MRes in Translational Cancer Medicine 2023/24 - ALL PROJECTS

Discipline(s)	Lab	Project title	Brief research description (i.e. bench or dry lab / example procedures / type of research)	Campus where lab based
Biochemistry / Biophysics	Dr Maria Thanou	Nanodroplets for non- invasive sonic tumour injections	Investigation of novel injectable nanomaterials that respond to non-invasive ultrasound and propel drug in tumours. Physical chemistry and cell cultures as well as in vivo tumour models	Franklin Wilkins Building, Waterloo Campus
Cancer Bioinformatics	Dr Anita Grigoriadis & Dr Cheryl Gillett	Characterisation of different immune cells in lymph nodes	This can be a wet or dry lab project: The presence of lymph node (LN) metastasis is one of the most important prognostic factors in breast and many other cancers, and the overall survival decreases as the number of cancerous (involved) LNs increases. Despite, a subset of these patients respond well to treatment and achieve long-term survival. Most commonly, regional LNs are excised, histopathologically processed and examined by a pathologist, to determine if LNs harbour cancerous cells. Although tumour cell metastasis is often preceded by alterations in the microenvironment of the metastatic organ in preparation for the arrival of and an effective colonisation by malignant cells, little attention is given to cancer-free (uninvolved) LNs and the progression from an uninvolved LN to an involved LN. In collaboration with Professors Tony Ng, Professor Sarah Pinder and Professor Ton Coolen, we were the first to report on morphological changes in the uninvolved LNs, being risk predictive of developing distant metastasis and are now elucidating the underlying biological and translational relevance of the pre-metastatic LNs.	Cancer Centre, Guy's Campus
Cancer Bioinformatics	Dr Anita Grigoriadis & Dr Cheryl Gillett	Characterisation of different immune cells in triple negative breast cancers	This is a bioinformatics project, in which you will study the immune cell infiltrates and modulators in triple negative breast cancers, based on spatial transcriptomics	Cancer Centre, Guy's Campus
Cancer Bioinformatics	Professor Agi Grigoriadis & Dr Anita Grigoriadis	Spatial transcriptomics profiling of normal and pathologic bone	In this project, we will use spatial transcriptomics to explore signalling pathways in normal bone and bone tumours.	Guy's Campus
Tumour Stroma Biology	Dr James Arnold	Tumour associated macrophages in cancer progression	Bench research project. We are a stromal biology/tumour immunology translational research lab working with in vivo models of cancer to develop novel strategies to target the stroma, and in particular macrophages, to prevent their role in tumour progression. Project likely to use flow cytometry, confocal microscopy, qRT PCR and primary cell culture.	Guy's Campus
Cancer Cell Biology	Dr Jeremy Carlton	Regulation of cell division and receptor degradation by the ESCRT-machinery	Bench research, molecular biology, biochemistry, live cell imaging, organelle repair and remodelling, cell division	Crick Institute
Cancer Cell Biology	Dr Gilbert Fruhwirth	Multi-modal in vivo imaging for monitoring cancer treatment	Our lab is focused on contributing to the development of new and the improvement of existing therapeutics through the application of imaging-based approaches spanning multiple lengths scales ranging from whole-body to microscopic levels. For details, see https://fruhwirthlab.org/. Wet lab including a variety of techniques (cell culture; genetic engineering; cell biological, biochemical and immunological methods; whole body cell tracking; fluorescence microscopy).	Cancer Centre, Guy's Campus
Cancer Cell Biology	Dr Claire Wells	Investigating the molecular mecahnims that drive cancer cell invasion	The Wells Lab seeks to develop migrastatics (drugs that stop cancer cell metastasis) for clinical use. We use cell biology and biochemistry techniques to investigate the signalling pathways that drive cancer cell invasion. This is a wet lab bench project. It will involve mammalian cell tissue culture, high resolution microscopy and analysis of protein function through western blotting and functional assays. The aim of the project is to make a contribution to our understanding of the molecular mechanisms that under pin cell migration and invasion.	Guy's Campus

