



THE UNIVERSITY OF
MELBOURNE

Faculty of Medicine, Dentistry
and Health Sciences

School of Biomedical Sciences

BIOM30003 - Biomedical Science Research Project

Undergraduate Research in the
Department of Biochemistry and Pharmacology



bio21
institute

General Overview



What is BIOM30003?

BIOM30003 is your opportunity to see what a real research laboratory is like! Students spend a semester working with our internationally regarded researchers in the Department of Biochemistry and Pharmacology. You will work on an exciting, research-based project, where you will learn a multitude of laboratory skills, access state-of-the-art technology, analyse data, think critically and communicate your research. This experience gives students a significant edge for future post-graduate research options in the Department, including Honours and Masters.

What are the entry requirements for BIOM30003?

1. Completed/passed at least 175 points towards their course (any discipline)
2. An average score of 75 or better in relevant second- and third-year subjects. Relevant subjects include those that start with ANAT, BCMB, BIOL, BIOM, CEDB, GENE, MIIM, NEUR, PATH, PHRM, and PHYS.
3. Completing the equivalent of a major in Biochemistry and Molecular Biology or Pharmacology.
4. You are expected to either be taking or have completed a third-year practical subject 'Advanced Techniques in Molecular Science' (BCMB30010), 'Drugs in Biomedical Experiments' (PHRM30009) or an equivalent practical subject in another department. This requirement is waived for students undertaking a computational project (i.e., not lab-based). Instead, students must have skills in a discipline that is relevant to that project (e.g., coding, bioinformatics, maths).
5. Support from a supervisor/laboratory head
6. Approval of the Discipline Coordinator

Note: final selection of students into projects is at the discretion of the laboratory head.

When is BIOM30003 offered?

Either Semester 1, 2 or over the Summer break.

What are the time commitments for BIOM30003?

The projects have flexible arrangements based around 10 weeks of laboratory work with about 80-100 hours of contact in the laboratory (~8-10 hours per week). There are possibilities for more intensive laboratory work either in the vacation period before the start of the semester, during the mid-semester break, during semesters or in Summer with intensive 3- to 4-week projects. The start date should be arranged with the laboratory head and documented on the application form. It is expected that students will spend an additional 80 hours preparing for laboratory work, attending workshops to improve their writing and presentation skills, developing their presentation, and writing their final report for assessment.

How is BIOM30003 assessed?

You will work closely with your laboratory supervisor who will give you feedback early in the project to let you know your progress and give guidance on areas in which you can improve or consolidate your skills. You are expected to submit a 1000-word literature review to your supervisor for feedback at week 4. This is not formally assessed but will form the introduction for your final research report.

Formal assessment includes:

- A 3000-word scientific report structured as a scientific paper (60%) – marked by the coordinators and an academic outside the research group.
- A 12-minute presentation on your research project with 3 minutes of questions (30%).
- Supervisor assessment of performance (10%).



Important information

What are the key dates?

Your time in the laboratory begins at the start of the semester. At the discretion of the supervisor, students may start in the lab prior to the start of semester, but the start date must be documented on the application form.

You will organize with your supervisor what times and days you will work in the laboratory; this may change regularly depending on the experiments you conduct.

Precise dates for submissions will be provided at the start of each semester.

	DUE DATES
Formal start of the semester including: information session, laboratory induction	Week 1
Workshop on developing a literature review	Week 2
Submission of literature review (draft of report introduction)	Week 4
Informal feedback on progress	Week 5
Workshop on presentation skills	Week 8
Workshop on writing skills	Week 9
Laboratory presentation	Week 12
Research report: Draft (informal feedback) Final submission	Friday of Week 12 Friday 11:30 pm of 1st examination week (via Turnitin)

How do I find a project?

Find out about specific research projects on offer in this booklet. Discuss research projects with staff members before applying. To meet staff members, contact them directly by email. You are free to approach different laboratories and supervisors to determine your preferred project but once you have reached an agreement to take a project you are obliged to continue in that laboratory. Considerable work and effort go into preparing projects and bench supervision. Agreements need to be honoured.

Where will my project be located?

Projects are supervised by departmental staff and their PhD students or senior scientists located in the Bio21 Molecular Sciences and Biotechnology Institute or the Medical Building. The Department of Biochemistry and Pharmacology has superb facilities and houses a large number of groups with strong interests in cellular, molecular, structural and chemical biology.

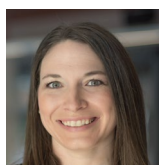
How do I apply?

1. Discuss potential projects with academic supervisors.
2. Complete the Biomedical Science Research Project Application Form – this form must be authorized and signed by the relevant discipline coordinator. <https://biomedicalsciences.unimelb.edu.au/study/current-student-information/biom30003-biomedical-science-research-project>
3. If you would like this subject to count as an elective to your major, please also discuss and get approval from the relevant major coordinator.

4. Add BIOM30003 to your study plan.
5. The form should be emailed to **BiomedSci-AcademicServices@unimelb.edu.au**
6. If the application is approved, you will be enrolled in the subject and sent a confirmation via email.
7. If your application is not approved, you will be contacted via email.

Who can I contact for general advice?

Students can obtain advice from the departmental coordinators for BIOM30003:



Laura Edgington-Mitchell
laura.edgingtonmitchell@unimelb.edu.au



Juliet Taylor
juliett@unimelb.edu.au



Debnath Ghosal
debnath.ghosal@unimelb.edu.au

Guide to projects offered

Researchers in the Department of Biochemistry and Pharmacology work on a large variety of exciting and important research topics. So how can you decide which project to do? We have prepared this visual guide to help you identify which projects you may wish to investigate in more detail. The general themes and techniques employed by our researchers are indicated in the circles below, and the names of respective researchers associated with each theme as indicated:

David Stroud
Justine Mintern
Diana Stojanovski
Malcolm McConville
Jose Villadangos

I want to use CRISPR/Cas9 and MASS SPECTROMETRY to understand complex systems

David Stroud
Justine Mintern
Diana Stojanovski
Elizabeth Hinde

I want to understand the TRAFFICKING AND ASSEMBLY proteins that are essential for our organelles and cells

Stuart Ralph

I want to develop COMPUTATIONAL tools to PREDICT how cancers, genetic and infectious diseases occur

Sequencing Efforts
Resistance Epitopes
Disease Predisposition
Molecular Mech of Genetic Di

Robyn Brown
Jose Villadangos
Elena Schneider-Futschik
Laura Edgington-Mitchell
Justine Mintern

I am interested in DISEASE MODELS and want to develop new THERAPIES to protect us from disease

Michael Griffin
Isabelle Rouiller
Michael Parker

I want to determine the ATOMIC STRUCTURE OF PROTEINS to aid in the design of novel therapeutics

