## Project Summary Table

| Project Name | Start Date | End Date | Cancer Area | Project Stage |
|---|---|---|---|---|
| P4-Gilbert-ASCC | | July '25 | Anal | Extended/Delayed |
| P6-Flint-Ovarian | | Feb '26 | Ovarian | Extended |
| P7-Flint-EC | | August '27 | Endometrial | Active |
| P9-Ladikou-AML | | Sept '27 | AML | Active |
| P10-Jones-Myloma | | Sept '27 | Myeloma | Active |
| P11-Chevassut-Park | | Aug '25 | AML | Completed |
| P12-Wheelwright-Cachexia | | Dec '25 | X (Cachexia) | Extended/Delayed |
| P13-Barrott-SACT | | Oct '27 | X (Treatment) | Active |
| P14-Robinson-Brain-Evs | | Mar '28 | Brain | Active |
| P15-Kennedy-CLL Stress | | Mar '26 | CLL | In Prep - not started |
| P16-Dekerle-BC Fatigue | | Apr '26 | X (Fatigue) | Active |
| P17-Herbertson-Radiotheraphy | June '25 | Oct '27 | X (Radiotherapy) | Active |
| P18-Wheelwright-CRF | | Oct '28 | X (Fatigue) | In Prep - not started |
| P19-Robinson Brain Prognosis | Oct-25 | Jul '26 | Brain | Awarded not started |
| P20-Rass-DNA2 | Sep-25 | Mar '26 | Pancreatic | Awarded not started |
| P21-Vareli-DLBCL | Nov-25 | Nov-26 | DLBCL | Awarded not started |
| P22-Oliver-AML | Oct-25 | Sep-26 | AML | Awarded not started |
| P23-Hodgson-CRC | Feb-26 | Oct-26 | Colorectal | Awarded not started |
| | | | | |
| Totals | | | | |

**P4-Gilbert-ASCC**

**Lay project update September 2025: Understanding the gut microbiome in relation to chemoradiotherapy for anal cancer - opportunities for intervention to improve patient outcomes.**

## Overview

Standard treatment for anal cancer involves radiotherapy combined with chemotherapy. The majority of patients are cured by their treatment, but up to 30% will either not respond or will relapse. Furthermore, many patients are troubled by long-term gastrointestinal side-effects of their treatments. Research in other cancers has demonstrated the importance of the bacteria that colonise the human bowel (known as the "gut microbiome") in modulating response and side effects to cancer treatment. Furthermore the bacteria within tumours themselves is being recognised as a potential factor that influences response to cancer treatment. Both the bacteria in the gut and bacteria within tumours represent a potential target for therapies that could improve outcomes for patients, however the microbiome of anal cancers and patients living with anal cancer is poorly understood.

This project aims to analyse the gut bacteria and the tumour bacteria of patients with anal cancer undergoing chemoradiotherapy treatment to assess how this changes during treatment, and assess for any correlations between the microbiome and treatment outcomes. There are two parts of this project:

Two parallel translational projects have been undertaken within the PLATO trial, a national phase III trial run by the University of Leeds.

1. PLATO microbiome sub-study: Collection of stool and urine samples, from patients before and after radiotherapy treatment.
   **Aim:** to assess how the gut microbiome changes during chemoradiotherapy.
   **Progress:** 21 patients from 11 UK centres were recruited prospectively. Dr Hamish Sinclair (SCF fellow), under the guidance of Professor Julian Marchesi, has analysed feces and urine samples at Imperial College London.
   **Timeline:** Sample analysis completed. Statistical analysis has been delayed while awaiting the clinical outcome data from the PLATO trial. This data was received in July 2025 and statistical analysis is underway.

2. PLATO intratumoral microbiome: Assessment of the bacteria in diagnostic tumour samples
   **Aim:** to assess baseline differences between responders and non-responders (does the bacteria within tumours affect responses to treatment?)
   **Progress:** Tumour samples from 446 patients were obtained retrospectively.
   **Timeline:** Sample analysis was performed at the University of Leeds. Statistical analysis of the data produced is currently underway (Dr Hamish Sinclair supervised by Dr Henry Wood from University of Leeds). Preliminary results show differences in the bacteria between high and low risk tumours which requires further in-depth analysis. We hope to submit preliminary results to scientific conference (ESTRO 2026).

**Project progress**
Sample collection and sample analysis of both projects has been completed. The results of the projects requires the translational lab data collected to be analysed alongside the trial outcome data (how patients responded to treatment, what were their side effects) from the PLATO trial which is held and controlled by the University of Leeds. The project progress has been impacted by this data release being delayed but I am pleased to update that this data has now been obtained ( as of July 2025). We are underway with our data analysis and are hoping to submit some results to ESTRO (European Society for Radiotherapy and Oncology) conference in may 2026 (Abstract submission will be November 2025).

**Conferences / publications**

Poster presentation – 2nd International multidisciplinary anal cancer conference (IMACC, Rome, 2023) ***Understanding the faecal microbiome in patients undergoing radical chemoradiotherapy: The PLATO microbiome translational sub-study*** *Hamish Sinclair (1,2), Sharon Ruddock (3), Alexandra Stewart (4,5), Tareq Abdullah (6), Deborah Williamson (7), Timothy Simmons (8), Bojidar Goranov (9), Maria A. Hawkins (10), David Sebag-Montefiore (11), Julian Marchesi (12), Duncan C Gilbert (2)*

**Why is this research relevant?**
Understanding the microbiome in cancer is a key research area being developed internationally. Better understanding of the microbiome might lead to better prognostication of treatment responses and may lead to new therapeutics to augment existing cancer treatments. Data investigating the microbiome in anal cancer specifically is lacking.

