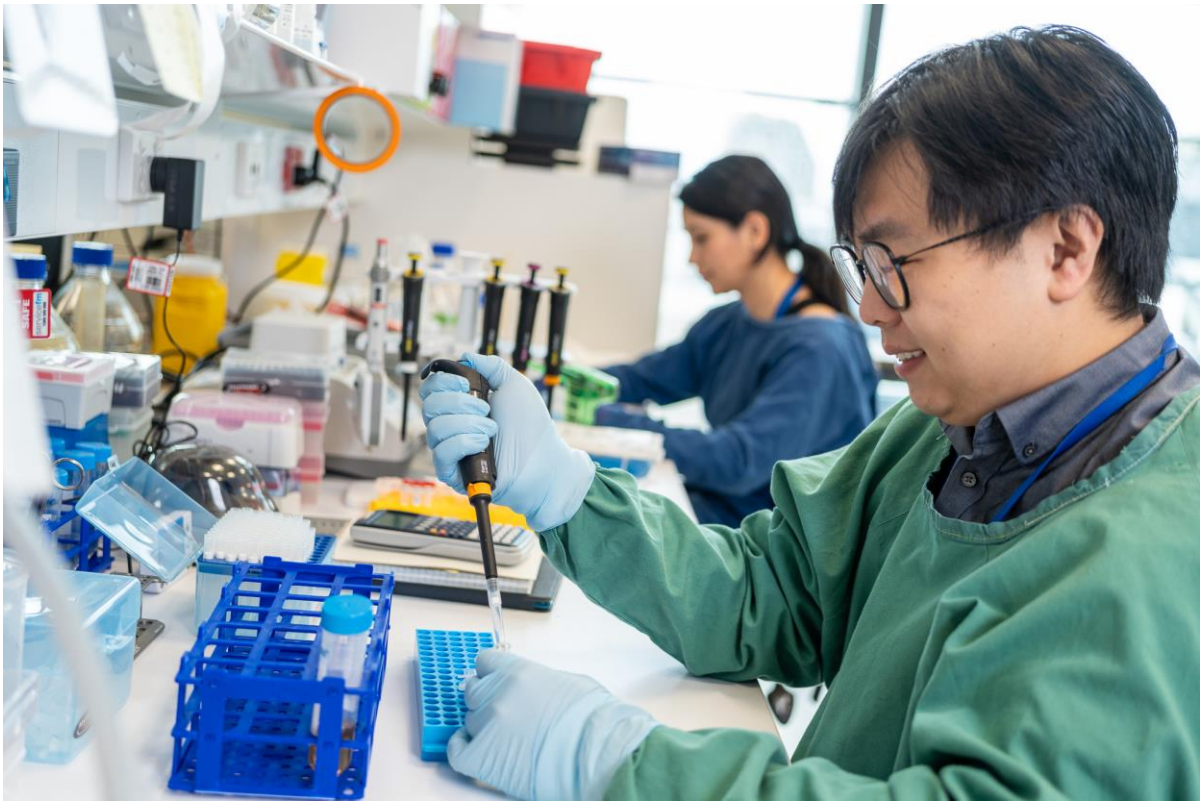


2026 Student Research Opportunities

SAiGENCI
SOUTH AUSTRALIAN iMMUNOGENOMICS CANCER INSTITUTE

adelaide.edu.au/saigenci

About SAiGENCI

The South Australian immunoGENomics Cancer Institute (SAiGENCI) was established as an independent cancer-focused medical research institute located within the University of Adelaide in South Australia. In 2026, SAiGENCI will become part of Adelaide University.

The Institute was made possible by an $80 million grant from the Commonwealth Government and is being jointly resourced by the Federal Department of Health, the Central Adelaide Local Health Network (CALHN) and the University of Adelaide/Adelaide University.

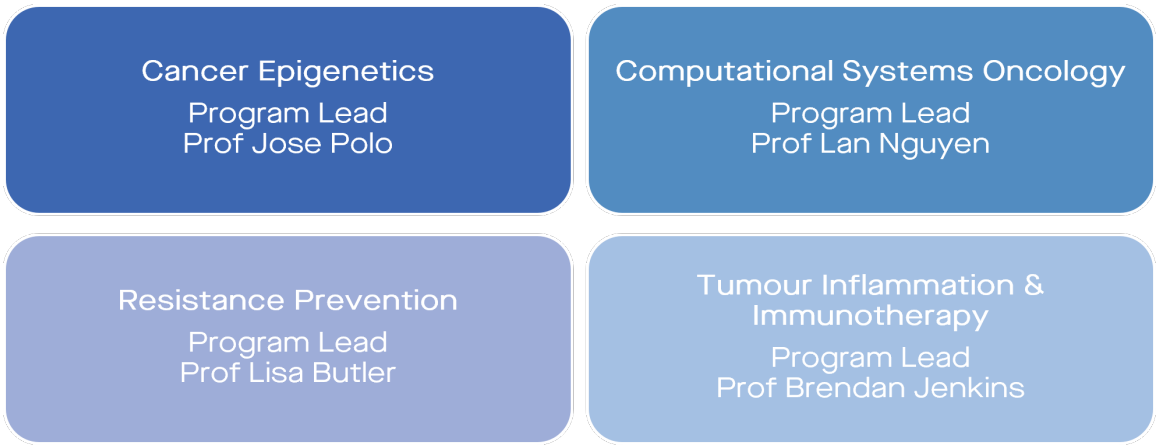
The overarching vision for SAiGENCI is to have a fundamentally positive impact on the conduct of cancer research in South Australia, so that fewer patients develop cancer, and the lives of those with cancer is improved.

To achieve this vision, the Institute aims to be a hub for scientific discoveries and development of transformative technologies that will translate into improved clinical outcomes through:

- Forging strong research collaborations
- Developing and testing new technologies and discoveries
- Improving treatment and care options for people living with cancer
- Training South Australian clinicians
- Commercialising new discoveries

SAiGENCI's Director and Medical Oncologist, Professor Christopher Sweeney, formerly of the Dana-Faber Cancer Institute, Boston, Massachusetts, and Professor of Medicine at Harvard Medical School, leads a core of high performing groups across four scientific programs.

SAiGENCI's Core Scientific Programs



SAiGENCI is comprised of a team of internationally leading cancer researchers and clinicians across these programs, who not only perform at an international level in their own right, but together are developing a distinct institutional culture focussed on excellence and clinical impact.

Our Institute members will also take a lead role across the state in supporting networks with other cancer research groups in South Australia and support a highly collaborative culture across Australia and internationally.

Learn more about SAiGENCI, its research and people via our website https://www.adelaide.edu.au/saigenci/

Training the Next Generation of Cancer Researchers

Are you looking for an opportunity to take the next step in your research career?

The Institute has a number of research projects on offer that are suitable for students at different stages of their scientific studies including; summer research projects for current undergraduate students (who have completed at least one year of study), Honours, Masters of Research (M Res), Masters of Philosophy (M Phil) and Doctor of Philosophy (PhD) candidates.

From 2026, projects will be based at SAiGENCI within the College of Health at Adelaide University, in either the Adelaide Health & Medical Sciences (AHMS) building, the South Australian Health and Medical Research Institute (SAHMRI) and/or the Central Adelaide Local Health Network (CALHN), all co-located on North Terrace in the Adelaide CBD.

SAiGENCI and Adelaide University will provide researchers early in their career with a stimulating and supportive environment to achieve highly ambitious research goals and build connections for their future careers.

Read on for program specific details, research groups and available projects.

Master of Philosophy and Doctor of Philosophy Research Opportunities

Who are we looking for?

SAiGENCI is looking for talented, enthusiastic and dedicated individuals who have a shared vision to undertake research that will lead to fewer patients developing cancer and improving the lives of those with cancer.

Perhaps you have or will soon complete an Honours or Master's degree in a scientific field related to cancer research, or maybe you're a clinician looking to add a research component to your skillset.

If you are a high achieving individual who meets the eligibility criteria (see below) and are committed to a two year Master of Philosophy (M Phil) or three to four-year Doctor of Philosophy (PhD) full-time research project (or part-time equivalent), we would like to hear from you!

What we will offer – The SAiGENCI Graduate Program

The Institute will provide a unique training experience for its students including:

- Immersion in a community of Australia's leading cancer researchers with access to world class facilities and technologies
- Regular research forums and master classes from experts in the field
- Workshops for developing research and data analytical skills as well as career development
- Travel funding support for students to present their research at national and international conferences
- For those enrolled in a PhD, opportunity to participate in a paid 3-month industry internship with a partner organisation

Eligibility Criteria for SAiGENCI Students

The Adelaide University Graduate Research School (AUGRS) administers all domestic and international postgraduate research degree applications. Positions are open to both domestic and international applicants who meet Adelaide University's entry requirements, including a minimum English language proficiency.

In addition to Adelaide University eligibility requirements, SAiGENCI M Phil and PhD applicants will need to have successfully completed an Honours degree (achieving a first-class final result), Master's coursework degree (achieving GPA > 6) that has

included a significant research component and thesis, or a Masters by Research degree. Individuals who have significant research experience and/or have contributed to peer-reviewed research publications will be viewed favourably.

Full details of the Adelaide Univesity M Phil and PhD degrees, including eligibility details, can be found on the following AUGRS websites:

Adelaide University Research Degree Opportunities
https://adelaideuni.edu.au/research/research-degrees/

Master of Philosophy
https://adelaideuni.edu.au/study/degrees/master-of-philosophy/

Doctor of Philosophy
https://adelaideuni.edu.au/study/degrees/doctor-of-philosophy/

HDR Scholarships

Adelaide University and SAiGENCI major/base scholarships

M Phil and PhD scholarships will be available for a period of two or three and a half years respectively with an indicative value of AUD $35,300 per annum (2025 rate). Students who meet the Adelaide University eligibility requirements can apply for these scholarships with applications assessed on a competitive basis.

Tuition fee waivers will be available for international students who are offered admission and a major Adelaide University/SAiGENCI scholarship.

SAiGENCI supplementary scholarships

In addition to the major scholarship, all students selected for a research project with SAiGENCI will receive a $5,000 per annum supplementary scholarship and will be eligible to apply for other competitive scholarships.

Finding a Supervisor and Project

Current or recently completed University of Adelaide students

If you have previously studied with the University of Adelaide or UniSA, contact the leader(s) of the project(s) or research areas listed below that excite you, to express your interest. Include in your email the level of study you want to undertake (i.e. M Phil or PhD), a copy of your CV, academic transcript(s) and English language test results (if relevant).

The supervisor will review your documents and arrange a time to speak with you about the project if they believe you have the right background and experience for the project. If, after talking with the supervisor, you still wish to proceed and you have received the supervisors written support to apply for a position in their group and be considered for a SAiGENCI scholarship, you can begin your online application.

All other applicants

If you have not previously studied with the University of Adelaide or UniSA, visit the AUGRS website (https://adelaideuni.edu.au/research/research-degrees/find-a-supervisor/) and follow the instructions to identify your Adelaide University research supervisor. This will involve a pre-assessment process where you can nominate three supervisors and upload a portfolio of documents. The AUGRS will review your enquiry for completeness, quality and eligibility before providing them to the nominated supervisors.

The supervisor(s) will review your documents and arrange a time to speak with you about the project if they believe you have the right background and experience for the project. If, after talking with the supervisor, you still wish to proceed and you have received the supervisors written support to apply for a position in their group and be considered for a SAiGENCI scholarship, you can begin your online application.

Applying Online for HDR Admission and Major Scholarship

All applicants will need to apply online through Adelaide University as outlined on the How to Apply webpage at https://adelaideuni.edu.au/study/how-to-apply/research/.

We strongly encourage you to apply during one of Adelaide University's main application rounds as shown on the Research Scholarships webpage at https://adelaideuni.edu.au/research/research-degrees/research-scholarships/. Please note application round dates differ for domestic and international students.

Follow the AUGRS instructions to create an account to complete your online application. You can save your application at any stage and do not need to complete it in one session. **We encourage you to begin your application well in advance of the application deadline.**

When applying for a SAiGENCI research project and scholarship, enter the details below that are relevant to your situation at the application headings shown.

Once all sections of the application are complete, review your details carefully before submitting.

Domestic applicants

Application Type: Select Admission and Scholarship.

Study Preferences: Enter the relevant details from the table below.

	M Phil Applicants	PhD Applicants
Study Type	Masters by Research	Doctor of Philosophy
Award	Master of Philosophy in Health	Doctor of Philosophy in Health
School	Pharmacy and Biomedical Science	
Research Area	Biomedical Sciences	

Scholarship Selection: Select the relevant Adelaide University Research Scholarship based on whether you are applying for an M Phil or PhD.

Research Interests: You will need to complete a short (500-800 word) research proposal on the Adelaide University Graduate Research Proposal form available within the application. The research proposal will include a title, summary, details, methods and references. Enter SAiGENCI as the proposed School/Discipline.

Structured Curriculum Vitae: You will also be required to provide your curriculum vitae on the Adelaide University Structured CV Template available within the application.

International applicants

Financial Support: Select seeking a scholarship from Adelaide University.

Study Preferences: Enter the relevant details from the table below.

	M Phil Applicants	PhD Applicants
Study Type	Masters by Research	Doctorate
Award Sought	Master of Philosophy	Doctor of Philosophy
Research Area	Biomedical and clinical sciences	

Research Interests & Proposal: You will need to complete a short (500-800 word) research proposal on the Adelaide University Graduate Research Proposal form available within the application. The research proposal will include a title, summary, details, methods and references. Enter SAiGENCI as the proposed School/Discipline.

Structured Curriculum Vitae: You will also be required to provide your curriculum vitae on the Adelaide University Structured CV Template available within the application.

SAiGENCI specific HDR application queries can be directed to:

Joanna Sundstrom
SAiGENCI Graduate Program
joanna.sundstrom@adelaide.edu.au
Please include “SAiGENCI HDR enquiry” in the email subject heading.

All other queries should be directed to the AUGRS using the online enquiry form available at https://adelaideuni.edu.au/study/enquire/ or via email to research.admissions@adelaideuni.edu.au.

One Year Research Project Opportunities

SAiGENCI offers students who have completed a three-year undergraduate degree the opportunity to work on a one-year research project through the following degrees.

Students interested in either Honours or a Master of Research should get in touch with a supervisor who works on a project or research area of interest (see projects below) to see if they have the capacity to take on a Honours or Master of Research student. Please include a copy of your CV, academic transcript and a brief description of why you are interested in doing Honours with the supervisor/in the area of research you have chosen.

Honours

Honours is a one-year qualification studied as an addition to an undergraduate degree. Completing an Honours degree provides an opportunity to investigate an area of interest in greater detail whilst gaining hands on research experience. To learn more about what is involved in an Honours degree, visit the Faculty of Health and Medical Sciences Honours page at https://health.adelaide.edu.au/study-with-us/honours.

The one-year Honours degree will be available to students who have completed a University of Adelaide or University of South Australia undergraduate degree and meet the relevant entry requirements.

Information on how to apply for admission to an Honours degree and any available scholarships will be made available later in 2025.

