MANCHESTER CANCER RESEARCH CENTRE

MB-PhD Summer Research Opportunities 2022

This year we are again offering University of Manchester MBChB and University of St Andrews Medicine Manchester-pathway students summer research opportunities to introduce them to MB-PhD supervisors and cancer research themes. Our MB-PhD training route enables aspiring clinician scientists to undertake the vocational training of a medical degree in tandem with the research expertise of a PhD in Cancer Sciences, leading to the awards of MBChB and PhD. We aim to recruit the best candidates each year who are passionate about clinical care and research. Substantial funding, including an undergraduate tuition fee bursary, is available to CRUK Manchester Centre MB-PhD students.

This document contains summer research opportunities. Further opportunities may become available throughout the summer period, with updates shared when available. Additional PhD projects are likely to also be offered during 2022-23 recruitment.

Summer research opportunities include lab visits and research placements. Lab visits will usually be 1 day in length and might include but are not limited to: shadowing a staff member/PhD student; attending lab group/journal club meetings; assisting with any applicable experiments. The length and start date of research placements will be agreed between staff and students but would usually be 1-2 weeks maximum. We would encourage students to apply for many different opportunities, to gauge interest in different supervisory teams.

Travel and accommodation reimbursements can be provided to summer research opportunity students where appropriate, with agreement from **Dr Georgina Binnie-Wright**, **Postgraduate Programme Manager**. Please apply for relevant opportunities and we can discuss this post-application.

How to apply

Students who are interested in any of the below opportunities should send the following details to georgina.binnie@manchester.ac.uk by **Wednesday 6 July 2022**:

- Your name
- Current year of study
- Are you intending to apply to the MB-PhD programme in future? (Yes/No/Undecided)
- Supervisor preference(s) [use staff members' names] – *please also indicate preference for research placement and/or lab visit with the relevant staff member/s if appropriate*
- 200 words maximum on why you are interested in the opportunities you have selected

Preference is likely to be given to students who are eligible to apply to the MB-PhD in the 2022-23 recruitment round.

Key Dates	Details
Wednesday 6 July 2022	***Students:*** Student expression of interest deadline
By Monday 18 July 2022	***Supervisors:*** To have chosen students to participate in their summer research opportunities.
WB Monday 18 July 2022	***Students:*** Decisions relayed to students
Friday 16 September 2022	***Supervisors and candidates:*** 2022 Summer research opportunities to have concluded [with opportunities for additional events/engagement throughout the 2022-23 academic year]

See below for the full list of current available opportunities.

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1. **Professor Andrew Renehan, Diabesity and Cancer**

Opportunity Details	Lab meeting; journal club
Location	Manchester Cancer Research Centre, 555 Wilmslow Road, Manchester, M20 4GJ
PhD Project Title	Diabetes and pancreatic cancer: prevention and Risk stratification through Mendelian randomisation (DiaRMid)
PhD Project Description [included for reference]	Increased adiposity is a risk factor for pancreatic cancer (PC) and type 2 diabetes (T2D). Evidence from observational epidemiology suggests that T2D, particularly as new-onset diabetes (NOD) compared with long-standing diabetes (SLD), may be a trigger for early detection of PC but these data are confounded, mainly by reverse causation. To address these limitations, this thesis proposes to build upon a recent PanGenEU study and explore the direction of causation between T2D subtypes (NOD and SLD) using Mendelian Randomisation (MR) approaches and assess the mediation roles of several adiposity measures including body mass index (BMI), and magnetic resonance-derived visceral fat (VAT) and hepatic fat fraction (HFF). We will derive a nested case-cohort study from the UK Biobank (estimated PCs: 2000; cohort of up to 100,000 with magnetic resonance-derived measurements) and access information on T2D, related factors and medications, BMI, VAT, and HFF; and on T2D and PC-related SNPs. This thesis will combine expertise in obesity-cancer research (Renehan, Sperrin); pancreatic cancer (Valle); MR (Martin, Gunter); and mediation analysis (Emsley) to develop four workstreams (WSs): • WS1: Write a comprehensive UK Biobank application to derive the forementioned nested case-cohort • WS2: Characterise T2D, related factors, BMI, VAT, and HFF by cases and non-cases • WS3: Use T2D and PC-related SNPs as instrumental variables in bidirectional RM to test for two-way causal associations between NOD, LSD and PC. • WS4: Determine indirect and direct effects of the T2D-PC associations with measures of adiposity using multivariable and mediation analysis. The end product will be a better understanding of new-onset diabetes as a trigger for PC early detection. The student will be MCRC-based (integrated into BRC PED theme), link with the HPB research theme, with opportunities for placements to the University of Bristol and IARC, Lyon.
Research Group Background	Professor Andrew Renehan has a track record in identifying and nurturing clinical students to achieve high-quality cancer science. He is a co-investigator on the awarded CRUK Clinical Academic Training (CAT) Award application and was one of the presenting team to CRUK in March 2019. His group already includes one MB-PhD student who has been ambassadorial with dissemination of information about the MB-PhD scheme and who has successfully passed her year 1 viva. The UoM clinical academics on Professor Renehan's supervisory team pledge to mentor a successful candidate beyond the MB PhD period into their early academic career. The Renehan research group is based at the Christie Hospital and MCRC Building (Christie campus). Projects are framed within epidemiology, data health science and advanced statistical methodologies. The resources and methodologies available in the lab are:

