Honours in Medical Research Handbook

2024

School of Biomedical Sciences

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Welcome to the School of Biomedical Sciences' Honours Program

This 2024 Handbook introduces the Honours in Medical Research program in the School of Biomedical Sciences at the University of WA.

An Honours in Medical Research is an invaluable postgraduate qualification that expands your employment opportunities and competitiveness and provides the training and launching pad for a wide variety of professional and postgraduate careers, including those in science, health-related disciplines, and/or postgraduate research.

For many of you, undertaking an Honours project will be your first real taste of scientific research, and you will be faced with exciting - and perhaps daunting - new challenges. You will have to confront the rigours of scientific writing, experimental design, time management, data analysis and oral presentations. You will learn to undertake and master cutting-edge scientific techniques and methodologies, and become familiar with a range of experimental tools, models and equipment. You will need to be both diligent and resilient, for in science (as in life) things often do not go as planned and there are hurdles and disappointments to be overcome. Your experienced supervisors will be there to guide you and help you to achieve your goals and do the very best you can.

For some of you this will be a transformative year in your life and will set you on a career path of lifelong research and discovery. For others it will be a stepping-stone to other ventures. For all of you it will be an invaluable learning experience that will teach you a range of technical, analytical, intellectual and communication skills that will prove invaluable wherever life takes you.

I encourage you all to embrace the challenges ahead, keep your minds open to new experiences and knowledge, become part of the school community, and make the most of being in a stimulating environment at the cutting edge of biomedical research.

Good luck!

Professor Jeffrey Keelan, BSc (Hons) Liv., MSc PhD Auck., FSRB

Head of School of Biomedical Sciences

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Introduction

The purpose of the Honours program in UWA's School of Biomedical Sciences is to introduce students to contemporary scientific medical research practices and develop their practical research and communication skills and competencies.

The Honours course comprises an academic year of full-time research and training, centered on an individual research project, resulting in the preparation and submission of a compact medical research thesis under the supervision of an experienced researcher and/or co-supervisors. Students will develop enhanced skills in critical and lateral thinking, experimental design, problem solving, time-management and scientific literacy and communication, as well as mastery of a variety of laboratory and/or analytical skills and an understanding of laboratory safety, professional responsibility and ethical conduct in research.

The Honours program is structured as a 48-point course (24 points per semester) composed of six units that encompass different components of the program. Some of the units are split into two parts that span both semesters (colour coded below). The course structure is summarized in the diagram below:

<table>
<tr><th>SEM 1</th><th>SEM2</th></tr>
<tr><td>BMED4001. 6 pts – Literature Review and Research Proposal in Biomedical Sciences</td><td>BMED4005. 6 pts – Research Communication in Biomedical Sciences - part 2</td></tr>
<tr><td>BMED4002. 6 pts – Research Communication in Biomedical Sciences - part 1 (assessment continuing)</td><td rowspan="3">BMED4006. 18 pts – Medical Research Thesis part 2: completion, assembly, submission and examination</td></tr>
<tr><td>BMED4003. 6 pts – Medical Research Thesis part 1: Preparation, induction and training (assessment continuing)</td></tr>
<tr><td>BMED4004. 6 pts – Research Ethics, Rationale & Design (ungraded pass/fail)</td></tr>
</table>

Final marks breakdown across the units:

- Literature review and research proposal: 15%
- Research communication parts 1 … plus… plus part 2 25%
- Research Ethics, Rationale & Design: Pass/fail
- Thesis part 1 …. plus… Thesis part 2: 60%

At the beginning of the year, students receive general training in biostatistics and chemistry, laboratory safety induction, and the appropriate use of research infrastructure. Additional specific training may also be required for certain types of research. For example, research using non-human animals will require completion of the PAWES training course offered by Animal Services; projects that involve radioactive isotopes will need completion of a radiation safety course, while research using genetically modified organisms will require OGTR approval. General laboratory training, student-specific training, and instruction in research design, results presentation and analysis will contribute to BMED4003. Training in research ethics, rationale and design will be covered in BMED4004.

Scientific communication skills are taught and developed throughout the Honours year. Research contributing towards the research thesis commences at the start of the year and continues throughout the

program, culminating in the submission of the thesis and presentation of the project at a conference-style event. Honours graduates who achieve a 2A or higher degree are eligible to enroll in a PhD programme.

Learning outcomes

Students who complete Honours in Medical Research should be able to:

1) Critically evaluate literature relevant to the area of research and compile references in an appropriate style;
2) Demonstrate advanced oral and written scientific communication skills;
3) Develop a research plan to address the aims of the project;
4) Execute a range of statistical analyses relevant to biomedical research;
5) Discuss considerations relevant to laboratory safety;
6) Demonstrate an advanced understanding of the responsible conduct of research in the biomedical sciences;
7) Demonstrate a thorough understanding of good clinical practice as it pertains to medical research;
8) Evaluate and design a research project based on a biomedical question;
9) Perform experiments, interpret data, solve scientific problems, identify limitations and future directions
10) Apply chemistry fundamentals in a laboratory setting

Entry Requirements for Honours in Medical Research

Students require a minimum weighted average mark (WAM) of 65 per cent in the Level 3 units of a Biomedical Science-related discipline, such as Genetics, Neuroscience, Pathology, Pharmacology, Microbiology, Immunology, Anatomy, Human Biology, Physiology, Biochemistry, Molecular Biology, Psychology, Public health. The student's undergraduate program should be pertinent to the topic of the project. Students must be accepted by at least one Academic supervisor from the School of Biomedical Sciences, UWA.

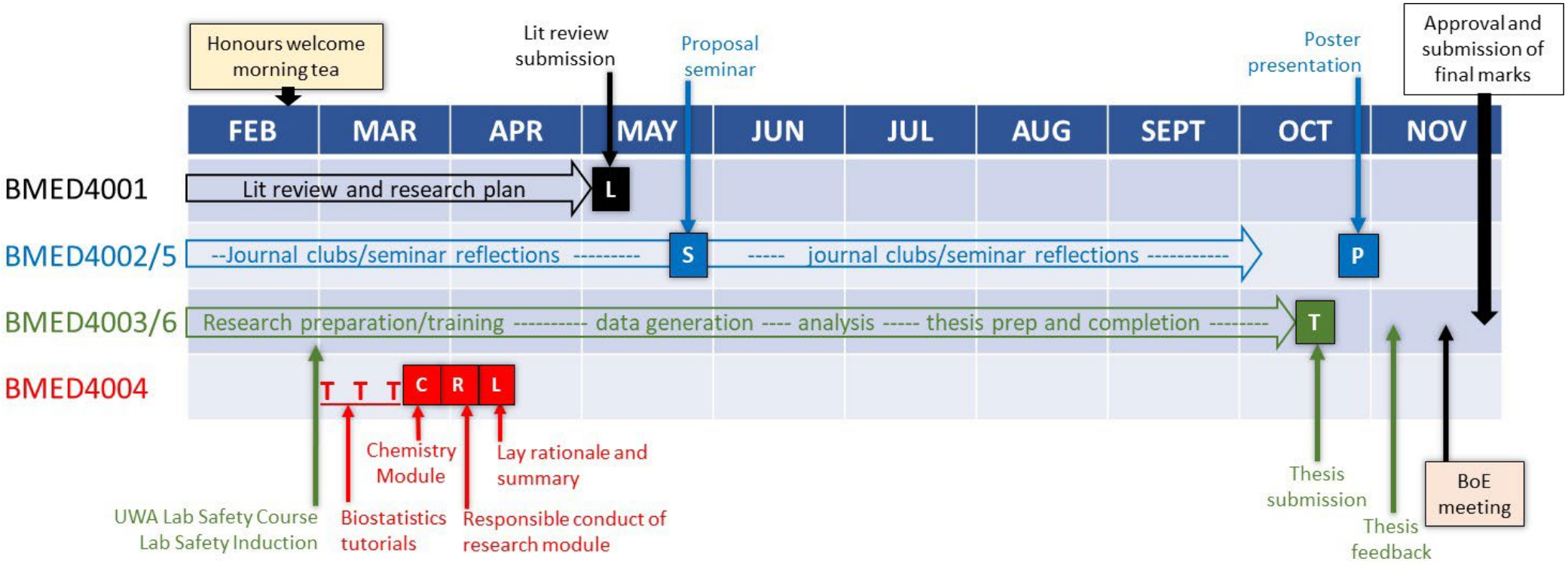
Details of the enrolment process can be found here

Outline and Structure of the Honours in Medical Research Program

The Honours program consists of a combination of research-based training modules and activities, attendance/presentation at research seminars and journal clubs, development and completion of an original research project with analysis and interpretation of the data generated, and submission of a written condensed literature review, research proposal and research thesis. These activities are organised and assessed via the six BMED units as outlined in the Table above: BMED4001, 4002, 4003, 4004, 4005, 4006. All units must be passed to complete the course. Failing any one unit will fail the course.