Master of Research

The Adelaide University Master of Research is a 1.5 year postgraduate degree which incorporates coursework exploring a range of topics including research methodologies and research skills. You will then use these skills to help plan and execute your own one-year independent research project. Domestic students pay no tuition fees for this program.

Full details of the Adelaide Univesity Master of Research degree, including eligibility and how to apply, can be found on the following AUGRS websites:

Adelaide University Masters of Research
https://adelaideuni.edu.au/study/degrees/master-of-research/

Summer Research Opportunities

A summer research project is a great opportunity for undergraduate students to get a taste of what it is like to work in a research lab. These opportunities are open to current University of Adelaide students through the Adelaide Summer Research Scholarships scheme.

Adelaide Summer Research Scholarships

SAiGENCI will offer summer projects through the Adelaide Summer Research Scholarships scheme to high achieving undergraduate students (on a competitive basis) who undertake a 6-week project with a SAiGENCI research group. Summer research scholarships will be valued at $250 per week for a maximum of 6 weeks.

Interested students should first get in touch with a supervisor who works on a project of interest (see projects below) to see if they have the capacity to host a student for 6 weeks over the summer months. Please include a copy of your CV, academic transcript and a brief description of why you are interested in doing a summer research placement with the supervisor/in the area of research you have chosen.

How to Apply

Students who find a supervisor able to host them for a summer research project should follow the application instructions on the following webpage: https://scholarships.adelaide.edu.au/Scholarships/undergraduate/all-faculties/adelaide-summer-research-scholarships.

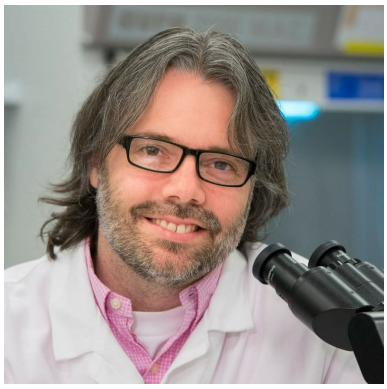
Applications for 2025/2026 Summer Research Scholarships open on Monday 18 August 2025 and close Friday 26 September 2025.

Summary of Available Research Projects

Program	Project Title	Supervisor(s)	Page
Resistance Prevention	Bioinformatic investigation of mRNA degradation in cancer	Dr Kristen Feher, Dr Kimberley Clark & Prof Christopher Sweeney	52
Tumour Inflammation & Immunotherapy	Identification of novel immune regulators in stomach (gastric) cancer	Dr Ruby Dawson & Prof Brendan Jenkins	54
	The role of innate immune regulators in pancreatitis and pancreatic cancer	Dr Mohamed Saad, Dr Joshua Chey & Prof Brendan Jenkins	55
	Identification of immune system regulators as therapeutic targets in lung cancer	Dr Mohamed Saad & Prof Brendan Jenkins	57
	Nanotechnology-based in situ vaccines for cancer immunotherapy	Dr Moustafa Mabrouk, Dr Than Loc Nguyen & Dr Yannan Yang	59
	Boosting response to immunotherapy in lung and pancreatic cancers	Dr Tamsin Lannagan & Dr Mara Zeissig	62
	KRAS inhibitors for the treatment of pancreatic cancer	Dr Tamsin Lannagan & Dr Mara Zeissig	63

Projects in Cancer Epigenetics

Epigenetic Processes in Pluripotency and Reprogramming Laboratory



Prof Jose Polo
Group Leader

Dr Wenjun Liu
Research Fellow

Dr Rudrarup Bhattacharjee
Research Fellow

Dr Ning Liu
Research Fellow

The relationship between epigenetics and cancer is well established.

The Polo Research Group is interested in understanding transcriptional and epigenetic mechanisms that govern cell identity.

We particularly focus on factors that regulate pluripotency of stem cells, reprogramming of somatic cells into induced pluripotent stem (iPS) cells and other cells, and regulate cancer growth and development.

Professor Jose Polo is the inaugural Director of the Adelaide Centre for Epigenetics (ACE) and Program Leader of the Cancer Epigenetics program of the South Australian immunoGENomics Cancer Institute (SAiGENCI).

Projects Available in the Epigenetic Processes in Pluripotency and Reprogramming Laboratory

Project Title: Pluripotency factors and cancer

Project Supervisor(s): Prof Jose Polo, Dr Wenjun Liu, Dr Ning Liu

Suitable for: Honours, M Phil, PhD

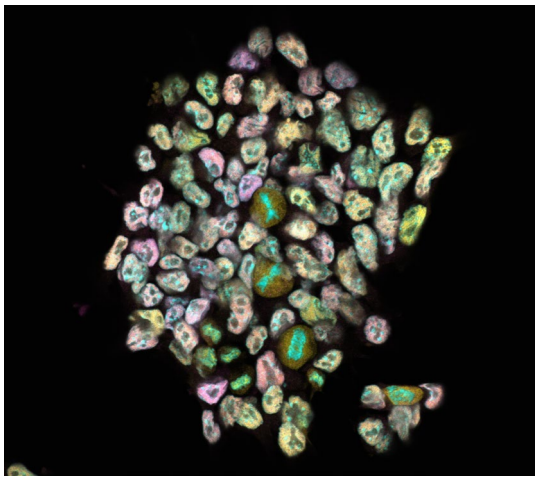
Location of project: Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Pluripotent stem cells can self-renew indefinitely and give rise to all cells of the adult organism. These remarkable capacities are the result of a core transcriptional network controlled by OCT4, SOX2 and NANOG, whose expression is lost upon differentiation. Several cancers have been shown to reactivate OCT4, SOX2 and/or NANOG, with high expression levels positively correlating with cancer progression and severity. Since they are linked to proliferative and multi-lineage differentiation capacity of cancer cells, they present attractive anticancer targets. However, they are considered "undruggable" since they lack catalytic active sites for molecules to bind.

To provide therapeutic alternatives, the Polo research group has adapted and developed various novel techniques to determine how expression and function of the pluripotency factors OCT4, SOX2 and NANOG are controlled in various physiological and pathological cell types, including embryonic stem cells and cancer respectively.

The candidate will develop skills/techniques in a combination of different molecular, biochemical, cellular techniques and genome wide approaches (RNA-seq, MS-MS, ATAC-seq, ChIP-seq, SC-RNA-seq, etc.) to dissect the nature and dynamics of such events.



Mouse embryonic stem cells stained for OCT4 (yellow), NANOG (magenta) and DNA (cyan).

Our ideal candidate will have high academic achievement and relevant experience and interest in stem cell and/or epigenetic and biochemical techniques.

This project encompasses both wet laboratory and bioinformatic components, making it suitable for students interested in cell-based and molecular biochemical wet lab techniques or bioinformatics and computational analysis, or a combination thereof.

For more information about this project contact:

Prof Jose Polo
The University of Adelaide
Email: jose.polo@adelaide.edu.au

Ms Suzanne Maiolo
The University of Adelaide
Email: suzanne.maiolo@adelaide.edu.au

Supervisor Researcher Profiles
https://researchers.adelaide.edu.au/profile/jose.polo
https://researchers.adelaide.edu.au/profile/wenjun.liu
https://researchers.adelaide.edu.au/profile/ning.liu

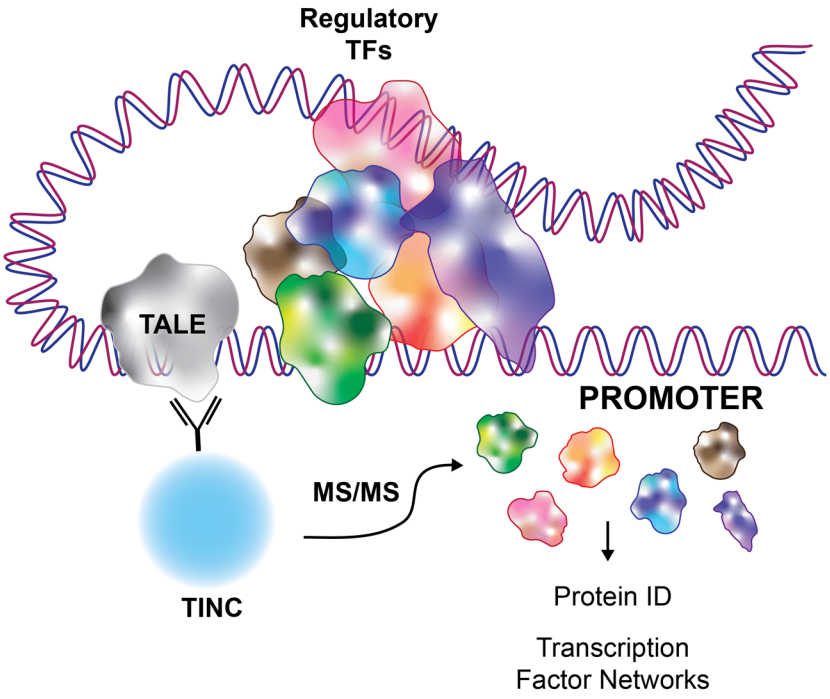
Project Title:	**Uncovering the regulatory complex of transcription factors in different cancers**
Project Supervisor(s):	Prof Jose Polo, Dr Rudrarup Bhattacharjee, Dr Wenjun Liu, Dr Ning Liu
Suitable for:	Honours, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Cellular identity is controlled by transcription factors (TFs), which bind to specific regulatory elements (REs) within the genome to regulate gene expression and cell fate changes. Recent advances in epigenome profiling techniques have significantly increased our understanding of which REs are utilised in which cell type, however, which factors interact with these REs remains largely elusive.

A major impediment to dissecting protein complexes at specific genomic loci is the shortage of appropriate techniques. The most common technique to assess TF binding is chromatin immunoprecipitation (ChIP), which relies on antibodies to interrogate the binding sites of a single TF. Yet, ChIP does not allow dissection of the composition of a multi-protein complex at a specific locus.

Importantly, the Polo research group has developed a novel epigenetic technique termed TINC (TALE-mediated Isolation of Native Chromatin), which allows us to do exactly that (Knaupp et al., Stem Cell Reports 2020). TINC relies on epitope-tagged TALEs, which are DNA-binding proteins engineerable to target specific genomic regions. Upon cross-linking of the cells, the target regions are isolated based on affinity purification of the TALE and associated nucleic acid and protein molecules are analysed by next generation sequencing and mass spectrometry, respectively. In our proof-of-concept experiments, we dissected the protein complex formed at the Nanog promoter, a key pluripotency RE. We identified TFs previously known to bind to this locus as well as novel proteins whose role in pluripotency we further validated (Knaupp et al., Stem Cell Reports 2020). Consequently, with this valuable technique at hand, this PhD project aims at deciphering how the key TFs drive and regulate different cancers, which in turn has major potential in identifying novel therapeutic targets.



Graphical representation of TINC: TALE-mediated isolation of nuclear chromatin.

The candidate will develop skills/techniques in a combination of different molecular, biochemical, cellular techniques and genome wide approaches (RNA-seq, MS-MS, ATAC-seq, ChIP-seq, SC-RNA-seq, etc.) to dissect the nature and dynamics of such events. Our ideal candidate will have high academic achievement and relevant experience and interest in stem cell and/or epigenetic and biochemical techniques.

This project encompasses both wet laboratory and bioinformatic components, making it suitable for students interested in cell-based and molecular biochemical wet lab techniques or bioinformatics and computational analysis, or a combination thereof.

For more information about this project contact:

Prof Jose Polo
The University of Adelaide
Email: jose.polo@adelaide.edu.au

Ms Suzanne Maiolo
The University of Adelaide
Email: suzanne.maiolo@adelaide.edu.au

Supervisor Researcher Profiles

https://researchers.adelaide.edu.au/profile/jose.polo
https://researchers.adelaide.edu.au/profile/rudrarup.bhattacharjee
https://researchers.adelaide.edu.au/profile/wenjun.liu
https://researchers.adelaide.edu.au/profile/ning.liu

Projects in Cancer Epigenetics

Molecular Epigenetics Research Group

Dr Luke Isbel
Group Leader

We seek to understand how epigenetic processes drive cellular identity, particularly in stem cells and disease states like cancer.

Transcription factors are the proteins that 'read out' DNA sequence to drive complex gene expression patterns that arise during development, or go awry in diseases like cancer. Of course, our genomes are not naked, instead, they are wrapped up by histone proteins to form chromatin. We are particularly fascinated by interactions between transcription factors and chromatin, as targeting this interface may enable a novel means of modifying transcription factor activity to treat cancer.

Projects Available in the Molecular Epigenetics Research Group

We are an inclusive and inquisitive functional genomics group, including 7 researchers, staff and students across all stages. Our primary drive is to utilise a variety of *in vitro* and *in vivo* systems to move beyond correlation and establish causation, an elusive but highly satisfying goal. At the end of the day, the information behind any disease is buried in our genome and it is our job to discover the 'how' of it all.

Please get in touch if you are an undergraduate student interested in a 2025-2026 summer research projects in our group.

We are currently at capacity for HDR students, but anticipate we will be recruiting again in late 2026, including Masters of Research, Masters of Philosophy and PhD candidates.

For more information about this project contact:
Dr Luke Isbel
The University of Adelaide
Email: luke.isbel@adelaide.edu.au

Supervisor Researcher Profiles
https://researchers.adelaide.edu.au/profile/luke.isbel

Projects in Cancer Epigenetics

Development & Epigenetics Research Group

Dr Adrienne Sullivan
Group Leader

Dr Kate Dredge
Research Fellow

Dr Ashleigh Geiger
Research Fellow

The identity of a cell is primarily determined by the specific complement of gene products it expresses. This expression program is highly dependent on the accessibility and activity of enhancers, which are non-coding regions of the genome that are bound by transcription factor proteins to regulate gene expression. But what happens when a cell changes identity? How does it remodel its repertoire of enhancers to 'forget' the previous type and establish a new one? And how are these processes impaired or co-opted in cancers?

The Development & Epigenetics Research Group seeks to understand how epigenetic remodelling of gene regulatory regions drives changes in cell identity and behaviour in development, as well as how misregulation of these processes can cause a cell to become cancerous or develop drug resistance. We use molecular biology techniques and multi-omics together with genetic engineering, 2D and 3D cell culture models of development, and live fluorescent readouts to study these fundamental processes.