Malcolm McConville
Debnath Ghosal
Michael Parker
Stuart Ralph

I want to develop new drugs to kill PATHOGENS and understand how they develop DRUG RESISTANCE

Elizabeth Hinde
Diana Stojanovski
Debnath Ghosal
Isabelle Rouiller

I want to SEE the dynamics and functioning of our cells and proteins by HIGH-RESOLUTION MICROSCOPY

Michael Parker
Laura Edgington-Mitchell
Robyn Brown
Debnath Ghosal
Isabelle Rouiller
Michael Griffin
David Stroud

I am interested in PROTEINS and how their FUNCTION is involved in the development of diseases

Projects offered

Robyn Brown - Gut-brain mechanisms underlying the negative and positive health outcomes following bariatric surgery	6
Laura Edgington-Mitchell - Validating proteases as biomarkers and therapeutic targets for oral cancer	7
Debnath Ghosal - Deciphering structures of bacterial and viral molecular machines that inject toxins into our cells	8
Michael Griffin - Probing the chaperone mechanisms of small heat-shock proteins	9
Elizabeth Hinde - Imaging transcription factor DNA target search in a living cell	10
Malcolm McConville - Identifying new metabolic drug targets in parasitic protozoa	11
Justine Mintern - Designing effective vaccines to fight infection and tumours	12
Michael Parker - Overcoming cancer drug resistance	13
Stuart Ralph - Protein translation in human malaria parasites as targets for therapeutics	14
Isabelle Rouiller - Understanding how the unfoldase protein p97 functions in health and disease	15
Elena Schneider-Futschik - Cystic fibrosis receptors and inflammation	16
Elena Schneider-Futschik - Cystic fibrosis receptors during developmental stages	17
Diana Stojanovski - Mitochondrial protein biogenesis in health and disease	18
David Stroud - Understanding how mitochondrial machines are built and maintained	19
Jose Villadangos - Harnessing the cells and molecules that initiate adaptive immunity to fight infections, cancer, immunosuppression and autoimmunity	20





Robyn Brown – Gut-brain mechanisms underlying the negative and positive health outcomes following bariatric surgery

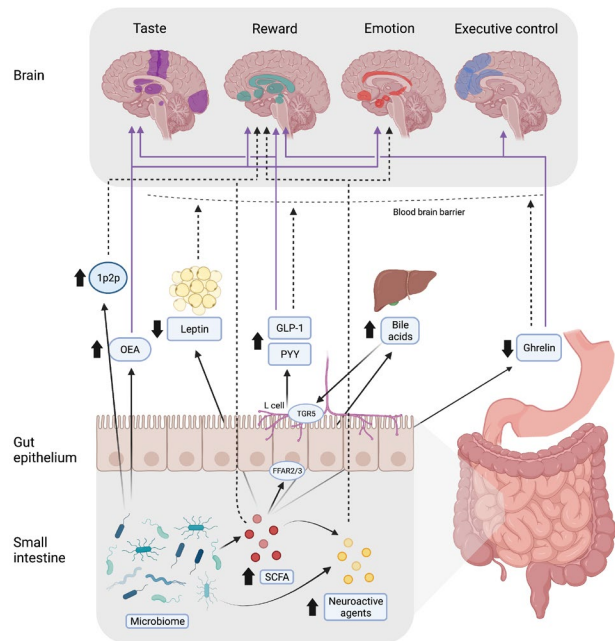
BENCH SUPERVISOR:

Eva Guerrero-Hreins (PhD candidate)

OFFERED:

Semester 1 & 2

Bariatric surgery is remarkably successful as it produces profound and sustained weight loss in combination with metabolic benefits. These benefits are thought to occur via actions on the gut-brain axis which lead to alterations in the neuroendocrine regulation of appetite and glycaemia. Furthermore, the hedonic responses to high-fat, high-sugar foods are dampened after bariatric surgery and decreased levels of compulsive forms of eating behaviour such as emotional eating and binge eating are observed. The precise mechanism responsible for these positive effects on eating behaviour is currently unknown. Evidence is also emerging which shows that subset of patients experience adverse mental health effects, including suicide, self-harm, depression and substance use disorders. The causative and contributing factors behind these adverse effects are not well understood. This project explores the utility of using a mouse model of bariatric surgery to determine the mechanisms underlying the impact of this procedure on affective behaviour including depression-like and anxiety-like behaviour, as well as operant responding for palatable food and drugs of abuse. Neurochemical analysis of brain tissue will investigate the changes in central gut hormones and their receptors potentially responsible for these changes in behaviour.



Techniques used may include:

1. Behavioural models e.g. operant self-administration
2. Surgical techniques
3. Immunohistochemistry
4. Fibre photometry
5. RNAScope

Recent papers from the lab:

Guerrero-Hreins et al., 2021 <https://doi.org/10.1007/s11154-021-09696-4>

Brown et al., 2021 <https://doi.org/10.1038/s41574-021-00520-2>

Contact Dr Robyn Brown to arrange an appointment:

robyn.brown@unimelb.edu.au



Laura Edgington-Mitchell – Validating proteases as biomarkers and therapeutic targets for oral cancer

BENCH SUPERVISORS:

Dr. Laura Edgington-Mitchell

OFFERED:

Semester 1-2

Oral squamous cell carcinoma is the most common head and neck cancer. It is an extremely painful disease for which treatments are limited. Oral cancer often spreads to cervical lymph nodes, and once metastasis occurs, patient survival rates drop below 40%. Current methods to predict the spread of oral cancer are ineffective; thus, most patients undergo radical elective neck dissection to remove all cervical lymph nodes prior to the appearance of metastatic lesions.

Our laboratory is investigating the contribution of proteases to oral cancer pain and metastasis. Proteases are a large family of enzymes that function as tiny molecular scissors to cut proteins. This process facilitates protein degradation and turnover, but also contributes to many cellular signalling events that underlie the growth and metastasis of oral cancer.

We are applying innovative proteomics techniques to identify novel protease substrates and improve our mechanistic understanding of how proteases contribute to health and disease. This project aims to validate recently identified protease substrates and explore their function. This knowledge is essential for validating proteases as drug targets for the treatment of this deadly disease.

