THE UNIVERSITY OF MELBOURNE

Faculty of Medicine, Dentistry and Health Sciences

School of Biomedical Sciences

BIOM30003 - Biomedical Science Research Project

Semester 2 Online Projects

Undergraduate Research in the Department of Biochemistry and Molecular Biology

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 Molecular Biology. 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. 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.
3. You are expected to either be taking or have completed the third year Biochemistry and Molecular Biology practical subject 'Advanced Techniques in Molecular Science' (BCMB30010) or an equivalent practical subject in another department. This requirement may be 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?

These projects are currently offered in Semester 2.
They may be offered over the Summer semester.

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 additional 80 hours in preparing for laboratory work, 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 15-minute presentation on your research project to the laboratory group (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.

	ASSESSMENT	DUE DATES
Formal start of the semester including: laboratory induction		Week 1
Submission of Literature review, informal feedback on progress		Week 4
Laboratory presentation	30%	Week 12
Laboratory performance	10%	End of semester
Research report: Draft (informal feedback) Final submission	60%	Friday of Week 12 Monday 11:30 pm of 2nd 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 will be conducted on-line.

Projects are supervised by departmental staff and their PhD students or senior scientists located in the Bio21 Molecular Sciences and Biotechnology Institute.

You will meet them in regular Zoom meetings and join in the laboratory meetings currently being conducted using Zoom.

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:

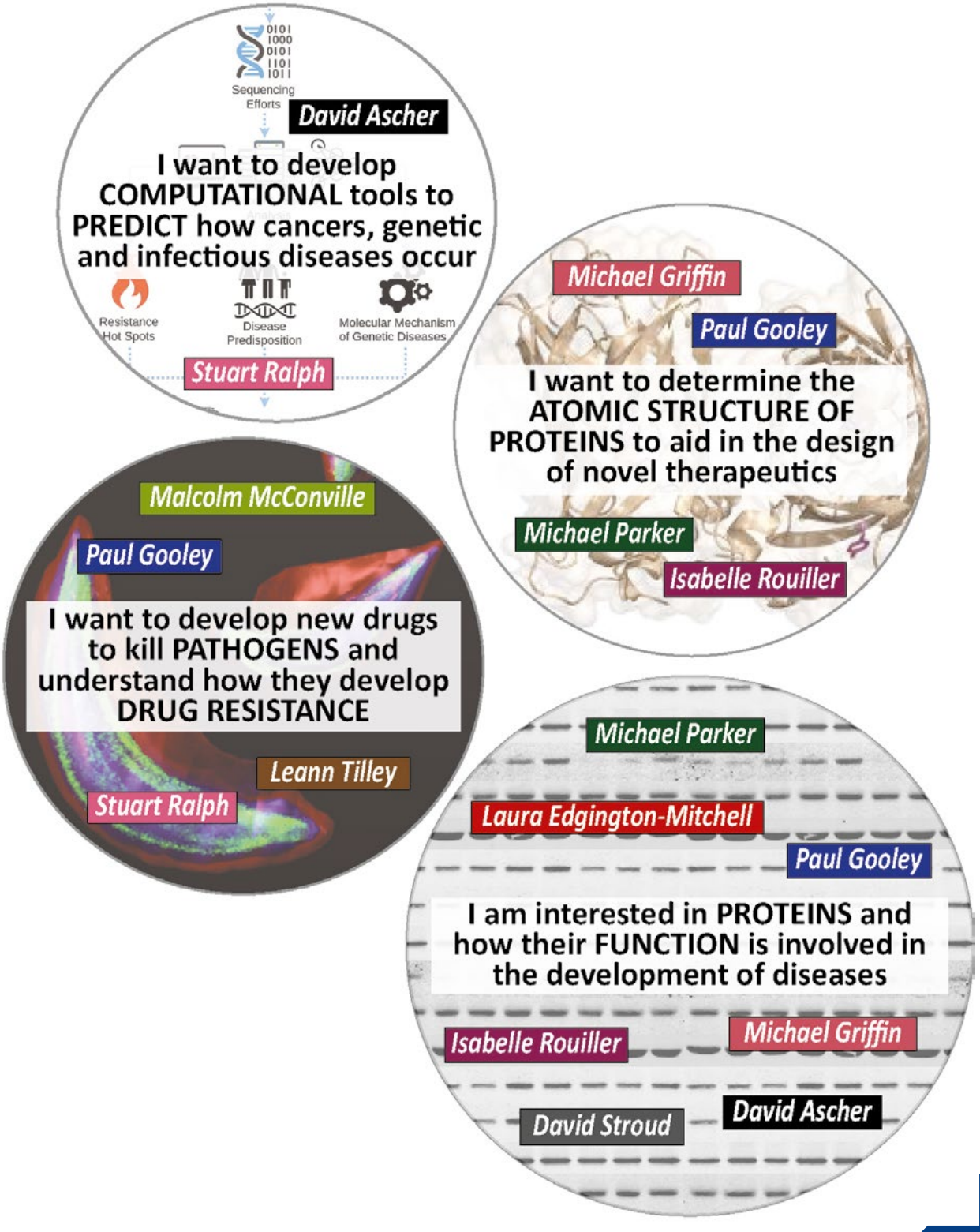
   https://biomedicalsciences.unimelb.edu.au/departments/biochemistry/study/undergraduate-research-training
4. Email the department coordinator, Leon Helfenbaum (**leonh@unimelb.edu.au**), to set up a meeting to arrange administrative enrollment procedures. Please do this as soon as you have completed the application form.