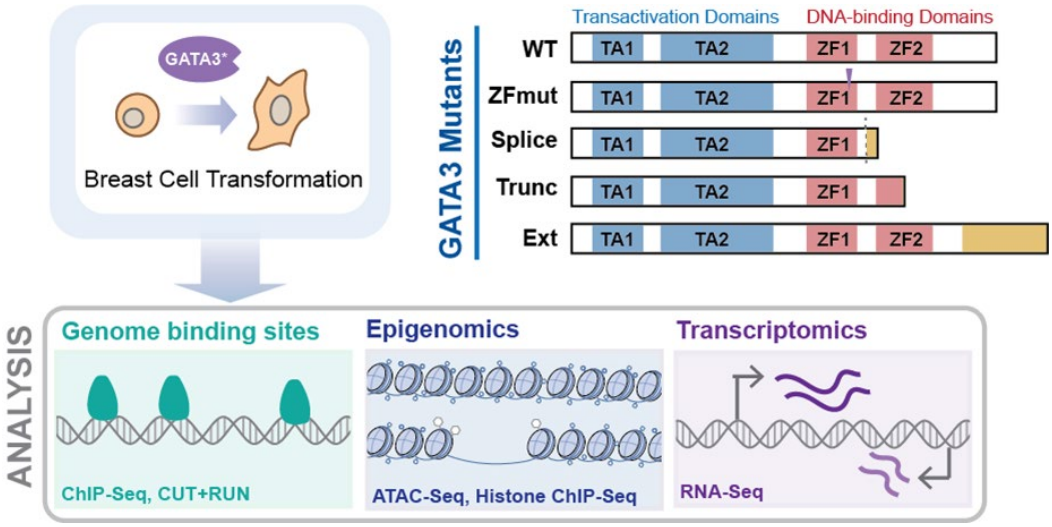
Dr Adrienne Sullivan is a Group Leader with the Adelaide Centre for Epigenetics (ACE) and the Cancer Epigenetics Program at SAiGENCI.

Projects Available in the Development & Epigenetics Research Group

Project Title:	**Aberrant epigenetic remodelling by cancer-associated GATA3 mutants**
Project Supervisor(s):	Dr Adrienne Sullivan & Dr Ashleigh Geiger
Suitable for:	Summer Placement, Hons, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

The transcription factor GATA3 is a 'master regulator' of cell identity, capable of regulating gene transcription and driving both activation and silencing of enhancer regions to change the epigenetic landscape of the cell. Mutations in GATA3 are frequent in luminal breast cancers (> 10% of all breast cancers), and more often affect younger, pre-menopausal women. These mutations produce a range of different variant GATA3 proteins which commonly have altered These mutations produce a range of different variant GATA3 proteins which commonly have altered DNA binding activity, but the effects of mutant GATA3 on the cellular epigenetic profile, and whether different GATA3 cancer mutants produce distinctly different effects, remain to be fully understood. Identifying how mutant GATA3 reshapes the identity of mammary gland cells is essential to understand how GATA3 mutations drive breast cancer onset and development.



GATA3 has 2 transactivation (TA) and 2 zinc finger (ZF) domains. Different mutations found in breast cancer change the protein and affect interactions with DNA in comparison to the normal (WT) protein. We aim to use multi-omics to determine how this may change normal breast cells to a cancerous identity.

This project aims to investigate the function of cancer-associated GATA3 mutant proteins in both activating and silencing enhancer regions in normal mammary gland epithelial cells.

The candidate will develop skills/techniques in cell biology (including culture of cancer lines), and molecular biology (including ChIP, ATAC and plasmid cloning). M Phil and PhD candidates will also develop bioinformatics skills for working with large sequencing datasets.

The ideal candidate will have a strong academic record and relevant experience and interest in cancer biology, gene regulation, epigenetics, and molecular biology.

For more information about this project contact:
Dr Adrienne Sullivan
The University of Adelaide
Email: adrienne.sullivan@adelaide.edu.au
Ph: +61 8 8313 3006

Supervisor Researcher Profiles
https://researchers.adelaide.edu.au/profile/adrienne.sullivan
https://researchers.adelaide.edu.au/profile/ashleigh.geiger

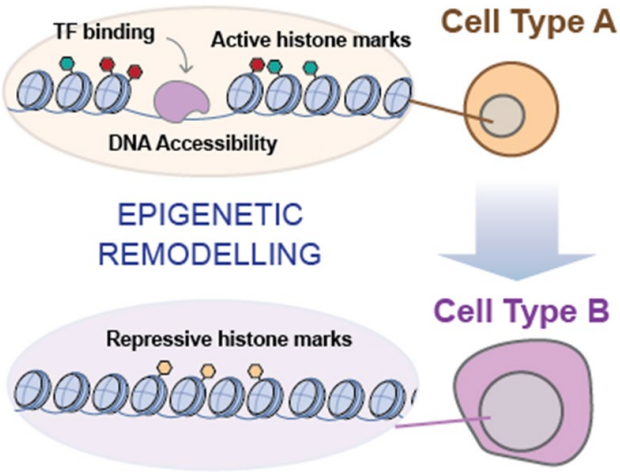
Project Title:	**Investigating the impact of enhancer misregulation using CRISPR/Cas9**
Project Supervisor(s):	Dr Adrienne Sullivan
Suitable for:	Hons, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Studies of the effect of epigenetic silencing on cell identity typically use global perturbation methods such as knockout or inhibition of key epigenetic remodellers. While informative, these approaches mean that effects on individual enhancers and genes can be masked by global de-regulation.

This makes it challenging to answer the fundamental question: why are certain enhancer subsets silenced as cells change identities, for example during differentiation? If these enhancers remain accessible, what happens to the associated gene? What happens to the cell? And furthermore, is there a 'window' of remodelling during differentiation, beyond which the enhancer will be maintained?

To answer these questions, this project aims to use existing CRISPR/Cas9-based targeted perturbation (such as CRISPRa), as well as design new Cas9-based tools to recruit chromatin remodellers and perturb silencing of select enhancers.



When a cell changes type, some regulatory regions become silenced and inaccessible through epigenetic remodelling. Why does this need to happen? We aim to perturb this process using targeted Cas9-based tools and use multi-omics tools to analyse the effect on the enhancer and the cell.

The candidate will develop skills/techniques in cell biology (specifically the culture and differentiation of stem cells), and molecular biology (including ChIP, ATAC, cloning of expression constructs, and CRISPR/Cas9 genome editing). M Phil and PhD candidates will also develop bioinformatics skills for working with large sequencing datasets.

The ideal candidate will have a strong academic record and relevant experience and interest in gene regulation, epigenetics, and molecular biology.

For more information about this project contact:

Dr Adrienne Sullivan
The University of Adelaide
Email: adrienne.sullivan@adelaide.edu.au
Ph: +61 8 8313 3006

Supervisor Researcher Profiles

https://researchers.adelaide.edu.au/profile/adrienne.sullivan

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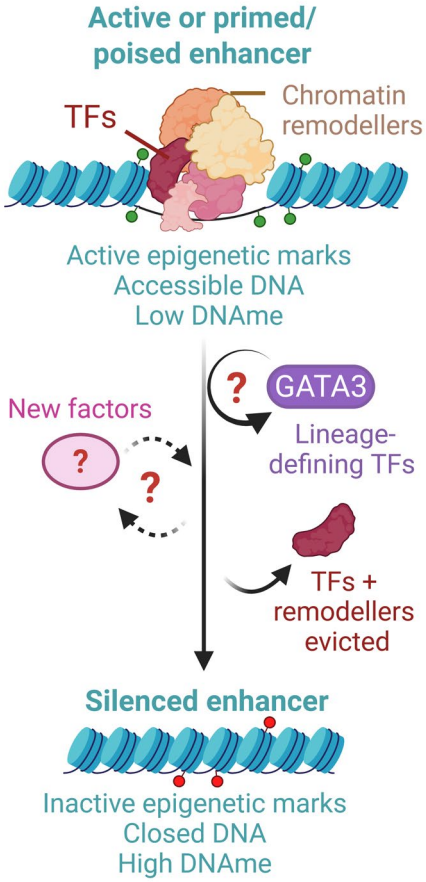
Project Title:	**An epigenetic roadmap to silencing: the molecular events of enhancer remodelling in stem cell differentiation**
Project Supervisor(s):	Dr Adrienne Sullivan, Dr Ning Liu, Dr Kate Dredge
Suitable for:	Hons, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

When cells differentiate, they change which genes are expressed – activating expression of genes associated with their new identity, and switching off expression of genes associated with their old identity. This switching can also be impaired or misregulated to drive cancer development. To do this, the repertoire of active enhancers needs to be extensively remodelled. However, the molecular processes that underly enhancer decommissioning are still poorly understood.

To start answering the critical question of how enhancers are decommissioned, we must first define which epigenetic changes occur, and in what order, as enhancers are shut down. The Development & Epigenetics Research Group has recently generated matched ChIP-Seq samples for different histone marks and transcription factors, ATAC-Seq, and RNA-Seq datasets capturing the state of differentiating stem cells across 7 timepoints. This project will analyse these datasets to characterise the molecular events of enhancer decommissioning.

Under the supervision of Dr Liu (Polo Lab), the candidate will develop skills in sequencing data analysis and performing integration of various multi-omics datasets, such as ChIP-Seq, ATAC-Seq, RNA-Seq and DNA methylation.



When a cell changes type, some regulatory regions become silenced and inaccessible through epigenetic remodelling. What molecular events underly this silencing? This project will characterise when and where different epigenetic changes occur as enhancers are decommissioned in differentiating cells.

HDR candidates will have the opportunity to train in wet-lab techniques or work together with wet-lab scientists for follow-up experiments to determine the epigenetic events that are critical for enhancer shut-down, with the ultimate goal being to understand how misregulation of these events contributes to cancer development.

The ideal candidate will have a strong academic record with experience in programming/data science and/or machine/deep learning and interest in gene regulation and epigenetics.

For more information about these projects contact:

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Supervisor Researcher Profiles

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Projects in Cancer Epigenetics

Epigenetics and Gene Regulation Laboratory

Dr Qi Zhang
EMBL-Australia
Group Leader

Despite all cells within a multicellular organism sharing the same DNA sequences, their individual cellular identity is determined by epigenetic processes. Dysregulation of these processes is highly relevant in pathologies such as cancer, developmental growth disorders and other human diseases.

We are interested in understanding the basic mechanisms of epigenetic regulation, with the ultimate goal of translating fundamental lab-based discoveries into novel therapeutic strategies. The current focus of the lab is to investigate the role of chromatin-modifying complexes in gene regulation and cancer. To achieve this, we employ a diverse range of methods, including biochemistry, structural biology, cell biology, genomics, and bioinformatics.

Projects Available in the Epigenetics & Gene Regulation Research Group

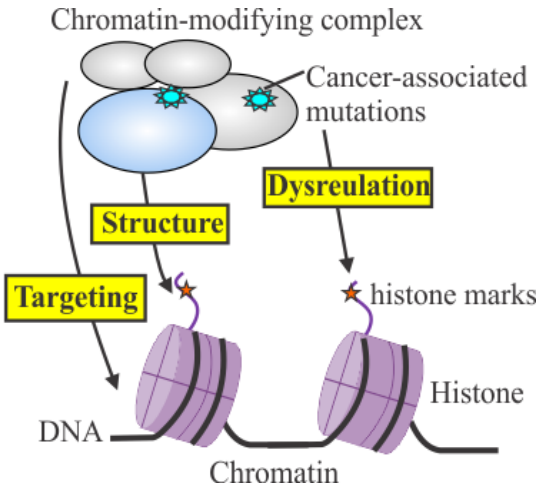
Project Title:	**Chromatin-modifying enzymes and cancer**
Project Supervisor(s):	Dr Qi Zhang
Suitable for:	Summer Placement, Hons, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Our DNA is wrapped around histones to form chromatin. Chromatin-modifying enzymes, which add or reverse post-translational modifications to chromatin, play a crucial role in the dynamic regulation of gene expression. These enzymes often form multi-subunit protein complexes to ensure precise targeting to chromatin and regulation of their enzymatic activities. Dysregulation of these complexes is associated with various diseases, including cancer and developmental disorders.

This project aims to address the following three questions through multidisciplinary approaches:

1. How are multi-subunit chromatin-modifying enzymes assembled, and how do they bind and modify chromatin substrates?
2. How are these enzymes recruited to their target genes?
3. How do the cancer-associated mutations dysregulate these enzymes?



Potential students can choose to focus on one or several questions, depending on their interests, and will have opportunities to gain hands-on experience in at least ONE of the following methodologies:

- **Biochemistry and Biophysics:** including but not limited to expression and purification of multi-subunit protein complexes, and biophysical characterisation.
- **Structural Biology:** including but not limited to Cryo-EM and various proteomic-based methods.
- **Molecular and Cell Biology:** including but not limited to cancer and stem cell lines and genome editing.
- **Genomics and Bioinformatics:** including but not limited to ChIP, CUT&RUN, ATAC etc and data analysis with bioinformatic tools.

Ideal candidates should be highly motivated and have a background in life sciences, chemistry and/or computer science, with a strong INTEREST (experience not required) in gene regulation and epigenetics.

For more information about this project contact:

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Supervisor Researcher Profiles

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Projects in Computational Systems Oncology

Artificial Intelligence for Biological Innovation Research Group

Dr Fuyi Li
Group Leader

Dr Jie Liu
Research Fellow

Our group specialise in the intersection of Artificial Intelligence (AI) and Big Data in Bioinformatics. Our research revolves around harnessing the power of AI and leveraging Big Data analytics to address various bioinformatics challenges in cancer studies. By developing AI-driven bioinformatics tools, platforms, software, pipelines, and resources, our research aims to unravel the complexities of cancer and contribute to advancements in the field.

One key aspect of our research involves exploring gene regulation mechanisms in cancer. We aim to uncover the intricate interplay between genetic factors and their impact on cancer development and progression by utilising AI algorithms and analysing large-scale genomic and epigenomic data. Understanding these mechanisms can provide crucial insights into identifying biomarkers, potential therapeutic targets, and novel treatment strategies.

Additionally, our research focuses on developing innovative approaches for multi-omics data processing in cancer research. With the integration of diverse omics datasets, such as genomics, transcriptomics, proteomics, and metabolomics, we aim to unravel the complex molecular networks underlying cancer.

By developing advanced machine learning approaches, our research aims to extract meaningful patterns and correlations from multi-omics data, enabling a comprehensive understanding of cancer biology. Through our research endeavours, we strive to contribute to the field of Bioinformatics by providing novel insights and tools that facilitate precision medicine, personalised therapies, and improved patient outcomes in cancer research and treatment.

We are excited to invite you to delve into the captivating realm of AI-driven Bioinformatics in cancer research. If you are passionate about leveraging cutting-edge technologies, such as Artificial Intelligence and Big Data analytics, to unravel the mysteries of cancer, we would be thrilled to explore potential research projects with you.

By joining our research team, you will have the opportunity to work on developing state-of-the-art bioinformatics tools and platforms, unravel gene regulation mechanisms, and delve into the analysis of complex multi-omics data in the context of cancer. If you are motivated to make a meaningful impact in the field of cancer research, we encourage you to reach out to us. Let's embark on a collaborative journey where we can contribute to advancements in AI in bioinformatics, cancer biology, and precision medicine. We look forward to discussing your research interests and the potential for us to work together.

Projects Available in the Artificial Intelligence for Biological Innovation Research Group

Project Title:	**Robust multimodal learning for cancer prognosis analysis**
Project Supervisor(s):	Dr Fuyi Li
Suitable for:	Honours, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Accurately predicting the prognosis of cancer patients is crucial for aiding clinicians in planning appropriate treatment, reducing cancer-related medical expenses, and significantly enhancing patients' quality of life. Multimodal prediction of cancer patient prognosis offers a more comprehensive and precise approach.

This project will focus on the development of advanced multimodal learning techniques that can seamlessly fuse information from different data modalities to enhance the accuracy and reliability of cancer prognosis models. By integrating diverse molecular and clinical features, the proposed approach aims to capture the complex interplay between genetic alterations, molecular signatures, and clinical characteristics that influence cancer progression and patient outcomes.