**Why is this research relevant to Sussex?**
Although anal cancer is a rare cancer, its prevalence is higher in certain patient populations, including people living with HIV and men who have sex with men (MSM). As a result, University Hospitals Sussex treats a high number of anal cancers compared to other centres across the UK. (A recent audit of 21 UK oncology centres found that University hospitals Sussex ranked 5th (5/21) for the volume of anal cancer patients treated between 2017 and 2020). Anal cancer shares similarities with other cancer tumour types including cervical cancer and head and neck cancer which means that the results from this study may be applicable across a wider patient group than those living with / diagnosed with anal cancer alone.

While the results of this study are observational, it is hoped that the preliminary results will inform the development of further studies that may benefit patients in Sussex. A presentation about the gut microbiome and an outline of this project was given at the science café held at the Macmillan Horizon centre in July 2023. The discussion garnered great interest and enthusiastic feedback.

**P6-Flint-Ovarian**

**The impact of psychological stress on cancer burden and recurrence of tubo-ovarian cancer and primary peritoneal cancers. PI Melanie S. Flint. Start date: 01/09/2021**

The overarching hypothesis of this proposal is to determine the role of psychological stress, through release of the stress hormone cortisol, on tumour spread and to investigate the molecular mechanisms through which this phenomenon occurs. We hypothesize that stress hormones have a two-pronged attack by inducing proliferation and invasion directly on cancer immune cell co-cultures, manifesting in increased metastasis and suppressing the immune system.

**Objective 1:** Determine whether stress hormones accelerate metastatic growth via immune suppression. We have shown the presence of cortisol receptors on ovarian cancer cells and that this receptor can be modulator by drug; relacorilant. We have also shown that cortisol, with or without the blocker, alters the amount of signalling molecules made by the immune system in the presence of ovarian cancer cells. Specifically, one of these signalling molecules from the immune cells is Interferon-gamma and this causes ovarian cancer cells to create and give off proteins called PD-L1 which are known to suppress the immune system. We have conducted cytokine arrays to gain an insight into immune profiles and examined how cells signal (talk) to each other. This aim has been completed and final data analysed planned manuscript submission October 2025.

**Specific Aim 2:** Examine stress levels and fear of recurrence in patients with ovarian cancer and explore if high stress levels correlate to disease behaviour and response to treatment. This Aim is ongoing. However, we are now successfully recruited 31 patients. We follow up each participant 3 monthly for 12 months with the final participants follow up completing at the end of Feburary 2026. We have analysed most of the stress questionnaires and completed all the immune profiling for each patient. We have also successfully generated patient derived organoids (mini tumours outside the cells) for several patients. We have also developed a high throughput assay which would allow researchers across Sussex the chance to test their own treatments etc. Using these organoids we have shown the compelling novel the drug relacorilant could potentially be used as a remission maintenance therapy. This will be presented on Sept 18$^{th}$ at the Corcept conference in San Francisco.

The next milestones are to consider relacorilant as maintenance therapy, Determine if relacorilant can improve drug resistance, develop organoids for each patient and continue tracking each patient over time. Once we have all the patient data, we can correlate stress reports with disease outcomes, tumour recurrence and immune profiling. Successful completion of this hypothesis would then provide an avenue to set up a clinical trial to test the effects of high cortisol levels on accelerating recurrence. This work benefits patients in Sussex because we are addressing a key reported concern; psychological stress and paving the way to develop novel models for other researchers in Sussex (and beyond) to test new treatment/drugs.

**Conference poster presentations for this work:**

National Trainees Conference, UK 2024

British Gynaecological Cancer Society, UK 2024

**P7-Flint-EC**

**Psychological Stress, glucocorticoids and gynaecological cancers**. PI Melanie Flint Start date Oct 2023. End Date oct 2026.

The incidence of endometrial cancer (EC) is increasing worldwide with approximately 400,000 women diagnosed every year. The role of stress in cancer progression is well established but very few studies have asked how stress can make EC worse. To understand EC, we need to understand which molecules can promote EC. Additionally, studies must also consider the quality of life (QOL) implications of the disease. The project aim is to measure stress levels in patients with EC and how this varies over time. We also aim to examine if the stress response differs between patients with early vs advanced disease and assess how stress may worsen EC. Upon receiving ethical approval for our study and completing the set-up process at University Hospitals Sussex NHS Foundation Trust, our endometrial cancer study is now open and actively recruiting participants. We have recruited 23 patients so far and are on track for an on time project completion. We have collected samples at various timepoints throughout their participation period (e.g., saliva, questionnaires, blood, tissue, hair), which we can use to understand how stress affects endometrial cancer. Following participants' stress levels over the course of 12 months will give us an idea about how long-term stress may be affecting someone living with endometrial cancer. We have began to analyse the stress questionnaires and early indication suggest that patients show variable levels of stress and this is high as expected during surgery. Follow-on assessments at 3 months suggest that stress also varies between patients. Our next milestones are to correlate stress levels with how the disease progresses and responds to treatment. Additionally, where possible, we will monitor the clinical outcomes e.g., local, and spread by a scan. Our goal at this stage is to identify whether stress can be correlated with cancer aggressiveness.