Electronic health records	**Consortium data**	**Methodologies**
• CPRD linked with HES, IMD, OHS & NRCAS • Salford Integrated Records • SNOW (Wales)	• OCTOPUS – colorectal cancer (7 trials: > 13,000 individuals • OCTOPUS – endometrial cancer (3 trials: > 4,000 individuals	• Advanced survival analyses • Multi-state modelling • Latent class modelling • Advanced met-analysis techniques including Bayesian and IPD

			• ABaCUS – 5 cohorts > 0.5M participants with repeated BMI	
Supervisory Style	Lead supervisor meetings are weekly in the first 6 months; fortnightly thereafter. There are monthly lab meetings and monthly virtual journal clubs. Students will present their work and bring new ideas to lab meetings. All PhD studentships include multi-disciplinary inputs with quarterly face-to-face supervisor meetings. As the student matures, they are encouraged to develop autonomy and independence. The 'lab' culture is one of **integration, continuity, synergism, cross-covering, and collaboration**. Examples are: • Integration: sharing of ICD codes for obesity-related cancers; • Continuity: a year 3 student directing a year 1 student to optimal resources; • Synergism: running models of similar hypothesis testing for different cancer types; • Cross-covering: named individuals deputising to recruit patients into studies measuring liver fat using advanced MR imaging. Collaboration: includes several collaborations within the Manchester NIHR Biomedical Research Centre Cancer Prevention and Early Detection (PED) theme (lead: Renehan).			
Career Development	The Renehan group will sign up to the ethos of an integrated MB-PhD student to "Train the Next Generation of Clinical Academic Leaders within a Cancer Team Science Environment". To this end, the MB-PhD student will be educated in academic pathways after PhD including ACF, and ACL posts. The student will be introduced to other aspirating clinical academics and will attend relevant workshops, for example, the Academy of Medical Sciences. As part of the student's training, they will attend and present at national and international conferences in cancer (e.g. NCRI conference) and in obesity-relevant fields. The student will be aspirational and will be encouraged to develop autonomy and independence including writing grants for young investigators projects/ awards.			

2. Professor Robert Bristow, Translational Oncogenomics

Opportunity Details	Lab visit; lab meeting; journal club
Location	Manchester Cancer Research Centre, 555 Wilmslow Road, Manchester, M20 4GJ
PhD Project Title	The Role of Chromosomal Gains in Defining Clinical Aggression in Prostate Cancer
PhD Project Description [included for reference]	Aggressive cancer phenotypes result from the imbalance of one or more dosage-sensitive genes in a particular chromosomal segment. An exemplar is the chromosomal gain of the right arm of 8q (Chr.8q) in prostate, ovarian and breast cancer; this gain is associated with poor clinical outcome. Up to 20% of prostate cancer (PCa) cases present with Chr. 8q, which harbours the c-Myc oncogene with co-amplification of up to 30-40 other genes. This usually is detected by sequencing techniques based on bulk DNA from a tumour section, but whether sub-clones exist at a cellular level showing cell to cell heterogeneity for gains is not known. This project will use molecular pathology approaches (in situ FISH, chromosomal instability assays, genomics and spatial transcriptomics) to understand the intra-prostatic cell heterogeneity of chromosomal gains using spatial 'omics on tumour foci within individual patient's prostate glands removed at surgery. The validation of DNA and RNA endpoints will lever whole genome/RNA sequencing and outcome data within the Pan Prostate Cancer Group (international consortium with over 1200 PCa annotated genomes). Functional genomic studies to validate pathology findings is an option using prostate epithelial cells (PrEC) transfected with engineered Human Artificial mini-Chromosomes (HACs). These HAC-Chr. 8q cells would mirror the genetics of Chr. 8q gains (e.g.