The course is a 1 year program of fulltime study, with research training commencing in February and the final assessment completed in November. There is no mid-year entry into the course. A typical timeline for the activities and assessments of the course is depicted in the diagram below:

Honours 2024 Schedule and Timeline



Unit content, learning outcomes and assessment structure

BMED4001 (6 pts)

Literature Review and Research Proposal in Biomedical Sciences

UNIT Coordinators: *Professor Jeffrey Keelan and Dr Mitali Sarkar-Tyson*

Students will write a literature review summarising the knowledge base and rationale underpinning the project, and a research plan outlining the principal aims of the study and an overview of the design and methodology used to achieve the study objectives.

Learning outcomes: students will be able to:

a) Compile, read and critically evaluate literature relevant to the area of research;

b) Format bibliography in an appropriate style;

c) Identify gaps in current knowledge;

d) Formulate aims to address the gaps in research;

e) Develop a research plan to address the aims of the project

f) Demonstrate high level written communication skills.

The literature review and research plan is assessed by the two independent examiners nominated by the project supervisor(s); they will also assess the thesis. The literature review and research plan will comprise the first chapter of the thesis. It can be edited and improved following feedback after assessment prior to inclusion in the final thesis. The document can be up to 5000 words (not including references); a word count must be included at the end of the document. The mark for the Literature Review and Research Plan represents 100% of the mark for this unit.

Further details can be found in the **Assessment Details and Timelines** section below.

BMED4002 and BMED4005 (6 pts each)

Research Communication in Biomedical Sciences Parts 1 and 2

UNIT Coordinators: *Professor Jeffrey Keelan and Dr Mitali Sarkar-Tyson*

BMED4002 Part 1 and BMED4005 Part 2 are paired communications units taken over semester 1 and 2. These units have similar outcomes and assessments, with BMED4002 Part 1 being “assessment continuing”.

These two units are comprised of four components:

1) Research proposal seminar (50% of mark, received in the 1st semester)

2) Specific engagement with/presentation at weekly lab journal clubs (both semesters; ungraded pass/fail)

3) Attendance at School seminars and submission of structured personal reflections (both semesters; ungraded pass/fail)

4) Conference poster presentation and oral defence (50% of mark; 2nd semester)

These units deliver and assess key advanced biomedical research communications skills, including:

a) Oral presentation to staff and students in the School of Biomedical Sciences of the project proposal (an in-depth overview of the literature pertaining to the field of study; an outline of the principal aims of the study and an overview of the approaches used to achieve the aims)

b) Review and analysis of scientific papers in a discipline-related journal club;

c) Attendance at the School Seminar program (or equivalent) and completion of Seminar Reflection Worksheets

d) Final conference poster presentation and oral defence

BMED4003 (6 pts)

Medical Research Thesis part 1

UNIT Coordinators: *Professor Jeffrey Keelan and Dr Mitali Sarkar-Tyson*

This unit represents the preparative portion of the student's research project and training, which culminates in the submission of a medical research thesis at the end of semester 2 (BMED4006). It covers all aspects of laboratory safety, specialist training requirements, development of wet-/dry-lab bench skills, equipment operation/credentialing, ethical compliance issues, laboratory management awareness, and preliminary work on project establishment, rationale and design.

This unit is designated as 'assessment continuing', with thesis submission and examination occurring in BMED4006 at the end of semester 2. There are no specific marks allocated to this unit.

In addition to the preparative work undertaken on the research thesis, the unit encompasses a number of modules and courses that students may need to take to comply with safety and training regulations, in addition to project-specific training and upskilling. These include:

1) Basic biomedical statistics: Between-subjects and within-subjects designs, time-series and formal qualitative design; concepts of Bayesian and frequentist approaches to statistical analyses; standard group comparison methods (e.g., t-tests, ANOVAs, ANCOVAs, regression including correlations, methods of curve fitting, and nonparametric statistics); the concepts of power analysis and effect size;
2) General laboratory safety training (online);
3) Reading and sign-off on the School Laboratory Safety manual;
4) Project-specific training on individual equipment and infrastructure;
5) PAWES course for those working with animals;
6) Radiation Safety Course for those working with isotopes;
7) Gene Technology Awareness Session for those working with genetically modified organisms;
8) First-aid and aggressive incident management for those working with clinical samples;

Not all students will need to take all courses/modules. Completion of modules is pass/fail, but they are not graded and do not contribute to the marks for the unit.

BMED4004 (6 pts)

Research Ethics, Rationale and Design

Unit Coordinator: *Dr Lynette Fernandes*

Knowledge and understanding of medical research ethics are integral to research. In this unit, students participate in a face-to-face discussion of an interactive movie at the start of semester. Students are required to subscribe to the BMED4004 Discussion Forum on LMS and check their UWA emails every day for updates.

Students will also complete two online courses:

1. Global Health Training Centre Research Ethics Online Training Modular course

2. Global Health Training Centre Good Clinical Practice short course
3. Chemistry refresher module (via LMS)

Students will also be required to submit a clinical OR scientific rationale for their thesis project written in lay language in the format of a grant or ethics application summary.

All components of this unit are required to be completed satisfactorily to pass the unit. The unit is pass/fail and is not graded.

More details will be provided by the beginning of the first semester of 2024.

BMED4006 (18 pts)

Biomedical Research Thesis Part 2

UNIT Coordinators: *Professor Jeffrey Keelan and Dr Mitali Sarkar-Tyson*

This 2nd semester unit follows on from BMED4003 (Thesis part 1); collectively these two units comprise the medical research thesis component of the course and are worth 24 credit points in total.

In brief, the thesis a body of original research consisting of a title page, statement of contributions and acknowledgment, abstract, introduction and literature review, aims and objectives, methods, results, discussion, references/bibliography and appendices. The first section of the thesis (literature review, aims and objectives) is submitted in the first semester and examined independently (BMED4001). This allows first semester feedback to the student on progress and the opportunity to edit the literature review and make changes to the project if suggested by the examiners. The final completed thesis is submitted (BMED4006) for examination at the end of the program.

For this Honours course, the structure and length of the Medical Research Thesis is carefully prescribed and all students must follow the guidelines carefully (*see page 15*). Students must adhere to strict work limits for the various sections; this is to ensure the thesis is concise and readable. Word limits are frequently imposed on research publications, so learning how to write within space constraints is a valuable "real world" skill. There are also strict instructions regarding referencing and attribution that must be followed, similar to those that apply to submission of research manuscripts for publication. Full details are provided below in the Assessment Instructions and Deadlines section.

The marks for the Medical Research Thesis (encompassed in BMED4003 and 4006) represent 60% of the total marks for the course. Completion of the thesis teaches students how to:

a) Present, cite and critique biomedical literature supporting their research
b) Describe appropriate methodologies and statistical techniques used in their studies
c) Generate, analyse and present research findings clearly, accurately and professionally
d) Critically appraise and discuss their research in the context of the existing knowledge in the field and identify any strengths and weaknesses in their findings

Detailed assessment instructions and deadlines

BMED4001 Literature Review and Research Proposal

Students will write a literature review introducing the background and rationale behind the project, and research plan outlining the principal aims and objectives of the study and an overview of the approaches and methodologies used to achieve the objectives. The submitted document is examined by two independent external examiners, who will provide comments and feedback via the examination process. The work undertaken to prepare this document will form the basis of your proposal seminar presented at the end of semester 1.

Layout: The structure, scope and breadth of the literature review should be decided in consultation with the supervisor, who will also edit drafts and give guidance on content, quality and style. Students will need to demonstrate an understanding of the literature supporting the project and its significance, identify areas where there are gaps or inconsistencies in knowledge, and demonstrate they are able to synthesise and interpret the findings of others in their own words. Mastery of written scientific English is a key aspect of this unit. Grammar, punctuation, layout and readability will all be taken into account in the marking process.

Students should work with their supervisor to establish the topic and order of the headings and sub-headings; structure and flow is very important in a review. A logical hierarchical numbering system should be employed, which should be used consistently and adhered to.

The title of the review should be stated on the first page in bold text (NB: this does not contribute to the page count or word count). It does not need to be the same as the title for the research thesis, but should accurately and succinctly describe the topic of the review.

The body of the text must be in Calibri 12 point font, single spacing throughout. A4 page size should be used. Figure/table legends should be single space, 11 point font. Page margins should be 20 mm for left and right, and 25 mm for top and bottom.

Following the literature review, the hypothesis, aims and objectives of the project should be stated. The research proposal should contain an outline of the experimental design, the primary and secondary outcomes of the study (where appropriate), a justification of the numbers of samples/animals/repeats, the main methodological / analytical approaches to be used, and a description the planned statistical analyses.

