHSC, in particular, provides the opportunity to accelerate progress towards early detection and prevention

Engagement with stakeholders to develop impact
Our research strategy is structured into four Pillars, and the fourth is "Making it Count". Engaging with key stakeholders and members of the public ensures that our research results are translated into truly fit-for-purpose innovations and increases our industrial collaborations.

We expanded our interactions with the business community to ensure that our laboratory discoveries can be rapidly developed for the benefit of cancer patients. Our approach focusses on early-stage engagement and collaborative research, licensing of technology, establishment of spin-out companies, scientific consultancy and co-ordinating with colleagues on public outreach and policy work.

- A joint "Science Day" with AstraZeneca was held in November 2019 and brought together more than 100 researchers from the ICR, RM and the company.
- All ICR researchers are provided with opportunities to develop commercial and entrepreneurial skills. We run workshops on how to develop successful interactions with industry and exploitation of IP as well as training in related skills such as public speaking and science communication. During the assessment period, almost 200 researchers undertook this training.
- Researchers can utilise up to six hours per week of their time for external activities such as providing consultancy services for companies or sitting on policy committees and may set up these interactions either independently or through the ICR's Business and Innovation Office.
- We are setting up an "Entrepreneur in Residence" programme.
- We engage with small and medium-sized enterprises to help translate their products into clinical practice. For example, we undertook the user testing and will assess the accuracy of the world's first handheld blood cell analyser in a controlled clinical environment followed by the assessment of the usability and acceptability of the device as used by patients in their own homes. The device, developed by Entia Ltd, a spin-out from Imperial, will be used as a home monitoring system for optimised delivery of chemotherapy to cancer patients.
- We are one of the two UK Centres of Excellence of the Roche imCORE™ Network, a unique international network of 27 leading cancer immunotherapy research institutions from ten countries committed to advancing immuno-oncology research.
- Our ability to conduct "smart" and efficient clinical trials has made us a partner of choice for pharmaceutical companies worldwide both for the development of ICR's drug candidates and their own drugs. We are a preferred partner for Phase I studies with major pharmaceutical companies such as Astex, AstraZeneca, Genentech/Roche, GSK, Merck, Novartis, Genmab, Medivation/Astellas, ESAI, Pfizer, Millennium, Bayer, Taiho and Vertex.
- In 2018, we formed a strategic alliance with CRUK and Merck KGaA. This is a multi-project collaboration and licensing deal aiming to progress the discovery and development of potential cancer drugs, from target discovery to the nomination of a preclinical drug

candidates. Scientists working under the collaboration will also develop new tests to guide the selection of patients with specific tumour types to take part in clinical trials.

The 2020 U-Multirank survey placed the ICR 11th worldwide for the proportion of our publications featuring an industry co-author and a UK patent office report showed the ICR filed a higher proportion of its patent applications with an industry partner than any other higher education institution.

It is important to ensure that innovative new drugs and treatment regimens can be brought to patients quickly and in a manner that is affordable to our healthcare systems. We carried out analysis which showed the higher the level of innovation of a cancer drug, the longer it was taking to pass through clinical trials, licensing and appraisal for availability on the NHS. We hosted a Summer Summit in 2019 bringing together experts from 16 leading academic institutions, charities, stakeholder groups and pharmaceutical companies to create a nine-point plan looking at practical recommendations to improve access to new cancer treatment and published a report (Yap, Workman) which received coverage across the national media and led to debate across the among patients and policy makers.

We highlighted to policy makers the barriers our researchers face in setting up clinical trials in children. We worked with others in the paediatric oncology community to raise the problem with politicians and policy makers, working with MEPs and MPs to keep the pressure on the European Commission through parliamentary questions, and responding to two EU consultations. We also worked to raise awareness more widely, running a press briefing at the Science Media Centre, and coordinating a joint letter in The Daily Telegraph from cancer charities. Ultimately, European regulators listened to these messages and changed the way that the EU Paediatric Regulation governing clinical trials is implemented.