Techniques used may include:

1. Protease activity assays
2. In vitro culture of oral cancer cells
3. Protein biochemistry (SDS-PAGE, western blotting)
4. Confocal microscopy
5. Histological evaluation of cancer tissue
6. Proteomics

Recent papers from the lab:

Anderson et al., *Biochemistry* 2020

Anderson et al., *Sci Rep* 2020

Mountford et al., *ACS Chem Biol* 2020

Tu et al. *J Neurosci* 2021

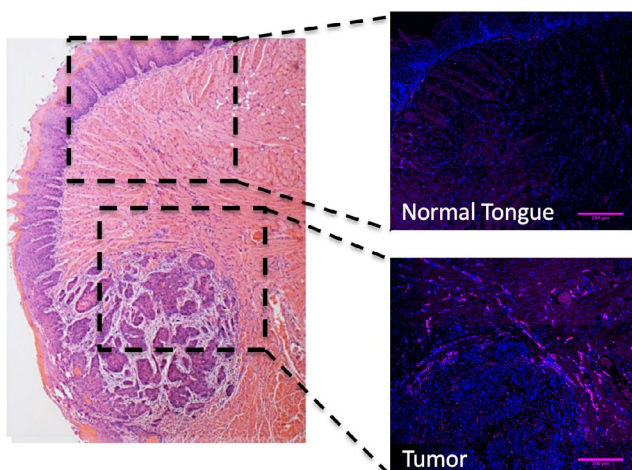
Tu et al. *Cancers* 2021

Contact Dr Laura Edgington-Mitchell to arrange an appointment:

laura.edgingtonmitchell@unimelb.edu.au

Oral Squamous Cell Carcinoma

Protease/Nuclei





Debnath Ghosal – Deciphering structures of bacterial and viral molecular machines that inject toxins into our cells

BENCH SUPERVISOR:

Debnath Ghosal

OFFERED:

Semester 2 and Summer

Bacteria harbour at least nine different types of secretion systems to transfer macromolecules across cellular envelope. These are sophisticated multi-protein nanomachines that secrete myriads of substrates including proteins, nucleoprotein complexes and variety of small molecules and are central to pathogenesis of multiple human diseases. For example, many pathogenic bacteria utilize the Type III Secretion System (T3SS) to cause diseases such as dysentery (*Shigella*), typhoid (*Salmonella*), plague (*Yersinia*) etc. Other human pathogens employ the Type IV Secretion System (T4SS) to mediate gastric cancer (*Helicobacter*), brucellosis (*Brucella*), typhus and spotted fevers (*Rickettsia*), as well as Legionnaires' disease (*Legionella*). The T4SS is also associated with the spread of antibiotic resistance, which currently presents a major threat to public health. Therefore, these molecular machines are attractive targets for drug development to enrich our present repertoire of antibiotics. Structural studies with these molecular machines are extremely challenging due to their large number of components, flexibility and tight integration into the bacterial cell envelope

Electron cryotomography (cryo-ET) has unrivalled power to visualize the native structure of macromolecules *in situ*. In recent years, improvement in software, detectors and subvolume averaging methods have allowed us to investigate macromolecules *in situ* at subnanometer resolution. We are harnessing this unique power of cryo-ET and combining it with correlative light and electron microscopy (CLEM), and Focused Ion Beam (FIB) milling to elucidate the structure and function of different bacterial injection modules at molecular resolution.

Techniques used may include:

1. Bacterial and mammalian cell culture
2. Protein biochemistry (SDS-PAGE, western blotting)
3. Host-pathogen interaction
4. 3D atomic structure determination (cryoelectron microscopy, X-ray crystallography)
5. Electron cryotomography

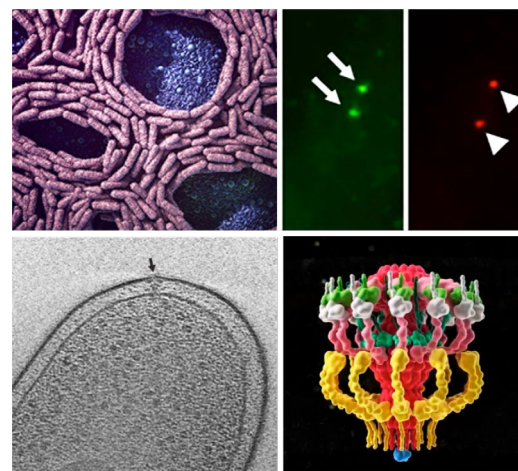
Recent papers from the lab:

Ghosal et al, *Nature Microbiology*, 2019a

Ghosal et al *Nature Microbiology*, 2019b

Contact Dr Debnath Ghosal to arrange an appointment:

debnath.ghosal@unimelb.edu.au





Michael Griffin – Probing the chaperone mechanisms of small heat-shock proteins

BENCH SUPERVISOR:

TBA

OFFERED:

Semester 2 and Summer

Protein misfolding and amyloid fibril formation is implicated in debilitating diseases such as Alzheimer's disease, Parkinson's disease, dementia and type II diabetes. Our lab is interested in how small molecules and molecular chaperones modulate amyloid formation. Small heat-shock proteins (sHsps) are a class of molecular chaperones that are well known to inhibit amyloid formation. However, the mechanisms by which sHsps inhibit this process are poorly understood. Many existing studies have focused on investigating how sHsps interact with proteins prior to their aggregation, however sHsps have also been shown to bind to preformed aggregates. We have previously shown that this binding may induce the formation of larger inclusion body-like aggregates, which are thought to be less toxic. We have also recently discovered that sHsps inhibit the elongation and naturally occurring end-to-end joining of amyloid fibrils and that this may occur via a specific interaction between sHsps and the ends of amyloid fibrils.

We are therefore interested in determining how sHsps interact with amyloid fibrils. Specifically, this project aims to investigate how effectively various wild-type and mutant forms of sHsps interact with amyloid fibrils. Students will analyse the rates of amyloid fibril formation, and the sizes

of amyloid fibrils formed and how these parameters are affected by wild-type and mutant forms of sHsps.

Techniques used may include:

1. Protein expression and purification
2. Protein biochemistry such as gel electrophoresis
3. Analysis of reaction rates
4. Analytical ultracentrifugation
5. Electron microscopy

Recent papers from the lab:

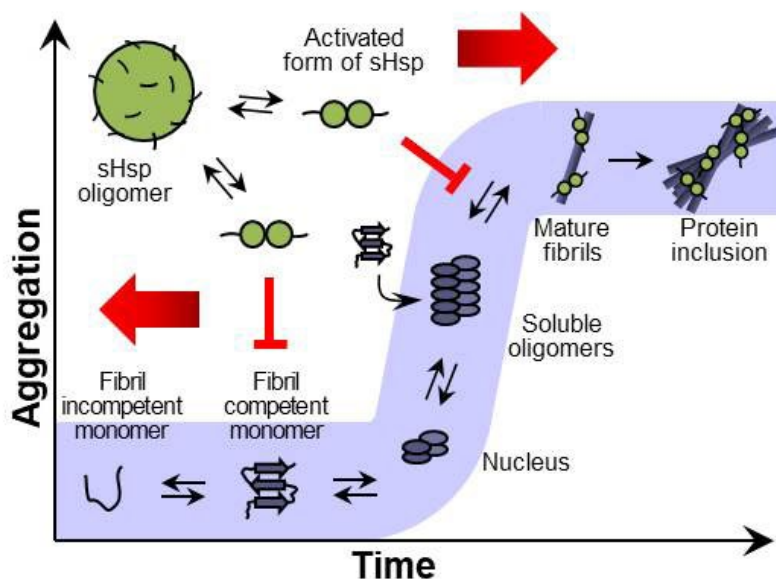
Cox D et al., *J Biol Chem* 2016

Todorova et al., *Biochemistry* 2017

Scott DJ et al., *Sci Rep* 2018

Contact Assoc Professor Michael Griffin to make an appointment:

mgriffin@unimelb.edu.au





Elizabeth Hinde – Imaging transcription factor DNA target search in a living cell