We have also successfully generated organoids (mini tumours) from the patients. We have also shown that using these mini tumours that cortisol increases growth and the stress hormone blocker relacorilant can decrease this growth which is a novel finding. We hope that by better understanding the effects of stress on endometrial cancer we can improve overall patient care and outcomes in the long-term, considering not only the disease but the person living with it. Because there is a lack of quality of life data or mechanistic work are available for patients with endometrial data this work will support patients with this disease by helping them manage stress responses and also potentially if successful offer an alternative treatment e.g. relacorilant for high grade cancers.

## P9-Ladikou-AML

**Characterising and targeting chemo-resistant acute myeloid leukaemia (AML) cells utilising a novel in vitro model of the bone marrow microenvironment**

**PhD student:** Imogen Mould
**Supervisors:** Dr Eleni Ladikou, Dr Andrea Pepper, Dr Fabio Simoes
**Start** 01/10/2024, **End** 30/09/2028
**Grant**: Sussex Cancer Fund Research Grant

**Acute myeloid leukaemia (AML)** is an aggressive blood cancer that affects about 3,000 people very year in the UK. In AML, the bone marrow (the factory where blood is made) starts producing large numbers of abnormal, immature white blood cells, called *blasts*. These blasts don't work properly and crowd out the healthy cells. Because of this, patients often develop:

- Anaemia (too few red blood cells) → feeling tired and weak.
- Easy bruising or bleeding potentially life threatening (too few platelets).
- Frequent infections (too few healthy white blood cells).

Only 14% of patients survive for 5 years or more either because they don't respond well to treatment, they relapse (the disease comes back) or from complications of the treatment. One reason is that some AML cells hide in the bone marrow's protective environment, where they stick to support cells and become resistant to treatment — a process called cell adhesion-mediated drug resistance (CAM-DR). Standard drugs for AML, such as **cytarabine** or the combination of **venetoclax and azacitidine,** can kill most AML cells. However, the few blasts that cling to the bone marrow support cells often survive and may cause the cancer to return. To study this, we created an artificial bone marrow in the lab called the Bone Marrow Adhesion System (BMAS). We have previously shown this protects AML cells from **cytarabine** induced cell death the same as in the patient bone marrow.

**Main objective**: To use the BMAS to study how the bone marrow environment contributes to venetoclax and azacitidine resistance and find novel ways to overcome this.

What has been delivered so far?

The project has delivered the essential foundations to study how the bone marrow environment influences drug resistance in AML. A thorough literature review was completed to guide the choice of AML cell lines representing different types of AML (different genetic backgrounds and drug sensitivity). The BMAS model, previously developed by our group, has been further characterised and optimised. In parallel, new protocols for spectral flow cytometry were implemented and refined, allowing AML blasts to be accurately distinguished from the support cells and their drug induced death measured with high precision.

Using this optimised BMAS system, AML cell lines were tested with venetoclax and cell death measured. Surprisingly, no significant BMAS protection against venetoclax was observed. To validate the assay, the assay was repeated using cytarabine and the BMAS reproduced the protective effect seen in our previous studies, confirming the setup is working as intended. This indicates that the absence of venetoclax protection is a true finding rather than a technical limitation.

However, venetoclax is rarely given to patients alone and is usually given with azacytidine. Therefore, initial experiments with azacitidine in combination with venetoclax, reflecting clinical treatment practice, have been carried out. As expected, in the absence of the BMAS, the combination was more effective at killing AML cells than venetoclax alone. Importantly, when AML cells were cultured on the BMAS our preliminary experiments suggest it can protect AML cells from the added effect of the azacitidine, suggesting the bone marrow environment may interfere with the ability of azacitidine to enhance venetoclax activity. We are currently repeating these experiments to validate initial results. In addition, we are opening an additional avenue of investigation that will focus on the potential role of the immune system in venetoclax resistance. Together, these strands of work set the stage for the next phase of the project and highlight promising new directions.

What are the next key milestones?

- Investigate whether the bone marrow environment is offering any protection against the combination of Venetoclax and Azacitidine which is what is used frequently in clinic to treat AML.
- Explore the role of immune cells such as macrophages in conferring resistance against chemotherapy.

Have you hit any significant issues that endanger any of the projects objectives?

We have **not** encountered any major issues that threaten the objectives of the project. As is typical in laboratory research, we have observed some unexpected results, which have proven to be very interesting and have prompted us to plan additional experiments.

The BMAS model we developed in the lab includes several bone marrow cell types such as stromal cells, endothelial cells, and bone cells. These are all non-immune cells. While we confirmed that they contribute to chemo resistance against cytarabine, when we tested Venetoclax (the drug we are particularly interested in), we did not observe the protective effect we anticipated. Based on this and further reading, we hypothesised that innate immune cells—specifically macrophages—may provide the missing signals that reprogram BCL-2 family dependence and enable protection against Venetoclax. We are therefore planning new experiments to investigate the role of these immune cells, as they may be the key to resistance.

Interestingly, while BMAS alone did not confer protection against Venetoclax, when Venetoclax was combined with Azacitidine (the combination commonly used in clinical practice), BMAS did protect the cells. These experiments are still at a very early stage, and we now need to validate these findings and explore the mechanisms behind this effect.

Any conference presentations or papers written if applicable?

