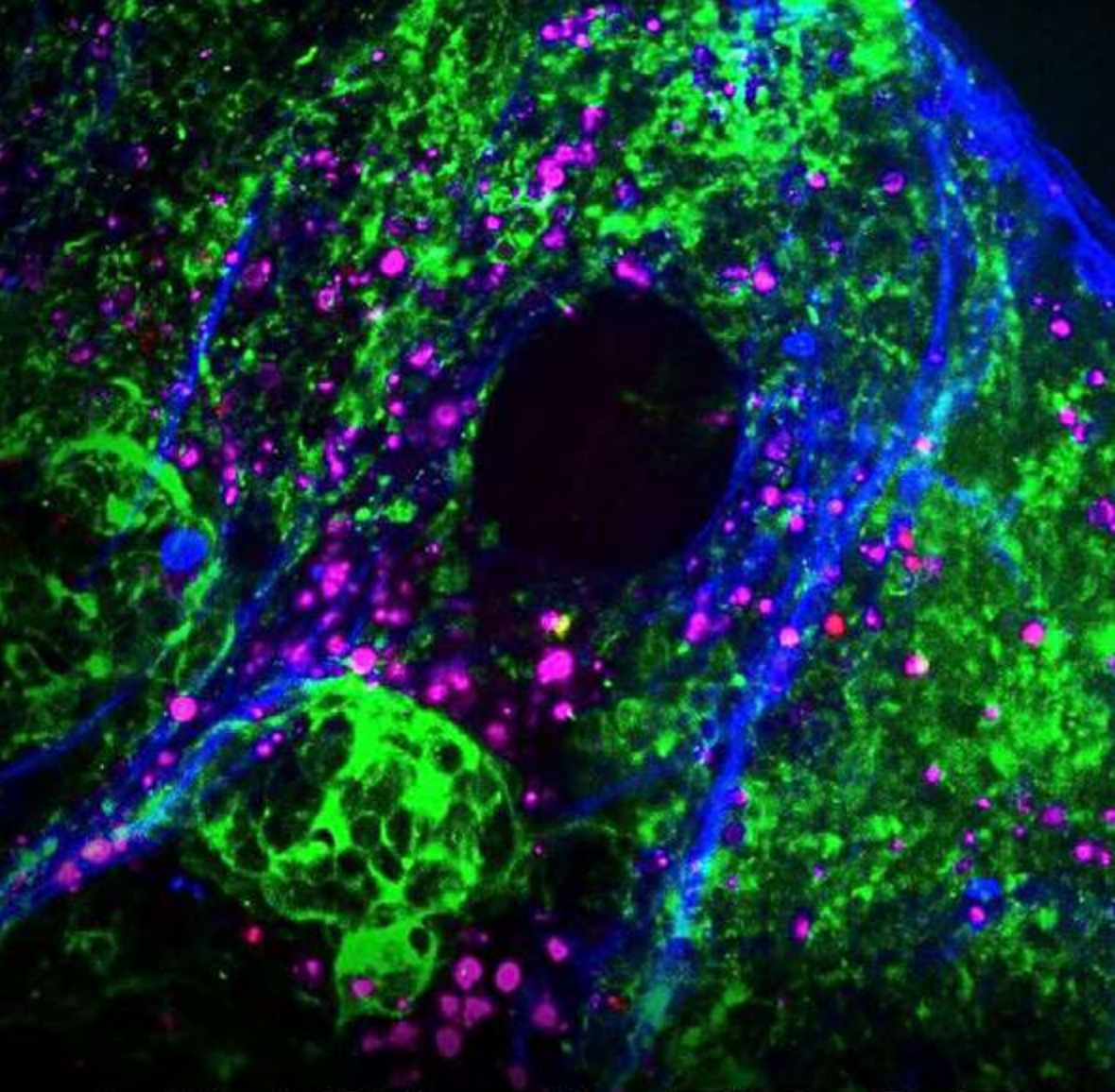

KNOWLEDGE IS POWER

WORKING TOGETHER TO OUTSMART CANCER

CELEBRATING TWO DECADES OF DISCOVERY
AT BARTS CANCER INSTITUTE
QUEEN MARY UNIVERSITY OF LONDON

20 CELEBRATIONS | Barts Cancer Institute

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Queen Mary University of London

CANCER RESEARCH UK | City of London Centre

Cover Image: The Eye of the Tumour

Captured by Dr Florian Laforêts (Professor Fran Balkwill's lab).

Lay summary: This microscope image shows a slice of living, ovarian cancer tissue, donated by a patient. The tumour is carefully nourished and kept alive in the lab, enabling our researchers to study the behaviour of the tumour cells (green) and surrounding immune cells (pink and red), providing insights into how we might more effectively treat the disease.

Scientific summary: An image of the live microenvironment in an *ex vivo* human high-grade serous ovarian cancer tumour slice. The fresh sample came from an omental metastatic tumour. The picture is the maximum intensity projection of a 3D image, acquired with a fluorescent confocal spinning disk microscope. Green represents tumour cells, stained with EpCAM; the red cells are CD4+ T cells; the purple cells are CD8+ T cells; and the blue represents the extracellular matrix, stained with fibronectin 1.

Knowledge is Power

Edited by Dr Charlotte Ridler

Disclaimer: Although the authors and editors have made every effort to ensure that the information in this book is accurate at the time of publication, the book is a work of memory. Chapters represent the recollections, personal views and opinions of individual authors and do not necessarily reflect the positions or opinions of any organisation, institution, or individual with which each author is affiliated. The content presented herein is based on the authors' perspective and interpretation of the subject matter. Neither the publisher nor any associated parties shall be held responsible for any errors, omissions, or consequences arising from the opinions or interpretations expressed within this book.

First Printing: 2024

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www.bci.qmul.ac.uk

Dedicated to staff and students,
past, present and future,
of Barts Cancer Institute

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Acknowledgements

Twenty years ago, Queen Mary University of London's leadership had a vision to bring together some of the most eminent cancer research teams in London, creating the Barts Cancer Institute. We would like to express our gratitude to everyone who has supported us.

We owe a debt of thanks to Professor Sir Nicholas Wright, Warden of Barts and the London School of Medicine and Dentistry, which has evolved into Queen Mary's Faculty of Medicine and Dentistry. Sir Nick spearheaded the establishment of the institute with the support of Queen Mary's Principal, Sir Adrian Smith, and the medical school's Chief Operating Officer, Peter Davies. Without their vision and investment, none of the achievements chronicled in this book would have been possible.

We would also like to thank Queen Mary's Vice-Principals for Health, Professor Richard Trembath (2011–2016), Professor Steve Thornton (2016–2022) and Professor Sir Mark Caulfield (our current Vice-Principal for Health), as well as our previous President and Principal, Professor Simon Gaskell, and current Principal, Professor Colin Bailey, for their enduring belief and support. We are proud to be a part of a university that values academic excellence, inclusivity and diversity of thought, which are central to our efforts to expand the limits of medical knowledge and create tangible progress for people with cancer.

Our heartfelt thanks go to our funders, including our major funders Cancer Research UK and Barts Charity, and the donors, volunteers and staff who enable their work. Their generosity has been essential to the continuing success of our research.

Finally, we extend our sincere gratitude to all our dedicated staff and students, past and present, as well as to the patients and other individuals who kindly participate in our research. Your contributions help to provide new hope to people affected by cancer.

Introduction

Professor Kairbaan Hodivala-Dilke

Happy 20th Birthday, Barts Cancer Institute. Here's wishing you many, many more.

In 2004, Facebook was launched, NASA landed the Opportunity Rover on Mars, and the Barts Cancer Institute (BCI) was born. And now, here we are, celebrating the BCI's 20th birthday. As I reflect on the past 20 years, the most overwhelming emotion is how much the BCI family has grown and grown, from strength to strength.

In 2003, I remember visiting the John Vane Science Centre at Charterhouse Square for the first time with some of the giants of the institute. Professor Sir Nick Wright – the Medical School Warden (now termed Vice-Principal for Heath) at that time – led the way, striding strong and laughing loudly. Professor Nick Lemoine – a hugely ambitious young clinician scientist with a spark in his eye – was excited and confident, knowing exactly how he would build and direct this institute to become a world-class cancer research beacon. Professor Ian Hart – the first BCI Deputy Director – was a truly kind-hearted scientist. He started as a veterinarian ('too clever to become a doctor', in his own words) and is someone I am so proud to call a mentor, teacher and friend. On that day, behind these giants, walked the young and keen Dr John Marshall, who actually brought his tape measure with him to work out bench lengths. And finally, there was me, just finishing my Imperial Cancer Research Fund (ICRF, now Cancer Research UK) tenure track position, pregnant with my first baby, and struggling to keep up the pace.

My first impression was: such a beautiful leafy square! Especially compared with the

lonely, concrete Rayne Institute at St Thomas's Hospital, where Ian, John and I started. At Charterhouse Square, we were greeted by smiling Jimmy, the gardener who cared for the grounds until his retirement in 2024. At that time, the John Vane Science Centre housed corridors of tiny office-like rooms on the ground floor, with hospital trolleys and beds randomly scattered about and no one, apparently, around. There were no working laboratories on the ground floor, but there was an out-of-place library for the Queen Mary Law department, where the Centre for Tumour Biology now has part of its laboratories. But mostly, what I remember is being so excited at the thought of being there at the beginning of what was clearly going to be an amazing journey to grow this new Barts Cancer Institute.

Top: Charterhouse Square Campus in spring time. Bottom, left to right: Professor Nick Lemoine (BCI Director), Professor Ian Hart (Tumour Biology Centre Lead), Dr Delphine Purves (BCI Institute Manager), Professor Sir Nick Wright, (Medical School Warden) and Peter Davies (Medical School Chief Operating Officer).

Sir Nick, Nick and Ian, the *Three Musketeers*, were together hooking in the biggest and the best talent to join us, and I can tell you that people were beating at the door to be let in. Right at the start, Dr Delphine Purves was appointed Institute Manager and instantly became the hub of the institute. A young woman in high-heeled shoes from the Wellcome Trust, Delphine's drive and financial wizardry meant that when she cracked the whip, things happened. She is still the single person who holds the BCI together. She was appointed and mentored by the Chief Operating Officer, Peter Davies – the "Dumbledore" of financial wizardry who taught her almost everything she knows and was always willing to invest in the BCI to make Sir Nick's vision a reality. Not long after, Kaye Yeung was onboard as Delphine's Cagney to her Lacey. The team was set! Nothing was stopping us.

The establishment of the BCI also meant joining with major forces who were already running ICRF-supported laboratories embedded in the John Vane Science Centre. The Centre for Medical Oncology (which later transformed into the Centre for Haemato-Oncology) was run by the great Professor Andrew Lister, who had been at the ICRF Medical Oncology Unit since 1977. To this day, you'll recognise him by being the only one in the building wearing a dapper bow tie, peering over half-moon glasses at you and setting the facts straight. As Clinical Director of the Cancer Services at Barts, he developed one of the largest units treating haematological malignancies in the country. He impressed us all by always putting the patients first and was famous for serving Christmas dinner in the wards before he and his family ate. He was truly adored by his patients and hugely respected by his colleagues. His right-hand team, Simon Joel (Professor of Pharmacology), Bryan Young (Professor of Medical Oncology) and the young Jude Fitzgibbon (later to become Professor of Personalised Cancer Medicine), welcomed us into the building.

Also in the John Vane Science Centre was Professor Fran Balkwill, who ran the Centre for Translational Oncology, which later turned into the Centre for Cancer and Inflammation and now the Centre for Tumour Microenvironment. Fran was the only woman to hold a Centre Lead position at the time. She is also a famous author of children's books – with over 500,000 copies sold, bringing science to life in twelve languages. An inspiration to scientists, both men and women, Professor Balkwill was ahead of her time in reminding people that cancer is more than malignant cells!

At the very beginning, Nick, Ian and Delphine had an inspired idea that was not

commonplace in other institutes. They decided to shape the BCI into centres, each with multiple laboratories and principal investigators (PIs). We take this for granted now, but I had only worked in places where each lab worked alone, like the old ICRF at Lincoln's Inn Fields and the Massachusetts Institute of Technology, where I worked as a postdoc. Being a relatively new PI at the time, I can tell you that there is nothing more frightening than being given an empty room and told to get on with it! Organising the BCI into centres was an insightful move because everyone was instantly part of a team, working together and immediately productive. This was a colossal draw, attracting others to join us. The strengths and fun that came with being part of a team were second to none. Of course, the inter-centre 'healthy' competition did exist – more in the name of pride than anything else. All gloves were off when it came to the BCI summer sports day, with becoming the winning centre the only goal.

In those early years, we had six integrated Centres:

On the ground floor: the Centre for Tumour Biology led by Ian Hart. Not long after his arrival, Ian, together with John Marshall, began to build a rapidly growing snowball of new recruits. Louise Jones (a.k.a. 'Jones the Breast') came from Leicester and proved to have a boundless capacity. She not only is a truly world-leading breast pathologist and teacher but also leads the Breast Cancer Now National Biobank (that we all rely on) and is the most inspiring and compassionate laboratory head and collaborator. Richard Grose (a.k.a. 'Uncle Dickie') and Professor Stephanie Kermorgant – both cell signalling aficionados – joined us from ICRF Lincoln's Inn Fields, after completing their postdoctoral fellowships with the hugely respected Clive Dickson and Peter Parker labs. Hemant Kocher – a hepatobiliary surgeon with a lust for academic research – was famous for his brightly coloured schematics and his deep commitment to two things: cricket and making a difference in pancreatic cancer research (which he certainly has, through his work on all-trans-retinoic acid (ATRA) as a novel therapy).

Spread across the ground floor and basement was the Centre for Molecular Oncology, led by our inaugural Director, Nick Lemoine. He brought with him a core team from Imperial College London and Hammersmith Hospital: Yaohe Wang, Gunnel Hallden and Tatjana Crnogorac-Jurcevic. Yaohe – another pathologist and young lecturer – always seems to be smiling and never seems to age. His eagerness

allowed him to create an incredible impact on viral therapy that has now exploded into a spin-off company, VacV, led by him and Nick. Gentle and modest Gunnel is now Director of Oncolytic Virotherapy and Antibody-drug conjugate (ADC) Biology at AstraZeneca. Meanwhile, Tatjana's interest in the molecular pathology of pancreatic cancer has led to a patented novel non-invasive diagnostics test for the early detection of pancreatic cancer. Soon after, they were joined by Yong-Jie Lu – a perpetually eager scientist with a passion for predicting prostate cancer onset – and another of Nick's recruits, Iain McNeish – a tall and kind medical oncologist with a focus on translational research and therapy development in ovarian cancer, who used to walk around the lab in his cycling lycra, whistling. He later took over leading the Centre. Michelle Lockley arrived as Iain's clinical research fellow and eventually joined as a young Clinical Senior Lecturer, employing her poise and drive to improve treatment for women with ovarian cancer. Soon after, Claude Chelala and Jun Wang (a.k.a Alex) arrived to lead our bioinformatics initiatives. Bringing numbers to our observations was a new idea at the time, and the bioinformatics service would ultimately transform research across the BCI, thanks in large part to Claude and Alex's active and collaborative natures.

On the third floor, the Centre for Haemato-Oncology was taken over by Professor John Gribben, an eminent haemato-oncologist who had flown all the way from Harvard to be with us. Stepping into Andrew Lister's shoes, John was in exactly the right place. It wasn't long before the Centre began to expand, becoming the home of the vast majority of BCI's clinical colleagues, including Ama Rohatiner, Vaskar Saha,

The grand opening of the CRUK Barts Centre. Left: CRUK Chief Executive Sir Harpal Kumar and BCI Director Professor Nick Lemoine cut the ribbon. Right, from left to right: Professor Sir Nick Wright, Professor Nick Lemoine, Sir Harpal Kumar and Peter Morris (Chief Executive of Barts Health NHS Trust).

Louise Jones, Heather Oakervee, Silvia Monoto, Rebecca Auer, Finbar Cotter, Li Jia, Jeff Davies and David Taussig, all underscoring our essential links with patients. Not long after John's arrival, Jessica Okosun was also recruited under Jude's umbrella as a Clinical Research Fellow. A highly talented and intelligent young scientist thirsty for discovery research, Jessica exudes a calmness that infiltrates those around her like a hot milky drink before bedtime. After her fellowship, she came back as a Clinical Senior Lecturer in 2017 and today has become Deputy Centre Lead of HaemOnc.

The Centre for Cancer and Inflammation, led by Fran Balkwill, was also home to the young Peter Szlosarek, who exemplifies bench-to-bedside achievements in melanoma and mesothelioma research. Peter started as a Clinical Research Fellow in Fran's lab in 1997, started his postdoc with her in 2005, and then left and came back in 2008 as a Clinical Lecturer. Over several decades, Peter has translated his early lab observations into an arginine-depleting agent, ADI-PEG20, which is creating an impact in several hard-to-treat cancers (and I should say, he is also one of the best dancers at BCI parties). Toby Lawrence also joined us as a Senior Lecturer and has become a leading expert in macrophage biology, now based at King's College London. David Propper is our resident clinical expert, who provides insight and direction to our research from the perspective of his patients. The centre, today known as the Centre for Tumour Microenvironment, is now home to some of Fran's home-grown new group leaders, including Oliver Pearce – a chemist by training who brings elegance to our understanding of the extracellular matrix – and most recently, Samar Elorbany – a young clinical surgical lecturer with a passion and drive to beat drug resistance in ovarian cancer for good.

Not long after the initial set-up of the BCI, the Centre for Cell Signalling was formed. This was led by Bart Vanhaesebroeck, who had made discoveries in PI3K signalling that we were all envious of. Bart brought with him Pedro Cutillas, a young and brilliant scientist with the inventiveness and foresight to invest in one of the first 'omics' platforms of the time – phosphoproteomics. Today, Pedro runs a successful spinout company, Kinomica, and he remains our go-to BCI proteomics expert: patient, knowledgeable and always happy to collaborate.

In the basement, Stephen Mather and Jane Sosabowski moved from the Nuclear Medicine Department at St Bartholomew's Hospital, bringing their world-class *in vivo* imaging to strengthen the BCI's foundations even further. This gave the BCI one

of its most important and unique selling points. Almost nowhere else in the UK was conducting *in vivo* imaging at this level, and it was exciting to watch this group grow from strength to strength over the years, even after Steve's retirement.

The BCI also recruited a couple of extremely talented young scientists, Melania Capasso and Sarah Anne Martin, working on B cells and DNA, respectively. Sarah also went on to become our Director of Graduate Studies. Always compassionate, calm and supportive to all our PhD students, she was a linchpin of our community. Nick and Ian set the expectation bar ridiculously high for Melania and Sarah's probation, and they both rose to the challenge without flinching. I am so proud of them both. It was just the first of many exciting opportunities to see young scientists really flourish, thanks to being nurtured at BCI.

By 2008, in less than five years of existence, the BCI was ranked third in the country for cancer research in the UK's Research Assessment Exercise (now the Research Excellence Framework) – you can't argue with that.

In 2014, Ian wrote beautifully about the first ten years of the Barts Cancer Institute in the first volume of this series, where he waxed lyrical about the transition from the Imperial Cancer Research Fund to Cancer Research UK (CRUK) and more, so I'll let you read all about that in his words. But what about since then?

When Professor Hart retired (and after much partying, weeping and a little drinking), Iain McNeish took the reins as Deputy Director. Tyson Sharp arrived – a young scientist from York, bringing his expertise in LIMD1, a gene that causes lung cancer. Tyson soon became the lead of the renamed Molecular Oncology Centre (now our Centre for Cell and Molecular Biology). Meanwhile, Sir Nick graciously took the lead for the Centre for Tumour Biology. I remember that at the first Tumour Biology centre meeting, Sir Nick said that he considered being our Centre Lead a promotion from being the Medical School Warden! He always started each centre meeting with, 'So, what's the good news?' – a true gentleman.

Sir Nick soon brought with him a team that would turn out to be one of the strongest assets to BCI. Trevor Graham came to us from the USA – a very young and seemingly quiet mathematician, Trevor introduced us to cancer evolution and has been a rising star since then, leaving us in 2022 to become the Director of the Centre for Evolution and Cancer at the Institute of Cancer Research. Stuart McDonald also

joined us, bringing his special expertise to the causes of oesophageal cancer that we were sorely lacking at BCI.

Getting these world-class scientists to all work together was so exciting, and it seemed that the BCI was unstoppable. But there's no success without funding. In those early years, CRUK changed its style of support and many of us moved from CRUK to Queen Mary University of London employment contracts. This was all part of CRUK's great plan to start to spread funding across what they called Centres of Excellence to support the training and technical facilities of their best researchers.

Celebrating the renewal of the CRUK Barts Centre. Top: the institute gathers on the green. Bottom: members of the Centre for Cancer Inflammation gather under the CRUK Barts Centre banner.

So, in 2009, the BCI combined forces with the CRUK-supported Centre for Cancer Prevention in Queen Mary's Wolfson Institute of Preventive Medicine (now the Wolfson Institute of Population Health) to become London's first CRUK Centre of Excellence. With only a handful of such Centres scattered across the country, we were certainly shoulder-to-shoulder with the elite class of cancer researchers in the UK.

The Wolfson was led by Professor Jack Cuzick, a Californian-born mathematician whose focus shifted into epidemiology. Jack sat firmly at the international forefront of preventative cancer research, transforming the identification of women at high risk of breast cancer and pioneering modern prevention breast and cervical screening strategies that have been adopted worldwide. Together with his colleagues, Professor Stephen Duffy (a true Scottish gentleman and statistician) and Professor Peter Sasieni (tall in stature and scientific ambition), Jack brought early detection of cancer research to a globally recognised level.

The CRUK-funded Barts Centre, as it was then known, was renewed in 2014 for a further five years, with extra funds offered. I don't think I have ever heard of CRUK giving more money than was applied for, but I think it was a true recognition of our strengths and their faith in us and cancer research.

With the CRUK Barts Centre looking to invest in the future, our first cohort of Early-Career researchers joined us around that time: Katiuscia Bianchi, Gabriella Ficz, Susana Godinho, Trevor Graham, Sarah McClelland, Paulo Ribeiro and Angus Cameron (who recently has become our new Director of Graduate Studies, following Sarah Anne Martin's departure to head up student programmes at the Crick). Soon after, we were also joined by Andrejs Braun (now our Director of Education), Bela Wrench, Prabhakar (Prabs) Rajan, Kevin Rouault-Pierre, Sergey Krysov, John Riches, Zuzana Horejsi and Faraz Mardakheh. Spread across the BCI, these eager scientists were keen and hungry to succeed at a level we couldn't have imagined. They work across the institute in a diverse array of disciplines, including signalling, epigenetics, chromosome biology, *Drosophila* modelling and metabolism. We are all so proud of how they have all exceeded the high bars of performance set before them.

As the years went on, CRUK's stance on funding began to change once again, and whispers of merging CRUK Centres of Excellence to become CRUK Major Centres became a reality. In 2018, we joined forces with University College London (UCL), King's College London, and the then gleaming and new Francis Crick Institute to

become part of the CRUK City of London Major Centre.

Long meetings over several months shaped this new idea and brought together the kings of cancer research from each of these organisations. Together, they would amalgamate into a super-force: Professor Tariq Enver, a stem cell biologist by trade who leads the Cancer Centre at UCL; Professor Peter Parker, a PKC signalling expert from King's and the Crick; Sir Richard Treisman, Director of Research at the Crick who discovered serum response factor (a central factor in MAPK signalling), and our own Nick Lemoine. The idea that a cross-organisational Major Centre would ever materialise was totally alien to me, but Nick knew that he could make it work. It's another example showing that if I say 'it won't fly', Nick will prove me wrong and make it a massive success.

The City of London Major Centre in Biotherapeutics had three cross-organisational themes: developing biological therapies, cross-disciplinary approaches in enhancing biotherapeutics and cancer evolution and tumour heterogeneity. The City of London Centre was renewed in 2022, at which point the individual CRUK Centres of Excellence at Queen Mary, King's and UCL were merged. It continues to support many of our essential facilities and clinical and non-clinical PhD students. It is the absolute exemplar of cross-organisational work, cleverly blending collaborative work through cross-organisational joint supervision of projects and PhD students. This approach has seeded joint projects that would have otherwise never happened. It is this teamwork that puts our CRUK City of London Centre firmly at the epicentre of international cancer research. We must remember that cross-organisational work is rarely found and provides immense strength to the work at all partner institutes. Around this time, Trevor and Jude also set up the BCI's new Centre for Genomic and Computational Biology, which enabled us to shuffle people to work together on cancer evolution and mathematics, setting us up with a flag of international recognition in the field.