Cancer Head/Neck	Prof Mahvash Tavassoli	Predictive Biomarkers of Treatment Resistance in Head and Neck Squamous Cell Carcinoma	Predominantly bench research, some dry lab bio-informatic analyses. Treatment and management of head and neck cancers (HNSCC) is an unmet medical need. Conventional therapies (surgery, chemo-radiotherapy) are highly toxic and have severe side-effects. Only one FDA approved targeted drug (cetuximab) is available and since 2016 immunotherapy has been approved for the treatment of metastatic HNSCC, but only a minority of patients respond to both therapies. We are using a multidisciplinary approach including gene expression profiling and imaging CyTOF to determine genetics/immune/tumour microenvironment signature of patients to stratify patients for appropriate individualised treatment.	Guy's Campus
Cancer/ Haemato-Oncology	Dr Shahram Kordasti	The effect of chronic inflammation on Tregs function	Student will work with a senior member of the team to investigate the effect of "inflamed" MSCs on the function and phenotype of regulatory T cells. This project is mainly wet lab based but student will also be engaged on data analysis, using in-house developed pipeline(s).	Guy's Campus
Clinical Tumour Immunology	Dr Debashis Sarker	Factors affecting patient recruitment and experience in Phase 1 trials		Guy's Campus
Molecular Cancer Epidemiology	Dr Aida Santaolalla and Prof Mieke Van Hemelrijck	Molecular epidemiology of cancer: real world evidence using large datasets of routinely collected cancer data.	This dry lab project will be conducted as part of the epidemiological research in the TOUR team. You will be using large clinical datasets and various analytical techniques to answer clinically relevant questions. All required epidemiological and analysis skills can be taught during the project.	Guy's Campus
Cancer Epidemiology/big data/ Real World Evidence	Prof Mieke Van Hemelrijck and Dr Beth Russell	Clinical epidemiology of cancer – predicting clinical outcomes	This dry lab project will be conducted as part of the epidemiological research in the TOUR team. You will be using large clinical datasets and various analytical techniques to answer clinically relevant questions. All required epidemiological and analysis skills can be taught during the project.	Guy's Campus
cancer Epidemiology/big data/ Real World Evidence	Prof Van Hemelrijck and Dr Gincy George	Clinical epidemiology of cancer – an application using data from Guy's Cancer;	This dry lab project will be conducted as part of the epidemiological research in the TOUR team. You will be using large clinical datasets and various analytical techniques to answer clinically relevant questions. All required epidemiological and analysis skills can be taught during the project.	Guy's Campus
Translational lymphoma research	Dr Alan G. Ramsay	Investigating the tumour microenvironment (TME) and immunotherapy in lymphoma	Investigating the tumour microenvironment (TME) and immunotherapy in lymphoma. Using immunofluorescence multiplex FFPE tissue staining and scanning (microscope and confocal), tissue culture (cell lines and pramry patient samples) and flow cytometry to model how tumor cells modulate stromal cells and their immunomodulatory function. The development of 2D and 3D imaging (live and fixed) encouraged to address novel research questions.	Guy's Campus
Haemato-Oncology	Dr. Robbert Hoogeboom	Targeting antigen-dependent BCR signalling in B cell malignancies	Bench research project in a lab that uses cell lines, primary patient cells and in vivo models to investigate the role of antigen stimulation in the development of B cell cancers and how this can be targeted using small molecule BCR signalling inhibitors. Project likely to invovle confocal microscopy, Flow cytometry and cell culture	Denmark Hill
Leuukemia Biology	Prof Eric So	Studying of cancer cell heterogeneity in human AML		Denmark Hill
Pharmaceutics	Dr Bahijja Raimi-Abraham	Infectious Diseases and Cancer: Exploiting their hidden connections	The link between cancer and infectious diseases is of great interest. This can include their comorbidity and impact on patient outcomes or repurposing of treatment to treat either condition. The work in this area investigates both these themes either using real life data, drug development laboratory work or drug repurposing and screening laboratory work.	Franklin-Wilkins Building, Waterloo Campus

Stem Cells and Bone Cancer	Prof Agamemnon Grigoriadis	Mechanisms of bone tumour growth and metastasis		Guy's Campus