BENCH SUPERVISOR:

Dr. Jieqiong Lou and Dr. Elizabeth Hinde

OFFERED:

Semester 2 and Summer

Transcription factors have evolved DNA target search strategies that allow them to efficiently navigate the nuclear space and arrive at their specific DNA sequence. This target search strategy is underpinned by molecular diffusion, which in turn is controlled by the architectural organisation of the cell nucleus and oligomeric state of the transcription factor. Until recently no imaging approach could track the molecular mobility of protein oligomers within the nuclei of live cells. To address this research gap, we recently established a new microscopy method to image the transport and binding dynamics of different oligomeric species in live cells. The overall aim of this project is to use this technology to uncover how the spatial compartmentalisation of the cell nucleus regulates transcription factor complex formation and DNA target search in a living cell.

Techniques used may include:

1. Cell culture of the HeLa cell line.
2. Preparation of expression vectors, including GFP vectors.
3. Cell transfection.
4. Confocal laser scanning microscopy of transfected cells.
5. Fluorescence correlation analysis of molecular diffusion within microscopy data.

Recent papers from the lab:

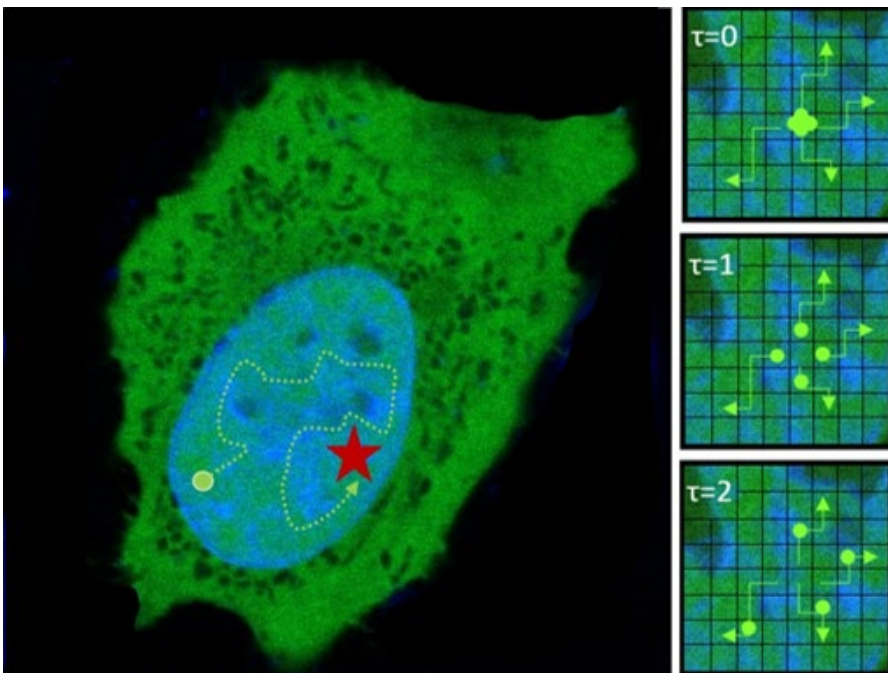
Hinde E et al., *Sci Rep* 2015

Hinde E et al., *Nat Comm* 2016

Hinde E et al., *Nat Nanotech* 2017

Contact Dr Elizabeth Hinde to arrange an appointment:

elizabeth.hinde@unimelb.edu.au





Malcolm McConville – Identifying new metabolic drug targets in parasitic protozoa

BENCH SUPERVISORS:

TBA

OFFERED:

Semester 2

Protozoan parasites cause a number of important human diseases including malaria, toxoplasmosis, and leishmaniasis, that collectively infect more than a third of the world's population. As current drug treatments for these diseases are inadequate or are being undermined by the emergence of resistant strains there is an urgent and ongoing need to identify new therapeutic targets. We have developed a dual approach for drug target identification. The first approach involves the systematic detection of all metabolic pathways that active in relevant parasite stages using mass spectrometry-based metabolite profiling and stable isotope labelling studies. Genetic studies (i.e CRISPR/Cas9) are then used to determine the role of novel or up-regulated metabolic pathways in pathogenic stages. In the second approach, we first use high through-put screening approaches to identify new compounds that kill relevant parasite stages and then define the mode of action of top hits using metabolomic approaches. These approaches have led to the identification of new metabolic pathways in all of these parasites, as well as potential lead inhibitors that will be further characterized in these projects.

Techniques used include

1. Cell culture (parasite and mammalian host cells)
2. Metabolomic profiling and stable isotope labelling approaches
3. CRISPR/Cas9 gene knock-out studies in Leishmania and Plasmodium
4. Enzyme assays on parasite cell extracts and recombinant proteins
5. Live-cell metabolic analysis (Seahorse XF platform)

Recent papers from the lab:

Saunders et al., *Molecular Microbiology* 2018

Kloehn J et al., *Curr Opin Microbiol* 2016

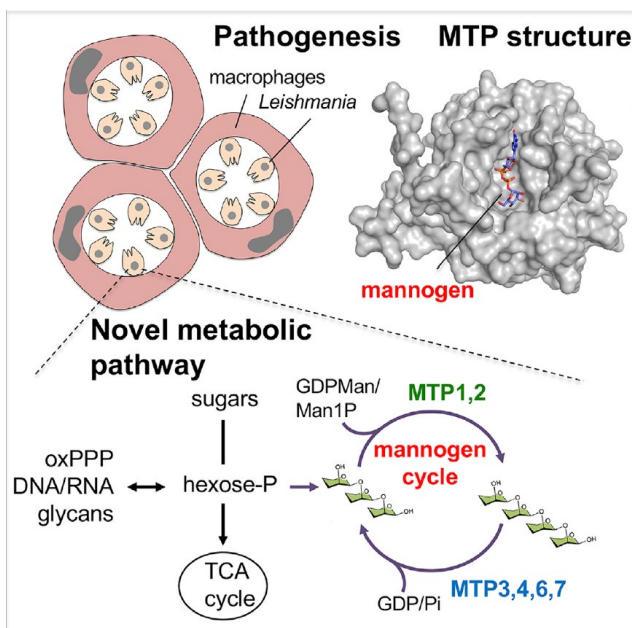
Uboldi et al., *Cell Host Microbe* 2015

Blume et al., *Cell Host Microbe* 2015

Sernee et al. *Cell Host Microbe* 2019

Contact Professor Malcolm McConville to arrange an appointment:

malcolmm@unimelb.edu.au





Justine Mintern – Designing effective vaccines to fight infection and tumours

BENCH SUPERVISORS:

TBA

OFFERED:

Semester 2

Vaccination currently represents the most effective strategy for eliminating infectious disease. While many vaccines are in use worldwide, for several pathogens our current vaccines fail with ensuing uncontrolled disease. This is the case for HIV, malaria and tuberculosis resulting in disease and devastation worldwide. Vaccines also have the potential to prevent and/or treat cancer, however this is currently not a clinical reality. Therefore, vaccine design must be advanced, and to do so, we require a more comprehensive understanding of the cell biology involved. A key question in vaccine biology is how is the antigen cargo delivered to specialised compartments inside immune cells. This project will identify mechanisms of antigen trafficking for effective immunity.

Techniques used may include:

1. CRISPR/Cas9 deletion of genes
2. Preparation of lentiviral vectors
3. Use of bioengineered nanoparticles

4. Isolation of primary cell types
5. Flow cytometry
6. Next generation sequencing
7. Immunoprecipitation, western blotting
8. Proteomics
9. Animal models of immunity and infection

Recent papers from the lab:

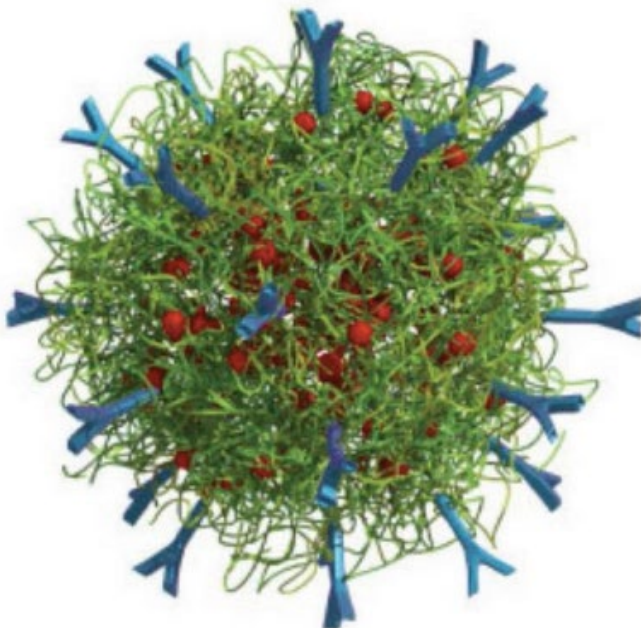
Liu H et al., *J Exp Med* 2016

Liu H et al., *Methods Mol Biol* 2016

Dumont C et al., *Traffic* 2017

Contact Assoc Professor Justine Mintern to arrange an appointment:

jmintern@unimelb.edu.au





Michael Parker – Overcoming cancer drug resistance

BENCH SUPERVISOR:

Dr Claire Weekley

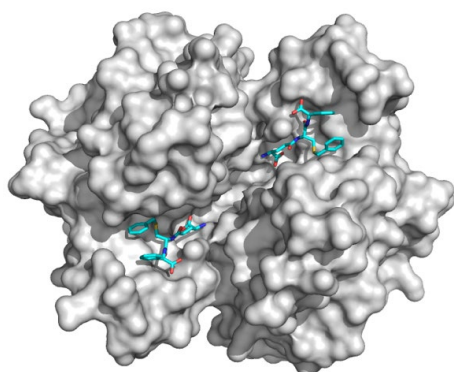
OFFERED:

Semester 2

Conventional cancer chemotherapy kills rapidly growing cells indiscriminately, causing significant side-effects and can lead to disease re-occurrence and resistance to the drugs. One of our interests is the Glutathione S-Transferase (GST) family of proteins that function by recognising foreign small molecule toxins in the body, causing them to be eliminated from the cell. Unfortunately, commonly used anti-cancer drugs are also recognised as toxic by GST, which is often overexpressed in cancer tissues and is associated with transformation to malignancy and the adaptive resistance to anti-cancer drugs. There is thus an urgent need for the design of new anti-cancer drugs that circumvent the development of GST-mediated resistance to treatment. Very recently, there has been an increasing interest in the development of metal-based drugs as effective and potent protein targeted chemotherapies. We are investigating, through structural and biochemical means, how a range of ruthenium, arsenic and osmium-based drugs and drug-like compounds interact with GSTs. Students will investigate how these compounds work, as well as any drug-like molecules we develop, using X-ray crystallography and a range of biophysical techniques.

Techniques used may include:

1. Protein expression.
2. Protein purification.



3. Protein characterisation (circular dichroism, differential scanning fluorimetry, dynamic light scattering, analytical ultracentrifugation, mass spectrometry).
4. 3D atomic structure determination (X-ray crystallography, cryo electron microscopy, synchrotron).
5. Protein-drug interactions (surface plasmon resonance, isothermal calorimetry, microscale thermophoresis, nuclear magnetic resonance spectroscopy, computational docking).
6. Structure-based drug discovery (virtual screening, fragment screening, computer-aided drug design).

Recent papers from the lab:

Baell JB et al., *Nature* 2018

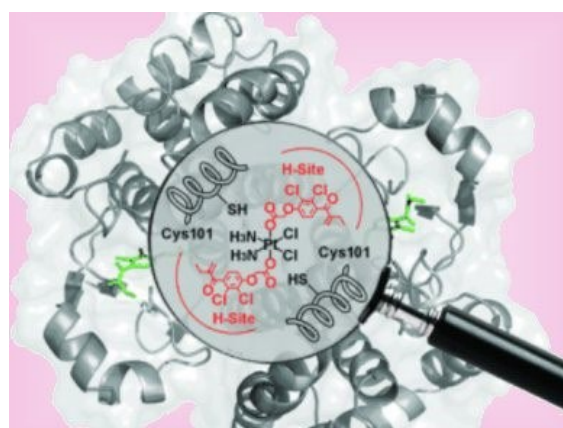
Broughton SE et al., *Nature Commun* 2018

De Luca A et al., (2019) *Proc. Natl. Acad. Sci. USA* **116**, 13943-13951

Koach J et al., (2019) *Cancer Res.* **79**, 5652-5667.