BCI's contribution to the City of London Centre also relied heavily on the internationally recognised successes of our Barts Health Cancer Centre leads, Tom Powles and Peter Schmid, who have worked tirelessly, spending much of their lives on planes, to cement international industrial sponsorship and accelerate the clinical successes of immunotherapy in urogenital and breast cancers and who have taken our outputs to the heady heights of publications in *Nature*, *Nature Medicine* and *New*

England Journal of Medicine – truly inspirational members of the family.

We have also worked with our colleagues in Queen Mary's Faculty of Medicine and Dentistry (FMD) on some ground-breaking projects. In 2013, Professor Sir Mark Caulfield – at that time the Director of the William Harvey Institute and today our Vice-Principal for Health – was appointed Chief Scientist for Genomics England and charged with delivery of the 100,000 Genomes Project on whole genome sequencing. It was our Professor Louise Jones who linked BCI into this amazing venture, taking on the role of Lead for Molecular Pathology for Genomics England amongst everything else that she does. More recently, Louise Jones and Tom Powels, together with our colleagues from the William Harvey Institute, were instrumental in ensuring the establishment of the first National Institute for Health and Care Research (NIHR) Barts Biomedical Research Centre and became co-leads of the Precision Cancer Care Research Theme taking the FMD's science from strength to strength.

In 2020, the COVID pandemic closed down the building for a while, but not the research – Delphine and the fantastic lab support teams, including Vipul Bhakta and Bex Gresham, made sure of that. The renewed CRUK City of London Centre attracted a second cohort of early-career scientists to the BCI: Roberto Bellelli, Lovorka Stojic and Tanya Soliman – all hardcore molecular biologists; Mirjana Efremova – single-cell

Barts Cancer Institute staff and students on The Green, Charterhouse Square, at our Welcome Back event, September 2021.

The Barts Cancer Institute community comes together: pictures from social events held across the years, including Sports Day and Christmas Parties.

transcriptomics wizard; Miguel Ganuza Fernandez – haematopoietic stem cell expert; Luigi Ombrato – metastasis and tumour microenvironment specialist; Barrie Peck and Andy Finch – both enriching the cancer metabolism energy even further; and Bennie Werner – cancer mathematician with an incredible ability to explain cancer evolution using numbers. And as if that was not enough, BCI attracted the talent of Vicky Sanz-Moreno, formally at King's College London – an amazing tornado of expertise in the cancer metastasis tumour microenvironment; and Kamil Kranc from Edinburgh – a super-driven stem cell and hypoxia expert. John Marshall and Richard Grose took over leading the Centre for Tumour Biology, and I had the honour of working more closely with Fran in leading the Centre for Tumour Microenvironment.

Since 2022, our most recent newcomers have enriched the BCI even further with Diu Nguyen – with her expertise in leukaemia; Ozgen Deniz – with her expertise in epigenetics; Marco Gerlinger – from ICR, working on cancer cell heterogeneity; and Paolo Gallipoli – a clinical reader in experimental haematology. All of these new starters have also brought in fellowships and funding at an amazing level. In 2023, we welcomed Francesca Ciccarelli, who came to us from the Crick and King's College London to head up the Genomics and Computational Biology Centre at BCI – a vibrant mathematician with a fervour for understanding cancer evolution. This year, we welcome the young Vivek Singh and Oscar Maiques Carlos – both bringing digital pathology with AI to BCI.

I can't close without dedicating the end of this chapter to honouring Nick Lemoine, CBE, MD, PhD, FRCPath, FMedSci. Nick has truly been the beating heart of BCI, driving it from the 75 staff that we started with in 2003 to over 420 in 2024. I am so proud to have had the opportunity to serve as his Deputy. I remember seeing him through the Boardroom window, working late into the night and at the weekends without tiring. It is his work and constant dedication to BCI (literally blood, sweat and tears) that has made us one of the top-ranking cancer institutes nationally and internationally. His legacy is immense, and I can highlight only a few of his accomplishments here.

Over the years, Nick has not only run his own laboratory and centre but nurtured all our careers and personally mentored over 150 discovery and clinical postdocs and students. He has published over 280 papers and personally held no less than three CRUK programme grants simultaneously in the earliest years of the BCI. He knows

Then and Now. On this page: celebrations for the Barts Cancer Institute's 10th Anniversary in 2014. Top, left to right: Richard Le Vay (editorial assistant), Dr Delphine Purves and Professor Nick Lemoine, celebrating publication of the 10th Anniversary Book: "Every Rational Attempt: The Stories Behind the Contribution of Barts in the Fight Against Cancer". Bottom: Professor Nick Lemoine awards some of our 10-year long-service awards (left to right) to Professor Kairbaan Hodivala-Dilke, Professor John Gribben and Professor John Marshall. On the opposite page: Barts Cancer Institute long-service awards in October 2024. Top: our 20-years long-service award winners. Bottom: our 5, 10 and 15 years long-service award winners.


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all of us and our science. He has always remained calm and collected, an iron rod of stability, and an advocate for transparency and honesty. And all of this without ever boasting about his own successes.

Nick has also provided important service to the FMD, representing BCI at Queen Mary Council and Senate. He was the original Chair of the Athena Swan committee, which successfully brought the first Athena Swan Bronze accreditation to FMD. He has been the FMD representative for Barts Health NHS Trust, where he was also the Director of Cancer Services. Since 2013, he has been the Medical Director of the NIHR. He has served and chaired countless national and international funding committees, including at the MRC Foundation and CRUK. In 2017, Nick was elected Foreign Academician of the Chinese Academy of Engineering – one of only 18 people worldwide – in recognition of his work on engineering new therapies for cancer in the Sino-British Center for Molecular Oncology (established as a joint venture between Queen Mary and Zhengzhou University in 2006) and his creation of the Academy of Medical Sciences in China.

He was appointed Commander of the Order of the British Empire (CBE) in the 2022 New Year Honours for services to clinical research, for taking a leading role in orchestrating the NIHR's coordinated response to the COVID-19 pandemic. This included chairing the Urgent Public Health group, which identified and ensured the delivery of the 100 most vital COVID-19 studies and leading the Long COVID awards scheme, which has seen more than £50m invested into 19 studies on this disease. I know I speak for us all when we thank him for being a devoted mentor and unwavering leader. If you've worked with Nick, he will have changed your life. After 20 years of leadership as Director of the BCI, Nick is stepping down to continue his work in the Centre for Cancer Biomarkers and Biotherapeutics lead. We wish his successor, Nitzan Rosenfeld, the very best as he takes on the role of Director of BCI from 2024 onwards.

So, in 20 years, we've grown from 75 to 421 staff at BCI. We've raised cumulative funds in excess of £100m in just the past five years. The BCI is a place where people really work together, and we now cover all angles of cancer biology, signalling and molecular regulation, bioinformatics, stem cell biology, evolution, metabolism, biotherapies, tumour microenvironment, multi-omics analysis, spinout companies rising and much more.

I think sometimes we take the BCI community and working together for granted. But it's true: it is the core of our success and hard to find elsewhere. I apologise here if I have excluded any details of your contribution since space was limited, but rest assured that your contribution to the team is valued. There's no 'impact factor' for working together, but if there were, we would score higher than any other institute that I know. Even those who have flown the nest along the way will say that there is something special about the Barts Cancer Institute that they can't substitute for anywhere else.

Happy 20th birthday BCI. Here's looking forward to even more success over the many, many years to come.

New Therapies
Professor John Gribben

A long history of cancer innovation treatments at Barts

Barts boasts a rich history in pioneering cancer treatments, dating back to 1970 when the Imperial Cancer Research Fund established the UK's first Medical Oncology Unit at St Bartholomew's Hospital. Professor Gordon Hamilton Fairley, an eminent figure in the field, was appointed as its Director. Under his leadership, the Fund endowed a chair in Medical Oncology at the hospital in 1971, with Professor Fairley becoming the inaugural Professor of Medical Oncology in the UK. This marked a new era in establishing medical oncology as a recognised area of training in the United Kingdom.

Professor Fairley trained at Magdalen College, Oxford, and St Bartholomew's Medical College and graduated in 1954. After house jobs at Barts and the Royal Postgraduate Medical School, he returned to St Bartholomew's as a registrar and later as a senior registrar. This marked the beginning of his pioneering work in the field of malignant disease, particularly in cancer immunology. His doctoral thesis focused on the immune mechanisms underlying chronic lymphatic leukaemia and other reticuloses, laying the groundwork for many subsequent contributions to the field. In 1965, Professor Fairley joined the staff of St Bartholomew's Hospital, followed by a position at the Royal Marsden Hospital two years later. His exceptional abilities, relentless drive, and captivating personality propelled the research unit to immediate success, earning him international acclaim in medical oncology. Renowned for his captivating lectures, Professor Fairley's expertise was sought after across the globe, with invitations pouring in from the United States, Australia, and various European

nations. Tragically, his life was cut short at the age of 45 by the detonation of a terrorist bomb intended for his neighbour. However, his visionary work laid the foundation for the continued success of the academic ICRF Unit at Barts through ongoing pioneering work led by Professor Bodley Scott, Professor Jim Malpas, Professor Andrew Lister, Professor Tim Oliver and Professor Fran Balkwill.

The ICRF Department of Medical Oncology later evolved into the Barts Cancer Institute at Queen Mary University of London that we know today. The BCI, in partnership with the Cancer Research UK City of London Major Centre, continues the long tradition at Barts and remains steadfast in its commitment to translating basic research findings into innovative cancer treatments. At the time, BCI identified five key research themes: cancer prevention & risk reduction, cancer screening & early diagnosis, genetics & evolution of cancer, targeting tumour cells, and targeting the tumour microenvironment. These research themes served as focal points for multidisciplinary integration and collaboration, facilitating the translation of scientific discoveries from the laboratory to the bedside. Working in tandem with the Experimental Cancer Medicine Centre (ECMC), BCI continues to

Professor Gordon Hamilton Fairley

The Gordon Hamilton Fairley Lecture & Medal

The BCI commemorates Professor Fairley with the Gordon Hamilton Fairley Lecture & Medal, awarded to those with an outstanding and distinguished career in the field of cancer research.

Previous winners include:

- 2011: Professor John Gribben
- 2015: Professor Sir Alex Markham
- 2018: Professor Charles Swanton
- 2023: Professor Iain McNeish
- 2024: Professor Thomas Powles

bridge the gap between research and clinical practice, bringing novel treatments to patients with cancer.

Innovative cancer treatment and the evolution of the Centre for Experimental Cancer Medicine

The ECMC Network was launched in 2007 by Cancer Research UK and the Department of Health with a view to ensuring that the UK remains at the forefront of international efforts to beat cancer. Today, this initiative connects world-leading laboratory and patient-based clinical research from 17 adult and 12 paediatric centres of excellence across the country. The network supports local collaborations between universities and NHS hospitals to promote efficient delivery of early-phase cancer studies and enable faster and more personalised patient benefit. To date, the ECMC network has provided more than £150m in funding, made possible by support from Cancer Research UK, the Little Princess Trust, the National Institute for Health Research (NIHR) in England, and the Health Departments for Scotland, Wales, and Northern Ireland.

The ECMC network's focus on pioneering 'bench to bedside' medicines – clinical applications borne out of early scientific discoveries – fit perfectly with our ethos at Barts. Professor Nick Lemoine and I submitted a successful application for funding from Cancer Research UK and the National Institute for Health Research in the first wave, and in 2010, Barts ECMC was the first centre in the UK to launch amid a blaze of national publicity. At the time, I already led the North East London Cancer Research Network (NELCRN), which supported later-phase cancer clinical trials. With a keen eye for synergy, Nick and I combined the early-phase clinical trial activity in the Barts ECMC with the later-phase clinical trial resources of the NELCRN to set up the newly formed Centre for Experimental Cancer Medicine within the BCI.

An old photo of a (slightly) younger Professor Nick Lemoine and Professor John Gribben at the Barts ECMC opening.

Barts ECMC quickly established itself to help bridge the gap between scientific discovery underway at the BCI and clinical application in London's patient population. Its mandate was ambitious and encompassed a multifaceted approach to delivering excellence in translational cancer research, conducting clinical trials with ethical and scientific integrity, strengthening governance and the evidence base for cancer management and expanding access to innovative treatments for cancer patients.

Barts ECMC rapidly earned its stripes, broadening its scope to encompass novel therapeutic modalities and a diverse array of tumour types. With an annual capacity to serve over 9,000 patients, the centre has stood as a testament to the power of collaborative research.

Under the visionary leadership of Professor Peter Schmid, Barts ECMC embarked on a journey of creative discovery. Peter spearheaded a transformative agenda, leveraging his expertise in breast cancer, early drug development and cancer immunotherapy (the approach of stimulating the host's immune system to recognise and attack malignant cells, which has revolutionised treatment in recent decades). Peter's pioneering work epitomised the centre's commitment to pushing the boundaries of scientific inquiry, with a keen focus on translating preclinical research into clinical breakthroughs. In particular, his work centred around newly emerging areas of cancer immunotherapy and resulted in Barts leading the field in a number of innovative trials, changing the face of how we treat many cancers today.

For example, Peter led the KEYNOTE-522 study, which found that adding the immune-checkpoint inhibitor Pembrolizumab to chemotherapy prior to surgery benefits patients with stage II or III triple-negative breast cancer, a notoriously aggressive and hard-to-treat subtype. Immune checkpoint inhibitors such as Pembrolizumab block proteins that enable cancer cells to evade immune detection, enhancing the body's ability to mount an effective immune response against tumours. This combination therapy led to a 37% decrease in the recurrence of this type of cancer. In addition, Peter also led the Impassion130 trial, which prolonged progression-free survival in patients with metastatic triple-negative breast cancer and resulted in the first approval of an immunotherapy for breast cancer patients. As such, his work has created a tangible improvement in the lives of women with this challenging cancer type.

Barts became an immunotherapy Centre of Research Excellence (imCORE centre) in

2016, forming part of a global network of basic and clinical scientists from 26 leading academic research institutions in cancer immunotherapy established by Roche. Centres in the imCORE network work together to accelerate the characterisation of complex biology and drive novel immunotherapy combination strategies to identify ways for more patients to benefit from immunotherapy.

The Barts ECMC team now comprises an academically led Trials Team responsible for the development and management of investigator-led clinical trials as well as a Cancer Research Delivery Group (CRDG) responsible for the recruitment and clinical management of Barts Health NHS Trust patients participating in clinical trials. The Clinical Trials Team has greatly enhanced Queen Mary's ability to lead academically sponsored clinical trials. The centre's vision and strategic priorities remain to facilitate the transfer from preclinical research undertaken at the BCI into the clinic, using biomarker-driven strategies to better understand the biology of novel treatments, thereby expanding our translational research and developing a programme of rational combinations of immunotherapy.

Meanwhile, Professor Thomas Powles has become a leading force in the field of genitourinary oncology. Professor Powles is Professor of Genitourinary Oncology at Queen Mary and is the Director of Barts Cancer Centre at St Bartholomew's Hospital. Tom's contributions have heralded a new era in cancer therapeutics, and he has led innovative clinical trials. Notably, Tom and his team published groundbreaking results of the EV302 trial, which revealed that a combination of enfortumab vedotin (an antibody drug conjugate) and pembrolizumab (an immunotherapy drug) doubled life expectancy in people with advanced bladder cancer from around 16 months to two-and-a-half years. This advance has been referred to as "the biggest breakthrough in the treatment of advanced bladder cancer that we've had in roughly 40 years".

Tom's pioneering work was recognised in December 2023, when he was named by *Nature* in their annual list of ten influential individuals around the world who have contributed to some of the year's key scientific developments. In May 2024, he was also recognised in *TIME* Magazine's inaugural TIME100 Health, a new annual list of 100 individuals who most influenced global health that year. These accolades recognise Tom's work on new treatments for metastatic bladder cancer as a world-class contribution to science.

From the bench to the bedside

A prime example of the translational work being performed here at BCI is the research conducted by Professor Peter Szlosarek, Professor of Medical Oncology at Queen Mary. Leading a team from the Centre for Cancer Biomarkers and Biotherapeutics at BCI, Peter's primary research focus revolves around understanding the aberrant expression of *ASS1* (encoding a protein that enables cells to manufacture the amino acid arginine) in human cancers and elucidating how this knowledge could be leveraged for effective anticancer therapy. Spearheading an active translational program, he orchestrates the progression of discoveries from laboratory experimentation to clinical application, particularly in the realm of arginine-depleting agents such as ADI-PEG20. Professor Szolarek's endeavours extend across various challenging cancer types, including those under investigation in the ADAM, TRAP, and ATOMIC clinical studies. Additionally, his leadership extends to his roles as Chair of the National Cancer Research Institute (NCRI) mesothelioma subgroup and as a member of the European Organisation for Research and Treatment of Cancer (EORTC) lung and melanoma groups.

An exemplary testament to this innovative translational effort is the treatment pioneered by his work, which led to a novel phase III clinical trial that was recently published in *JAMA Oncology* and sponsored by Queen Mary and Polaris Pharmaceuticals. This represents a significant breakthrough in combating malignant pleural mesothelioma (MPM), a rare yet devastating cancer primarily linked to asbestos exposure, which historically presents limited therapeutic avenues. The trial unveiled a novel combination therapy involving traditional chemotherapy alongside the innovative drug ADI-PEG20, resulting in a remarkable increase in median survival by 1.6 months and an astounding quadrupling of survival rates at the 36-month mark, compared to placebo-chemotherapy.

These findings carry profound implications, considering that MPM boasts one of the most dismal 5-year survival rates among solid cancers, hovering around a mere 5-10%. This pioneering approach signifies the first successful integration of chemotherapy with a metabolism-targeting drug for this disease in over two decades, offering a beacon of hope for patients and clinicians alike. The culmination of this achievement is embodied in the ATOMIC-meso trial, representing two decades of dedicated research at BCI, all initiated by Peter's seminal discovery during his PhD

in Professor Fran Balkwill's lab, concerning the absence of ASS1 protein in malignant mesothelioma cells – a pivotal insight driving the quest for effective MPM treatments.

Ongoing investigations continue to explore the potential of ADI-PEG20 across diverse cancer types, including sarcoma, glioblastoma multiforme, and others reliant on arginine metabolism. The success witnessed in MPM treatment underscores the prospect of this drug in addressing multiple cancer types, promising a paradigm shift in therapeutic strategies.

In this area, Dr Bela Wrench and Dr Michael Austin from the Centre of Haemato-Oncology at BCI are exploring how ADI-PEG20 might enhance the effectiveness of CAR-T cell therapy (immunotherapy that reprogrammes T cells to better target malignant cells) in treating B-acute lymphoblastic leukaemia. They have proposed that this treatment could increase the sensitivity of leukaemia cells to CAR-T therapy by priming key cell death pathways.

Although CAR-T therapy has revolutionised the management of relapsed or refractory B cell leukaemia, particularly in children and young adults, it still faces obstacles such as resistance and relapse, which can curtail its long-term benefits for many patients. Bela and Michael's research delves into the intricate mechanisms of cellular immunotherapy, shedding light on the role of arginine deprivation with ADI-PEG20 in sensitising ASS1-deficient cancers to apoptosis-inducing signals. By elucidating these mechanisms, their findings provide a compelling framework for optimising CAR-T therapy, with potential implications for refining future strategies in cellular immunotherapy development.

Ongoing translational work

Translational work continues across the BCI, with a number of promising approaches progressing towards the clinic. I discuss a few examples here, but there are many more to be found throughout the remainder of this book.

Professor Hemant Kocher is leading a clinical trial, STARPAC, which is investigating a new approach to treat pancreatic cancer by targeting cells in the tumour microenvironment. This work arose from research in Hemant's laboratory, which found that using a form of vitamin A helped to subdue pancreatic stellate cells, preventing them from building dense stroma around the pancreatic cancer, which

shields it from immune and therapeutic attack. Treatment with a form of vitamin A, ATRA, led to a reduction in cancer cell proliferation and invasion. The phase I STARPAC trial showed that the addition of ATRA to standard chemotherapy caused no additional harmful effects in patients when compared with standard chemotherapy alone and suggested that the combination modifies the pancreatic cancer stroma in patients. A phase II trial is now underway to investigate this approach further.

Professor Yaohe Wang and his team, working with Professor Nick Lemoine, are researching the use of oncolytic, cancer cell-infecting viruses for the treatment of pancreatic cancer. This approach could work alone or in combination with current immunotherapies to improve their efficacy. In 2022, Yaohe and Nick launched a new spin-out company, VacV Biotherapeutics, building on more than 20 years of research from his and Nick's teams. VacV aims to develop Vaccinia virus-based cancer therapeutics that both destroy the cancer and create an immune response that activates and recruits more immune cells to fight the cancer. The company is currently in the preclinical phase of development.

My own work has focused on the mechanisms whereby cancer cells induce immune defects. In particular, we have demonstrated that leukaemia and lymphoma cells induce T cell defects with impaired actin polymerisation, resulting in decreased immune effector cell function. We have explored ways to reverse these defects and found that the drug lenalidomide could address several of them. I led the phase III trial that led to the approval of lenalidomide and rituximab for follicular lymphoma based on this research work. I have led the introduction of CAR-T cells at Barts, and we are now an approved treatment centre for this modality. Our research work has focused on steps to improve CAR-T function, including the use of BTK inhibitors.

We all await the next exciting translations of the research work at BCI to improve the lives of our patients with cancer.

Understanding the Tumour Microenvironment

Professor Fran Balkwill

When asked what they understand by the term 'cancer', most people refer to cells becoming malignant, using phrases such as 'cells out of control' – but that is only half the story. Cancers are not just made of malignant cells but also 'normal' cells that have been recruited and corrupted to help the tumour grow and spread. Cancers are more like rogue tissues. This combination of malignant cells and normal cells, embedded in a fibrous extracellular matrix (ECM), is called the tumour microenvironment (TME). The mixture of cells in this complex, abnormal and dynamic environment communicate using molecules such as integrins (see the next chapter) and cytokines, which are locally acting signalling molecules especially important in controlling our immune responses.

I first became fascinated by TME research way back in 1986, when I read an article entitled 'Tumors: Wounds that do not heal', by an American scientist called Professor Harold Dvorak. Nearly 40 years later, his hypothesis is clearly proven: in most, if not all, cancers, cells that normally repair damage and fight infections are, unfortunately, also involved in every stage of cancer development and spread. And I believe that the greatest progress in understanding the TME has been made in the past 10 years.

However, Barts Cancer Institute has a reputation for TME research that goes back further. In the first years of the Institute, the Centre for Cancer and Inflammation focused on the role of the cells and cytokines of the innate immune system in the TME. Before moving to BCI, we discovered that an inflammatory cytokine (maybe inappropriately known as tumour necrosis factor, TNF) was necessary for development of some skin tumours in mice. Eventually, this research led us to test

antibodies that neutralised TNF in patients with advanced cancer. Although these were ineffective in advanced cancers, the lessons learnt may still be useful 20 years later (see the end of this chapter). In 2019, we expanded the centre to encompass the ground-breaking work of Professor Kairbaan Hodivala-Dilke (Kebs) on tumour blood vessels and renamed it the Centre for Tumour Microenvironment under Kebs's leadership.

Deconstructing the TME of ovarian cancer

I will continue this chapter by describing my group's research on a common type of ovarian cancer: high-grade serous ovarian cancer (which I will subsequently refer to as ovarian cancer for simplicity). Although research into this TME has been our focus for the past 10 years, our work has only been possible because we were simultaneously learning from TME research in other BCI labs and around the world.

The project began in 2013, when I was fortunate to obtain a European Research Council 'Advanced' grant and a Cancer Research UK programme grant: our aim in both of these grants was to improve our understanding of the ovarian cancer TME. As ovarian cancer is normally diagnosed when it has spread, we decided to study the TME of the advanced cancer: the different cells, the fibrous ECM, the cytokine proteins that allow cell communication and the physical characteristics (stiffness). This 'deconstruction' phase was to act as a template and validation for our attempts to develop new experimental models that would help us find new treatments for patients. This is important because, although many cancer treatments target the malignant cells, newer biological therapies, especially immunotherapies (see previous chapter), tackle the interactions between malignant cells and the other cells of the TME, aiming to turn the TME from cancer-promoting to cancer-destroying.

