CCRCB
Centre for
Cancer Research
& Cell Biology

CCRCB ANNUAL REPORT 2015

Queen's University Belfast

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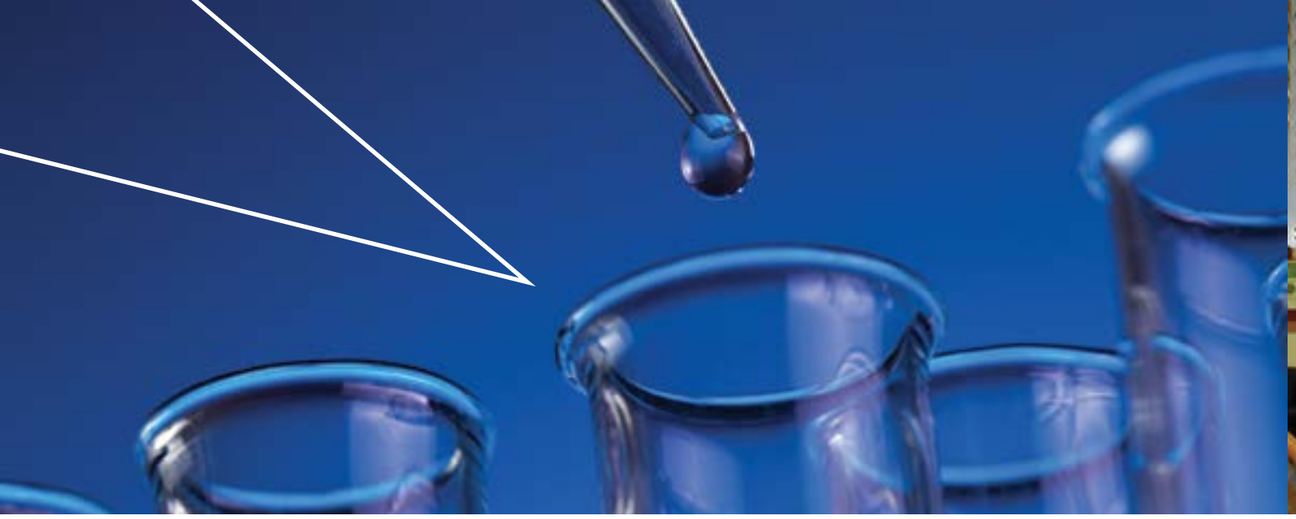
DIRECTOR'S INTRODUCTION

The Centre for Cancer Research and Cell Biology (CCRCB) is the beating heart of a comprehensive cancer research programme in Belfast, focused on accelerating the delivery of scientific discovery to clinical application. CCRCB is the research hub of the Belfast Cancer Research UK Centre and the Belfast Experimental Cancer Medicine Centre (ECMC), operating in partnership with the Belfast Health and Social Care Trust. Our integrated clinical and scientific programmes address clinically unmet needs. Our principal objective is to promote evidence-based, innovative clinical trials in order to underpin improved patient outcomes in high incidence solid tumours of Gastro-Intestinal, Prostatic, Breast and Ovarian origin, and in specific Blood Cancers. Our unifying research theme is to develop translational outputs, in the form of biomarkers and/or novel therapeutic strategies that enable our Centre to be at the forefront of personalized cancer medicine in these prevalent diseases.

This report will capture the major activities and successes of CCRCB researchers over the 2015 calendar year. We hope that reading this brochure will inform you about the dynamic research environment within CCRCB and inspire you and your organization to support and/or partner with our teams to achieve our mission on behalf of cancer patients here in Northern Ireland and across the world.

I extend my sincere thanks to all Staff, Researchers and Students for their dedication to the cause and for the significant support that we receive from the NI Cancer Research Consumer Forum and the many other volunteers in our community that continue to inspire us.

David Waugh,
CCRCB Director

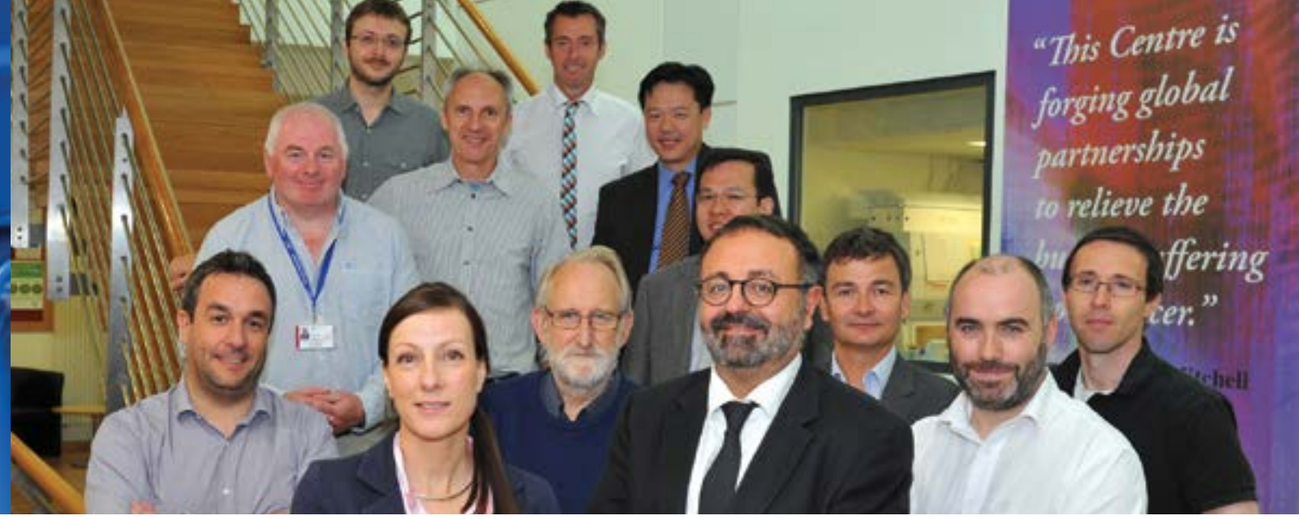


OVERVIEW OF CENTRE STRATEGY

The Centre's research strategy has been shaped to accelerate the translation of pre-clinical discovery to clinical application. Investigators operating in inter-disciplinary teams through our disease-focus groups are driving important pre-clinical discovery and knowledge relevant to improving patient treatment and care. Our partnerships with Biotech and Industrial partners, drawn from within and outwith Northern Ireland, are bridging the innovation gap by informing the development of products that will have future clinical utility. Through the expertise of the Northern Ireland Clinical Trials Centre, our Centre can then undertake the early clinical development of these products. As such, through this pipeline of collaborative research activity underpinned by core partnerships, CCRCB is now able to point to a substantive and exciting innovative early phase clinical trials programme operating within the Northern Ireland Cancer Centre and Belfast Health and Social Care Trust. Our continued focus remains on growing the scale of the trials portfolio, concentrating on increasing the number of biomarker-enabled patient enrichment and biologically-informed clinical trials that we can offer to patients in Belfast.

The Centre is well served by dedicated and talented senior academics that constitute an ambitious management team. Professor Kevin Prise and Professor Manuel Salto-Tellez have provided invaluable support in their capacity as Deputy Directors of the Centre, while simultaneously providing national and international leadership in Radiation Biology and Molecular Pathology, respectively. Our ECMC innovative clinical trials programme continues to go from strength-to-strength under the leadership of Professors Kennedy and Wilson, with a record number of patients electing to enrol in clinical research. In Professor Paul Harkin and Professor Tim Harrison, the Centre benefits from both academic and commercial expertise in biomarker discovery and cancer therapeutic development, enabling the wider scientific community within the Centre to also consider the pathway required to develop science towards clinical impact. Finally, three industrious Associate Directors in Professor Ken Mills, Professor Mark Lawler and Dr Dan Longley have worked continuously to update, refresh and innovate our undergraduate, postgraduate and post-doctoral training programmes. In addition, the Centre is fortunate to also call upon the leadership of Dr Karen McCloskey, who serves as Director of the Gender Equality Office for the School of Medicine, Dentistry and Biomedical Science.

The Centre is now home to 38 Principal Investigators, has a total annual grant income in excess of £14M, and is home to over 300 researchers. Our expansion has been underpinned by successful team working to develop competitive externally-funded research programmes, and by leveraging key academic-industrial-healthcare partnerships to populate our research pipeline. Growing the entire academic and industrial life science sector in Northern Ireland also provides new employment opportunities for our postgraduate and undergraduate researchers. Our new Masters programmes are now providing comprehensive education in Translational Medicine, and in addition to our established PhD training programme, we are offering a new International Doctoral Training Programme in Precision Medicine beginning in 2016. This four year Programme will provide QUB students with an unrivalled opportunity to perform cutting edge research at the National Cancer Institute (NCI) in Washington, positioning them as future leaders in an area that is revolutionising how we deliver 21st century medicine to cancer patients.



CENTRE PROGRAMMES

CCRCB has served as a catalyst for change by focusing the resource leveraged from external funders to develop and grow essential activities that directly impact on patient care. Cancer Research UK (CRUK) remains a major funder of research activity within the Centre. The renewal of the Belfast CRUK Centre and ECMC programmes continues to underpin the core infrastructure for our Centre in developing state-of-the-art capabilities in molecular diagnostics, clinical trials and molecular pathology. Importantly, the research advances being realised in our programmes in Belfast is underpinning a closer partnership with other Centres in the CRUK network. This not only ensures that research discoveries made in Belfast are impacting on patient care nationally but also enables us to import other discoveries so that patients in Belfast can benefit from new improvements in treatment and care.

The Movember FASTMAN Centre of Excellence officially launched in July 2014 continues to build momentum. This £5M programme in partnership with Manchester is driving a multi-disciplinary programme to understand optimal approaches to improve radiotherapy and radionuclide response in prostate cancer patients. Furthermore the Drug Discovery Programme in partnership with Almac Discovery continues to advance several projects towards clinical development.

The CRUK Accelerator award of £3.7M, which commenced in July 2015, brings together a consortium of cancer pathologists, biologists and immunologists from the Belfast Cancer Research UK Centre, who will work in partnership with researchers from the Universities of Southampton, Manchester and Newcastle, University College London and the Institute of Cancer Research. Already recognised as experts in identifying faulty genes and molecules in tumours, the Belfast team will now lead this nationwide research programme dedicated to expanding the application and use of digital pathology to quantify specific tumour markers. The programme will be supported using software from PathXL, a Queen's University spin-out company which specialises in high resolution imaging of tumours and cloud-based digital pathology.

CCRCB researchers are at the heart of a new £5M research programme that aims to fundamentally change how we treat bowel cancer patients, both across the UK and globally. The Medical Research Council (MRC) and Cancer Research UK (CRUK) jointly launched a Stratified Medicine Consortium to help personalise bowel cancer treatment by matching patients to the most effective therapies. Programmes like S-CORT (Stratification in COloRecTal cancer) emphasise CCRCB's vision of Precision Cancer Medicine, using precise state-of-the-art technologies to translate excellent science into clear patient benefit.

With support from Invest Northern Ireland, California-based CV6 Therapeutics Ltd has chosen to partner with the Centre for Cancer Research and Cell Biology at Queen's University Belfast for a highly innovative Research and Development project. The project, which aims to develop a new drug with the potential to make chemotherapy more effective, represents a total investment of £5.5M in R&D. Invest Northern Ireland has offered assistance of £2.5M towards the collaboration which includes part funding from the European Regional Development Fund (ERDF), under the Sustainable Competitiveness Programme for Northern Ireland.

The Centre for Cancer Research and Cell Biology has been launched as a new UK Centre of Excellence to understand and treat patients' illnesses more precisely. The Precision Medicine Catapult in Belfast, which will commence in 2016, will be one of six initial locations for its regional centres of excellence network, alongside Cardiff, Glasgow, Leeds, Manchester and Oxford. Each centre will act as a hub for research and development in precision medicine, which uses diagnostic tests and data-based insights to understand a patient's illness more precisely and select treatments with more predictable, safer and cost-effective outcomes. The Precision Medicine Catapult has been established to harness the breadth of UK expertise, developing innovative technologies and solutions for broader use across the UK's healthcare sector.

Financial funding from local charities and individual bequests also continues to provide generous and welcome funding to the Centre.

CENTRE LIFE

CCRCB has played host to a busy calendar of visits from academics and key stakeholders over 2015. Our annual Mitchell Lecture was delivered by Professor Lisa Coussens, a pioneer of immune cell targeting in the tumour microenvironment and Director of the Knight Cancer Centre in Oregon. During her visit Professor Coussens also participated in the first CCRCB Women in Science event. This took the format of an informal interview with Professor Coussens, who shared her career pathway and her life as an international scientist.

A further CCRCB Women in Science event was held in July when Dr Francoise Meunier, Director General of the European Organisation for Research and Treatment of Cancer (EORTC) visited the Centre. A large audience learned of the history and development of the EORTC and of Dr Meunier's strategic vision to improve the lives of cancer survivors. Dr Meunier received an honorary degree from QUB at the SMDBS graduation ceremony in July 2015. Professor Richard Marais from the CRUK Manchester Institute gave the 2015 Cancer Research UK Lecture entitled 'Precision Medicine in Melanoma', rounding up another successful year long seminar programme. Following the announcement of the merger of Breast Cancer Campaign and Breakthrough Breast Cancer, Dr Elizabeth Robertson (Head of Research of the merged Charity) visited CCRCB in March 2015. The Centre was also privileged to have a visit from Dr Howard Soule, Executive Vice President and Chief Science Officer of the Prostate Cancer Foundation (PCF) in November 2015. Dr Soule coordinates global academic, government and biopharmaceutical sector research activity and is responsible for the implementation of PCF's global research strategies. Dr Soule's visit also coincided with CCRCB's Movember fundraising coffee morning.

The Centre has also played host to a number of important patient information events across our major diseases. Most significantly was the first ever CCRCB Open Day which was held on Saturday 9 May 2015 when the Centre welcomed over 350 visitors to the Centre. Visitors included patients and their families, supporters of the charities who fund research in CCRCB and the general public. The attendees could choose from a wide range of activities throughout the day such as lab tours, talks by senior scientists, and interactive activities. Visitors were able to talk to the CRUK cancer research nurses and members of the NI Cancer Research Consumer Forum about clinical trials. Epidemiologists from the Centre for Public Health also had a large stand where they had activities aimed at raising awareness of cancer prevention through lifestyle changes. Representatives from Almac and PathXL were also on hand to talk about their work carried out in partnership with CCRCB. Plans are currently underway to hold a further CCRCB Open Day in October 2016.

Our academic and research staff have contributed significantly to many major cancer conferences and symposia. In particular, the All-Ireland Cancer Consortium Conference 'New Horizons for Cancer: removing Boundaries' was held at Queen's University in May 2015. In addition to the major contribution of our young researchers to the Irish Association for Cancer Research and the Haematology Association of Ireland meeting, our postgraduates and research fellows have presented at a range of important conferences across the UK, Europe and the US. Members of our academic staff have also been prominent in both organizing and speaking at a range of key European and UK wide conferences, highlighting the increasing impact and dissemination of our findings across the cancer research community.

The life of the Centre has been enriched by a number of new academic appointments to consolidate our translational research programmes. Dr Jaine Blayney and Dr Darragh McArt were appointed to lectureships in Translational Cancer Bioinformatics and took up post early 2015. Dr Melissa LaBonte Wilson joined the Centre in April 2015 from the University of Southern California to a lectureship post in Molecular Oncology. Dr Robert Ladner was appointed to a Readership position and is leading the collaborative CV6 Therapeutics and QUB programme to accelerate the translation of novel drug development to improve clinical care. Dr Ian Mills has also been appointed to a Readership position and his research focuses on the impact of transcriptional regulation on prostate cancer metabolism and stress responses. Moreover, the Centre has made a further significant clinical academic appointment. Mr Stuart McIntosh has been appointed as a Clinical Senior Lecturer and this appointment will provide expertise in breast cancer research and further expand the clinical trials portfolio. I would also like to give a special mention to Paul Mullan who was promoted to Reader during the academic year.

RESEARCH AWARDS

The Centre takes great pride in recognising the outstanding achievements of our staff in 2015. A synopsis of the major and notable awards of our staff includes:

- Vice-Chancellor of Queen's University Belfast, Professor Patrick Johnston was awarded an Honorary Fellowship of the Royal College of Surgeons in Ireland (RSCI). The award, the highest distinction the RSCI bestows, was presented to Professor Johnston in recognition of his contribution to cancer research. A globally-recognised cancer specialist over the last 20 years, Professor Johnston, from Derry, has also led the development of a world-leading Institute of Health Sciences at Queen's University. His research has resulted in a number of prestigious landmark publications, over 20 patents and almost £100 million in grants being secured from research and philanthropic bodies. Professor Johnston was presented with the award by RCSI President, Declan J Magee, at a conferring ceremony at RCSI in Dublin, on 7 February 2015.

- Professor Kevin Prise was elected as Vice-President-Elect of the US Radiation Research Society, having been nominated via a ballot of all its members. Professor Prise leads the Radiation Biology Group at CCRCB, which is working on improved approaches for treating cancer with radiotherapy. In collaboration with Professor Joe O'Sullivan (Clinical Director) and Professor Alan Hounsell (Clinical Physics Research Lead), Professor Prise plays a major role in the Prostate Cancer UK Movember Centre of Excellence at CCRCB, which is researching new approaches for treating men who are likely to fail current treatments for prostate cancer. Professor Prise will take up the position of Vice-President in September 2016 and will serve as President from September 2017.