Who can I contact for general advice?

Students can obtain advice from Leon Helfenbaum (**leonh@unimelb.edu.au**), the departmental coordinator for BIOM30003 and coordinator of BCMB30010 'Advanced Techniques in Molecular Science'.

Guide to projects offered

Researchers in the Department of Biochemistry and Molecular Biology work on a large variety of exciting and important research topics. Here are the on-line projects offered by our laboratories this semester. The general themes and techniques employed by our researchers are indicated in the circles below, and the names of researchers associated with each theme is indicated:



Projects offered

David Ascher – Treating the person not the disease	6
Michael Parker – Overcoming cancer drug resistance	7
Stuart Ralph – Protein translation in human malaria parasites as targets for therapeutics	8
Isabelle Rouiller – Understanding how the unfoldase protein p97 functions in health and disease	9

David Ascher – Treating the person not the disease

BENCH SUPERVISOR:
Dr David Ascher

OFFERED:
Semesters 2

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 webservers 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:

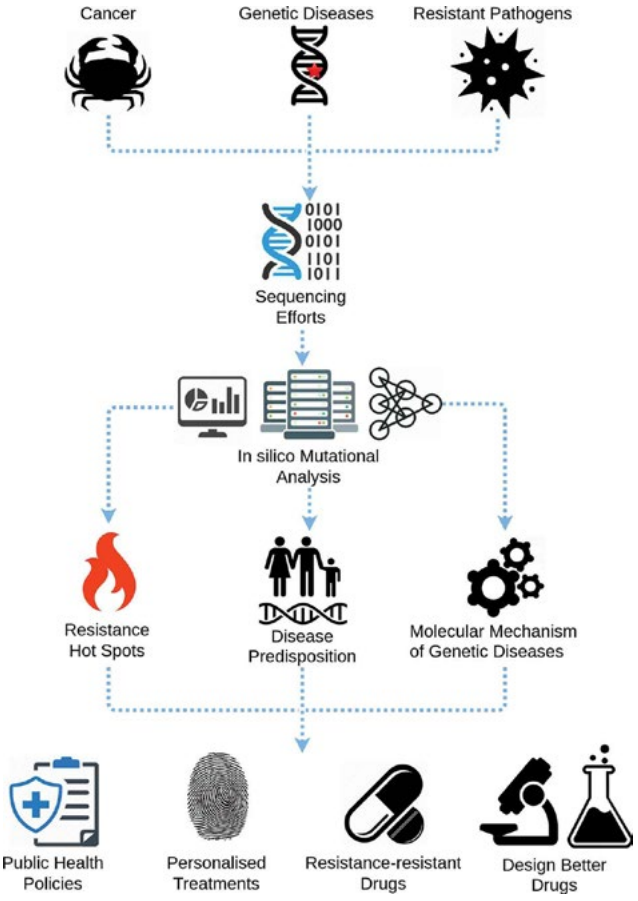
1. Protein structure analysis
2. In silico mutation analysis
3. Machine learning and neural networks
4. Webserver development