	a mini-chromosome, with c-Myc and other co-amplified genes) to inform upon genetic instability, mutations and cell growth autonomy. The student will gain skills and integrate knowledge in molecular pathology, with bioengineering and genetics. The work will be completed primarily in the laboratory of Prof. Robert Bristow at the CRUK Manchester Institute (in vitro models; DCS-FBMH) in collaboration with Prof. Patrick Cai (HAC systems; FSE-Manchester Institute of Biotechnology), Prof. David Wedge (cancer genomics; DCS-FBMH) and Dr. Pedro Oliveira (Christie pathology). A better understanding of cell to cell heterogeneity could drive new therapies against aggressive subclones.
Lab Background	As a clinician scientist, projects and mentees that reflect an interest in wanting to improve patient care are welcome approaches in my translational lab. Open/honest communication and clear expectations between mentor and mentee are central to a successful graduate training experience. Work-life balance is very important as happiness and fulfilment in one reflects positively on the other.
Supervisory Style	Creativity, innovation and team science with collaborations are key features to developing a state-of-the-art research programme. When aligned with a mastering of the literature and critical appraisal, this approach leads to impactful peer-reviewed publication(s). My mentees are expected to develop their own research approach with my input. Mentees are expected to attend weekly lab meetings and journal clubs. During the week, I will make myself available for 1:1 meetings, to discuss data or to have bespoke teaching sessions. I encourage my mentees to actively seek out appropriate internal and external collaborators for: best hypothesis generation; technologic advances to improve laboratory work; and optimising the impact of their research.
Career Development	Students will have the opportunity to write reviews and participate in the development of research proposals to support their scientific professional development. They will also have the opportunity to attend a national/international meeting to present mature data; this increases their understanding of the field, critical appraisal of their work and networking. Writing is a skill that requires consistent application and practice. Therefore, I strongly encourage my mentees to participate in grant proposal writing workshops and other mechanisms to improve their writing skills in order to prepare their initiatives in writing manuscripts or their thesis and authorship on manuscripts will always occur early in a research activity. I am strongly committed to a vibrant, safe, collegial and supportive research environment where all researchers from diverse perspectives and backgrounds are valued; I expect that the mentee has the same ethos. Research in my lab will be of the highest research integrity. There is zero tolerance bullying or harassment consistent with confidential hotline availability for mentees and CRUK, Christie and UofM guidelines.

3. Dr Adam Hurlstone, Cell and Cancer Biology

Opportunity Details	Research placement; lab visit; lab meeting; journal club
Location	Michael Smith Building, Dover St, Manchester M13 9GB
Project Title	Engineering T Cells to Kill Ovarian Tumour Cells
Research placement [PhD project to also be	T cells are our most potent defence against cancer cells, having evolved to puncture holes and dissolve cells that they recognise as being abnormal. However, cancer cells make themselves hard to spot by T cells. We can assist T cells to see cancer cells by engineering them to express a novel receptor put together from bits of antibody and bits of T cell signalling molecules. The