- Professor Kevin Prise was also appointed Editor-in-Chief (Scientific) of the British Journal of Radiology, and has been appointed to the UK Department of Health Expert Committee on Medical Aspects of Radiation in the Environment (COMARE).

- Professor Patrick Morrison was elected Vice President of the Ulster Medical Society for 2016.

- Dr Sandra Irvine was appointed to the NCRI Clinical Studies Group for colo-rectal cancer as PPI representative for 3 years from July 2015.

- Dr Kirtiman Srivastava was awarded the Roche Prize for 2015 and was presented with a medal and cheque for £400. His winning presentation was based on his publication in Oncotarget entitled: 'p63 drives invasion in keratinocytes expressing HPV16 E6/E7 genes through regulation of Src-FAK signalling.'

- Dr Peter Bankhead was awarded joint first place in the Cancer Research category at the All Ireland Cancer Consortium Conference in May 2015 for his poster presentation entitled 'QuPAth: A general framework for visualisation and quantification of tissue biomarkers in whole slide images.'

- Dr Lisa Crawford received a UK Myeloma Forum (UKMF) travel award to present her work at the International Myeloma Workshop in Rome in September 2015 with an associated invited talk at the UKMF Scientific Day in November 2015.

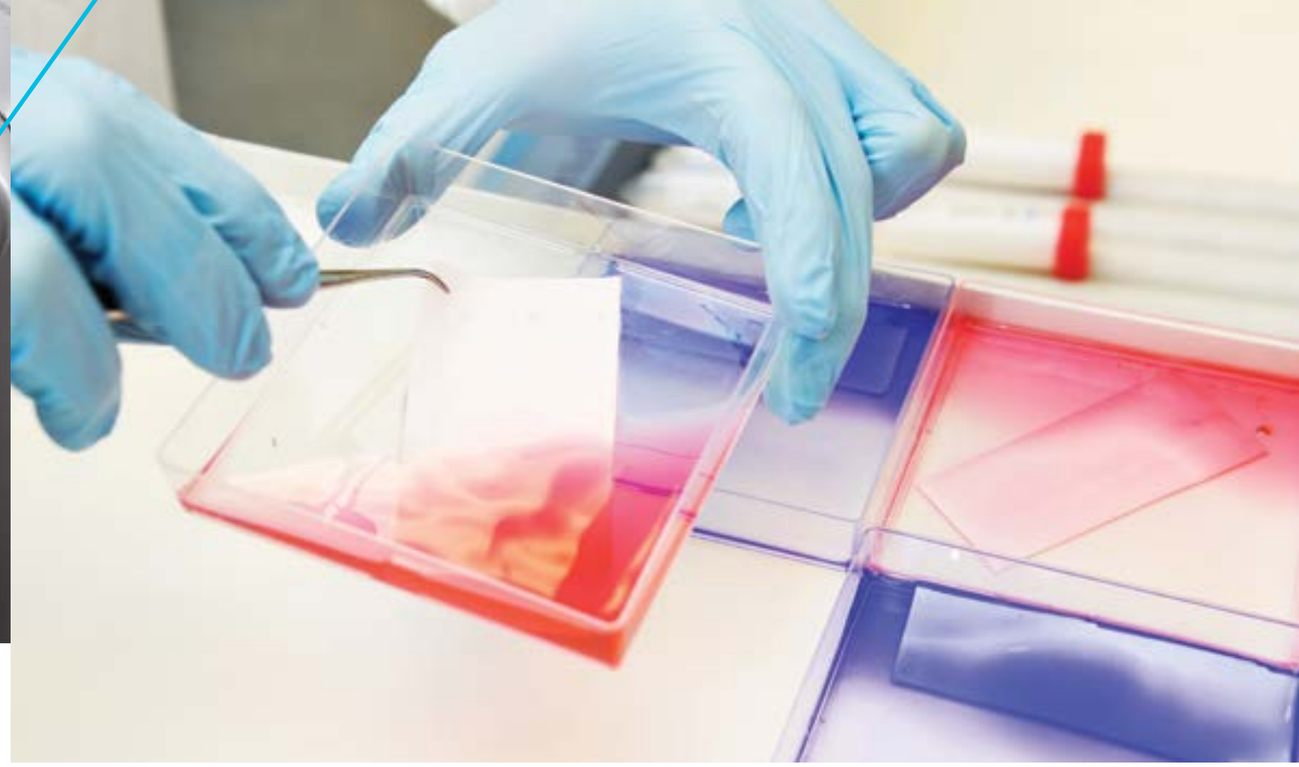
- Dr Philip Dunne was awarded the Proffered Oral Presentation prize based on his work on tumour cell invasion at the IACR Annual Meeting held in Limerick on 26 - 27 February 2015.

- Dr Mihaela Ghita was awarded a Young Scientist Travel Award to present her work at the 12th International Workshop on Microbeam Probes of Cellular Radiation Response held in Tsuruga, Japan, on 30 May - 1 June 2015.

- Dr Kerry Hughes and Dr Rich Williams were awarded £3,400 from the Royal Society of Chemistry's Outreach fund to carry out chemistry outreach activities for schools and events with the centre.

- Dr Kyle Matchett was awarded the inaugural Professor John Fitzpatrick Prize for the Best Oral Poster Presentation at the IACR Annual Meeting held in Limerick on 26 - 27 February 2015.

FOCUS GROUPS



ADVANCED RADIOTHERAPY

The Advanced Radiotherapy Group (ARG) is a multidisciplinary team of clinicians, physicists, radiation biologists, radiographers and physiologists whose remit is to research, initiate and develop new and advanced radiation treatments using basic laboratory research, pre-clinical studies and clinical treatments. Members of this translational research group are leading experts in radiation and radiotherapy physics, cell biology, mathematical modelling, radiation biology, bladder physiology, and radiation oncology.

A number of clinical trials and studies (BUSTIN, RBM, ADRRAD, SPORT, CASPIR) have been developed and are led by members of the ARG. These clinical trials and studies are open for recruitment within the NI Cancer Centre and cover the key themes of the ARG; biomarker development, advanced radiotherapy treatments and radionuclide therapies. Previous research arising from the ARG has directly impacted patient care, such as the study of PET/CT for Radiotherapy Planning in Lung Cancer which has directly changed clinical practice and been incorporated into international radiation treatment guidelines.

Concurrent with on-going Trial recruitment, the ARG applies state-of-the-art pre-clinical radiotherapy technologies to model clinical treatments and drive hypothesis driven advanced radiation oncology research. A leading strength and area of focus of the ARG is mathematical modelling of advanced radiotherapy treatments from in-vitro through in-vivo to clinical treatment plans and patient outcome data. Work is also on-going investigating the combination of advanced radiotherapies (such as Stereotactic Radiotherapy and Intensity Modulated Radiotherapy) with new molecularly targeted agents; in the application of image-guided therapies; in ion beam therapies; in the application of fibre optic sensors in radiotherapy; and in radionuclide approaches to cancer treatment. Some aspects of the work are disease specific, with a particular focus on prostate cancer as part of the PCUK/Movember Centre of Excellence. Other interests of the group are in breast, lung and brain tumours with some members also contributing to other CCRCB focus groups such as breast, ovarian and genito-urinary/prostate.

Members of the ARG are involved in national and international collaborations based around a wide range of studies. The group holds current funding from Prostate Cancer UK, Cancer Research UK, MRC, EPSRC, UK Department of Health, Friends of the Cancer Centre, The R&D Office and the European Commission. Industry support comes from PTW, GW Pharmaceuticals, XStrahl Life Sciences, OSL and the National Physical Laboratory. Group members have formal collaborations with key international organisations such as the International Atomic Energy Agency and members of the ARG are part of key national clinical and research bodies such as the UK's National Radiotherapy Board, CTRad and the NCRI Clinical Studies Groups. The ARG has a number of cross-faculty links with members of the Faculty of Engineering and Physical Sciences (EPS) with on-going projects in ion beam therapies and radiation studies using nanoparticles.

Alan Hounsell
Chairperson

The objective of the Advanced Radiotherapy Group is to maximise our input into Radiation Oncology Research and Development by:

- Developing new collaborative research programmes in Advanced Radiotherapies;
- Maximising the translational opportunities of our research;
- Inputting into new radiation-based clinical studies at the Northern Ireland Cancer Centre (NICC);
- Maximising training opportunities in radiation sciences;
- Initiating collaborative projects with other focus groups and external partners;
- Profiling radiation-based work at Queen's, nationally and internationally.

Our research covers three component areas:

- Radiation Biology;
- Radiotherapy Physics;
- Clinical Radiotherapy Research (including radiographer led research).

Focus Group Membership:
Dr Karl Butterworth
Dr Mihaela Ghita
Dr Gerry Hanna
Dr Simon Horn
Dr Suneil Jain
Dr Raymond King
Dr Ciara Lyons
Dr Karen McCloskey
Dr Conor McGarry
Dr Stephen McMahon
Ms Angela O'Neill
Dr Sarah Osman
Professor Joe O'Sullivan
Professor Kevin Prise
Dr Philip Turner

BREAST CANCER

The Breast Cancer Focus Group is comprised of Oncologists, Surgeons, Pathologists, Geneticists and laboratory-based Scientists.

Its role is to facilitate the transition of novel biomarkers or therapies from the laboratory into prospective clinical trials run in the Belfast Experimental Cancer Medicine Centre (ECMC) for the benefit of patients affected by breast cancer.

Clinical research:
Ultimately this focus group aims to translate laboratory research findings such as the identification of novel biomarkers or the development of novel therapies and incorporate them into prospective clinical trials. Significant progress has been made within the last year to establish the research infrastructure necessary to deliver such translational research.

Beyond the development of clinical studies from discoveries made within CCRCB, the Clinical Team in the Cancer Centre aim to provide a range of National and International Clinical Studies for patients with breast cancer. The Breast Cancer Focus Group aims to provide strategic advice on the composition of the breast cancer clinical trials portfolio within the Northern Ireland Cancer Trials Network.

A summary of some of the studies is available at: http://www.qub.ac.uk/research-centres/nictc/ClinicalTrials/Bycancertype/BreastCancer/

If you are a patient and are interested in taking part in a clinical trial, please speak with the Doctor who is responsible for your care.

Basic and translational research:

Breast cancer research within CCRCB is centred around the following themes:

- DNA damage signalling;
- DNA Repair;
- Hormone therapy resistance;
- Triple Negative and BRCA phenotypes;
- Angiogenesis;
- Biomarkers of response;
- Chemoprevention in women at high risk of breast cancer;
- Breast tissue response to ionising radiation.

Focus Group Membership:
Dr Niamh Buckley
Dr Jackie Clarke
Dr Alison Clayton
Professor Paul Harkin
Dr Jane Hurwitz
Dr Colin James
Professor Richard Kennedy
Dr Tong Lioe
Dr Seamus McAleer
Dr Nuala McCabe
Dr Shane McKee
Dr Paul Mullan
Dr Eileen Parkes
Professor Kevin Prise
Professor Tracy Robson
Professor Manuel Salto-Tellez
Dr Kienan Savage
Dr Laura Taggart
Dr Stephen Walker

Stuart McIntosh
Chairperson

Gerry Hanna
Deputy Chairperson

BLOOD CANCER

The Blood Cancer Focus Group has research activities across the spectrum of diseases represented by the umbrella term, Blood Cancers. The focus group encompasses a wide range of translational and clinical scientists, bio-informaticians, medicinal chemists, pathologists and academic clinicians from the CCRCB and the Belfast Health and Social Care Trust. The research laboratory is focussed on developing and applying pre-clinical models of disease that are complemented by active collaborations with the haematology consultants across Northern Ireland.

Myeloid malignancy, itself a spectrum of diseases covering Myelodysplastic Syndromes (MDS), Myeloproliferative Neoplasms (MPN) and Acute Myeloid Leukaemia (AML), has an unmet need for new effective and less intensive therapies as the survival rates, particularly in the elderly (over 65 years old) are still poor. One angle of our research has been an emphasis on identifying potential therapeutic agents repurposed from treatments for other diseases including those used for dementia or diabetes. This also interacts with our studies on the epi-sensitisation of leukaemia cells by combining epigenetic therapies with novel, repurposed or existing therapies to improve their effect and reduce toxicity. Other studies have involved using the CRISPR-CAS system to introduce or repair mutations associated with myeloid malignancies in order to understand their molecular contribution to disease development and evolution.

Myeloma, also known as multiple myeloma, is a blood cancer arising from plasma cells and is considered to be incurable but treatable. Myeloma has a remitting-relapsing disease course, with remissions induced with steroids, chemotherapy, proteasome inhibitors or immunomodulatory drugs but these do not have long term benefit so our research has been to identify new targets around the ubiquitin pathway that can improve patient outcomes.

A vital part of the Blood Cancer Research Group's activities are the interactions with clinical colleagues. This is represented nationally and internationally by our participation in trials for MDS, AML, MPN and CML supported by the Bloodwise Therapy Acceleration Programme (TAP) portfolio within the NI Cancer Trials Centre. Locally, Focus Group members as registered clinical scientists attend multi-disciplinary team (MDT) meetings, assess quality of bone marrow harvests, have developed assays for AML mutations that have transitioned into the clinical diagnostic laboratories and are developing next-generation sequencing panels to further extend/enhance the diagnostic and prognostic capability for blood cancers across Northern Ireland.

Focus Group Membership:
Dr Lesley Anderson
Dr Mark Catherwood
Dr Lisa Crawford
Dr Gerald Gavory
Professor Tim Harrison
Dr Sandra Irvine
Professor Terry Lappin
Dr Fabio Liberante
Dr Kyle Matchett
Professor Mary Frances McMullin
Dr Suzanne McPherson
Dr Melanie Percy
Dr Kienan Savage
Dr Alex Thompson
Dr Lakshmi Venkatraman
Dr Paul Winter
Dr Shu-Dong Zhang

Associate Membership:
Dr Claire Arnold
Dr Gary Benson
Dr Robert Cuthbert
Dr Mary Drake
Dr Damian Finnegan
Dr Mervyn Humphreys
Mrs Amy Logan
Dr Christine Macartney
Dr Scott McCloskey
Dr Peter McGrattan
Dr Bethany Mitchell
Dr Michael Quinn
Dr Oonagh Sheehy

Ken Mills
Chairperson

BRAIN TUMOURS

A Brain Tumour Focus Group is building activity at CCRCB, in partnership with Brainwaves NI, to develop new translational research programs and critical mass in this area. Brain tumour research is a highly under resourced area of research (receiving less than 1% of funding from UK charities and health agencies) even though it is the leading cause of cancer deaths in children and adults under the age of 40, and outcomes for patients show little improvement over the past 20 years.

There are currently very few opportunities for brain tumour patients in Northern Ireland to be enrolled in national trials and there is a pressing need to build capacity and develop programs, which will improve patient outcomes.

The Brain Tumour Focus Group is a multidisciplinary team having strengths in Neurosurgery, Cancer Biology, Radiation Physics, Biology and Oncology, Bioinformatics and Molecular Pathology. The membership includes basic scientists, clinical scientists and clinicians. The aim is to bring new researchers with experience in other areas or tumour sites together with existing clinicians and clinical scientists working with brain tumour patients to deliver new innovative translational research programs.

The focus group aims to develop three key strands of activity. Firstly to build translational programs based on existing research areas, which the group members are working on. This includes the development of targeting strategies against the protease Cathepsin S, which plays a role in invasive processes of brain tumours and may underpin resistance to radiotherapy, by optimising the use of radiation based therapies alongside Cat S inhibitors. Secondly, new molecular pathology analysis of a range of markers, in clinical samples from patients with primary and recurrent brain tumours, to allow the discovery of specific markers, which may be predictive for treatment outcomes and allow stratified approaches in patients. This is being developed in collaboration with the Northern Ireland Molecular Pathology Laboratory. Finally we are developing clinical trial opportunities for brain tumour patients initially linking into national on-going trials but with the longer-term goal of translating the research of the focus group into new trial opportunities. The work includes basic research, preclinical and trial activity in these areas feeding into key themes in CCRCB including biomarker, drug development and combinations of advanced radiotherapies, such as stereotactic radiotherapy with new molecularly targeted agents.

Additional members will be recruited into the focus group and invited along to ad hoc meetings depending on the focus of the current research of the group.

The overall objectives of the Brain Tumour Group are to maximise our input into new approaches for treating brain tumours by:

- Developing new collaborative research programmes in Brain Tumour Research;
- Maximising the translational opportunities of our research;
- Inputting into new clinical studies for Brain Tumour patients at the Northern Ireland Cancer Centre (NICC);
- Maximising training opportunities in Brain Tumour research;
- Initiating collaborative projects with other focus groups and external partners;
- Profiling brain tumour related research at Queen's, nationally and internationally;
- Engagement with local patient groups and funding stakeholders.