Finally, a bibliography should be included, listing all the publications and sources of the literature cited in the review and research plan. The Vancouver style of citation and bibliographic referencing must be used. Students must comply with the University's referencing requirements, and are strongly encouraged to use Endnote or a similar referencing software package to insert citations and manage/format their bibliography. The UWA library has several helpful online referencing resources to help students navigate the demands of referencing:

https://guides.library.uwa.edu.au/referencinguwa/referencing

Diagrams and Tables: The use of figures and diagrams is strongly recommended to improve the clarity and readability of the review. Each figure, diagram and table should be accompanied with an explanatory legend; avoid splitting the figure/diagram and legend across different pages. Figures and diagrams should be embedded within the pages of text; they do not need to be on a separate page.

The inclusion of original figures is strongly encouraged; however, images or figures may be reproduced from published sources. They must, however, be appropriately referenced and cited in the bibliography to comply with the University's plagiarism policy. Poor quality, pixelated figures with small illegible text should be avoided.

Word length and formatting: The literature review and research proposal should be no more than 5000 words (not including title and bibliography); a word count must be included at the end of the document. If

the word count is exceeded, the document will be returned to the student for editing. Page numbers should be positioned in the footer at the bottom right of each page, commencing with the first page of the literature review and ending with the last page of the bibliography.

Submission and assessment: On or before the due date (which will be posted on LMS), one copy of the literature review and research proposal must be submitted in electronic format as a PDF document via LMS. The document will be assessed by two examiners against the following criteria:

(a) How well does the literature review demonstrate an understanding of the central concepts in the field of study?

(b) To what extent does the review summarise the current state of knowledge and identify gaps in that knowledge?

(c) Does the review contain an appropriate number of figures, diagrams and tables and are they of high quality?

(d) Does the review have a well-designed, logical structure and appropriate use of subheadings?

(e) Does the review comply with the wording and formatting guidelines?

(f) Does the document demonstrate an appropriate use of grammar and punctuation? Has care been demonstrated to avoid spelling mistakes and typographical errors?

(g) Have the source materials been properly cited and formatted in a bibliography according to the style guide?

(h) Are the *hypotheses* and *aims* clearly stated?

(i) Is the proposed methodology and statistical analysis clear, appropriate and accurate?

(j) Does the research proposal clearly establish how the hypotheses will be tested and the aims accomplished?

Marks and feedback: Marks will be deducted for late submission – *5% for every day late*, unless an extension has been granted. Remember, supervisors are busy and need time to read and edit their students' work. Students should not demand a response within 24 hours to meet a deadline!

Students will receive their marks at the end of semester 1. The marks for the literature review and research plan constitute 100% of the marks for this unit, which represents 15% of the entire grade for the course.

Following completion of the assessment process, students will receive written comments from the examiners, including a list of any typographical or stylistic changes recommended before final inclusion as part of your final research thesis submitted at the end of the year. Any changes made as a result of feedback will not be re-assessed and will not contribute to your final mark. However, the feedback gives students a final chance to do minor editing before a permanent thesis is submitted. The examiners may also comment on the content of the research plan and suggest changes if they have significant concerns regarding the proposed approach, power, methodology or feasibility.

BMED4002 and BMED4005 Research Communication Parts 1 and 2

The two research communication units contain four assessable items: *a research proposal seminar; participation in a journal club; attendance at the School Seminar program; and a conference-style poster presentation with oral defence*. The marks for these two units comprises 25% of the total marks for the Honours course.

1. Proposal seminar

Students are required to give an in-depth PowerPoint presentation of the literature pertaining to their field of study, an outline of the principal aims of the study and an overview of the approaches used to achieve

the aims; this will be scheduled in mid-April. Preliminary data may be included if available. Students can and should receive guidance from their supervisors with respect to preparing the PPT presentation for this seminar and rehearsing the delivery of the seminar.

The seminar will consist of a 20-minute presentation followed by a 5-10 minute question and answer session. The seminar will count towards 50% of the Unit mark and will be assessed via a rubric given to all attending academics (with the exception of the supervisor(s)) in the audience against the following criteria:

(a) Clarity and quality of the overall presentation: oral and visual	33%
(b) Quality of the scientific content of the seminar	33%
(c) Ability to answer questions in a clear and logical manner	33%

Seminar marks will be released to students at the end of semester 1 of their seminar, with feedback where available.

2. Journal club

Students must regularly attend and participate in a lab journal club (or equivalent), presenting at least once to the group for discussion during the year. The supervisor will provide the Unit Coordinator a confirmation of attendance and participation. This activity is not directly assessed, and is a pass/fail component.

3. School seminars

Students are required to attend at least six School Seminars and fill out a one-page Seminar Reflection Sheet, which must be forwarded to the Unit Coordinator within 24 h of the seminar. The Seminar Reflection Sheet will be located on LMS. This is a pass/fail component and is not graded. Attendance at an alternative, equivalent seminar program is allowable, but must be approved by the Unit Coordinator.

4. Poster presentation and oral defence

At the end of the year, after submission of the thesis, students will prepare and present a 'conference-style' poster. This provides a concise overview of the entire research project completed by the student during the year. Examples of high-scoring posters from previous years will be made available via LMS. Formatting guidelines are listed below:

- Dimensions: up to 1 m wide and 1.41 m high (B0 page size)
- Material: uncoated paper (160 gsm) or fabric; gloss or lamination not necessary
- Title: located at the top of the poster in lettering of 4 cm or greater
- Content: Introduction; Methods: Results: Conclusions; References; Acknowledgements
- Style: the visual style, colours, font and layout are determined by the student.
- Pointers: Keep the poster simple, with logical flow/layout, and as concise as possible; rely on your presentation to expand, add clarity and explanation. Ensure text is large enough to be legible from 2 m away. Avoid jargon/acronyms. Ensure figures are clearly labelled. Employ consistent formatting/colour options. Employ use of boxes and emphasis techniques to make key aspects stand out.

Posters can be printed by Uniprint or commercial suppliers such as Officeworks or Clockwork Print; note, printing may take up to 3 days.

Posters will be presented at a conference-style format, at a time and venue chosen by the discipline coordinator approximately 2 weeks after the thesis submission deadline. All students in the discipline will

have their posters on display in the same session and are encouraged to view others' posters and actively engage with their colleagues to learn more about their project. Students are advised to bring a copy of their thesis along in case it needs to be referred to.

Students will individually present their poster to their examiners, supervisor and discipline coordinator, where they will be expected to explain the basic rationale and description of the study, present the findings, and discuss the significance and implications of the work. The examiners will then question the student on various aspects of the project over 10 minutes. Students may be asked to defend the use of specific methodology or approaches, their interpretation of the findings, or an aspect underpinning the rationale for the study.

During the presentation and Q&A session, it is important to speak loudly, fluently and clearly, avoid long rambling statements, and demonstrate a solid depth of knowledge and understanding of the topic. Students are advised to rehearse their presentations in front of a supportive audience and get feedback. The poster and presentation will be marked against the following criteria:

a) Visual clarity, impact and effectiveness of the poster (50% of poster grade)

b) Quality of the oral interpretation of the poster (20%)

c) Student's ability to answer questions and demonstrate in-depth knowledge of the topic and area of research (30%)

Collectively, the poster presentation is worth 50% of the marks for the two communication units BMED4002 and 4005 (which equates to 25% of the marks for the Honours course).

BMED4003 Medical Research Thesis part 1

This unit encompasses the commencement of research that will contribute to the medical research thesis (completed in BMED4006), in particular the initial training, credentialing and induction required. The unit is "assessment continuing" and contributes (with BMED4006) to the 60% of marks allocated to the thesis.

A variety of various modules and credentialing/training activities are undertaken as part of the preparative work are required to safely undertake a research project; they are classed as pass/fail, but do not contribute to the grade. A copy or screenshot of the badge/certificate of completion must be uploaded into LMS as confirmation of completion.

Specific training modules

General lab health & safety training typically involves Building Safety Inductions, reading and certifying the lab safety manual and the UWA Biosafety 1 (Biohazards) unit, an online quiz that is completed via LMS (look under the *Community* tab, find *Biosafety* under "organizations" and enrol under *'UWA-Biosafety-Induction'*). A range of information on health services can be accessed here:

http://www.student.uwa.edu.au/experience/health

Students who are using laboratory animals during their Honours Project must complete the PAWES (Program in Animal Welfare, Ethics and Science) course, taught by the UWA Office of Research. Please note that this course fills up quickly and students should reserve a space as early as possible. The course is time-tabled on the Research UWA website and usually becomes available in January of the year of your Honours:

http://www.Research.uwa.edu.au/staff/animals/pawes

Students undertaking an Honours project that involves the use of radiolabelled drugs or reagents must also complete the Unsealed Radioisotope Handling Course run by the Safety and Health Office at UWA. See:

https://www.safety.uwa.edu.au/induction-and-training/courses/unsealed-radioisotope

The online Gene Technology Awareness Session is essential for students who work with Genetically Modified Organisms (GMOs), and for anyone who works within (or administers) a facility certified by the Office of the Gene Technology Regulator (OGTR). Details can be found at:

https://www.class2go.uwa.edu.au/enroll/3MHEFE

Students carrying out clinical research involving recruitment of patients may need to do additional training (e.g. CPR; Defibrillation; Aggressive Incident Management; Manual Handling; How to obtain Informed Consent; etc); supervisors will need to be aware of these requirements and organise the appropriate modules for their students.