Three important TME discoveries of the past 10 years

So, what have we, and others, learnt about the ovarian cancer TME in the past 10 years and how does it relate to other cancer TMEs? I would suggest that there have been three major advances in TME research. First, while there are many places in the body where cancers can develop and many reasons why they develop, their TMEs are quite similar. Although all cancer biopsies will contain some immune cells, abnormal blood vessels, 'builder' cells called fibroblasts and the fibrous ECM, the

proportions of these elements vary between patients and even in different biopsies from the same patient. TME types can be roughly divided into 'immune desert' with few immune cells, 'inflammatory' with many immune cells, 'fibrotic' with high fibroblast numbers and ECM proteins and 'immunosuppressed' with dysfunctional and 'exhausted' immune cells. Importantly, these four TME types are found in cancers from all around the body, not only ovarian, but, for instance, breast, bowel, lung, pancreas, bladder, skin and liver. This is why some immunotherapies, such as immune-checkpoint blockade, work in different cancers. The reason they work has more to do with the TME type rather than the origin of the malignant cells, although we don't fully understand the TME features that make a cancer especially susceptible to some current immunotherapies. For instance, although we and many others have found that ovarian cancers have immune cells in their TME that have the potential to recognise and destroy malignant cells, current immunotherapies have not been successful in this cancer type.

The second important TME finding of the past 10 years is that some of the proteins that are found in the TME are just as important as the cells. When we were 'deconstructing' ovarian cancer, we found that its fibrous ECM was made from around 150 different proteins, and there was one mixture of these proteins that was especially bad news. Patients who had this mixture of ECM proteins had a poorer prognosis. Moreover, this type of ECM was found in 12 other common cancer types and was associated with the worst outcomes in all of them.

Oliver Pearce, who worked on our original ovarian cancer TME project and is now a Senior Lecturer at BCI with his own group, has been exploring why this pattern of molecules inhibits anti-tumour immune responses in the TME. He has found that the structure of these molecules differs across TME types. In tumours where immune cells infiltrate and contact the cancer cells, there is more space between ECM fibres. He thinks differences in fibres explain why the immune cells can penetrate deep inside the tumour. To test this idea, he has built a decellularised tumour model, comprising the ECM environment of a tumour stripped of its native cells, in which new cells can be introduced. In this model, immune cell behaviour and malignant cell killing can be measured in real-time. Using this model, his group recently found that the tumour ECM on its own can make immune cells cancer-promoting. Small modifications to the ECM may be able to change them into immune cells that can help fight against the malignant cells. Oliver is currently developing ECM-targeting treatments in

collaboration with an industry partner. To make his decellularised model available to the community he has established a service within our centre called Matrix Dynamics, which academics and industry can access for either fundamental studies or as a drug testing platform with a relevant tumour ECM.

In my group, postdocs Dr Bella Kotantaki and Dr Florian Laforêts are also studying drugs that can reduce ECM stiffness in our mouse ovarian cancer models to see if these can increase the penetration of anti-cancer immune cells deep inside the tumours.

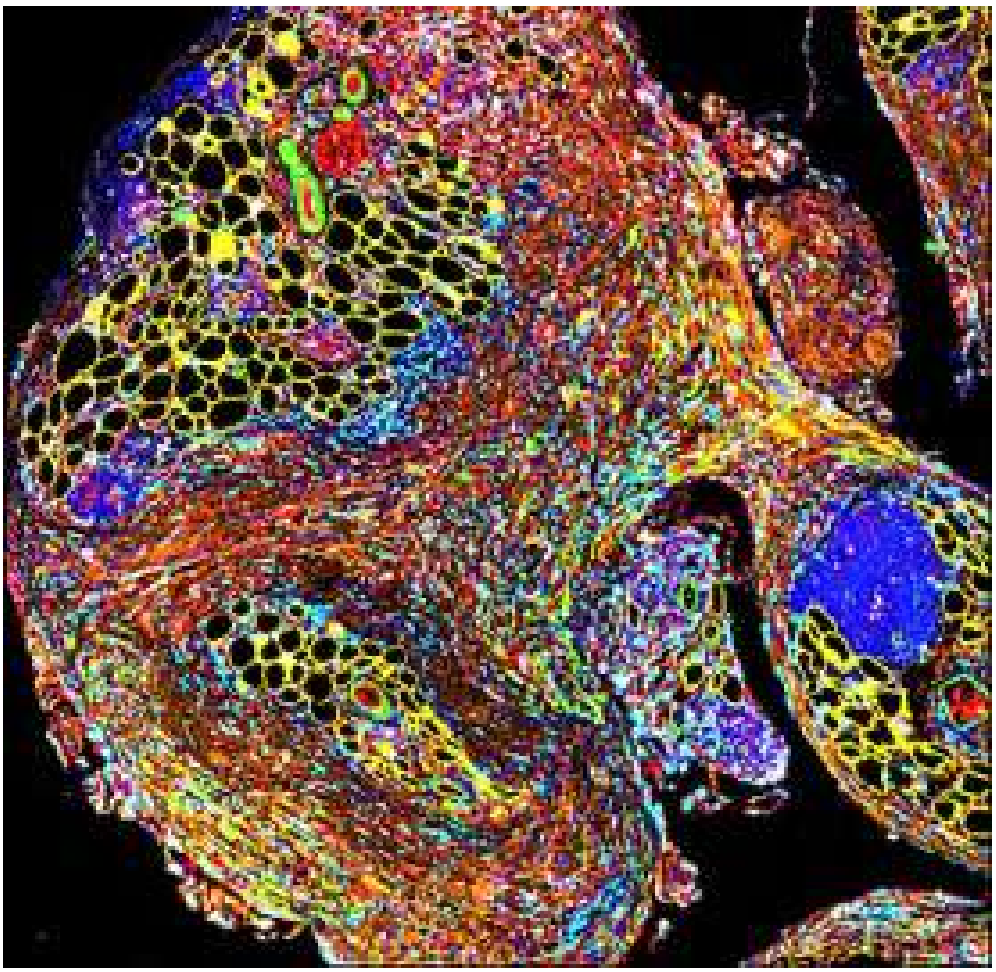
While you may think that drugs such as chemotherapy kill rapidly dividing malignant cells, that is, again, only half the story. We, and others, have found that cancer treatments such as chemotherapy and radiotherapy also affect other cells in the TME, as well as the ECM. I believe this is the third important finding in TME research in the past 10 years. When the entire cancer mass (i.e., the rogue tissue) is damaged by a treatment, the immune cells, fibroblasts and blood vessel cells in the TME react to danger and damage signals in an acute way that can stimulate a useful immune response to the cancer. This is in contrast to the chronic harmful actions of immune cells in the TME that usually help the cancer grow and spread. In fact, many chemotherapies and radiotherapies also can be considered immunotherapies, at least in some of their actions.

Because many ovarian cancer patients have chemotherapy after diagnosis but before surgery, we have been able to study the effects of chemotherapy in patient samples – by taking tumour samples before and after treatment. We have discovered not only that three cycles of chemotherapy destroy some of the malignant cells, but also that this destruction attracts and stimulates immune cells in the TME to destroy even more malignant cells.

Unfortunately, at the same time, the 'good' effect of chemotherapy is countered by immune-suppressive molecules being made by the malignant and other TME cells. We believe that this knowledge can be exploited to benefit patients by combining chemotherapy with immunotherapies. If we can find the right combinations it may also mean that only three cycles of chemotherapy will be needed instead of the usual six that are given to ovarian cancer patients. This is a special focus of BCI clinical lecturer Dr Samar Elorbany.

New techniques for studying the TME

One of the reasons for progress in TME research is that we have been able to use an exciting number of new techniques in the past 10 years. One of the most useful has been a technique called single-cell RNAseq. This allows us to study the RNA profiles of tens of thousands of individual cells in a cancer. We can then identify types – and sub-types – of cells and the proteins they are likely to make from this RNA in an unbiased manner. We have begun to decipher the 'language' of the TME – the signal proteins that the different cell types use to communicate and control.



Cell DIVE imaging of a mouse ovarian tumour. Each colour identifies a different cell type: the red cells are malignant cells and all other colours identify 'normal' cells that make up the tumour microenvironment. This work is by Dr Bella Kotantaki and Dr Florian Laforêts together with Joe Hartlebury who is funded by the CRUK City of London Major Centre.

We also need to know what proteins the TME cells are making and where they are made, and there are new techniques for this as well, such as Cell DIVE. We are seeing the TME in more detail than ever before and beginning to understand its complexities and the ways it differs from normal well-behaved tissues and organs (see figure on p30).

Novel TME models

As I mentioned above, TME research has implications for patients because many treatments that are now being tested aim to disrupt the unhealthy relationship between the malignant and other cells and molecules of the TME. Cancer models in mice have been important in testing treatments currently in use today, but for TME research we need to be sure that any models we use have TMEs that closely resemble their human counterparts. Most mouse cancers grow much more rapidly than human tumours, and we cannot be certain that they will have a relevant TME. Dr Chiara Berlato and Dr Ganga Gopinathan in my group made some new ovarian cancer mice that grew more slowly and then, using the same techniques that we used in the 'deconstruction' phase of the human ovarian cancer project, Dr Eleni Maniati, Chiara and Ganga compared the mouse to human TMEs. The figure on p30 shows an example of one of these models where we have evidence for a complex TME in a mouse tumour. Although there were some differences between mouse and human tumours, the results were generally reassuring and showed that we could use these models to research new biological therapies alone or in combination with chemotherapy.

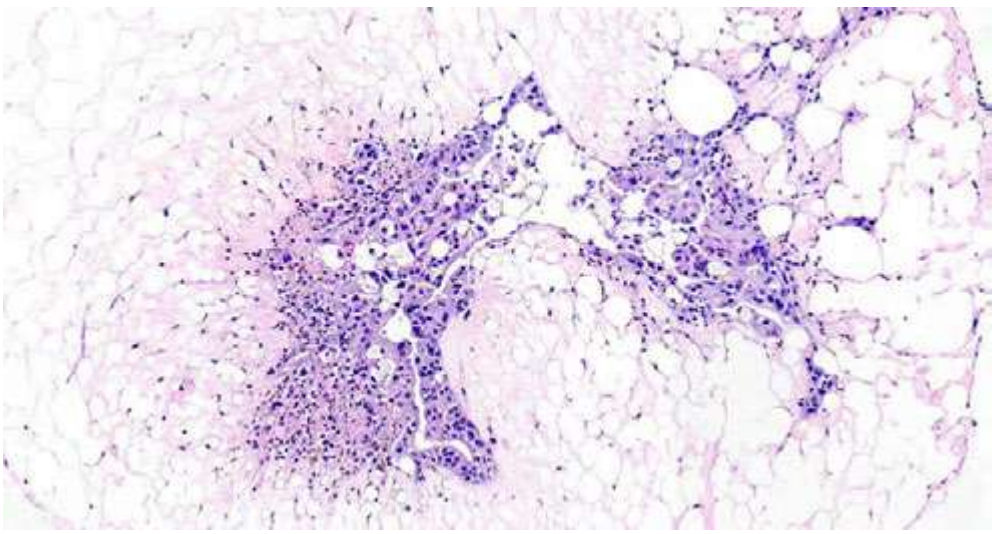
It is critically important to always start TME research with study of the human cancer, and therefore alongside better mouse models with well-characterised TMEs, we also need to study the dynamics of the TMEs of human cancers. We have developed three ways of modelling the human TME to understand and intervene therapeutically. First is a technique that allows us to study, for a short period of time (one to three days), an entire human TME using a technique first developed by Dr Emmanuel Donnadieu in Paris. Florian takes 320 micron (about ⅓ of a millimetre) slices of live cancers and using special fluorescent dyes, measures the movements of immune cells in the TME. He has found that the immune cells in samples from chemotherapy-treated patients or mice have altered patterns of movement and that there is good agreement in results with mouse and human samples. As this

technique studies the entire TME, we think it may be a stepping-stone between preclinical models and patients.

The second advance is to develop TME models made entirely from human cells. Postdoc Dr Bea Malacrida is growing mini-human tumours made of five different cell types, four 'normal' cell types and ovarian cancer cells. When they are combined in three-dimensional gels, we find that they organise themselves in a similar way to the human tumours. Also, malignant cells from different patients have distinct effects on the structure and behaviour of the 'penta-cultures' even though they are from the same type of tumour. These human cell models are giving us new insights into TME regulation and are allowing us to test new treatments that target the TME.

The third advance is to take these mini-tumours and give them a blood supply in a 'microfluidic chip'. In these 'chip' models, postdoc Dr Joash Joy in my group can deliver T cells that have been genetically engineered to attack ovarian cancer cells through tiny blood vessels. We believe this will help us understand why CAR-T cells work in some blood cancers but are of no benefit in cancers such as ovarian.

Multi-cellular models of breast cancer using normal and malignant human cells are also being grown in other BCI labs, for instance, those of Professor Richard Grose, Professor John Marshall and Dr Luigi Ombrato. I believe that this way of modelling the TME has the potential to help us understand basic mechanisms of communication



Human ovarian cancer penta-cultures These are made from human fat cells, fibroblasts, mesothelial (lining) cells, macrophage immune cells and ovarian cancer cells. This work is by Dr Beatrice Malacrida.

between malignant and normal cells and will allow for more rapid preclinical screening of potential TME-targeting treatments.

Chicken or egg – how is the TME established?

Although we know a lot about the different cells that make up the TME, there is still much to learn about how TMEs are established, both as a tumour first develops and when a metastasis is established. Understanding the TMEs of the earliest stages of primary tumours and metastases could lead to new treatments that prevent cancer development and spread.

Dr Stuart McDonald's group at the BCI is studying TME changes that may identify why some people with non-malignant abnormalities of the oesophagus will go on to develop cancer. A fundamental question is whether the cells that surround the pre-malignant cells are important in causing cancer development. As people age, cells in many tissues have mutations that could lead to cancer, but they don't. This raises the question: are the other cells of the TME the trigger and not the cancer-causing mutations?

Dr Luigi Ombrato's group is studying the very earliest stages of breast cancer metastasis. This is very difficult to do, even in mouse cancer models, because the metastases are extremely small and not visible to the naked eye. Luigi solved this problem by inventing a technique called 'cherry-niche'. In mouse models, when malignant cells containing the cherry-niche dye grow as lung metastasis, they stain TME cells close by with the red dye allowing Luigi to see the very first cells that are recruited by the malignant cells and hence how the TME develops in a metastasis.

Blood vessels in the TME

This chapter has not so far, mentioned another critical component of the TME, blood vessels. Tumours cannot grow without a blood supply but in cancers the vessels are leaky and abnormally structured. Kebs's work has led to important new insights into the development and regulation of the TME vasculature, not only the endothelial cells that line these vessels but also the mural cells that were thought to form a protective scaffold for the vessels. Kebs's group showed that these mural cells can interact with other TME cells, especially by the production of tumour-promoting molecules that stimulate malignant cell growth. This discovery suggests a new

approach to targeting tumour blood vessels that can be exploited in clinical trials. Kebs's discoveries are covered in detail in the next chapter.

Treatments that target the TME

The knowledge that cancers are made of a dynamic and complex mixture of cells and ECM suggests new ways of treating cancer by disrupting the TME. Immunotherapies are a successful example. Immune checkpoint blockade allows cytotoxic T lymphocytes to overcome suppression by malignant cells. But this single treatment only works in a minority of patients and in some cancer types. The knowledge that we have gained over the last 10 years suggests that combinations of TME treatments are most likely to be successful in the future. We probably need to devise a combination or sequence of drugs that stimulate or re-educate immune cells in the TME from their suppressed and exhausted state; inhibit and normalise blood vessels; loosen the stiff matrix and dampen cancer-promoting inflammation (maybe with antibodies to inflammatory cytokines that we first tested 20 years ago) alongside selective targeting of the malignant cells.

The future of TME research

As described above, I believe that we have enough knowledge to devise combination therapies that attack different aspects of the cancer-promoting TME and will benefit more patients. However, the information we are now obtaining, especially from techniques like CellDive we described above, will require machine learning and AI approaches to devise and personalise the best approaches. The result of this TME-targeted approach to cancer treatment needs to be long-lasting immune memory that keeps at bay any remaining malignant cells.

Integrins in Cancer

Professor John Marshall

Integrins are molecules that integrate (hence their name) the world outside of the cell with that inside of the cell. They are present on the surface of all cells with a nucleus and are composed of two chains: an alpha (α) and a beta (β) chain, forming pairs containing one of each chain. Upon binding to molecules outside of the cell, integrins help to deliver signals inside the cell that can change its behaviour. In cancer cells, these signals might result in cells moving, invading or a combination of both, resulting in them spreading to another organ (metastasis). In addition, blood cells need integrins to exit the blood to fight infections, and integrins also control whether cells divide.

Both Professor Kairbaan Hodivala-Dilke (Kebs) and my lab have worked on integrins in cancer for two decades. My own fascination with integrins began during my PhD with Professor Ian Hart at the ICRF's Lincoln's Inn Fields labs in the 1980s. When new data suggested that these molecules might be playing an important role in metastasis, our whole lab shifted to study integrins, with my work focusing on melanoma. Nobody had done this work before, and everything was new – it was enormous fun. Then, late one Wednesday night, I looked at a band on one of my gels and realised that I had discovered a new integrin that nobody had described before. But by a cruel coincidence, the following morning, a paper was published in *Nature* by another group announcing the discovery of that same molecule – now known as αvβ1. I had been scooped, and yet I simply felt excited to have found something so important, even if that discovery was only mine for an evening. My work has focused on the study of integrins ever since, and it has never been a more exciting field than

it is today.

But before discussing my own work, I will begin by introducing Kebs' research. Kebs' early work changed our understanding of how new blood vessel growth (angiogenesis) in cancer is controlled. This process is crucial, as tumours must cultivate and plumb themselves into a blood supply of their own to acquire sufficient nutrients and oxygen to grow beyond a few millimetres in size. In the late 1990s, research from the USA showed that the integrin αvβ3 appeared at high levels on endothelial cells (cells that line the blood vessels). These data eventually led to the hypothesis that αvβ3 is required for the growth of cancer blood vessels and that blocking αvβ3 would therefore limit the ability of tumours to grow and spread.

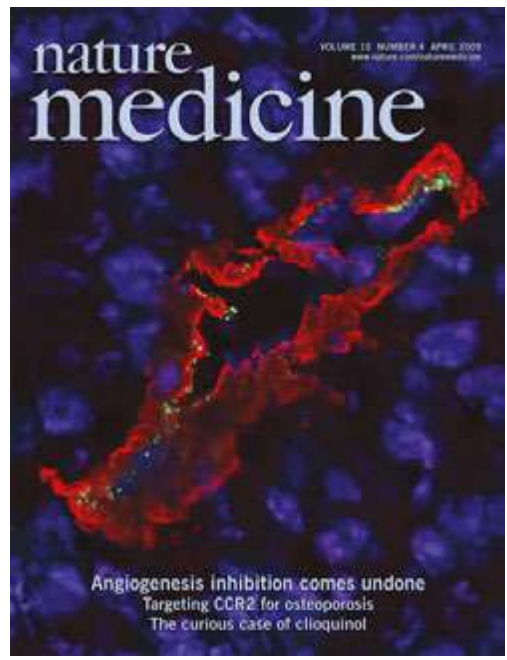
Billions of dollars were spent by pharmaceutical companies generating antibodies and other drugs that stopped αvβ3 signalling for the treatment of cancer. Unfortunately, none of these anti-cancer clinical trials targeting αvβ3 worked. Kebs first began research in this area as a postdoc with Professor Richard Hynes in Boston, USA. When Kebs returned to the UK she joined Ian Hart's lab. Within just a few years, with her amazing team, especially the outstanding Dr Louise Reynolds and Dr Stephen Robinson, she studied genetically modified mice that lacked αvβ3 and/or the related αvβ5. Surprisingly, they showed that mice that had no αvβ3 on their endothelial cells actually grew *larger* tumours that had *higher* numbers of blood vessels. They showed the reason for this counter-intuitive result was that αvβ3 signalling *reduced* how much of the endothelial growth factor receptor (VEGFR) appeared on endothelial cells – a molecule that promotes blood vessel growth. So removing αvβ3 in transgenic mice using genetic tricks increased the amount of VEGR significantly and caused *more* blood vessels to develop, allowing *bigger* tumours to grow. These results suggested that we needed a better understanding of integrins and the effects of potential cancer therapies that target these molecules.

More recently, Kebs has studied the effect of αvβ3 in cells that form part of the blood vessel wall, known as mural cells. Mural cells include smooth muscle cells and pericytes, multi-functional cells that wrap around the endothelial cells that line capillaries. Kebs showed that the genetic loss of αvβ3 from these cells changes the way they signal to their local environment. Her team has coined this type of paracrine signalling from pericytes 'pericrine' signalling. This change in pericrine signalling, controlled by the loss of β3 from these cells, stimulates the surrounding

tumour cells to survive and grow more. Looking at human breast cancer, lymphoma and melanoma, the team found that cancers in patients with low levels of muralβ3 integrin grow faster and more aggressively, and the mechanisms in mouse models and humans are likely to be similar. This work defined a possible new way in which cancer is controlled.

Kebs and her team have also extensively explored the role of a molecule called Focal Adhesion Kinase (FAK), which plays a fundamental role in integrin signalling. They reported that loss of FAK from endothelial cells prevented the initiation of tumour angiogenesis but had no effect on the number of blood vessels in already established tumours. However, loss of endothelial cell FAK in established tumours sensitises these tumours to DNA-damaging therapy, like radiotherapy. It does this by altering the protective chemical cocktail made by endothelial cells that usually behaves like the 'invisibility blanket' to stop DNA-damaging therapies from effectively killing cancer cells.

Finally, Kebs has challenged the widely accepted belief that stopping angiogenesis is a good way to prevent tumour growth. A study, published in *Nature Medicine*, led by Dr Andy Reynolds in Kebs' lab showed that a molecule designed to block αvβ3 function and, therefore, actually significantly increased angiogenesis when used at extremely low concentrations over one thousand times lower than is used usually to block αvβ3 function. When Dr Tony Wong combined these low, angiogenesis-promoting doses of αvβ3 inhibitor with therapeutic doses of cytotoxic drugs, he was able to deliver higher concentrations of cytotoxic drugs to experimental tumours. This significantly increased the effectiveness of therapy whilst reducing side effects, even in models of pancreatic cancer that formerly did not respond to treatment.



The cover of Nature Medicine, featuring the work of Reynolds et al. (2009).

The likely explanation is that tumour blood vessels are often poorly organised and, in some cancers, such as pancreatic cancer, low in number. By transiently increasing the number of blood vessels in a tumour, delivery of therapy to the cancer cells is far more efficient and thus far more effective. Kebs is trying to translate these key findings into a clinical trial.

My own work has focussed on a particular integrin molecule, αvβ6. This molecule was discovered in the 1990s and found to be exclusively present on epithelial cells (the cells that line the inner and outer surfaces of the body). Usually, however, it is only detectable during wound repair, development and cancer: all processes that require tissue remodelling. Then, in the early 2000s, my lab discovered that integrin αvβ6 promoted cancer cell migration and invasion, suggesting that the increased levels of this molecule seen on cancer cells may actually be promoting disease. Dr Gareth Thomas (now a professor), who was working with Professor Paul Speight, worked in my team as part of his PhD and showed that αvβ6 promoted the release of the inactive forms of enzymes that break down collagen – a major component of the extracellular matrix, the molecular scaffolding that surrounds our cells and gives our tissues structure. This helps tumour cells breach the structures confining them within a tissue, enabling them to proliferate and spread through connective tissues. Inhibition of the function of these enzymes, or indeed αvβ6, inhibited the ability of the cancer cells to invade collagen-rich gels (which mimic the extracellular matrix), raising the possibility that targeting αvβ6 may present a new way to treat cancer in the future.

My team developed a lab model system called organotypic cancer mimetic gels, consisting of a collagen gel that mimics human tissue, on which we could grow cancer cells. This setup allowed us to recreate the interface between the tumour and its environment. By chemically or genetically manipulating the cells in this model, we showed that αvβ6-dependent invasion of oral carcinoma cells required the presence of fibroblasts and the activity of cyclo-oxygenase-2 (COX2). When these organotypic gels were transplanted under the skin of mice, the oral cancer cells formed invasive carcinomas that resembled human disease closely, with invasion being dramatically suppressed by treatment with COX2 inhibitors.

These data set the scene for Ian and my teams' arrival at BCI on the hottest day in August 2003. My team had already stained 1,200 breast cancers for αvβ6. With the

help of Professor Louise Jones, then still at the University of Leicester, we observed a clear link between high levels of αvβ6 expression and poor survival in patients with breast cancer, especially in those with HER2-positive cancer, a type of breast cancer that is quick to grow and spread.

Dr Kate Moore joined my team and eventually published the first histopathology study linking αvβ6 to poor overall survival and distant metastasis in breast cancer. Kate showed that αvβ6 promotes breast cancer cell invasion by working together with HER2. Using the αvβ6-blocking antibody 264RAD that my lab was helping AstraZeneca to develop, Kate reported that blocking αvβ6 and HER2 could inhibit or even reverse tumour growth in experimental animals. This treatment also lowered the levels of both αvβ6 and HER2 protein. These and other data show that these two molecules work together and that the presence of both indicates one of the highest-risk breast cancer types.