Kevin Prise
Chairperson

Focus Group Membership:
Dr Shahnaz Al Rashid
Dr Roberta Burden
Dr Tom Flannery
Dr Gerry Hanna
Dr Jackie Harney
Dr Estelle Healy
Dr Perry Maxwell
Dr Darragh McArt
Dr Philip Dunne
Dr Paul O'Reilly
Ms Maggi Whyte (Brainwaves NI)
Professor Manuel Salto-Tellez
Professor Chris Scott
Professor David Waugh

GENOMICS

The cross-discipline Genomics Focus Group has the aims of:

- Coordinating genomic and epi-genomic activities across the CCRCB in collaboration with the other research centres;
- Identifying novel areas of collaboration for research and grant applications;
- Improving the infrastructure associated with 'omics' research including bioinformatics training, analysis potential and storage issues.

The members of the group are drawn from most of the other disease based focus groups and include laboratory scientists, bioinformaticians, clinical academics and laboratory researchers. The Group has had presentations on epigenetic studies, novel bioinformatics analysis methods, Global Alliance for Genomic Health (GA4GH) and molecular pathology.

Overall, the group is aimed at improving patient outcomes through genomic or epigenetic based research activities.

Focus Group Membership:
Dr Jaine Blayney
Dr Niamh Buckley
Dr Tim Davison
Dr Gerald Gavory
Dr Sandra Irvine
Dr Jackie James
Professor Mark Lawler
Dr Fabio Liberante
Dr Darragh McArt
Dr Simon McDade
Professor Mary Frances McMullin
Dr Julia Miskelly
Professor Patrick Morrison
Professor Manuel Salto-Tellez
Dr David Simpson
Dr Alex Thompson
Dr Stephen Walker
Dr Kate Williamson
Dr Shu-Dong Zhang

Ken Mills
Chairperson

GASTRO-INTESTINAL CANCER

The Gastro-Intestinal Focus Group has established a comprehensive collaboration between basic and translational scientists, clinician scientists, clinical academics, epidemiologists, oncologists, surgeons, pathologists, bio-informaticians and medicinal chemists from CCRCB, CII, School of Pharmacy and CPH in QUB and the Belfast Health and Social Care Trust (BHSCT). It addresses a number of important clinical problems, both in the early and advanced disease settings.

The main activity in this focus area is on colorectal cancer. This has built on the foundation of a basic/translational research group in CCRCB and an early and late phase clinical trials group in the clinical Cancer Centre, which have come together closely over the last few years. Scientifically, its major goals and achievements to date are the identification of novel targets, in particular for specific molecular subtypes of colorectal cancer (eg: mutant *p53, Kras* and *Braf*), and the identification of biomarkers of response to chemotherapy and targeted agents. Moreover, it is the ultimate goal of the focus group to translate this research into the clinical trials arena. For example, GI Focus Group members (Van Schaeybroeck, Lawler, Johnston, Salto-Tellez, Wilson) are leading Mercuric, one of the first early phase, European-wide, multi-Centre clinical trials based on science generated by the group and which is supported by European Union funds.

In addition to Mercuric, national and international clinical trials in GI cancer are led by investigators from the GI Focus Group including the innovative FOCUS4 adaptive clinical trial in metastatic CRC, the Add-Aspirin adjuvant CRC trial, the pre-operative Vitamin D CRC trial, the BALLAD adjuvant trial in small bowel adenocarcinoma and the Easi-Switch trial. Members of the group are also involved as clinical or scientific partners in other national and international phase I-III trials and are members of the NCRI Colorectal Clinical Studies Groups and Supportive and Palliative Care CSG as well as the EORTC GI group and International Rare Cancer Initiative Small Bowel Adenocarcinoma Working Group.

In the recent MRC Stratified Medicine call, CCRCB researchers (Lawler, Johnston, Salto-Tellez, Kennedy, Wilson) were successful in securing a Stratified Medicine Programme Grant entitled Stratification in COloRectal cancer: from biology to Treatment prediction (S-CORT). S-CORT is a ~£5M programme funded by the MRC and CRUK. It involves researchers at Queen's, Oxford, Leeds, Birmingham, Cambridge, London and Aberdeen, Industry partners including Almac Diagnostics and patient advocacy/PPI groups including the Northern Ireland Cancer Research Consumers Forum. S-CORT will develop new approaches for molecular stratification of patients with colon and rectal cancer, utilising a cohort of 2,000 clinically annotated samples from patients in clinical trials throughout the UK. CCRCB researchers are leading three of the six Workstreams in this Programme, emphasizing our central role in securing this prestigious funding.

GI Focus Group members have had notable recent success in leading CRUK New Agents Committee (NAC) first-in-human clinical trials. Wilson and Longley are the PI and Scientific Lead respectively for the phase I trial of MedImmune's MEDI3039 a novel 2nd generation TRAIL receptor agonist. Wilson and McDade are the PI and Scientific Lead for the phase I trial of LY3177833, a novel CDC7 inhibitor developed by Eli Lily. Wilson, Coyle and others are also involved in other early phase trials sponsored or co-sponsored by CRUK NAC.

Dan Longley
Chairperson

Parallel to the long-standing and established research in the CRC arena, the group has started to expand its work in focused projects in other areas of gastrointestinal oncology, including oesophageal and gastric cancer, pancreatic cancer and small bowel cancer, building on clinical trials activity and previous research in these disease domains. The advancement of biobanking through the International Cancer Genome Consortiuum OCCAMS trial allows the collection of tissue and plasma samples to drive future translational research in oesophago-gastric cancer. Combined with the enhancement of radiotherapy practice through participation in the Neo-SCOPE and SCOPE-2 trials in oesophago-gastric cancer and the SCALOP-2 and PIONEER trials in pancreatic cancer, we seek to further develop multi-modality and personalized oncology in these disease sites. Work is also ongoing in rarer diseases of the GI tract, with a recent publication by Salto-Tellez on novel prognostic biomarkers for small bowel cancer.

Focus Group Membership:

Dr Aidan Armstrong
Professor Charles Campbell
Dr Marie Cantwell
Dr Declan Carey
Dr Mark Catherwood
Dr Helen Coleman
Dr Vicky Coyle
Dr Nyree Crawford
Dr Sonali Dasgupta
Dr Michael Devlin
Dr Philip Dunne
Dr Martin Eatock
Mrs Cathy Fenning
Dr Caroline Forde
Dr Donna Graham
Mr Ronan Grey
Professor Peter Hamilton
Dr Claire Harrison
Dr Caitriona Holohan
Dr Jackie James
Professor Brian Johnston
Professor Patrick Johnston
Dr Claire Jones
Dr Paul Kelly
Professor Mark Lawler
Mr Jack Lee
Dr Maurice Loughrey
Dr Jane McClements
Dr Simon McDade
Dr Damian McManus
Dr Stephen McQuaid
Dr Liam Murray
Dr Bode Oladipo
Dr Colin Purcell
Professor Manuel Salto-Tellez
Dr Richard Turkington
Dr Sandra Van Schaeybroeck
Dr Rich Williams
Professor Richard Wilson
Dr Shu-Dong Zhang

GENITO-URINARY AND PROSTATE CANCER

Prostate cancer is the third most common accounting for 13% of all new cancer diagnoses. Over half a million people are diagnosed with this malignancy every year in the US and Europe combined. Progression to metastatic disease occurs in around 20-30% of cases and there is a pressing need to improve detection of the disease but also risk stratification at the time of diagnosis to ensure that effective treatment is appropriately targeted. Major treatment options include radical prostatectomy and radiotherapy and Belfast is internationally recognised as a clinical and translational centre for radiotherapy for prostate cancer. The award of the Movember/Prostate Cancer UK Centre of Excellence to CCRCB in partnership with Manchester has further catalysed this work and 2015 has been a productive and successful year for Belfast.

One focus has been on the development of a molecular test to improve the stratification of prostate cancers between indolent cases and those likely to fail treatment and progress to metastasis. Professor Richard Kennedy and his team have now developed two signatures, one that predicts response to radiotherapy and other DNA-damaging agents and another which predicts progression to lethal metastatic disease. A vital component in the development of these signatures is international collaboration with clinical centres worldwide to obtain appropriately annotated samples for test validation. Both tests are now entering this phase and our partners in the Movember Centre Manchester but also beyond that in the rest of Europe are contributing to this to accelerate the ultimate clinical implementation of these findings. Dr Simon McDade is working on some of the molecular drivers for these signatures along with researchers in Professor Kennedy's team. More broadly molecular stratification and improved testing is vital to the delivery of high-quality cancer care and the leading role that Belfast plays in this work has been reflected in the two major national awards, a CRUK Accelerator Award in support of digital pathology and the announcement that Belfast is to be the UK Precision Medicine Catapult Centre for Oncology. These awards will certainly enable these and other tests to rapidly transition from the validation stage to routine clinical practice.

Radiotherapy is at the heart of prostate cancer treatment in Belfast and a comprehensive clinical and scientific research focus is on more effective delivery of radiotherapy with enhanced response and minimised toxicity. The year ended with the largest profiling study yet undertaken on responders and non-responders to radiotherapy and data analysis and reporting on this major study will take place in 2016. New forms of radiotherapy, such as Radium-223, also have had dramatic impacts on metastatic disease and there is an active programme to explore the biological basis for the efficacy of Radium-223 and further enhance its' clinical impact. Professor O'Sullivan is leading the next generation of clinical trials of this agent, including the investigator-initiated trial ADDRAD, working closely with Dr Suneil Jain and Dr Phil Turner. An ongoing MRC-funded study on toxicity due to radiotherapy (Dr Karen McCloskey) will improve the monitoring of treatment and the delivery of other forms of radiotherapy is being improved through collaboration between CCRCB and Pharmacy on the utilisation of nanoparticles.

From a clinical trials perspective 2015 has been a momentous year for the (Systemic Therapy in Advancing or Metastatic Prostate cancer: Evaluation of Drug Efficacy) STAMPEDE Trial, a multi-arm, multi-stage study bringing together Belfast and other major clinical translational centres across the UK. Major studies by the STAMPEDE groups reported significant survival benefits from combination therapy in locally advanced disease. In the coming year STAMPEDE will initiate trials arms to repurpose metabolic inhibitors beginning with Metformin and this metabolic focus may provide opportunities in the future to test other clinically approved metabolic inhibitors as sensitisers for standard therapies. Distinct from the STAMPEDE Trial, Belfast also participated in a targeted trial of Olaparib, a PARP inhibitor, reporting significant benefits for patients who had failed standard therapies and were carrying mutations in DNA-repair genes. The work of Belfast researchers on signatures predicting therapy response will enable additional trials to be designed and undertaken based on molecularly selected companion therapeutics. The Movember Centre and the other multi-centre trials structures provide exciting opportunities to accelerate this important work. The publication of a pre-clinical study showing an enhanced by prostate cancer cells carrying mutations in PTEN to ATM inhibition provides one example of how molecular stratification can inform therapeutic response and potentially trials design in the future (Dr Nuala McCabe). Complementing this study, the molecular pathology team (Professor Manuel Salto-Tellez) reported on a method to sensitively detect PTEN expression in tumour tissue using in situ hybridization and this, and other methodologies, will be implemented to complement other molecular profiling studies on treatment response cohorts which will report in 2016.

Ian Mills
Chairperson

In addition to therapeutic strategies targeting DNA-repair pathways, researchers have continued to develop programmes targeting IL8/CXCR signalling (Professor David Waugh), legumain protease (Dr Rich Williams and Dr Paul Mullan) and anti-apoptotic proteins (Dr Dan Longley). In each case these programmes have been supported by molecular profiling and motivated by the desire to use these targets to enhanced response to standard therapies. These programmes are supported by additional grant funding from the Medical Research Council, Prostate Cancer UK and the Wellcome Trust with clear strategies to progress from pre-clinical studies into clinical trials. Much however remains to be learnt about the mediators of treatment resistance in prostate cancer and new programmes are being initiated to assess the contribution of epigenetic factors, the unfolded protein response and the Type I interferon response to multi-treatment resistance prostate cancers (Dr Ian Mills, Dr Melissa Labonte-Wilson, Dr Karl Butterworth).

The year has been punctuated by focus group meetings and gatherings of the Manchester and Belfast prostate cancer research teams to discuss progress and findings. A high point of 2015 was a two-day visit by Howard Soule, the Chief Scientific Officer and Executive Vice President of the Prostate Cancer Foundation (PCF). PCF is the largest private research foundation funding prostate cancer in the world and is the designated charitable partner of the Movember Foundation in the USA. His visit provided an opportunity for researchers to present the full spectrum of prostate cancer research being undertaken in Belfast for the first-time in a single programme. His excitement and enthusiasm for the work was contagious and I feel a much more eloquent testimony to the outstanding research community that has developed here in Belfast than this attempt to summarise it. By continuing to reach out to each other, and to the global research community, 2016 will be a year to further build visibility and recognition for the outstanding research undertaken here.

Our goals continue to be:

- To promote molecularly-stratified approaches that identify high risk patients;
- To characterize novel therapeutic strategies and accompanying biomarkers for molecular stratified, high-risk groups;
- To identify increasingly effective treatments of advanced castrate-resistant prostate cancer, especially in the context of bone metastasis;
- To characterize novel therapeutic strategies and biomarkers of radio-resistant prostate cancers.

Focus Group Membership:
Dr Francesca Amoroso
Dr Chris Armstrong
Dr Karl Butterworth
Dr Mark Catherwood
Dr Catherine Davidson
Dr Sharon Eddie
Miss Dominique French
Miss Gemma Gregg
Professor Tim Harrison
Dr Simon Horn
Professor Alan Hounsell
Dr Suneil Jain
Dr Jackie James
Professor Richard Kennedy
Dr Raymond King
Dr Adrien Kissenpfennig
Dr Melissa LaBonte Wilson
Dr Dan Longley
Dr Ciara Lyons
Dr Darragh McArt
Dr Nuala McCabe
Dr Karen McCloskey
Dr Simon McDade
Dr Pamela Maxwell
Dr Paul Mullan
Dr Declan O'Rourke
Dr Sarah Osman
Professor Joe O'Sullivan
Dr Konstantin Panov
Dr Adam Pickard
Professor Kevin Prise
Miss Lorna Rainey
Professor Manuel Salto-Tellez
Dr Philip Turner
Dr Steven Walker
Dr Rich Williams
Professor David Waugh
Dr Shu-Dong Zhang

OVARIAN CANCER

Progress in the key project areas is as follows:

1) Early detection/prevention
Drs Beirne and Mullan have focused on the discovery of blood biomarkers of HGSC, as this is an area of significant need. Gene expression and DNA Methylation (DNAme) array profiling of formalin fixed paraffin embedded (FFPE) matched tissue samples from 6 cases of HGSC has been performed. Given the current consensus that the cell of origin of HGSC is actually the fallopian tubes, the tissues collected were: normal fallopian tube epithelium (FT), normal ovarian surface epithelium (OSE), serous tubal intraepithelial carcinoma (STIC), primary HGSC and omental metastases (OMT). RqPCR validation of target genes was initially performed including 14 novel secreted protein targets. Eight targets were selected to be taken forward into an ELISA-based screening experiment. Eight ELISAs were performed on a small cohort of serum samples from "normal" patients versus "HGSC" patients. They identified two targets that appear to be statistically significantly better than CA125 (routine NHS diagnostics) at discriminating "HGSC" from "Normal".

2) Novel therapeutics
Together with Almac Discovery, Professor Robson led the development of therapeutic peptide derivatives based on FKBPL's active anti-angiogenic domain. ALM201, a 'first-in-class' FKBPL-based anti-angiogenic therapeutic peptide entered phase I/II cancer clinical trials in ovarian cancer in July 2015 (EudraCT number: 2014-001175-31) at centres in Belfast, Manchester and Newcastle; early indications in a handful of patients demonstrate that the drug has no dose-limiting toxicity, with some patients showing signs of stable disease.

3) Biomarker/Diagnostic development
Richard Kennedy's group have identified and validated a biomarker for activation of the MEKK pathway in ovarian cancer and have shown that this is an important determinant of primary and acquired resistance to carboplatin-based agents. This group has also characterised a novel immune response to abnormal DNA in ovarian cancer that upregulates expression of PD-L1 and may be a determinant of response to immune-checkpointing targeted therapies.

Glenn McCluggage has been part of the last 2 WHO groups formulating the classification of Tumours of the Female Genital Tract. He has recently been involved in a group which has proposed criteria for assessment of primary site in extrauterine high grade serous carcinoma (papers in press in Gynecologic Oncology and International Journal of Gynecological Pathology).

Fiona Furlong's research focuses on the role of microRNA mediated mechanisms of chemoresistance in high grade serous ovarian cancer in which she has demonstrated that overexpression of the miR-433 microRNA mediates increase resistance to both paclitaxel and carboplatin in epithelial ovarian cancer cells. This work has led to the analysis of miR-433 and the miR-433 gene targets as biomarkers of chemoresistance in which she has screened ~500 tumour samples. She has also demonstrated that miR-433 is a critical regulator of the cell cycle in which it may have important tumour suppressor functions.

Kienan Savage's group has identified mutations in RNA splicing factors as potential biomarkers of risk for ovarian cancer. He is now collaborating with the Department of Genetics to validate these in families with familial ovarian cancer not due to BRCA1/2 mutations.