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



Contact:

Dr David Ascher to arrange an appointment by Zoom
david.ascher@unimelb.edu.au

Michael Parker – Overcoming cancer drug resistance

BENCH SUPERVISOR:
Dr. Craig Morton and Dr Tracey Nero

OFFERED:
Semester 2

Our primary focus is to understand how proteins function using structural biology and to use this information for drug discovery. As a first step we need to identify proteins that might be involved in particular diseases of interest. Sometime this happens through the work of collaborators or through a critical analysis of publications and online databases. In a recent example we were seeking proteins that might be involved in Alzheimer's disease. We started the process by a thorough search of the literature and online data bases following by a critical analysis of interesting proteins. Did they have a genetic or other validation of being involved in the disease? What does the protein do and would interfering with it be dangerous? Has the gene been expressed in quantities and purity that are sufficient for structural biology? Does the protein adopt a stable 3-D atomic structure? Is there is an existing structure? and does it have suitable pockets for drug binding? Is anyone else working on the protein and, if so, what are they doing? What sort of drug could be designed to modulate the protein's function? Are there other proteins that interact with it that might be targets for drug discovery? Students will be given the opportunity to take part in the development of new drug discovery projects and will gain an appreciation of the strategy behind new project selection in a world leading structural biology lab.

Techniques used may include:

1. On-line literature searches and critical appraisal.
2. Analysis of protein structure data bases.
3. Analysis of interactome data bases.
4. Interrogation of drug discovery and development data bases.
5. Detailed report ranking proteins as drug discovery targets in diseases such as COVID-19 and Alzheimer's disease.
6. Structure-based drug discovery (virtual screening, computer-aided drug design, molecular dynamics simulations) of chosen targets.

Recent papers from the lab:

Miles LA et al., (2019) Science **19**, 110-119

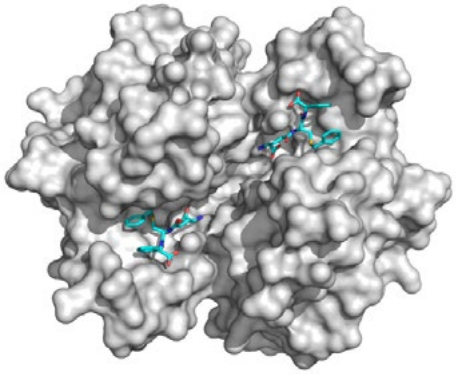
Thilakasen P et al., (2019) EMBO Mol Med **11** e9539

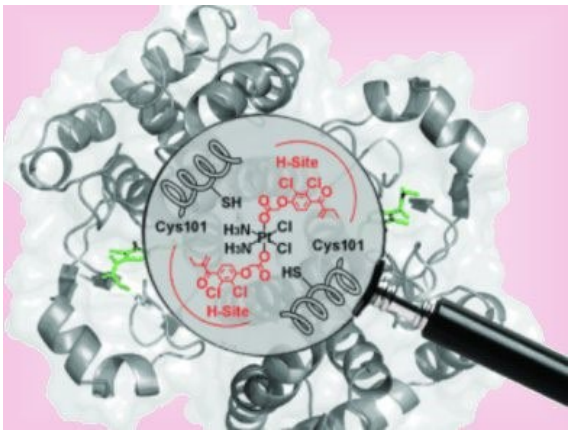
Nero TL et al., (2018) *Biochem Soc Trans* **46**, 1367-1397

Baell JB et al., (2018) *Nature.* **560**, 253-257-5667.