Extending these studies to pancreatic cancer, PhD students Claire Reader and Sabari Vallath in my lab discovered that most human pancreatic ductal adenocarcinomas (PDAC) expressed high levels of αvβ6 on their surface, and importantly, so did the matched metastases. With help from colleagues at the Beatson Cancer Research Institute in Glasgow, Clare showed in several preclinical studies that the αvβ6 drove PDAC development and shortened overall survival. However, this outcome could be significantly improved if we used our 264RAD antibody to stop αvβ6 from working, again heralding a potential of αvβ6-directed therapy in the future.

Professor Louise Jones and her team have also observed the expression of αvβ6 in many cases of ductal carcinoma in situ (DCIS), a pre-malignant form of breast cancer in which cells in the breast milk ducts take their first steps to becoming cancerous. Only 20-50% of DCIS actually progresses to life-threatening invasive ductal carcinoma. Nevertheless, all women diagnosed with DCIS are treated as though they will develop breast cancer and suffer invasive local surgery or, in some cases, total mastectomy. This means thousands of women are over-treated for a disease they will never get. Unfortunately, we do not yet know for sure which DCIS will progress to invasive disease and which will remain harmless, so markers that enable us to distinguish between the two are much needed.

To address this, Dr Michael Allen, working with Louise, analysed many hundreds

of DCIS samples and explored the expression of αvβ6 in DCIS. Normal breast ducts comprise an inner layer of luminal epithelial cells surrounded by a myoepithelial cell layer. Michael showed that it was the outer myoepithelial cells, not the luminal epithelial cells, that sometimes expressed high levels of αvβ6. They also discovered that almost all high-grade DCIS, DCIS showing signs of invasion, and DCIS located alongside invasive ductal carcinoma expressed high levels of αvβ6. In contrast, DCIS that histologically looked low grade had little or no αvβ6. In fact, studying DCIS samples from the UK, Australia, and New Zealand (UK/ANZ) DCIS trial where patients had local excision and no evidence of adjacent disease in the margins, women with αvβ6-positive DCIS had a median time to recurrence of just 2.3 years versus 11.4 years for women with αvβ6-negative DCIS.

In the lab, Mike also showed that when myoepithelial cells expressed αvβ6 they were able to promote cancer cell invasion by activating MMP9 – a protease capable of breaking down the extracellular matrix. This potentially provides a mechanism for the relationship between αvβ6 expression and the transition of DCIS to invasive cancer. Relevant to these observations, Mary-Kate Hayward, then a PhD student in Louise's team, discovered that stretching myoepithelial cells stimulated them to express αvβ6. Thus, the proliferation of cancer cells within the milk duct could eventually stretch the duct and force myoepithelial cells to transition to an αvβ6-expressing cell that promotes their escape across the basement membrane by generating active collagenases. We now believe that the increased presence of αvβ6 and the biological changes that it causes will help to develop clinical tests to indicate the risk that DCIS poses to individuals and help guide decisions around surgery and mastectomy.

In separate studies, Dani DiCara, a PhD student in my lab, identified a 20 amino-acid sequence in a surface protein of a specific serotype of foot-and-mouth-disease virus, which she called A20FMDV2. This peptide bound specifically and with high affinity to integrin vβ6. Clinical fellow Dr Antonio Saha, under the guidance of Professor Jane Sosabowski, was able to radiolabel A20FMDV2 and use it to perform Positron Emission Tomography (PET) imaging of αvβ6-expressing breast cancer tumours. The peptide was subsequently used by GSK in their Idiopathic Pulmonary Fibrosis (IPF) programme since the inflamed lung tissues of IPF mice (and patients) expressed high levels of αvβ6. Dr Kate Moore, a postdoctoral researcher in my group, showed that the αvβ6 -specificity of A20FMDV2 could also be used to deliver

therapy. In collaboration with ADC Therapeutics, who conjugated the fungal-derived cytotoxic drug pyrrolobenzodiazepine (PDB) to A20FMDV2, Kate showed that low concentrations of this peptide-drug conjugate effectively stopped the growth of or completely eliminated experimental PDAC tumours that expressed αvβ6. Translation to the clinic remains the goal for A20FMDV2, and this may happen in labs outside of BCI that have adopted A20FMDV2 αvβ6-targeting for oncolytic viral therapy.

Thus, BCI continues to break boundaries in our pursuit of understanding and targeting integrins in cancer. The past 20 years have gone by in a flash. It has been wonderful working with such a fabulous group of dedicated, smart people. And despite studying αvβ6 for 20 years, it has never been more exciting to study this molecule than it is right now because there are so many new things that I never knew this molecule could do. Over the years, my mindset has shifted from that of solely being a basic discovery researcher to being strongly focussed on translation, as I believe that the observations we have made in the lab have huge potential to benefit patients in the clinic – we have received a lot of interest from industry partners, and this gives me huge encouragement.

Computational Biology & Bioinformatics

Professors Claude Chelala & Trevor Graham

The need for computational biology and bioinformatics is becoming ever more important. New technologies are generating an exponentially increasing quantity of data of differing types (multimodal data), whether genetic and molecular data, histology, or health records. High-throughput approaches produce vast data sets allowing us to characterise these changes over space and time. In addition, healthcare providers are gathering huge quantities of information and samples from patients over months and years as their disease progresses. This poses many challenges for data management, analysis, integration and interpretation. However, it also offers huge opportunities for unlocking new personalised approaches, where we can monitor patients' disease and tailor their treatment accordingly.

Ambitious, translational-driven projects using high-throughput technologies on large cancer patient sample collections can only achieve their full potential if adequate computational capacity and skills are available. Professor Claude Chelala and Professor Trevor Graham were recruited to the BCI as part of the expansion of our computational biology and translational bioinformatics research programmes.

Professor Claude Chelala – bioinformatics in precision medicine

I was working at the Pasteur Institute in Paris when I saw the advert for a postdoctoral bioinformatician to join Professor Nick Lemoine's group, which first brought me to the BCI in 2006. Nick's group had recently received a big European grant for a project focussing on pancreatic cancer that would generate a huge quantity of data. It was a great opportunity, allowing me to work in a big European

collaboration alongside Nick and Professor Tatjana Crnogorac-Jurcevic and engage in a lot of networking. The project ultimately shaped a lot of my ongoing interest in the genomics and molecular pathology of pancreatic cancer.

After a year, I was awarded a lectureship at the BCI. I enjoyed teaching Bioinformatics to MSc students and recruited my first PhD student (Dr Emanuela Gadaleta). Over the years, I established an interdisciplinary research team of excellent postdoctoral researchers and PhD students with complementary expertise in translational bioinformatics, molecular biology, health data science and software engineering to exploit the power of data-driven approaches for precision medicine.

At the time, bioinformatics was becoming ever more important for cancer researchers to analyse the increasingly vast and complex data sets being generated. In 2007, alongside my research work, I established the BCI's bioinformatics core service with two staff members, Dr Jun (Alex) Wang, a geneticist and bioinformatician and Dr Ai Nagano, who has a background in quantum physics. Over the years, we have accelerated the publication of a huge number of papers at the BCI, some of which could not have been completed without the service and input from my own research team when demand was too high. Alex now leads the bioinformatics core alongside a dedicated MSc course training the new generation of data scientists.

The BCI's links to the clinic have been key to my work. Being connected to local hospitals enables us to tailor the analysis we do to the London populations served by Barts Health and to address questions that present current clinical challenges. Access to patient specimens is also vital. The BCI provided the opportunity for me to work with my long-term collaborators and clinical colleagues Professor Louise Jones and Professor Hemant Kocher, who are internationally renowned for their outstanding work in breast pathology and pancreatic cancer, respectively, to acquire funding and create innovative biobanking infrastructures for health informatics and bioinformatics in pancreatic and breast cancers. I now lead the Health Informatics and Bioinformatics for two national biobanks (Breast Cancer Now Tissue Bank and Pancreatic Cancer Research Fund Tissue Bank, with over 12 NHS Trusts). These banks form the centre of an ecosystem that brings together clinical, *in vivo*, *in vitro* and *in silico* resources. This allows us to analyse a combination of clinical data and molecular findings to uncover new knowledge that informs personalised strategies for patient benefit.

My work in breast cancer focuses on combining different data types to explore

differences linked to individuals' ancestry. This is an area of research that I am particularly passionate about; current clinical approaches historically have been designed and tested predominantly in people of European descent, and so do not adequately serve people from other backgrounds.

Another branch of my research using bioinformatics and pathology showed that histologically normal appearing tissues adjacent to breast cancer in pre-menopausal women can be stratified into molecular subtypes, each with defining features and distinct prognostic potential. This is the most extensive characterisation of normal adjacent tissues showing clinical promise for young breast cancer patients.

I have also researched the use of sequential, non-invasive liquid biopsies for tracking tumour dynamics in pancreatic cancer. This approach was able to predict the course of disease in individual patients as their disease progresses and in response to the treatment they received so clinical decisions could be tailored to patients' personal risk profiles. My team also led the development of SNPnexus, a popular software that fills the gap between genomics and biological interpretation for prioritising sequencing variants for disease and phenotype studies.

Nick has always encouraged us to be collegiate in our work, and during my time at the BCI, I have been grateful to be surrounded by excellent colleagues at other Queen Mary institutes. Professor Michael Barnes at the William Harvey Research Institute and I together secured funding from UK Research and Innovation (UKRI)'s Medical Research Council (MRC) to attract four Rutherford early career research fellows to Queen Mary, with two based at BCI (Dr Dayem Ullah and Dr Kathleen Curtius). I also co-led the Centre for Computational Pathology, one of four centres within Queen Mary's cross-faculty Life Sciences Initiative, with Professor Conrad Bessant at the School of Biological and Behavioural Sciences, bringing together a large network of experts from across the university. Most recently, working with Barts Life Sciences, Barts Charity and Barts Health, I am co-leading the Precision Medicine research award with Professor Carol Dezateux at the Wolfson Institute of Population Health. This award funds a large research team at the BCI and WIPH, working with longitudinal electronic health records and multi-modal data to carry out research that will help us develop the best precision tools to serve our patients in Northeast London and beyond. With generous funding from Barts Charity, this programme has attracted specialists in digital pathology to BCI (Dr Vivek Singh and Dr Oscar Maiques

Carlos) and in health data science and biostatistics to WIPH (Professors Rohini Mathur and Jianhua Wu).

I also believe that training the next generation of health data researchers is important and that this must begin at school age. With the help of my team, I have worked with science festivals and schools to encourage interest in data science. For example, we talk about DNA sequencing using Lego blocks and dinosaurs. I think it is important to communicate with the public and help the young generation to get excited about these topics.

Professor Trevor Graham – mathematical understanding of cancer genetics and evolution

I joined the BCI in 2013 as one of a cohort of seven new early career researchers who were recruited at the same time (Professor Susana Godinho, Dr Katuisia Bianchi, Dr Angus Cameron, Dr Gabi Ficz, Dr Paolo Ribeiro and Professor Sarah McClelland). My background was in maths, and accordingly, I set about creating the first mathematical theory-led lab in the BCI, which aimed to take ideas from evolutionary theory and apply them to make sense of cancer. We called ourselves the "evolution and cancer lab", or affectionately EvoCa for short.

The first year was a little tough: my first application to CRUK for a fellowship was rejected, and I found it hard to attract mathematically trained people to join the lab, probably because neither I nor the BCI had any visibility in mathematical biology. But the following year, my reapplication to CRUK – which had improved tremendously with input from the fantastically supportive faculty of the BCI, especially Jude Fitzgibbon – was funded. I persuaded some maths PhD students from interdisciplinary programs at UCL to join the group (Marc Williams and Danny Temko), recruited two brilliant postdocs (Dr Annie Baker and Dr Pierre Martinez) and two BCI students (Will Cross and clinical fellow Ryan Choi) and the lab felt like it had taken off.

A theme that has run through my entire research career is to bring mathematical population genetics theory to make sense of cancer genomes. I have always worked closely on the topic with my colleague Dr Andrea Sottoriva – who was then a new

group leader at the ICR in London. It was on this theme that the lab had its first major publication success in *Nature Genetics*. The paper derived mathematical formulas that showed that if cancers evolved neutrally (which meant that all cells in the cancer had the same chance of producing surviving offspring), then intra-tumour genetic heterogeneity (the genetic differences between cells in a tumour) should follow a characteristic pattern (a 1/f power law). The paper found that this characteristic pattern was very widespread across many different kinds of cancer.

The study – which admittedly sounds rather dry when written like this – turned out to be extremely controversial in the field of cancer genomics. It was controversial because the prevailing view at the time was that the extensive intra-tumour heterogeneity that had recently been recognised to be present in every cancer was shaped by the strong selective forces that made the cancer grow and progress. My paper claimed that the opposite was, in fact, true – that most intra-tumour heterogeneity was just random mutational noise that was inconsequential for tumour biology. A vigorous and, at times, heated debate followed at many conferences all around the world, and no less than five letters were written to *Nature Genetics* critiquing the Williams *et al.* paper. But the idea has stood the test of time (and the analyses have been refined and improved in later work) and that first paper spawned a host of subsequent work that has been the bedrock of the lab ever since.

In 2019, together with Jude Fitzgibbon, I helped to form a new Centre for Genomics and Computational Biology (GCB, now known as the Centre for Cancer Evolution) at the BCI. The creation of GCB exemplified the increasingly central role of computational methods in cancer research and the need for the BCI to invest in this area. In GCB, Jude and I led the recruitment of new computational biology research groups: Dr Mirjana Efremova and Dr Ben Werner, who have both thrived in GCB.

The rate of technological advancement in biological research continues to be breathtaking – genome sequencing, single-cell sequencing, spatial transcriptomics and AI were technologies that were no more than ideas when the BCI was first created, but which are now mainstays of modern molecular cancer research. The huge datasets generated by these technologies can only be made sense of by innovative computational methods, and it is great to see the foundation that the institute now has in this area. Computational and mathematical biology are now firmly embedded in the BCI.

Genetics & Lymphoma

Professor Jessica Okosun

Before I regale you with the journey of our lymphoma discoveries, I must start from the beginning. Long-lasting success can only come with the right foundations. At the BCI, these were established before I arrived. The discoveries and successes of the lymphoma research group were built on several key pillars: first, interactions bridging the lab and the clinic were crucial. The geographical proximity of our research with the Haemato-Oncology Department at St Bartholomew's Hospital ideally placed us to bring together the strengths of our scientists and clinical academics with those of physicians and pathologists in the clinical lymphoma service. Another important pillar was the huge investment in the Haemato-Oncology Tissue Bank with the allied clinical database (thanks to the foresight of Andrew Lister, Emeritus Professor of Medical Oncology). These pillars allowed the BCI to become a leading lymphoma research centre capable of attracting and training many clinical fellows, such as myself. Many of these fellows have gone on to become internationally renowned lymphoma experts, including Professor Peter Johnson (former Chief Clinician at CRUK, Director of the Southampton CRUK Centre and current National Clinical Director for Cancer at NHS England) and Professor Andrew Davies (now Director of Southampton NIHR/CRU Experimental Cancer Medicines Centre).

I am of course incredibly biased, but lymphomas are a fascinating type of blood cancer. Over 80 different forms of lymphoma have been described, each with its own nuances – different clinical behaviour, treatment approach and outcomes. At the BCI, lymphoma research initially focused on asking clinical patient-orientated questions and observing the disease. For example: what is the natural history of a

common type of incurable slow-growing lymphoma, follicular lymphoma? Why does it behave the way it does? And why does the lymphoma go away for a few years after treatment and then return again in a continual pattern? Professor Andrew Lister, Professor Ama Rohatiner and Dr Silvia Montoto led these investigations. These clinical observations generated a growing need to probe the molecular pathogenesis of these lymphomas, particularly with a genetics lens. Jude Fitzgibbon, who later became Professor of Personalised Cancer Medicine, was appointed in 2001 to tackle these research questions.

Initial research in follicular lymphoma centred around monitoring minimal disease using standard quantitative PCR methods. This work, driven by Dr Sameena Iqbal, Dr Lindsey Goff and Professor Jude Fitzgibbon, focused on detecting a specific genetic change, the chromosomal translocation *BCL2-IGH*, that could be used to track the disease in the blood or bone marrow of follicular lymphoma patients. The lymphoma genetics programme gradually began to expand, in part through the strength of the legacy lymphoma tissue bank collections but also the participation in international collaborative initiatives such as the Leukaemia and Lymphoma Molecular Profiling Project (National Cancer Institute, US, led by Dr Lou Staudt) and The Lunenberg Lymphoma Biomarker Consortium (Led by Professor Anton Hagenbeek, Utrecht, *in memoriam*). These international collaborations marked a period of tremendous genomic discovery in B-cell lymphomas. For example, the seminal study using gene expression of the microenvironment to dichotomise follicular lymphoma patients into two groups with different clinical outcomes was published in *The New England Journal of Medicine* in 2004.

Another important driver of the genetic discoveries in follicular lymphoma came in the guise of a swathe of clinical research fellows who undertook their PhDs in Jude's research group, drawn from a range of medical backgrounds, from haematology to pathology. An area that was always of interest to the lymphoma research group was a pivotal clinical inflection point when patients with a seemingly indolent follicular lymphoma transformed into an aggressive lymphoma, an event associated with dismal outcomes even in this contemporary era. Between 2005–2009, clinical research fellows Drs Derville O'Shea, Ciaran O'Riain and David Wrench (all clinical consultants now) studied large cohorts of biobanked samples from follicular lymphoma patients and made important first steps in identifying genetic biomarkers of aggressive behaviour including *TP53* mutations and DNA methylation signatures. This work

resulted in a number of publications in *Blood*, the flagship journal for haematology. At that time, many of the discoveries were enabled by genetic approaches that either focussed on single genes or implemented low-resolution sequencing technologies.

In my mind, the next critical turning point in our lymphoma research came with the advent of next-generation genomic sequencing. While giving a talk abroad, Jude met Dr Csaba Bödör, who at that time was a postdoctoral fellow and today is Professor and Head of Molecular Diagnostics in Onco-Haematology at Semmelweiss University, Hungary. In 2009, Csaba arrived to undertake a postdoctoral position in Jude's lab, fresh-faced from Budapest on the back of a European Haematology Association Research Mobility Grant. A few years later, in 2011, I arrived on the scene, another haematology clinical fellow keen to learn the intricacies of laboratory work and the genetics of lymphoma. Csaba's research demonstrated that mutations in *EZH2*, a gene that regulates our epigenetics, were very common in follicular lymphoma patients. This work helped to increase recognition that epigenetic dysfunction was at the heart of follicular lymphoma biology. Following this, a number of small-molecule EZH2 inhibitors were developed, one of which, Tazemetostat, received FDA approval for patients with follicular lymphoma in 2019 – one of the few bench-to-beside moments that I witnessed.

In truth, the beginnings of my career in lymphoma research at the BCI were rather serendipitous. I originally received CRUK Clinical Research Fellowship funding for a project in acute myeloid leukaemia but decided at the last moment to seek external funding to work on a lymphoma genomics project with Jude. Around this time, we were particularly fortunate to be one of nine projects selected as part of the highly competitive Genomics Initiative funded by CRUK's Catalyst Club. This funding allowed us to use whole-genome sequencing and other high-throughput sequencing to chart the genetic changes in a patient's follicular lymphoma over time, from an indolent to an aggressive transformed lymphoma using patient samples collected at multiple time points. We were one of the few centres in the world with this truly unique resource.

At the time of the project, Jude's lab consisted of just three members – including Csaba and me. Even with the camaraderie and enthusiasm of a small team, it was a mammoth task to analyse and interpret the tsunami of sequencing data generated – our first experience of 'Big Data' analyses. During this project, we built a close

working relationship with Dr Jun (Alex) Wang, at the time a bioinformatician in Professor Claude Chelala's lab. Together with many other national and international collaborators, we published this study in *Nature Genetics*. It served as an important contribution to the field, shining a light on the concept of tumour evolution. Our results strongly supported the notion that a specific residual population of tumour cells (which we termed common progenitor cells, CPCs) could be driving the lymphoma relapse on several occasions. I distinctly remember Jude's words following the successful publication: "Let's enjoy this moment, a fantastic accomplishment that we might not replicate again". Thankfully, we had other ideas, and many other discoveries came after.

Ultimately, this study set the wheels in motion for our adoption of next-generation genomics, bioinformatics and big data analytics in our lymphoma research, which underpins our approach to this day. A few years later, we identified recurrent mutations in a gene called *RRAGC*, which opened our eyes to the potential contribution of metabolic pathways in follicular lymphoma pathogenesis. Our other

Csaba Bödör, Jessica Okosun and Jun (Alex) Wang, who led the Nature Genetics study, at the American Society of Hematology meeting, New Orleans, 2013.

studies showed that these lymphomas are genetically diverse (heterogeneous) both in time and in space. These discoveries paved the way for further studies exploring alternative therapeutic mechanisms and formed the basis of Jude's CRUK Programme Grant in Follicular Lymphoma to evaluate epigenetic therapies.

Despite the great strides we and others had made, we recognised that to tackle the next questions, we needed to bring together the international community. This led to the hugely successful Follicular Lymphoma Workshop supported by the Greg Wolf Foundation held in North Berwick, Scotland in 2017. The charisma and reputation of Jude and Professor John Gribben, Centre Lead of Haemato-Oncology, were instrumental in allowing us to gather many of the world's foremost researchers in follicular lymphoma research, over three days, to take stock of where the field stood and the challenges and questions that we faced over the coming decade. The highlights of this meeting were the many presentations of unpublished ideas and data, alongside the brainstorming sessions by established and emerging leaders in the field on areas in basic biology, animal model systems, biomarkers and next-generation clinical trials. It was inspiring for me at that time and helped shape my next questions. I returned to the BCI as a newly minted CRUK Clinician Scientist Group Leader later that year.

Our research reputation paved the way for new international collaborations. It has been a privilege to be part of a £4.8 million CRUK Accelerator Award that built a multi-country, multi-institution consortium, EDITOR, enthusiastically led by Professor Jesús San-Miguel (University of Navarra, Spain). EDITOR has focused on developing state-of-the-art tools and models to understand the transition from pre-cancerous to overt haematological malignancies, including follicular lymphoma, providing resources with a significant impact on the wider scientific community. The UK hub was ably led by Jude initially, and more recently by myself, coordinating the follicular lymphoma research efforts across the groups in the UK, Italy and Spain. Through this consortium, it has been exciting to develop collaborations with Dr Dinis Calado at the Francis Crick Institute (who focuses on mouse modelling) and Dr Simone Ferrero at the University of Turin, Italy (who focuses on minimal residual disease and clinical trials).

A salient next question was how to take translational lymphoma research to the next level. I had recognised early on that there were very few UK lymphoma clinical

trials that had in-built parallel correlative or translational science. This seemed like such a missed opportunity to maximise our learnings (both clinically and biologically) from patients in clinical trials. With that in mind, I set myself a mission to integrate correlative science into upcoming lymphoma clinical trials. Working with many expert clinical colleagues through the National Cancer Research Institute (NCRI) Lymphoma Network, I feel fortunate and proud to have led and shaped the development of the infrastructure needed to integrate successfully correlative translational projects alongside several ongoing UK phase II and III lymphoma clinical trials. This has enabled us to establish a powerful biomarker discovery and evaluation platform.

Looking forward, our groups have begun to broaden our research interests into other harder-to-treat lymphomas including diffuse large B-cell lymphoma, primary central nervous system lymphoma (a form of lymphoma restricted to the brain) and T-cell lymphomas. We have continually embraced new technologies, including, most recently, single-cell methods to investigate one cancer cell at a time. We have also recognised the need to study and understand the many biological layers of these lymphomas (not just their genomics) that contribute to the lymphomas' heterogeneity and shape how they behave. We look forward to seeing what we can learn preclinically and directly from patient samples from clinical trials, which in turn

Left to right: Jun (Alex) Wang, Kevin Rouault-Pierre, Jessica Okosun, Trevor Graham and Jude Fitzgibbon, BCI team members of the UK hub of the CRUK Accelerator Award project, EDITOR.

will bring our discoveries even closer to the patients.

As I reflect on the humbling and rewarding lymphoma research journey of my predecessors and myself, I believe we benefitted immensely from several key ingredients: our patients' altruism that resulted in the legacy biobank, the adoption of new technologies, the power of collaborations and team science. My mantra remains: keep the challenges faced by patients at the heart of our research questions. The work is not over and there is much still to do.

New Diagnostics

Professors Jane Sosabowski, Tatjana Crnogorac-Jurcevic & Yong-Jie Lu

New diagnostic imaging – Professor Jane Sosabowski

Radiopharmaceuticals – drugs containing radioactive isotopes – play a crucial part in cancer care, including as agents for positron emission tomography (PET) and single-photon emission computed tomography (SPECT) imaging, techniques that support cancer diagnosis, prognosis and monitoring. Innovative radiopharmaceutical therapies are also emerging as a safe, effective and targeted way to deliver radiation to tumours.