Richard Kennedy
Chairperson

4) Preclinical model system development
Niamh Buckley and Sharon Eddie have been working towards developing a number of different *in vivo* models of ovarian cancer. First they have used a modified cre/lox approach to developing a GEMM model. They can virally deliver cre recombinbase to the tissue of origin of interest into an *in vivo* model with floxed ovarian cancer specific genes (e.g. BRCA1). The advantage of this strategy over conventional promoter driven cre is that often it is very difficult to identify a tissue specific promoter that does not lead to "leaky" expression of cre and therefore gene knockout in other tissues. Furthermore, as lentivirus has a high packaging capacity, polycistronic vectors can be used to allow simultaneous overexpression or knockdown of additional genes. This can also be utilised to allow bioimaging though co-expression of luciferase or GFP.

This group have spent considerable time obtaining both Home Office and Health and Safety approval. As this is now in place, pilot studies will be starting to establish latency periods etc. In addition, they are obtaining a conventional cre/lox model whereby BRCA1 knockdown is under the control of Pax8 through our focus group collaborator, Professor Ronny Drapkin. This will provide an established model while the other viral driven model is being developed. A second approach is to use a murine derived fallopian tube cell line obtained through a focus group collaborator, Joanne Burdette. These cells can be syngeneically allografted into immune competent host allowing us to study tumour/host interactions which is not possible using human derived xenograft models. The group are also currently developing a number of isogenic lines from these cells with modulation of key ovarian cancer genes and plan to utilise these *in vivo*.

Focus Group Membership:
Dr James Beirne
Dr Paul Buchanan
Dr Niamh Buckley
Dr Elaine Craig
Dr Sharon Eddie
Dr Aya El-Helali
Dr Fiona Furlong
Professor Paul Harkin
Dr Ian Harley
Professor Tim Harrison
Dr Nuala McCabe
Dr Karen McCloskey
Professor Glenn McCluggage
Dr Sarah McKenna
Dr Joanne Millar
Professor Patrick Morrison
Dr Paul Mullan
Dr Eileen Parkes
Dr John Price
Professor Tracy Robson
Dr Kienan Savage
Professor Manuel Salto-Tellez
Dr Claire Thompson
Ms Laura Webster

ENABLING TECHNOLOGIES

DRUG DISCOVERY

Tim Harrison
Lead Investigator

The capabilities of the Drug Discovery group include:

- Medicinal chemistry expertise in hit identification, hit to lead and lead optimisation;
- Biology expertise in target validation and assay development using multiple formats;
- Fragment screening (using a range of orthogonal biophysical techniques);
- Computer aided drug design and chemoinformatics;
- Bioinformatic expertise in data mining;
- Measurement and interpretation of Absorption, Distribution, Metabolism and Excretion (ADME) and physicochemical properties of molecules;
- State of the art compound storage and data management facilities;
- Pre-clinical and clinical project management;
- International network of collaborators and outsourced service providers.

It has become increasingly clear that rather than being a single disease, cancer is a heterogeneous collection of diseases. In order to diagnose and treat cancer effectively, strategies for patient selection must be combined with the development of molecularly targeted therapeutics so that patients can receive the drug or combination of drugs which is most appropriate for the treatment of their disease, at the appropriate time. This approach necessitates the involvement of multi-disciplinary teams of basic researchers and clinicians, working within an infrastructure which allows for effective knowledge transfer.

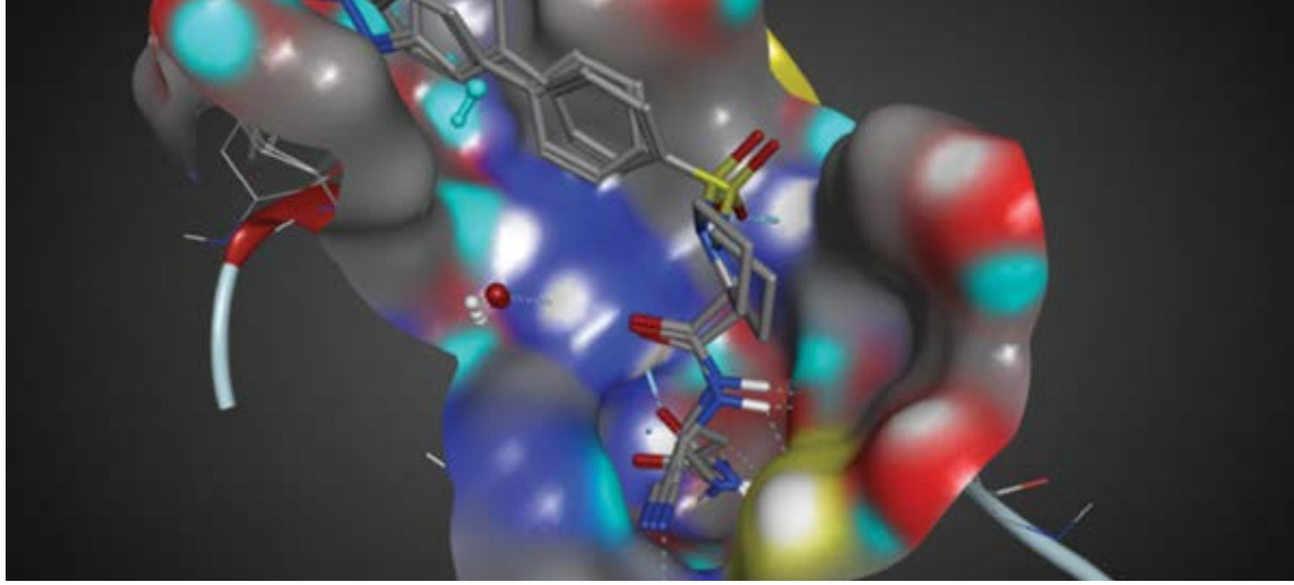
The Drug Discovery group at the Centre for Cancer Research and Cell Biology (CCRCB) integrates both academic and industrial scientists as part of a strategic collaboration between Queen's University Belfast and Almac Discovery, to facilitate the translation of basic research discoveries into products which can ultimately derive value for patients. Working in close partnership with researchers from across the University and local hospitals, as well as with external researchers, the mission of the Drug Discovery group is to identify molecular targets which are relevant to disease and to develop strategies to modulate their function. Working closely with colleagues within the Centre (which includes the Northern Ireland Molecular Pathology Laboratory and Northern Ireland Biobank), a strong emphasis will be placed on the early development of biomarkers, both to aid patient selection, and to establish that the drug is interacting with its intended target in patients.

Key to the progression of any drug discovery programme is the identification of a chemical compound (either small molecule or peptide/protein based) which can interact with the target. This drug "hit" is then optimised to provide a compound (often termed a Preclinical Candidate) which has the potency, specificity and pharmaceutical properties to interact with the target in humans at a therapeutic concentration which does not cause unacceptable side effects. This candidate molecule is further evaluated in pre-clinical development studies before progressing into clinical trials.

Research is currently focussed on the discovery of inhibitors of proteases with a specific focus on deubiquitinase enzymes and other ligases involved in the ubiquitin-proteasome system. There is also a strong interest in developing new strategies for the disruption of protein-protein interactions, focussed on the anti-apoptotic protein cFLIP and its role in therapeutic resistance. A third area of interest, which takes advantage of our expertise in peptide and protein engineering, is in the development of novel protein-based delivery vehicles for the specific targeting of therapeutic agents to tumours. Based on these drug discovery capabilities, it is anticipated that molecules will emerge that may be developable into the next generation of clinical medicines. The multidisciplinary environment within the Centre for Cancer Research and Cell Biology, itself situated within easy reach of other QUB research faculties and Clinical Centres, offers an exciting opportunity for chemists, biologists, bioinformaticians, physicists, radiographers and clinicians to combine their expertise to facilitate the drug discovery process.

CCRCB Drug Discovery Lab
(Dr Rich Williams, Academic Medicinal Chemist)

Our lab is an academic medicinal chemistry group focused on the development of small molecule protease inhibitors that are relevant in human diseases, such as cancer and Cystic Fibrosis. Working with experts in the field of both protease chemical biology and cancer biology we have developed a number of small molecule inhibitor programmes, such as the Legumain project with Dr Paul Mullan. We are also involved in the CRUK accelerator programme in structural biology with Professor Richard Bayliss (Leeds). This programme allows us to put forward nascent drug discovery projects from Queen's University that would be enhanced significantly by access to fragment screening (Beatson), protein production (Newcastle, Leicester), computational chemistry (ICR) and x-ray crystallography (Leeds, Leicester). In addition, through interactions with Professor Harrison and the Almac Discovery group we have been able to drive the identification and development of a significant number of molecular starting points for further exploration.



Legumain Inhibitor Program
(Dr Paul Mullan, CCRCB)

Research carried out in the lab of Dr Paul Mullan identified Legumain, a cysteine protease from the C13 clan, as a marker of poor prognosis in breast cancer (D'Costa, Z., et al, *Oncotarget*, 2014, 5, 1609). Further research has revealed similar findings in a number of other human cancers, such as ovarian, pancreatic and prostate cancer. Interestingly, depletion or suppression of Legumain has shown that these cancers have a significant addiction to this protease. Unlike in the cancer setting similar experiments with normal cell lines have revealed no impact upon cell viability suggesting that Legumain could be a powerful anti-cancer target that will spare human toxicity which is observed with current treatment options.

Using multiple starting points for hit finding, we have now identified potent, selective and cellular active inhibitors of Legumain with improved physiochemical properties (Higgins, C.A., et al., *Bioorg. Med, Chem. Lett.*, 2014, 24, 2521; Ness, K.A., et al., *Bioorg. Med, Chem. Lett.*, 2015, 25, 5642; Ness, K.A., et al., *Bioorg. Med, Chem. Lett.*, 2015, 25, online asap). The lead compound from this research is currently being scaled up for *in-vivo* testing in early 2016. We have also provided tool compounds from this project to research groups across the globe.

Cathepsin S Inhibitor Program
(Professors Scott (School of Pharmacy), Taggart and Elborn (Centre for Infection and Immunity)

Cystic fibrosis (CF) is an autosomal recessive disorder that is caused by mutations in both copies of the CFTR gene (Cystic Fibrosis Transmembrane conductance Regulator). CFTR is known to be involved in the secretion of bodily fluids, such as sweat and mucus. CF can affect a number of organs in the human body including the pancreas, liver, intestine and kidneys, but is mostly commonly associated within the lung. Loss of CFTR in the lung is associated a thickening of mucus and a decrease in lung function over time. Patients suffering from CF have difficulty in clearing mucus which provides an ideal bed for infections. Recent numbers published by Cysticfibrosis.org (http://www.cysticfibrosis.org.uk/about-cf) show that there are currently over 10,000 people suffering with CF in the UK alone.

Through our collaborative research into CF, we have discovered that Cathepsin S (CatS), a potent elastolytic enzyme, plays a major role in the progression of the disease in the lung. We have observed, through a number of studies using small molecule inhibitors of CatS an impact on multiple hallmarks of CF confirming CatS as a *bona fide* drug target.

We have initiated a drug development program around the identification of a small molecule CatS inhibitor that can be delivered directly to the lung. The design features of this class of compound are somewhat different to either oral or IV drugs. To aid this program through to pre-clinical development we have been working with experts in the field, such as Dr John Dixon (former head of research at AZ) and scientists in Argenta.

Cathepsin S in Cancer
(Professor Chris Scott and Dr Roberta Burden)

Recent studies have interrogated the impact of CatS with regards to the tumour microenvironment. We have identified that tumour-derived and microenvironment-derived CatS both have significant roles to play in facilitating tumour growth, through proliferation, apoptosis and angiogenesis (Small, D., et al, *Int J Cancer*, 2013, 133, 2102). Furthermore, the importance of macrophage-derived CatS has also been examined, with studies demonstrating its contribution in murine tumour model growth and more recently in mediating breast-to-brain metastasis (Gocheva, V., *et al*, 2010, 24, 241; Sevenich, L., *et al*, 2014, 16, 876).

Extensive work has been carried out to identify protease substrates in order to elucidate protease-specific roles within biological processes. We have ascertained that CatS can regulate the expression of several pro-tumourigenic factors, most notably the pro-inflammatory chemokine, CCL2. We showed that this regulation appears to occur through CatS cleavage of CD74, which in turn transcriptionally regulates CCL2 expression, through the activation of NFkB. Interrogation of patient microarray datasets has confirmed the clinical correlation between CatS and CCL2, highlighting physiological significance and strongly suggests that CCL2 may be a potential biomarker of CatS activity within disease (Wilkinson, R.D.A, et al., *Oncotarget*, 2015, 6, 29725).

MOLECULAR PATHOLOGY AND BIOBANKING

Manuel Salto-Tellez
Lead Investigator

Jackie James
Lead Investigator

Other members:
Peter Hamilton
Perry Maxwell
Darragh McArt
Stephen McQuaid

The Molecular Pathology Programme at CCRCB is at the forefront of academic Molecular Pathology and Molecular Diagnostics in the UK. It includes the Northern Ireland – Molecular Pathology Laboratory (NI-MPL), the Northern Ireland Biobank (NIB) and the Digital Pathology / Bioinformatics programme. NI-MPL is a self-contained, purpose-designed, nationally accredited (CPA / UKNEQAS) hybrid operation capable of performing molecular pathology translational research and molecular diagnostics of solid tumours. The molecular pathology diagnostic unit is a partnership between CCRCB and the Belfast Health and Social Care Trust (BHSCT).

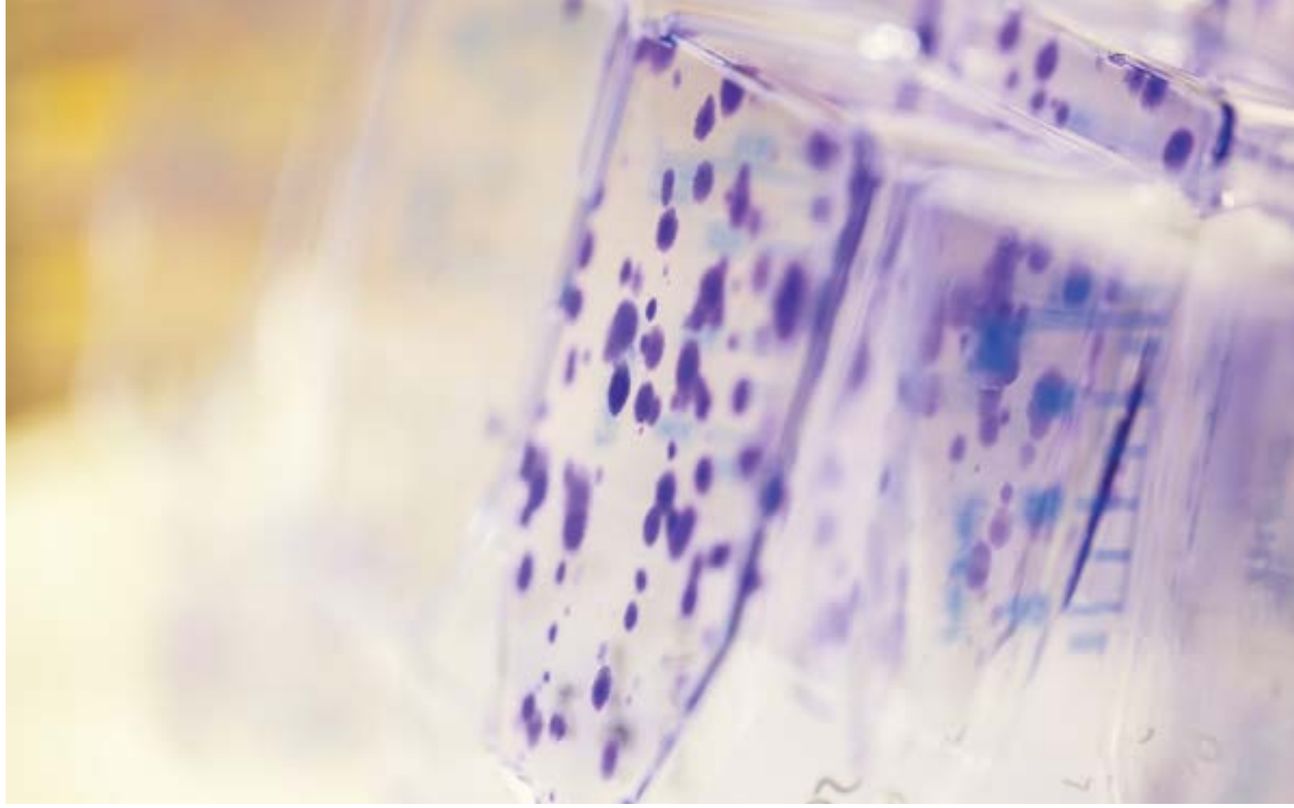
The laboratory environment ensures the proper SoPs, procedure manuals and QA/QC schemes to exercise its hybrid role. This laboratory is able to provide research support to basic scientists willing to understand the clinical relevance of their research findings, academic oncologists willing to have biomarker analysis or validation in the context of clinical trials, and all those in need of high-quality, affordable molecular diagnostic testing in oncology.

Although it is in its early days, the Molecular Pathology Programme:

- Analyses more than 1,000 samples for molecular diagnostics and more than 5,000 samples for research purposes annually;
- Is a pillar of some of the key research programmes in CCRCB (Movember, MErCuRIC, S:CORT, CRUK and ECMC Centre status, etc.) totalling almost £20M;
- Is the leading laboratory for the CRUK Accelerator programme on digital pathology and immune checkpoints (£3.9M);
- Has been instrumental in the acknowledgement of Belfast as a Centre of Excellence for Precision Medicine (Innovate UK);
- Has collaborated in some of the key industry developments in the area of molecular pathology / personalised medicine, such as the Tissue Mark Test (PathXL) and the DDRD test (ALMAC);
- Supports key clinical trials in the Northern Ireland context;
- Has generated more than 100 papers over the last 3-4 years, in key pathology journals (J Pathol, Modern Path) and general cancer and biology journals (CCR, CR, JNCI, Mol Cell, Oncotarget, EMBO MM);
- Leads a new teaching programme for routine pathologists in molecular pathology.

