Sid Faithfull
Brain Cancer Laboratory

Bringing us closer to more effective treatments for brain cancer patients and their families
All of us in the Sid Faithfull Brain Cancer Laboratory are thankful for your personal commitment and generous and important financial support of our work.

Your investment in our work enables us to build capacity, obtain resources and instigate trials that ultimately lead to better treatments and improved quality of life for many people. In this research update I will introduce to you the people who have been working hard with the help of your support, tell you about the progress of our trials and resource collection and provide you with information about our current projects and where we see our next steps.

Thank you again for not only sharing your vision with us of a better future for those diagnosed with brain cancer, but for also partnering with us to enable critical, life-saving research to continue.

With many thanks,

[Signature]

Professor Bryan W Day
Professor Bryan W Day

Team Head

Professor Bryan W Day obtained his PhD from the University of Queensland in 2008. He heads the Sid Faithfull Brain Cancer Laboratory at the QIMR Berghofer Medical Research Institute and is the current Sid Faithfull Fellow.

Bryan and his team focus on the most common and aggressive form of brain cancer, Glioblastoma (GBM) in adults and the most common brain cancer in children, Medulloblastoma.

He is a past Director for the Australian Society of Medical Research (ASMR) and is passionate about maintaining the ongoing success and sustainability of medical research in Australia.

Among Bryan’s achievements have been the development of a brain tumour bank at QIMR Berghofer and the characterisation of the receptor EphA3 as a therapeutic target in brain cancer. This research has led to clinical testing of a novel EphA3 therapeutic antibody for aggressive treatment refractory brain cancers.

Professor Day’s main research focus is on understanding brain cancer cell biology and identifying novel therapeutic agents to treat these aggressive diseases in order to develop more effective treatments for patients and improve their quality of life.
Sid Faithfull Brain Cancer (SFBC) Laboratory

Our laboratory studies the most common and aggressive form of both adult brain cancer, Glioblastoma (GBM) and paediatric brain cancer Medulloblastoma.

The focus of our research is on understanding the molecular mechanisms which are responsible for the initiation and recurrence of brain cancers and to develop and test new and effective therapies to treat these aggressive diseases.

Our goal is to develop more effective treatments for patients and improve their quality of life.

Current Laboratory Research Projects

- Defining Eph receptors as therapeutic agents in brain cancer.
- Defining novel therapies for the treatment of brain cancer.
- Understanding intratumoural heterogeneity and interclonal cooperativity in brain cancer.
- Understanding brain cancer stem cell plasticity and the stem cell niche.
- Brain cancer tissue and culture bank development.
Our vision

To continue to build an internationally competitive translational research program at QIMR Berghofer MRI in both adult and paediatric brain cancer. Our focus and commitment is to investigate the biological processes critical for the development of these aggressive refractory cancers and bring these basic findings to clinical trials.

The challenge of identifying new targeted therapies with efficacy in brain cancer is immense, especially since a combination of agents will almost certainly be required. The SFBC Laboratory is investigating several promising projects, aimed at developing strategies to firstly, target tumour-initiating cells and secondly, to better understand GBM heterogeneity and validate combined approaches to achieve greater responses for brain cancer sufferers. Better outcomes are urgently needed as overall survival for brain cancer sufferers has increased by months only in the last 50 years.

QIMR Berghofer Brain Cancer Tissue and Culture Bank

We have been able to establish an active and ongoing collaboration with the Royal Brisbane and Women’s Hospital (RBWH), neurosurgeon Dr Rosalind Jeffree and oncologists Dr Po Inglis and Dr Zarnie Lwin. The SFBC Laboratory at QIMR Berghofer has collected over 300 high grade brain cancer specimens. This resource has been absolutely critical in driving brain cancer discoveries in our laboratory and numerous laboratories all around the world. We have generated 50+ primary GBM cell lines isolated from brain cancer patient tissue. These lines are essential tools for research and enable us to study the biological aspects responsible for GBM tumour initiation and test numerous novel therapeutic approaches both in the dish and in cutting edge animal models.
Our progress: SFBC Laboratory clinical trial involvement