Tumour Immunology	Prof Tony Ng/Dr Luigi Dolcetti	Investigations of the impact of chemotherapeutic/targeted therapies on the cancer: immune stromal microenvironment interface	Pathways, triggered in cancer cell line by different chemotherapeutic compounds, will be screened by means of various techniques that challenge the transcriptional, translational and post-translational levels, i.e. real-time PCR, nano-strings/ chip based microarray or RNA-seq for, respectively low, medium and high throughput; westernblot/ dotblot, immunofluorescence staining/ mass cytometry, FACS/ CyTof staining will offer the counterpart analysis at the protein tier. Once identified those pathways that are elicited at the cellular level, we will test their systemic consequences by means of in-vitro co-culture of both cancer cell line/ healthy donor PBMC and tumor derived organoids/ matched patients PBMC testing the effects of chemotherapeutic-induced stress that might either elicit or suppress an antitumor immune response. This functional approach will relay on both cellular biology techniques such as mixed lymphocyte culture/ mixed peptide lymphocyte culture (MLC/ MLPC or polyclonal stimuli) and gene silencing/editing (siRNA, shRNA, CRISP/CAS9) of specific gene targets.	Guy's Campus
Tumour Immunology	Dr John Maher	Genetic targeting of T-cells against cancer	Bench research: Isolation, activation and genetic engineering of peripheral blood T cells; assessment of cytotoxic activity and cytokine release; flow cytometric characterisation of CAR T cells	Guy's Campus
Tumour Immunology	Dr Sheeba Irshad	Immunophenotyping of cancers	Wet lab project/ example procedures: IHC, FACS, co-culture in vitro assays	Guy's Campus
Epithelial and cancer biology	Professor Jody Rosenblatt	Can extrusion remove senescent epithelial cells?	Bench research/ cell culture studies and microscopy-mouse and zebrafish, possily/ we take a cell biology approach to studying the origins of cancer and how it spreads	Guy's Campus
Haemato-oncology	John Strouboulis	GATA1 deregulation and ineffective erythropoiesis in sickle cell disease and Diamond Blackfan Anemisa	Bench project, will involve cell culture, protein analysis (Western immunoblotting, immunoprecipitations), CRISRP/Cas9 gene editing, RNA analysis, ChIP assays etc.	Denmark Hill
Physiology and Medicine	Dr Elizabeth Davies	Drug repurposing for cancer therapy:an electronic health record and molecular biological approach	Dry/wet lab blended project	Guy's Campus
Cancer Immunology	Dr Paul Barber and Dr Shahram Kordasti	Tissue immune profiling, using Imaging Mass cytometry.	Imaging CyTof is a highly multiplexed tissue imaging technique that can capture information on around 40 cellular markers simultaneously. This allows the identification of many immune and cancer cell types within the tissue and enables the investigation of their interactions and response to therapies. However, identifying individual cells from complex tissues is not trivial and requires sophisticated image processing. This project will help develop novel techniques to segment individual cells from images by validating imaging against liquid CyTof using peripheral blood samples from healthy donors and patients. This project may involve wet lab and dry lab and the student will learn novel computational approaches for data analysis.	Guy's

Cancer Bioinformatics	Dr Mohammad Mahdi Karimi & Prof Ghulam Mufti	A bioinformatics approach to investigate the aberrant expression of transposable elements in Acute myeloid leukemia (AML)	Acute myeloid leukemia (AML) remains one of the most lethal of adult malignancies with long term survival rates of <20% in patients under 65. Epigenomic patterns are profoundly altered in cancer. The genomes of cancer cells are characterized by localized regions of de novo hypermethylation, frequently in CpG island promoters of tumor suppressor genes and microRNA genes. Paradoxically transposable elements (TEs), which make up over 40% of the human genome, are frequently hypomethylated in different types of cancers, including AML. While DNA demethylation of such TEs is widespread in cancer, the role of hypomethylation of these elements in tumorigenesis remains controversial. The specific aims of this proposal are: 1) to determine the magnitude of TE-mediated aberrant gene expression in AML using RNAseq data and 2) to investigate histone marks and DNA methylation at candidate genes and TEs, with the goal of delineating the perturbed regulatory mechanisms or epigenetic pathways responsible for TE-mediated aberrant gene transcription. This project involves applying bioinformatic tools such as LIONS (https://doi.org/10.1093/bioinformatics/btz130) for next-generation sequencing data analysis to survey the chimeric transcripts derived by TEs in AML patients (see Karimi et al. Cell Stem Cell, 2011). For this we will use an existing RNA-seq dataset of AML samples generated by the Cancer Genome Atlas (TCGA) and TARGET AML cohorts. This project will also involve analysis of DNA methylation and histone modification data generated from the same patient samples, and "intersection" of this epigenetic information with the expression information obtained from the matching RNAseq datasets. The potential candidate should have basic programming skills in Python or R and be able to work within an interdisciplinary group of biologists and bioinformaticians. Having a degree in statistics or computer science is a plus.	Social Genetic and Developmental Psychiatry Centre (SGDP), Denmark Hill