Molecular Pathology research in Belfast involves academics at QUB and clinicians within the BHSCT Tissue Pathology laboratories and is underpinned by the Northern Ireland Biobank (NIB). The NIB is funded primarily by the Health and Social Care (HSC) Research and Development (R&D) Division of the Northern Ireland Public Health Agency; it is also supported in part through the CRUK Centre grant, Prostate Cancer UK and a local charity, the Friends of the Cancer Centre.

The Northern Ireland Biobank (NIB) is a member of the International Society for Biological and Environmental Repositories (ISBER) and works closely with the UKCRC Tissue Directory and Coordination Centre. It participates in the UK Confederation Of Cancer Biobanks Standards Programme and will seek to become ISBER compliant during 2016.



The NIB enhances translational cancer research through the quality assured targeted collection of tissues and bodily fluids (including normal and tumour tissues and blood samples) all linked to reliable clinical and pathological data sets. The ability to apply for samples from the NIB has been active since August 2011; as of January 2016, the NIB has processed over 190 researcher applications and has distributed over 27,000 samples to 110. The NIB has recently put in place a robust infrastructure to complement ongoing targeted collections with additional tissue collections associated with phase I-III trials run in the Belfast Experimental Cancer Medicine Centre.

The NIB is supported by a secure, information management system. A close working relationship exists between the NIB and the NI Cancer Registry to ensure all samples processed for the bank are linked with robust de-identified clinical and pathological information collected from state of the art data repositories.

Further information about the NIB can be found at www.niobiobank.org. Researchers wishing to access samples can do so via the online application system www.nibiobank.qub.ac.uk/nibresearcher.

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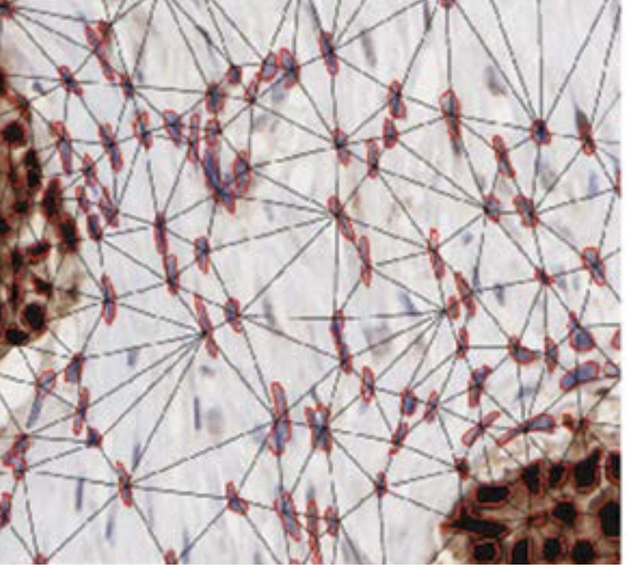

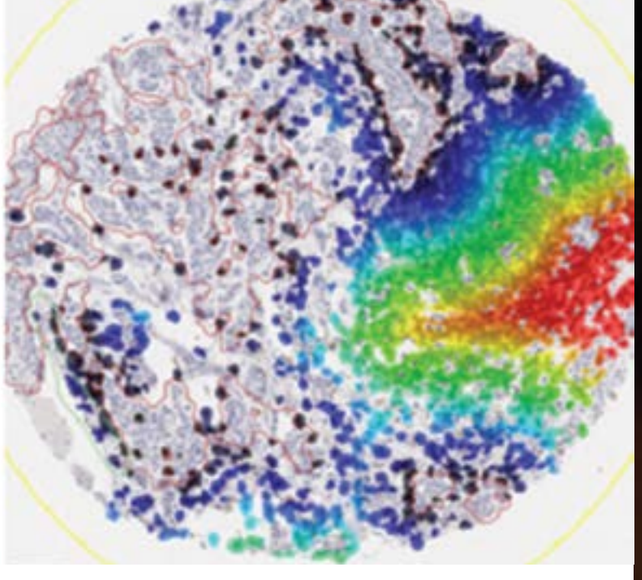

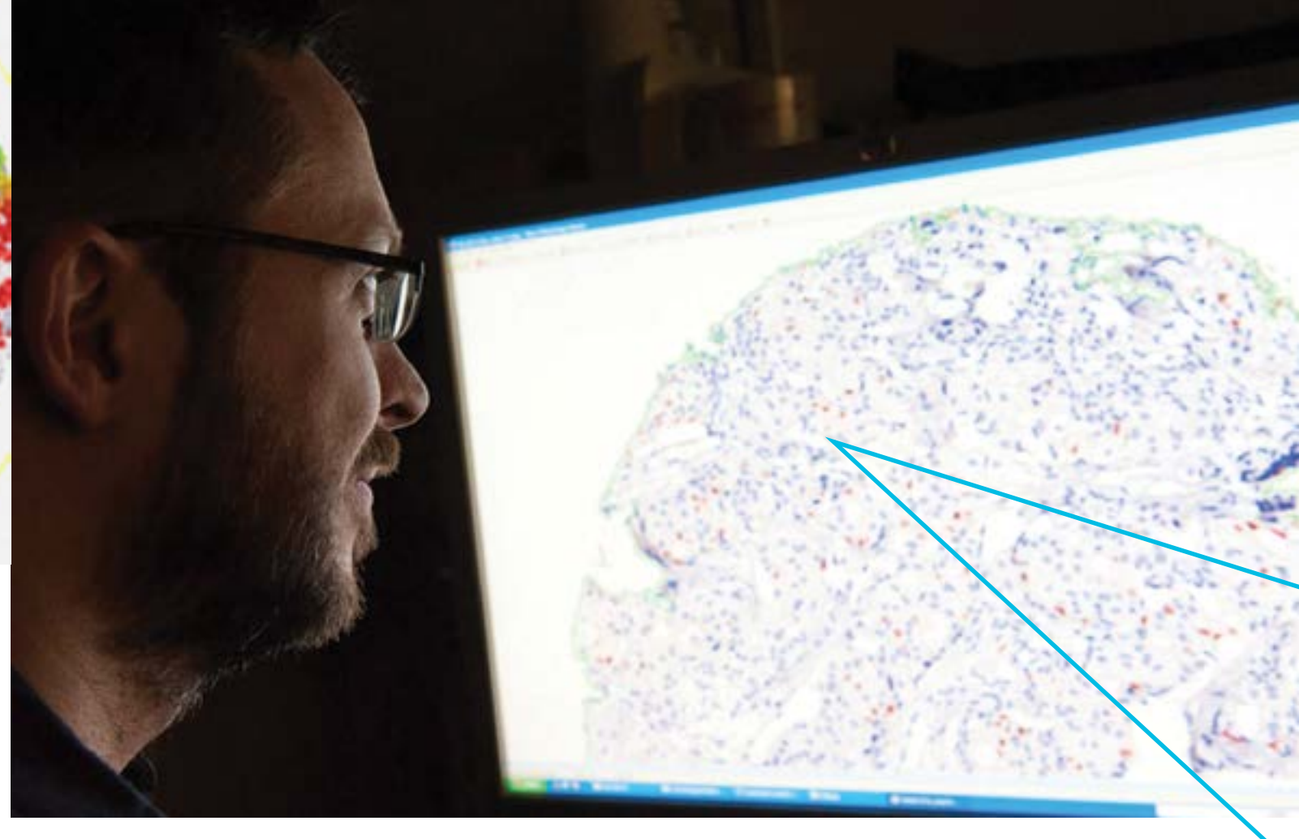

TRANSLATIONAL BIOINFORMATICS AND IMAGING

The Cancer Bioinformatics and Imaging group consists of scientists with expertise across a broad spectrum of subjects including Computational Biology, Computer Vision, Machine Learning, Data Integromics, Systems and Network Biology. The group is leading on high-throughput big data analysis in cancer genomics, molecular oncology and tissue pathology for molecular diagnostics and precision medicine. With a focus on solid cancers, they provide a vital key in deciphering the complex genomic and phenotypic landscape of cancer, and in identifying prognostic and predictive biomarkers. This is strongly allied to the rapid developments in molecular pathology and the translation of new genomic and tissue-based tests into practice. Digital pathology, image analysis and tissue informatics provide important technologies to support high throughput computerised analysis of solid tumour tissue samples and to understand the complex interplay between genotype and phenotype.

The aim of the group is to lead internationally on the development of novel computational and statistical methods in the analysis of genomic and image data, and to support interdisciplinary collaborative research by working closely together with biologists, oncologists and pathologists within the Centre for Cancer Research and Cell Biology (CCRCB).

Key research areas include:

- Computational biology and biostatistics;
- Pathway analysis, causal inference of regulatory networks, and integration of genetics and genomics data;
- Digital pathology, tissue imaging, image analysis and tissue biomarker discovery;
- High-throughput analysis of genomic and image data;
- Quantitative methods in linking genomes to targeted therapeutic compounds;
- Data "Integromics";
- The development of new computational methods and their application to translational cancer research.

Next generation sequencing and genomics
Using the high-throughput sequencing platforms centred within the Northern Ireland Molecular Pathology Laboratory (NI-MPL), we generate a wealth of data across a range of cancer specific projects. Using the latest analytics software, in-house algorithms and novel high performance computing architectures, research is undertaken across a range of solid cancers including prostate, breast, gastrointestinal and brain tumours. Key hypotheses are generated and tested with the aim of generating novel genomic biomarkers and multivariate signatures for cancer diagnostics and prognostics.

Data Integromics and PICAN
Through collaboration with the Northern Ireland Biobank (NIB), NI-MPL and Digital Pathology, the Cancer Informatics team have also developed a novel bioinformatics integration platform called PICAN (Pathology Integromics in Cancer) for the management of clinical, phenotypic and genotypic data from cancer tissues. This allows novel but complex biomarker signature analysis across large numbers of tissue samples. Recent initiatives aim to build new compute architectures and big data pipelines to enhance data search and accelerate biomarker discovery in cancer genomics.

Peter Hamilton
Lead Investigator

Tissue Imaging, QuPath and Immuno-oncology algorithms
The group has a strong interest in tissue and biomarker imaging and works closely with the NI-MPL and the NIB to drive innovative solutions in cancer research. We have established one of the most extensive digital pathology laboratories in the UK, with scanning technologies, image and tissue microarray (TMA) management software, along with image analysis software for quantitative biomarker discovery, validation and translation. Expansion of this capability will be possible through a recent £3.9m grant as part of the CRUK Accelerator programme. We have developed QuPath – a sophisticated image analysis platform for the high resolution analysis of tissues and cells. This is now supporting a wide range of cancer biomarker imaging programmes within the Centre and is allowing us to develop novel approaches to quantifying immune cell response in cancer patients, as powerful prognostic and predictive markers in disease.

This strong track record is underpinned by strong industrial links, primarily through PathXL Ltd which was spun out from these activities and is now a leading digital pathology software company with customers worldwide. It has been working closely with the group on automated tumour identification using image analysis and has established TissueMark™ as a leading software platform for tumour markup and analysis in molecular diagnostics and next generation sequencing.

Educating the next generation of bioinformaticians
Finally, the group takes a leading role in the education, training and mentoring of students, staff and scientists to provide them with a deeper knowledge and understanding of modern methods in bioinformatics, computational biology and tissue imaging. This includes a comprehensive MSc course in Bioinformatics and Computational Genomics aimed at establishing the next generation of bioinformaticians and equipping researchers with the tools necessary to drive discovery in genomics, molecular diagnostics and translational cancer research.

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NORTHERN IRELAND CANCER TRIALS CENTRE AND NETWORK

Until the establishment of the Northern Ireland Cancer Trials Network (NICTN) in 2007, cancer clinical trials had been conducted in Northern Ireland, but were predominantly co-ordinated and conducted in central Belfast, with only a few trials being conducted in isolation at the four Cancer Units spread across the province. Today, the Northern Ireland Cancer Trials Network (NICTN) aims to deliver the highest quality and standard of care to cancer patients across Northern Ireland through leading edge clinical and translational research. The NICTN Coordinating Centre (NICTN CC) based at the NI Cancer Centre acts as an enabling technology within CCRCB at QUB and facilitates the early phase and translational research activities of the Belfast Experimental Cancer Medicine Centre (ECMC) and all clinical and translational research activities of the Belfast Cancer Research UK Centre. Belfast is one of 18 Experimental Cancer Medicine Centres (ECMC) and one of 15 Cancer Research UK Centres within the UK.

Role of NICTN:

- To co-ordinate and promote cancer clinical trials, and run the full range of first-in-human phase I to phase IV trials, along with genetic epidemiology, questionnaire, quality of life, translational and other high quality studies. Clinical trials can be designed locally (investigator-initiated) or adopted as part of a multi-centre study. Investigator-initiated trials often involve collaboration with other academic groups within local universities or hospitals;
- To act as the co-ordinating centre for the NICTN responsible for the co-ordination of cancer clinical trial and translational research activity throughout Northern Ireland, particularly phase III trials and epidemiology studies;
- To manage an academic early phase clinical trials unit running a portfolio of Cancer Research UK, commercial, academic and local investigator-initiated experimental cancer medicine studies including phase I, II and translational trials.

Performance

Over the period of this report, our target recruitment of at least 10% incident cancers was exceeded (target number 850) with 1409 participants, or 16.6% of incident cancers (excluding non-melanoma skin cancer) being recruited into 87 cancer clinical trials and other adopted clinical research studies. Interventional trials recruited 218 participants (2.6%) compared to our target of 7.5%; a reflection, in part, of interventional trials becoming more molecularly targeted resulting in larger numbers of patients having to be screened to identify niche populations of eligible patients. Delivery of cancer trial activity again mapped against our Cancer Services in Northern Ireland with 66% of overall recruitment activity being delivered at the regional Cancer Centre in Belfast. Cancer Unit activity at the other four Trusts contributed 34% of regional recruitment activity. Although recruitment was to a wide range of studies covering most disease areas, recruitment to urology, breast and haematology cancer clinical trials far exceeded other disease areas accounting for 65% of the overall annual recruitment. Recruitment to non-disease site specific trials accounted for 28% of our annual regional recruitment activity and was the main recruitment activity reported by the Cancer Units.

NICTN gratefully acknowledges the funding received from the Northern Ireland Health and Social Care Research & Development Division, Friends of the Cancer Centre, Cancer Research UK, Leukaemia and Lymphoma Research TAP and Prostate Cancer UK.

Richard Wilson
Lead Investigator

EDUCATION AND TRAINING

CLINICAL ACADEMIC TRAINING PROGRAMME

The Clinical Academic Training Programme (CATP) at Queen's University Belfast was established in conjunction with the Northern Ireland Medical and Dental Agency (NIMDTA) and the Belfast Health and Social Care Trust in 2008 to provide a unique opportunity for highly motivated individuals who want to excel in both clinical and academic training.

The three programmes available are: **Academic Foundation (AF2)** – a four month placement which enables the trainee to gain insights into clinical academic medicine at an early stage through regular interaction with academic clinical supervisors and scientific staff. The **Academic Clinical Fellow (ACF)** is targeted at doctors in the early years of specialty training. This is a two-year funded programme, attracts a National Training Number (academic), and allows the ACF to develop academic skills simultaneously with specialty clinical skills. This academic training environment is aimed at helping the ACF prepare a competitive application for a training fellowship to undertake a higher degree. The **Academic Clinical Lecturer (ACL)** post offers exciting opportunities for aspiring trainees who are considering a career in clinical academic medicine. These posts are designed for doctors who have already obtained a higher degree. Trainees will finish their clinical training while continuing academic development at post-doctoral level.

The CATP Committee oversees the academic progression of the trainee in ACL, ACF and AF2 programmes. The CATP Committee is comprised of members from the School of Medicine, Dentistry and Biomedical Sciences at Queen's University Belfast, NIMDTA and the Belfast Health and Social Care Trust. The Committee approves and appoints supervisors and allocates trainees to the appropriate Research or Education Centre within the School of Medicine, Dentistry and Biomedical Sciences. Progress is reviewed at the end of each AF2 placement and at six monthly intervals for the ACF and ACL trainees.

In CCRCB we have successfully had trainees on all levels of the Clinical Academic Training Programme and the current trainees within the Centre are listed in the table below.

For further information on the Clinical Academic Training Programme contact the Programme Administrator, Ms Valerie Reid (v.reid@qub.ac.uk), School of Medicine, Dentistry and Biomedical Sciences.

Programme	Name	Period
AF2	Henry, Aimee (Supervisor: M McMullin)	2 December 2015 - 1 April 2016

POST DOCTORAL PROGRAMME

In addition to the training of PhD students, CCRCB is a major Centre within the School of Medicine, Dentistry and Biomedical Sciences for further research training and career development. It attracts researchers from the UK, Ireland and across the world due to the breadth and quality of the research, and the emphasis on international and cross-disciplinary collaborations. Researchers at all stages of their career development benefit from the very active programme of seminars and internal research meetings and the availability of courses to learn key scientific and complementary skills. Our aim is to continue to attract enthusiastic scientists and clinicians to work with our established staff and to draw on their experience and also to independently generate new ideas in a stimulating research environment.