1. Clinical Assessment of Ifabotuzumab (anti-EphA3) in Relapsed or Refractory GBM

This clinical trial has been instigated based on Professor Day’s and Professor Andrew Boyd’s discoveries of the role of EphA3 in GBM. The trial is a multicentre, phase I dose escalation study to evaluate the safety and efficacy of KB004 when given weekly by two hour IV infusion to patients with relapsed or refractory GBM. The study is being conducted in both Melbourne (Austin) Dr Hui Gan/Professor Andrew Scott and Brisbane (RBWH) Dr Po Inglis/Dr Paul Thomas. This trial is supported by a generous donation of $500,000 from the Cure Brain Cancer Foundation.

2. Clinical Assessment of HDAC Inhibitors in GBM

A clinical trial is currently underway in collaboration with Associate Professor Jennifer Martin to measure the efficacy of histone deacetylase (HDAC) inhibitors in GBM. The SFBC Laboratory has been actively involved in trial design and is responsible for collecting specimens from patients recruited to the trial for assessment of HDAC inhibitor concentration in the CSF.

3. Assessment of the EphA2 mAb, 4B3 as an Effective GBM Imaging Agent

In collaboration Professor Stephen Rose (UQCCR) and the Herston Imaging Research Facility (HIRF) and Dr Simon Puttick (AIBN) we are preparing a first-in-man study as a proof of concept that the EphA2 mAb (4B3) can be used as an effective imaging agent in GBM. Our animal studies show that 64Cu-4B3 is better able to discriminate tumour from normal brain with less non-specific uptake than 18F-DOPA.

4. Using molecular-guided PET/MRI imaging to target hypoxia in glioblastoma

A preclinical study to identify novel pathways and define molecular signatures associated with hypoxia and poor patient outcome. In collaboration Professor Stephen Rose (UQCCR) and radiation oncologist Dr Benjamin Chua (RBWH) we are undertaking a study to collect tissue from GBM patients. Pre-operatively we will assess hypoxic versus normoxic regions via PET/MRI imaging at the HIRF, using an [18F]-FMISO radiotracer (Professor Rose and Dr Chua). Imaging information will be used to guide surgery. Resected regions of hypoxia versus normoxia will be isolated and tumour tissue transferred to the SFBC Laboratory for molecular analysis. (Dr Jeffree, Dr Inglis, Dr Lwin). Hypoxic versus normoxic tissue will be analysed using the digital genomic NanoString technology, RNA sequencing and proteomics analysis (Dr Lim and Professor Day).
SFBC Laboratory Research Capabilities

1. Orthotopic tumour xenografting in laboratory animals for assessment of oncogenes and novel therapeutic agents.
2. Intravital animal imaging.
3. Whole genome sequencing (WGS) and RNASeq and proteomics analysis.
4. Molecular biology and cell culture-based laboratory techniques:- western blotting, QPCR, high throughput in-vitro image based drug screens, CRISPR and shRNA gene technologies, lentiviral transduction, immunohistochemistry, immunoprecipitation, immunofluorescence, ex-vivo GBM patient tumour tissue slice assays, cell culture development, Nanostring analysis and DNA and RNA isolation.

While these capabilities may not inspire great excitement in the hearts and minds of our patients and their families, they are vital in the facilitation of our work in progress.
Emeritus Professor Andrew Boyd

Professor Andrew Boyd is the long term mentor of Professor Day; they have worked together on brain cancer since 2004 at QIMR Berghofer. Professor Boyd’s research focus is the biology of cancer, particularly the elucidation of potential targets for cancer therapy and Eph receptor biology.

Together the achievements of Professor Boyd and Professor Day and their respective groups have led to the development of a successful and diverse international competitive brain cancer research program at QIMR Berghofer.