BMED4004 Research Ethics, Rationale and Design

1. **Basic Chemistry for Lab Researchers module:** Students will be required to successfully complete this refresher module available via the LMS. Students must obtain a minimum of 80% in the associated quiz to pass this module.
2. **Research Ethics module**: Students will watch and actively participate in interactive videos, provided via the LMS, at the start of semester. Students will successfully complete the following online courses: i) Research Question (Global Health Training Centre), ii) Essential Elements of Ethics (Global Health Training Centre) and iii) Good Clinical Practice (Western Australian Health Translation Network). Students must obtain a minimum of 80% in quizzes associated with each course to obtain a certificate and pass this module.
3. **Project rationale:** Students will also be required to prepare and submit a project summary and rationale by late March (this allows timely feedback for preparing the literature review and research plan). The objective of this task is for the student to clearly and succinctly describe the study rationale, objectives and design in lay-friendly language similar to that required for a grant or ethics application. The project rationale must be no more than two A4 pages in length (Submission must be in English, typewritten using 12 point, Times New Roman Font, 1.5-spacing throughout. Each page should consist of a single column of text with the following margins: 15 mm for left and right, and 25 mm for top and bottom) including references; figures and tables are not allowed. Feedback will be provided by the unit coordinator. Students must obtain at least 50% to pass this module.
4. **Statistics in Medical Research module:** An understanding of basic statistical approaches and techniques is necessary to design a robust study and properly analyze and interpret research data. The statistics module will be run as three weekly workshops, using real-world data to teach practical biomedical statistical analytical principles. Attendance at all workshops is required and completion of short assessment pieces are required in order to pass this module.

Note: where specialised statistical approaches and facilities are required (e.g., genetic analysis, multivariate statistics, 'omic data analysis), these will be taught by your supervisor using the own tools and platforms employed within their labs.

The Statistics in Medical Research module will cover the following:

- *Descriptive statistics:* Mean, median, mode; standard deviation and standard error; confidence intervals; normalcy of distribution; statistical outliers; data visualization, graphing and plotting.
- *Parametric statistics:* Probability testing; t-test, ANOVA, ANCOVA, analysis of repeated measures.
- *Nonparametric statistics:* Chi-Square, Fisher's exact test, Wilcoxon (paired or unpaired), Kruskal-Wallis ANOVA, Survival Analysis, etc.
- *Curve fitting*: Correlations, smoothing, linear regression, multiple linear regression, non-linear regression (e.g., dose-response curves), logistic regressions (where the dependent variable is categorical), factor analysis, principle component analysis.
- *Power analysis*: hypothesis testing, assumptions, effect size, sample size.

The modules will include training on the use of the free software package ***Jamovi*** to conduct statistical analyses and presentation of data (https://www.jamovi.org/download.html).

Students are required to pass each module in order to pass BMED4004. Furthermore, failure in any or all of these components will result in failure in the entire Medical Research Honours course**.** Attendance at all workshops is required and completion of short assessment pieces are required in order to pass this module. More details on teaching delivery and deadlines for completing each module will be provided by the beginning of the first semester.

BMED4006 Biomedical Research Thesis Part 2

At the completion of the Honours program, students will be required to submit a compact medical research thesis, consisting of a written presentation of their research methods, findings and conclusions, for marking. The Thesis should include updated versions of the literature review and research proposal, having incorporated any typographical and grammatical corrections suggested by the examiners. The original bibliography should be included and updated at the end of the thesis, retaining the original references from the literature review plus others relating to the Materials & Methods, Results and Discussion.

The thesis must be submitted as a PDF file for examination. Supervisors can and should provide feedback to the student before submission with respect to writing style, content, formatting and referencing. Feedback can be provided on the Introduction, Methods and Results, but **NOT** the discussion, which should entirely reflect the student's own work. The size and content of the thesis is outlined below; students must note the structure, layout and word limits and ensure these are followed. **Word limits are NOT optional.**

Structure and layout:

The thesis should be laid out according to the following guidelines:

1. Title page: stating the title of the thesis, the name and number of the submitting student and the name(s) and affiliations of the supervisor(s).
2. Contribution statement page: A signed statement indicating the contribution of the student to the work contained in the thesis submitted as part of the requirement for the Honours degree (a pro forma page will be provided). Contributions by others should be specifically stated, quantified if necessary.
3. Acknowledgement page: formal acknowledgement and thanks to those who helped with the project or who provided materials, data or other support.
4. Table of contents: neatly formatted and accurately paginated, listing major and minor headings.
5. Abstract: A single page summarising the background, rationale, aims, methods, results and conclusions of the project.
6. Literature review and research plan: as previously submitted and assessed for BMED4001 (edited as necessary). The original bibliography should be retained and augmented to encompass references cited in the remainder sections. Sources should be numbered according to the order in which they are cited (Vancouver referencing style).
7. Materials and Methods: relatively brief description of the methodological and analytical aspects of the study, written so that a suitably trained reader will be able to understand the approaches and procedures undertaken and replicate them. Reagents, platforms and equipment should be briefly defined in text as per a research manuscript. All methods and approaches should be properly referenced.
8. Results: A concise listing and description of the data and findings generated by the project; the use of properly formatted and labelled diagrams, figures and tables is strongly recommended. Statistical significance of findings should be clearly annotated. Discussion and interpretation should be avoided in this section.
9. Discussion: A structured, logical, informed and balanced discussion of the findings and significance of the project, noting any strengths, flaws or gaps in the study, and identifying opportunities or

requirements for further study. Importantly, the Discussion must not be read or edited by the supervisor – it should reflect the student's work alone.

10. Bibliography: A full, complete and accurate listing of all of the papers and sources of information cited in the thesis, numbered according to the order in which they are cited. Students are encouraged to use recent, high quality reviews to support general statements and the state of knowledge around broad topics, while specific studies of particular relevance (old and/or new) should be cited individually.
11. Appendices: supplementary information, figures or data generated during the research, supplied for information but not formally assessed.

Word limits:

It is intended that the Honours research thesis should be a compact, readable document that provides a vehicle for students to adequately present their research work in a concise, lucid and easily examinable format. Word limits are in place to prevent the thesis becoming too large and unwieldy, and to reflect the reality of research practice where size constraints are commonplace when publishing or reporting research.

The word limits for the various sections of the thesis are as follows:

Section	**Word limit**
Title	25 words
Abstract	500 words
Acknowledgments	No limit
Table of Contents	No limit
List of Figures/List of Tables/Abbreviations	No limit
Literature review and project proposal	5000 words
Materials & Methods*	*3000 words combined
Results	
Discussion	2500 words
Bibliography	No limit
Appendices**	No limit

*Combining the Materials & Methods and Results in a single word limit is intended to allow projects that have a major method development/optimisation component (with few results) to be properly and adequately presented without being penalised.

** Appendices will not be formally assessed by the examiners (no word limit).

Printing and formatting:

The Thesis should be formatted in Word, in colour, and saved as a PDF file for submission and printing if desired. File size should be less than 10 MB if possible. The page size should be A4 with margins of 2 cm (width) and 2.5 cm (height). All pages from the Introduction onward should be numbered, with the page number located on the bottom right of the footer. The header should be left blank.

Electronic submission (as a PDF file) is required for the Honours thesis submission; these will be emailed to the examiners. Hard copies can be printed at the student's expense if needed.

Submission

Thesis is to be submitted electronically for examination via LMS.

Assessment grade guidelines

The marking bands for assessment are as follows:

Class	When apportioning marks please take into account the grades used by UWA
First class	90% - 100% H1: HD+ 80% - 89% H1: HD- Outstanding ability in research and communication.
2A Honours	75% - 79% H2A: D+ 70% - 74% H2A: D- Very competent. Candidate still very worthy of consideration for a postgraduate research award.
2B Honours	60% - 69% H2B: CR Competent but some inadequacies in content, scope understanding and/or presentation such that the person would be unlikely to make a good independent research worker.
Third class honours	50% - 59% H3: Pass Evidence of effort but inadequacies in research competence, understanding and/or presentation.
Fail	Fail: N+ Less than 50 % Unsatisfactory. Very serious inadequacies in all or most areas.