Haemato-Oncology	Dr Piers Patten	Immune mapping of the lymphoma microenvironment to understand differential response to emerging immune based therapies.	Wet/dry project (blended). Cellular and other immune based therapies are transforming the way that non-Hodgkin lymphomas are being treated in the clinic. In low grade lymphomas such as follicular lymphoma responses to date have been highly successful, with significantly worse responses seen in closely related disease such as chronic lymphocytic leukaemia/small lymphocytic lymphoma and marginal zone lymphoma. This project will used advanced imaging techniques to examine the tissue based immune microenvironment of these different diseases to assess the hypothesis that the localised tumour immune microenvironment is a major influencer on outcome. The project will encompass both bench based hands on experience using primary patient material, and application of computational frameworks to analyse the large datasets generated.	Between Guy's/Denmark Hill
Molecular Oncology	Dr. Anthony Kong and Paul Barber	Assessing immune biomarkers of breast cancer patients with brain metastases and combination treatment in organoids	This will be a wet lab experiment. The candidate will learn to assess various immune markers in tumours and peripheral blood in order to uncover potential predictive biomarkers for breast cancer patients with brain metastases undergoing various treatments. The candidate will also learn to grow patient-derived organoids +/- co-culturing experiment with immune cells in parallel with the biomarker work in patients' samples.	New Hunt House, Guy's
Haemato-Oncology	Dr Lynn Quek	Single cell transcriptomics and chromatin states in TP53-mutant Myeloid Cancers	Myelodysplastic syndrome (MDS) and Acute Myeloid Leukaemia (AML) are closely related, cancers of the bone marrow. Patients with MDS/ AML that have mutations in the TP53-DNA damage repair pathway have an abysmal prognosis. We are studying how these aggressive cancers develop from a pre-cancer stage called clonal haematopoiesis of indeterminate potential (CHIP) to try to discover ways we can prevent disease progression. This is a mixed wet/ dry lab project (60:40). Techniques used will include single cell RNAseq and ATACseq experiments, next generation sequencing and guided data analysis which requires some basic knowledge of working in a Unix environment and R (however, these can also be taught on the project). The student will learn about haematopoiesis, cancer genomics and chromatin biology.	Denmark Hill

Haemato-Oncology	Dr Lynn Quek	Epigenetic reprogramming to restore haematopoietic function in Isocitrate dehydrogenase-mutant AML	Mutations in isocitrate dehydrogenase (IDH) are found a many cancers, including ~20% of Acute Myeloid Leukaemia (AML). Mutant IDH produces an oncometabolite, 2-hydroxyglutarate (2HG) which disrupts enzymes that regulate the epigenome of haematopoietic cells, leading to differentiation arrest and leukaemia. Patients with IDH mutations can be effectively treated with IDH inhibitors, used in combination with drugs including DNA hypomethylating agents. We are studying how combining novel therapies for IDH-mutant AML can epigenetically reprogramme AML cells to restore normal haematopoietic function using single cell multi-omic techniques combined with detailed functional analysis of haematopoietic cells. This is a mixed wet/ dry lab project (70:30). Techniques used will include single cell RNAseq and ATACseq experiments, next generation sequencing and guided data analysis. Basic knowledge of working in a Unix environment and R is an advantage (however, these can also be taught on the project). The student will learn about haematopoiesis, cancer genomics and epigenetics, working with patient samples from a clinical trial.	Denmark Hill