The student will gain expertise in developing and implementing multimodal learning algorithms to integrate diverse data modalities for cancer prognosis analysis. The ideal candidate will have proficient programming skills in languages such as Python and R, and experience in machine learning and deep learning techniques.

For more information about this project contact:

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Supervisor Researcher Profiles

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Project Title:	AI-driven drug-target interaction prediction
Project Supervisor(s):	Dr Fuyi Li
Suitable for:	Honours, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Accurate prediction of drug-target interactions is fundamental in drug discovery and development processes, facilitating the identification of potential drug candidates and reducing the time and cost associated with experimental validation.

This project focuses on leveraging AI-driven approaches to enhance the prediction of drug-target interactions through the integration of diverse data modalities. By combining molecular, structural, and pharmacological data, advanced multimodal learning techniques will be developed to provide a comprehensive understanding of the complex interactions between drugs and their targets. The project aims to develop robust predictive models that capture the intricate relationships between chemical structures, biological activities, and target properties, ultimately improving the efficiency and success rate of drug discovery pipelines.

The student involved in this project will gain hands-on experience in developing and implementing AI-driven algorithms for drug-target interaction prediction. Proficiency in programming languages such as Python and R, along with a strong background in machine learning and deep learning techniques, will be essential for effectively integrating and analysing diverse data sources. The ideal candidate will have a keen interest in computational biology and drug discovery, coupled with a proactive attitude towards exploring innovative solutions to address challenges in predicting drug-target interactions.

For more information about this project contact:

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Supervisor Researcher Profiles

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Projects in Computational Systems Oncology

Computational Cancer Immunogenomics Laboratory

Dr Stefano Mangiola
Group Leader

The Computational Cancer Immunogenomics group, led by Dr Mangiola, is interested in applying cutting-edge computational methods for the study of the immune system's role in cancer progression and treatment response. Dr Mangiola's hybrid laboratory is at the edge of artificial intelligence and multi-omic data production.

By profiling a patient's immune system through modern spatial and single-cell technologies, we model the propensity to enter metastatic progression and be resilient to metastatic spread (e.g., in breast cancer). Similarly, we intend to identify systemic immune features that explain local immunity (within the tumour microenvironment) and predict resistance to neoadjuvant therapy in breast and other cancer types.

The immune system is diverse across the human population. We have pioneered population-scale immune system modelling using large-scale single-cell data (Human Cell Atlas) and quantified its heterogeneity across tissues. This heterogeneity includes tissue-specific ageing programs, sexual dimorphism, and ethnic diversity in immunotherapy targets. Now, we aim to use artificial intelligence (AI) models (i.e. large language models) to extend our immune map to cancer. Specifically, we are interested in building foundation models that can identify stable immunotherapy targets across ethnic groups.

Our work includes the construction of scalable infrastructure and interfaces that allow multi-atlas-level analyses and annotation. This includes tidyomics, CuratedAtlasQuery and HPCell.

We are particularly interested in the following areas:

- Integration of spatial and single-cell transcriptomics and proteomics.
- Machine learning and classification.
- Large-language AI models applied to cellular biology.
- Cancer immunodiagnosis.
- R tidy programming applied to multi-omics.
- Large-scale inference from single-cell multi-atlases.

Projects Available in the Computational Cancer Immunogenomics Laboratory

Project Title:	**Large-language AI models to study the immune system**
Project Supervisor(s):	Dr Stefano Mangiola
Suitable for:	PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Demographic factors like age and sex critically influence disease outcomes and treatment responses, including cancer treatments targeting the immune system (immunotherapy).

Australia has an ethnically diverse and ageing population. Despite its importance, a unified resource to test the population-level diversity of therapy and diagnosis targets is missing. The current paradigm of population-level investigation of complex cancer traits still relies on homogenised tissue data, such as the 15-year-old Cancer Genome Atlas (TCGA) database.

With a recent breakthrough, we pioneered the population-level immune system investigation from massive-scale single-cell resources. Across 12,981 healthy individuals and 30 organs, we mapped profound immunological changes across ages, sex and ethnicity, uncovering diversity in key pathways used in immunotherapy (e.g. LAG3, SLAMF7 and CD83).

As the lead researcher on this project, you will translate cutting-edge technology. You will adapt and implement our existing infrastructure to generative single-cell large-language models, akin to ChatGPT, but specifically tailored to identify novel immune targets conserved in ageing and across sexes. Your role will involve pushing the boundaries of AI in cell biology, pivoting this technology to analyse our extensive clinically annotated cancer cell compendium. This will allow for the identification of critical therapeutic targets in cancer, which is a step towards more personalised and effective treatments. You will contribute to the next generation of AI models by extending beyond the current static-cell paradigm, working towards a dynamic representation of cells. This will involve creating models that capture cellular behaviour's complexity and variability in different biological contexts.

Skills you will learn:

- **Single-cell Analysis:** Master state-of-the-art techniques in single-cell RNA sequencing, understanding cellular heterogeneity at an unprecedented resolution.
- **Artificial Intelligence and Machine Learning:** Gain expertise in developing and applying generative models and large-language models to biological data, equipping you with skills that are at the forefront of AI-driven research.

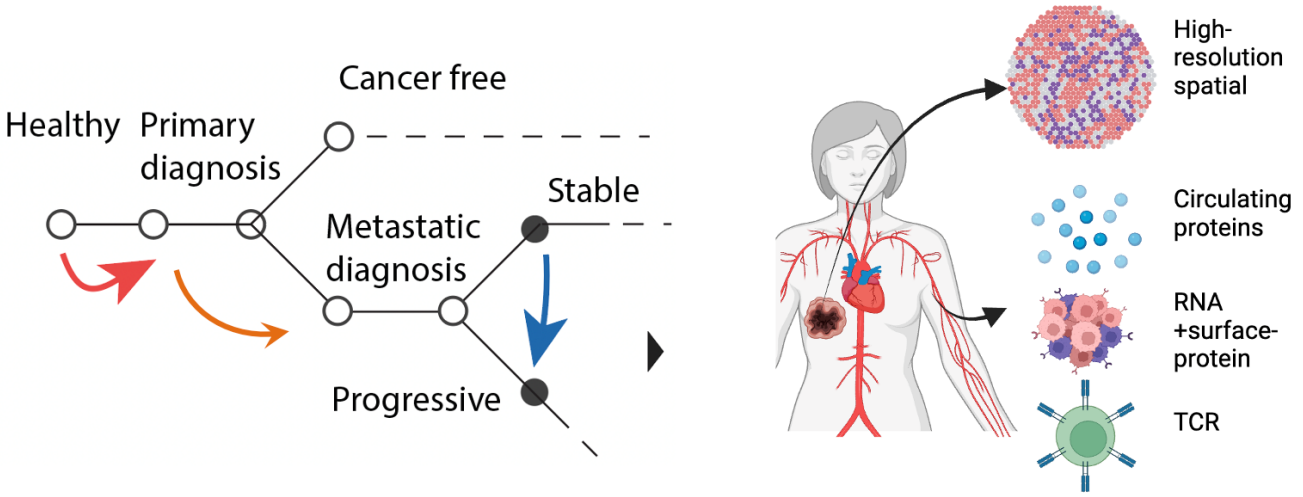
- **Bioinformatics:** Develop strong bioinformatics skills, including data processing, integration, and analysis of large-scale, clinically annotated datasets.
- **Computational Modelling:** Learn how to build and refine dynamic cell models, moving beyond static representations to capture the temporal and spatial variability of cellular behaviour.
- **Translational Research:** Engage in translational research by applying computational findings to clinically relevant questions, bridging the gap between basic science and potential therapeutic applications.

The ideal candidate for this PhD project will have a strong background in computational biology, bioinformatics, or a related field, with experience in handling large-scale datasets. Proficiency in programming languages such as Python or R is essential, as well as familiarity with machine learning techniques and AI applications. Prior experience with single-cell RNA sequencing or other omics data would be highly advantageous. The candidate should be highly motivated, with a keen interest in translational research and a desire to apply computational methods to solve clinically relevant problems. Excellent problem-solving skills, attention to detail, and the ability to work independently as well as part of a multidisciplinary team are also crucial.

Project Title:	**Integration of spatial and single-cell multi-omics to predict neoadjuvant response in cancer with locally-assisted systemic immunodiagnosis**
Project Supervisor(s):	Dr Stefano Mangiola
Suitable for:	PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

The effective prediction of neoadjuvant therapy outcomes in cancer treatment remains a pivotal challenge. This project proposes a novel approach by integrating spatial and single-cell multi-omics analyses to enhance the precision of neoadjuvant response predictions. Our methodology leverages cutting-edge techniques in both spatial omics and single-cell sequencing to capture a comprehensive molecular landscape at the tumour site. By delineating the intricate interplay between tumour cells and the immune environment, this approach aims to uncover specific biomarkers and signalling pathways indicative of therapy responses.



Representation of the multi-omics study design, to probe the local and systemic immune response as the disease progresses.

Further innovation lies in implementing locally-assisted systemic immunodiagnosis, which utilises local tumour data to inform systemic immune profiling. This dual approach promises to improve the accuracy of predicting patient responses to neoadjuvant therapies and aims to personalise treatment plans, thereby potentially enhancing clinical outcomes.

The projects multi-disciplinary framework combines advanced bioinformatics tools with clinical oncology insights, enabling a more targeted and efficient diagnostic process. By predicting therapeutic efficacy before treatment initiation, this strategy seeks to spare patients from the adverse effects of ineffective therapies and streamline clinical decision-making.

The key skills and techniques the PhD candidate will learn by working on this project include:

- **Multi-omics Data Integration:** Learn how to integrate and analyse multi-omics data, including high-resolution spatial, circulating protein, RNA, and TCR data, to understand immune responses.
- **Single-Cell Sequencing Techniques:** Gain expertise in cutting-edge single-cell sequencing technologies, particularly in the context of immune profiling.
- **Spatial Transcriptomics:** Develop skills in spatial transcriptomics, allowing for high-resolution mapping of gene expression within tissue samples.
- **Bioinformatics and Computational Analysis:** Build proficiency in bioinformatics tools and computational techniques for processing and interpreting large-scale datasets.
- **Translational Research:** Engage in research that connects basic scientific discoveries to clinical applications, focusing on immune responses as diseases progress.
- **Data Visualisation and Interpretation:** Enhance your ability to visualise complex biological data and extract meaningful insights that contribute to the understanding of disease mechanisms.

The ideal candidate for this project should have a strong foundation in bioinformatics or computational biology, with some experience with gene/protein expression data. Proficiency in the programming language R is beneficial, as well as familiarity with single-cell sequencing techniques and spatial transcriptomics. A background in immunology or related fields would be highly advantageous, particularly if combined with knowledge of translational research. The candidate should be analytical, detail-oriented, and capable of working with large, complex datasets. Strong communication skills and the ability to work collaboratively in a multidisciplinary team are also important for this role.

Project Title:	**Build large-scale and scalable computational infrastructure for analysis, deployment and exploration of the single-cell universe**
Project Supervisor(s):	Dr Stefano Mangiola
Suitable for:	PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Single-cell and spatial omic technologies have fundamentally transformed biological research by generating vast quantities of data. This influx challenges existing bioinformatics pipelines and individual users' capacity to keep up with the rapidly evolving demands of impactful data-driven research.

As part of this project, you will collaborate with our industry partner to enhance the capabilities of CuratedAtlasQuery and HPCell, focusing on establishing a privately deployable intelligence hub for single-cell and spatial data. You will expand the existing CuratedAtlasQuery database, which has already facilitated extensive profiling of the immune system at the human population level, by integrating biological annotations and developing data summarisation techniques. This effort will help democratise access to large-scale single-cell analyses. Additionally, you will contribute to developing HPCell, an analytical language designed to execute massively parallel single-cell analysis workflows in a tidy R style and enable their deployment on high-performance computing platforms. This project allows you to work at the forefront of computational biology and translational research.

The key skills and techniques the PhD candidate will learn by working on this project include:

- **Single-cell and Spatial Data Analysis:** Gain expertise in analysing and managing large-scale single-cell and spatial datasets.
- **Bioinformatics Tool Development:** Develop skills in enhancing and expanding bioinformatics tools like CuratedAtlasQuery and HPCell, focusing on integrating biological annotations and data summarisation techniques.

- **High-performance Computing:** Learn to execute and optimise single-cell analysis workflows on high-performance computing platforms using the HPCell analytical language.
- **Data Integration and Summarisation:** Master techniques for integrating diverse biological datasets and creating summarised outputs that facilitate large-scale analyses.
- **Collaborative Industry Research:** Experience working directly with an industry partner, gaining insights into the application of bioinformatics in a commercial setting.
- **R Programming and Tidyverse:** Enhance your proficiency in R, particularly in the tidyverse style, for organising and analysing complex data.
- **Translational Research**: Engage in translational research by applying computational methods to address clinically relevant questions.

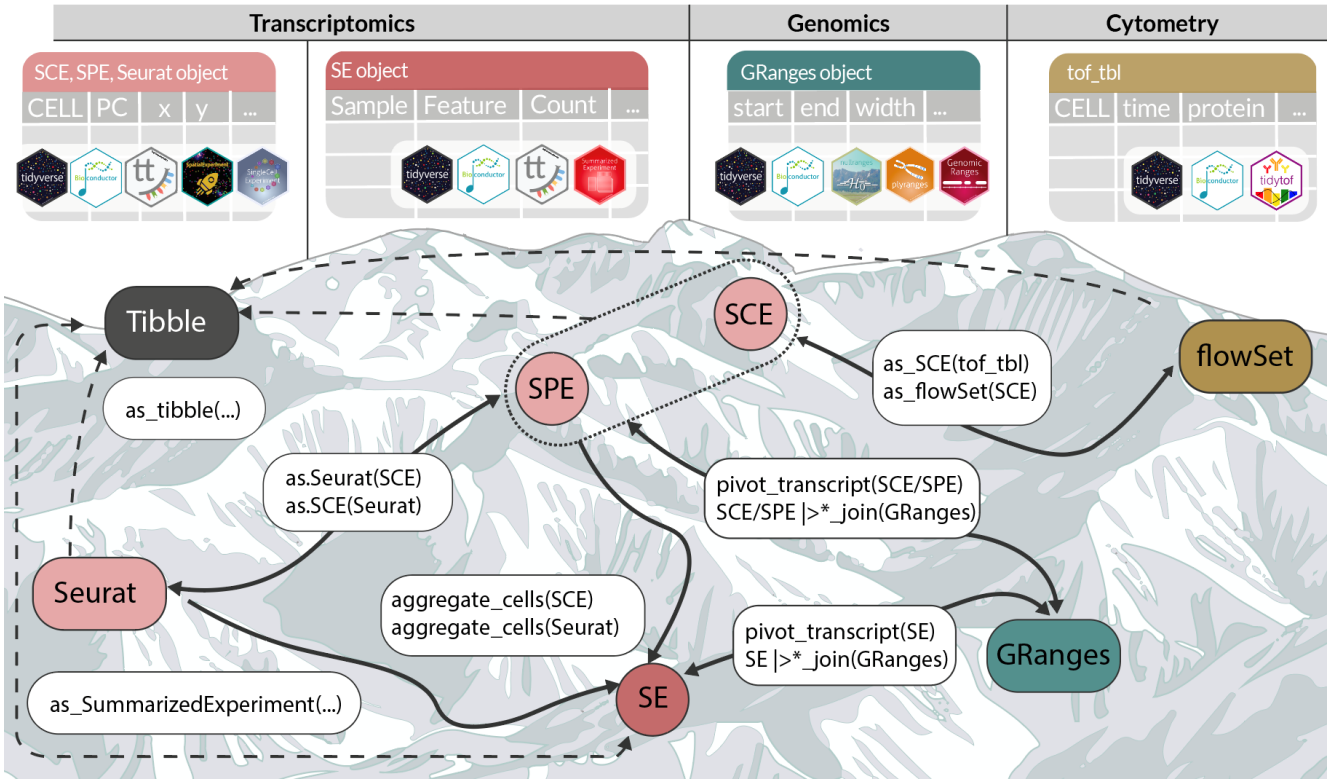
The ideal candidate for this project should have a strong background in bioinformatics, computational biology, or a related field, with experience in analysing single-cell and spatial data. Proficiency in R programming, particularly with tidyverse, and familiarity with high-performance computing environments are essential. Prior experience in developing bioinformatics tools or working with large-scale biological datasets would be highly beneficial. The candidate should also possess strong problem-solving skills, the ability to work collaboratively with industry partners, and a keen interest in translational research. Excellent communication skills and a demonstrated ability to manage and interpret complex data are also important for success in this role.