Central to the post-doctoral programme within the Centre is a weekly seminar programme at which Post-Doctoral Research Fellows present their work to their peers and colleagues and gain skills in introducing speakers and leading questioning.

As part of encouraging active career development for our post-doctorate, we also run a mentoring scheme within the Centre which aims to take forward a small group of post-docs and assist them with preparing applications for fellowships to be held at CCRCB or elsewhere. This is supported by Staff Training and Development Fellowship workshops. Currently several post-docs are in the CCRCB Fellowship mentoring programme, and several fellowship applications have been submitted to funders including CRUK, the MRC, EU and Breast Cancer Now. In the last few years, several prestigious fellowships have been awarded to post-docs on the mentoring programme, and several post-doctoral researchers have been successful in obtaining faculty positions.

The Centre's post-doctorate continue to be major players in the School-wide Post-Doctoral Society. Initially setup by members of CCRCB, the committee is currently chaired by Dr Sharon Eddie Parkinson. The Society acts as a forum to provide a voice for the postdoctoral community within the School and to promote opportunities for career advancement, personal development and social interaction. The society holds an annual symposium featuring both scientific presentations from the postdoctoral body and career-focussed talks from invited speakers. The next symposium will be held in Riddel Hall on 11 March 2016.

Throughout the period covered by this report, a number of our postdoctoral fellows obtained awards for their academic achievements, some of which are highlighted below:

- Dr Kirtiman Srivastava was awarded the Roche Prize for 2015 and was presented with a medal and cheque for £400. His winning presentation was based on his publication in Oncotarget entitled: 'p63 drives invasion in keratinocytes expressing HPV16 E6/E7 genes through regulation of Src-FAK signalling.'
- Dr Peter Bankhead was awarded joint first place in the Cancer Research category at the All Ireland Cancer Consortium Conference in May 2015 for his poster presentation entitled 'QuPAth: A general framework for visualisation and quantification of tissue biomarkers in whole slide images.'
- Dr Lisa Crawford received a UK Myeloma Forum (UKMF) travel award to present her work at the International Myeloma Workshop in Rome in September 2015 with an associated invited talk at the UKMF Scientific Day in November 2015.
- Dr Philip Dunne was awarded the Proffered Oral Presentation prize based on his work on tumour cell invasion at the IACR Annual Meeting held in Limerick on 26 - 27 February 2015.
- Dr Mihaela Ghita was awarded a Young Scientist Travel Award to present her work at the 12th International Workshop on Microbeam Probes of Cellular Radiation Response held in Tsuruga, Japan, on 30 May - 1 June 2015.
- Dr Kerry Hughes and Dr Rich Williams were awarded £3,400 from the Royal Society of Chemistry's Outreach fund to carry out chemistry outreach activities for schools and events with the centre.
- Dr Kyle Matchett was awarded the inaugural Professor John Fitzpatrick Prize for the Best Oral Poster Presentation at the IACR Annual Meeting held in Limerick on 26 - 27 February 2015.

Dan Longley
Associate Director for Post-Doctoral Studies

SEMINAR PROGRAMME

An important aspect of our work and success is the Centre's seminar programme which provides an opportunity to talk about our research and share ideas with colleagues. We have a post doctoral seminar programme where each week the post doctoral research fellows present and discuss their work with colleagues in other research groups within the Centre. In addition we have an external seminar programme (advertised on our website www.qub.ac.uk/ccrcb) in which we host guest speakers to encourage collaborations and interactions with other research institutions.

Our distinguished **Mitchell Lecture**, which was initiated in 2007 and is held annually to honour the previous Chancellor of Queen's University Belfast, Senator George Mitchell, for his enormous contributions to the University and the wider community, took place on 5 March 2015. The lecture was given by Professor Lisa Coussens from the Oregon Health and Science University. Professor Coussens' talk was entitled "Inflammation and Cancer: Good Cells Behaving Badly."

This year's prestigious **CRUK Lecture**, held annually as part of the Belfast Cancer Research UK Centre initiative, was delivered on 10 December 2015 by Professor Richard Marais, CRUK Manchester Institute. Professor Marais' talk was entitled "Precision Medicine in Melanoma."

The following external seminars were held during the period of this annual report:

Dr Markus Rehm,
Royal College of Surgeons in Ireland
"Cell death regulation - Mechanistic insight and translational applications";

Professor Carol Mackintosh,
University of Dundee
"Cancer and diabetes as disorders of the 2R-signalling networks that shaped vertebrate evolution";

Dr Cassio P de Campos,
Queen's University Belfast
"Learning Graphical Models with Biomedical Applications";

Dr David Gonzalez de Castro,
The Institute of Cancer Research
"Genomic cancer medicine: work in progress";

Professor Esther Baena,
Cancer Research UK Manchester Institute,
University of Manchester
"Understanding prostate cancer biology as a route to novel therapeutics";

Dr Shahram Kordasti,
King's College London
"From Trex to Tregs; the immune response in bone marrow failure syndromes";

Dr Andrea Pellagatti,
University of Oxford
"Interconnections among mutations, gene expression, clinical variables and outcome in patients with myelodysplastic syndromes";

Professor Robert W. Sobol,
University of South Alabama
Mitchell Cancer Centre
"Base excision repair, ADP-ribosylation adn NAD metabolism: A convergence of processes to maintain the genome";

Professor Lisa Coussens
2015 Mitchell Lecture Speaker

Professor Eric O'Neill,
University of Oxford
"Genomic instability in sporadic solid malignancies - epigenetic silencing of RASSF1A and BRCAness in cancer";

Professor Ian Tomlinson,
University of Oxford
"Ultramutator cancers, predisposition and pathogenesis";

Dr Patricia Muller,
University of Leicester
"How do mutations in p53 turn a tumour suppressor into an oncogene?";

Dr David Clark,
Argenta Discovery Services / Charles River
"Charles River: Drug Discovery Support for Academic Groups";

Professor Jim Huntington,
University of Cambridge
"In Search of the Holy Grail: An Antithrombotic that doesn't cause Bleeding";

Professor Timothy Humphrey,
University of Oxford
"Chromosome breaks, chromatin and cancer";

Professor Vincenzo D'Angiolella,
University of Oxford
"Insights into the regulation of Ribonucleotide Reductase (RNR) during the cell cycle and the DNA damage response";

Professor Christian Ottensmeier,
University of Southampton and Southampton University Hospital
"Cancer Immunotherapy: Head and Neck cancer as a clinical model";

Dr Aude Echalier,
University of Leicester
"Targeting the ubiquitin system: the Cullin RING E3 ubiquitin ligases";

Professor Steven Narod,
University of Toronto
"The Treatment of Hereditary Breast Cancer";

Dr Francois Paris,
University of Nantes
"New radiobiology dedicated to hypofractionnated radiation therapy";

Professor Richard Edmondson,
University of Manchester
"DNA damage repair as a stratification tool for the treatment of ovarian cancer";

Dr Pradip Majumder,
Mitra Biotech
"Predicting clinical response to anticancer drugs using CANScript - an ex vivo platform that captures patient tumour heterogeneity";

Professor Jean-Baptiste Cazier,
University of Birmingham
"WGS500, 1KG, UK10K, 1M Projects: The Reality of Translating NGS Research to Clinical Applications";

Dr Laura Marcu,
University of California
"Fluorescence Lifetime Techniques: Benchtop to Operating Room";

Professor Jessica Downs,
University of Sussex
"Protective packaging for DNA: chromatin and the maintenance of genome stability";

Dr Matt Smalley,
Cardiff University
"Wnt and Erbb2 signalling interact to determine tumour phenotype in a mouse model of HER2 breast cancer";

Professor David Beech,
University of Leeds
"Calcium entry and non-selective cationic channels: should cancer biologists and oncologists be interested?"

CCRCB Postgraduate Symposium winners Niamh McGivern, Peter Gilliland and Stephanie Craig with Associate Director for Postgraduate Studies Professor Mark Lawler.

POSTGRADUATE PROGRAMME

Our Postgraduate Training Programme in CCRCB provides an enriched environment for incoming clinical fellows/scientific graduate students to perform high quality research and to achieve their career goals. It combines scientific rigour with appropriate skills development opportunities to empower our students to perform excellent research for publication in international peer review journals and to acquire new skills sets to advance their careers.

2014-2015 was an excellent year for the CCRCB Postgraduate Programme with a significant increase in the number of postgraduate students since 2011-2012. A total of 13 new PhD students started their research in the Centre. Currently, we have 56 postgraduate students in CCRCB (66% female/34% male) with over 26% EU/ international students, reflecting our commitment to QUB's internationalisation agenda. Funding of our evolving **Doctoral Training Programme in Precision Cancer Medicine** is achieved through the Department of Education and Learning, and from competitive grant funding through Research Councils, charities, the European Commission and other funding sources. In addition, we provide opportunities for self-funding students to undertake research in the Centre. Self-funding candidates are invited to discuss their research project preferences and supervisory team at the time of application, to ensure that their research interests and career development are best addressed.

The Research Project is the fulcrum of the Postgraduate Programme with the student undertaking internationally competitive research under the direction of one of the 38 Principal Investigators within the Centre. All students are assigned a Primary and a Secondary Supervisor for the duration of their PhD. Students are encouraged to present their research at national/international conferences, which not only expands their research experience but also provides an opportunity for networking for future career opportunities. Where appropriate, students also undertake short visits to collaborators' laboratories in the UK, Europe, the USA or other international centres, in order to advance their research and knowledge. Communicating science to both peer and lay audiences forms part of our training programme, with specialist training available for participation in public engagement events.

We are dedicated to providing an overarching skills and career development programme as part of our postgraduate offering. In pursuit of this goal, incoming PhD students this year undertook two modules, Cancer Biology and Translational Cancer Medicine, which provided the expert skills and knowledge that can contribute both to their PhD and their developing career. Further career development skills modules are planned as we continue to develop a premier Doctoral Training Programme in Precision Cancer Medicine.

Mentoring of students is achieved through a combination of an Annual CCRCB Symposium for each PhD cohort and an Annual Progress Review (APR), which also ensures that students are "on track" for the timely completion of their PhD. Winners of the Oral Presentation awards in 2014-2015 at the Annual CCRCB Symposia were:

1st Year PhD: Stephanie Craig (Supervisors: Dr Jackie James, Dr Simon McDade)
2nd Year PhD: Peter Gilliland (Supervisors: Dr Rich Williams, Dr Sandra Van Schaeybroeck)
3rd Year PhD: Niamh McGivern (Supervisors: Dr Paul Mullan, Dr Richard Kennedy)

Mark Lawler
Associate Director for Postgraduate Studies

Our students also participated in the School of Medicine, Dentistry and Biomedical Sciences' Postgraduate Education and Research Forum, which took place at Riddel Hall. As part of this Forum, there was a "3-2-1" style series of oral presentations and a poster presentation session.

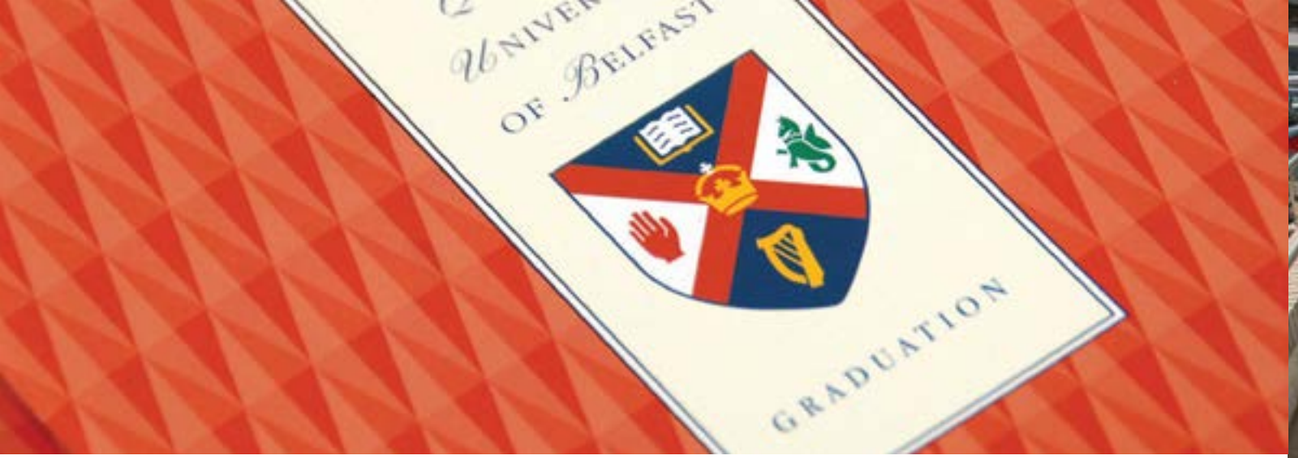
Alexander McIntyre (Supervisors: Dr Simon McDade and Dr Dan Longley) won overall first Prize in the 3-2-1 presentation sessions while Luke Humphreys (Supervisors: Dr Dan Longley and Professor Richard Kennedy) secured the first prize in the poster session.

In addition to the leadership role that CCRCB has taken in the development of the Postgraduate Research and Education Forum, CCRCB has also demonstrated significant leadership in the newly developed Masters of Research (MRes) in Translational Cancer Medicine (http://www.qub.ac.uk/schools/mdbs/pgd/PT/MRes/). Sixteen students are undertaking the Precision Cancer Medicine stream of the MRes in Translational Medicine Programme in 2015-2016.

A number of our postgraduate students have received awards during the period of this report:

- Mr Matthew Alderdice was awarded the Teenage Cancer Trust Stephen Sutton Prize (first prize) at the NCRI 2015 Annual Conference in Liverpool for his paper entitled 'Natural Killer Cell-like signature observed in locally advanced rectal cancer after neoadjuvant chemoradiotherapy in a tumour regression grade dependent manner.'
- Miss Kathryn Clarke was awarded a prize for her oral presentation entitled 'Integrated analysis of both biological and molecular effects of the epigenetic modifying agent Romidepsin in MDS/AML', presented at the All Ireland Cancer Consortium Conference in Belfast in May 2015.
- Miss Dominique French and Miss Emma Waring were awarded prestigious Scholars in Training Awards from the US Radiation Research Society to present their work at its annual meeting being held in Weston, Florida, USA in September 2015.
- Miss Laura Kettyle was awarded best poster presentation for 'Differential HOXA Dependency in Normal and Leukaemic Haematopoiesis' at the School of Medicine, Dentistry and Biomedical Sciences Postdoctoral Society Symposium (SMDB PS) in March 2015. In addition Laura was awarded best oral poster presentation for 'Criticality of the Hoxa cluster in novel models of MLL-AF9' at the Cancer Translational Research Group (CTRG) conference in September 2015. Laura was also awarded best poster presentation for 'Criticality of the Hoxa cluster in novel models of MLL-AF9' at the Haematology Association of Ireland (HAI) conference in October 2015.
- Dr Eileen Parkes was awarded a Dr Gary McGowan Friends of the Cancer Centre Scholarship of £2000. This annual award is given in memory of Dr McGowan, an oncology registrar who died in 2010.
- Dr Philip Turner won best complex case presentation at the All Ireland Annual Radiation Oncology Update Meeting which took place in April 2015 in Cork.

An exciting new initiative in 2015 involved the announcement of a joint **CCRCB-NCI Doctoral Training Programme in Precision Cancer Medicine** with the world renowned National Cancer Institute in Washington, USA. This initiative provides Queen's PhD students with the unrivalled opportunity to perform their research at the NCI, allowing them to produce excellent science in a premier international institution. The first participants will take up their positions in this prestigious programme in late 2016.



SUMMARY OF THE POSTGRADUATE DEGREES AWARDED

Chris Armstrong, PhD
July 2015
Inhibition of treatment-induced cell survival signalling enhances radiosensitivity of PTEN-deficient prostate cancer

Emma Arnold, MD
July 2015
Intracellular signalling pathways in Myeloproliferative neoplasms

Eliana Barros, PhD
July 2015
Transcriptional role of BRCA1 in the DNA damage response

Conor Bradley, PhD
December 2015
The role of the JAK1/2-STAT3 signalling pathway as a key mediator of drug resistance in early stage colorectal cancer

Laura Campbell, PhD
July 2015
Identification of the genetic contexts underpinning CXCL8 potentiation in colorectal cancer and characterisation of its role in tumour progression

Robert Carson, PhD
December 2015
Targeting oncogenic BRAF in colorectal cancer

Lynsey Chatham, PhD
December 2015
Studies of SEPT6 Expression

Conor Hanna, PhD
July 2015
The Radiation Targeting of PTEN - Deficiency in Castration - Resistant Prostate Cancer in Combination with Modulations of DNA Damage Repair

Laura Kettyle, PhD
December 2015
Criticality of the HoxA cluster in normal and malignant haematopoiesis

Gemma Logan, PhD
July 2015
An investigation of the role of Ankyrin Repeat and SOCS Box Proteins (ASBs) in normal and malignant haematopoiesis

Niamh McGivern, PhD
December 2015
Identification of Novel Therapeutic Approaches for Clear Cell Ovarian Cancer

Michael Moran, PhD
July 2015
HPV-related Oropharyngeal Squamous Cell Carcinoma in Northern Ireland: A molecular and population based study

Jessica Neisen, PhD
July 2015
Chemokine regulation of microenvironment - enhanced invasion in prostate cancer

Christine Young, PhD
December 2015
Identification of activated pathways following epigenetic combination therapies in myeloid leukaemia cell lines

CCRCB's 2015 Summer Research Students

UNDERGRADUATE PROGRAMME

The role of Associate Director for Undergraduate Studies is to coordinate and link the CCRCB teaching contribution to the various activities in the School Education Centres. CCRCB researchers coordinate and lecture on a range of biomedical, medical and dental modules across all levels of the undergraduate courses.