Cancer Immunology	Dr Rachel Evans	Characterising changes in the macrophage landscape in preclinical NSCLC in response to radiation therapy	NSCLC is an area of clinical unmet need with a poor prognosis. Tumours in the lung are often surrounded by macrophages that can drive tumour progression. Radiation therapy (RT) is a mainstay of NSCLC treatment. RT often initiates an inflammatory response however a long-term wound healing response often causes an influx of pro-tumourigenic macrophages that can drive residual tumour development. We are using immune competent NSCLC mouse models (Kras/TP53 mutant) and assessing how macrophage populations change in response to radiation therapy. This project will make use of preclinical tumour tissues that we are generating in our group. The main aims will be to characterise phenotypic and spatial changes in macrophages in preclinical NSCLC +/- RT using i) confocal microscopy of immunofluorescently stained tumour tissues ii) multicolour flow cytometry of disaggregated tumour tissues. Data will be correlated with human genomic data sets mined for key signatures as part of a collaboration with AstraZeneca	New Hunt's House, Guy's Medical School campus
Cancer Immunology	Dr Rachel Evans	Characterising the effects of immune checkpoint blockade on macrophages in 3D tumour/macrophage co-cultures	NSCLC is an area of clinical unmet need and tumours in the lung are often surrounded by macrophages which can drive tumour progression through a range of different behaviours. Macrophages exhibit a high degree of plasticity in response to their surroundings. Recent clinical trials have seen success in the use of immune checkpoint blockade (ICB) therapeutics in NSCLC. The biological effect of ICB on T cells is well characterised but their effects on macrophages is unclear. In our group 2D experiments coculturing healthy monocytes with different human NSCLC cell lines have indicated differences in tumour-educated macrophages dependent upon the mutation status of the tumour cells. Initial experiments will involve improving the physiological relevance of our cocultures by optimising growth of a NSCLC cell line panel as 3D spheroids. Monocytes isolated from healthy donor blood will be added to the tumour spheroids and allowed to mature to form macrophages. Changes in macrophage phenotype from different NSCLC cocultures +/- ICB will be characterised using multi-colour flow cytometry of disaggregated spheroids. Tumour spheroids and their migration patterns imaged using multiphoton microscopy to more comprehensively understand macrophage	w Hunt's House, Guy's Medical School campus
Cancer Cell Biology	Dr Ximena Montano	Identification of prognostic biomarkers and signal transduction pathways induced by nerve growth factor receptor, NTRK1 when activated by TP53 dependant repression of the phosphatase PTPN6 expression in neuroblastoma.	Neuroblastomas are the most frequent extracranial tumours of infancy. Long-term survival with high-risk type tumours is poor. Prognosis depends upon patient age and tumour biology. Good-prognosis neuroblastomas have differentiated/ganglionic characteristics and express the nerve growth factor receptor (NGF) tyrosine kinase NTRK1, whereas poor prognosis tumours show undifferentiated/neuroblastic features and express the neurotrophin receptor tyrosine kinase NTRK2. We have shown that NTRK1 activated by TP53 dependant repression of PTPN6 expression induces neuroblastoma cell differentiation in the absence of ligand stimulation, and that this module is associated with good prognosis. Given that poor prognosis tumours have heterogeneous biology and histology, the identification of prognosis biomarkers is of significance for patient outcome. We aim to identify potential differentiation associated signalling cascades and biomarker(s) induced by the NTRK-1-TP53-PTPN6 module that could be used as prognostic indicator(s) and treatment targets for neuroblastoma. Signalling cascades will be assessed by techniques that address changes of protein and transcriptome expression, and protein phosphorylation. These include RT-PCR, RNA-seq, western blot, dotblot, immunofluorecence and FACs. In collaboration with Dr Cheryl Gillet, expression of key signalling genes involved in differentiation will be tested in FFPE tissue by immunostaining and scanning (microscope and cell imaging) and analysed for their prognostic value.	Cancer Centre, Guy's Campus
Haemato-Oncology	Dr Pramila Krishnamurthy & Dr Giorgio Napolitani	Evaluating immunological response to Donor Lymphocyte Infusion following Allogeneic Haematopoietic Stem Cell Transplantation for Acute Myeloid Leukaemia and Myelodysplastic Syndrome	The project will involve the use of CyTOF to deeply characterise the immunological response to Donor Lymphocyte Infusions using samples banked from patients entered onto the PRO-DLI clinical trial. Wet lab work (CyTOF) alongside data analysis using established pipelines and with bioinformatics support will be the major elements of this project.	SGDP (Denmark Hill)