Project Title:	**Developing the Tidyomics ecosystem**
Project Supervisor(s):	Dr Stefano Mangiola
Suitable for:	PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

As part of this project, you will work on improving the Tidyomics R software ecosystem, which enhances the analysis and visualisation of high-dimensional omics data by applying the principles of tidy data analysis. Your primary responsibilities will include improving the documentation, robustness, and interoperability of the Tidyomics ecosystem, ensuring it remains accessible and user-friendly for the growing community of computational biologists. You will also focus on extending Tidyomics to support spatial profiling technologies, enabling its application to cutting-edge research in tissue biology at the single-cell level. In addition, you will contribute to the development of a user-friendly grammar that facilitates the manipulation of popular data containers across various omics (genomics, transcriptomics, cytometry) and platforms (Bioconductor,

Seurat). As part of your work, you will engage with the international Tidyomics community, collaborating with developers and users across five continents, and contribute to the ongoing roadmap for the ecosystem through our community GitHub Project space. This project offers you the opportunity to be at the forefront of computational biology, with a focus on interfacing with large-scale single-cell atlas collections like The Human Cell Atlas and Curated Cancer Atlas.



The key skills and techniques the PhD candidate will learn by working on this project include:

- **R Programming and Tidyverse:** Enhance your proficiency in R, focusing on tidy data principles and the tidyverse ecosystem for data manipulation and analysis.
- **Software Development:** Gain experience in improving and extending bioinformatics software, focusing on documentation, robustness, and interoperability of the Tidyomics ecosystem.
- **Spatial Profiling Technologies:** Learn to apply and integrate spatial profiling technologies within the Tidyomics ecosystem, enabling advanced analysis of tissue biology at the single-cell level.
- **Data Visualisation:** Develop skills in visualising high-dimensional omics data, making complex biological data more accessible and interpretable.
- **Community Collaboration:** Engage with a global community of developers and users, contributing to an international network that spans five continents.
- **GitHub Project Management:** Participate in collaborative software development using GitHub, contributing to the ongoing roadmap and development of the Tidyomics ecosystem.

- **Interfacing with Single-Cell Atlas Collections:** Work with large-scale single-cell data repositories like The Human Cell Atlas and Curated Cancer Atlas, enhancing your understanding of cutting-edge single-cell research.

The ideal candidate for this project should have a solid background in bioinformatics, computational biology, or a related field, with strong proficiency in R programming and a deep understanding of tidy data principles and the tidyverse ecosystem. Experience in software development, particularly in improving and documenting bioinformatics tools, would be highly advantageous. Familiarity with spatial profiling technologies and single-cell analysis is also beneficial, as is prior experience with large-scale omics data. The candidate should have excellent problem-solving skills, be comfortable working collaboratively within a global community of developers and users, and have a keen interest in contributing to advancing computational biology through open-source software development. Strong communication skills and a proactive approach to learning and innovation are essential for success in this project.

For more information about these projects contact:

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Supervisor Researcher Profiles

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Projects in Resistance Prevention

Prostate Cancer Research Group

Prof Lisa Butler
Group Leader

Dr Maggie Centenera
Research Fellow

Dr Zeyad Nassar
Research Fellow

Prostate cancer is a major public health issue, killing approximately 3,300 men in Australia annually.

The Prostate Cancer Research Group (PCRG) is tackling localised and metastatic prostate cancer by developing more robust diagnostics tests, biomarkers for responsiveness to current treatments and new drugs for clinical development.

Professor Lisa Butler leads the PCRG which consists of some 18 researchers, support staff, PhD and honours students.

Visit the prostate Cancer Research Group for more information:
https://health.adelaide.edu.au/our-research/prostate-cancer-research-group

Projects Available in the Prostate Cancer Research Group

Project Title:	**Exploiting prostate cancer metabolic dependencies to develop new therapeutics and prognostic and predictive biomarkers**
Project Supervisor(s):	Dr Zeyad Nassar & Prof Lisa Butler
Suitable for:	Summer internship, Honours, M Phil, PhD
Location of project:	South Australian Health & Medical Research Institute (SAHMRI), North Terrace, Adelaide

Project outline

Due to the dependence of prostate cancer cells on androgens for growth and survival, androgen deprivation therapy (ADT) is the frontline strategy for advanced prostate cancer (PCa) management.

Although initially effective, patients inevitably develop resistance to ADT leading to emergence of lethal disease phenotypes such as castrate resistant PCa (CRPC) and neuroendocrine PCa (NEPC), with a median overall survival of less than 2 years. Co-targeting of adaptive pathways that are induced by these treatments is now considered essential to delay disease progression and engender more durable therapeutic responses. Metabolic rewiring is both a hallmark feature of cancer cells, a resistance mediator and a promising therapeutic vulnerability.

This project will employ in vitro, in vivo and ex vivo models coupled with state-of-the-art transcriptomics and mass spectrometry metabolomics techniques to discover new metabolic targets and evaluate their therapeutic potential for lethal castrate resistant (CRPC) and neuroendocrine (NEPC) PCa treatment.

The candidate will develop skills in molecular pharmacological techniques, gene editing, metabolomics, drug candidate testing (in vitro, in vivo and ex vivo models) and flow cytometry.

Our ideal candidate will have a first class Honours or Masters qualification in biomedical sciences, pharmacology or biochemistry.

For more information about this project contact:
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Supervisor Researcher Profiles
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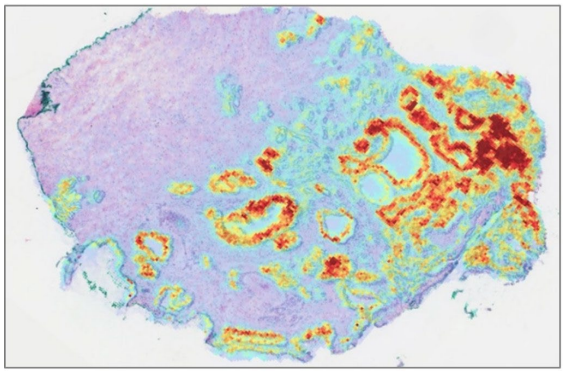
https://researchers.adelaide.edu.au/profile/lisa.butler

Project Title:	**Unravelling the molecular heterogeneity of clinical prostate tumours**
Project Supervisor(s):	Dr Paul Trim, Dr Maggie Centenera & Prof Lisa Butler
Suitable for:	M Phil, PhD
Location of project:	South Australian Health & Medical Research Institute (SAHMRI), North Terrace, Adelaide

Project outline

A hallmark of prostate cancer (PCa) is its dependence on androgen signalling, and the androgen receptor (AR) is the primary therapeutic target for advanced disease. However, resistance to antiandrogen therapies is inevitable and leads to lethal and aggressive forms of PCa that remain incurable. PCa is a highly heterogenous and multifocal disease, a characteristic that has posed a major challenge to the development of novel treatments. Spatial heterogeneity, a fundamental feature of the tumour microenvironment (TME), is critical to understand how the organisation and interaction of different cell types within the tumour drive disease progression and drug resistance.

This project will utilise cutting-edge spatial technologies and data integration to investigate how androgens influence the genes, lipids and proteins of the TME to promote PCa progression. This will identify novel tumour and TME-specific vulnerabilities for development of new targeted therapies to improve outcomes for men with prostate cancer.



Mass spectrometry imaging of phosphatidylcholine lipids in a clinical prostate tumour. Image: Dr Paul Trim

The candidate will develop skills in bioinformatics/computational biology and wet-laboratory based techniques including tissue imaging.

Our ideal candidate will have interest in bioinformatics and some microscopy skills. This project would also suit a clinical HDR candidate.

For more information about this project contact:

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Supervisor Researcher Profiles

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https://researchers.adelaide.edu.au/profile/margaret.centenera

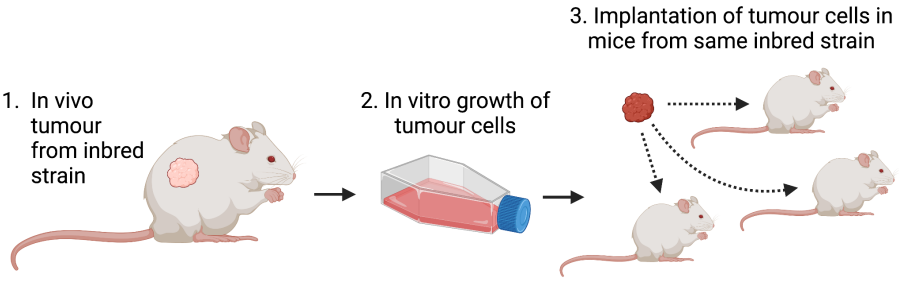
Project Title:	**Ceramides: from a metabolic biomarker to a targetable vulnerability**
Project Supervisor(s):	Prof Lisa Butler & Prof Lisa Horvath (Garvan Institute of Medical Research, NSW)
Suitable for:	Summer internship, Hons, M Phil, PhD
Location of project:	South Australian Health & Medical Research Institute (SAHMRI), North Terrace, Adelaide

Project outline

Plasma lipids (particularly ceramides) are prognostic for poor patient outcome across the natural history of prostate cancer (localised to metastatic).

This project will establish a high fat diet model of prostate cancer in mice (known to increase circulating ceramides) with an intact immune system to evaluate the link between circulating lipids, tumour metastasis and the interactions between tumour and host lipids. We will also test the ability of novel clinical inhibitors of sphingolipid metabolism to suppress cancer metastasis and improve survival.

The candidate will develop skills in animal studies and wet-laboratory techniques including lipidomic profiling.



Mouse model to study cancer metastasis.

For more information about this project contact:

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Supervisor Researcher Profiles

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3D Chromatin Organisation Research Group

Dr Joanna Achinger-Kawecka
Group Leader

Dr Daniel Thomson
Research Fellow

Dr Fiona Zhou
Research Fellow

Geraldine Laven-Law
Research Manager

The 3D Chromatin Organisation Research Group (PI Dr Joanna Achinger-Kawecka) is an experimental biology and bioinformatics laboratory studying the principles of 3D genome folding in cancer.

The 3D genome architecture brings together genes and distant regulatory elements to orchestrate gene transcription, and has been implicated in many diseases, including cancer.

Our research focuses on understanding the role of 3D chromatin alterations in driving cancer development, progression and treatment resistance, with a focus on hormone-dependent cancers, such as breast and prostate cancers. We use cutting-edge methods (multi-omics, single-cell, genome editing as well as various pre-clinical model systems) to study the interplay of the 3D chromatin, epigenome and transcriptome in cancer to increase our understanding of cancer biology and accelerate the development of new therapies.

Projects Available in the 3D Chromatin Organisation Research Group

Project Title: **Establishing the regulatory function of transposable elements in cancer (Bioinformatics)**

Project Supervisor(s): Dr Joanna Achinger-Kawecka and Dr Daniel Thomson

Suitable for:	Honours, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Transposable elements (TEs), also known as "jumping genes" are repetitive genomic elements that represent almost half of the human genome. While the majority of TEs in the human genome have lost the ability to transpose, their sequences hold a significant regulatory potential. TEs contain binding sites for transcription factors, enabling them to function as alternative promoters or enhancers regulating the gene expression.

TEs are frequently activated during tumorigenesis, promoting oncogenic gene expression. While some TEs have been previously documented to contribute to gene deregulation in cancer, a comprehensive view of the regulatory landscape of TEs in cancer remains incomplete.

This bioinformatics project, suitable for Honours, Masters, or PhD, will leverage large, publicly available pan-cancer transcriptome, chromatin, and 3D genome datasets to carry out a comprehensive systematic study of the contribution of TEs to the regulatory cancer genome.

We are seeking a candidate with prior research experience in next generation sequencing (NGS) data processing and analyses, working within a high-performance computing (HPC) environment, and knowledge of at least one computational language (e.g., Python, R). Datasets you will have access to include ATAC-seq (chromatin accessibility), RNA-seq (transcriptome) Hi-C (3D genome structure), ChIP-seq/CUT&RUN (transcription factor binding), ONT Nanopore DNA and RNA sequencing (long-read sequencing), and single-cell data. We have access to two HPCs, established bioinformatics pipelines (Nextflow nf-core), and strong in-house bioinformatics expertise to streamline any large data processing and machine learning applications, and grow your bioinformatics skillsets.

Please contact Dr. Joanna Achinger-Kawecka to discuss your suitability for this project.

Project Title:	**Dissecting transposable elements contribution to cancer**
Project Supervisor(s):	Dr Joanna Achinger-Kawecka, Dr Daniel Thomson and Geraldine Laven-Law
Suitable for:	Honours, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Transposable elements (TEs), also known as "jumping genes" are repetitive genomic elements that represent almost half of the human genome. While the majority of TEs in the human genome have lost the ability to transpose, their sequences hold a significant regulatory potential. TEs contain binding sites for transcription factors (TFs), enabling them to function as alternative promoters or enhancers regulating the gene expression.

TEs are often hijacked in cancer to drive oncogenic gene expression. Yet, paradoxically, reactivation of these TEs in cancer cells can trigger an innate immune response known as viral mimicry and inhibit tumour growth. Therefore, TEs may pose as double-edged sword, with not only an underexplored role in promoting tumorigenesis (see project #1), but also representing a key vulnerability that could be exploited in targeted therapy. A deeper understanding of the role of TEs in oncogene expression and viral mimicry is crucial for developing novel TE-based cancer therapies and biomarkers.