Dr Rochelle Dsouza obtained her PhD in November 2013 from the prestigious Ludwig Maximilian’s University, in Germany. She has over 7 years of experience (postgraduate and postdoctoral combined) working with mass spectrometry based cell signaling and has completed a PhD with Professor Matthias Mann at the Max Planck Institute for Biochemistry, who is among the top proteomics (the study of proteins and genomes) experts of the world.

Glioblastoma (GBM) is the most common malignant and aggressive primary brain cancer in Australia. Standard treatment involves surgical removal, post-operative radiation and temozolomide chemotherapy. With a median survival rate of less than 15 months and only approximately 10% of patients surviving two years without disease recurrence, research is vital to find new and more effective therapeutic approaches to treat this disease. Despite decades of intensive research to better understand the underlying biology of brain cancer, there has been no real meaningful change in the overall survival of patients in the last 30 years. It is Rochelle’s desire to change this situation that drives her.

The team in the SFBC Laboratory have set up a brain tumour and cell culture bank that has over 300 tumour specimens to-date from which they have generated >40 primary lines. This resource is crucial to the success of Rochelle’s current project where she is studying abnormal cancer cell signaling, analyzing changes in protein and cell behaviour.

One of the new advancements in therapeutic approaches leverages the discovery that the protein EphA3 belonging to the Eph-ephrin family, is elevated in glioblastoma and other cancers. Since EphA3 is found on the surface of cells and is known to transmit molecular signals into the cell, the protein as well as its signaling route is an attractive target. Rochelle and the team have generated compelling data showing discrete expression between the EphA3 and its binding partner, ephrinA5. EphA3 is present on the more proliferative stem cell-like GBM tissue, while ephrin A5 is present on the more differentiated slower proliferating tumour fraction. They hypothesise that ephrin A5 could drive glioblastoma cell differentiation, leading to a less aggressive tumour cell phenotype.

Employing a global and innovative protein analysis tool of mass spectrometry based phosphoproteomics; Rochelle is investigating what signals are activated by ephrin A5 and identifying novel druggable targets that could better treat this devastating disease.
Seçkin Akgül
Research Officer

BSc (Molecular Biology and Genetics), PhD (Cellular and Molecular Biology)

Dr Seçkin Akgül is a post-doctoral fellow at the SFBC Laboratory. Before joining Dr Day’s team, he received his Bachelor degree at Bilkent University in Turkey, and completed his PhD education at the University of Michigan Medical School in the USA. Being well aware of the cutting-edge science conducted at QIMR Berghofer when he was in the USA, Seçkin was determined to fly to Australia and become part of Brisbane’s medical research community.

Seçkin’s motivation and drive to work with Bryan and the team comes from his desire to contribute to the scientific progress of brain cancer research and through improved treatments, ultimately serve society.

Having the desire to comprehend how a perfectly normal cell transforms into a tumour, Seçkin is driven to do whatever he can to help people with cancer. His research is therefore dedicated to better understand a phenomenon called “intratumoural heterogeneity”, which is one of the major factors behind the varying treatment responses observed in brain cancer patients.

Individual cells or compartments within a single tumour mass are associated with different molecular characteristics leading to many different tumour behaviours. Since current diagnosis schema is unable to fully recognize this molecular diversity to guide specific treatment plans, the majority of patients succumb to this disease while only a minority respond well to treatment.

Seçkin and his colleagues have designed novel models in our laboratory to create a comprehensive spectrum of human brain cancer in order to determine which unique tumour elements are resistant to current therapies and to potentially personalise therapeutic interventions to maximize therapeutic benefit.

Our ultimate goal is to identify novel therapeutic strategies which are able to target resistant tumours to prolong patient survival, and create more effective options for the incurable patient population.
Dr Carolin Offenhäuser
Research Officer

MSc (Biochemistry), PhD (Cell Biology)

After an undergraduate degree in biochemistry at the University of Tübingen, Germany and a PhD in cell biology at the University of Queensland, Dr Carolin Offenhäuser joined QIMR Berghofer as a postdoctoral researcher in 2012.