I first joined the BCI as a postdoctoral researcher in Professor Steve Mather's cancer imaging laboratory, which moved over to Charterhouse Square from the Nuclear Medicine Department at St Bartholomew's Hospital. I took over leadership of the lab after Steve's retirement in 2012 when I was appointed as Lecturer. In this role, I continued the lab's focus on preclinical development of radiopharmaceuticals for PET and SPECT imaging and therapy. I was supported by two fantastic friends and colleagues in my work: Dr Roxana Kashani in the radiochemistry lab and Dr Julie Foster in the preclinical imaging facility. New commercial imaging agent work came into the lab via Ciara Finucane's move to Invicro (our imaging contract research organisation (CRO) partner to this day). The radiochemistry work was done by Steve in his new part-time Emeritus Professor role, split between grandchildren, golf and radiochemistry (in that order!).

At that time, there were many barriers to the clinical translation of agents due to

the difficult regulatory environment. In addition, the Barts Health Radiopharmacy Investigational Medicinal Products (IMP) licence (needed to manufacture radiopharmaceuticals for clinical trials) had been deactivated. The Nuclear Medicine Department lost its last Nuclear Medicine clinical academic when Dr Teresa Szyszko moved to King's College London, so the patient impact of the Cancer Imaging Lab was pretty limited: we were developing Gallium-68 PET imaging agents in the lab but had no route to the clinic at Barts Hospital as the only manufacturing capability in the Barts Radiopharmacy was for SPECT agents (Tc-99m and In-111). At that time, Professor John Marshall was trying to test his F-18-αvβ6 peptide PET radiotracer at Imanova in West London. However, it meant the patients had to travel across London for a scan, making it almost impossible to recruit.

Against this backdrop, in early 2017, a delegation came from the Nuclear Medicine Department at Barts Hospital to Professor Nick Lemoine's office at BCI to ask for help from us in bringing new Ga-68 PET imaging agents to Barts patients. This kickstarted a new era of collaboration between my lab and the hospital. Myself, John, Hikmat Jan (Lead Nuclear Medicine Consultant, ably supported by fellow Nuclear Medicine consultants Dr Athar Haroon and Dr Ewa Nowosinska) and Dr Neil Hartman (Head of Nuclear Medicine and Head of Radiopharmacy) applied for a Barts Charity Large Project Grant to set up a new Ga-68 PET Clinical Imaging Service, as part of the BCI's Targeting Tumour Cells theme. Our goal was that the hospital Ga-68 PET imaging service be sustainable: the Ga-68 generator cost at that time was ~£60k per annum, so we needed to scan a good number of patients (about 250 per annum) to make it pay for itself.

Our case to Barts Charity revolved around improved imaging and new radiopharmaceutical therapies for prostate cancer. At that time, exciting new imaging and therapy agents for prostate cancer were coming into use and being tested in clinical trials: Ga-68-PSMA and Lu-177-PSMA. These agents bind to Prostate Specific Membrane Antigen (PSMA) on the surface of prostate cancer cells, enabling targeted imaging and radiotherapy. Despite Ewa's heroic efforts, Barts Health had missed out on being commissioned by NHS England to give Lu-177-DOTATATE therapies for neuroendocrine tumours, and we didn't want to be in the same position with the new Lu-177-PSMA radiopharmaceutical therapies, especially in view of the large numbers of patients it would affect.

We were successful in our bid. However, as soon as the project started, Neil announced that he was moving to Wales. So, I called on the expertise of Dr Maggie Cooper (ex-Head of Radiopharmacy at Barts Health and currently at King's College London) to help. Along with the excellent Radiopharmacy Production Manager, Maria Tsionou, we did the initial enabling work to buy equipment and bring a Ga-68 generator on site and recruited an excellent postdoc (Dr Jennifer Young) to start setting up the manufacturing process.

The best way to ensure NHS England commissioning at Barts Health was to participate in VISION, a multicentre Phase III clinical trial of a Lu-177-PSMA therapy, which we knew was being planned by the biopharmaceutical company Endocyte at many hospital sites around the world. Supported by Dr Maria Burniston (Interim Head of Nuclear Medicine), I approached Endocyte, who said they already had enough sites in the UK. However, by persisting and pointing out that we could supply the Ga-68-PSMA imaging agent for the patient pre-treatment scans (very few other UK departments had this capability), Endocyte was persuaded to include us, with Dr Jonathan Shamash (consultant medical oncologist at Barts Health) as principal investigator. This was agreed in October 2018, and the race was on to catch up with the other sites and get the manufacturing process up and running in time to open in early 2019. Thanks to the ECMC (including Kelly Mousa and the BCI Setup team fronted by Wassilah Russool), we fast-tracked the research governance approval, Administration of Radioactive Substances Advisory Committee (ARSAC) licences, and other approvals and contracts needed to eventually hold the Site Initiation Visit in record time in early 2019.

In the meantime, the setup of the Ga-68-PSMA manufacturing process in the radiopharmacy was ongoing, with Jen validating new equipment, generators and processes, writing documentation and carrying out training. Under Good Manufacturing Process (GMP) regulations, four staff members are required to manufacture, quality control and release a patient imaging dose.

Progress had been frustratingly slow without a Head of Radiopharmacy to enable the generation of new standard operating procedures and other documentation, but this changed when Busola Ade-Ojo moved over from the pharmacy to be the Head of Radiopharmacy and made it her mission to get the manufacturing of the Ga-68-PSMA up and running on time. Finally, Jen was able to drive the process forward, with

help from Joaquim Ramada-Magalhaes (Quality Assurance Manager) and Richard Skidmore (Head of Quality). Emily Trahair, in the Nuclear Medicine Physics team, set up the patient administration equipment and procedure for the Lu-177-PSMA therapies.

We scanned our first patient in the VISION trial on 15th April 2019 (with the Ga-68-PSMA dose manufactured by Jen and QC'd by me!), and this was followed by their first Lu-177-PSMA therapy dose a few weeks later (administered by Emily, overseen by Ewa). The VISION trial ultimately found that Lu-177-PSMA prolonged imaging-based progression-free survival and overall survival when added to standard care. The Barts Health Ga-68 PET clinical imaging service has been up and running ever since, initially with our help, but gradually completely handed over. Despite the interruption of the pandemic, the VISION trial was followed by Barts Health patients being able to participate in the PSMAFore and PSMAddition trials. Reinstatement of the IMP licence, effected by Busola, allowed imaging CT-IMP trials to take place.

Currently, we are setting up the Ver-A-T1D trial, which uses the novel agent Ga-68-NODAGA-Exendin to image pancreatic beta cell mass in type I diabetes and measure the effect of a blood pressure medication, Verapamil, on preserving beta cell function. By having the capability to manufacture the diagnostic imaging agents needed to recruit patients, we aim to enable trials of novel alpha-particle emitting radiopharmaceutical therapies at Barts – our own as well as those currently causing a frenzy of investment from large pharmaceutical companies running to tens of billions of pounds. The current hospital management team is strongly supportive of new trials in nuclear medicine, and we hope that this excellent relationship between BCI and Barts Health Radiopharmacy and Nuclear Medicine will continue to have a positive impact on patients.

Biomarkers for earlier detection of pancreatic cancer in urine – Professor Tatjana Crnogorac-Jurcevicz

My scientific career path has led me through three different countries, where I worked on a number of diverse research projects. As part of my work, I utilised various animal models – including pig, mouse and fish – and learned a number of biochemical, cellular and molecular biology techniques. While this empowered me to tackle any form of scientific challenge, the real one revealed itself when I joined

Professor Nick Lemoine's lab, first at CRUK Molecular Oncology Unit at Imperial College (Hammersmith Hospital) and then here at the BCI, where I started working on pancreatic cancer and still continue to do so.

Pancreatic cancer is one of the deadliest and likely the most challenging of cancers. Around 11,000 patients are diagnosed with this cancer in the UK each year, the majority of whom will present with advanced disease and survive less than a year. Fewer than 10% will still be alive after five years. The combination of being an uncommon cancer type and a traditionally late diagnosis offered limited possibility to obtain research samples, which is crucial if we are to understand the disease.

Through several fruitful national and international collaborations, we performed global 'omics' analyses of precursor lesions and primary and metastatic tissues. However, I fairly quickly realised that if we want to make a real difference for pancreatic cancer patients, it has to be through non-invasive early detection. Thus, we started looking for biomarkers that would enable us to detect this disease while it is still resectable and opted to do this in urine – a body fluid that is obtainable completely non-invasively.

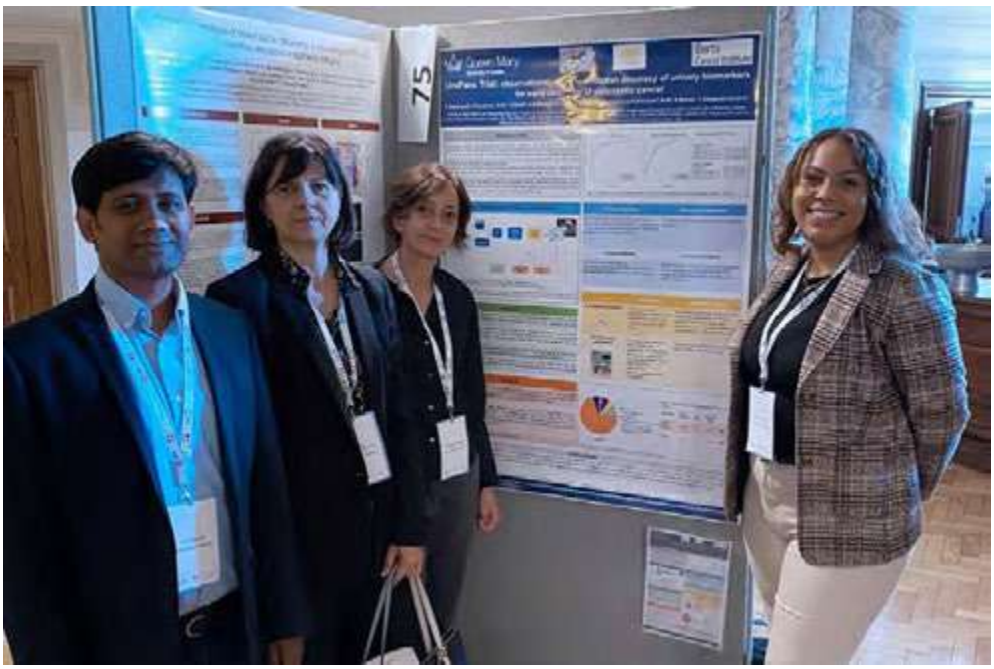
This was somewhat uncharted territory, as the biomarker field 15 years ago was not yet fashionable. Moreover, urine as a biofluid was an additionally unfavourable choice despite uroscopy and urinalysis having over 6,000 years of recorded history. Although I was able to prove that urine is indeed a valid biofluid for detecting a signature of pancreatic cancer, which we published in 2008, it still took several years before I obtained the necessary funding to continue this promising work. In the last couple of years, with funding support from Pancreatic Cancer Research Fund and their CEO Maggie Blanks' belief in me, we have come a long way. We discovered and validated three urinary biomarkers, REG1B, LYVE1 and TFF1, and validated them on a large number of urine samples, showing that they are robust. Finally, we recently demonstrated that these biomarkers can detect pancreatic cancer up to two years before clinical diagnosis.

To facilitate the biomarker panel data analysis, our collaborator, Dr Oleg Blyuss from Wolfson Institute of Population Health, constructed a logistic regression algorithm named PancRISK. The algorithm is based on the three biomarkers and patients' age, enabling the stratification of patients as having an average or an elevated risk for developing pancreatic cancer. Only those in the elevated risk category should

undergo further, usually invasive and expensive, clinical workup.

We are currently running the UroPanc study (www.pcrf.org.uk/uropanc-study), which is a large observational clinical trial funded by Pancreatic Cancer Research Fund and supported by the trials team at the Centre for Experimental Cancer Medicine (Mariam Mahamood, Tommy Chan and Ismita Chhetri). The aim of the trial is to establish the accuracy of our biomarker panel and its affiliated PancRISK in two cohorts at risk of developing pancreatic cancer – individuals with hereditary predisposition to pancreatic cancer (familial history and genetic syndromes) and patients with vague but suggestive symptoms of pancreatic cancer. We are recruiting such patients at Royal London Hospital (Dr Patrick Wilson and team), at UCLH (Professor Steve Pereira and team), and in Liverpool through the EUROPAC registry (Professor William Greenhalf and team). In addition, within UroPanc, we will also assess the economic and social impact of implementing the urine test in clinical practice with Dr Melody Ni's team at Imperial College London.

If the urine test is proven to stratify patients accurately, it could be implemented into a new and improved diagnostic pathway for pancreatic cancer patients. Interim



From left to right: Nurshad Ali, Tatjana Crnogorac-Jurcevic, Silvana Debernardi and Evelyn Kurotova presenting a poster on UroPanc at The Early Detection of Cancer Conference in London, 2023.

analysis of data from around 800 assayed clinical samples was presented on 10th October 2023, at The Early Detection of Cancer Conference in London.

We are now at the stage of developing and manufacturing a commercial-grade kit that will be submitted for CE-marking. Once approved, it will be ready for real-time application to benefit patients at risk of developing pancreatic cancer.

Prostate cancer diagnosis from tissue to liquid biopsy – Professor Yong-Jie Lu

Early in my research journey, I became interested in cancer cytogenetics, the study of the structure and properties of cancer cell chromosomes. This approach aims to understand the genetic changes in human cancer cells both globally and at the individual cell level. It considers all genomic alterations within a cell and the intra-tumoural heterogeneity among cancer cells within a patient.

From the 1970s to the 1990s, this approach contributed significantly to our understanding of cancer development. It has also been instrumental in developing genetic diagnostic tools for cancer detection, subtyping and the development and application of targeted cancer therapy. For example, the discovery of the Philadelphia chromosome alteration and, subsequently, the identification of the bcr:abl fusion gene led to the development of Gleevec, a groundbreaking Chronic myelogenous leukaemia (CML therapy targeting the bcr:abl fusion gene that vastly improved the survival of patients with this genetic abnormality. Advances in cytogenetics and molecular cytogenetics technologies eventually led to the development of DNA microarrays and next-generation sequencing (NGS), including current single-cell NGS approaches.

Through my efforts in the development of molecular cancer cytogenetics technology and its application in studying a number of human cancers during my postgraduate and postdoctoral training, I was offered a senior lecturer post at the Barts and the London School of Medicine and Dentistry at Queen Mary in June 2003, just before the establishment of the Barts Cancer Institute. I was therefore fortunate to witness the initiation, growth and flourishing of the institute under the leadership of Professor Nick Lemoine over the past 20 years.

My research at BCI would not have been possible without the Orchid charity, which Professor Tim Oliver and his patient Colin Osborn founded to support the establishment of my lab within the Queen Mary medical school, including supporting my salary for a number of years. My research also benefited tremendously from close collaboration with Professor Daniel Berney, a clinical academic and consultant specialising in male urological pathology who served as the secretary of WHO in the section of urological pathology. Before my arrival at Queen Mary, Professor Oliver also established the male urological tissue bank, which became crucial to my work and was later led by Professor Berney.

I started my research team within the Department of Medical Oncology, where my team was the only one working on prostate cancer and other male urological tumour genetic studies. The other research teams all focused on haematological malignancy research. However, in this department, I benefited from the scientific discussions with Professor Bryan Young, a world leader in cancer genetics. After the creation of the BCI, Professor Lemoine invited me to move to his Centre of Molecular Oncology, where

Professor Yong-Jie Lu (centre) and his research team in 2012.

people were working on solid tumours. In 2019, this centre was split into two centres, the Centre for Cancer Biomarkers & Biotherapeutics and the Centre for Cancer Cell & Molecular Biology, due to its healthy growth.

Prostate cancer is the most common cancer among Western men, but its prevalence is much lower in Asian countries. My team performed genetic studies on prostate cancer using molecular cytogenetic and microarray technologies. Our aim has been to understand the genetic alterations and molecular mechanisms driving cancer development, thereby identifying novel cancer biomarkers and therapeutic targets.

One particular interest of our research is the underlying causes of the differences in prostate cancer prevalence between populations. We were the first to discover that certain genetic changes are common in cancer cells from patients of European ancestry but rarely occur in cancer in patients of Chinese ancestry. This genetic difference between Western and Asian populations was later confirmed by other studies in Chinese, Japanese and Korean patient samples. Based on the difference in genetic changes in cancer cells between populations, I hypothesised that the *TMPRSS2:ERG* fusion, one of the most common fusion genes in human malignant diseases that occurs in half of the prostate cancer cases in Western men, may be induced by the male hormone, androgen. This was experimentally confirmed by our lab's investigations. This discovery of the induction of genetic alterations by the male hormone was highlighted by dozens of national and international media as research news, including BBC1 lunchtime news.

Unlike many other cancers, prostate cancer is commonly diagnosed at an early clinical stage, partly owing to prostate-specific antigen (PSA) testing, a cheap and easily performed blood serum protein test. However, more than half of prostate cancer cases diagnosed at an early stage are indolent (non-lethal even without curative treatment). Therefore, the diagnostic issue for prostate cancer is not early cancer detection but the early detection of clinically significant prostate cancer to reduce the overdiagnosis and overtreatment of indolent cancer.

One of my genetic studies aims to identify genetic biomarkers that can distinguish between indolent and aggressive, clinically significant prostate cancers – so-called 'separating the tigers from the pussycats' – using surgically removed cancer tissues. This work has been performed by analysing tissue samples, partly in collaboration

with Professor Jack Cuzick, Professor Berney and the transatlantic prostate cancer group, who have developed Prolaris, the only FDA-approved prostate cancer prognostic biomarker.

However, tissue sampling is very invasive, and many patients with or without indolent prostate cancer should avoid the tissue biopsy process. For patients with indolent cancer, monitoring cancer progression under an active surveillance programme to avoid an invasive biopsy procedure would be preferable. MRI has been investigated and clinically implemented to reduce biopsies. However, more accurate non-invasive or minimally invasive biomarkers need to be developed to reduce unnecessary biopsies. Liquid biopsy is a promising alternative for this purpose.

My biomarker research focused on circulating biomarkers, as blood is a rich resource for cancer marker development. When cancer cells die, they release cancer cell proteins, DNA and RNA into the blood circulation. Cancer cells can also secrete these molecules and extracellular vesicles into the blood circulation and even invade the blood circulation, an essential step for cancer metastasis. All these cancer cell-derived materials in the blood can be used as biomarkers. In addition to products released from cancer cells, normal cells in the blood circulation, primarily immune cells, may alter their status in response to the presence of cancer cells, thus also holding potential as cancer biomarkers.

The development of cancer biomarkers using circulating tumour DNA and RNA, a field pioneered by our new Director, Professor Nitzan Rosenfeld, has seen extensive exploration for clinical use in recent years. My biomarker studies have focused on circulating tumour cells (CTCs), and we have shown that analysing different subtypes of CTCs is valuable for predicting prostate cancer prognosis, metastasis and treatment response. We are also investigating the potential of using CTC analysis to predict cancer recurrence and metastatic development after the apparent complete removal of cancer lesions by surgery. Most importantly, CTCs can be released at the early stage of cancer development, and their presence indicates a high risk of metastasis progression. Therefore, CTCs may be an effective biomarker for distinguishing aggressive disease from indolent cancers and useful for diagnosing clinically significant cancers. This is critical for prostate cancer but is also applicable to other cancer types. We have demonstrated in a single-centre study that CTCs are a promising biomarker for diagnosing clinically significant prostate cancer, a finding

that attracted significant media attention. We are now interested in validating this exciting finding in a large cohort muti-centre study. Once validated, it would change the paradigm of prostate cancer diagnosis. Building on the opportunity provided by the blood samples collected for CTC analysis, my team also investigated other circulating biomarkers, such as circulating megakaryocytes for advanced prostate cancer prognosis and plasma exosomal miRNA to predict hormone therapy resistance.

Finally, for translational studies with potential clinical impact, collaboration with clinicians, clinical trial design experts and statisticians is critical. My successful prostate cancer genetic and biomarker research has benefited greatly from close collaboration with Dr Jonathan Shamash (consultant oncologist), Professor Greg Shaw (consultant urological surgeon), Professor Rhian Gabe (Barts Clinical Trial Unit lead) and Dr Adam Brentnall (biomedical statistician), in addition to Professor Berney (pathologist). While my recent research has focused on circulating biomarkers, particularly for cancer early detection, I continue to be involved in cancer genetics studies. As a member of both the Prostate International Cancer Genome Consortium (ICGC) and the International Consortium for Genetic Predisposition Study (PRACTICAL), I contribute to the global effort to understand the genetic mechanisms driving prostate cancer development and progression, thereby aiding in the development of better diagnostics and therapeutics.

Cancer Screening, Prevention & Early Diagnosis

Professors Stephen W. Duffy & Jack Cuzick

In November 2002, what was at that time called the Department of Mathematics, Statistics and Epidemiology at Cancer Research UK in Lincoln's Inn Fields was moved to Queen Mary University of London. Our new home was the Wolfson Institute of Preventive Medicine, now named the Wolfson Institute of Population Health, on the Charterhouse Square campus. Over the years, the department's name has changed several times, and it is now called the Centre for Cancer Screening, Prevention and Early Diagnosis. The aim has remained the same: to research and evaluate interventions to prevent cancer or to diagnose it at an early stage, to increase the likelihood of effective treatment and reduce mortality from the disease. As a partner in the Cancer Research UK Barts Centre, we have maintained strong links with Barts Cancer Institute during these last two decades.

When we arrived in Charterhouse Square, our centre had essentially three teams: Professor Jack Cuzick's, focussing on cancer prevention; Professor Peter Sasieni's, working mainly on the evaluation of cervical cancer screening; and Professor Stephen Duffy's, researching various aspects of screening for breast cancer. The experience of being 'dragged and dropped' from Lincoln's Inn Fields to Charterhouse Square was a painless one. Thanks to Sir Nicholas Wright, then Warden of Barts and the London, and Sir Nicholas Wald, Director of the then Wolfson Institute of Preventive Medicine, we were made very welcome by Queen Mary centrally, and locally by the Wolfson Institute and Barts Cancer Institute.

As the centre of London goes, the Charterhouse Square area is a particularly pleasant and historic location in which to work. Some of us were gratified to note

that we were working almost next door to Florin Court, the block of flats used to represent Hercule Poirot's residence in the classic television series.

The early years of our tenure at Charterhouse Square saw some particularly important results for cancer control. These included:

- The publication of the IBIS-1 trial, and the accompanying review confirming that selective oestrogen receptor modulators can prevent breast cancer as well as treat it;
- The development of the Tyrer-Cuzick breast cancer risk prediction model, now used in genetic and family history clinics worldwide;
- Results indicating that human papillomavirus (HPV) testing would be superior to cytology in cervical cancer screening;
- The findings that cervical cancer screening is minimally effective under age 25, and can be safely done less frequently in women aged 50 years or more – these results fed directly into the redesign of the cervical screening programme;
- Findings from breast cancer screening trials and screening programmes internationally that breast cancer screening can work in women aged 40-49 as well as in women aged 50 or more.

Although a relatively recent building in this historic area, the Wolfson Institute in Charterhouse Square has its quirks and its history. The building houses a mix of laboratory, teaching and office space, the last probably most important for the critical mass of statisticians in our centre, who spend most of their time at computer screens. Stephen was puzzled to note that one wall of his office had a rectangular pattern of rawl plugged holes. He later found out that the room had previously housed a telephone exchange.

Around the end of the noughties, a number of further results in cancer screening emerged from our centre. These included further consolidation of the evidence that HPV testing should replace pap smear testing as the frontline cervical screening tool, with the research encompassing a comprehensive range from basic laboratory work to population-based studies of testing. The work in our centre, in collaboration with colleagues worldwide, was highly influential in the shift in thinking of HPV testing as

triage for those with a positive pap smear to the other way round, with HPV testing as the first screening test. We were also a partner in the UK Flexible Sigmoidoscopy Trial, which demonstrated substantial reductions in the number of bowel cancer cases and deaths following a once-in-a-lifetime flexible sigmoidoscopy examination. In breast cancer screening, we found that annual screening was effective in women aged 40–49 with a significant family history of breast cancer.