Similar general expectations to these will apply to the other items of assessment, that is, the Literature Review & Research Plan, the Preliminary Seminar, and the Poster Presentation & Interview.

ALL UNITS MUST BE PASSED TO PASS HONOURS.

LATE PENALTIES: All late submissions will incur a 5% mark penalty per day.

Responsibilities of the Honours Student

One of the exciting challenges of the Honours year is that you will encounter many challenges and learning curves. The inevitable downside of this is that each task will take longer than anticipated, so it is important to be highly organised. As an Honours students you should:

- Ensure you are aware of all the important dates and deadlines, as penalties for late submissions do apply.
- Ensure you manage your time carefully so that the requirements of the Honours course are completed within the stipulated time limits. Although it is understood that many students need to take on part-time work for financial reasons, ensure that this is kept to a reasonable level (e.g. less than 8 hours per week).
- Obtain a Medical Certificate to receive a special consideration if you are ill during the year.
- Ensure you are aware of Unit requirements, particularly with respect to security and the safe and responsible usage of facilities such as the Internet and core equipment. If in doubt, consult your Supervisor, the Honours coordinators or the Senior Technical Officer (Sarah Power).
- Document all your experimental work in a laboratory book and show it to the Supervisor on a regular basis. It is a requirement that the laboratory notebook is accurately completed and remains the property of the Supervisor for up to five years post-Honours. Make sure that you protect electronic data by backing it up regularly (where your supervisor can get access) and having copies saved on several different sites. Don't store data where it can be lost or stolen.
- Be aware of the Guidelines on Research Ethics and Research Conduct, as outlined in http://www.Research.uwa.edu.au/policies3/guidelines_on_Research_ethics_and_Research_conduct
- Arrange regular meetings with your Supervisor to discuss all aspects of your work.
- Be open to suggestions and advice from your Supervisor, particularly during the early stages; as the year progresses you should grow in confidence and show signs of independence and initiative.
- Ensure that any conflicts that might develop with Supervisors or others are brought to the attention of the Honours Coordinators so that problems can be resolved quickly and amicably.
- Uphold the academic standards and good reputation of the School of Biomedical Sciences.

Responsibilities of the Honours Supervisor

The Supervisor is responsible for all matters directly related to the Research project. Specifically, the Supervisor should:

- Provide academic guidance with respect to the overall direction, day-to-day running of the research project, and editing and feedback on written and oral tasks.
- Meet frequently with the student, and establish open and good communication
- Ensure the appropriate level of support and training is provided to the student, including resourcing and regulatory approvals
- Be a good listener, and offer encouragement for good ideas and well-developed thoughts, with constructive criticism where appropriate.
- Keep the student informed about relevant regulations and administrative processes in the Unit, School and University
- Guide, advise, help, constructively criticise, but not push – it is the student's responsibility to be motivated to succeed and to assume ownership of the research project.

- Make arrangements for continuing supervision during periods of absence.
- Provide advice and guidance on the preparation of the:

  Research proposal seminar,

  Literature Review & Research Plan,

  Research thesis, and

  Poster presentation & defence
- Provide relevant feedback to the Honours Coordinator and Examiners by completing the 'Supervisor's Assessment' form (Appendix B).
- Participate as an observer during the poster presentation and defence.
- Attend an Examiners Meeting at end of year, if required, to enable major differences in thesis marking between examiners to be resolved.

Responsibilities of the Honours Examiner

Each student will have two examiners with expertise in the area of the project. The Examiners take part in multiple aspects of assessment of students. Specifically, the Examiners should:

- Attend and assess the research proposal seminar (late April)
- Read and assess the literature review & research plan and provide feedback on the work.
- Read and mark the research thesis (late October)
- Attend and participate in the Poster Presentation & defence (late October/early November)
- Contribute to achieving a fair and equitable grade for the student through discussions and negotiation with the Course Coordinator(s) via email, phone or online communication (early November)

Responsibilities of the Honours Coordinator

The Honours coordinator is responsible for organising and overseeing the entire Honours course. Specifically, the Honours Coordinator will:

- Call for Honours projects (July) and prepare the Honours booklet (September).
- Coordinate conditional enrolment of Honours students (from September onwards).
- Ensure all students are correctly enrolled and installed in the supervisors' labs (January/February).
- Organise Honours Orientation program and safety/training modules (for late-February).
- Organise welcome function for Honours students (late-February) and introduce them to the structure, assessment expectations and timelines of the course.
- Assign examiners to each student (late February).
- Organise Project proposal seminars (early May)
- Collect Literature Review/Research Plan from Students and distribute to examiners (late May); provide feedback to students from the examiners.
- Informally check on students' progress (May to August).
- Distribute the Research Thesis to examiners, together with marking guidelines (mid-October) and coordinate with examiners regarding the final grade.

- Organise and run the conference Poster Presentation sessions (late October) and collate the examination marks.
- Present the final marks and grades to the Board of Examiners for approval and submission.

Plagiarism

Plagiarism is defined as appropriating someone else's words or ideas without acknowledgment. New ideas and findings are crucial to the advancement of knowledge and are typically published in international journals under particular authors' names. It is extremely important that this credit be properly assigned for personal, financial and historical reasons. As scholars, we have to rigorously acknowledge previous contributions if we are to expect that in turn, we will be acknowledged in the future.

Copying material from a published source without properly citing the source, or copying from another Honours student or other thesis constitutes plagiarism. The University has strict rules about academic integrity, and views plagiarism within a thesis as major misconduct.

If you are in doubt as to what constitutes plagiarism, make sure you consult your Supervisor or Honours Coordinator, and/or consult the University policy on Academic Misconduct:

https://www.uwa.edu.au/students/-/media/Project/UWA/UWA/Students/Docs/UWA-Academic-Conduct-Policy.pdf

Appendix A: Marking Guides

Literature Review and Research Plan Assessment Sheet

Page 1 of 2, please see below

Examiners: please complete the ***assessment sheet (page 2) and email it back to the Honours Coordinator within*** 2 weeks of receipt.

Some criteria to aid in your assessment have been listed below:

The review:

- Provides a review of the relevant literature to support their hypothesis and does not include irrelevant Literature?
- Demonstrates critical thinking.
- Follows a logical flow and progression?
- Identifies gaps in knowledge leading into research question.
- Contains high quality and appropriately labelled diagrams and tables.
- Discusses the potential significance and impact of the project?

The proposal:

- Describes a well-designed program of research.
- Includes an overall hypothesis that is subdivided into well-defined objectives or specific aims?
- Provides an overview of the proposed experiments that are linked to the proposed aims? This should include experimental materials and methods, data management, analysis and statistics, ethics and recruitment of participants as required.
- Demonstrates that the student understands their project.

Grammar and formatting:

- Is there use of clear and concise scientific English with accurate spelling, punctuation & grammar?
- Is the document formatted correctly (page size, numbering etc) with appropriate use of the correct font (12 point Calibri) and headings?
- Are all figures/tables labelled and referred to in text?

Referencing:

- Are all scientific/factual statements and descriptions correctly referenced?
- Is the formatting of in-text citations uniform?
- Does the bibliography include an appropriate mix of reviews, original research, and recent plus older publications?
- Is the bibliography content and format consistent and accurate?

Student Name: _____ Assessor Name_____

Assessment Criteria	Mark
Literature review (50 marks) a) Does it provide a review of the relevant literature to support their hypothesis and does not include irrelevant Literature? b) Demonstrate critical thinking? c) Follow a logical progression? d) Identify gaps in knowledge leading into research question. e) Appropriate use, quality and labelling of diagrams and tables. f) Include an overall hypothesis that is subdivided into well-defined objectives or specific aims? g) Discuss the potential significance of the project?	
Research proposal (35 marks): a) Provide a well-designed program of research? b) Provide an overview of the proposed experiments that are linked to the proposed aims? This should include experimental materials and methods, data management, analysis and statistics, ethics and recruitment of participants as required. c) Demonstrate that the student understands their project?	
Grammar, formatting and referencing (15 marks): a) Is it clear and concise scientific English? b) Is the document formatted appropriately and the spelling, punctuation & grammar correct? c) Is the document 12pt font text – Calibri, Arial or Times New Roman? d) Is the page size A4 with margins of 2 cm (width) and 2.5 cm (height) used consistently throughout the text? e) Are subheadings, page numbers, headers/footers consistent? f) Are all figures/tables labelled and referred to in text? g) Is the document fully and accurately referenced: • Statements correctly referenced. • Formatting of in-text citations is uniform. • Inclusion of reviews, original research, and recent plus older publications in the bibliography. • Consistency and accuracy of the bibliography content and format.	