In January 2017 Carolin joined the SFBC Laboratory under Professor Bryan Day. The use of cutting-edge technology, access to primary cell lines and patient samples through the lab’s glioblastoma (GBM) tumour bank, and availability of antibodies for preclinical studies are enabling highly translational research projects as well as important functional studies. Carolin is exceptionally motivated by the opportunity to contribute to some of these projects, all aiming to find greatly needed, more effective therapies for brain cancer patients.

Building on recent findings from Bryan’s lab and her previous experience, Carolin is investigating two proteins called EphA2 and EphA3 as therapeutic targets in brain cancers. In GBM, EphA2 and EphA3 are involved in propagating tumours and promoting their invasive nature.

This makes complete surgical resection impossible and contributes to tumour recurrence.

The lab has identified that targeting of EphA3 with antibody-drug conjugates (ADCs) improves outcome in preclinical GBM models. Carolin and the team now have exciting preliminary data suggesting this is also true for a subset of paediatric medulloblastoma brain tumours.

EphA2 and EphA3 often exist together on GBM stem cells. This suggests to the team that targeting EphA2 and EphA3 together might be more effective than either one alone.

Dual targeting is another avenue that the SFBC Laboratory are currently pursuing with the hope to improve therapeutic options for both GBM and medulloblastoma patients in the future.
Zara Bruce is a Research Assistant with the SFBC Laboratory. Her love of science developed from an early age and growing up she was always very curious about the world around her. At age six she had set her sights on dinosaurs, excitedly declaring that, “When I grow up I want to become a paleontologist”. As expected, with time and further education Zara’s interests and ideals changed.

After high school she started studying a Bachelor of Forensic Science at Griffith University, majoring in Forensic DNA Profiling. (This had nothing to do with CSI by the way). It was a culmination between two interests, the study of law and genetics. One subject that marked a significant turning point in Zara’s studies was Cancer Immunology. It resonated with her both personally and professionally. Here was a subject that was not just interesting; the science had the potential to be translated, positively affecting the lives of many. Consequently it was not long after she completed a Bachelor of Science with Honours that Zara found herself working as a Research Assistant in the Sid Faithfull Brain Cancer Laboratory, at the time headed by Professor Andrew Boyd.

In the last seven years Zara's primary role has been focused on creating and maintaining primary cell lines used in the study and characterization of GBM. With such poor survival outcomes and an absence of new therapies available, drawing upon her love of cancer immunology, it is Zara’s goal to translate the science into hope for patients and their loved ones during a time when it is most needed.
Fiona Smith
Research Assistant
BSAppSc (Medical Technology), GradDip (Biotechnology)

Fiona Smith joined the SFBC Laboratory in 2017 after many years working as a Research Assistant. She began her association with medical research straight from high school at the Walter and Elisa Hall Institute for Medical Research in Melbourne where she was employed as a laboratory technician.

Fiona loved science at school but deferred university to get some real world experience. While she was working she commenced a degree in applied Science (Medical Technology) which she completed over the next six years while working full time. It was at the Walter and Elisa Hall Institute that Fiona began working with Professor Andrew Boyd, a renowned leader in Eph receptor biology and cancer. Moving to Brisbane to continue working with Andrew in the Leukaemia Foundation Laboratory at QIMR Berghofer, her main focus was studying Eph receptors and the role they played in Leukaemia and other cancers. This was also the laboratory that Professor Bryan Day started his scientific training (honours and PhD) and where he first researched EphA3 as a potential therapeutic target for Glioblastoma.

When Andrew retired at the end of 2016 Fiona took the opportunity to transfer to the SFBC Laboratory. Fiona’s hope is that her laboratory skills and knowledge of Eph receptors can now be utilised to learn more about brain cancer and ultimately help in the challenge of finding better treatments for patients. Fiona enjoys coming to work each day and working with a fantastic group of scientists committed to cancer research.