Contact Professor Michael Parker to arrange an appointment:

mwp@unimelb.edu.au





Stuart Ralph – Protein translation in human malaria parasites as targets for therapeutics

BENCH SUPERVISORS:

Stuart Ralph, Dr Emma McHugh

OFFERED:

Semester 2 and Summer

Our laboratory is interested in the characterization of potential drug targets in the malaria parasite *Plasmodium falciparum*. Several anti-malarial drugs in clinical use act against the protein translation machinery, validating this as a target for therapeutic intervention. We are particularly interested in the aminoacyl tRNA synthetases (ARS) family of enzymes, which are responsible for attaching amino acids to their cognate tRNA.

Our laboratory uses biochemical, bioinformatic, molecular, and cell biological techniques to characterize *Plasmodium* enzymes as drug targets we need to be able to assay the activity of purified enzymes. To do this we will overexpress *Plasmodium* tRNA synthetases in *E. coli*, fused to a tag that facilitates their subsequent purification. We will perform kinetic assays for these enzymes, and microscopy to determine the subcellular localisation of tagged tRNA synthetases within parasites. We will also perform inhibitor assays to determine the growth response of parasites to inhibitors of tRNA synthetases.

Techniques used may include:

1. CRISPR/Cas9 manipulation of parasite genome
2. Bacterial protein overexpression and purification
3. Enzyme assay of malaria tRNA synthetases
4. Microscopy of *in-vitro* grown malaria parasites
5. Drug assays for *in-vitro* grown malaria parasites
6. Computational prediction of drug mode of action
7. Computational analysis of enzyme evolution
8. Bioinformatic prioritization of drug targets

Recent papers from the lab:

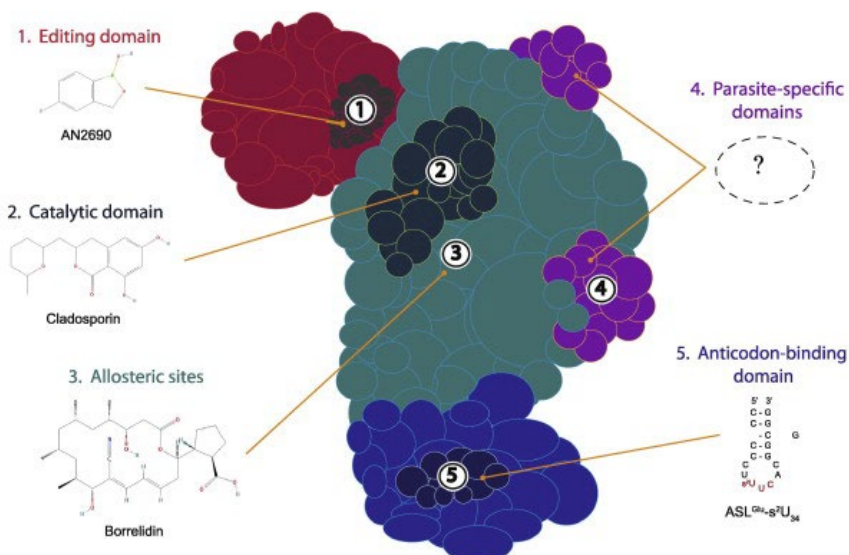
Goodman CD et al., *Trends Parasitol* 2016

Wong W et al., *Nat Microbiol* 2017

Yeoh LM et al., *BMC Genomics* 2017

Contact Assoc Professor Stuart Ralph to arrange an appointment:

saralph@unimelb.edu.au





Isabelle Rouiller – Understanding how the unfoldase protein p97 functions in health and disease.

BENCH SUPERVISORS:

TBA

OFFERED:

Semesters 2 and Summer

Cells need to efficiently discard unwanted proteins to stay alive and healthy. Improper protein degradation leads to numerous diseases including Alzheimer and Parkinson. In these neurodegenerative diseases, improperly folded proteins accumulate as aggregates in brain and muscle cells instead of being degraded. Inhibition of protein degradation is also a strategy for killing unwanted cells such as cancer cells, and invading bacteria and protozoa.

We are interested in the molecular mechanisms by which an abundant and essential protein, named p97, unfolds unwanted proteins. To do this, we use a combination of structural biology approaches (mainly cryo-EM) and biochemical assays. Students undertaking this project will take assess how p97 functions in human, mycobacteria or protozoa at the molecular level, using a combination of protein science, biochemical assays, cryo-EM and computational approaches.

Techniques used may include:

1. Single particle electron microscopy.
2. Protein structure analysis.
3. Protein expression and purification.
4. Biochemical and biophysical assays.
5. Proteomics.

Recent papers from the lab:

Makarkov et al., *Npj Vaccines* 2019

Alsahafi et al., *Cell Host & Microbe* 2019

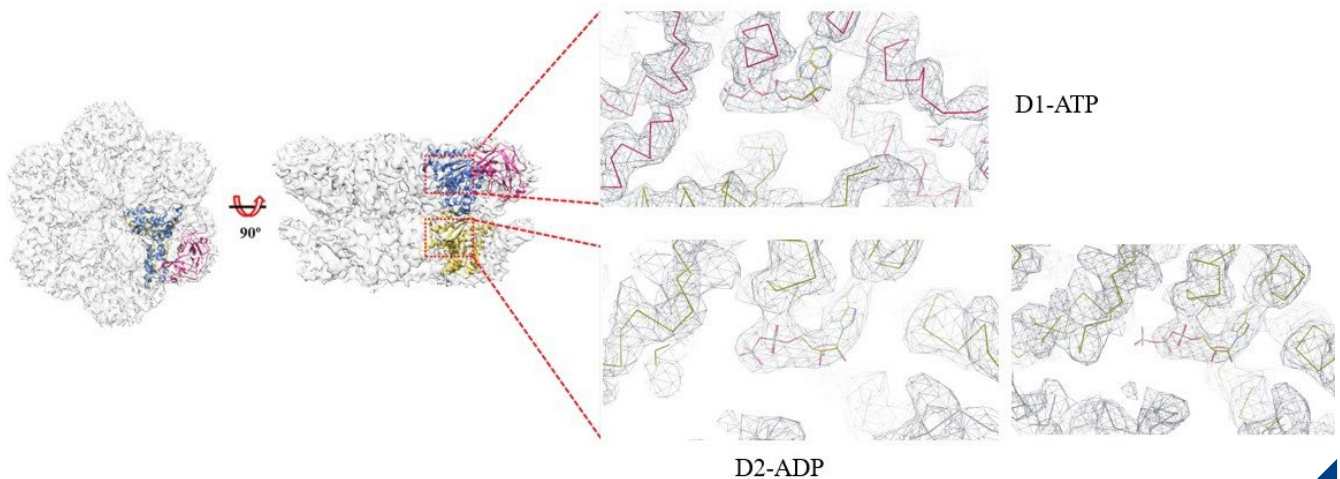
Carlson et al., *eLife* 2018

Lindsay et al., *Vaccine* 2018

Fabre et al., *J Biol Chem* 2017

Contact Assoc Professor Isabelle Rouiller to arrange an appointment:

isabelle.rouiller@unimelb.edu.au





Elena Schneider-Futschik – Cystic fibrosis receptors during developmental stages

BENCH SUPERVISORS:

Fiona Qiu (PhD student), Dr Elena Schneider-Futschik

OFFERED:

Semester 2

The cystic fibrosis modulators (called caftors) have transformed clinical outcomes for many patients with cystic fibrosis (CF) by improving survival and general health. However, the much greater prevalence of CF women reaching childbearing age means increasing numbers of women taking these medications face very difficult decisions when it comes to having a family. This study will aid clinicians in prescribing -caftor modulators to pregnant women on how these drugs will transfer across essential barriers during different developmental stages.