Assessor Signature_____ Date_____

Scales: ***H1-D+*** (90 – 100%); ***H1-D-*** (80 – 89%); ***H2A-D+*** (75 – 79%) ***H2A-D-*** (70 – 74%); ***H2B*** (60 – 69%); ***H3*** (50 – 59%); ***F*** (<50%)

Thesis Assessment Sheet
Page 1 of 2, please see below

Thesis Assessment Criteria	Mark
Abstract, Introduction, Aims and hypothesis (5 marks) a) Did the Abstract summarise succinctly and accurately the aims and outcomes of the study, and could it be understood without reading the rest of the Thesis? b) Did the Introduction provide appropriate scientific background, as well as identify limitations of the literature and areas of controversy? c) Did the Introduction include the key articles within the scientific literature? Were the Aims and Hypotheses clear and valid? d) Did the student adequately address the examiners feedback?	
Materials and Methods (15 marks) a) Were the Materials and Methods clearly described and fully referenced? b) Were the Methods used appropriate and valid for the stated aims?	
Results (30 marks): a) Does the Results section represent an adequate body of work? b) Are the results presented clearly and accurately? c) Were appropriate choices of experimental conditions, such as doses, concentrations, time-points, etc. used? Were sufficient controls and replicates performed? d) Were appropriate numbers of observations performed? e) Was there sound and appropriate use of statistical analyses and tests? f) Was the presentation of results (Figures, Tables, etc.) clear and logical?	
Discussion (30 marks): NB Please take into account that the discussion is written by the student with NO input from the supervisor. a) Is the Discussion relevant to the Introduction, Methods and Results? b) Is it logical in presentation and content? c) Is there evidence of critical and creative analysis? d) Does it place the findings in the context of past studies? e) Are there suggestions for future studies? Is there evidence of over-interpretation of data? f) What is frequency and extent of bias in interpreting the data? g) Have unexpected or inconsistent results been fairly and skilfully discussed?	
References (10 marks): a) Is the in-text citation style appropriate and consistent? b) Is the reference list free from careless errors? c) Is the content of the Thesis supported with appropriate in-text primary research citations, or is there over-reliance on reviews?	
Style and Presentation (10 marks): a) Is the Thesis well-organised (e.g. appropriate use of subheadings), succinct and clear? b) Is it of an appropriate length? c) Does the Thesis demonstrate an appropriate use of grammar? d) Has care been demonstrated to avoid spelling mistakes and typographical errors? Has the nominated journal style been followed consistently	

Assessor Signature_____ Date_____

Scales: ***H1-D$^+$*** (90 – 100%); ***H1-D$^-$*** (80 – 89%); ***H2A-D$^+$*** (75 – 79%) ***H2A-D$^-$*** (70 – 74%); ***H2B*** (60 – 69%); ***H3*** (50 – 59%); ***F*** (<50%)

Student Name: _____ Assessor Name_____

Thesis Assessment Criteria	Comments
Abstract, Introduction, Aims and hypothesis (5 marks)	
Materials and Methods (15 marks)	
Results (30 marks):	
Discussion (30 marks): NB Please take into account that the discussion is written by the student with NO input from the supervisor.	
References (10 marks):	
Style and Presentation (10 marks):	

Comments:

Assessor Signature_____ Date_____

School of Biomedical Sciences

Honours in Medical Research

Seminar Reflection Worksheet

Student name and date:

Seminar presenter (name):

Seminar title or topic:

Background and rationale:

Design & methodology:

Findings and take-home message:

Presentation lessons:

Enrolment in Honours in Medical Research for 2024

DECIDING ON AN HONOURS PROJECT

A list of Honours projects for 2024 is provided in the final section of this Booklet. Once you have identified a project of interest you should promptly contact the project Supervisor(s) to discuss the project. If you and a Supervisor agree to you undertaking a particular project you should then you can formally apply for entry to the Honours program.

All students must identify a project and supervisor before attempting to enrol.

Note: supervisors often have other projects that may not be listed in this booklet; if you are interested in undertaking an Honours project with a specific supervisor, arrange to meet with them and discuss options.

Identify the appropriate Entry Requirements

Students with a Biomedical Sciences or Biomedical Major:

If you have completed a Biomedical Science Major with an average of 65% or better in third year Units contributing to the major, you are eligible to apply directly online:

https://handbooks.uwa.edu.au/undergraduate/honoursdetails?code=HON-BIOMS

Students without a Biomedical Sciences or Biomedical Major:

The key requirement is that both UWA- and non-UWA applicants can demonstrate the equivalent of a 65% average in third year major units in disciplines that are relevant to their proposed project. Supporting documentation uploaded must include a brief research proposal with confirmation from the relevant supervisor, School or Research Institute that general facilities are available to support the project.

Submit an application

Step 1: Register your agreed project with the UWA Biomedical Sciences office.

Once you have met with your prospective supervisor, the project has been confirmed, and the necessary induction programmes have been advised, please complete the yellow 'Application for Medical Research Honours form' included in this Handbook. This Form must be submitted to the Administrative Office, School of Biomedical Sciences, UWA, prior to enrolling so that the School knows that a project and Supervisor have been assigned to you, when making a decision regarding approval of your on-line application.

Step 2: Apply to the Honours Programme.

Visit the UWA Honours page for links to the UWA application portals
http://www.studyat.uwa.edu.au/courses-and-careers/honours#aust
Use the following codes when applying:
BMED (Honours), Course Code: BH006, Major/Program Code: HON-BIOMS,

Step 3: Enrol in the appropriate units.

You will need to enrol in the Bachelor of Biomedical Science (Honours) six units shown below: BMED4001, BMED4002, BMED4003, BMED4004, BMED4005, BMED4006.

Please refer to Student Central for advice on enrolment dates and fees.

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Application for Honours in Medical Research 2024

To be filled in by STUDENT:

Name: Student No:

Primary Supervisor:

E-mail address: Contact Number:

Mailing address:

Biomedical Sciences Supervisor (if different from above):

E-mail address: Contact Number:

Mailing address:

Project Title:

Honours Booklet Page No: (if applicable)

To be filled in by SUPERVISOR:

Names of **two** suitably qualified examiners who have agreed to examine the student:

Name:

Position & Institution:

Email address: Contact number:

Name:

Position & Institution:

Email address: Contact number:

Honours Induction Checklist *– Supervisors, please indicate whether the above student will need to take any of the following induction programmes or ethics approvals:*

☐ PAWES (Program in Animal Welfare, Ethics and Science)

☐ Gene Technology

☐ Radioisotope handling course

Other programmes required:

☐

☐

Ethics Requirements:

Non-human animal Research ethics approval - required ☐ already approved ☐

Human Research ethics approval - required ☐ already approved ☐

I agree to supervise this student in honours for 2024.

Supervisor's signature: Date:

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Honours Projects Available in 2024

Primary Supervisor(s)	Project Title	Page
Dr. Lucy Furfaro	Active induction of Group B Streptococcus bacteriophages	33
Dr. Sharon Perrella	Postpartum pain and analgesia use in breastfeeding women after a Caesarean section birth	35
Prof. Yuben Moodley	Cellular stress responses of IPSC-derived alveolar epithelial cells with SFTPC gene mutation	37
Dr. Jasreen Kular	Group A *Streptococcus* colonisation of heart endothelium in the pathogenesis of Acute Rhematic Fever	39
A/Prof. Lynette Fernandes	Identifying the processing demands of summative assessments in pharmacology	41
A/Prof. Lynette Fernandes	Cultivating teamwork skills to prepare Science graduates for the workplace	42
A/Prof. Jason Waithman	Improving the Immune Response to Cancer	43
A/Prof. Allison Imrie	Immunoglobulin responses induced after immunization with different SARS-CoV-2 vaccines.	45
Dr. Liz Johnstone	Investigation of G Protein-Coupled Receptor Molecular Pharmacology	47
Dr. Omar Kujan	The Expression of Chemokines in Premalignant to Advanced Oral Cancer	48
A/Prof. Nathan Pavlos	Development of a human cell model to study rare bone diseases	49
A/Prof. Kate Hammer	Interactions between antimicrobial components and physicochemical parameters in honey	51
Dr. Baca Chan	Harnessing viruses to combat cancer.	53
Dr. Jonathan Chee	Developing a novel T cell biomarker of islet pathology	54
Dr. Jonathan Chee	Repurposing anti-copper drugs to improve mesothelioma immunotherapy	56
Dr. Kelly Martinovich	Immunostimulatory effect of respiratory bacteria on respiratory epithelium to inform development of novel therapies	58
Dr. Jessica Mountford	Investigating causative factors of early-onset myopia in zebrafish as a model of refractive error.	60
Dr. Andrew Stevenson	Identifying fibroblasts subtypes in skin and investigating their role in skin repair, scar formation and fibrosis	62
Dr. Andrew Stevenson	The impact of matrix stiffness on skin fibroblasts	63
Dr. Belinda Guo	Next-generation sequencing of platelets to monitor blood cancers	64
Prof. Mark Nicol	Identification of probiotic bacteria to prevent mastitis in breastfeeding women.	65
Prof. Mark Nicol	*Development of next-generation probiotics to prevent childhood pneumonia.*	67
Dr. Christian Tjiam	Defining the surface-ome of mucosal tissue-resident memory B cells	70