Tumour Immunology and Antibody Immunotherapy	Dr Chara Stavraka and Prof. Sophia Karagiannis	Mechanisms of action of monoclonal antibodies for the treatment of solid tumours	This project will investigate the impact of monoclonal antibodies on the phenotype and functions of human immune cells from patient blood and tissue explants such as those derived from skin and tumours. This project will involve isolation of immune cells from human blood and tissues, ex vivo culture of patient-derived specimens, cell culture, multiparameter flow cytometry, microscopy and immunohistochemistry.	Guy's Campus
Cancer Bioinformatics	Dr Mohammad Mahdi Karimi	A bioinformatics approach to investigate the aberrant expression of transposable elements in Acute myeloid leukemia (AML)	Acute myeloid leukemia (AML) remains one of the most lethal of adult malignancies with long term survival rates of <20% in patients under 65. Epigenomic patterns are profoundly altered in cancer. The genomes of cancer cells are characterized by localized regions of de novo hypermethylation, frequently in CpG island promoters of tumor suppressor genes and microRNA genes. Paradoxically transposable elements (TEs), which make up over 40% of the human genome, are frequently hypomethylated in different types of cancers, including AML. While DNA demethylation of such TEs is widespread in cancer, the role of hypomethylation of these elements in tumorigenesis remains controversial. The specific aims of this proposal are: 1) to determine the magnitude of TE-mediated aberrant gene expression in AML using RNAseq data and 2) to investigate histone marks and DNA methylation at candidate genes and TEs, with the goal of delineating the perturbed regulatory mechanisms or epigenetic pathways responsible for TE-mediated aberrant gene transcription. This project involves applying bioinformatic tools such as LIONS (https://doi.org/10.1093/bioinformatics/btz130) for next-generation sequencing data analysis to survey the chimeric transcripts derived by TEs in AML patients (see Karimi et al. Cell Stem Cell, 2011). For this we will use an existing RNA-seq dataset of AML samples generated by the Cancer Genome Atlas (TCGA) and TARGET AML cohorts. This project will also involve analysis of DNA methylation and histone modification data generated from the same patient samples, and "intersection" of this epigenetic information with the expression information obtained from the matching RNAseq datasets. The potential candidate should have basic programming skills in Python or R and be able to work within an interdisciplinary group of biologists and bioinformaticians. Having a degree in	Social Genetic and Developmental Psychiatry Centre (SGDP), Denmark Hill
Cancer Bioinformatics	Dr Mohammad Mahdi Karimii & Giorgio Napolitani	A multi-omics bioinformatics pipeline for identification of non-coding tumour-specific antigens	Tumour-specific antigens (TSAs) are proteins or other molecules found only on cancer but not normal cells. TSAs can assist the body in mounting an immune response against cancer cells and are ideal targets for cancer immunotherapy, but only a few have been discovered so far. Mutated TSAs (mTSAs), also known as neoantigens, have received a lot of attention in the search for vaccines against solid tumours. This is due to the superior immunogenicity of mTSAs attributed to their selective expression on cancers, minimizing the risk of immune tolerance. However, mTSAs are generally patient-specific and are less common than previously thought. Aberrantly expressed TSAs (aeTSAs) are another class of TSAs derived from a variety of genetic and epigenetic changes leading to the transcription and translation of genomic sequences normally not expressed in normal cells, such as non-coding genomic regions. While mTSAs are patient-specific, aeTSAs can be shared by multiple patients with the same type of tumour and are preferable for vaccine development. Systematic detection of aeTSAs can only be achievable by high-throughput mass spectrometry (MS) analysis of major histocompatibility complex class I (MHC I)–associated peptides. To detect aeTSAs in each patient, we need to use MS analysis software searching MHC I–associated peptides in a personalized protein database derived from tumour RNA sequencing (RNA-seq) data containing the expression of both coding and non-coding regions in each patient. Using public datasets of matched MS and RNA-seq data for tumours, we will optimise and apply the current proteogenomic analysis workflows to create personalised protein databases from RNA-seq libraries and search MHC I–associated peptides on them.	Social Genetic and Developmental Psychiatry Centre (SGDP), Denmark Hill