Thirty six Biomedical Science Level 3 students and Intercalated students undertook laboratory research projects within the CCRCB. Other students were supervised for their literature review module including one by Bronagh McCabe on repurposing drugs for blood cancer that was published in the Annals of Hematology. The CCRCB also hosted students from the School of Biological Sciences for their 46 week placements and these projects have also contributed to recently published research articles.

The successful "Research Discovery Days" for 1st and 2nd year students, in collaboration with the Biomedical Education Centre, were continued. These enabled the students to be introduced to the CCRCB research themes and the focus groups' research activities. The students also benefit from discussion with a research mentor who can discuss specific topics in more depth and address options for future careers.

The CCRCB Summer Research Programme continues to be a popular and successful scheme supported by a variety of funding sources including the School of Medicine, Dentistry and Biomedical Sciences, CCRCB, Centre for Biomedical Education, Centre for Dental Education, Queen's Foundation, Leukaemia & Lymphoma NI and Almac Diagnostics. The programme provides an opportunity for aspiring research scientists to undertake a short laboratory based research project for eight weeks over the summer period. The students benefit from learning laboratory techniques, data analysis and interpretation and are required to write a research report and present their work at a CCRCB summer student symposium. The popularity of the CCRCB programme is reflected in over 115 applications for the 23 studentships that were awarded to dental, medical or science students from QUB, Ulster University, Cambridge University, Limerick College of Technology, Córdoba University in Spain and Krems University in Austria.

Details of all the Undergraduate Education Programmes offered within the School of Medicine, Dentistry and Biomedical Sciences can be found at www.qub.ac.uk/schools/mdbs/students.

Ken Mills
Associate Director for Undergraduate Studies

PUBLIC ENGAGEMENT ACTIVITIES

PUBLIC ENGAGEMENT ACTIVITIES

The role of CCRCB's engagement activities is to share our pioneering research – and its impact on prevention, diagnosis and care in the future – with people across Northern Ireland. In this section we highlight the successes of our engagement programme during 2015.

Public engagement is central to the Belfast CRUK Centre strategy – it brings to life the ground-breaking research taking place at CCRCB and builds support for this work within the local community. Our researchers are the key to all our engagement work, regularly talking to people about their projects, hosting interactive lab tours, and volunteering their time outside work hours to help with public events and fundraising activities.

CCRCB is part of the Belfast Cancer Research UK Centre – one of 15 Cancer Research UK (CRUK) designated Centres of Excellence across the UK. This virtual Centre encompasses a network of scientists, doctors and nurses based at the Northern Ireland Clinical Trials Centre and the five Cancer Units located in hospitals across the region, as well as the CCRCB and the Centre for Public Health. The Centre brings doctors, scientists and nurses closer together so that developments in cancer research can be taken swiftly from the bench to the bedside.

Other charities provide funding to CCRCB and also contribute to our public engagement activities and outreach programmes. For example, CCRCB regularly welcomes supporters and volunteers of local charities such as Leukaemia & Lymphoma NI, Prostate Cancer UK, Friends of the Cancer Centre, Cancer Focus NI, Brainwaves NI and others.

Raising the profile of research engagement within the centre
The CCRCB Engagement Committee which was established in 2014 has continued to grow and has improved communication of centre activities to all staff, and been instrumental in the development of engagement activities targeting new audiences. The Committee has managed several events over 2015 such as NI Science Festival and the CCRCB Open Day. It has also identified future training needs which will be delivered in 2016.

Bringing local research to life
People who have supported CRUK and others interested in local cancer research are regularly invited to the CCRCB to hear about our work from the researchers themselves. Our researchers lead groups on interactive tours of the laboratories – bringing local research to life and explaining the impact their work could have on cancer detection and treatment in the future. In 2015 over 200 people took part in these lab tours, and an additional 360 people participated in other events in the Centre.

Our researchers also take time to attend community events where they talk to people about our work. Our researchers volunteered at over 30 events this year, including the CRUK Race for Life in Belfast, a range of events targeting young people, and a number of community events throughout NI. Altogether there were over 700 people engaged at events outside the centre across the community.

CCRCB Open Day
We were delighted to welcome 350 guests on Saturday 9 May 2015 for our first ever CCRCB Open Day.

This was a unique opportunity for members of the public to meet our researchers, go behind the scenes in our labs and find out more about cancer research happening every day in Belfast. Our guests had the opportunity to participate in 12 lab tours or go to any of the 18 talks and chats running on the day. The feedback we received was overwhelmingly positive and the next Open Day is planned for October 2016.

Cancer awareness and prevention
Prevention and early diagnosis messages are important in the efforts to beat cancer sooner. During 2015, the CRUK Senior Research Nurse and other Research Nurses attended 10 health events, raising awareness of the signs and symptoms of cancer and healthy lifestyle factors.

About the Belfast Cancer Research UK Centre
The Belfast CRUK Centre is a partnership between Cancer Research UK, Queen's University Belfast, the Health and Social Care Research and Development Division of the Northern Ireland Public Health Agency, and the Belfast Health and Social Care Trust.

The Centre's public engagement strategy is delivered by Caroline Crothers, Cancer Research UK's Research Engagement Manager, who is based in the CCRCB. She manages the CCRCB Engagement Committee and works closely with researchers to identify opportunities to promote our research to a wide audience throughout Northern Ireland.

If you want to find out more about our public engagement programme, please email caroline.crothers@cancer.org.uk or ring 07900 748418.

STAFF LISTING

NEW APPOINTMENTS

Ian Mills
Reader in Translational
Prostate Cancer Biology

Dr Ian Mills was appointed as a Reader in Translational Prostate Cancer Biology in February 2015. His overarching research aims are to improve therapy responses and risk stratification in prostate cancer. His work focuses on the impact of transcriptional regulation on prostate cancer metabolism and stress responses. He is interested in metabolic changes as intrinsic drivers of drug resistance in prostate cancer through induction of phenotypes ranging from autocrine hormone biosynthesis to cytokine production.

He has previously established the Uro-Oncology Research Group in Cambridge working alongside Professor David Neal. In 2010 he set up a prostate research group in Oslo within the Centre for Molecular Medicine Norway (NCMM) within the University of Oslo/Oslo University Hospital. The group there works on the hexosamine biosynthesis pathway as a feedback modulator of the unfolded protein response and drug responses in prostate cancer cells.

Further exploring the relationship between metabolism and prostate cancer they have identified genetic risk loci that are enriched in both prostate cancer cases and hypercholesterolemia. The group is involved in identifying prognostic biomarkers for prostate cancer in urine and blood samples utilising Scandinavian cohorts with clinical follow-up data from the Norwegian and Swedish Cancer Registries and in conjunction with the Movember Global Action Plan initiative. CCRCB provides a great opportunity to apply this work to radiotherapy response within the framework of the newly established FASTMAN Centre and to further develop national and international collaborations.

Robert Ladner
Reader in Molecular Oncology

Robert D. Ladner, PhD was appointed to the post of Reader in Molecular Oncology at Queen's University Belfast in 2015. Dr Ladner was awarded his MSc and PhD from Rutgers University/The University of Medicine and Dentistry New Jersey, where he performed his graduate research. It was during this time that Dr Ladner identified and characterized the sequence of human dUTPase and its variants and was among the first to unravel the complex mechanisms and cellular consequences of the uracil-DNA misincorporation pathway and the mechanisms of resistance to a class of chemotherapies known as thymidylate synthase (TS) inhibitors. This was closely followed by the first report of a strong association between dUTPase overexpression and clinical resistance to 5-fluorouracil in colorectal cancer.

In 2004, Dr Ladner was subsequently recruited to the post of Assistant Professor at the University of Southern California Norris Comprehensive Cancer Center where he initiated a collaborative drug development strategy to develop novel chemotherapeutics targeting uracil-DNA repair and to develop new synthetic lethal strategies that exploit the uracil-DNA misincorporation pathway during treatment with TS inhibitors. In 2014 Dr Ladner became Founder and CEO of CV6 Therapeutics, a biotechnology company dedicated to developing novel treatments to improve the effectiveness of currently approved cancer drugs. In 2015, CV6 Therapeutics entered a collaboration agreement with QUB supported by Invest Northern Ireland to accelerate the translation of these novel drug development programs to improving clinical care.

Stuart McIntosh
Clinical Senior Lecturer
in Surgical Oncology

Mr Stuart McIntosh was appointed as a Clinical Senior Lecturer in Surgical Oncology at Queen's University Belfast in October 2015. A graduate of the University of Edinburgh, Mr McIntosh undertook the majority of his surgical training in Scotland, with spells in clinical research in Glasgow and Cambridge, before obtaining a National Oncoplastic Fellowship in Leeds at the end of his training. Initially appointed as a consultant surgeon in Aberdeen in 2005, he moved to Belfast in 2009 to take up a post as consultant breast surgeon in Belfast City Hospital.

Since his appointment six years ago, Mr McIntosh has overseen a variety of developments within the breast service in the City Hospital, including expansion of the clinical trials portfolio to allow increasing access to clinical trials for breast cancer patients. He was appointed as Deputy Clinical Director of the NI Cancer Trials Network in 2013, and is a member of the NCRI Breast Clinical Studies Group as well as of the Association of Breast Surgery's Academic and Research Committee.

Mr McIntosh's current research interests are focused around personalising the surgical management of breast cancer, including managing women at high risk of breast cancer, the pre-surgical treatment of breast cancer, and the role of three dimensional surface imaging technologies in breast reconstruction surgery.

Jaine Blayney
Lecturer in Translational
Cancer Bioinformatics

Dr Jaine Blayney was appointed as a Lecturer in Translational Cancer Bioinformatics in April 2015. After obtaining an MSc degree in Computing and Information Systems at the University of Ulster in 2002, Dr Blainey co-ordinated an IT network systems programme for adult-returners in the further education sector. She completed her PhD in Bioinformatics (protein tertiary structure prediction) at Ulster University (UU) in 2008. Dr Blainey's first post-doctoral position was with the European CardioWorkBench programme identifying biomarkers and drug targets in cardiomyopathy. She joined QUB CCRCB as a Post-Doctoral Research Fellow in 2009, initially working on characterising lung cancer sub-groups, later joining Professor Richard Kennedy's Stratified Medicine Group to work on ovarian and prostate cancer molecular sub-typing. In October 2013, Dr Blainey moved to the Stratified Medicine Centre at UU as a Lecturer in Computational Biology, co-ordinating two biostatistics/bioinformatics modules in the undergraduate and postgraduate Stratified Medicine degrees.

Dr Blainey's main interest is in translational bioinformatics, in particular identifying novel biostatistical methods for the transfer of prior knowledge, including gene signatures, across independent platforms and technologies e.g. microarray to next generation sequencing datasets. Using such methods Jaine has predicted, and subsequently validated, the tumour of origin and histology of epithelial ovarian cancer cell lines. She is also interested in data integration strategies and in identifying software solutions for computational bottlenecks in biostatistical analytical pipelines. Dr Blainey has a strong interest in promoting the recruitment and retainment of women in STEM, contributing to the SWAN self-assessment teams in both QUB and UU and serving on the committee of the Women in Technology and Science all-Ireland networking group.

Melissa LaBonte Wilson
Lecturer in Molecular Oncology

Dr Melissa LaBonte Wilson was appointed as a Lecturer in Molecular Oncology in April 2015. Dr LaBonte Wilson was awarded her PhD at the University of Southern California (USC), where she worked in the laboratory of Dr Robert D. Ladner who remains one of the world's foremost authorities on uracil-DNA repair and mechanisms of resistance to thymidylate synthase-targeted therapies. She also collaborated closely with Dr Heinz-Josef Lenz, a world expert in mechanisms of clinical drug resistance.

Dr LaBonte Wilson then accepted a Post-doctoral Fellowship with Dr Lenz and went on to explore the relatively new field involving the tumour microenvironment and its role in cancer. Her research established the potential for therapeutic targeting of both CXCL8 and Defensin β1 in colorectal cancer and led to the establishment of a multidisciplinary team of molecular biologists, clinicians and chemists in a focused medicinal chemistry-based drug discovery project at USC.

In 2012, Dr LaBonte Wilson accepted an Assistant Professorship at the Azusa Pacific University just outside Los Angeles. Melissa pursued both CXCL8 and Defensin β1 as the primary focus of her research and continued the drug development program through a collaborative project with Dr Lenz and Dr Nicos Petasis (USC Dornsife Department of Chemistry). This research identified novel, first-in-class small molecule inhibitors of CXCL8 and CXCR2 (the receptor for CXCL8) with significant therapeutic potential and the ongoing evaluation of these molecules and continued characterization of this critical pathway will be the primary focus of her ongoing studies.

Darragh McArt
Lecturer in Translational
Cancer Bioinformatics

Dr Darragh McArt was appointed as a Lecturer in Translational Cancer Bioinformatics in January 2015. His research focuses on integrative analysis of disparate datasets on multiple cancer types and the development of translational next generation sequencing and high throughput analysis in molecular pathology. Through collaboration with Molecular Pathology, Digital Pathology and NIB initiatives, Dr McArt co-leads on the development of a novel "integromics" platform called PICAN for the management of clinical, phenotypic and genotypic data. This system has been key to tissue biomarker discovery in breast cancer and other diseases. He is also be a key bioinformatics lead in the new genomic expansion in the CCRCB.

Dr McArt has worked as a postdoctoral researcher in QUB for the connectivity mapping research group under Dr Shu-Dong Zhang developing parallel programming architecture and perturbation models. Later, he became the lead bioinformatician for the Northern Ireland Molecular Pathology Laboratory under Professor Manuel Salto-Tellez. Darragh has also spent time training in NCI Fredrick, Maryland and in Darmstadt, Germany. He joins an expanding translational bioinformatics and molecular diagnostics programme within the CCRCB.

Caroline Crothers
CRUK Research
Engagement Manager

Caroline Crothers joined the Belfast Cancer Research UK's Centre as the new Research Engagement Manager in late September.

As the Research Engagement Manager, Caroline's role is to engage the public in Northern Ireland with the research taking place in their community. Caroline engages these different audiences in a variety of ways, arranging talks about CRUK funded research and bringing the research to life through interactive lab tours in CCRCB. Also finding opportunities for researchers to go out and speak about their work in the community in order to reach more people and build greater support for the world-class research taking place at the Centre.

Following on from the success of the inaugural Open Day in 2015, Caroline will be seeking to expand this for 2016 and increase the programme of events in the NI Science Festival which is also taking place in 2016.

Caroline works closely with the press teams at CRUK and the other Centre partners to ensure that exciting new developments make the news and raise the profile of the Centre and is an active member on twitter, tweeting about her activities and any cancer research developments.

Before joining us, Caroline worked for the past four years for Leukaemia & Lymphoma NI, who are also based in CCRCB.

To contact Caroline, email: caroline.crothers@cancer.org.uk, follow on twitter: @crukbelfast or call: 028 9097 2987.

Joanne Badger
Leukaemia and Lymphoma NI Coordinator

Joanne Badger joined the centre as the Coordinator for Leukaemia & Lymphoma NI in late November.

As Coordinator Joanne's role is to drive support for LLNI and the Centre by increasing local engagement with the life-saving research that happens here. Providing more long term and sustainable funding for the research here is a priority and Joanne is working closely with the Central Committee, researchers, clinicians, fundraisers, volunteers and external stakeholders in order to make this happen.

Using the press and social media campaigns Joanne has been trying to raise awareness of the impact of LLNI on blood cancers and the benefit this has for local people. A recent development where the charity have agreed to fund ten leukaemia patients on a clinical trial here in Belfast has been of particular interest as it is the first occasion where local people are directly benefitting from the work being done here.

Prior to working for the charity Joanne had been living in Hong Kong, the UAE and Australia where she worked as a Fundraising Coordinator for the Peter MacCallum Cancer Centre.

To contact Joanne or find out more about her role please email: j.badger@qub.ac.uk or call: 028 9097 2928.