- Presented her work to the Sussex Blood Cancer Research group meeting
- Presented at a patient-directed research open-day session run by our laboratories and the Sussex Cancer Fund
- Co-delivered a "Lighting Lecture" at the Markus Taylor's Pharmakon exhibition, winning a prize for best "lightning lecture" as voted for by the audience
- Currently preparing a review for publication on targeted therapies in AML within the bone marrow environment, in collaboration with another PhD student, to be submitted in the coming month

Set the update in the context of broader research in that area? How does your project fit into research in other UK locations/overseas?

Acute myeloid leukaemia (AML) remains a major unmet clinical need worldwide. Despite advances in treatment, relapse and drug resistance are the primary barriers to long-term survival. Current UK and international research is heavily focused on:

1. **Understanding drug resistance mechanisms** – Many groups are studying how AML cells survive chemotherapy and targeted therapies. Our project using the BMAS and extended plans to study immune components will add to the knowledge.
2. **Improving targeted therapies** – Venetoclax, often combined with azacitidine, has emerged as a promising treatment for older or unfit AML patients. However, resistance is a growing problem. By exploring resistance mechanisms our project aligns with international efforts to refine its use and identify biomarkers of response or resistance.
3. **Informing new therapeutic strategies** – Insights from our project could inform combination treatments that disrupt protective bone marrow interactions or target specific resistance pathways. This resonates with international efforts to design rational drug combinations that overcome resistance, a priority area for both UK charities (e.g., Blood Cancer UK, Leukemia UK) and global consortia (e.g., NIH-funded studies, European LeukemiaNet).

In summary, our project contributes directly to the global effort to tackle AML relapse and drug resistance. By focusing on the protective bone marrow niche and Venetoclax resistance, it addresses a key question at the frontier of AML research in the UK and overseas, with strong potential for translational impact.

**Contribution to patient benefit**

This project is ultimately aimed at improving outcomes for patients with AML, a disease where survival rates remain poor. In the long term, our project could translate into:

- More effective treatments that reduce the chance of relapse.
- Better use of existing drugs such as venetoclax and azacitidine by understanding who will benefit most.
- Development of novel combination approaches to improve remission rates and survival.

**Impact in Sussex**

Sussex patients with AML are treated primarily at Brighton and Sussex University Hospitals and may be referred to tertiary centres in London for specialist therapies. Relapsed AML remains a major challenge for these patients, often with limited treatment options locally. By carrying out this research in Sussex, we are:

- Strengthening local capacity in blood cancer research, helping attract clinical trials to the region.
- Offering Sussex patients earlier access to innovative treatments and trial participation.
- Building collaborations between laboratory researchers and local clinicians, ensuring that discoveries are translated more quickly into patient benefit.

In summary, this project not only contributes to the international effort to improve AML treatment but also enhances the research and care environment for patients in Sussex, ensuring that local communities directly benefit from advances in this challenging area of cancer care.

**P10-Jones-Myeloma**

**Project Name:** **Unravelling the role of gain(1q) in multiple myeloma – year 1 update**

**Supervisor/Student:** Dr John Jones / Miss Abbie Bentley
**Project Dates:** October 2024 - October 2027

## Project Background

Multiple myeloma is the second most common blood cancer. It develops from antibody producing cells that live in the bone marrow. Myeloma causes anaemia, infections, bone damage and kidney failure. It accounts for 15% of blood cancers and 2% of all cancers, with around 6200 new myeloma cases diagnosed each year in the UK. Despite the development of new therapies, myeloma is not curable, resulting in patients requiring many different treatments during their disease journey. A key driver of aggressive disease and treatment failure is the development of new genetic changes. This is called disease evolution, meaning that the disease can overcome treatment and progress.

In this project we are looking at how the presence of the most common genetic change, called gain(1q), influences the myeloma cancer cell behaviour. Gain(1q), is found in approximately 40% of newly diagnosed patients, and up to 70% of patients at relapse. Gain(1q) is very important in the way the myeloma cells behave and escape treatment, but the reasons why are unknown. In addition, patients with gain(1q) have worse outcomes.

## Project objectives

We aim to find out how the gain(1q) genetic change affects myeloma cell behaviour. With this information we will look to create personalised therapies for patients with gain(1q). To do this we are comparing the genetic profiles of cell lines and patient samples with gain(1q) to those without. Several techniques are being used to generate the information we need to answer our questions. Examples include genetic profiling (sequencing), protein studies (mass spectrometry) and computer simulations (mathematical modelling).

## Current Progression

The project has been running for one year and we are well on track to achieve our objectives. No significant barriers to progress have been encountered. Firstly, myeloma cell lines with different copy numbers of gain(1q) were used to provide preliminary data and optimise experimental methods. Flow cytometry (visualisation of cell components) and western blotting (looking at proteins) techniques enabled us to characterise the expression of proteins thought to be important in gain(1q) myeloma cell behaviour, including IL6R, MCL1, and CKS1b.

Following this patient samples were assessed. Cancerous plasma cells were isolated from the patient bone marrow, enabling extraction of DNA, RNA, and protein. Using mass spectrometry, we compared protein levels in patients with gain(1q) to those without it. This has included samples from 17 patients. We have recently received the data and are now looking for proteins that are different in the gain(1q) cohort. Our next step is to confirm these differences, explore how the proteins impact on myeloma cell activity and if therapies can be made to target them.

The study is gaining international support. We are collaborating with a team in the USA, who have been helping with the genetic analysis and will continue working with us during the next steps. The SCF Grant is a very important stepping stone for the ultimate aim of this work, improving treatment and outcomes for patients with gain(1q) myeloma. Although the work will have international impact, local patients are key to this project. All patient samples have been taken from myeloma patients who are being treated in Sussex, either at Eastbourne or Brighton Hospitals. We are excited to move to the next stage of the project, which will revolve around finding targets for therapy development.