In our second decade in Charterhouse Square, there were some major breakthroughs. These included the finding that aromatase inhibitors can be used for primary prevention of breast cancer in postmenopausal women and the development of a method which uses tissue samples to differentiate aggressive from indolent prostate cancers, thus saving substantial numbers of patients from treatments with serious side effects. Our Centre was augmented with the Cancer Prevention Trials Unit, led by Professor Peter Sasieni, and the Molecular Epidemiology Laboratory, led by Professor Attila Lorincz. Both contributed to the development and evaluation of self-sampling for the human papillomavirus, which has great potential for cervical screening in women who do not wish to undergo the test with sampling by a doctor or nurse.

We were also awarded 13 years of funding from the Department of Health and Social Care and the National Institute for Health Research for The Policy Research Unit in Cancer Awareness, Screening and Early Diagnosis. This enabled us to extend our work in cancer screening, in particular, finding that the NHS Breast and Bowel Cancer

The Centre for Cancer Prevention, as was, in 2017. Photograph by permission of Chris Mathews.

Screening Programmes were fulfilling the promise of the previous clinical trials and saving lives from breast and colorectal cancer. Our centre was the methodological lead on the UK Lung Screening Trial, which showed the feasibility of targeted lung screening in the UK, now adopted as practice by the NHS. It also facilitated collaborations in the field of health behaviour, in which we identified a number of interventions which could increase participation in cancer screening, particularly in deprived and otherwise underserved communities.

In November 2017, Peter Sasieni moved to King's College London, taking the Cancer Prevention Trials Unit with him. This left a major gap in our research activities. Since then, however, generous funding from Barts Charity, matching the funding for the Cancer Research UK Barts Centre, allowed us to expand in other areas. We have further extended our behavioural research profile with the recruitment of Dr Sammy Quaife, Professor Suzanne Scott and Dr Georgia Black.

In 2021, Professor Fiona Walter took over as Director of the Wolfson Institute, now known as the Wolfson Institute of Population Health, and joined our centre, bringing a dimension of early diagnosis in primary care to our research. The Centre's research profile now includes a major drive to improve the stage of diagnosis of ovarian cancer and the CanDetect programme to develop tools to diagnose upper digestive tract cancers at an earlier stage. We also now incorporate the research programme of Professor Ranjit Manchanda, which includes an ambitious nationwide study of high-risk gene testing in the general population for ovarian cancer.

In 2023, we were fortunate to lure Peter Sasieni back to the Centre, which now bears the name The Centre for Cancer Screening, Prevention and Early Diagnosis. Peter brings back the Cancer Prevention Trials Unit and adds to our profile the NHS Galleri Trial of a blood test for early detection of several cancers at once and his work on estimating the joint effects of cervical screening and HPV vaccination. Peter is accompanied by Professor Jo Waller, a specialist in cancer screening behaviour, further adding to our already distinguished group of health behaviour scientists. Health behaviour can be thought of as the final building block in the edifice of cancer screening, prevention and control. Our laboratory colleagues can develop a new faecal test for bowel cancer, and we can evaluate its effect in clinical practice. However, how do we persuade the public to carry out a faecal sampling test, which although it may save one's life, is not fun to perform?

The centre's programme now has a strong dimension of addressing inequalities, and we are particularly anxious to address these in the local population in East London. Current projects within our local area include a study to identify early signs of ovarian cancer in general practice and evaluations of interventions to promote participation in breast and bowel cancer screening, including a health education intervention delivered in mosques in East London.

The landscape of cancer prevention, screening and early diagnosis is changing, and for the better. System failures such as emergency presentation of cancer are declining year by year, survival for many cancers has been improving steadily over the last three decades, and following disruption by the COVID-19 pandemic, screening and diagnostic services have made Herculean efforts to recover. However, there remains considerable pent-up potential for the prevention of cancer, whether behaviourally, medically or surgically. There are still too many cancers diagnosed at a late stage. Further evaluation of multi-cancer testing and home self-sampling for markers of cancer are major targets for future research. Issues of tailoring screening and prevention to individual risk remain to be resolved, and there is great potential for expanding the cancer testing tools available to general practice. There is still plenty for us to do.

The Early Career Researcher Programme

Professor Susana Godinho

The Early Career Researchers (ECR) Programme was established by Barts and the London School of Medicine and Dentistry (now the Queen Mary Faculty of Medicine and Dentistry) in 2013. The aim was to introduce new talent, revitalise the faculty's research portfolio, and build a cohort capable of becoming future research leaders. This concerted recruitment exercise, funded by Queen Mary, formed an important part of a new strategy to improve the research outcomes of the Research Excellence Framework (REF; the UK's system for assessing the excellence of research, which is used to inform allocation of public funding in higher education). The programme was spearheaded by Professor Tom MacDonald (Professor of Immunology at the Blizard Institute) and Professor Richard Trembath (former Vice-Principal for Health), with the support of Professor Bill Spence (former Vice-Principal for Research) and Professor Simon Gaskell (former Principal).

The first cohort of ECRs was established in 2013 and comprised 18 new researchers, 14 of whom are now consolidated in tenured academic posts (from Senior Lecturer to Professor). The success of the ECR programme can be measured at multiple levels. It enabled the faculty to recruit young, intermediate investigators to establish new lines of research, often complementary to existing areas of excellence within the faculty. These new researchers also brought home highly prestigious awards that enabled the creation of research hubs and the generation of 3* and 4* publications (signifying 'internationally excellent' and 'world-leading' quality research, respectively, as graded in the REF). After the initial three-year period (2013–2016), the scientists had raised £2.962m of Research Council funds collectively, plus £6.842m from other

sources (of which £1.107m was from Barts Charity).

The ECR Programme was a simple and successful strategy that could easily be replicated. Timely investment in ECRs and start-up packages allowed individuals to start their independent scientific research programmes and apply for further funding to expand their teams. This initial investment was instrumental in attracting many talented ECRs looking for opportunities to establish their labs. In addition, the ECR cohort received mentorship both as a group and as individuals at their respective institutions, co-ordinated by Professor Tom MacDonald and Professor Denise Sheer at the Blizard Institute, Professor Nick Lemoine and Professor Kairbaan Hodivala-Dilke at the Barts Cancer Institute and Professor Mauro Perretti at the William Harvey Research Institute. The combination of investment, talent and mentorship is the reason for the remarkable success of this programme.

New ECR Rising Star Programme

On the back of the wave of success and positive experiences generated by the first cohort of ECRs, Queen Mary established a new ECR Recruitment Programme aligning with their planned phase of growth to increase overall research power. The 'Rising Star Programme' was established in 2018 by Professor Steve Thornton (Vice-Principal for Health), Professor Mauro Perretti (former Dean for Research) and Professor David Kelsell (Professor of Human Molecular Genetics at the Blizard Institute), with £6.1m of generous support from Barts Charity that funded the recruitment of 16 new ECRs between 2019–2020. Similarly to the previous cohort, the majority (12 of 16) of the new appointments now have tenured academic posts, an extraordinary achievement that further underscores the programme's success. The new ECRs have attracted significant funding, including Research Council funds and other major awards (such as from Cancer Research UK and British Heart Foundation), and have contributed to the recent REF2021 with 3* and 4* publications.

The faculty has established an Academy of ECRs and intermediate Fellows to enable mentoring and career support to create and nurture the new cluster of scientific talent – a strategy that is expected to continue to attract and foster talent at Queen Mary. In line with this commitment, the Academy has been revamped as a forum to promote cross-fertilisation between the new ECRs who form part of the 'Rising Stars Programme' and several other ECRs (lecturers and senior lecturers)

funded by Queen Mary as well as fellows funded by third parties (including Medical Research Council, Cancer Research UK and British Heart Foundation). This inclusive platform provides support, training and mentorship to ECRs across Queen Mary.

Bringing the Faculty of Medicine and Dentistry together

One initially underappreciated achievement of the ECR programme was its ability to bring the faculty together. Being part of a cohort with much in common and a strong motivation to interact, the ECRs, particularly those from the first cohort, organised and ran annual retreats for several years since the programme's inception, supported by the faculty. These retreats provided invaluable opportunities for discussions on research plans and opportunities, extensive networking, and practical help and advice around developing as successful independent group leaders. These informal occasions for exchanging ideas have nurtured collaborative projects and led to the establishment of long-term collegial relationships throughout the faculty. It is also partly thanks to the ECRs that groupings such as the London Inflammation

ECR Retreat in 2015 at Chicheley Hall.

Network, the Epigenetics Hub, the Metabolism Group and the Extracellular Vesicles Group were established. These groups operate in a collegiate fashion, providing hubs for cutting-edge research, the exchange of expertise and grant applications.

When asked how the ECR Programme changed the faculty, Professor Mauro Perretti replied: "The 2013 ECR Programme implemented in faculty has been very successful in rejuvenating our academic faculty while at the same time strengthening specific streams of research." He also highlighted that in addition to the scientific quality of the ECRs, "a particular benefit has been their collegiate attitude and their drive towards collaborations and joint projects. This fresh approach has helped to shape the research strategy of the faculty for the years to come."

Success at Barts Cancer Institute

In 2013, I started my independent career at the BCI as one of the seven ECRs in the first cohort of the ECR Programme. As a group of young, energetic (and at times naïve) scientists, we brought our enthusiasm and determination to succeed to our institute. Being part of a cohort was incredibly productive and enjoyable. It is difficult to express how much support we have provided to one another, particularly during the first years of establishing our labs. From helping with grant writing, joint lab retreats and of course a healthy dose of pub outings, we laughed, celebrated and commiserated together when needed. We shared the frustrations and the absolute joys of mentoring and managing people in our own teams, and we were always

The 1st ECR cohort: Before and after. Left to right: 2013 – Paulo Ribeiro, Angus Cameron, Gabi Ficz, Susana Godinho, Katiuscia Bianchi, Sarah McClelland and Trevor Graham. 2023 – Paulo Ribeiro, Angus Cameron, Gabi Ficz, Susana Godinho, Katiuscia Bianchi and Sarah McClelland.

there to cheer for each other's successes.

In 2023, we celebrated our 10-year anniversary as a group. On a glorious sunny day in July at the beautiful Charterhouse Square Campus, we brought together our teams, past and present, to commemorate this incredible milestone. With plenty of group photos, drinks and pizza, the party was a celebration of the ECR Programme and its success at the BCI.

Ten years since the first cohort of ECRs started, it is fascinating to go back to the early days, to the 'beginners' enthusiasm and ask: 'did the ECR programme at the BCI stand the test of time?' Unarguably yes. The six academics currently working at the BCI brought a total of ~£14m in grant income, of which £4m is from Research Council Funds. We also brought 37 new PhD students so far, of which 20 have completed their PhD, and generated numerous 3* and 4* publications that were part of the university portfolio for both REF2014 and REF2021. We have been instrumental in supporting the growth of existing facilities and in setting up new ones, such as the Metabolomics and Single-Cell Platforms, for the benefit of the entire institute. To

First ECR Cohort – 2013

- Katiuscia Bianchi, Reader
- Angus Cameron, Reader
- Gabi Ficz, Reader
- Susana Godinho, Professor
- Trevor Graham, Professor (moved to Institute of Cancer Research)
- Sarah McClelland, Professor
- Paulo Ribeiro, Reader

Second ECR Cohort – 2019/2020

- Roberto Bellelli, Senior Lecturer
- Mirjana Efremova, Senior Lecturer
- Andrew Finch, Professor
- Miguel Ganuza, Senior Lecturer
- Ioanna Keklikoglou, Assistant Professor (moved to University of Crete)
- Luigi Ombrato, Senior Lecturer
- Barrie Peck, Senior Lecturer
- Tanya Solimon, Senior Lecturer
- Lovorka Stojic, Senior Lecturer
- Ben Werner, Reader

date, all researchers in our cohort have successfully been promoted to Readers or Professors, recognising our contributions as senior academics and teaching leads.

A new ECR cohort started at the BCI between 2019–2020 and was initially composed of six researchers. This number was expanded to 10 with additional funds from Barts Charity, which recognised the ECR Programme as a major asset to the faculty for bringing new talent. At the BCI, the new ECRs have established their teams, secured tenured academic posts and brought in an impressive grant income of ~£13m, of which ~£6m is from Research Council funds. They have also attracted 17 new PhD students. It is wonderful to see the new ECRs bringing the same enthusiasm and motivation to make the BCI an even better place. There is no doubt that this incredible group of scientists will continue to thrive at our institute.

Together, both cohorts make up approximately 25% of the current group leaders at the BCI, which is a remarkable achievement. This will undeniably have a significant positive impact on the institute, not only in the quantifiable metrics highlighted above but also through the development of a collegiate research environment that has been enabled by the support and mentorship received over the years. Indeed, it is important to acknowledge that our success at the BCI is also due to the incredible support we received from senior colleagues: in particular, Professor Nick Lemoine (the BCI's inaugural Director) and Professor Kairbaan Hodivala-Dilke (BCI Deputy Director), who were involved in the recruitment and mentorship of the ECRs at the BCI.

The impact of the ECR Programme at the BCI is best illustrated by Prof Nick Lemoine's words: "With each successive round of recruitment of Early Career Researchers, the BCI has been invigorated by the injection of new blood and fresh thinking in novel and emerging areas of science. Their energy and ambition generate a wave of optimism and innovation that lifts the vision of the whole faculty to explore innovation and make new discoveries." We hope the past, current and future generations of ECRs will continue to invigorate the BCI for years to come.

Professor Susana Godinho would like to thank Professor Mauro Perretti for providing valuable information regarding the ECR Programme crucial to writing this book chapter.

Education, Training & Engagement

Professor Andrejs Braun, Professor Richard Grose, Dr Sarah-Anne Martin & Professor John Marshall

Postgraduate taught courses – Professor Andrejs Braun & Professor Richard Grose

Educating the next generation of scientists and clinicians forms an important part of the BCI's mission to drive progress for people with cancer. Our postgraduate teaching began in 2005, shortly after the institute's establishment. Before the launch of our cancer-specific courses, Professor Bijendra Patel established a specialist Surgical Skills programme, which took place in the basement of the Old Anatomy Building at Charterhouse Square – coincidentally, the same place where Professor Nick Lemoine and many others had previously studied anatomy during their medical school training at Barts and the London. Years later, the same basement hosted nine aspiring surgeons honing their craft through advanced surgical simulators.

The BCI's first cancer-specific courses took shape in 2006 following discussions between Institute Manager Dr Delphine Purves and the Medical School's CMO, Peter Davis. Delphine proposed the idea to Nick, who nominated two directors to run our first two cancer-focused courses: Professor Louise Jones to oversee Molecular Pathology and Genomics and Dr Simon Joel to oversee Cancer Therapeutics. Both courses continue to this day. The BCI's teaching initially drew around 30 students in total to the institute but expanded year by year. The growing educational programme was overseen by Kaye Yeung, first as Academic Coordinator and later as Deputy Institute Manager. Professor John Marshall also played an instrumental role

in the development of our programmes. Today, BCI offers six courses and welcomes a global student body of around 200 annually, both onsite and through distance learning platforms. By sharing our expertise, we hope to train and inspire the next generation of cancer experts.

Multiple faces of diversity

Diversity in professional background is one of the most notable features of our MSc students. In addition to attracting MBBS and biomedical sciences graduates worldwide, we've welcomed engineers, dentists, nurses and even horticulture biologists and MBAs to our cancer courses. Interestingly, although the learning curve for some of these students is usually steeper in the first semester, they often turn out to be some of the most motivated and, in turn, successful in their chosen cancer research niche. Within this context, I can't help recalling Niels Bohr's "*Contraria Sunt Complementa*" (contrary things are complementary things), emphasising that the most interesting things in science and education happen when two or more seemingly opposite fields merge. The latter is definitely true for the BCI level seven (Master's and equivalent level qualifications) educational agenda.

Students join us from all over the world, both in person and online – giving us an alumni network that stretches from South America to Australasia. We were pioneering Distance Learning Provision long before COVID-19 and the introduction of mixed-mode education. Our family of global learners have benefitted from the increasing influence of technology, taking us from a position nearly twenty years ago where students were listening to audio capture, to current digital platforms that enable real-time communication, virtual labs, and interactive webinars, erasing traditional geographical barriers to classroom teaching. Now, a student in Brazil can, in essence, sit alongside a peer in Germany, listening to a lecturer from London, discussing, debating, and learning the hallmarks of cancer, all thanks to the power of online education.

Yet, the Digital Education itself is not without its challenges. Differences in time zones, varying levels of access to resources, and contrasting educational backgrounds can sometimes be challenging in the distance learning provision. For example, organising viva voce assessments with a cohort ranging from GMT-8h to GMT+8h can test logistics and awareness. Markers may sometimes be surprised to

be greeted with "good morning" from a student during the late afternoon in the UK. Equally, not all our online students are from locations that far-flung – I remember the Chinese surgeon being examined in cancer biology, who, when asked the ice-breaker: "Sorry if it's late at night for you – where are you joining us from?" replied: "Acton…"

Equally diverse are the destinations of our alumni. Many of our graduates continue their careers in academic or research institutions. Equipped with robust knowledge of cancer biology and scientific thinking skills, about half of our students pursue a PhD, including in some of the best universities in the world – from Oxbridge to Zurich to Vancouver. It is delightful, some years down the line, to read high-impact papers authored or co-authored by our former students, getting a sense of fulfilment about training the next generation of cancer researchers.

Since our curriculum heavily features a clinical translational agenda, some alumni aim to bridge the gap between discovery research and patient care. Therefore, a sizable proportion of our students, especially clinically trained ones, work in hospitals, including large cancer treatment centres. There, they progress as clinical or medical oncologists and clinician scientists. Retrospectively, such alumni are particularly grateful for the opportunity to learn advanced statistics and principles of clinical trial design, subsequently making them some of the best in clinical academia.

Further, since the biotech and pharmaceutical sectors continually seek individuals with in-depth knowledge of cancer mechanisms and drug development, around a third of our graduates continue their professional journey in industry, ranging from senior executive to research and development, drug testing and clinical trial coordination.

Next, with the expanding interface between science and society, we see an increasing number of BCI graduates going into public health, policymaking, and cancer advocacy, where they become proficient in shaping health policies and resource allocation, ensuring that scientific advances translate into societal benefits. It is particularly inspiring to see our alumni taking active roles in patient advocacy activities such as VOICE (the BCI's five-day science for patient advocates programme, bringing together people with personal experiences of cancer and cancer researchers under the same forum).

Expanding the MSc programmes

Over the past ten years, it has become increasingly clear that computational biology and data sciences will be a significant driving force in biomedical sciences, including cancer research. This understanding was further backed by the rapidly expanding bioinformatical agenda in major cancer centres, including BCI, and, in turn, a large demand for graduates trained in computational cancer research.

Luckily, this window of opportunity coincided with the significant expansion of the Centre for Cancer Genomics & Computational Biology, led by Professor Jude Fitzgibbon at that time. The computational research firepower defined the BCI's capacity to develop a brand-new course specifically focused on data analysis in cancer research. Dr Jun (Alex) Wang led the development of our new Cancer Genomics & Data Sciences MSc, officially launched in the 2022/23 academic year.

The course itself is unique due to its exclusive focus on cancer research and abundance of "hands-on" student experience analysing vast amounts of raw computational data accumulated within the centre. As of the beginning of 2023/24, the enthusiasm for joining the course is enormous, with the intake increasing sixfold over a year.

Academic collaborations are increasingly becoming the norm, especially in fields like cancer research, which demand diverse perspectives and shared knowledge. With the research agenda in mind, we were always keen to develop collaborative educational programmes with other universities worldwide to expose their level seven students to joint academic efforts early. Within this context, we attempted to identify any unmet educational needs globally where our contribution would be especially valuable in addressing clinical and societal challenges. One such challenge could be identified in Southeastern Asia, where most level seven programme equivalents included a large amount of laboratory research work, often at the expense of taught programme components. While such a Master of Research arrangement is an excellent way to train the next generation of discovery scientists, such courses would be prohibitive to those trying to combine education with employment, including medics undergoing postgraduate professional training.

Therefore, our will and ability to contribute to an inclusive and diverse online education in cancer led us to establish a collaboration with Universiti Sains Malaysia

(USM), one of Asia's leading science and research universities. Supported by the Queen Mary Digital Education portfolio, we developed a distance-learning Cancer Biology programme aiming to educate postgraduate students who otherwise would be unable to join research-oriented programmes. As a tailored approach to this cohort of students, we opted to increase academic flexibility, allowing students to shape their academic portfolios as much as possible. The programme is scheduled to start in the 2024/25 academic year and will epitomise the integration of Western and Eastern academic excellence, aiming to equip students with a comprehensive understanding of the multifaceted realm of oncology.

Excellence through scholarships

Since the launch of our cancer programmes in 2005, a sizable proportion of our students have been joining us as part of their international scholarship. As a globally orientated, research-led institute, we were proud to contribute to the causes of international foundations that provide access to cutting-edge postgraduate education to students from developing countries. Merck Foundation, as well as Chevening and Commonwealth scholarship schemes, are some of the supporters of our star students who are keen to establish or develop cutting-edge clinical or academic leadership in their countries.

Indeed, selecting candidates for such scholarships proved to be one of the most challenging tasks, given the high number of intelligent and highly motivated professionals applying. In a way, it taught us that multiple other factors, apart from academic achievements per se, are to be taken into account when deciding who would benefit most from doing a Master's course.

Projecting the societal contributions of our students was particularly important when assessing Commonwealth Scholarship applicants, as the distance learning nature of the programme is particularly suitable for practising clinicians. So far, we have been delighted by our scholars who, with rare exceptions, were graduating with distinctions and moving to highly successful post-BCI careers. Moreover, it was particularly inspiring to read and mark dissertations of students who chose to do data analysis, systematic or literature reviews around cancer care in their home countries, clearly defining healthcare system strengths, shortfalls and areas for future focus. From that perspective, we can safely say that the impact of BCI postgraduate

education on national healthcare systems far exceeds the UK and is truly global.

Dissertations as an exercise in academic freedom

Those familiar with the Bologna Declaration and the UK Quality Code for Higher Education would probably know that one of the most important descriptors for level seven degrees is the ability to create new scientific information based on existing evidence. This exercise comprises a sizable proportion of an MSc, ranging from 60 to 100 credits out of 180 required. For most of our students, a lab project or dissertation marks the high point of their studies. By the time they reach the third semester, students are already more or less clear about their favourite areas in cancer research. To further develop the passion for a particular area of cancer, we allow students to come up with their own dissertation topic and then find an appropriate supervisor as close as possible to their chosen field. This approach complements the mainstream administrative pipeline of project selection, where students choose from pre-ordained suggestions.

Left to Right: Professor Andrejs Braun, Dr Kevin Rouault-Pierre, Dr John Riches and Dr Angus Cameron

Indeed, the title repertoire of self-made projects is remarkable, often placing our output creativity into many understudied areas of cancer research. Ranging from an analysis of the relationships between primary care and cancer clinics, through rare and overlooked cancer types, to the impact of circadian rhythms on cancer susceptibility and prognosis – these topics are a true contribution to the overall knowledge of cancer as a disease. Needless to say, a sizable proportion of dissertations are published in respectable journals as literature or systematic reviews.

The description of the semester three creativity exercise would be incomplete without highlighting the contribution students make to the BCI lab-based research agenda. In this semester, students on lab-based courses are embedded into ongoing research projects, working alongside PIs and postdocs where they contribute to the advancement of cancer research at Queen Mary's.

This hands-on experience is instrumental in not only honing the students' practical and analytical skills but also in fostering their scientific thinking and learning to collaborate in the lab. The project placements are allocated according to students' research interests, ensuring a high level of motivation and a mutually beneficial exchange with the research group: while the students gain a realistic insight into the rigours and rewards of laboratory research, the ongoing projects, in turn, are enriched by fresh perspectives and newly generated data that are often incorporated into publications. In some cases, standalone lab projects form a basis for the transition from MSc to PhD, and there are at least five such examples over the last four years.

Students graduate with an enormously developed skill set, having honed their skills in critical analysis, communication and research, all underpinned by a deep understanding of cancer, from inception to treatment. But they never truly leave us at Barts Cancer Institute, remaining lifelong members of our burgeoning alumni network – now numbering well into the thousands!

PhD programmes – Dr Sarah Anne Martin

One of the major successes of our postgraduate taught programmes has been the progression of many of our MSc students to undertake PhD degrees within the BCI and beyond. This is a testament to the research-driven content incorporated within

our postgraduate research courses, driving real scientific curiosity.

The success of our PhD programmes is largely due to the diverse nature of our student population and the scientific opportunities available to them. Over the past decade, our student cohort has grown by 30% and has been one of the leaders in postgraduate research student recruitment across the faculty. Significantly, 40% of our postgraduate research student cohort are international students from around the world including countries such as Malaysia, Egypt, Saudi Arabia, Belgium, Croatia, Germany, Cyprus, Italy, Switzerland, Ireland, Mexico, France, Spain, USA, Kazakhstan, India, Hong Kong, Turkey, Netherlands, Nigeria, China, Hungary, Greece, Austria, South Korea, Slovakia, Bulgaria, Lithuania, Bangladesh, Sweden, Portugal and Belgium.