Fiona loves working in this team, especially knowing that work done in this laboratory will potentially translate to better outcomes for patients suffering with brain cancer.
Michelle Li is a second year PhD student working under the supervision of Professor Bryan Day in the SFBC Laboratory. Prior to joining this passionate group, Michelle worked in an affiliated hospital of Peking University (Beijing, China) as a tumour biology Research Assistant for 5 years. This lab was located close to the radiotherapy department in the hospital. Young patients, especially children, came to the department with their parents for post-surgery radiation therapy. Big surgical scars and radiation skin markings were very visible on their heads. Watching the children and their parents deal with brain cancer prompted Michelle to rethink her career path.

Michelle's hope is that someday her research can help these young patients to survive cancer. Being aware of the limitations of doing independent research without resources and proper training, Michelle decided to pursue a PhD in Professor Bryan Day's laboratory. Currently, her work involves establishing and characterising primary lines derived from medulloblastoma patients, and using these cell lines to investigate Eph-ephrin signalling system in medulloblastoma.

Medulloblastoma is the most common malignant brain tumour in children. Current treatments improve patient survival but lead to severe side effects due to high-dose chemotherapy and craniospinal irradiation given at a young age. Michelle has a keen interest in establishing a reproducible protocol for culturing of primary paediatric medulloblastoma tumours as building blocks to study Eph receptors as therapeutic targets.

Additionally, she would like to establish and characterise a patient-derived xenograft medulloblastoma model for preclinical drug evaluation. These in vitro and in vivo studies will provide us with a better understanding of how Eph-ephrin signalling pathways involved in medulloblastoma development and progression, so that we can design personalised target therapies to minimise toxicity and improve patients' quality of life.
Dr Manasi Jiwrajka
Student

BA Hons (Neuroscience), MBBS, MPhil Candidate

Dr Manasi Jiwrajka is an MPhil student working under the supervision of Professor Bryan Day. Manasi’s background has been in the field of neuroinflammation. She has studied at Vassar College, New York, USA and the University College London in the UK where she completed her undergraduate degree and honours thesis. Subsequently, Manasi underwent medical training at the University of Queensland, and is currently a clinical doctor at the Royal Brisbane and Women’s Hospital.

Her interest is in the immune cells of the brain, and more specifically, researching the involvement of immune cells in brain cancer pathogenesis. The focus of her Master’s degree is investigating the interaction between microglia (a type of immune cells) and Eph receptors in the context of glioblastoma. Manasi was drawn to the SFBC Laboratory and QIMR Berghofer as they are one of the world’s leaders in brain cancer research. Additionally, the large glioblastoma tumour bank received from the Royal Brisbane and Women’s Hospital is an incredible resource available for the team’s research.

Manasi is passionate about translational medical research, and through her work hopes to provide a link between laboratory research and patient care.
Courtney Jurd joined the SFBC Laboratory in June 2018. She is a Bachelor of Business graduate with a professional background in Business Administration and Human Resource Management. Prior to joining the SFBC Laboratory, Courtney worked in a number of paediatric and adult hospitals across Queensland, Australia. She thoroughly enjoyed contributing her administration skillset within the healthcare sector, an area she is truly passionate about.

This passion combined with the belief that evidence-based research is integral for patients wishing to attain optimal health led her to join Professor Bryan Day’s team.

Courtney’s focus as a member of the SFBC Laboratory is to provide the best administrative support possible so that Professor Bryan Day and the wider team can concentrate first and foremost on the vital research being conducted. She hopes that her organisational skills and love of efficient and accurate processes will aid the team in carrying out the day to day tasks of running a research laboratory.

Courtney enjoys working with this highly skilled and motivated team and hopes to learn much more about innovative brain cancer research techniques over her time within the lab.
Thank you again for your investment with us.

With your support our research has advanced and better treatments and patient outcomes are closer than they have ever been.