offered 22-23]	summer student will work alongside a PhD student who is testing how best to engineer these novel receptors for ovarian cancer.
PhD Project Title	Engineering TIL to Overcome Glucose Competition in the Ovarian Tumour Microenvironment
PhD Project Description [included for reference]	Tumour infiltrating lymphocytes (TIL) are a critical component of the body's immune response to cancer. They limit cancer development and augment response to a range of therapeutics. The infusion of ex vivo expanded autologous TIL in melanoma patients has been shown to lead to complete and durable tumour regression in a significant fraction of patients and we are currently recruiting patients to TIL trials across a range of tumour types in Manchester. However, complete responses occur in only a minority of patients, indicating that TIL therapy is suboptimal. A factor inhibiting TIL activity in the solid tumour environment is access to nutrients due to poor tumour vascularisation and competition with tumour and stromal cells for nutrients, and notably access to sufficient glucose which is essential for T cell activation. Through the proposed research the student will evaluate whether alternative carbon sources (ACS) recently shown to be utilisable by T cells can enhance TIL activity in low glucose concentrations. The student will also address whether the ability of TIL to utilise these ACS can be further enhanced by engineering them to express enzymes implicated in the import or catabolism of these ACS, thereby armouring TIL to function in the solid tumour environment. The Edmondson laboratory has shown that TIL can be readily harvested from resected ovarian cancer and expanded ex vivo and has generated a biobank of matched autologous ovarian cultures and TIL. The Hurlstone laboratory has established a platform for engineering T cells using viral constructs. This project utilizes the knowledge and skill base of the supervisor's teams to innovate TIL therapy with a line of sight to the clinical trials being undertaken in Manchester.
Lab Background	Dr Hurlstone is a cancer biologist based in the Michael Smith Building on the university's central campus, which provides excellent physical space, cutting edge research facilities, and a stimulating intellectual environment. Professor Edmondson is a gynaecological surgeon, specializing in ovarian cancer. His laboratory is located in nearby St Mary's hospital, sited for optimal access to surgical theatres. The Hurlstone and Edmondson laboratories comprise several post-doctoral research associates, clinical research fellows, PhD students, Masters students and undergraduates performing laboratory-based research who support training at the bench. Professor Thistlethwaite runs an extensive clinical and translational programme at The Christie for adoptive cell therapy in solid tumours. She is the Director of the multi partner iMATCH consortium.
Supervisory Style	Both Dr Hurlstone and Prof Edmondson have extensive experience in supervising PhD students, including clinicians. As a former MB PhD student herself, Prof Thistlethwaite has personal insight into the particular needs of MB-PhD students. A successful applicant will receive regular guidance from their supervisory team through one-to-one meetings and also from peers at group meetings. These meetings provide regular opportunities for students to discuss data and receive feedback and help with troubleshooting. They also provide a forum for practicing talks and discussing literature.
Career Development	The primary goal of the student is to complete their doctoral thesis and successfully defend it in an oral exam (viva). Most students in the Hurlstone and Edmondson laboratories also publish their research in leading scientific journals and present their research as posters or oral presentations at national and international meetings. An MB-PhD enhances career prospects within academic medicine, but the primary motivation should be intellectual curiosity and a passion for research. The research vocation requires commitment, flexibility and consistent effort but this should be compatible with a good work-life balance.