Diversity within our postgraduate research community

As of September 2023, we have 130 students enrolled within BCI postgraduate research programmes via numerous doctoral training programmes in collaboration with FMD institutes, across Queen Mary and beyond. One such doctoral training programme is our Medical Research Council (MRC) funded doctoral training programme (DTP) which runs in collaboration with the University of Southampton. This is the first MRC-DTP awarded to Queen Mary and has been running since 2016 with a successful renewal in 2022 for a further five years. This four-year PhD Programme with integrated Master of Research combines two world-leading research centres, the University of Southampton and Queen Mary, to deliver a DTP with excellence in Translational Biomedical Sciences around three main themes: 1. Cancer, neurological and inflammatory diseases 2. Infectious disease and anti-microbial resistance 3. Global health.

A tangible demonstration of the success of our postgraduate research students is evidenced by the wide range of destinations following their award both within academia and beyond. These include postdoctoral research positions within the UK (26%) and internationally (11%); clinical training (24%); pharmaceutical companies (21%); research funding (1%); science communication (1%); management (1%) and scientific consultancy (1%).

Here, two former BCI PhD students who have advanced into senior roles look back on their experiences:

Professor Jessica Okosun – Professor of Translational Cancer Research and CRUK Clinician Scientist at Barts Cancer Institute (BCI PhD student 2011–2015)

"I was a fortunate recipient of a Kay Kendall Leukaemia Fund (KKLF) Junior Clinical Research Fellowship to join Professor Jude Fitzgibbon's lab in 2011 to undertake a PhD. As a fresh-faced PhD student, I was particularly keen to understand the genetic heterogeneity in lymphoma patients and relished the themes of the lab: bringing the challenging questions from the clinic to the bench, leveraging patient samples and adopting cutting-edge technologies in the pursuit of answering these questions. These approaches really dared me to think more deeply about how I could achieve precision medicine for our patients. This period was highly successful, working with post-docs at the time (Csaba Bödör and Alex Wang) under the outstanding mentorship of Jude, who gave me the room for research creativity and opened several doors of opportunities and collaborations by introducing me to the wider lymphoma biology field. I distinctly remember flying to Washington as a first year PhD student to give an oral presentation in a closed workshop amongst many lymphoma biology luminaries – it was both an inspiring and frightening experience! Our important contributions to the field opened the door, unsurprisingly, to more questions and proved highly instrumental in solidifying my desire to become a clinician scientist and shaping my trajectory and current translational lymphoma research program that I lead at the Barts Cancer Institute."

Dr Prabhu Arumugam – Director of Clinical Data and Imaging at Genomics England (BCI PhD student 2012–2016)

"I trained in Medicine at Barts and the London and had lectures during medical school from some of the faculty at the BCI. It was both inspiring and motivational to hear about the work that was being undertaken. During medical school, I did a short summer project in the Kocher Lab at the BCI and during my early medical training, finalised a plan to return to do a formal period of research, leading to a PhD. Stepping into a research laboratory as a clinician is not something to be underestimated. The basics of laboratory life of cell culture were novel and my mind was blown when I first saw a gel electrophoresis. It can be challenging moving to a new field of research as there is a lot of background work that you need to become familiar with and I spent my first few weeks wondering how I could do this and what on earth I was doing

amongst these brilliant and incredible researchers. However, working in an institute that specialises in cancer research makes that transition a lot easier. The collaborative atmosphere at the BCI is superb and there is always someone around to help with troubleshooting a problem in the lab or during data analysis. It was always reassuring hearing from a range of scientists, from BSc students to PIs that research is littered with moments when things don't work and go to plan. PhDs take a long time. There are highs and lows, and I could only have finished with the support of friends and colleagues at the BCI. The key takeaways for me were to learn from problems and to make the most of collaboration, learning from the mistakes of others as well".

BCI public engagement – Professor John Marshall

One of the greatest qualities of the BCI's staff and students is their enthusiasm for public engagement activities, sharing their knowledge and passion for science with audiences young and old. Before the COVID-19 pandemic, the BCI benefited from a dedicated Cancer Research UK public engagement and fundraising officer, who worked specifically with the institute. Every month, groups of patients, carers, and funders were invited to tour our labs and research facilities, guided by a senior scientist who would show them cancer cells under microscopes and describe the essential and often expensive technologies we need to remain at the cutting edge of science. Annually, BCI welcomed 700–800 visitors in this way.

Centre of the Cell

One of the most inspiring examples of public engagement connected to BCI is the Centre of the Cell – the first informal science learning centre to be located within a research laboratory. Situated in Queen Mary's Blizard Institute, the Centre was founded by and is directed by BCI's Professor Fran Balkwill. Fran's responsibilities include strategy, operations, and fundraising, having raised over £7.5 million since 2003 for its unique learning spaces: the STEM Pod and the Neuron Pod. The Centre engages schools and community groups through innovative science shows such as 'Snot, Sick and Scabs', and offers a Youth Membership Scheme with opportunities for work experience, mentoring, and university application advice for teenagers in East London. The Centre also runs evening events, including the Big Question Lecture series co-produced with youth members, as well as concerts that combine science,

Centre of the Cell's STEM Pod, with Nucleus station (centre) and surrounding interactive stations.

music, and art. Since its opening in 2009, Centre of the Cell has reached over 239,000 participants in its sixteen original science shows.

In 2022, Queen Mary University of London invested £438,000 to refurbish the Centre's immersive STEM Pod, which reopened on time and within budget in Summer 2023. With a further £100,000 donation from LifeArc, the STEM Pod experience was enhanced by a Projection Mapping sequence 'The Orchestra of You' in December 2023. New digital interactives for STEM Pod are under development, and a website redevelopment project is underway to bring the Centre's unique content to national and international audiences. Future priorities include expanding provisions for young people with special educational needs, increasing patient involvement initiatives, and evaluating the long-term impact of the Centre.

Although Centre of the Cell covers many aspects of cell biology and biomedical science, increasing understanding of cancer and cancer research is an important aim. The STEM Pod includes two cancer research-focused interactive games: Lab Bench Chaos, where visitors grow cancer cells (featuring two BCI postdocs), and Tumour Takedown, which challenges players to destroy tumour microenvironments using different immunotherapies. BCI staff also appear in the Centre's film sequences, and

postdocs and PhD students volunteer as STEM Ambassadors to assist with workshops and shows.

With funding from research grants and industry, Centre of the Cell is developing a new science show and workshop exploring how cancer treatments are developed, working with BCI scientists. Aimed at teenagers and families, this programme will cover artificial intelligence, big data, multi-cellular 3D models, mouse cancer models, and clinical trials.

STARS (Science Training for Aspiring Research Scientists)

BCI's STARS programme, which I first developed in 2003, aims to encourage and inspire A-level pupils from London schools where progression to higher education is below the national average to pursue their career ambitions. Each year, 25 students identified by the Mayor of London's Schools Accession Team visit BCI teaching labs to learn cell and molecular biology techniques directly from PhD student demonstrators, who show them how to perform cell and molecular biology experiments that are used daily for our research at BCI. This includes how to perform tissue culture, analyse proteins using electrophoresis and western blotting, and isolate and clone DNA. The Queen Mary admissions team also provide a brilliant talk covering all matters related to applying to and attending university. Feedback from participants is very positive, and many achieve their aspirations of entering medical, dental, or veterinary school. This year, we extended the STARS programme across other sites in the City of London Centre, enabling us to expand the horizons of many more children in London.

VOICE (Vision On Information, Confidence and Engagement)

The BCI also runs VOICE (Vision On Information, Confidence and Engagement) – a course that teaches basic and clinical science to cancer patient advocates. Conceived by Dr Adrienne Morgan, a founder of the Independent Cancer Patient's Voice (ICPV) and a breast cancer patient herself, the programme was designed and delivered by Professors Louise Jones, Richard Grose and myself, together with guest speakers to deliver cancer-specific talks and many volunteers to run the practical sessions. In 2024, patient advocate Dave Chuter joined the organising team as Chair of ICPV.

VOICE aims to enable individuals who have little or no formal science training

to grasp the fundamentals of what cells are, why changes in DNA can result in the development of cancer, how normal and cancer cells 'talk' to each other and their environments, how to access and how to read scientific research articles. Throughout the week, experts deliver talks about specific cancers that correspond to those that the students may have themselves. Each afternoon, the students don lab coats and gloves and perform experiments in our teaching labs. One highlight is a demonstration by Louise in which she prepares a freshly removed breast cancer for the pathology lab. This is a highly emotional time for many who may have, or have had, breast cancer themselves. Evening activities include guest speakers, visits to other sites, (such as the Centre of the Cell), and opportunities for some much-needed relaxation.

VOICE programme participants with BCI staff and student volunteers.

VOICE's reputation increases each year, and the course now attracts participants from around the globe, with recent participants travelling to us from Australia, Canada, and Mexico. Cancer Research UK funds five students annually, and almost every CRUK Grand Challenge team now has one or more VOICE-trained patient representatives. The importance of VOICE cannot be underestimated.

Looking ahead

Public engagement is considered an important responsibility by staff at BCI. This gives me confidence that our current programmes will continue long into the future and hopefully will be expanded further with novel ideas developed by our outstanding staff.

Future Horizons at the BCI: A Glimpse into the Next Era of Cancer Research

Professor Tyson V. Sharp

At the BCI, we conduct research with a clear line of sight to the clinic, always aiming to uncover knowledge that we can translate into tangible improvements for preventing, diagnosing and treating cancer. This book has covered many examples from the past 20 years in which our research has already progressed to the clinic and has impacted patients' lives. But these advances begin decades earlier, in the laboratory, with fundamental breakthroughs in our understanding of the disease.

Much of the BCI's research is of this fundamental kind, unpicking the intricate processes driving cancer. Ultimately, these are the studies that feed the translational pipeline leading from bench to bedside. Discoveries happening in the lab today may represent the start of new clinical breakthroughs that will benefit patients in years to come. In this chapter, I will cover a few of the many examples of research at the BCI today where we are leading the way in exploring exciting new horizons.

RNA biology

RNA biology was once perceived merely as a conduit between DNA and proteins. However, its important role in health and disease has drawn attention in recent years, particularly during the COVID-19 pandemic, which propelled RNA biology into the public consciousness. Researchers around the world raced to understand this RNA virus and develop RNA-based vaccines. However, interest in RNA therapeutics had been growing rapidly even before 2020, with innovative RNA-based drugs seeing remarkable success in neurological disorders such as spinal muscular atrophy.

Understanding and targeting RNA biology in cancer has a huge potential to reveal new ways to halt tumour growth, stop metastasis, overcome treatment resistance and more. At the BCI, we have recruited an incredible cadre of early-career research talent focusing on RNA biology, who collaborate as part of our RNA hub. We've become one of the biggest cancer RNA centres of excellence in the UK, sitting at the forefront of this new field. Our researchers are also helping to drive collaboration throughout the UK, such as by hosting RNA UK, a conference that brings together RNA-focused cancer researchers nationally and internationally. Here, I feature the work of just a few of our researchers investigating RNA biology in cancer.

Dr Lovorka Stojic's research has profoundly reshaped our understanding of long non-coding RNAs (lncRNAs) in cancer biology. These RNA molecules are not translated into proteins, yet research is revealing that they carry out an extensive array of vital functions. Lovorka's work has shed light on the multifaceted roles of these molecules in gene expression, chromatin organisation, and their potential implications in oncogenesis.

Lovorka has published important work demonstrating how to modulate lncRNA expression using CRISPR interference, a technique that holds promise for targeted cancer therapies. This work provides vital insights for researchers aiming to harness the therapeutic potential of lncRNAs in cancer treatment. In other work, she has also unpicked the intricate involvement of lncRNAs in cell division. Given that aberrant cell division is a hallmark of cancer, understanding these roles is paramount for developing innovative cancer interventions.

In addition, Lovorka performed a comprehensive evaluation of 'loss-of-function' methods – tools designed to specifically reduce the expression of particular genes to aid researchers in inferring their function. Lovorka's work provides a framework for understanding the unintended effects of these methods on genes other than their intended target and explores how to mitigate them to improve the use of these tools in pinpointing the exact roles of genes and RNAs in cancer progression. In collaboration with Dr Faraz Mardakheh and team (who at the time were based at the BCI but have since moved to the University of Cambridge), Lovorka also helped to develop TREX, a technique that identifies RNA-binding proteins interacting with specific RNA regions in living cells – a previously impossible task.

Meanwhile, Dr Diu Nguyen is improving our understanding of RNA cancer

biology, particularly in the realm of cancer stem cells (CSCs). These rare cells can self-renew and differentiate into proliferating cancerous cells, often evading traditional treatments like chemotherapy or radiotherapy. As a result, CSCs have been identified as culprits behind drug resistance and disease recurrence.

Diu's lab focuses on the intricate roles of RNA-binding proteins in post-transcriptional gene expression. Her research has highlighted RNA-binding proteins' significance in cancers, especially leukaemia. Despite their potential, only a fraction of known RNA regulators have been explored in leukaemia. Therefore, the team's primary aim is to delve into the dysregulated processes related to RNA-binding proteins in leukaemia, especially acute myeloid leukaemia (AML). Their end goal is to identify and understand potential RNA-binding protein therapeutic targets, which could lead to innovative AML treatments while preserving normal stem cells.

Epigenetics

Epigenetics is often termed the 'software' of our genes, operating above our DNA's 'hardware' to switch genes on and off in the right cells at the right time. Central to this is a process called DNA methylation, in which chemical tags are added to our DNA to alter its expression. Investigators are increasingly recognising that cancer development involves not only genetic alterations, but also epigenetic ones, which often precede the onset of the disease, and research in this field is expanding rapidly.

Dr Gabriella Ficz is a leader in the field of epigenetics research, and her contributions have significantly advanced our understanding of cancer biology. Her studies into the dynamics of DNA methylation have revealed important implications for epigenetics in cancer predisposition.

Gabriella co-leads the Queen Mary University of London Epigenetics Hub with Dr Miguel Branco of the Blizard Institute. This is a £3 million collaboration, funded by Barts Charity, that brings together world-leading expertise at Queen Mary and Barts Health NHS Trust to investigate how epigenetics could aid the early detection of a range of diseases, including cancer. BCI's Dr Özgen Deniz and Dr Lovorka Stojic are also members of this hub.

A key example of Gabriella's research found striking similarities between the DNA methylation in human embryonic stem cells grown in the lab and cancer cells,

raising interesting questions about how cancer cells develop and how this process may reflect a return to a more naïve, stem-cell-like state. Moreover, reversing specific methylation patterns offers a promising avenue for future therapeutic interventions in cancer.

Dr Özgen Deniz's research focuses on understanding how epigenetic modifications regulate transposable elements – segments of genetic code with the ability to jump around to different locations in our DNA – and how these elements impact blood cancer such as AML. Özgen and her team aim to use transposable elements to create new and effective ways to treat cancer. A notable study by Özgen and her team delves into the role of endogenous retroviruses as enhancers with the potential to drive oncogenesis in AML. This research underscores the significance of understanding epigenetic modifications in the context of cancer biology.

Epigenetics holds immense promise for the future of cancer biology. Research like that of Gabriella and Özgen's labs is helping to move us closer to a comprehensive understanding of cancer and paves the way for devising innovative new therapeutic strategies.

Metabolism

A hundred years ago, Dr Otto Warburg published a seminal paper describing how cancer cells switch to using glycolysis for energy, a less efficient but rapid energy-producing process compared with oxidative phosphorylation (the metabolic pathway usually employed in aerobic respiration). Cancer's propensity to adopt a unique pattern of metabolism, driven by their insatiable hunger for growth, is now recognised as one of the hallmarks of the disease.

For many years, research into cancer metabolism fell quiet, but the field has seen a renaissance in the past decade, with components of metabolism presenting promising targets for new therapies. Professor Nick Lemoine and others at the BCI spotted the potential in cancer metabolism research before its resurgence and chose to invest in this area at a time when most were still unwilling to do so. This foresight yielded great success, thanks in part to the support of Barts Charity, who invested in the recruitment of talented new group leaders focussing on metabolism to the institute.

Dr Andy Finch is at the cutting edge of cancer cell metabolism research, with a keen focus on lipid dynamics. Lipids, sometimes incorrectly perceived merely as energy reservoirs, are pivotal for various cellular functions, including the formation of cell membranes and intricate signalling processes. Andy's research has shown that when oncogenes like *MYC* and *RAS* are activated, they can drastically alter the biosynthetic needs of cancer cells. For example, his recent work showed that cells with the oncogene *MYC* require more energy to function and that this makes them more susceptible to apoptosis (cell death). Revealing weaknesses such as this hints at promising new possibilities for therapies.

Dr Barrie Peck researches the interplay between cancer metabolism, diet and the tumour microenvironment. His work delves into the adaptive mechanisms that cancer cells employ, particularly in response to varying environmental stimuli. One current focus is investigating the impact of a high-fat diet on the development of cancers and whether inhibition of lipogenesis presents a promising treatment strategy. His research has previously uncovered a number of metabolic genes that are essential in cancer and could present therapeutic targets.

Dr Katiuscia Bianchi researches how inflammation modulates cancer metabolism, with a particular focus on how obesity-associated inflammation can increase the risk of breast cancer. During obesity, macrophages infiltrate the breast tissue, leading to low-grade chronic inflammation, a factor considered responsible for the higher risk of breast cancer. Katiuscia's research showed that these macrophages exert this effect via the breast cancer oncogene IKKε. She has also shown that IKKε can reprogram cell metabolism, affecting the function of the mitochondria and increasing serine metabolism. Blocking the action of IKKε delays tumour formation in mice and reduces cancer cell proliferation, suggesting that this pathway could present a valuable therapeutic target. Katiuscia also spearheads the Metabolomics Mass Spectrometry core facility at BCI – a state-of-the-art facility that is pivotal to the cutting-edge metabolic research being conducted across the institute.

Dr Paolo Gallipoli's work focuses on myeloid leukaemias – a group of blood cancers that develop in the bone marrow – including AML. A clinical academic working between BCI and Barts Hospital, Paolo is investigating new targets for leukaemia therapies, focusing on how cancer cells rewire their metabolism in AML. His research recently revealed a potential new way to tackle treatment-resistant leukaemia by

blocking an enzyme called mannose-6-phosphate isomerase, which is involved in glycosylation – the process of attaching sugar molecules to proteins. Blocking this process caused leukaemia cells to fill with toxic fatty acids, making them more vulnerable to chemotherapies.

Dr Kevin Rouault-Pierre is studying how two blood cell disorders – myelodysplastic syndromes (MDS) and AML – develop and progress. He is particularly interested in how normal production of stem cells goes awry and develops into cancer. His team recently showed that people with MDS lose an enzyme called COASY – which is important in regulating the production of red blood cells – disrupting cells' metabolism and leading to anaemia. However, vitamin B5 boosted red blood cell production in MDS patient cells, suggesting a potential approach to treat anaemia in these individuals.

Altogether, the study of metabolism in cancer offers a window into the core processes supporting cancer cell survival and growth. Research from labs such as Andy, Barrie, Katiuscia, Paolo and Kevin's are bringing us ever closer to understanding and potentially disrupting cancer cells' complex metabolic wiring.

Navigating new horizons

After 20 years, the BCI is ushering in a new chapter as we warmly welcome Professor Nitzan Rosenfeld as our new Director. Nitzan is renowned for his ground-breaking contributions to the realm of liquid biopsies, where his expertise is unparalleled. His research has consistently pushed the boundaries of our understanding, offering novel insights into early cancer detection and the molecular intricacies of tumour evolution.

Looking ahead, the future of the BCI – and of cancer biology more broadly – seems bright. The BCI is driving exciting progress in some potentially transformative areas of research. We have many challenges to overcome to reach our ambitious goals. It will be fascinating to see how far we and the field of cancer research have come a further 20 years from now.

Conclusion: Reflections on 20 Years as Director

Professor Nick Lemoine

After twenty years as Director of the Barts Cancer Institute, it is time for me both to look back and to look forward. You have read the chronology of events in Keb's introductory chapter, so I will not repeat those here but I will take the opportunity to reflect on the key factors that made things possible.

It makes a difference who your boss is

Sir Nick Wright is a visionary leader who transformed the fortunes of our medical school during his tenure as Warden. Founding the Barts Cancer Institute was just one example of his courage and perspicacity, but of course, the most important for us as history has shown. He had previously been my boss as Dean of the Royal Postgraduate Medical School at Hammersmith Hospital in the 1990s when I was appointed as the first Clinician Scientist for the Imperial Cancer Research Fund (now Cancer Research UK), so I already knew about his commitment to developing the next generation of researchers and enabling them to be creative and ambitious. However, it was only when he recruited me to Barts that I realised just how far that commitment extended. When Nick believed in you, all things were possible and while I often felt my autonomy as Director was unearned it was really exciting and inspiring to be given the freedom to operate without the micromanagement so common in our sector. He also taught me that it is possible to have fun while doing serious business, as the often hilarious Medical School Executive meetings that he chaired showed us. When he stepped down as Warden and joined us in the Barts Cancer Institute as a Centre Lead, it was wonderful to have his wit and wisdom close by.

There is no I in team

Right from the start, the BCI has been blessed with an outstanding leadership team, with Delphine Purves as the consummate Institute Manager (or *Consigliere* as she might put it) and Ian Hart and Kairbaan Hodivala-Dilke as successive Deputy Directors. I often say 'It doesn't matter whether you like them or not, it's "can they do the job"', but it really makes a difference when they can do the job **and** you like them. Ian always referred to the two of us as Good Cop, Bad Cop and it was never clear to me then which of us was which, but when Kebs succeeded him in the role it was immediately apparent what he had meant! The dynamics of a senior team are critical to how it functions, and for any organisation 'the tone comes from the top'. Our shared commitment to healthy attitudes for a healthy organisation has been the rock on which we have built the values of the BCI. Excellence in all that we do has been a guiding principle and that extends beyond our science to everything that you experience as staff and students in the Barts Cancer Institute. We believe that a culture of mutual understanding and support is critical for our success.

In it for the long haul

Discoveries do not come easily and there are always trials and tribulations along the way. We have always recognised that we need to invest in the long term if we really want to see a return. Giving people the confidence to aim high is so important – we are here for the big wins, not the quick wins. It might be aligned with investment guru Warren Buffett's strategy – he chooses stocks that he believes offer solid prospects for long-term growth. Spotting those stocks is a skill that few possess. Many of the highlights of the 2024 BCI Showcase event were the result of up to twenty years of work by those involved, including truly transformational discoveries in basic science and ground-breaking clinical trials of novel therapeutics and diagnostics.

Making the big calls when the time is right

The BCI does not follow the crowd in its science. Instead, we have identified areas with the most unrealised potential for translation into clinical benefit for patients with or at risk of cancer, even when those themes were not in vogue. Ten years ago, biological therapies were out of fashion for the large funding bodies (committee

feedback on our grant application for development of oncolytic virotherapy said that it was unlikely ever to work) but today we have a Queen Mary spin-out company supported by UKRI grants and several million pounds of venture capital. We identified that DNA damage repair and genome stability held potential for discoveries to be translated into new therapeutic approaches and recruited the country's most talented scientists into our Early Career Researcher Programme. Building on fundamental discoveries in genome control with very significant investment in computational biology, the BCI has been at the forefront of understanding tumour evolution. Starting from a discovery of abnormal arginine metabolism in cancer cells nearly twenty years ago, our programme in cancer metabolism has grown into one of the most exciting in the country and has been translated into successful clinical trials in some of the most challenging cancer types.

What does the future hold for the BCI?

Antibody-drug conjugates are one of the most exciting developments in cancer therapy to reach the clinic, and BCI is at the forefront of trials of these agents. Already, Tom Powles has been recognised as one of *Nature*'s Top Ten Scientists as well as being named in the *TIME* 100 Health List for his breakthrough achievements in advanced bladder cancer.

Biological therapies will play a growing role in cancer treatment, and BCI clinicians and scientists are actively driving these from lab to clinic. As well as the anti-metabolic therapy pioneered by Peter Szlosarek in mesothelioma, the oncolytic virotherapy programme led by Yaohe Wang is poised to enter early-phase clinical trials in pancreatic and other cancers. CAR-T therapy is being advanced in blood cancer patients by John Gribben and our team of haemato-oncologists, and the translational work of John Marshall to develop CAR-T therapy for solid cancers is immensely promising. Our clinical trial programme includes studies of mRNA therapeutics for a number of tumour types, and in light of the success of such agents as vaccines against COVID-19, we could be entering a new era for molecular oncology.