CURRENT STAFF

(as at 31 December 2015)

Academic Staff

Professors:
Professor Charles Campbell
Professor Karl Hale
Professor Peter Hamilton
Professor Paul Harkin
Professor Tim Harrison
(McClay Professor of Medicinal Chemistry)
Professor Patrick Johnston
Professor Richard Kennedy
(McClay Professor of Medical Oncology)
Professor Mark Lawler
Professor Mary Frances McMullin
Professor Ken Mills
Professor Joe O'Sullivan
Professor Kevin Prise
Professor Manuel Salto-Tellez
Professor Chris Scott
Professor David Waugh
Professor Richard Wilson

Readers:
Dr Fred Currell
Dr Robert Ladner
Dr Dan Longley
Dr Karen McCloskey
Dr Ian Mills
Dr Marie Migaud
Dr Paul Mullan

Senior Lecturers:
Dr Vicky Coyle
Dr Gerry Hanna
Dr Suneil Jain (Friends of the Cancer Centre)
Dr Jackie James
Mr Stuart McIntosh
Dr Richard Turkington
Dr Sandra Van Schaeybroeck
Dr Kate Williamson

Lecturers:
Dr Jaine Blayney
Dr Karl Butterworth
Dr Emma Evergren
Dr Melissa LaBonte Wilson
Dr Darragh McArt
Dr Simon McDade
Dr Konstantin Panov
Dr Kienan Savage (Cancer Focus NI)
Dr Alex Thompson
Dr Richard Williams
Dr Shu-Dong Zhang

Honorary Staff

Dr Ian Banks
Ms Ruth Boyd
Dr Mark Catherwood
Dr Graham Cotton
Dr Tim Davison
Dr Deirdre Donnelly
Dr Martin Eatock
Professor Dean Fennell
Dr Tom Flannery
Dr Gerald Gavory
Dr Alan Gilmore
Dr Robert Grundy
Dr Ian Harley
Professor Alan Hounsell
Dr Sandra Irvine
Dr Colin James
Dr Iain James
Professor Terry Lappin
Dr Maurice Loughrey
Dr Tom Lynch
Dr Perry Maxwell
Dr Nuala McCabe
Professor Glenn McCluggage
Dr Conor McGarry
Dr Damian McManus
Dr Stephen McQuaid
Dr Melanie Morris
Professor Patrick Morrison
Dr Colin O'Dowd
Dr Declan O'Rourke
Dr Melanie Percy
Dr Giuseppe Schettino
Dr Steven Walker

Scientific Fellows

Dr Niamh Buckley (Breast Cancer Now)
Dr Stephen McMahon (EU)

Clinical Research Fellows

James Beirne (HSC R&D Division)
Aideen Campbell (CRUK)
Catherine Davidson (CRUK)
Rosalie Douglas (HSC R&D)
Aya El-Helali (Almac)
Caroline Forde (CRUK)
Donna Graham (Tom Simms Bequest)
Ciara Lyons (Tom Simms Bequest)
Jane McClements (Tom Simms Bequest)
Suzanne McPherson (Leukaemia & Lymphoma NI)
Angela O'Neill (HSC R&D Division)
Eileen Parkes (CRUK)
Philip Turner (Friends of the Cancer Centre)
Adam Upritchard (FASTMAN)

Research Staff

Shahnaz Al Rashid (Brainwaves NI)
Abdullah Alvi (QUB)
Chris Armstrong (PCUK)
Peter Bankhead (CRUK)
Paul Buchanan (QUB)
Conor Bradley (Wellcome Trust)
Robbie Carson (CRUK)
Pankaj Chaudhary (EPSRC)
Lisa Crawford (BHSCT Charitable Funds)
Nyree Crawford (Astex Therapeutics Ltd)
Sabine Dalleau (Invest NI)
Ravi Deevi (CRUK)
Pablo de Vera (EU Marie Curie)
Philip Dunne (MRC/CRUK)
Sharon Eddie (PCUK)
Jose Fernandez (CRUK)
Mihaela Ghita (MRC)
Catherine Higgins (Wellcome Trust)
Caitriona Holohan (CRUK)
Simon Horn (PCUK)
Raymond King (PCUK)
Gerald Li (Invest NI)
Fabio Liberante (Leukaemia & Lymphoma Research)
Joanna Majkut (Wellcome Trust)
Adnan Malik (Wellcome Trust)
Kyle Matchett (Leukaemia & Lymphoma NI)
Pamela Maxwell (CRUK)
Katherine McAllister (SFI-DEL)
Anna McCormick (Breast Cancer Now)
Leona McGirr (MRC)
Julia Miskelly (MRC)
Wendy Moore (QUB)
Zsuzsanna Nemeth (Wellcome Trust)
Paul O'Reilly (BBSRC)
Sarah Osman (HSC R&D)
Adam Pickard (PCUK)
Kelly Redmond (MRC)
Soraia Rosa (EU Marie Curie)
Abigail Savage (Invest NI)
Francesca Saveria Amoroso (PCUK)
Kirtiman Srivastava (MRC)
Leanne Stevenson (Tom Simms Bequest)
Gayathri Thillaiyampalam (CRUK)
Christine Young (Leukaemia & Lymphoma NI)

Almac Staff

Laie Abello
Oliver Barker
Christina Bell
Caroline Boyd
Frank Burkamp
Stephanie Burton
Eamon Cassidy
Joana Costa
Anthony Dossang
Ulrich Dyer
Leanne Fegan
Katherine Gibson
Beronia Gorges
Matthew Helm
Ashling Henderson
Peter Hewitt
Gemma Logan
Martin McCann
Keeva McClelland
Mary McFarland
Estelle McLean
Sara McQuillan
Hugues Miel
Krzysztofa Odzywol
Natalie Page
Lauren Proctor
Shane Rountree
Ewelina Rozycka
Sarah Scullion
Steven Shepherd
Laura Taggart
Adam Treder
Mark Wappett
Steven Whitehead
Martin Wiles

Technical Staff

William Andrews (MRC)
Victoria Bingham (CRUK)
Conor Breen (MRC)
Alan Coffey
Elaine Craig (BHSCT Charitable Funds)
Lara Maria Dura Perez (PCUK)
Josephine Dutton
Cathy Fenning (CRUK)
Marc-Aurel Fuchs (Friends of the Cancer Centre)
Kym Griffin (Invest NI)
Paula Haddock (Breast Cancer Now)
Anne Jordan (Leukaemia & Lymphoma NI)
Oksana Lyubomska (MRC)
Angelina Madden (Cancer Focus NI)
Karen Magill Young (Invest NI)
John McCotter
David McGibbon
Claire McGready (CRUK)
Gordon McGregor
Leanne McIlreavey (Invest NI)
Kirsty McLaughlin (CRUK)
Gaurang Patel (CRUK)
Maria Rea
Peter Stewart (MRC/CRUK)

Administrative

Joanne Badger
(Leukaemia & Lymphoma NI Administrator)
Margaret Carr
(CRUK Public Affairs Manager)
Priscilla Clark
(NI Biobank Administrator)
Caroline Crothers
(CRUK Research Engagement Manager)
Sharon Dunwoody
(CRUK Centre Administrator)
Beryl Graham
(Centre Manager)
Paula Langham
(Project Officer, Movember Centre of Excellence)

Clerical

Jane Arbuthnot
Claire Atchison (Leukaemia & Lymphoma NI)
Ruth Beattie
Jenni Byers (CRUK)
Julie Hunter
Jill Loughlin
Frances McCormick
Anne McRoberts (CRUK Accelerator)
Linda Megrath
Noreen Rafferty
Julie Skelly (Almac/Invest NI)
Katie Stewart

MAJOR SOURCES OF FUNDING

FUNDING BODIES

The work of our research groups would not be possible without the substantial grant funding from our sponsors and from generous donations. Our major sources of funding include:

Research Councils
Biotechnology and Biological Sciences Research Council (BBSRC)
Engineering and Physical Sciences Research Council (EPSRC)
Medical Research Council (MRC)

Charities
Action Cancer
Association for International Cancer Research (AICR)
Bloodwise (formerly Leukaemia and Lymphoma Research)
Brainwaves Northern Ireland
Breast Cancer Now (formerly Breast Cancer Campaign)
British Heart Foundation
British Lung Foundation
Cancer Focus Northern Ireland
Cancer Research UK (CRUK)
Friends of the Cancer Centre
Leukaemia and Lymphoma NI
Nuffield Foundation
Prostate Cancer UK
Wellcome Trust

Companies
Almac Diagnostics
Almac Discovery
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Bristol-Myers Squibb
Celgene
GW Research Ltd
PathXL
Leica
Merck Serono
Pfizer Ltd
PharmaMar
Pierre Fabre
Randox
Roche

Government
British Council
Health and Social Care (HSC) Research and Development (R&D) Division of the Public Health Agency of Northern Ireland
Belfast Health and Social Care Trust (BHSCT)
Department for Employment and Learning (DEL)
EU Framework 7
EU Marie Curie Scheme
National Institute for Health Research (NIHR)
National Institutes of Health (NIH)
National Physics Laboratory (NPL)
Science Foundation Ireland
Technology Strategy Board
UK Home Office

Societies
Association of the British Pharmaceutical Industry
Biochemical Society
European Haematology Association (EHA)
Haematology Association of Ireland
Pathological Society
Royal Society

Agencies
Invest Northern Ireland

GRANTS AWARDED

(from 1 January 2015 – 31 December 2015)

This section specifically highlights new grants awarded within 2015. The funding bodies of our numerous ongoing research programmes are acknowledged in the previous section.

Investigator(s)	Sponsor	Title of Project	Amount	Period
Butterworth, Karl	GW Research Ltd	Investigation of radiobiological efficacy of cannabinol derivatives	£14,800	01/08/15 - 29/02/16
Campbell, Charles	Astra Zeneca	CASE MRC Studentship	£17,500	01/10/14 - 30/09/18
Coyle, Vicky McMullan, Ronan McAuley, Danny Clarke, Mike Wilson, Richard	NIHR	Early switch to oral antibiotic therapy in patients with low risk neutropenic sepsis (The EASI-SWITCH Trial)	£972,319	01/08/15 - 30/04/19
Coyle, Vicky	Cancer Research UK	Predicting Response to Treatment of Neutropenic Sepsis in Adult Patients with Cancer – Clinical Research Fellowship (Caroline Forde)	£260,000	01/10/15 - 30/09/18
Hanna, Gerry Butterworth, Karl Prise, Kevin	Cancer Research UK	Assessment of tumour efficacy and normal tissue toxicity using AZD6738 in combination with radiotherapy for non-small cell lung cancer	£48,200	01/09/15 - 31/08/16
Irvine, Sandra	Leukaemia & Lymphoma NI	Consumables	£10,000	01/04/15 - 31/03/17
Irvine, Sandra	Leukaemia & Lymphoma NI	Travel Grant	£2,000	01/04/15 - 31/03/17
Irvine, Sandra	Leukaemia & Lymphoma NI	Salary for Post Doctoral Research Fellow – Dr Lisa Crawford	£23,310	01/08/15 - 31/01/16
James, Jackie	Cancer Research UK	ECMC – Stratified Medicine	£10,500	01/01/15 - 31/12/15
James, Jackie Hamilton, Peter	HSC R&D	NI Biobank Renewal	£1,908,000	01/09/15 - 31/08/20
Ladner, Robert	Invest NI	Developing Novel Combination Therapies to Overcome Critical Drug Resistance Pathways in Cancer	£670,439	01/04/15 - 31/03/17
Lawler, Mark Johnston, Patrick Kennedy, Richard Wilson, Richard Salto-Tellez, Manuel	Medical Research Council / Cancer Research UK (MRC-CRUK)	Stratification in COloRectal Cancer: from Biology to Treatment Prediction (S-CORT)	£5,000,000	01/04/15 - 31/03/20
Lawler, Mark Gavin, Anna Murray, Liam	Cancer Focus NI	Cancer Health Economist	£149,908	01/01/16 - 31/12/18
Longley, Dan Scott, Chris Andrews, Gavin Bell, Steven	Medical Research Council CiC	Development and Delivery of Gold Nanoparticles for Oesophageal Adenocarcinoma	£67,688	01/07/14 - 31/08/16
Longley, Dan Wilson, Richard Kennedy, Richard Kissenpfennig, Adrien	SFI-DEL	Development of personalised medicine approaches for the clinical application of IAP antagonists	£637,289	01/09/15 - 31/08/19

Investigator(s)	Sponsor	Title of Project	Amount	Period
McArt, Darragh	Cancer Research UK	The Integrative Landscape of Primary and Recurrent Glioma for Dynamic Biomarker Discovery – PhD Studentship (Aideen Roddy)	£141,390	01/10/15 - 30/09/19
McArt, Darragh McDade, Simon	Medical Research Council	Integrative environment for data acceleration, analysis and biomarker discovery	£20,000	01/03/15 - 31/08/16
Mills, Ken	Leukaemia & Lymphoma NI	Summer Studentships	£6,000	01/07/15 - 31/08/15
Mullan, Paul McDade, Simon Williams, Rich	Breast Cancer Now (formerly Breast Cancer Campaign)	Exploiting the TBX2 Repression of CST6 as a Novel Treatment Strategy for Poor Prognosis Breast Cancers	£193,552	01/03/15 - 28/02/18
Mullan, Paul McArt, Darragh	British Medical Association	T P Gunton Grant – James Beirne (DNA Methylationa Markers for Early Detection of Ovarian Cancer: the Key to Successful Population Screening)	£42,782	01/09/15 - 31/08/18
Buckley, Niamh McCloskey, Karen	BHSCT Charitable Funds	Investigating KCNK Proteins as Potential Novel Biomarkers and Therapeutic Targets in Ovarian Cancer	£44,748	01/02/15 - 31/01/16
Prise, Kevin	National Physics Laboratory	PhD Studentship (50%)	£30,000	01/10/14 - 30/09/17
Prise, Kevin	Brainwaves NI	Brain Tumour Research	£58,600	01/11/15 - 31/10/16
Salto-Tellez, Manuel Hamilton, Peter James, Jackie Kennedy, Richard Lawler, Mark Waugh, David	CRUK Centres Network Accelerator	A National Digital Pathology and Image Analysis Platform for Solid Tumours, complemented by A Comprehensive Clinical Fellowship Programme in Molecular Pathology	£3,753,474	01/07/15 - 30/06/20
Salto-Tellez, Manuel	Technology Strategy Board	STRATFix: Enabling Stratified Medicine with Novel Fixatives for improved Pre-Analytical Pathology	£46,864	01/10/14 - 30/09/17
Turkington, Richard	HSC R&D	Clinical Research Fellowship – Dr Rosie Douglas	£198,716	01/08/15 - 31/07/18
Van Schaeybroeck, Sandra	Cancer Research UK	To investigate the effect on tumour volume of the AZD0424 and MEK inhibitor	£69,247	01/08/15 - 31/07/16
Williamson, Kate	Randox	Haematuria Biomarker Study	£120,000	01/01/05 - 31/12/15
Waugh, David	Cancer Research UK	CRUK Centre Core Infrastructure Support	£512,500	01/04/15 - 31/03/16

The following publications were published within the period of this report:

ALVI, M.A., McART, D.G., KELLY, P., FUCHS, M.A., ALDERDICE, M., McCABE, C.M., BINGHAM, V., MCGREADY, C., TRIPATHI, S., EMMERT-STREIB, F., LOUGHREY, M.B., McQUAID, S., MAXWELL, P., HAMILTON, P.W., TURKINGTON, R., JAMES, J.A., WILSON, R.H. and SALTO-TELLEZ, M. (2015) Comprehensive molecular pathology analysis of small bowel adenocarcinoma reveals novel targets with potential for clinical utility, *Oncotarget*, 6(25), p20863-74.

ANDERSON, L.A., JAMES, G., DUNCOMBE, A.S., MESA, R., SCHERBER, R., DUECK, A.C., DEVOCHT, F., CLARKE, M. and McMULLIN, M.F. (2015) Myeloproliferative neoplasm patient symptom burden and quality of life: Evidence of significant impairment compared to controls, *American Journal of Hematology*, 90(10), p864-870.

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BADUSHA MOHAMED YOOSUF, A., MITCHELL, D.M., WORKMAN, G., JONNADA, S., NAPIER, E. and JAIN, S. (2015) Sector analysis provides additional spatial information on the permanent prostate brachytherapy learning curve, *Brachytherapy*, 14(5), p707-710.

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BALIAKAS, P., HADZIDIMITRIOU, A., SUTTON, L.A., MINGA, E., AGATHANGELIDIS, A., TSANOUSA, A., SCARFO, L., DAVIS, Z., YAN, X.J., SHANAFELT, T., PLEVOVA, K., SANDBERG, Y., VOJDEMAN, F.J., BOUDJOGRA, M., TZENOU, T., CHATZOULI, M., CHU, C.C., VERONESE, S., GARDINER, A., MANSOURI, L., SMEDBY, K.E., PEDERSEN, L.B., MORENO, D., VAN LOM, K., GIUDICELLI, V., FRANCOVA, H.S., NGUYEN-KHAC, F., PANAGIOTIDIS, P., JULIUSSON, G., ANGELIS, L., ANAGNOSTOPOULOS, A., LEFRANC, M.P., TRENTIN, L., CATHERWOOD, M., MONTILLO, M., GEISLER, C., LANGERAK, A.W., POSPISILOVA, S., CHIORAZZI, N., OSCIER, D., JELINEK, D., DARZENTAS, N., BELESSI, C., DAVI, F., ROSENQUIST, R.,GHIA, P. and STAMATOPOULOS, K. (2014) B-cell receptor stereotypy defines distinct clinical subgroups of chronic lymphocytic leukemia: Implications for individualizing treatment, *Lancet Hematology*, 1(2), e74-84.

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Acknowledgements

We are grateful to everyone who provided information for this Annual Report, everyone who supplied images or gave us permission for their images to be used, and the CCRCB staff who helped to produce this report.

Design:
www.darraghneely.com

Printed by:
Corporate Document Services (CDS)

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