Techniques used may include:

1. Analytical quantifications techniques.
2. Drug entry and distribution studies.
3. Immunohistological analysis.
4. Animal models of cystic fibrosis and pregnancy

Recent papers from the lab:

Qiu et al., *ACS Pharmacol. Transl. Sci.* 2020

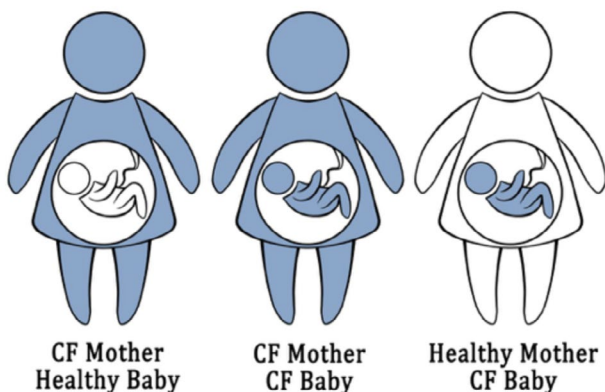
Schneider-Futschik, *Gene Ther.* 2019

Masson et al., *J Cyst Fibros.* 2019

Schneider et al., *ERJ Open Res.* 2018

Contact Dr Elena Schneider-Futschik to arrange an appointment:

elena.schneider@unimelb.edu.au





Elena Schneider-Futschik – Cystic fibrosis receptors and inflammation

BENCH SUPERVISORS:

Dr Andrew Jarnicki (co-supervisor), Dr Elena Schneider-Futschik

OFFERED:

Semester 2

In this study, we will correlate the functional manifestations of cystic fibrosis (CF) with pathological changes in histopathology; and investigate whether administration of ivacaftor, the first CF gene modulator that has significantly improved the life of patients with CF; is beneficial in improving inflammation.

Techniques used may include:

1. Immunohistochemistry
2. Immunoprecipitation, western blotting.
3. Imaging
4. Analytical quantifications
5. Animal models of immunity and infection.

Recent papers from the lab:

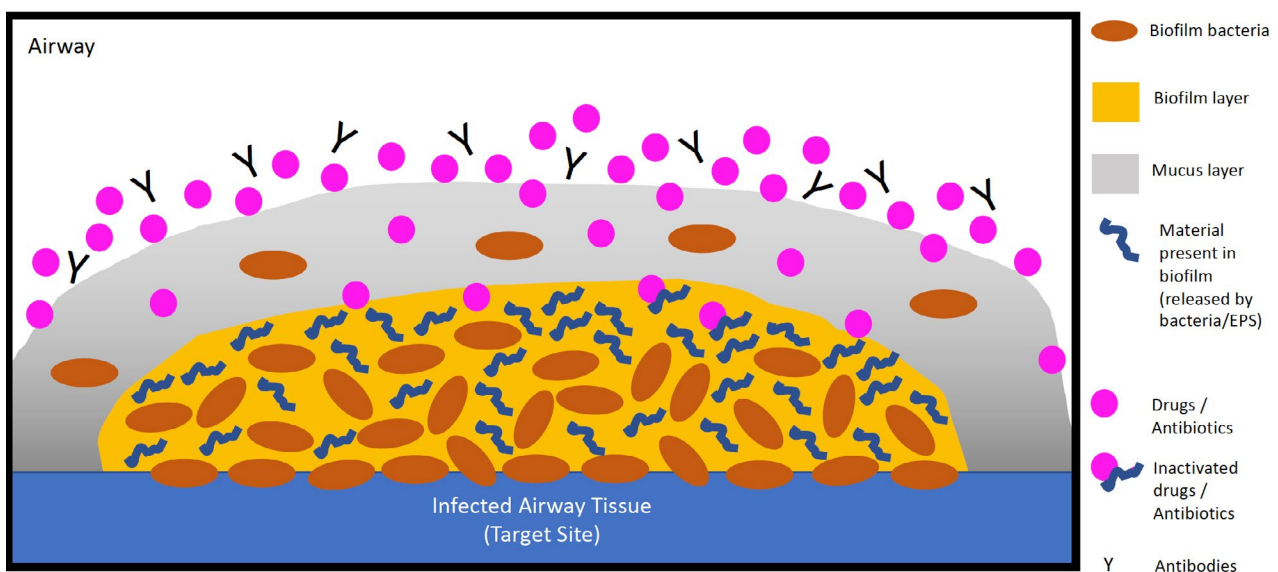
Reyes-Ortega et al., *ACS Pharmacol. Transl. Sci.* 2020

Schneider-Futschik *Gene Ther.* 2019

Masson et al., *J Cyst Fibros.* 2019

Contact Dr Elena Schneider-Futschik to arrange an appointment:

elena.schneider@unimelb.edu.au





Diana Stojanovski – Mitochondrial protein biogenesis in health and disease

BENCH SUPERVISORS:

TBA

OFFERED:

Semester 1 and 2

Mitochondria are dynamic organelles that play a central role in diverse aspects of cell biology, including ATP production, regulation of metabolic processes and apoptosis. Mitochondrial function is dependent on the 1200 proteins that reside within mitochondria, but are nuclear-encoded. The biogenesis of these proteins is highly regulated and involves: (i) synthesis on cytosolic ribosomes; (ii) targeting and import into mitochondria through dynamic and multimeric machines known as translocases; and (iii) folding and assembly into complexes.

The Stojanovski lab investigates how protein biogenesis events are executed in human cells and how their dysregulation leads to mitochondrial disease, a group of long-term, genetic, often inherited disorders that occur when mitochondria fail to produce enough energy for the body. We do this by using state-of-art gene-editing (CRISPR/Cas9) and proteomics tools. Creation of cell models of disease and biochemical interrogation of these models allows us to uncover molecular mechanisms of mitochondrial disease to drive downstream therapeutic interventions.