**P11-Chevassut-AML**

**Project title:** Identifying Novel Treatment Strategies in Acute Myeloid Leukaemia (AML)
**Researcher:** Dr. Hyun Park (Clinical Research Fellow in Haematology/PhD student at Brighton & Sussex Medical School)
**Supervisors:** Professor T Chevassut, Dr R Morgan

**Positive outcomes of funding**

Through the generosity and support of the SCF and donors, I have had a wonderful experience during my PhD studies at Brighton & Sussex Medical School/University of Sussex. This has been a time of immense personal and professional development, with the attainment of scientific skills in molecular biology that will be critical in the next stages of my clinical academic career. The below are some notable achievements that I know will not have been possible with the incredible support from the SCF:

1. So far, we have published **two papers** in the field of AML, and hope to expand on this in the near future:
    a. https://www.nature.com/articles/s41388-025-03470-5
    b. https://www.nature.com/articles/s41388-025-03415-y
2. I was awarded the **Early-Stage Research Start-up Grant** from the **British Society for Haematology (BSH)** to supplement my consumable funding for this year, as well as a Travel Scholarship to present the findings of my PhD at the BSH Annual Meeting in April 2025. This was a fantastic experience to network with experts within the field and develop a greater understanding of the current research scope in Haematology.
3. I was awarded the competitive National Institute for Health and Care Research (NIHR) **Academic Clinical Fellowship** commencing August 2025. This fellowship will allow for 25% of my time in the next three years to be dedicated to research and is also coupled to formal specialist training in Haematology within the NHS. This marks a significant milestone in the progression of my clinical and academic training towards becoming a consultant Haematologist.

**Project update**

**Background:**

- Acute myeloid leukaemia (AML) is a type of cancer in which the bone marrow produces a large number of abnormal cells.
- Despite decades of research, AML is associated with extremely poor survival outcomes. Less than 30% of patients diagnosed with AML survive for longer than 5 years, highlighting the importance of research in this field for the development of new treatments for patients.
- I have been studying the **'Wnt/β-catenin pathway'**, which is known to be important in AML patients.
- Previous studies have shown that β-catenin works together with lots of **'protein partners'** to promote blood cancers. Therefore, understanding this '**protein network**' may help to develop new therapeutic strategies.

- In 2019, the Morgan Lab performed an experiment known as **'mass spectrometry'**, to identify novel protein partners of β-catenin for the first time in leukaemia cells – one of these partners, and the focus of my PhD, was a protein called **TOE1 (Target of EGR1)**. TOE1 has important functions in solid tumours, but has never been studied in leukaemia
- Research questions:
    - To understand the role of TOE1 in AML
    - To understand how TOE1 may impact the Wnt/β-catenin pathway

**Update from the last report:**

- Previously, we were able to reveal that TOE1 is an important protein in promoting the **growth** of leukaemic cells.
- To identify **how** TOE1 may be achieving this, we performed a '**mass spectrometry**', experiment (which quantifies protein levels), under the below conditions:

| | |
|---|---|
| **Control** leukaemia cells | Leukaemia cells with **reduced** TOE1 levels |

  i.e. we artificially reduced the level of TOE1 within leukaemic cells, and assessed how this affects other protein levels, compared to a leukaemic cells with normal levels of TOE1.
- For further experiments, we focussed on the proteins that changed the **most significantly** following the change in TOE1 levels
- We also looked into existing studies, to suitable identify targets to explore – from this, we identified that TOE1 may be affecting leukaemic cell growth through its activity on another protein known as **PAK2 (p21 (RAC1) activated kinase 2)**
- Whilst from the mass spec data we found that PAK2 levels go down if we artificially reduce TOE1 levels, this does not necessarily prove that TOE1 is affecting leukaemia growth through PAK2 - so, we also performed a couple of 'subsequent experiments': 1) we confirmed that PAK2 has an effect on leukaemia growth through artificially reducing its levels and 2) in cells with artificially reduced TOE1 (and hence PAK2), we restored the level of PAK2 to show that the effect on leukaemic cell growth was recovered.
- From this,we determined that TOE1 is affecting leukaemic cell growth, at least in part, through affecting PAK2 levels
- Alongside this, our data suggests that TOE1 may also affect the level of a partner known as **LEF-1 (lymphoid enhancing factor 1)**, which is an important part of the Wnt/β-catenin pathway.
- Therefore, our data suggests that may be a **possible therapeutic target** in TOE1.
- Next steps: I will now be writing up my thesis, with the viva voce planned for later this year. I will also be returning to clinical training in August.