This wet laboratory and bioinformatics project, suitable for Honours, Masters, or PhD, is focused on understanding the role of TEs in cancer, particularly their impact on transcription, viral mimicry and immune evasion. To do this, you will use various molecular (Hi-C, RNA-seq, ATAC-seq) and functional (CRISPR, DEGRON) methods to study selected TEs and establish their role in gene regulation and treatment response in cancer.

We are seeking a candidate with prior research experience and proficiency in cellular and molecular biology. Prior experience in interpreting next-generation sequencing data, and knowledge of at least one computational language (e.g., Python, R) would be an advantage. Wet laboratory techniques and datasets you will have access to include Hi-C (3D chromatin structure), CUT&RUN/ChIP-seq (transcription factor binding), ATAC-seq (chromatin accessibility), RNA-seq (transcriptome), ONT Nanopore DNA and RNA (long read) sequencing, and single-cell data. We have access to high performance computing (HPC) and established analytical pipelines to streamline any large data processing and machine learning applications. You will be supported by two senior bioinformaticians and an experienced wet laboratory researcher to further develop your molecular biology and computational skillsets

Please contact Dr Joanna Achinger-Kawecka, Dr Daniel W. Thomson, or Geraldine Laven-Law to discuss your suitability for this project.

Project Title:	**Activating p53 to target transposable elements in treatment-resistant ER+ breast cancer**
Project Supervisor(s):	Dr Joanna Achinger-Kawecka and Dr Fiona Zhou
Suitable for:	Honours, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Estrogen-receptor positive (ER+) breast cancer is one of the most commonly diagnosed cancers in Australia. Advanced ER+ breast cancers are treated with cyclin-dependent kinase 4/6 inhibitors (CDK4/6i). Unfortunately, resistance to CDK4/6 inhibitors can develop within ~2-3 years.

Normal function of tumour suppressor protein p53, long known as the "guardian of the genome" for its role in preventing oncogenesis, is frequently impaired in ER+ breast cancer, despite p53 mutations being relatively rare. We have shown that restoration of p53 function via pharmacological inhibition of its negative regulator MDM2 inhibits tumour growth in CDK4/6i-resistant ER+ breast cancer.

This wet laboratory project, suitable for Honours, Masters, or PhD, will use a multi-omics approach to characterise the molecular mechanisms of p53 activation and therapeutic response in patient-derived xenograft (PDX) and organoid (PDxO) models of breast cancer on the 3D genome, epigenome and transcriptome.

We are seeking a candidate will possess prior research experience with *in vitro* and/or *in vivo* cancer models (cancer cell or *ex vivo* tissue culture, mouse models, and/or organoid culture), molecular biology techniques (DNA and RNA extraction, protein isolation, expression profiling etc), a keen interest in epigenetics, and drive to understand the fundamental mechanisms of breast cancer progression. Key experimental techniques established in the lab include Hi-C, ATAC-seq, RNA-seq, ChIP-seq/CUT&RUN, ONT Nanopore DNA and RNA sequencing, and single-cell and spatial profiling. The project will also involve establishing CRISPR-based technologies for functional studies. You will be supported by experienced wet laboratory researchers and bioinformaticians to further develop your molecular biology and computational skillsets.

Please contact Dr Joanna Achinger-Kawecka or Dr Fiona Zhou to discuss your suitability for this project.

For more information about any of these projects contact:

Dr Joanna Achinger-Kawecka
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Supervisor Researcher Profiles

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Projects in Resistance Prevention

Molecular and Proximity Discovery Laboratory

Dr Michael Roy
Group Leader

The Molecular and Proximity Discovery (MPD) Laboratory (PI Dr Michael Roy) is a cutting-edge, multidisciplinary research group working at the intersection of chemical biology and cancer drug discovery.

We focus on understanding and manipulating protein-protein interactions (PPIs) to rewire faulty cancer cell signalling pathways — paving the way for safer, more effective cancer therapies.

Our lab specialises in PPI inhibitors and Chemically Induced Proximity (CIP) techniques like Targeted Protein Degradation (TPD), using small molecules (PROTACs and molecular glues) to hijack the cell's recycling system and eliminate disease-causing proteins.

Our research dives deep into protein structure and function — including ubiquitin E3 ligases, kinases/pseudokinases, and epigenetic regulators — to understand biology, uncover targetable cancer vulnerabilities and design innovative molecules that can reprogram cellular signalling.

Our key research toolbox includes:

- Synthetic/Medicinal Chemistry
- Structural Biology & Biophysics
- Cellular Biology
- Computational Tools & AI-driven Discovery

Projects Available in the Molecular & Proximity Discovery Laboratory

Researchers in the Molecular & Proximity Discovery Laboratory use a broad range of techniques and skills to undertake their research. These include: synthetic organic and medicinal chemistry, protein biochemistry and structural biology (e.g. recombinant protein production, X-ray crystallography), biophysics, cell culture, flow cytometry and proteomics, and incorporation of computational approaches (e.g. machine learning, *de novo* design) for design and analysis of proteins and small molecules.

Students with a background in biomedical sciences, chemistry, biochemistry, pharmacology or computational biology are encouraged to contact Dr Roy to discuss potential research projects in areas of mutual interest.

For more information about projects contact:
Dr Michael Roy
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Supervisor Researcher
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Sweeney OncoTherapeutics and Biology Laboratory

Prof Christopher Sweeney
Group Leader

Dr Katherine Morel
Research Fellow

Dr Mark Bunting
Research Fellow

Dr Kimberley Clark
Research Fellow

Dr Kristen Feher
Research Fellow

The Sweeney OncoTherapeutics and Biology Laboratory has a translational research focus and works to better understand the underlying biology of prostate cancer and improve therapies for patients.

Prostate cancer is a complex disease that affects millions of men globally. Development of prostate cancer involves corruption of the normal prostate transcriptional network, following deregulated expression or mutation of key transcription factors. The group is interested in understanding how many of these transcription factors affect prostate cancer development, from localised disease to castration-resistant metastatic prostate cancer, and subsequently finding viable therapeutic approaches to benefit patients.

The research team is led by Professor Christopher Sweeney, who has devoted his clinical and academic career to developing strategies to improve the care of patients with genitourinary malignancies with a major focus on prostate cancer and testicular cancer.

Projects Available in the Sweeney OncoTherapeutics and Biology Laboratory

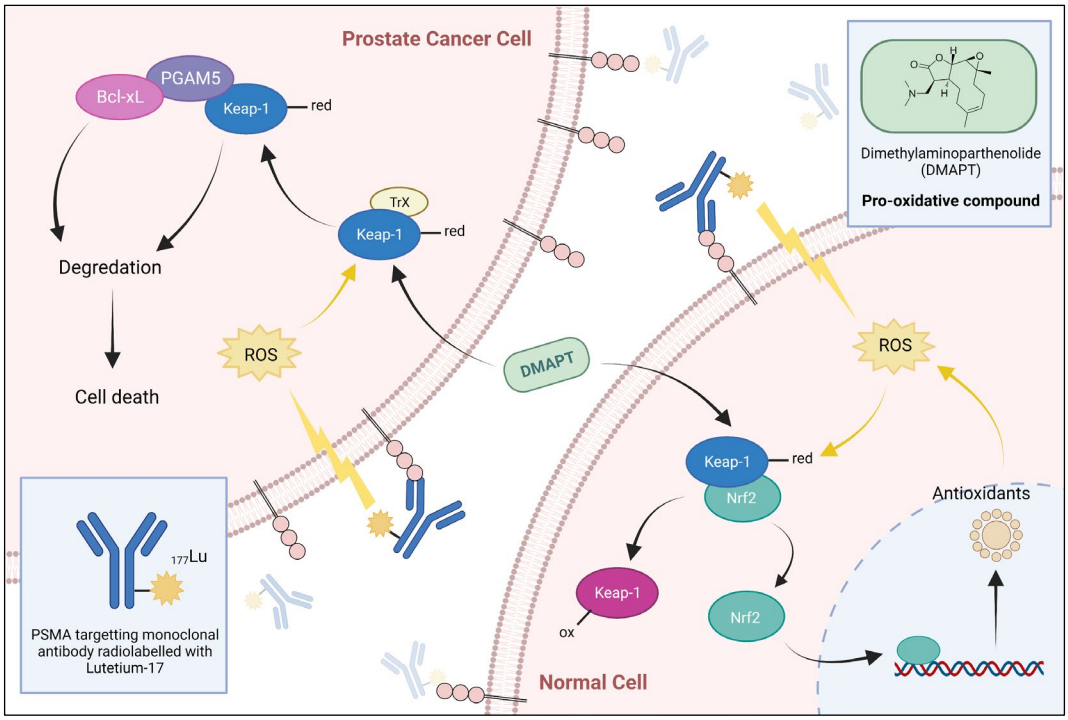
Project Title:	**Modulating oxidative stress responses to augment radiation therapy efficacy in prostate cancer**
Project Supervisor(s):	Dr Katherine Morel & Prof Christopher Sweeney
Suitable for:	PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Radioligand therapy (RLT), which targets the prostate specific membrane antigen (PSMA), is a recent development in the treatment of metastatic castration resistant prostate cancer. The limiting factor in RLT is to keep the absorbed dose to normal tissue low while delivering high absorbed doses to cancer cells. Strategies to reduce damage to normal tissues are key to more effective PSMA-targeted RLT. Elevated oxidative stress is observed more frequently in cancer cells than in normal cells. It is therefore expected that additional exposure to a low level of reactive oxygen species will push cancer cells toward death, whereas normal cells might maintain redox homeostasis through adaptive antioxidant responses. This would allow for lower radiation doses to be used, reducing toxicity in normal tissues. We aim to investigate the ability of pro-oxidative compounds to increase efficacy of RLT in prostate cancer and understand the underlying mechanisms of this effect.

This project will involve a range of techniques which may include molecular biology and cloning (qPCR, primer design, PCR sequencing, bacterial work, cell line modification), protein analysis (western blotting, ELISA), histology (IHC and IF analysis of tissues) and microscopy. This project will utilise multiple models of prostate cancer, including animal models, 3D organoids and 2D cell lines.

Candidates are required to have a first-class Honours or Master's qualification, ideally with experience working in a molecular wet-laboratory research environment. Candidates working on this project may be required to register as a radiation worker.



Proposed mechanism of action for modulation of radioligand therapy (RLT) by DMAPT: Pro-oxidant compound, DMAPT, sensitises cancer cells to RLT, in part, by maintaining Keap1 in a reduced state and enhancing its interaction with PGAM5 and Bcl-xL, resulting in degradation of Bcl-xL in mitochondria. In contrast, DMAPT protects normal cells against radiation via oxidation of Keap1 and release of the Nrf2 transcription factor for activation of mitochondrial antioxidant enzymes.

For more information about this project contact:

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Supervisor Researcher Profiles

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https://researchers.adelaide.edu.au/profile/christopher.sweeney

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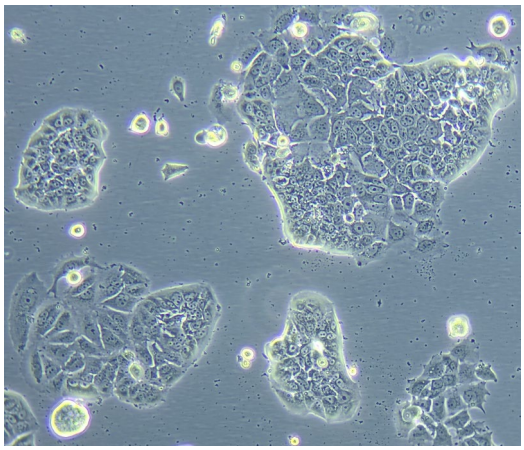
Project Title:	**Role of NF-kB-mediated therapy resistance in estrogen receptor positive breast cancer**
Project Supervisor(s):	Dr Mark Bunting & Prof Christopher Sweeney
Suitable for:	Hons, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

NF-kB hyperactivation has previously been shown to promote breast cancer progression. Mechanistically, one way this can occur is through loss of tristetraprolin (TTP), an RNA binding protein that regulates mRNA stability, including NF-kB, and is commonly lost in late stage cancers. Estrogen receptor positive breast cancer can initially be responsive to standard-of-care therapies but later develop resistance, leading to cancer recurrence and poor survival outcomes for patients. We hypothesise that loss of TTP and hyperactivation of NF-kB activates pathways involved in therapy resistance and can be targeted with NF-kB inhibitors to re-sensitise tumour cells to therapeutic intervention.



MCF-7 estrogen receptor (ER) positive breast cancer cell line shown growing in 2D culture. This cell line will be used to model NF-kB activation together with loss of TTP in ER+ breast cancer.

This project will investigate the efficacy of NF-kB inhibitor treatment of estrogen receptor positive breast cancer using in vitro and in vivo models.

The project will involve a range of techniques which may include molecular biology and cloning (primer design, PCR, qPCR, sequencing, bacterial work, cell line modification), protein analysis (western blotting, ELISA), histology (IHC and IF analysis of tissues), microscopy, and flow cytometry. This project will utilise multiple models of breast cancer, including animal models, 3D organoids and 2D cell lines.

Candidates are required to have a first-class Honours or Master's qualification, ideally with experience working in a molecular or cancer biology wet-laboratory research environment.

For more information about this project contact:

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Supervisor Researcher Profiles

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https://researchers.adelaide.edu.au/profile/christopher.sweeney

Project Title:	Bioinformatic investigation of mRNA degradation in cancer
Project Supervisor(s):	Dr Kristen Feher, Dr Kimberley Clark & Prof Christopher Sweeney
Suitable for:	Summer placement, Hons, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

mRNA are precursors to proteins but the amount of mRNA is not tightly correlated to the amount of corresponding protein. mRNA degradation is one of multiple mechanisms behind this phenomenon, and is mediated by RNA binding proteins (RBP) that target AU-rich elements (ARE) in the 3' untranslated regions of mRNA. One such RBP is tristetrapolin (TTP), which regulates NF-kB stability and is commonly lost in late stage cancers.

This project will use bioinformatics to investigate the role of mRNA degradation in rewiring cell signalling and its contribution to treatment resistance, senescence and metastatis. It will also investigate the role of RBPs such as TTP in the regulation of mRNA degradation.

The project will involve analysis of public and in-house data, including gene expression, RNA and protein sequence, spatial transcriptomics, image analysis, flow cytometry.

Candidates are expected to have a First Class Honours or Master's qualification. The ideal candidate will have a strong quantitative background, such as Bioinformatics, Mathematics, Statistics, Computer Science or Physics. Students with a wet laboratory background may also be suitable, depending on their prior bioinformatics experience and interest. Please contact Dr Kristen Feher to discuss suitability for this project.