Wider contributions to economy and society

UOA1 has an outstanding track record in delivering against its mission and taking scientific discoveries through to the clinic and thereby improving outcomes for cancer patients worldwide. These impacts changed clinical policy, improved outcomes for patients and also had considerable economic impact. This success is exemplified by the Impact Case Studies and the following additional examples:

- Before 2010, there were no approved treatment options for patients with advanced prostate cancer progressing after first-line docetaxel. The ICR was involved in research that led to the widespread approvals of four new therapies. The ICR discovered and clinically developed the drug abiraterone (see Impact Case Studies). Based on the ICR-led phase III TROPIC clinical trial, cabazitaxel is now marketed in over 75 countries with sales of 484M Euros in 2019. Data from the ICR-led AFFIRM trial resulted in widespread enzalutamide approvals in over 70 countries worldwide. Our trials showed that radium-223 improves survival and quality of life for patients with metastatic bone disease, reducing the risk of symptomatic skeletal events and hospitalisation.
- An ICR team developed a rapid-capture NGS panel. This panel determines both the incidence and the prognostic value of common mutations in paediatric solid tumours—including ALK mutations originally modelled at ICR. The ICR is now offering the panel to paediatric patients with solid tumours across the country.
- We pioneered a more flexible, patient-centred mainstreamed model for *BRCA* testing whereby patients are consented to testing at a routine oncology appointment by trained clinicians. The pathway resulted in around a 4-fold reduction in time and 13-fold reduction in cost compared to the tradition genetic pathway.

Engaging with a diverse community

Our public engagement strategy stresses our responsibility as a publicly funded higher education institution and charity to communicate openly about our work. We focus on engaging with schools and local communities in Sutton and Chelsea, encouraging support for projects such as the London Cancer Hub and on engaging with undergraduate students to encourage talented people into cancer research.

The Communications and Policy Directorate is responsible for our public engagement and policy work. We have a Public Engagement Forum, which has ICR-wide membership and coordinates engagement activities. We also have a Science Communication Forum, comprising of researchers, which ensures our approach to communication and engagement represents our science effectively and supports key priorities for knowledge exchange.

ICR and RM worked with our BRC Patient Representatives to develop a strategy for our joint BRC to engage and involve patients. We have:

- Eight Patient Representatives, one for each of the eight BRC themes and two Patient Representatives sitting on the BRC Steering Group.
- An active Patient and Public Involvement (PPI) colleagues network, of approximately 90 patients, carers and members of the public who contribute to our research in various ways (e.g. by reviewing patient information sheets and other documents by email and attending public engagement events).
- A Patient and Carer Research Review Panel, which meets quarterly, reviews protocols and research material. Between 12 and 20 PPI colleagues from our network usually attend the face-to-face meetings of the Panel.
- Patients work alongside our research teams as co-applicants and co-producers.
- Open engagement events, which raise awareness around research developments and innovations. Four to five events are organised per year, bringing together scientists and 75 to 170 patients, carers and members of the public to learn about medical advances and innovations in specific tumour types.

We are initiating new activities, such as the PPI Digital Platform, to ensure patient representatives are drawn from diverse groups reflecting the UK population, i.e. young people, minority ethnic groups, those with uncommon cancers.

The ICR recently completed a major review of its public engagement strategy. We received feedback from researchers that we should strengthen the focus on engagement with schools, and with under-served groups—especially work to reach children from disadvantaged backgrounds who might not consider a career in science. We also received feedback from BAME staff that outreach activities could play an important role in helping equalise access to science. We are therefore included outreach to ethnic minority groups as a key element in the forthcoming strategy.

Indicators of wider influence, contributions to and recognition by the research base

UOA1 researchers winning significant prizes and markers of esteem:
Three Fellows of the Royal Society (Workman, Houlston, Rabbitts), six Fellows of the Academy of Medical Sciences (de Bono, Eeles, Houlston, Rabbits, Swerdlow, Workman) and seven NIHR Senior Investigators (Bliss, Dearnaley, de Bono Eeles, Harrington, James, Yarnold), three Fellows of the European Academy of Cancer Sciences (Houlston, Workman, Yarnold), AACR-Joseph H. Burchenal Memorial Award for Outstanding Achievement in Clinical Cancer Research (de Bono), AACR Outstanding Investigator Award for Breast Cancer Research (Turner), Raymond Bourgine Award for Cancer Research (Workman), BACR/AstraZeneca Young Scientist Frank Rose Award (Valeri), Weiss Medal (Yarnold), Ian Donald Award for Technical Merit (ter Haar), Sutton Women in STEM award (Rossanese) and ESTRO Lifetime Achievement Award (Yarnold).