**P12-Wheelwright-Cachexia**

**Preliminary evaluation of a psychoeducational digital intervention to support coping with cancer and weight loss for cancer patients and caregivers (CHANGES2 project): Update 17 September 2025**

- CHANGES was funded by an educational grant via the Gilead UK and Ireland Fellowship Programme. The aim of CHANGES is to produce a digital intervention (basically a website) to support cancer patients with unintentional weight loss and their carers (family/friends). SCF has provided funding to support the completion of CHANGES and extension of the project (CHANGES2), including a preliminary evaluation.
- The website features a film, an explainer animation, tips and interactive elements. Different sections on the website explain why people with cancer lose weight, how to eat well with cancer if losing weight, strategies to help with a small appetite and coping with the psychological impact of the condition. A knowledge test is also included which users complete before and after working their way through the intervention. The knowledge test, along with a brief feedback survey will be used in the preliminary evaluation.
- User testing is complete
- Ethical approval for the pilot testing and preliminary evaluation was received on 23 June 2025.
- There have been delays with the pilot testing and preliminary evaluation. This delay is due to three factors

1. Staffing issues at the site have hampered the setting up of the study in the main recruitment centre (Dorset County Hospital Foundation Trust)
2. The research fellow working on the project has, unfortunately, been on long term sick leave. She is now due to start a phased return to work in October.
3. Charities have not engaged when approached about advertising the project. Although this is disappointing, it is informative for our dissemination strategy

- The Horizons Centre at the Royal Sussex has recently started to allow research projects to advertise for participants, so we hope this will lead to some recruitment for the pilot study, alongside our main site.
- Our plan for the preliminary evaluation study is now to focus on patients across University Hospitals Sussex NHS Foundation Trust, recruiting via the digital information shared with patients and in adverts in outpatients.
- The project is currently due to end 31 October 2025. Given the delays, we would like to extend this by 6 months (at no cost to SCRF) and propose a new end date of 30 April 2025

# P13-Barrott-SACT

**Project Title:**
A Qualitative exploration of how patients and members of the multi-professional team experience nurse and pharmacist delivered Systemic Anti-Cancer Therapies (SACT) on-treatment review clinics in oncology services in England. (SORCE)

**Study summary:**
Some nurses and pharmacists working in hospitals where people diagnosed with cancer are treated with SACT, also known as chemotherapy, have developed specialist skills to review patients during their SACT treatment instead of doctors. This helps patients to get the right care at the right time from healthcare professionals with the skills needed to assess how they are responding to their treatment. This means that patients may see or speak to a nurse or pharmacist, instead of a doctor, before each treatment to assess them and any side effects they may have, to confirm if they are well enough to have their next treatment. Nurses and pharmacists may be able to prescribe the SACT, and other drugs, make decisions about whether to stop, delay or change the treatment or change the drug doses being given. There is evidence that nurses and pharmacists working in this way is safe and good for patients' experience in a variety of hospital and primary care services. Little is known about how people with cancer having SACT and being reviewed by nurses and pharmacists instead of doctors experience these reviews. There is also little evidence of how nurses, pharmacists, and doctors feel about these new ways of working with patients. With increasing numbers of people being diagnosed with cancer who are suitable to have SACT and the development of new SACT drugs that are helping people with cancer to live longer, cancer services need more nurses and pharmacists to support the review of patients during their treatment.
Also, more and more SACT review clinics are being delivered remotely by oncologists, nurses, and pharmacists via the telephone or virtually on a computer or smart phone instead of in a face-to-face clinic. There is evidence that patients are equally satisfied with telephone and face-to-face consultations and that healthcare professionals find these types of clinics an efficient and effective method for managing patient care. There is very limited research, however, into how the increased use of these types of review clinics have impacted patient experience and care when undergoing SACT treatment, and how the healthcare professionals managing these consultations experience them.
To ensure that new ways of working are safe and good for patient experience and care, it is important to understand what is working well now and what is not and what patients prefer and why.

**Project Aims and Objectives**
The aim of this PhD study is to explore how patients and members of the multi-professional team experience nurse and pharmacist delivered SACT on-treatment review clinics in oncology services in England.

**Study Objectives:**

- To explore the experience of nurses and pharmacists delivering SACT on-treatment review clinics and if there are differences in this experience between the professional groups.
- To explore how patients experience SACT on-treatment review clinics delivered by nurses and pharmacists.
- To explore if patients experience nurse/pharmacist delivered SACT on-treatment review clinics differently from how they experience these clinics when delivered by consultant oncologists.
- To explore if patient experience varies between nurse-delivered and pharmacist-delivered SACT on-treatment review clinics.
- To explore how nurse and pharmacist-delivered SACT on-treatment review clinics are experienced by consultant oncologists.

- To explore how the experience of delivering SACT on-treatment review clinics varies for nurses, pharmacists, and consultant oncologists between face-to-face (F2F) and virtual/telephone consultations.
- To explore how the experience of receiving SACT on-treatment review clinics delivered by nurses, pharmacists and consultant oncologists varies for patients between F2F and virtual/telephone consultations.

The study involves undertaking semi-structured interviews with Consultant Oncologists, Nurses, pharmacists and patients.

**Study start date:** March 2025
**Study end date:** October 2027 (This is the end of PhD date)
**Supervisor:** Dr Wladyslawa Czuber-Dochan (King's College London)

**Is the project currently on track?** Yes
**Delivered to date:**
Participant interviews commenced in April 2025 at 5 of the 6 included sites (x1 site only recently received R&D approval 0n 11/09/25). Up to 30 Healthcare professionals and patient participants who meet the inclusion criteria will be recruited. To date the following interviews have been completed:

- Consultant Oncologists: 7 (with one arranged for 07/10/25). A maximum of 10 will be included
- Nurses: 8. A maximum of 10 will be included
- Pharmacists: 5. A maximum of 10 will be included
- Patients: 11

All interviews to date have been transcripted and initial data analysis is underway.
**What are the next key milestones?**

Next steps include:

- Complete recruitment of participants- it is hoped that with the final site now open that this can be completed by December 2025
- Continue with data analysis
- Continue to draft background, methods & methodology chapters for thesis

**Conference presentations or papers:**
The systematic review undertaken prior to starting the study has been published:
https://onlinelibrary.wiley.com/doi/full/10.1111/jan.15512?msockid=1867a225c03c66a13505b6a7c11b6736
Further publications are currently being considered.