For more information about this project contact:

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Supervisor Researcher Profiles

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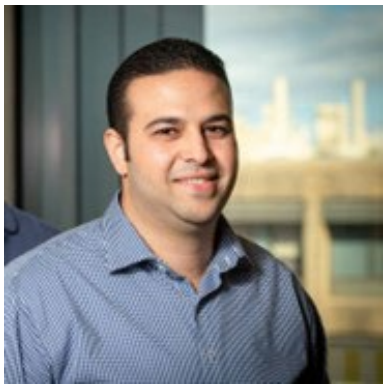
https://researchers.adelaide.edu.au/profile/kimberley.clark
https://researchers.adelaide.edu.au/profile/christopher.sweeney

Projects in Tumour Inflammation & Immunotherapy

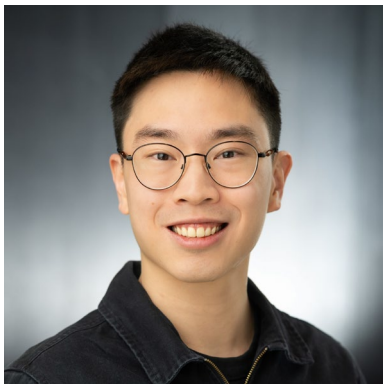
Cancer and Immune Signalling Laboratory

Prof Brendan Jenkins
Group Leader



Dr Mohamed Saad
Research Fellow

Dr Ruby Dawson
Research Fellow



Dr Joshua Chey
Research Fellow

The projects undertaken in our group combine molecular biological and genetic approaches in pre-clinical disease models, together with human translational studies, to identify the mechanisms by which key regulators of the innate immune system promote the pathogenesis of inflammation-associated cancers of the stomach, lung and pancreas.

Key molecular targets of innate immunity include:

- pattern recognition receptors (e.g. toll-like receptors, cytosolic DNA sensors)
- inflammasomes
- ADAM and iRhom family proteases
- cytokine signalling pathways (e.g. interleukin (IL)-6 cytokine family, JAK-STAT axis)

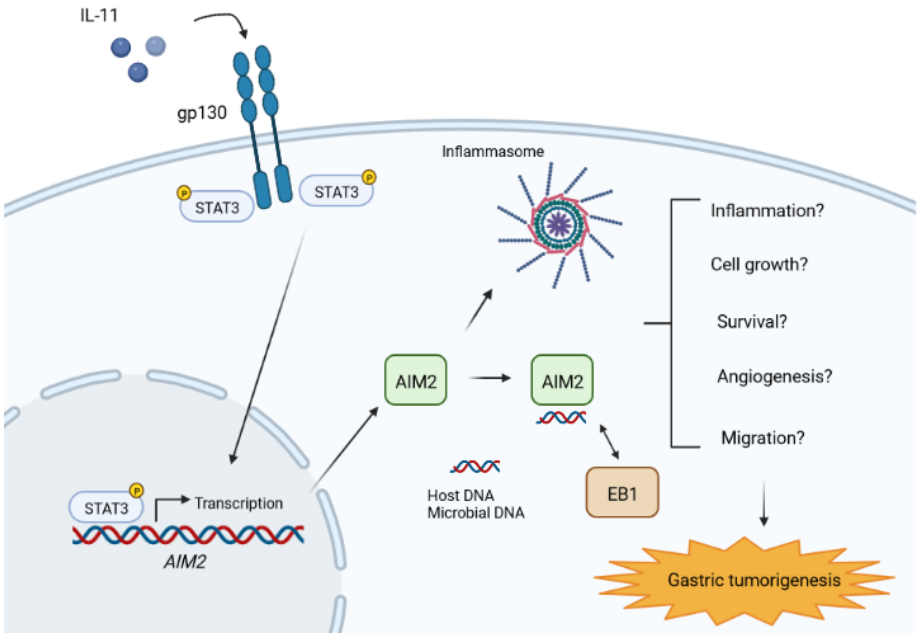
The research team is led by Professor Brendan Jenkins, who is a leading international authority on innate immunity and cancer, impacting on multiple fields (oncology, immunology, gastroenterology, respiratory medicine).

Projects Available in the Cancer and Immune Signalling Laboratory

Project Title:	**Identification of novel immune regulators in stomach (gastric) cancer**
Project Supervisor(s):	Prof Brendan Jenkins, Dr Ruby Dawson
Suitable for:	Hons, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Stomach (gastric) cancer is among the most common cancers worldwide, and is strongly linked with a deregulated immune response, leading to chronic inflammation. However, the identity of regulators of the innate arm of the immune system with oncogenic potential in the stomach remains largely unknown.



Schematic overview of the cross-talk between the IL-11/JAK-STAT3 cytokine signalling cascade and the AIM2 pattern recognition receptor in promoting gastric cancer.

Using preclinical genetically engineered and xenograft mouse models for gastric cancer, we aim to identify and understand how novel immune regulators (pattern recognition receptors, inflammasomes) in the stomach trigger chronic inflammatory and oncogenic responses that lead to gastric cancer.

This project encompasses a wide range of molecular and cell biological and genetic approaches (including CRISPR/Cas9).

Ideal candidates will have at the least a Bachelor's or first-class Honours degree in the broad biomedical science discipline, ideally with experience in a molecular wet-laboratory research environment. Candidates must also have a willingness to work with animal models.

For more information about this project contact:
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Supervisor Researcher Profiles
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https://researchers.adelaide.edu.au/profile/ruby.dawson

Project Title:	**The role of innate immune regulators in pancreatitis and pancreatic cancer**
Project Supervisor(s):	Prof Brendan Jenkins, Dr Mohamed Saad, Dr Joshua Chey
Suitable for:	Hons, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Pattern recognition receptors (PRRs) are key molecules of the innate immune system that recognise microbial- and/or host-derived products to trigger the inflammatory response.

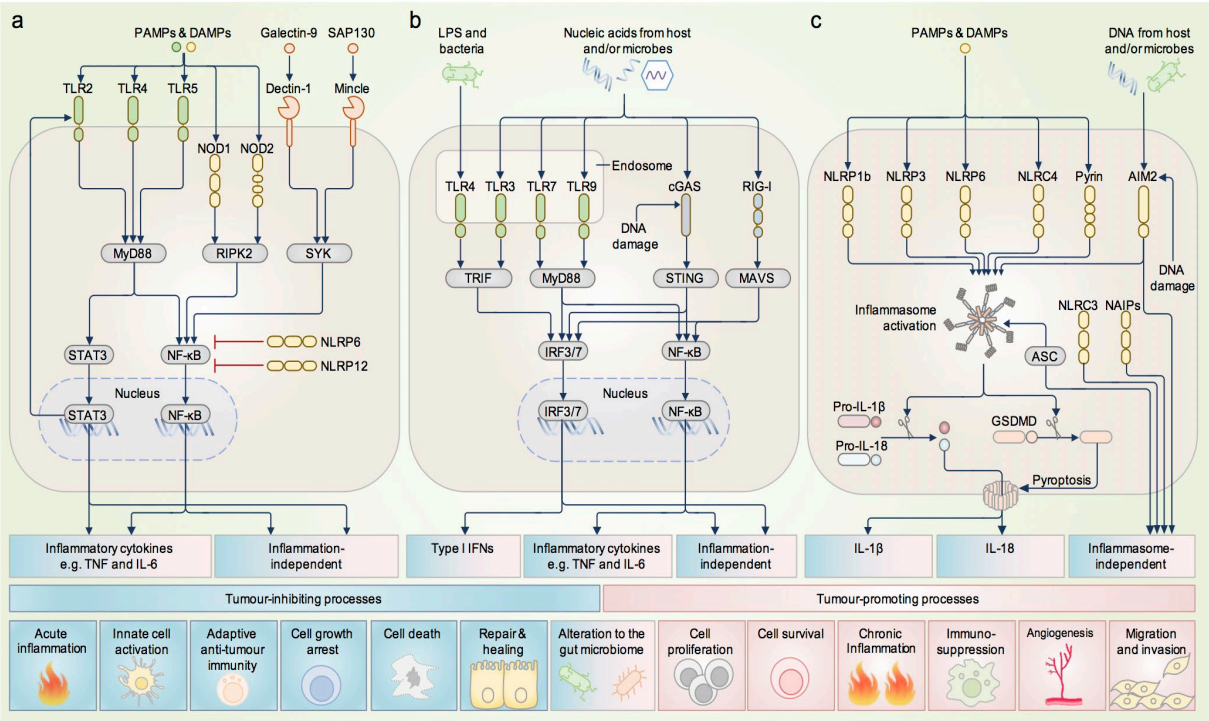


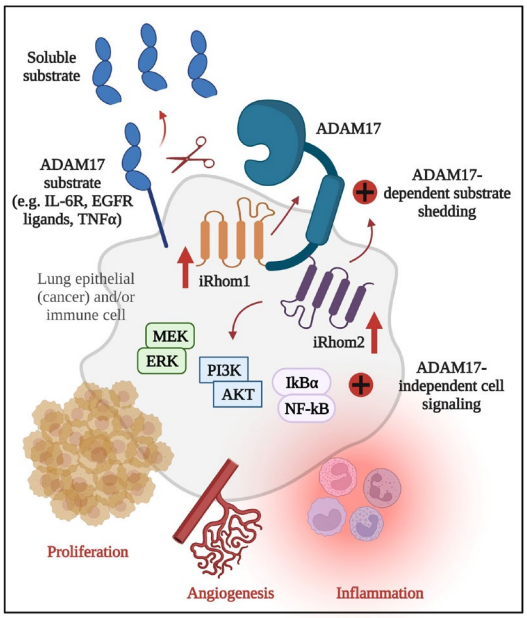
Figure 1

Pattern recognition receptors orchestrate diverse cellular processes relevant to cancer development and progression. a | Membrane-bound Toll-like receptors (TLRs) sense numerous pathogen-associated molecular patterns (PAMPs) and damage- associated molecular patterns (DAMPs) released by dying or tumour cells. The cytoplasmic nucleotide-binding oligomerization domain-like receptors (NLRs) NOD1 and NOD2 can sense peptidoglycan of bacteria. The C-type lectin receptors dectin 1 and Mincle can sense PAMPs but also tumour-associated molecular patterns. These pattern recognition receptors signal via their respective adaptor proteins MyD88, RIPK2 and SYK, and activate the transcription factors NF-κB and STAT3, coordinating the production of inflammatory cytokines (for example, TNF and IL-6) and type I interferons that stimulate inflammatory or non-inflammatory processes. Some NLRs, such as NLRP6 and NLRP12, inhibit NF-κB signalling and suppress inflammation. b | Endosomal TLRs, the DNA sensor cGAS and the RNA sensor RIG-I activate their respective adaptors TRIF, MyD88, STING or MAVS, and via the transcription factors interferon regulatory factor 3 (IRF3), IRF7 or NF-κB trigger inflammatory or non-inflammatory processes. c | The cytosolic NLRs pyrin and absent in melanoma 2 (AIM2), via the adaptor protein ASC, form inflammasome complexes to induce proteolytic cleavage of pro-IL-1β, pro-IL-18 and gasdermin D (GSDMD). AIM2, NLRC3, members of the NLR family, apoptosis inhibitory proteins (NAIPs) and ASC also have inflammasome-independent functions in cancer.

This project aims to understand the molecular basis by which specific PRRs promote pancreatic cancer, one of the most lethal and aggressive cancers in the world that is strongly linked with a dysregulated immune response.

The project will also investigate the mechanisms by which the iRhom (rhomboid-like pseudoprotease) family of proteases, recently implicated in inflammatory conditions, contributes to pancreatitis and pancreatic cancer.

This research employs preclinical genetically engineered and xenograft (including patient-derived) mouse models, as well as translational studies using our large collection of biobanked pancreatic cancer patient samples. Such research will ultimately assist identifying genes for potential use as biomarkers for targeted therapy.



Schematic diagram of ADAM17 biological activity and its regulation by the iRhom pseudoproteases. Also shown are downstream signalling pathways activated and the pro-tumourigenic cellular processes.

Ideal candidates will have at the least a Bachelor's or first-class Honours degree in the broad biomedical science discipline, ideally with experience in a molecular wet-laboratory research environment. Candidates must also have a willingness to work with animal models.

For more information about this project contact:
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Supervisor Researcher Profiles
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https://researchers.adelaide.edu.au/profile/mohamed.saad
https://researchers.adelaide.edu.au/profile/yuchinnjoshua.chey

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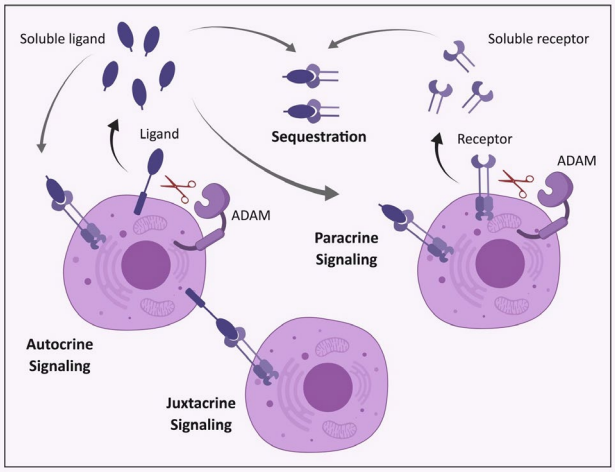
Project Title:	**Identification of immune system regulators as therapeutic targets in lung cancer**
Project Supervisor(s):	Prof Brendan Jenkins, Dr Mohamed Saad
Suitable for:	Hons, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

iRhoms and ADAMs are key protease families whose role in the immune system and inflammation-associated cancers remain poorly defined.

This project studies the role of the ADAM and iRhom families of proteases as key upstream oncogenic regulators in the lung. This will fully elucidate the mechanistic basis by which ADAM and iRhom family proteases can influence lung carcinogenesis, and in doing so also identify how they potentially impact on innate immune responses triggered by pattern recognition receptors.



Modes of action of ectodomain proteins. Schematic representation of the various autocrine, paracrine and/or juxtacrine modes of action by which biologically active processed ADAM17 substrates (i.e., ectodomains) act on cells.

This project employs a combination of *in vivo* lung cancer mouse models (genetically engineered, xenograft - including patient-derived), CRISPR gene editing and clinical biopsies to foster translation, as well as a vast range of molecular and cellular biological techniques.

Ideal candidates will have at the least a Bachelor's or first-class Honours degree in the broad biomedical science discipline, ideally with experience in a molecular wet-laboratory research environment. Candidates must also have a willingness to work with animal models.

For more information about this project contact:
Prof Brendan Jenkins
The University of Adelaide
Email: brendan.jenkins@adelaide.edu.au

Supervisor Researcher Profiles
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https://researchers.adelaide.edu.au/profile/mohamed.saad

Projects in Tumour Inflammation & Immunotherapy

Biomaterials and Immune Engineering Laboratory (BIEL)

Dr Yannan Yang
Group Leader

Dr Moustafa Mabrouk
Postdoctoral Researcher

Dr Than Loc Nguyen
Postdoctoral Researcher

BIEL aims to leverage state-of-the-art biomaterials and nanotechnology-based approaches to modulate immune systems and create translational immunotherapy strategies with improved therapeutic efficacy and minimised adverse effects.

Our laboratory is specifically interested in designing and fabricating biocompatible nanoparticles, hydrogels, scaffolds and cell/bacteria derived biomimetic materials with immunomodulatory activities and controlled drug release profiles for engineering immunity. We stand at the materials-bio interface and investigate how biomaterials at different scales (nano, micro and bulk) can interact with bio-systems and tumour microenvironments, and how these interactions can be further controlled to benefit the outcome of immunotherapy that aims to prevent and treat cancer.