Contact:

Professor Michael Parker to arrange an appointment by Zoom
mwp@unimelb.edu.au





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

BENCH SUPERVISORS:
Stuart Ralph, Dr Emma McHugh, Emily Crisafulli, Madel Tutor, Vern Lee (PhD Students)

OFFERED:
Semester 2

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. Analysis of images of *in-vitro* grown malaria parasites
2. Analysis of drug assays for *in-vitro* grown malaria parasites
3. Computational prediction of drug mode of action
4. Computational analysis of enzyme evolution
5. Bioinformatic prioritization of drug targets

Recent papers from the lab:

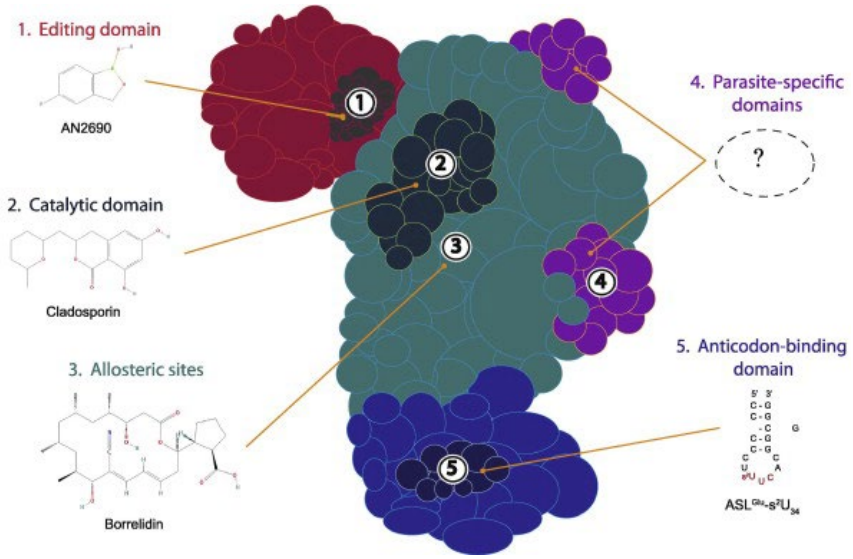
Goodman CD et al., *Trends Parisitol* 2016

Wong W et al., *Nat Microbiol* 2017

Yeoh LM et al., *BMC Genomics* 2017

Contact:

Assoc. Professor Stuart Ralph to arrange an appointment by Zoom
saralph@unimelb.edu.au



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

BENCH SUPERVISORS:
Sepideh Valimehr, NGeorge Kobakhidze MeysamMirzadeh, Dr Ashish Sethi, and Dr Mohsen Kazemi

OFFERED:
Semesters 2

Control of protein folding is central to keep cells healthy and alive. Cells need to discard unwanted and abnormal proteins efficiently else, these proteins could become toxic. Improper protein degradation leads to neurological diseases such as Alzheimer and Parkinson. In these diseases, improperly folded proteins accumulate as aggregates in brain and muscle cells. Inhibition of protein degradation could also be a strategy for killing unwanted cells such as cancer cells, bacteria and protozoa

We are interested in the molecular mechanisms by which an abundant and essential protein, named p97, unfolds unwanted proteins. The mechanisms by which p97 function is not fully understood, but we know that p97 interact with other proteins, called co-factors, to choose which proteins to unfold. Bioinformatics analysis will bring novel insight into this process of selection.

We are also interested in developing inhibitors of p97 in order to kill susceptible human cells such as cancer cells or cells from diseases causing parasites (e.g. malaria and tuberculosis). Bioinformatics analysis, including virtual drug screens will help define specificity for drugs development.

Techniques used may include:

1. Online literature search and critical appraisal.
2. Protein structure analysis and structure prediction.
3. Virtual proteins and protein docking.
4. Virtual drug screening.
5. Molecular Dynamics simulations.

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 by Zoom
isabelle.rouiller@unimelb.edu.au