**How does this project benefit patients?**
As detailed in the study summary above, it is important to better understand the experience of patients being seen by nurses and pharmacists in SACT clinics to ensure that further service developments are patient-focused not service-led. Also, how HCP experience the delivery of these clinics, and how both HCPs and patients experience telemedicine need to be better understood to ensure that future services are developed in a sustainable & resilient way and are again focused on good patient care rather than service challenges.

## P14-Robinson-Brain EVs

**Developing a BRAIN metastasis extracellular vesicle based liquid biopsy, BRAINCELL**
Sussex Cancer Fund Reference: P14-Robinson-Brain EVs

The BRAINCELL study is a prospective longitudinal sample collection research project that is investigating the possibility of using a blood test to identify and monitor secondary brain tumours (brain metastases) a significant challenge with current techniques.

This project will collect blood, urine and tear samples from patients before, during and after high dose radiotherapy treatment for their brain metastases and represents a collaboration between the University of Sussex, the Royal Marden Hospital (the regional treatment centre for high dose radiotherapy for Sussex patients with brain metastases), the Institute of Cancer Research and the University of Manchester.

Since the successful approval of the funding for this project at the end of 2024, and since our last update, we have successfully amended the study protocol, including the amendments to the consent form and patient information leaflet, and received sponsor and ethical approval for these amendments.

Additionally, the complex multi-party Data Sharing Agreement, Material Transfer Agreement, and Collaboration Agreement between the University of Sussex, the Royal Marsden Hospital and the University of Manchester is in final stages of negotiation. This has taken slightly longer than expected due to the inclusion of two additional research groups at no additional cost (Professor Alan Melcher's team at the Institute of Cancer Research who will investigate immune cell changes within the samples and Professor Petra Hamerlik's team at the University of Manchester who will investigate tear samples). This significantly strengthens the potential new knowledge that can be generated from this project and no extra cost to the Sussex Cancer Fund.

Regarding personnel associated with this project, Professor Giamas (the primary applicant's supervisor has now left the University of Sussex and his role has been taken over by Professor Erika Mancini. Further, a new clinical fellow associated with the overarching SAFER study, the main point of contact for this liquid biopsy sub study, has been appointed and is fully onboarded with the amended protocol.

Patient recruitment to SAFER is matching expected timelines, and with the collaboration agreement expected to go live within the next month, we are therefore on track to start transferring samples to the University of Sussex for processing shortly. Given the known timescales for the samples initial processing at the University of Sussex, we are therefore hopeful to meet our expected outcomes at the end of the first year.

**P15-Kennedy-CLL Stress**

## Investigating the effect of stress hormones on treatment responses in Chronic Lymphocytic Leukaemia.

This project provides consumables to support a PhD studentship to investigate the role of stress in CLL which will commence in October ’25. A student with relevant skills and familiar with the Brighton team has been appointed. Ethics have been applied for and granted in order to recruit patients into the study from Eastbourne hospital.

A subset of the consumables have been purchased in readiness for the project kickoff on October 1st 2025.

## P16-Dekerle-BC Fatigue

**Project: A proof-of-concept investigation of a new model to explain fatigue experienced post breast cancer treatment.**

**Principal Investigator**: Dr Jeanne Dekerle, University of Brighton.

**Co-investigators**: Dr. Ollie Minton - Clinical Lead for Palliative Medicine, University Hospitals Sussex NHS Foundation Trust; Dr. Nadia Terrazzini - Principal Lecturer in Clinical Immunology, University of Brighton; Dr. Jessica Eccles - Clinical Reader in Brain-Body Medicine, Brighton and Sussex Medical School

**Project dates:** 01/2025 - 06/26.

**Brief summary of the project**

Our brain constantly processes information coming from our senses. According to new scientific models, when impaired, these processes lead to feeling fatigued. While people with and beyond cancer are likely to experience fatigue, these models have yet to be tested in cancer patients. With this project, we therefore want to see how cancer patients process information coming within the body compared to healthy participants. We also want to see if our two groups perceive fatigue differently during a physical task and if these differences relate to sensory abilities. Finally, we will draw immune profiles and record other measures such as body composition, physical activity and sleep disturbance, to help explain our findings fully.

Breast cancer is the most common cancer in the UK (15% of new cancer cases) with a higher prevalence (>50%) of moderate to severe fatigue than for other cancers. So we will study this patient group first. Cancer-related fatigue is recognized as a significant and distressing symptom, and both causes and management strategies are key research priorities in the UK. This project will enable us to study its cause so patients and carers can understand the symptom better, to then move on to developing interventions to help all beat it.

We are a newly formed team of oncologist, psychiatrist and researchers from Sussex. This project is also enabling us to find the best way to collaborate as we ambition to carry out more together. We also have new facilities (Falmer campus; University of Brighton) and want to evaluate how to best do research there with people who live with and beyond cancer.

**Is the project on track?** Yes – We aim to complete data collection in June 2026.

**What has been delivered so far?**

- 01/25 – 08/25: Institutional and NHS ethical submissions – Approvals now received
- 07/25: Recruitment of a research assistant (starting date: 06/10/25)
- Preparatory work in our labs to ensure suitability of protocol, facilities, bookings, etc: 05-08/25

**What are the next key milestones?**

- Welcoming our new research assistant; allotting time for induction and familiarisation to the study, health and safety procedures, equipment, and facilities.
- Advertising the project and start recruiting (Sept-Oct 25).