4. **Dr Amaya Viros usandizaga, Skin Cancer and Aging**

Opportunity Details	Research placement; lab visit; lab meeting; journal club

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Location	Cancer Research UK Manchester Institute, The University of Manchester, Alderley Park, SK10 4TG [free shuttle bus provided with additional funding for transport costs also available – to discuss with **Dr Georgina Binnie-Wright**, **Postgraduate Programme Manager**]
Project Title [PhD project to also be offered 22-23]	*Research placement in the area of* the aged microenvironment in the outcome of skin cancer and the response to immunotherapy. *Full content to be defined by Dr Viros usandizaga and the student post-application, prior to their summer start date.*
Research Group Background	My lab is based on the Alderley Park Cancer Research UK Manchester Institute, University of Manchester campus. I am a Wellcome clinician scientist, and my research is mainly funded by Wellcome, in addition to Cancer Research UK, Melanoma Research Alliance, the Rosetrees Trust and the Harry J Lloyd Trust. My lab primarily focuses on the role of the aged microenvironment in the outcome of skin cancer and in the response to immunotherapy, and we are also interested in understanding sexual dimorphism in cancer. Cancer Research UK Manchester is the ideal environment to undertake the research in this proposal. I have been a Wellcome Clinician Scientist since 2017, and my interests have focused on why melanoma and skin cancer kill the elderly population disproportionately. My group has established a key role for the aged extracellular matrix, immune response to early cancer, diet and aged stromal cells driving skin cancer onset and progression. Students and post docs in the lab use a range of cell biology, high end imaging and 'omics approaches.
Supervisory Style	Lab members are expected to interact and collaborate within the group and the wider research environment. We foster an atmosphere where people at all levels freely communicate with each other about their work and ideas, both informally on a day-to day basis and at scheduled meetings. We share protocols, methods, results and conduct active discussions between all members, formally and informally, to discuss key results and plans. I would expect to see the student individually once a week on a formal basis, but in reality, interactions would be more frequent. I operate an open-door policy where students and postdocs are encouraged to discuss things at any time. We share lab space and the above meetings with three other groups, including two independent research fellows. All the groups have related interest that span ageing and cancer, and the range of topics provides a vibrant research environment with exposure to different experimental approaches, from in vivo models to mathematics. We promote an atmosphere where everyone in the four groups communicate and collaborate. CRUK MI has weekly internal student, weekly postdoc and weekly external seminar invited speakers that hugely enrich the experience and enhance learning and development. There are multiple activities organized to promote interactions between students and postdocs, both scientific and social.
Career Development	Senior or more experienced lab members will take on supervision of undergraduate student projects, but students will also contribute and validate to all group efforts. All lab members are encouraged to talk to and interact with each other. All students are strongly encouraged to think about their work in terms of publication as well as a thesis, as this will ultimately be the basis for a future academic research career and fellowship applications. We expect students and postdocs to take responsibility for writing their own papers. We would provide input in the initial paper planning and data interpretation, as well as lots of encouragement, but then the student would be expected to undertake writing the first draft and preparation of figures. There is an expectation that they would actively keep up with the research literature (essential for writing papers) and attend conferences to present their work. Students are encouraged to apply for travel grants whenever they submit posters to conferences, enhancing their CV, and actively encouraged to apply for further funding schemes.

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5. **Professor Marcel van Herk, Radiotherapy Related Research (RRR) Advanced Radiotherapy**

Opportunity Details	Research placement; lab visit; lab meeting; journal club
Location	Related Research 58, The Christie NHS Foundation Trust, Wilmslow Rd, Manchester M20 4BX
Project Title	Detecting heart beat signals in clinical 4D CT scans
Research Placement	Recent studies have shown that an excess dose of radiation to specific substructures of the heart during radiotherapy of lung cancer patients can increase the chance of major cardiac events and worsen survival rates post treatment. Sparing of these substructures is thought to be implemented in radiotherapy treatment of NSCLC patients in the near future. This brings with it the need for better visualisation of the heart and its substructures. The aim of this project is to take routine 4DCT (respiratory gated CT) data, used in the radiotherapy planning of NSCLC patients, process it with existing algorithms to correct for respiration and cardiac motion and evaluate their impact on the visibility of a number of heart structures, that are known to be sensitive to radiation. We will both score the visibility of the structure qualitatively, as well as quantitatively; by asking several observers to put landmark points on selected anatomical points and measure their variability. We anticipate that this project will take two weeks at the end of August. This work introduces the student to medical imaging, radiotherapy planning, and provides knowledge of motion of the heart due to respiration and heartbeat. The effect of radiotherapy on the heart is a main focus of the group and the summer placement prepares the student for a potential PhD in our group.
Research Group Background	I lead the University of Manchester radiotherapy physics group physically based within department 58 of The Christie NHS Foundation Trust Hospital, who provide world leading cancer treatments and are the largest cancer centre in Europe. I lead a large multi-disciplinary team consisting of scientists and health care professionals, focused on improving the treatment of cancer with radiation. In particular, my group aims to improve the survival of cancer patients while reducing the side effects of radiation, which can be severe. For example, in lung cancer we work to increase the chance of cure, by precisely defining and targeting the tumour, while also avoiding the most sensitive parts of nearby organs. This close association with the Christie, ensures access to vast clinical data and enables the results of our studies to be directly implemented in the clinic to ensure we are able to improve the treatment of cancer patients both within the Christie and across the globe. I have worked at the interface of physics, computer science and cancer treatment for over 3 decades, focusing on optimising the precision and personalisation of radiotherapy, a high-tech treatment modality used for ~50% of cancer patients. I have pioneered the concept of Image-guided radiotherapy (IGRT), leading to a new standard of care and change in clinical practice. My role in this step-changes in clinical practice led to my involvement in published national guidelines of the Royal College of Radiologists for image-guided radiotherapy (as physics editor) and in the international teaching course on IGRT delivered by the European Society of Radiotherapy and Oncology (> 100 participants each year since 2006). After years of improving the use of imaging in radiotherapy and given the current technical accuracy achieved, I am now focusing on two main knowledge gaps 1) lack of knowledge of tumour boundary and spread, and 2) lack of understanding of the biological effect of treatment for individual patients.
Supervisory Style	A core value of our research is multi-disciplinarity: our group mixes physicists, computer scientists, oncologists and radiographers, with an active flow of ideas between the clinic and researchers. We are a large group with over 40 members who meet regularly and all contribute to the success of the research programme. This atmosphere is fully inclusive with all members of the group, regardless of role, expected to interact and collaborate effectively with those

