BIOM30003 - Biomedical Science Research Project

Undergraduate Research in the Department of Biochemistry and Pharmacology
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 postgraduate research options in the Department, including Honours and Masters.

What are the entry requirements for BIOM30003?
1. An average score of 75 or better in relevant second and third year subjects.
2. Completing the equivalent of a major in Biochemistry and Molecular Biology or Pharmacology.
3. 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).

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 1 week mid-semester break during semesters or in Summer with intensive 3-4 week projects. 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 your supervisor and an academic outside the research group.
• A 12-minute presentation on your research project (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. However, students and laboratories may find it useful if you start a week or two earlier to begin the process of learning experimental techniques and methods.

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.

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<td>60% Friday of Week 12 Monday 11:30 pm of 2nd examination week (via Turnitin)</td>
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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. Read the project descriptions in this book and arrange a meeting with the supervisor(s) you are interested in.
2. Obtain a provisional offer in the project by the supervisor.
3. Complete the online application form on the BCMB department website: [https://biomedicalsciences.unimelb.edu.au/study/current-student-information/biom30003-biomedical-science-research-project](https://biomedicalsciences.unimelb.edu.au/study/current-student-information/biom30003-biomedical-science-research-project)
4. Email the form to the departmental coordinators listed below to arrange administrative enrollment procedures.

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:
# Projects offered

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Genomic sequencing is being more routinely used to diagnose patients with genetic diseases, including cancer, and optimise treatment strategies. In order to realise the power of genomic information in clinical settings, we need new tools to rapidly assess the functional impact of novel variants. We have developed a range of computational tools to deconvolute the molecular consequences of coding variants giving rise to different phenotypes and clinical outcomes. The same disease phenotype, in turn, may arise from many different mutations that alter a patient’s outcome or how they may respond to a particular treatment. By analysing these mutations and predicting their effects on protein structure and function we are trying to revolutionise treatment strategies, an important step towards personalised medicine.

We are currently working on a range of diseases including genetic diseases (Alkaptonuria, Urea cycle disorders, VHL), cancer (renal carcinomas, gangliomas, prostate cancer), and drug/vaccine resistance (TB, cancer, malaria, HIV, influenza). These projects will use computational (bioinformatics) approaches to unravel the molecular mechanisms driving these mutations and derive novel predictive methods to guide patient treatment. One of the ultimate goals of these projects will be the development of web servers enabling the rapid analysis of mutations to help guide clinical decisions.

This project will suit students with some familiarity with Linux operating systems and computer coding (Python).

Techniques used may include:
1. Protein structure analysis
2. In silico mutation analysis
4. Webserver development

Recent papers from the lab:
Pandurangan AP et al., Nucleic Acids Res 2017
Pires DEV, Ascher DB. Nucleic Acids Res 2017
Andrews KA, Ascher DB et al., J Med Genet 2018
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.

This mini-project aims to evaluate the activity of key proteases in oral cancer cell lines and tissues from patients. We will evaluate the utility of protease activity as a biomarker for predicting metastasis and as a potential drug target 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

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

Contact Dr Laura Edgington-Mitchell to arrange an appointment:
laura.edgingtonmitchell@unimelb.edu.au
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*, 2019b

Contact Dr Debnath Ghosal to arrange an appointment:
debnath.ghosal@unimelb.edu.au
While viruses are replicating in the cell they use their own proteins to hijack and subvert host cellular processes to avoid detection by the host. Many viruses, including the rabies virus, have few proteins to carry out all these processes, and to do so these proteins must be highly multifunctional. The phospho-protein (P protein) of rabies has over 20 functions ascribed to it. Due to leaky ribosomal scanning, the P protein is produced as five N-terminally truncated isoforms (P1 to P5), and importantly all isoforms do not have the same functions. The isoforms P2 to P5 lack an N-terminal binding site for the viral L protein which is important for replication, and so compared to P1, P2 to P5 are not involved in replication – due to truncation causing a loss of function. Remarkably, however, we have found that truncation does not always result in loss-of-function but also in gain-in-function. For example, truncation of the first 53 residues produces the isoform P3 in which an N-terminal nuclear localization sequence and a C-terminal microtubule association sequence have been activated. These sequences are in P1, but are inactive. We want to understand what are the structural differences between P1 and P3 that result in these functional differences.

Techniques used may include:
1. Bacterial overexpression of protein.
2. Protein purification.
3. Preparation of site-directed mutants.
4. Biophysical methods such as cross-linking and HDX Mass Spectrometry, Isothermal Calorimetry, Circular Dichroism, Fluorescence and Nuclear Magnetic Resonance.

Recent papers from the lab:
Sethi A et al., Nat Commun 2016
Hossain A et al., Cell Reports 2018
Wu F et al., J. Biol. Chem 2020

Contact Professor Paul Gooley to arrange an appointment:
prg@unimelb.edu.au
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:**
- 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
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.
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
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:
- Sernee et al. *Cell Host Microbe* 2019
- 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

### Contact Professor Malcolm McConville to arrange an appointment:
malcolmm@unimelb.edu.au
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:**

Dumont C et al., *Traffic* 2017

**Contact Assoc Professor Justine Mintern to arrange an appointment:**

jmintern@unimelb.edu.au
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, though 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).

**Recent papers from the lab:**

Baell JB et al., *Nature* 2018
Broughton SE et al., *Nature Communs* 2018

**Contact Professor Michael Parker to arrange an appointment:**

mwp@unimelb.edu.au
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
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:
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
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
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

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**BENCH SUPERVISORS:**
Dr Andrew Jarnicki (co-supervisor), Dr Elena Schneider-Futschik

**OFFERED:**
Semester 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 dysfunction is associated with the ageing process and the onset of numerous neurological disorders, including Alzheimer’s and Parkinson’s disease. Mitochondrial function is dependent on the 1000-1500 proteins that reside within one of the four mitochondrial sub-compartments: the outer membrane, intermembrane space, inner membrane and matrix. The cell faces a major conundrum when it comes to the mitochondrial proteome since the majority of proteins localized within mitochondria are encoded in the nucleus. The life or “biogenesis” of these proteins is highly regulated and involves their synthesis on cytosolic ribosomes, targeting to mitochondria, import into mitochondria, folding into the correct 3D structure, assembly into complexes and, once the protein has fulfilled it role turnover for removal of the protein from the system. We are interested in how proteins are trafficked to and within mitochondria and how the mitochondrial proteome is regulated through the interplay of these processes. We used both fungal and mammalian cells systems in our analysis.

Techniques used may include:

1. Tissue culture of mammalian cells
2. Pharmacology
3. Protein Techniques, including SDS-PAGE and Blue-Native PAGE
4. Mitochondrial Isolation
5. Yeast Genetics

Recent papers from the lab:
Kang Y et al., *elife* 2016
Kang Y et al., *Mol Cell* 2017

Contact Dr Diana Stojanovski to arrange an appointment:
d.stojanovski@unimelb.edu.au
Is 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
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