Projects Available in the Biomaterials and Immune Engineering Laboratory

Project Title: **Nanotechnology-based in situ vaccines for cancer immunotherapy**

Project Supervisor(s): Dr Yannan Yang, Dr Moustafa Mabrouk & Dr Than Loc Nguyen

Suitable for: Hons, M Phil, PhD

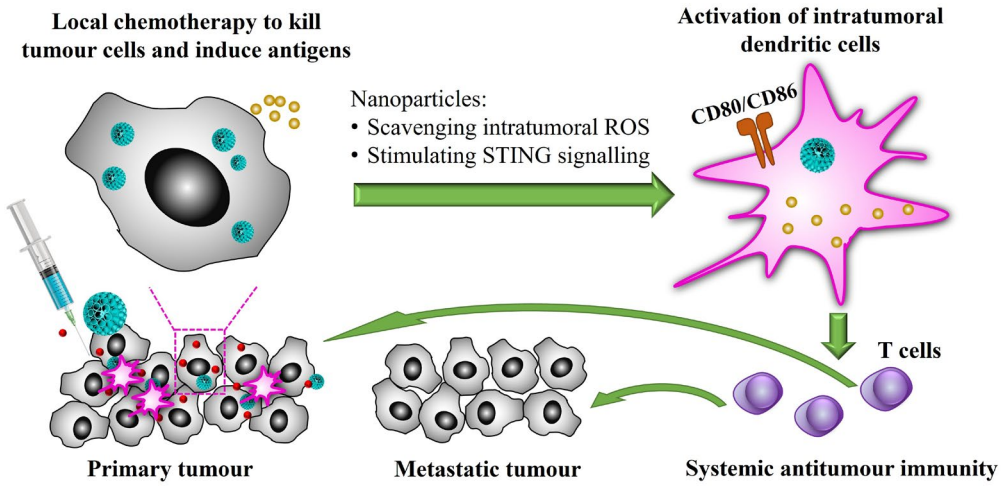
Location of project: Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

In situ cancer vaccines are a new type of vaccination strategy. It reshapes the tumour microenvironment and converts the tumour burden into tumour antigens to evoke adaptive immune response against tumours. As in situ vaccines harness a patients'

own tumours as the source of antigens, the tumour heterogenicity can be largely overcome. In situ cancer vaccines can be utilised as a neo-adjuvant therapy in clinical settings to eradicate metastatic tumours and reduce the recurrence rate after primary treatments such as surgery. In addition, as in situ vaccines are a local treatment which mostly uses an intra-tumoural administration route, the toxicity in normal tissues and other adverse effects can be largely mitigated. However, the limited immune response generated by in situ vaccinations remains a major bottleneck that hinders their clinical translation.

This project aims to develop nanotechnology based in situ vaccines by fabricating novel nanoparticles with a range of activities, including activation of stimulator of interferon genes (STING), reshaping immunosuppressive tumour microenvironment for tumour immunotherapy. We will further investigate and maximise the synergy between nanomaterials and drugs to evoke robust anti-tumour immunity. It is envisioned that the outcomes from this research program will provide a new solution to address the bottleneck that accounts for the numerous clinical failures of in situ vaccines, with the potential to attract industry interest for translation of the vaccine nanotechnology.



Schematic illustration of the working mechanism of the nanotechnology-based in situ vaccine: a local chemotherapy strategy for inducing systemic antitumor immunity.

The skills/techniques you will learn by doing this project include:

- Nanomaterials fabrication and characterisation
- Bioanalysis (Flow cytometry, Confocal imaging, Western-blot, etc.) on nanomaterials-cell interactions
- Establishing in vivo tumour models
- Performance and biosafety evaluation of vaccines in animal models

Candidates with skills, experience, or educational backgrounds in biomaterial fabrication, nanobiotechnology, immunology/immunotherapy, pharmaceutics or cancer biology are preferred to undertake this project.

For more information about this project contact:

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Supervisor Researcher Profile

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https://researchers.adelaide.edu.au/profile/thanhloc.nguyen

Projects in Tumour Inflammation & Immunotherapy

T Cell Immunotherapy Laboratory

Dr Mara Zeissig
Group Leader

Dr Tamsin Lannagan
Research Fellow

Immunotherapy has revolutionised the way we treat cancer. Immunotherapies such as CAR T cell therapy or immune checkpoint inhibitors all harness the ability of cytotoxic T cells to recognise and kill tumour cells. However, approximately 80% of solid cancer patients do not respond to immunotherapy.

The T Cell Immunotherapy Laboratory is focused on understanding how cancers evade the immune system to identify new ways to enhance response to immunotherapy. In particular, we work on cancers that are addicted to the oncogene KRAS such as lung, colorectal and pancreatic cancers. We utilise a range of tools including genetically engineered preclinical models of cancer, analysis of immune cell subsets and molecular biology techniques. We also harness large-scale genetic screening using CRISPR-Cas9 technology to find previously unknown targets and mechanisms that regulate response to immunotherapy.

Projects Available in the T Cell Immunotherapy Laboratory

Project Title: **Boosting response to immunotherapy in lung and pancreatic cancers**

Project Supervisor(s): Dr Tamsin Lannagan & Dr Mara Zeissig

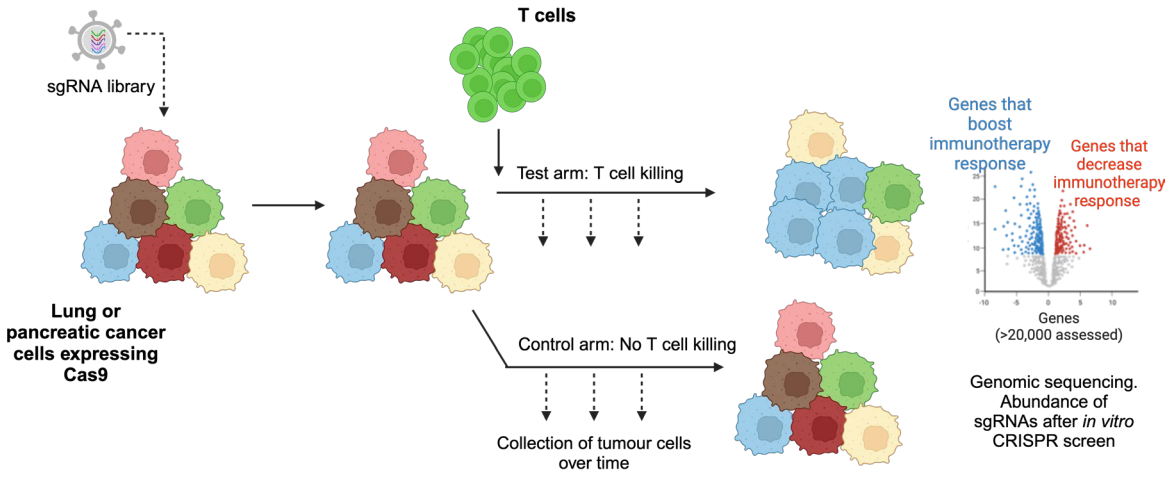
Suitable for: M Phil, PhD

Location of project: Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Lung and pancreatic cancers are two of the most commonly diagnosed cancers and have very poor survival outcomes. They are characterised by immune-cold tumours, with poor infiltration of cytotoxic T cells and a lack of response to immunotherapy.

This project will use unbiased, whole-genome CRISPR-Cas9 genetic screening, in combination with T cell co-culture to identify new targets that could enhance the response of these tumours to immunotherapy. New drug targets identified in the screens will be characterised in vitro and in vivo to assess the effects on tumour growth, immune infiltration and response to immunotherapy. Potential new drug combination therapies will also be tested in mouse models of lung and pancreatic cancers.



New drug targets to increase response to immunotherapy will be identified by co-culturing lung or pancreatic cancer cell lines (expressing Cas9 and harbouring sgRNAs that target the whole genome) with tumour-killing T cells and conducting an unbiased whole-genome CRISPR-Cas9 screen.

The student will learn a range of techniques, including in vivo modelling, CRISPR-Cas9 gene editing, cell culture, flow cytometry, next-generation sequencing, immunohistochemistry and qPCR.

Candidates are expected to have a First-class Honours or Masters degree in biomedical science and ideally have wet-lab experience. Candidates should also be willing to work with animal models of cancer.

Project Title:	**KRAS inhibitors for the treatment of pancreatic cancer**
Project Supervisor(s):	Dr Tamsin Lannagan & Dr Mara Zeissig
Suitable for:	Honours, M Phil, PhD
Location of project:	Adelaide Health & Medical Sciences Building, North Terrace, Adelaide

Project outline

Pancreatic cancer is the 4th biggest cancer killer in Australia. Almost all (95%) pancreatic cancers are driven by mutations in the oncogene KRAS. In the past few

years there has been the introduction of a new class of drugs that target KRAS. In clinical trials, KRAS inhibitors are only effective in a small number of patients but present a new therapeutic option that is targeted and has fewer side effects.

Tumour heterogeneity is a potential underlying driver of poor treatment response. KRAS-mutant pancreatic cancer has multiple genetic subtypes, with mutations in tumour suppressor genes such as TP53, CDKN2A, SMAD4 and ARID1A, frequently co-occurring with KRAS. Importantly, the effect of these mutations on response to KRAS inhibitors is poorly understood.

This project will focus on identifying resistance mechanisms and improving the efficacy of KRAS inhibitors for the treatment of pancreatic cancers. It will use genetically engineered mouse models to study the effect of the KRAS-mutant pancreatic cancer genetic subtype on tumour biology and response to therapies.

The student will learn a variety of techniques, including in vivo modelling, CRISPR/Cas9 genetic editing, cell culture, in vitro drug assays, flow cytometry and immunohistochemistry.

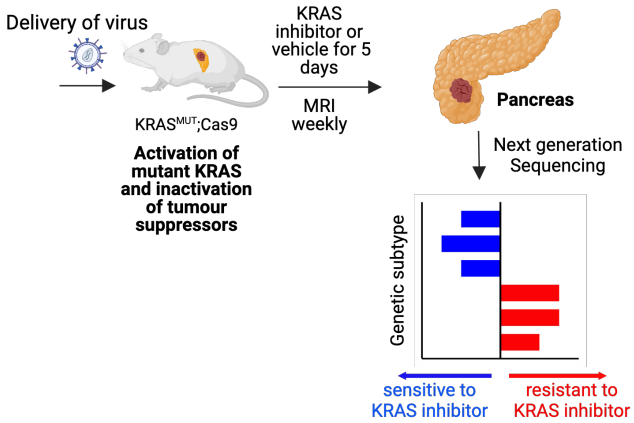


Figure 1. *In vivo* CRISPR-Cas9 screen to identify KRAS mutant subtypes resistant or sensitive to KRAS inhibitors

Lentiviral vectors harbouring guide RNAs targeting tumour suppressor genes will be delivered into the lungs of KRAS mutant;Cas9 mice. This drives the expression of mutant KRAS and the inactivation of tumour suppressor genes encoded for by the gRNAs, recapitulating the genetic subtypes observed in patients. These mice will be used to conduct an in vivo CRISPR-Cas9 screen to identify pancreatic cancers resistant or sensitive to KRAS inhibitors.

Candidates will have a Bachelors, First-class Honours or Masters degree in biomedical science and ideally have wet-lab experience. Candidates should also be willing to work with animal models of cancer.

For more information about these projects contact:

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Supervisor Researcher Profiles

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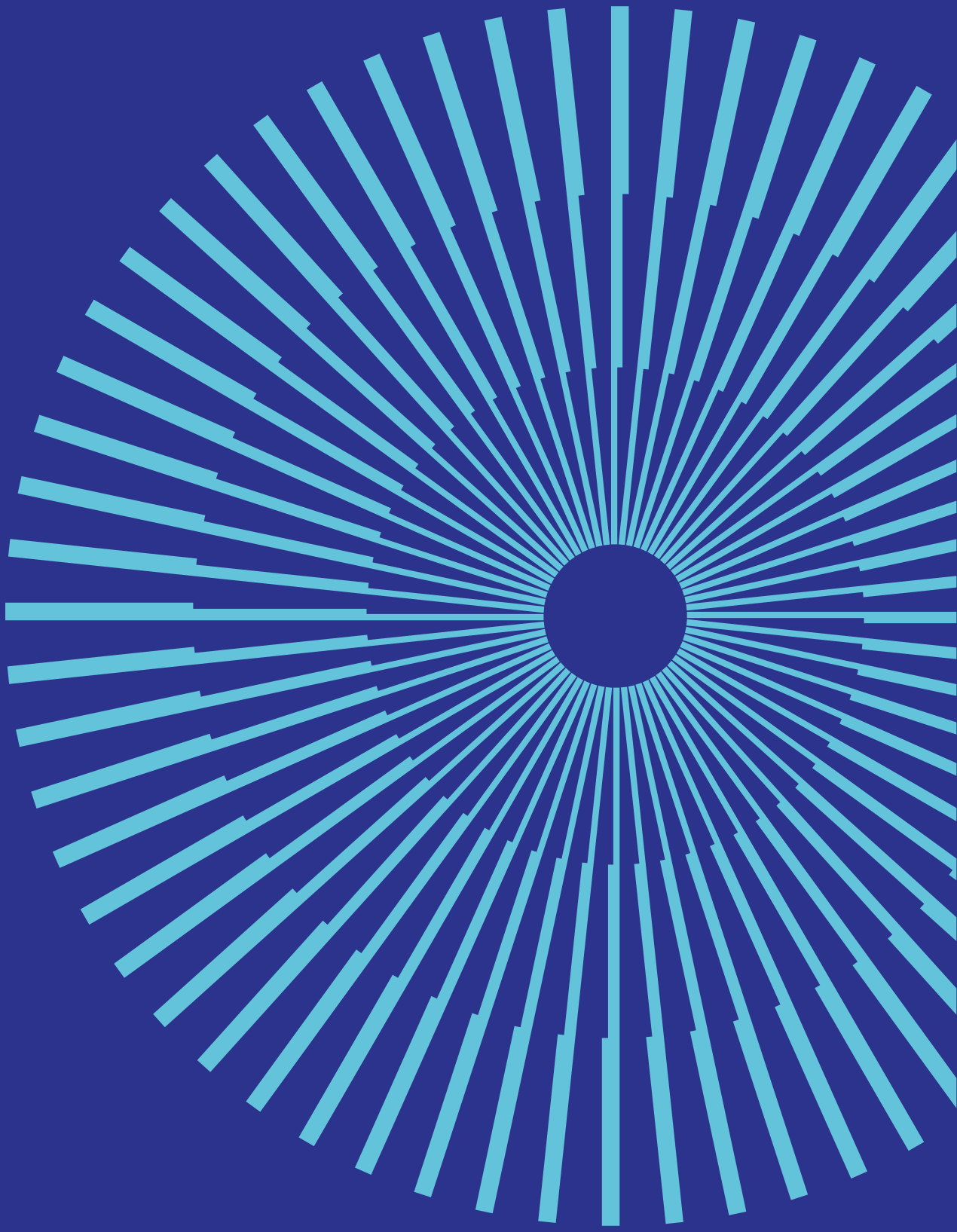

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