Precision medicine melds clinical interventions with laboratory analysis using technologies such as single-cell sequencing to learn more about the responses at the single-cell level, and spatial transcriptomics to analyse the geographical relationships

between multiple biomarkers on the same tissue sample and monitor the immune responses over time. Mathematical oncology will play an increasingly important part in guiding neo-adjuvant therapies, using ctDNA and cancer exosome approaches to determine whether surgery and radiotherapy can be minimised or maybe avoided altogether.

Molecular radiotherapy is gaining increasing traction, and the BCI has been invested in this field for twenty years. I anticipate that this will go from strength to strength, bolstered by our partnership in CRUK's RADNET programme through the City of London Centre consortium with the Crick, Kings and UCL. Jane Sosabowski's national leadership could transform the security of the UK's supply of clinical radionuclides through the reprocessing of nuclear waste.

The BCI is already a nationally recognised exemplar for patient and public involvement and engagement, with the STARS and VOICE programmes as well as our patient involvement group in the Experimental Cancer Medicine Centre. This is a key theme for the future and with such strong foundations, the BCI will continue to lead the way. There is so much exciting science going on and we want the world to know about it!

Reflecting on the past 20 years, I feel privileged to have had the opportunity to lead the BCI and see our plans come to life. I wish our new Director, Professor Nitzan Rosenfeld, an equally fulfilling experience.

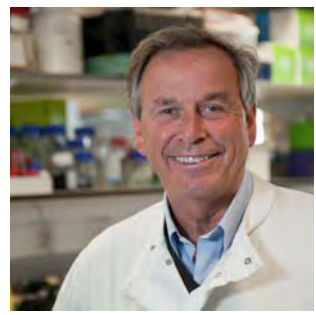
Professor Nick Lemoine's stepping down celebration in 2024.

Author Biographies

Professor Kairbaan Hodivala-Dilke

After completing her undergraduate studies at the University of Southampton in 1994, Professor Kairbaan Hodivala-Dilke earned a PhD in epithelial cell biology under Professor Fiona Watt at The Imperial Cancer Research Fund. She then conducted postdoctoral research with Professor Richard Hynes at MIT, gaining experience with genetically modified mice. Returning to the UK, she joined the Imperial Cancer Research Fund as a tenure-track fellow with Professor Ian Hart, working at St. Thomas' Hospital and later at Barts Cancer Institute. She was awarded tenure in 2004 and became Professor of the Tumour Microenvironment in 2009. She has served as Deputy Director of the Barts Cancer Institute since 2012 and Centre Lead of the Centre for Tumour Microenvironment since 2019. In 2015, she was awarded the British Society Cell Biologists Hooke Medal and was elected EMBO member and Fellow of the Academy of Medical Sciences.

Professor John Gribben



Professor John Gribben holds the Gordon Hamilton Fairley Chair of Medical Oncology at Barts Cancer Institute, Queen Mary University of London. He completed his doctoral studies at University College London with a Wellcome Trust Fellowship Award and continued postdoctoral training with Professor Lee

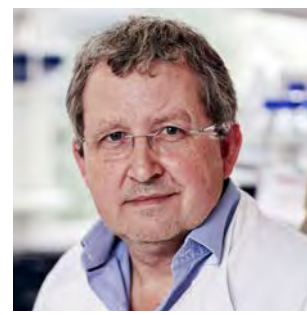
Nadler at the Dana-Farber Cancer Institute, Harvard Medical School. In 1992, he joined the Faculty at Harvard Medical School, becoming an Associate Professor of Medicine and an Attending Physician at the Dana-Farber Cancer Institute and Brigham and Women's Hospital. He returned to London in 2005, joining the Barts Cancer Institute. Professor Gribben is a founding member of the CLL Research Consortium, Associate Editor of Blood, and a Fellow of the Academy of Medical Sciences. He is currently the Centre Lead of our Centre for Haemato-Oncology.

Professor Fran Balkwill

Professor Fran Balkwill earned her BSc in Cellular Pathology from Bristol University in 1973 and her PhD from St Bartholomew's Hospital Medical College in 1977. She began her research career as a Postdoctoral Research Fellow at the Imperial Cancer Research Fund, where she later served as Head of the Biological Therapy Lab and Principal Scientist. In 2000, she joined Queen Mary University of London as Professor of Cancer Biology. She led the Centre for Cancer and Inflammation until 2019 and has been the Deputy Centre Lead for the Centre for Tumour Microenvironment since 2020.

In 2001, she founded and became Director of the Centre of the Cell at Queen Mary University of London. She is an accomplished communicator of science, especially to young audiences, and has written thirteen science books for children. In 2006, she was made a Fellow of the Academy of Medical Sciences and was elected a member of its Council. She was awarded an OBE in the 2008 Queen's Birthday Honours list. In 2024, she was elected as a Fellow of the Royal Society.

Professor John Marshall



Professor John Marshall began his research career in the Tissue-Interactions Laboratory of the Imperial Cancer Research Fund (ICRF) in 1983. In 1984, he moved within ICRF to study invasion and metastasis with Professor Ian Hart. Over six years, he developed photodynamic therapy while completing an MSc in Medical Immunology and an MPhil from the University

of London. He then pursued PhD studies on the role of integrins in melanoma. In August 2004, he and Ian Hart moved to the Barts Cancer Institute, where he was promoted to Professor of Tumour Biology in 2014. Since 2007, Professor Marshall has been designing and teaching research skills and sciences for two MSc courses, among other teaching responsibilities, at Queen Mary University of London. He became the Centre Lead for the Centre for Tumour Biology in 2020.

Professor Claude Chelala

Professor Claude Chelala was awarded a PhD in Computational Biology and Radiation Biology from Paris-Sud University and the Curie Institute and a degree in Structural Bioinformatics from Paris Descartes University in 2002. She then joined the National Centre for Scientific Research (CNRS) as a postdoctoral researcher. In 2004, she joined the Pasteur Institute in Paris to work on large-scale genetic variation analysis. In 2006, Professor Chelala joined the Barts Cancer Institute as a postdoctoral research assistant and was later promoted to academic posts, becoming Professor of Bioinformatics in 2015. She always had a strong motivation to translate her computational work into a patient setting. She established an interdisciplinary research team and now co-leads the Barts Life Sciences Precision Medicine programme and the Health Informatics and Bioinformatics for the Breast Cancer Now Tissue Bank and Pancreatic Cancer Research Fund Tissue Bank. She is Deputy Centre Lead for the Centre for Cancer Biomarkers and Biotherapeutics.

Professor Trevor Graham

Professor Trevor Graham completed his undergraduate training in Mathematics at Imperial College London before embarking on an interdisciplinary PhD combining Mathematics and Biology at University College London. He became a postdoctoral researcher, first in Professor Sir Nicholas Wright's lab at the CRUK London Research Institute, then in Professor Carlo Maley's lab at UCSF, where Trevor continued to mix

mathematics with molecular biology. Trevor became a group leader at the Barts Cancer Institute in 2013 and was promoted to Professor of Cancer Evolution in 2016. He co-led the development of computational biology as a core research theme at the BCI, culminating in the establishment of the Centre for Genomics and Computational Biology in 2019, where Trevor was deputy lead. He joined the ICR as Director of the Centre for Evolution and Cancer in spring 2022.

Professor Jessica Okosun

Professor Jessica Okosun graduated in Medicine at the University of Cambridge and undertook her medical and specialty registrar haematology training in London. Her research interests in lymphoma biology developed during her Kay Kendall Clinical Research Fellowship with Professor Jude Fitzgibbon at the Barts Cancer Institute, where she investigated the genetic heterogeneity and tumour evolution underlying follicular lymphoma and its progression. For this work, she was awarded the Royal College of Pathologists Specialty Research Medal. She earned her PhD from Queen Mary University of London in 2015. In 2017, she returned to the Barts Cancer Institute as a Clinical Senior Lecturer, and she was promoted to professor in 2023.

Professor Jane Sosabowski

Professor Jane Sosabowski completed a BSc (Hons) in Chemistry and an MSc by research on the photochemistry of sunscreen constituents at the University of Natal, Durban, South Africa. She then moved to the UK, joining the Joint Department of Physics at the Institute of Cancer Research in Sutton, Surrey, where she earned a PhD focused on developing PET radiotracers for assessing multidrug resistance in vivo. She later joined the Nuclear Medicine Research Laboratory at Barts and The London School of Medicine and Dentistry as a postdoctoral researcher with Professor Stephen Mather. This lab evolved into the Cancer Imaging Laboratory, which she now leads.

Professor Tatjana Crnogorac-Jurcevic

Professor Tatjana Crnogorac-Jurcevic obtained her MBBS degree and completed an MD thesis at the Medical Faculty, University of Zagreb, Croatia. She earned her PhD at the Imperial College School of Medicine, London. After postdoctoral work in molecular biology at CNRS in Toulouse, France, and molecular oncology at the CRUK laboratory at Hammersmith Hospital, London, she joined Barts Cancer Institute in November 2004 as a postdoctoral research assistant. She was later promoted to academic posts, culminating in her promotion to Professor of Molecular Pathology & Biomarkers in 2019.

Professor Yong-Jie Lu

Professor Yong-Jie Lu completed his undergraduate medical training at Henan Medical University in 1989 and postgraduate studies in Medical Genetics at Harbin Medical University in 1992. He earned his PhD in Pathophysiology from the Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, in 1995. He began his research career as a Visiting Scholar and Postdoctoral Scientist at the Institute of Cancer Research, Sutton, UK, later becoming a Senior Postdoctoral Scientist and then a Research Associate and Deputy Team Leader. In 2003, he joined the Barts Cancer Institute as a Senior Lecturer and Team Leader. He was promoted to Reader in 2010 and has been a Professor of Molecular Oncology since 2017. He is a member of the European Liquid Biopsy Society steering committee and the co-chair of the Circulating Tumor Cell Working Group.

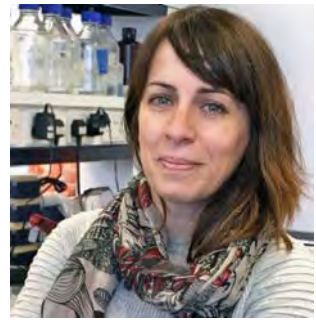
Professor Stephen W. Duffy

Professor Stephen Duffy is a statistician by training and was educated at the University of Edinburgh and Imperial College London. He has worked in the UK, Singapore, France, Sweden, and Russia. Much of his past work focused on randomised trials of cancer screening. As a result of his contributions to breast screening research, he has twice been awarded the Alexander Margulis Prize for Scientific Excellence by the Radiological Society of North America. Since 2010, Professor Duffy has been the Director of the Policy Research Unit in Cancer Awareness, Screening, and Early Diagnosis, a collaboration of primary care physicians, behavioural scientists, epidemiologists, and statisticians across seven institutions. He retired in 2024.

Professor Jack Cuzick

Professor Jack Cuzick received his BSc in Mathematics and Physics from Harvey Mudd College, Claremont, California. He then studied for an MSc in Mathematics at the University of London. He obtained his PhD in Mathematics from Claremont Graduate School, Claremont, California. Before his retirement in 2024, Professor Cuzick was the head of the Cancer Prevention unit within the Wolfson Institute of Population Health and held the position of John Snow Professor of Epidemiology at Queen Mary University of London. Until 2021, he was the Director of the Wolfson Institute of Preventive Medicine and head of the Centre for Cancer Prevention. His interests lie in cancer epidemiology and clinical trials, with a special focus on prevention and screening. He is a Fellow of the Royal Society, the Academy of Medical Sciences, the Royal Statistical Society, and the Institute of Mathematical Statistics, as well as an Honorary Fellow of the Royal College of Physicians. In 2017, he was awarded a CBE for services to cancer prevention and screening, as well as the CRUK Lifetime Achievement in Cancer Research prize.

Professor Susana Godinho

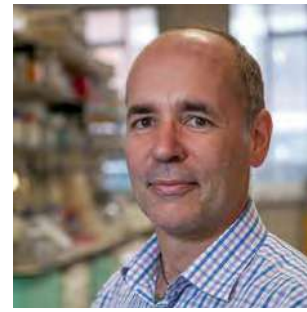


Professor Susana Godinho earned her BSc/MSc in Biology, specialising in Microbiology and Genetics, from the University of Lisbon, Portugal, in 1999. She completed her PhD in Cellular Biology at the Gulbenkian Institute of Science, Portugal, and Cambridge University in 2006, investigating the role of Polo kinase during mitosis. Following her PhD, she became a Postdoctoral Fellow at the Dana-Farber Cancer Institute and Harvard Medical School, USA, where she studied how cancer cells cluster extra centrosomes during mitosis. She then served as a Harvard-Portugal Programme Fellow at the same institutions, researching the role of centrosome amplification in cancer cell invasion using 3-D cell culture models. In 2013, she established her lab at the Barts Cancer Institute, where she continued to study how centrosome and cytoskeleton abnormalities impact cancer physiology and tumour progression. In 2016, Susana was awarded the prestigious Lister Prize, and in 2022, she was promoted to professor. In 2024, she became Deputy Centre Lead for the Centre of Cancer Cell and Molecular Biology and the AMS Springboard champion for Queen Mary's.

Professor Andrejs Braun

Professor Andrejs Braun graduated from Riga Stradins University in 2002, after which he moved to the University of Southampton as a visiting research fellow to study targeted cancer therapy and lymphoma biology. He continued his research at the University of Manchester, where he obtained his PhD in 2009. Following this, he moved to the Beatson Institute in Glasgow as a postdoctoral researcher, where he studied epigenetics of senescence and cancer with Professor Peter Adams. Andrejs then moved to the Barts Cancer Institute in London in 2014, where he was appointed as a lecturer being promoted to Professor in 2023. Professor Braun is Director of the Cancer and Therapeutics programmes and Director of Postgraduate Taught Programmes at the Barts Cancer Institute.

Professor Richard Grose



Professor Richard Grose read Zoology at the University of Bristol. He worked at Pfizer Central Research before undertaking a PhD at University College London, followed by postdoctoral research at ETH Zurich and Cancer Research UK London Research Institute. After joining Professor Ian Hart's Centre for Tumour Biology at the Barts Cancer Institute in 2004, Richard focused on examining links between developmental pathways and cancer and understanding cellular crosstalk, which has been the primary focus of his research group. He was promoted to Professor in 2019. Alongside running a research group, he is Dean for Global Engagement within the faculty and a committed educator - Directing an MSc Programme in Cancer and Molecular & Cellular Biology, as well as teaching on the Queen Mary-Nanchang programme.

Dr Sarah Anne Martin

Dr Sarah Anne Martin earned a BSc (Hons) in Microbiology and a PhD in Molecular Biology from the National University of Ireland, Galway, in 2003. She then joined the Mount Sinai School of Medicine, New York, as a postdoctoral fellow, investigating BRCA1 and its role in regulating caspase-3 activation. In 2006, she joined the Institute of Cancer Research, London. In September 2010, Professor Martin became a principal investigator at Barts Cancer Institute. Alongside her research, she served as Director of Graduate Studies for Research. In 2024, Dr Martin moved to The Francis Crick Institute, where she is now Head of Student Programmes.

Professor Tyson V. Sharp

Professor Tyson Valentine Sharp obtained his PhD from St. George's, University of London. After two postdoctoral positions in the Netherlands and the USA, he returned to the UK to take up a Senior Research Fellow position at the Institute of Cancer Research in London and then at UCL. In 2005, he moved to the University of Nottingham to establish his independent research group. He later relocated to the Barts Cancer Institute, where his research group studies the LIM domain family of adaptor proteins, focusing on their role in regulating microRNA-mediated gene silencing and the hypoxic response. He is the Centre Lead of the Centre for Cancer Cell and Molecular Biology and was promoted to Professor in 2018

Professor Nick Lemoine

Professor Nick Lemoine trained in medicine at St Bartholomew's Hospital Medical College, where he qualified with the University of London Gold Medal in 1983, specialising in pathology and oncology with posts in London and Cardiff. He earned his PhD in molecular oncology in 1988, working on the molecular genetics of thyroid cancer at The University of Wales College of Medicine in Cardiff. He then completed his MD in molecular oncology in 1992, researching growth factor receptor abnormalities at the Royal Postgraduate Medical School, London. He served as Professor of Molecular Pathology at Imperial College London, where he was Director of the Cancer Research UK Molecular Oncology Unit and the first Director of the National Translational Cancer Research Centre at Hammersmith Hospital. In 2004, he became the Director of the Barts Cancer Institute, serving in this role until 2024. He is the Centre Lead for our Centre for Cancer Biomarkers and Biotherapeutics. His own research focuses on the molecular genetics of cancer and gene therapy. Nick was elected as a Fellow of the Academy of Medical Sciences in 2006 and as a Foreign Academician of the Chinese Academy of Engineering in 2017. He was awarded a CBE in the 2022 New Year's Honours.

Our Emeritus Faculty

A number of individuals, now retired, were instrumental in founding and shaping the Barts Cancer Institute. Many of these emeritus researchers led practice-changing research at St Bartholomew's Hospital before our institute's establishment, creating the foundations for our research to build upon. Read more about the institute's roots in our previous 10-year anniversary book: *Every Rational Attempt: The Stories Behind the Contribution of Barts in the Fight Against Cancer.*

Professor Andrew Lister

Professor Bryan Young

Professor Ama Rohatiner

Professor Tim Oliver

Professor Rodney Reznek

Professor Steve Mather

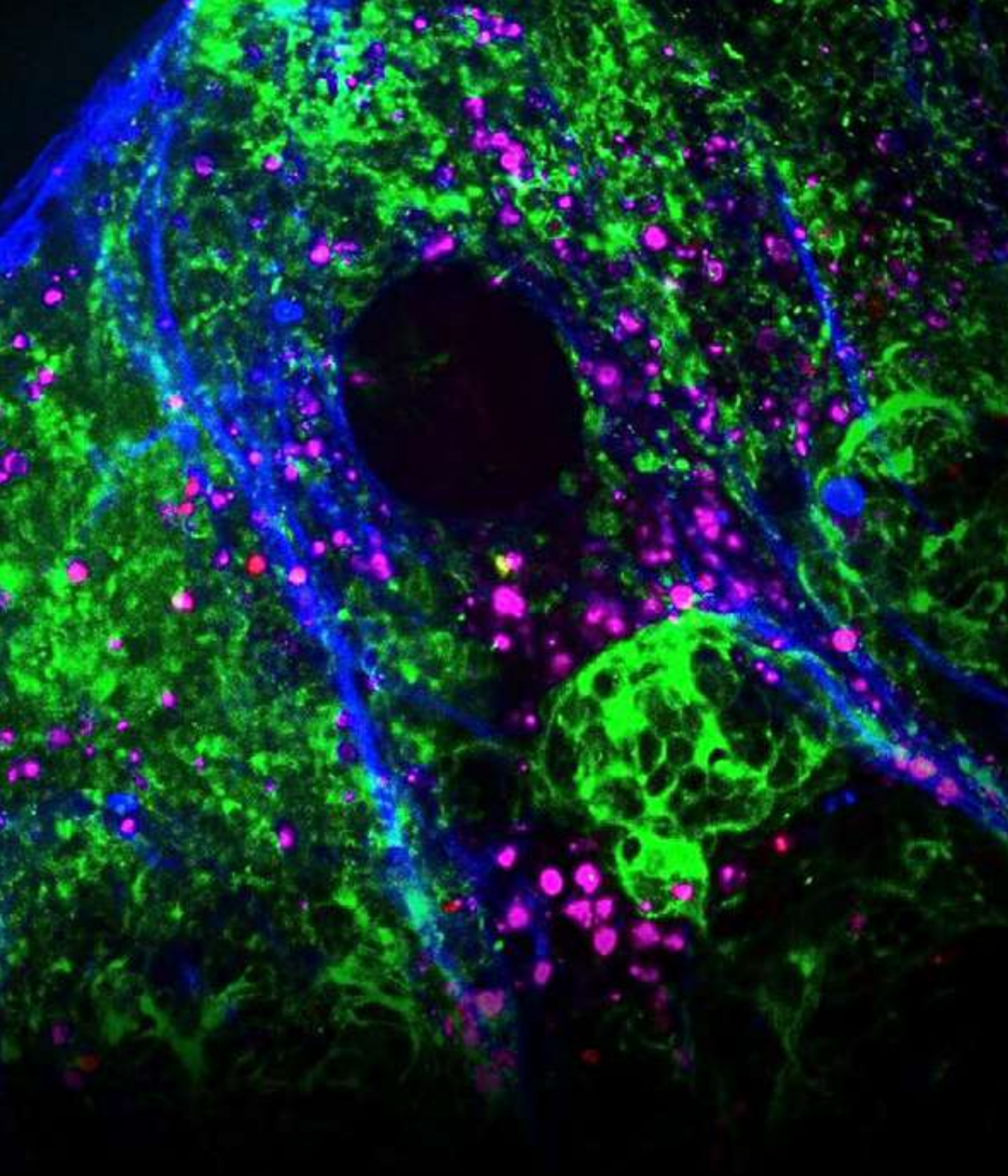
Dr Simon Joel

Professor Ian Hart

- **Professor Andrew Lister** is Emeritus Professor of Medical Oncology. He was Director of Cancer Services and Clinical Haematology at Barts NHS Health Trust and Director of the ICRF Medical Oncology Unit. He led the BCI's Centre for Medical Oncology, later renamed the Centre for Haemato-Oncology. His research focused on driving improvements for people with blood cancer.
- **Professor Bryan Young** is Emeritus Professor of Cancer Genomics. He headed the Barts Medical Oncology Unit before leading the Cancer Genomics Group at the BCI. His research focused on the genetics and genomics of acute myeloid leukaemia.
- **Professor Ama Rohatiner** is Emeritus Professor of Haemato-Oncology. She co-led the clinical leukaemia and lymphoma research programme at the Barts Medical Oncology Unit and later at the BCI. Her work drove the development of new treatment strategies for blood cancer.
- **Professor Tim Oliver** is Emeritus Professor of Medical Oncology. He directed the Barts Male Genito-Urinary Unit and led trials showing the efficacy of Carboplatin in testicular cancer. He founded Orchid, the UK's foremost male cancer charity.
- **Professor Rodney Reznek** is Emeritus Professor of Diagnostic Imaging. His radiology research led to improvements in the imaging of patients with gynaecological cancers.
- **Professor Steve Mather** is Emeritus Professor of Radiopharmacy. He was head of the ICRF Nuclear Medicine Research Laboratory at Barts, which later moved to the BCI. His research focused on developing improved radiolabelling methods for cancer imaging.
- **Dr Simon Joel** is Emeritus Reader in Cancer Pharmacology. He directed the Cancer Pharmacology group, studying novel cancer drugs. Dr Joel was Postgraduate Teaching Lead at the BCI and was instrumental in developing our courses.
- **Professor Ian Hart** is Emertius Professor of Tumour Biology. He was Deputy Director of the BCI and Centre Lead for Tumour Biology. His research focussed on the molecular underpinnings of cancer cell invasion and metastasis.

Abbreviations

AML	Acute myeloid leukaemia
BCI	Barts Cancer Institute
CAR-T	Chimeric antigen receptor T cells
CLL	Chronic lymphocytic leukaemia
CRUK	Cancer Research UK
CTC	Circulating tumour cell
DCIS	Ductal carcinoma in situ
ECM	Extracellular matrix
ECMC	Experimental Cancer Medicine Centre
ECR	Early career researcher
EMBO	European Molecular Biology Organization
FDA	Food and Drug Administration
FMD	Queen Mary Faculty of Medicine and Dentistry
HPV	Human papillomavirus
ICRF	Imperial Cancer Research Fund
Kebs	Nickname for Professor Kairbaan Hodivala-Dilke
MDS	Myelodysplastic syndrome
MRC	Medical Research Council
MRI	Magnetic resonance imaging
NCRI	National Cancer Research Institute
NIHR	National Institute for Health and Care Research
PDAC	Pancreatic ductal adenocarcinoma
PET	Positron emission tomography
PI	Principal investigator
REF	Research Excellence Framework
STARS	Science Training for Aspiring Research Scientists (our schools engagement programme)
STEM	Science, technology, engineering, and mathematics
TME	Tumour microenvironment
UKRI	UK Research & Innovation
VOICE	Vision On Information, Confidence and Engagement (our patient advocate course)
WHO	World Health Organization



Twenty years ago, Queen Mary University of London's leadership had a vision to bring together some of the most eminent cancer research teams in London, creating the Barts Cancer Institute. In this volume, researchers from the institute reflect on successes and challenges from two decades of deciphering cancer's complexities and look ahead to promising new horizons.

Queen Mary University of London

20 YEARS CELEBRATIONS Barts Cancer Institute

CANCER RESEARCH UK | City of London Centre