Primary Supervisor(s)	Project Title	Page
Dr. Alistair Cook	Exploring the role of macrophages in response to tumour irradiation	72
Prof. Jenette Creaney	Influence of mesothelioma cell plasticity in clinical outcomes	73
Prof. Jenette Creaney	Exploring mechanisms of mesothelioma chemotherapy resistance	75
Prof. Jenette Creaney	A combined radiotherapy and ferroptotic approach to treating mesothelioma	77
A/Prof. Alec Redwood	Understanding T cell diversity to cancer antigens	79
A/Prof. Alec Redwood	The impact of T cell exhaustion on cancer vaccination	81
Dr. Sebastien Malinge	Towards finding new cures for childhood leukaemia	83
Dr. Jua Iwasaki	A novel vaccine to prevent Group A Streptococcus attachments to the tonsils	85
Dr. Henry Hui	Detection of deletions of chromosome 13 in chronic lymphocytic leukaemia by immuno-flowFISH	87
Justine Bendo	Identifying the protein-protein interaction of the Macrophage infectivity potentiator (Mip) of *B. pseudomallei.*	88
Ashley Johnson	Characterisation of a novel folate biosynthesis fusion gene in *Burkholderia pseudomallei*	90
A/ Prof. Charlene Kahler	Interference patterns between Neisseria species.	92
A/Prof. Charlene Kahler	Ceftriaxone resistance in Neisseria meningitidis	94
A/ Prof. Charlene Kahler	Understanding MisR regulation in N. meningitidis	96
Dr. Warren Pavey	Optimising a new method of heart storage – gas persufflation	98
Dr. Amy Prosser	Mapping allospecific T cells in transplantation	100
Dr. Okhee Yoo	Taste masked microparticles for formulating bitter drugs into acceptable medicines for young children	102
Dr Shaun Teo	Developing educational resources to improve awareness and knowledge of Type 1 Diabetes within community sport settings	104
Dr Aveni Haynes	What is the burden of cardiovascular disease in Western Australian children and adolescents diagnosed with type 1 and type 2 diabetes?	106
Dr Aveni Haynes	Investigating geospatial patterns in the occurrence of childhood onset type 1 diabetes in Western Australia	108
A/Prof Mary Abraham	Exploring management of hypoglycaemia in day-to-day life in children with Type 1 diabetes.	110
Dr Craig Taplin	The impact of early morning exercise performance on acute post-prandial glucose time in range and 24h glycaemic control in youth with Type 1 Diabetes	111
Dr. Steven Mutsaers	Examining the efficacy of the Hck inhibitor RK-20449 in the mouse lung fibrosis model	113
A/Prof. Chris Bundell	Anti MDA5 antibodies: are they important,can we improve our diagnostics approach	115
A/Prof. Phil Burcham	A Novel Fluorescence Quenching Microplate Assay for Rapid Caffeine Estimation in Human Saliva	117
Dr. Anthony Akkari	Evaluating strategies to improve the awareness of pharmacogenetics in youth.	119
Dr. Belinda Kaskow	Multi-omic immunophenotyping of KIR+CD8+ T cells in Multiple Sclerosis	121

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Research Project Proposal 2024

Primary supervisor (name):	Lucy Furfaro
Contact details (phone; email; location)	Lucy.furfaro@uwa.edu.au UWA Crawley Campus
Other supervisor/s if any (name):	Prof Barbara Chang
Contact details (phone; email; location)	Barbara.chang@uwa.edu.au QEII Medical Centre
SBMS Coordinating supervisor (for non-SBMS supervisors)	
Contact details (phone; email; location)	
Conflict of Interest	None.
Project title:	**Active induction of Group B Streptococcus bacteriophages**
Project location:	UWA Crawley Campus
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Over a century since their discovery, bacterial viruses known as bacteriophages could provide an answer to the rapidly developing antibiotic resistance in bacterial pathogens. These viruses are ubiquitous and estimates of their abundance equate to a trillion bacteriophages (phages) per grain of sand on this Earth[1]. The lytic lifecycle of phages is an attractive option for therapy, due to the ability to infect specific ranges of host bacteria, replicate within them, kill the host bacteria and continue the process with the now exponential number of phages released. This is essentially a self-dosing antimicrobial agent[2]. *Streptococcus agalactiae* is a leading neonatal pathogen that is targeted during pregnancy to prevent vertical transmission[3]. This results in widespread antibiotic administration to colonised women during pregnancy and may be an ideal clinical scenario for phage therapy[4]. To date, no obligately lytic *S. agalactiae*-specific phages have been isolated, rather only temperate phages which have the ability to integrate have been characterised. Our group is interested in understanding the role these temperate phages play in *S. agalactiae*. Prophages are widespread in many organisms, however, some are remnants and inactive. This project will assess the phenotypically active prophages of *S. agalactiae* by inducing their entry to the lytic cycle. There are a number of different mechanisms of induction and we aim to compare common medications[5] and antibiotic agents impact on phage induction. Understanding how readily induction occurs and under what conditions will provide insight into this neonatal pathogen and equip us with candidates for bioengineering.

Aims

1. Compare the ability of different agents to induce prophages from clinical *Streptococcus agalactiae* isolates.
2. Isolate, purify and characterise induced phages to assess host range activity.
3. Assess the cross-infection of the induced phages in other phage-free *Streptococcus agalactiae* isolates.

Techniques

- Bacterial culture
- Growth and induction curves
- Plaque assays
- DNA extraction
- PCR
- Data analysis and bioinformatics

References

1. Keen EC. A century of phage research: bacteriophages and the shaping of modern biology. Bioessays. 2015 Jan;37(1):6-9.
2. Kutter EM, Kuhl SJ, Abedon ST. Re-establishing a place for phage therapy in western medicine. Future Microbiol. 2015;10(5):685-8.
3. Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease: revised guidelines from CDC, 2010. Recommendations and Reports. 2010;59(10):1-32.
4. Furfaro LL, Chang BJ, Payne MS. Applications for bacteriophage therapy during pregnancy and the perinatal period. Frontiers in Microbiology [Review]. 2018 2018-January-11;8(2660).
5. Sutcliffe SG et al. Common oral medications lead to prophage induction in bacterial isolates from the human gut. Viruses. 2022 Dec 21;15(1):25.

Research Project Proposal 2024

Primary supervisor (name):	Dr Sharon Perrella
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Conflict of Interest	
Project title:	**Postpartum pain and analgesia use in breastfeeding women after a Caesarean section birth**
Project location:	Geddes Hartmann Human Lactation Research Group, SMS
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Caesarean birth involves major abdominal surgery with associated pain and reduced mobility. Findings from our recent study show elevated pain scores across the first 2 weeks after Caesarean birth that impact a woman's ability to care for her newborn infant. A better understanding of maternal analgesia use after Caesarean birth is needed to inform postpartum care. **Aims:** To describe maternal pain scores in the early weeks after birth To describe analgesia use in the first 2 weeks after discharge To explore associations between maternal pain scores, surgical anaesthetic type, and analgesia use after discharge. **Design:** An anonymous online survey of Australian women that had birthed by Caesarean section within the previous 12 months was conducted May – July 2022, with > 1200 responses received. The primary aim was to describe women's experiences of establishing breastfeeding after a Caesarean birth. A secondary outcome was to determine women's experience of pain, with pain

	score ratings (immediately after birth, in the days following birth and in the first 2 weeks at home), anaesthetic type and analgesia use recorded. **Techniques** The retrospective quantitative data will be analysed using descriptive statistics to describe women's experiences of post-Caesarean pain and pain management. Experiences will be compared between the following subgroups using linear mixed models: • primiparous and multiparous women • non-elective and elective caesarean birth Associations between pain scores and analgesia use will be explored, and the appropriateness of selected analgesia will be evaluated against published standards. **Outcomes** Findings of this project will inform clinical practice as well as guidelines for postpartum women. The student will be provided with multiple opportunities to interact with and present to maternity health care providers. This project is ideally suited to a student with a pharmacology major, a women's health major, or particular interest in maternity health care. Please e-mail Dr Sharon Perrella if you would like to discuss this opportunity.