Cancer Bioinformatics	Dr Mohammad Mahdi Karimi	Identifying the Amplification of Extrachromosomal Circular DNAs in haematological malignancies	Extrachromosomal circular DNAs (ecDNAs) have recently been found to be prevalent in several human cancers. Elevated amounts of ecDNA have been considered an important biomarker for cancer pathogenesis. A well-characterized type of ecDNAs is double minute (DM), ranging in size from a few to several Mb, accumulated in tumour cells. Several studies have shown that the amplification of oncogenes and drug resistance genes found on DMs is a recurrent event that causes intertumoral genetic heterogeneity and offers a possible growth advantage of cancer cells. However, the underlying mechanism leading to the formation of DMs, as well as their structure and role in haematological malignancies remains elusive. Having access to the whole genome sequencing (WGS) and RNA-seq of a large cohort of Acute myeloid leukaemia (AML), myelodysplastic syndrome (MDS), and multiple myeloma (MM) patients in our research group, we will apply a number of bioinformatics algorithms including Amplicon architect1 to investigate the architecture of DMs and other forms of ecDNAs as well as the pattern of expression of DM-formed oncogenes in AML, MDS, and MM. Integrating multi-modal genomic data with available clinical information for these patients will allow us to: (1) Identify the frequency of ecDNAs and other types of DNA amplification events (2) Examine ecDNA amplifications enriched for highly amplified oncogenes (3) Integrate the somatic variations in these patients with ecDNA amplifications to find the ecDNAs harbouring somatic variations (4) find transcriptionally active ecDNAs that lead to phenotypic variation through full-length and/or truncated gene expression (5) examine highly relevant clinical and biological consequences of ecDNAs in haematological malignancies The bioinformatic findings can be validated by complementary molecular assays if the student is interested in performing wet-lab works in addition to bioinformatics analysis. One required assay for validation is Circle-seq expriment3. We have successfully applied Circle-seq to 8 primary human peripheral blood samples and the expertise is available in our research team to be applied to new blood samples.	Social Genetic and Developmental Psychiatry Centre (SGDP), Denmark Hill
Cancer Bioinformatics	Dr Mohammad Mahdi Karimi & Dr Lynn Quek	Integrative analysis of multi-modal single-cell datasets for myeloid malignancies	Clonal Haematopoiesis of Indeterminate Potential (CHIP) is a pre-cancerous state where there is age-associated acquisition of mutations in haematopoietic cells. CHIP is a precursor of myeloid cancers, particularly myelodysplastic syndrome (MDS), which then progresses to acute myeloid leukaemia (AML). We are studying CHIP and MDS using single-cell transcriptomic, epigenomic, and proteomic methods to understand clonal structure and biological heterogeneity of blood cells. We aim to create a multi-modal single-cell atlas of haematopoietic cells. This requires applying bioinformatics methods for noise reduction, cell annotation, and biomarker identification for single-cell data.	Social Genetic and Developmental Psychiatry Centre (SGDP), Denmark Hill
Cancer Immunology	Dr Lais Palhares, Dr Silvia Crescioli & Prof. Sophia Karagiannis	CSPG4 antigen shedding and its role in cancer immunotherapy	The aim of the study is to investigate the melanoma-associated antigen chondroitin sulphate proteoglycan 4 (CSPG4) cleavage (or shedding) from the cancer cell surface and whether the shedding is influenced by the binding of anti-CSPG4 monoclonal antibodies (mAb). This process can act as a 'sink', resulting in reduced drug binding to target cells and therefore reduced efficacy of anti-CSPG4 drugs. To investigate this, we will use melanoma patient serum samples, alongside appropriate serum controls, as well as melanoma cell culture supernatants. We will use different anti-CSPG4 antibodies produced in-house to evaluate shedded and membrane bound CSPG4 via ELISA, Western Blot and Flow Cytometry assays. We will also evaluate if the shedding affects antibody direct and cell mediated effector functions via MTS, three colour ADCC/ADCP assay and LDH assay. Furthermore, we aim to elucidate CSPG4 shedding within the in vivo environment by using a murine melanoma tumour model.	Guy's Campus