Our involvement in consultations, public policy committees, professional bodies, and charity advisory boards allows us to assist in enabling the transition of research evidence into public policy.

National Institute for Health and Care Excellence (NICE) and European Medicines Agency (EMA) committees

ICR researchers gave evidence to NICE at the Technology Appraisals for enzalutamide (2020, James), apalutamide (2020, James), palbociclib (2019, Turner), nivolumab (2016, Harrington)

and T-VEC (2016, Harrington). Harrington also testified to the EMA Committee for Medicinal Products for Human Use as part of the EMA approval of pembrolizumab in head and neck cancer and was an expert advisor at the EMA hearings that led to T-VEC's European approvals. Huddart was a member of the NICE Bladder Cancer Guideline development group 2012-2015.

Funding panel memberships in the period

- NIHR: Advanced Fellowship Panel (Bliss); Health Technology Assessment Commissioning Board (Bliss); Health Technology Agency Funding Committee (James); NIHR Early Phase Clinical Trials (Yap).
- Breast Cancer Now: Catalyst Committee (Melcher, Turner); Grants Committee (Cheang), Risk and Prevention Committee (Houlston).
- CRUK: Clinical Career Committee (Turner, Chesler, Eeles); Clinical and Trials Awards and Advisory Committee (Hall); Clinical Research Committee (deSouza, Yap, de Bono, Harrington), Early Detection Research Committee (Al-Lazikani); Multidisciplinary Expert Review Panel (Oelfke); New Agents Committee (Rossanese).
- MRC: Molecular and Cellular Medicine Board (Fletcher, Houlston).
- Royal Society: Sectional Committee (Workman).
- Sarcoma UK: Research Advisory Committee (Huang, Shipley).
- Wellcome Trust: Biomedical Resource Committee (Al-Lazikani); Genetics, Genomics and Population Research Expert Review Group (Turnbull).
- Worldwide Cancer Research: Scientific Advisory Committee (Rossanese).

Other contributions to wider discipline

Professor Nick James is a member of the Cross Whitehall Trial Advice Panel run by the Cabinet Office (2015–present). The Panel advises on and aims to extend use of trials methodology across all aspects of Government. ICR researchers are active in driving research and quality standards in clinical trials through: UK Clinical Research Collaboration Registered CTU Group Executive Committee (Deputy Chair 2019, Bliss), NCRI Cancer CTU Group (Chair 2013–2019, Bliss). At the outset of the COVID-19 pandemic Professor Bliss was appointed onto the NIHR Urgent Public Health Group (UPHG), as one of two reviewers of research methodology. The NIHR UPHG was established to provide advice directly to the Chief Medical Officer for England in order to prioritise and coordinate COVID-19 research. Professor Huddart was a member of the Bladder cancer guideline group for the European Society of Medical Oncology in 2019. Professor Workman was Deputy Chair for the NCRI Strategy Advisory Committee.

Professor Turner is the breast lead, Professor de Bono the prostate lead and Professor Turnbull the inherited cancer predisposition lead for the Genomics England Clinical Interpretation Partnerships, and through these roles shaped the implementation of the 100,000 genomes project to better interpret genomic data, which will lead to better clinical understanding and better patient outcomes.

The textbook Cancer Prevention and Screening: Concepts, Principles and Controversies, led and co-edited by Professor Ros Eeles, received the Council Chair's Choice Award at the British Medical Association's Medical Book of the Year Awards 2019.

Other relevant accolades:

- UK Pharmacology on the Map award recognising the ICR as one of four sites in the UK of importance for the discovery of cancer drugs (2015).
- Accreditation by the NCRI Clinical and Translational Radiotherapy Research Working Group (CTRad) as one of three Established Centres of Excellence in Academic Radiation Oncology (2016).
- Regius Professorship of Cancer Research awarded by Her Majesty the Queen to mark her 90th Birthday (2016).
- Queen's Anniversary Prize for world-leading research in cancer drug discovery and development (2017).