	around them. We encourage the sharing of ideas and research, both informally on a day-to-day basis with others within the group and at weekly lab meetings and scheduled meetings. I would expect to meet you 5 times during the placement (weekly would be normal for a PhD student), however myself and other members of the group are always available to discuss the project and answer questions. Although we support a hybrid working environment since Covid, we use the platform 'Slack' for daily discussions and zoom or teams for meetings if face to face meetings are not possible. Increasingly more members of the team are available in the office on a daily basis for discussions. We hold hybrid lab meetings once a week, including presentations from groups of researchers at every session which the student would be expected to attend. This meeting provides the opportunity for the researchers to share their data and encourages discussions on where more input or help is required. We also run daily drop-in coffee meetings and weekly topic meetings e.g. on data mining to allow more focused discussions.
Career Development	I am fully supportive of all members of my group and strive to ensure their future success in whatever career path they choose. We have a number of PhD, masters and undergraduate students. PhD students often provide supervisory support to masters and undergraduate student projects to ensure their success and provide daily help to the student, but the student is also encouraged to discuss their project with all members of the team. We will support the publication of results generated during the project, and often students with sufficient quality data can contribute as a named author on journal articles. We expect the student to contribute to writing of the publication and provide their data in a form that can be used and verified by the team. PhD students from my group have gone on to be leaders in academia, industry and clinically.

6. **Dr Douglas Dyer, Immunology**

Opportunity Details	Research placement; lab visit; lab meeting; journal club
Location	AV Hill Building, The University of Manchester, Acker Street, Manchester, M13 9PL
Project Title [PhD project to also be offered 22-23]	*Research placement in the area of* extracellular matrix in regulating the immune system. *Full content to be defined by Dr Dyer and the student post-application, prior to their summer start date.*
Research Group Background	My lab is based on the main University campus, within the AV Hill Building, I am a member of the Wellcome Trust Centre for Extracellular Matrix Research and the Lydia Becker Institute of Immunology and Inflammation. We are focused on the role of the extracellular matrix in regulating the immune system, specifically focusing on the interplay between the endothelial glycocalyx in chemokines in facilitating immune cell recruitment. We study this topic in a variety of areas including infection models and also in response to radiation therapy of resting tissues.
Supervisory Style	Our lab is focused on creating an open and collaborative learning environment to allow all members to advance their scientific understanding and career. In particular we emphasise creating an atmosphere where people are free to ask questions and not feel restricted in this area. I meet all members of the lab on a 1:1 basis every week on top of our weekly lab meetings. These lab meetings alternate between journal club and each member taking the chance to present their work in detail to the group. We share lab space with a number of other labs which gives us access to a range of equipment and fosters a strong learning environment.

Career Development	Most lab members will also take on supervision of masters or undergraduate student projects. This is usually given to PhD students in the second or third years of their study, but all lab members are encouraged to talk to and interact with these students, who they are treated as lab members for their period of study. All students are strongly encouraged to think about their work in terms of publication well as a thesis, as this will ultimately be the basis for a future academic research career and fellowship applications. We encourage lab members to develop their papers with regular input and learn how to do this in a collaborative fashion. We also expect engagement with the literature to stay up to date and to present your findings at meetings and conferences.