Breast Cancer Genetics	Prof Elinor Sawyer	Functional analysis of common variant rs11977670 on chromosome 7q34 which predisposes to Invasive Lobular Carcinoma	This project is a wet lab project and it will investigate the role of the lobular breast cancer risk variant, rs11977670, on gene expression in invasive lobular carcinoma. The project has the opportunity to learn essential molecular and cell biology techniques. It will involve culturing a panel of breast cancer cell lines, performing western blot and cell-based assays. It may also involve generating lentivirus stocks and/or CRISPRi and CRISPRa to modulate the expression of proteins of interest and test their effects on ILC biology.	Guy's campus in Guy's cancer centre, Innovation Hub

Cancer Immunology/Leukemia	Dr Giorgio Napolitani	Characterization of The Immunological Landscape in Myeloid Leukemias	The recent successes of immunotherapy in the management of cancer have eluded patients with myeloid malignancies such as Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML). A better understanding of the heterogeneity of lymphocytes in the Bone Marrow of patients with these forms of Leukemia could help us to design and develop new immunotherapeutic strategies. In our lab, we use a combination of single cells analysis and functional studies to find T-cell subsets in the Bone Marrow of MDS and AML patients that could be harnessed in immunotherapy.The projects will be wet lab, but 20% of their time will be dedicated to the analysis of their data. The methodologies will be: Primary Cells isolation and Culture Flow Cytometry Mass Cytometry T-cell assays (assessment of antigen specificity, proliferation and cytokine production)	Denmark Hill
Tumour Immunology	Dr Jacqueline Sheilds	Characterisation of therapy-induced immune changes in lymph nodes	Lymph nodes are key immune hubs, critical for the initiation of immunes responses. However, in pathologies such as cancer lymph node function can be hijacked to support tumour escape. We have previously shown that lymph nodes draining tumours undergo significant remodelling, with coincident changes to immune composition and organisation in response to tumour signals. We are now keen to understand how perturbation of the tumour microenvironment e.g. through therapy, impacts tumour draining lymph nodes. This project will employ techniques including multiparameter flow cytometry and state-of-the-art imaging approaches to profile immune repertoires and organisation within tumour draining lymph nodes following therapy.	Guy's Campus
Tumour Immunology	Dr Joanna Jackow & Prof Sophia N Karagiannis	Investigating the role of monocytes in initiation and progression of cutaneous squamous cell carcinoma (cSCC) development in recessive dystrophic epidermolysis bullosa (RDEB).	Cutaneous squamous cell carcinomas (cSCC) complicating the inherited blistering skin disease, recessive dystrophic epidermolysis bullosa (RDEB), is a strikingly aggressive cancer, with poor clinical outcome, with 87% of patients dying of metastatic disease by the age of 45 years. RDEB-cSCC arise at sites of scarring, chronic inflammation and aberrant wound healing associated with RDEB. Chronic activation of STAT3 signaling is linked to inflammation and malignant transformation. We have demonstrated that inhibition of STAT3 activation using a JAK kinase inhibitor leads to tumour regression in xenograft mouse and spheroid models of RDEB-cSCC (Jackow et al. 2021). However, systemic effects and immune system involvement has not been investigated in context of RDEB-cSCC development and progression. This project will examine the hypothesis that monocyte subtypes populations will have characteristic signature in RDEB patients compare to heathy controls and are driving the development and progression of RDEB-cSCC. To investigate this the objective of the project is to characterize monocytes populations in PBMC obtained from RDEB patient and establish a signature profile.	Guy's Campus
Behavioural science	Dr Jo Waller	Public acceptability of multi-cancer early detection blood tests in cancer screening	The NHS-Galleri trial has recruited 140,000 people to evaluate the potential for a multi-cancer early detection (MCED) blood test to pick up cancer earlier when outcomes are better. This dry lab project would use data from a related study exploring public acceptability of this type of blood test screening, which will be essential to inform any future implementation of MCED screening into the NHS. Data are being collected from a large, population-based sample and the project will involve statistical analysis of the data to understand patterns and predictors of acceptability of MCED screening.	Guy's Campus