**Have you hit any significant issues that endanger any of the projects objectives ?** No

**Broader research in the area of cancer-related fatigue:**

Jeanne (principal investigator) is carrying out a study on healthy participants to understand better the core mechanisms of exercise-induced fatigue. If the findings are positive, the next step will be to compare the results with participants who experience fatigue daily, such as cancer patients, to help understand the causes of fatigue.

Jeanne and Ollie (co-investigator) are core members of the Fatigue Research Group of the Sussex Cancer Research Centre and have had monthly meetings this past academic year to discuss aims, objectives, and research projects. Group lead, Sally Wheelwright, has recently secured funding for a PhD student to test if we can predict, at the point of cancer diagnosis, who will go on to develop significant cancer-related fatigue. This work would then allow us to target interventions to those most in need earlier, potentially reducing the

negative impact of cancer-related fatigue. This new research on cancer-related fatigue will enable us to grow our research capacity, expertise, and momentum.

**How does your project fit into research in other UK locations/overseas?** Jeanne (principal investigator) is attending a national conference in France in October 25 to present recent findings on the effect of experiencing fatigue on perceptions of physical exercise in multiple sclerosis. This work inspired the present study. Jeanne will be one of four speakers for a symposium on fatigue and exercise. The three other speakers have all carried out research in cancer-related fatigue. One of Jeanne's aims is to discuss prospects for international collaborative work.

## P17-Herbertson-Radiotherapy

**This project will assess the impact of additional research radiographer time on patient engagement with research and recruitment to radiotherapy clinical trials.**

There are a number of radiotherapy research trials open nationally at the moment, which we would be keen to open in Sussex and offer to our local patients, but we currently have limited trust funded research radiographer time.

This 2 day/week research radiographer role will provide greater capacity to open and run NIHR portfolio trials. This project aims to demonstrate that this post will enable more efficient timelines for opening studies and increased recruitment to radiotherapy studies. It will also aim to improve patient engagement with local research and nationally recruiting radiotherapy trials.

This role aims to facilitate opening and successfully recruiting to >3 new radiotherapy trials in the first 12 months in post.

Target recruitment for 1 first year will be >30 patients successfully recruited into radiotherapy studies

The following trials will be prioritised for feasibility assessment and set up;

- STAMPEDE2: Stereotactic radiotherapy to low volume metastases in advanced prostate cancer
- PEARLS: Extended field radiotherapy to abdominal lymph nodes in locally advanced prostate cancer
- SCC After: Adjuvant radiotherapy for skin cancer
- Fast forward boost: Hypo-fractionated trial of breast cancer radiotherapy with integrated boost
- APPROACH: Analysis of Proton vs. Photon Radiotherapy in Oligodendroglioma and Assessment of Cognitive Health

During this initial phase of funding from the Sussex Cancer Fund, data will be collected about the effectiveness of the role and subsequently used to demonstrate to the NHS Trust that longer term investment in such posts would be valuable.

Start date: 8/10/25 End date: 8/ 10/27

**Supervisors**

- Bex Herbertson, Consultant Medical Oncologist, Cancer division research director
- Angus Robinson, Consultant Clinical Oncologist, UHS radiotherapy Lead
- Kirsty Bracewell, Lead Cancer research nurse

**Grant funding**

£50000 approved (2 year pump primed total to support x2day/week Band 7 research radiographer). Awarded/approved 14/5/25, not yet invoiced by trust, as post due to start 8/10/25

Funding awarded is split into two phases:
1) £25,000 for the first year on condition that quarterly steering meetings are held and progress towards the opening of clinical trials is being made
2) A further £25,000 for the second year which is conditional on the end of year 1 deliverables being met

**Progress**
Louisa Karacochi was interviewed and appointed 2/9/25, due to start in her new role 8/10/25

There was significant delays in getting the post advertised – mainly waiting for cancer division finance and radiotherapy managers to approve and put on TRAC. An error in the job advert then meant it went off line after a few days and we had to ask for it to be re advertised. Despite annual leave and capacity constraints, the radiotherapy management team were very helpful in setting up the interview and subsequently arranging backfill of the radiographer hours to facilitate a quick start.
Other issues which could have a negative impact on the project's success is the capacity of the physics team in radiotherapy department and the physics department.

**Main targets for year 1:**

- Open >3 new radiotherapy trials
- Recruit >30 patients successfully into radiotherapy studies

Once in post Louisa will do a piece of baseline work looking at radiotherapy trial recruitment in Sussex, Surrey and nationally, to get an accurate picture of where UHS sits in terms of radiotherapy trials recruitment. She will also look at patient engagement with research locally and be part of a patient engagement event at one of the Macmillan/SCF Science café's.
Opening and successfully recruiting to more radiotherapy trials will have a significant benefit for patients in Sussex. Clinical trials are crucial in improving the management of cancer and lead to improvements in techniques, side effect profile and tolerability. It is also a way of improving the way we radiotherapy is delivered and hence impact on capacity issues and waiting times. Opening trials locally means our Sussex patients have the opportunity to take part and potentially access new treatment or techniques close to home.

**P18-Wheelwright-CRF**

**lDentifying Patients most at risk of developing cancer related fatigue.**

This project will kick off on October 1st 2025. A student has been recruited, ethics are in place and once the data sharing agreement has been signed with Southampton University the data can be released.