Techniques used may include:

1. CRISPR/Cas9 deletion of genes
2. Tissue Culture
3. Cell fractionation, including mitochondrial isolation
4. Protein Techniques, SDS-PAGE and BN-PAGE
5. Confocal Microscopy
6. Immunoprecipitation, western blotting
7. Proteomics

Recent papers from the lab:

Jackson et al., *PNAS*, 2022

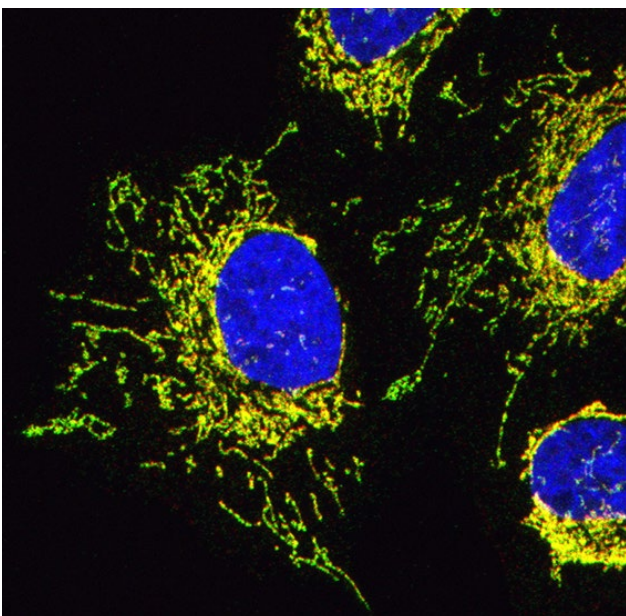
Jackson et al., *Mol. Biol. Cell*, 2021

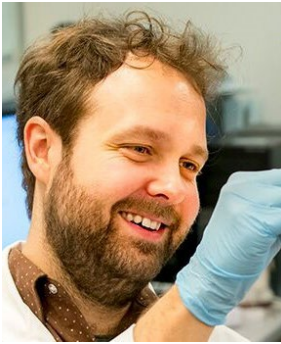
Kang et al., *eLife* 2019

Kang et al., *Molecular Cell*, 2017

Contact Dr Diana Stojanovski to arrange an appointment:

d.stojanovski@unimelb.edu.au





David Stroud – Understanding how mitochondrial machines are built and maintained

BENCH SUPERVISORS:

Dr. David Stroud

OFFERED:

Semester 2

It has been estimated that, even at rest, our bodies turn over ~70kg of ATP each day. More than 90% of this is generated through mitochondrial oxidative phosphorylation, which occurs on the five membrane protein complexes comprising the respiratory chain. Mitochondria are comprised of ~1500 different proteins. Over 80 of these are subunits of respiratory chain complexes and >100 others are needed for their biogenesis and regulation. Several hundred more mitochondrial proteins support energy production indirectly. Surprisingly, we still don't know the functions of ~200 human mitochondrial proteins!

We are interested in nfunctionalize these proteins, and to do this we use state-of-art gene-editing (CRISPR/Cas9) and proteomics tools. Students undertaking this project will take charge of their very own nfunctionalized mitochondrial protein, use CRISPR-Cas9 to generate knockout human cell lines and use these to study the proteins role in mitochondrial function.

Techniques used may include:

1. Tissue culture of mammalian cells
2. Pharmacology including gene-editing with CRISPR/Cas9
3. Fluorescence activated cell sorting
4. Protein electrophoresis techniques and western blotting

Recent papers from the lab:

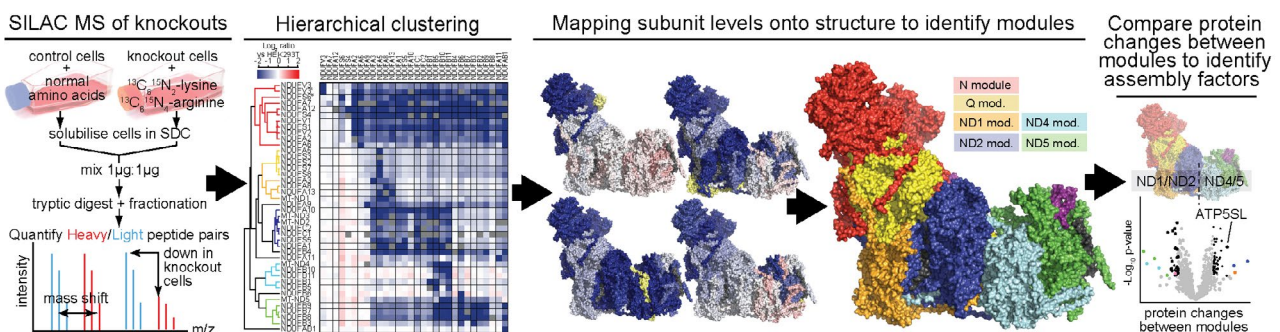
Stroud DA et al., *Nature* 2016

Hock DH et al., *Mol Cell Proteomics* 2020

Zhang et al., *Nature Communications* 2020

Contact Dr David Stroud to arrange an appointment:

david.stroud@unimelb.edu.au





Jose Villadangos – Harnessing the cells and molecules that initiate adaptive immunity to fight infections, cancer, immunosuppression and autoimmunity

BENCH SUPERVISORS:

TBA

OFFERED:

Semester 2

The Villadangos Laboratory studies the cells and molecules responsible for *Antigen Presentation*. This process is central to adaptive immunity, underpinning the initiation, regulation, persistence and termination of every T cell response. Antigen (Ag) presentation entails intracellular processing of foreign, self or tumour components into ligands that are displayed, bound to Major Histocompatibility Complex molecules, on Ag presenting cells. When naïve T cells recognise these Ags they become activated and an immune response ensues. Activated T cells acquire effector functions that also depend on Ag presentation and recognition e.g. the capacity to stimulate or suppress the activity of other immune cells, or ability to kill tumour cells or cells infected with viruses. Ag presentation can also cause inactivation of naïve or effector T cells, a reaction that prevents autoimmunity but can be exploited by tumours to escape immune surveillance. Another outcome of Ag presentation is the formation of memory T cells that protect against re-infections or tumour recurrence.

Understanding antigen presentation will allow us to design new and better vaccines against infections or cancer, boost immunity in immunocompromised patients and inhibit autoimmune and allergic reactions. We use interdisciplinary research to achieve this goal, implementing a research program that covers from the whole organism through intercellular interactions to the molecular level.

Techniques used may include:

1. Cell isolation, culture
2. Flow cytometry
3. Transcriptomics
4. Gene editing (CRISPR/Cas9 technology) in cells and whole organisms
5. Protein chemistry
6. Microscopy
7. Animal models of infection and cancer

Recent papers from the lab:

McWilliam HE et al., *Nat Immunol* 2016

Roquilly et al., *Immunity* 2017

Liu H et al., *J Exp Med* 2017

Contact Professor Jose Villadangos to arrange an appointment:

j.villadangos@unimelb.edu.au