Research Project Proposal 2024

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Conflict of Interest	None
Project title:	**Cellular stress responses of IPSC-derived alveolar epithelial cells with SFTPC gene mutation**
Project location:	Harry Perkins Institute for Medical Research Building (North), QQ Block, QEII Medical Centre, Nedlands WA 6009 Harry Perkins Institute of Medical Research (South), Fiona Stanley Hospital Campus, 5 Robin Warren Drive, Murdoch WA 6150
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Idiopathic pulmonary fibrosis (IPF) is a debilitating and ultimately fatal interstitial lung disease characterised by a progressive decline in pulmonary function and irreversible scarring of the lung. While the exact pathogenesis of IPF is not fully understood, persistent micro-injury from tobacco smoke, dust exposure and infectious disease is believed to cause dysfunction in lung tissue repair and remodelling. Furthermore, dysregulated alveolar epithelial type II cells (AECIIs) have been implicated as a mediator of lung fibrosis in IPF. AECIIs play a critical role in maintaining lung homeostasis through their regenerative properties and secretion of surfactant proteins. Mutations in surfactant protein C (SP-C) gene (SFTPC) resulting in a misfolded and

	malfunctional SP-C protein have been identified in both familial and sporadic IPF. Recently, a model of SP-C mutant-expressing AECIIs was developed from patient-specific induced pluripotent stem cells. Mitochondrial dysfunction was reported in this cell line however further studies are required to identify a potential role for other cellular injury pathways, such as endoplasmic reticulum (ER) stress, telomere length, senescence and apoptosis, in response to injury and how these pathways ultimately lead to fibrosis. This study aims to investigate the effect of SFTPC mutations on cell injury pathways in iPSC derived AECIIs and the order of stress events following injury. **Techniques:** Tissue culture, flow cytometry, real time PCR, confocal laser scanning microscopy, immunocytochemistry **References:** 1) Vazquez-Armendariz AI, Barroso MM, El Agha E, Herold S. 3D In Vitro Models: Novel Insights into Idiopathic Pulmonary Fibrosis Pathophysiology and Drug Screening. Cells. 2022; 11. 2) Winters NI, Burman A, Kropski JA, Blackwell TS. Epithelial Injury and Dysfunction in the Pathogenesis of Idiopathic Pulmonary Fibrosis. Am J Med Sci. 2019; 357: 374-8.

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**Group A *Streptococcus* colonisation of heart endothelium in the pathogenesis of Acute Rhematic Fever**
Project location:	Telethon Kids Institute
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	This project seeks to understand how a bacterial infection damages the heart valves in children, causing the chronic condition Rheumatic heart Disease (RHD). RHD results from a common childhood sore throat infection caused by Group A *Streptococcus* (GAS) bacteria. In some children, GAS infections can trigger an inflammatory disease called acute rheumatic fever (ARF). A symptom of ARF is inflammation and damage to the heart valves, and repeated ARF episodes can cause permanent heart valve damage known as RHD. While rare in most populations, Indigenous Australian children have the highest prevalence of RHD in the world, and account for 92% of RHD diagnoses in Australia despite only making up ~3% of Australia's population. Based on preliminary data from our team we hypothesise that ARF-causing GAS strains directly colonise heart endothelial cells, through an ARF-associated GAS surface protein. **The aims of the study will be to:** 1) Determine if ARF-causing GAS strains can directly colonise the heart. 2) Determine if an ARF-associated GAS surface protein is involved in the colonisation.

	3) Determine the endothelial cell response to GAS colonisation. **Techniques involved include:** Cell culture, bacterial culture, adhesion and invasion assays, molecular cloning, western blot, immunofluorescence staining

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**Identifying the processing demands of summative assessments in pharmacology**
Project location:	M Block QEII Medical Centre
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Assessment is probably the most important event to drive student learning. However, unless students understand what is being asked of them in exams, learning may be steered in the wrong direction. While students may readily address the knowledge demands of exam questions, they often address processing demands poorly or not at all. This may be due to a misinterpretation of the action words / phrases in exam questions. While many action words have universal meanings, others have nuanced meanings within certain disciplines. This project aims to research, document and address the processing demands associated with assessment literacy in Pharmacology. This project would appeal to students who are interested in working on a project that involves education research.

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**Cultivating teamwork skills to prepare Science graduates for the workplace**
Project location:	M Block QEII Medical Centre
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	"Being a team player is the most valuable quality a person should develop in order to thrive in the world of work and life" (Patrick M. Lencioni - The Ideal Team Player: How to recognize and cultivate the three essential virtues). Teamwork skills are teachable qualities that students need to succeed in a 21st century workplace. However, teamwork does not automatically occur as a consequence of putting people together. Teamwork is a dynamic skill that requires instruction, guidance, and mentorship. This project aims to develop resources to (1) assist staff to deliver Teamwork and modules and (2) assist students to grow their teamwork skills. This project would appeal to students who are interested in working on a project that involves education research.

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**Improving the Immune Response to Cancer**
Project location:	UWA M Block QEII Campus
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Our research program focusses on understanding and improving the immune response to cancer. Cancer immunotherapy as a discipline is delivering promising and vital alternatives for both adults and children in our efforts to control and cure cancer. However, immunotherapies overall provide vastly diverse outcomes between different patients and cancer types. Several key questions about why this might occur, or how to maximise the potential of immunotherapy, still remain. Our team deliberately seeks to answer the most complex immunological questions to provide meaningful, functional data so the full promise of immunotherapy can be realised. Our team harnesses the power of basic science, molecular biology, and genomics to forge tangible solutions that can dramatically improve the survival of people with cancer; with a specific focus on individual's with melanoma, sarcoma and leukaemia. Our current projects utilise a mixture of

	cell biology, animal models and multi-omics technologies, with the following focus areas: 1. Developing tailored immunotherapies by identifying novel tumour subtypes based on their molecular characteristics 2. Understanding and overcoming tumour heterogeneity using a novel and innovative adoptive cell therapy protocol 3. Investigating a treatment method using donated cells as alternatives for patients who cannot receive immunotherapy from their own cells The core values underpinning our team are research excellence and innovation, which we achieve by embracing an entrepreneurial mindset in all our studies and by applying a multi-disciplinary lens on our work with the help of our collaborators. We are applying the latest disruptive technologies, such as single cell sequencing, to challenge existing dogma and assumptions associated with many of the significant problems and frustrations faced in the clinic. Finding solutions to complex issues requires an exceptionally capable team, which we have assembled. While there is no doubt that future obstacles will impede our ability to treat every person successfully – a key goal of our team is to continue to train the next generation of great researchers with the requisite skills to overcome those challenges on the horizon. We encourage all interested students (PhD, Masters, Honours) to contact us and discuss specific project options.

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**Immunoglobulin responses induced after immunization with different SARS-CoV-2 vaccines.**
Project location:	Ist Floor, L block QEII Medical Centre
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	The most effective response to the SARS-CoV-2 pandemic has been the rapid development of vaccines and their deployment into the general population, resulting in significantly reduced human mortality 1. The vaccination program was the largest public health initiative ever undertaken in an immunologically naïve population and provides a unique opportunity to investigate the development of the immune response to a well-defined antigen, the SARS-CoV-2 spike protein 2. Initially, two vaccines were available for the development of immunological protection within the local Western Australian community, Pfizer BNT162b2 and AstraZeneca ChAdOx1-S were initially available to age-defined groups, and this was followed by Moderna mRNA-1273 several months later. Serum was collected both pre- and post-vaccination in 2021-2022 from a variety of vaccine recipients, many of whom received different vaccine formulations for their primary, secondary and tertiary vaccines. This study will evaluate the development of specific immunoglobulin generated towards the SARS-CoV-2 spike protein focussing particularly on the IgG and IgM isotypes and if time allows, the development of IgG subclass responses 3. Evaluation will be by an in-house ELISA and antibody responses will

	be measured using a commercially prepared spike protein formulation that has been developed to be conformationally stable 4. This dataset will provide important information about the human immune response to different vaccine formulations and will contribute to the improved knowledge of immune responses in a population that was broadly naïve to the SARS-CoV-2 spike protein in the times these samples were collected. 1 Fiolet, T., Kherabi, Y., MacDonald, C.-J., Ghosn, J. & Peiffer-Smadja, N. Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: a narrative review. Clinical Microbiology and Infection 28, 202-221, doi:https://doi.org/10.1016/j.cmi.2021.10.005 (2022). 2 Luo, J. et al. A Quantitative ELISA to Detect Anti-SARS-CoV-2 Spike IgG Antibodies in Infected Patients and Vaccinated Individuals. Microorganisms 10, 1812 (2022). 3 Vidarsson, G., Dekkers, G. & Rispens, T. IgG Subclasses and Allotypes: From Structure to Effector Functions. Frontiers in Immunology 5, doi:10.3389/fimmu.2014.00520 (2014). 4 Hsieh, C.-L. et al. Structure-based design of prefusion-stabilized SARS-CoV-2 spikes. Science 369, 1501, doi:10.1126/science.abd0826 (2020).

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**Investigation of G Protein-Coupled Receptor Molecular Pharmacology**
Project location:	Harry Perkins Institute of Medical research
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Background: G protein-coupled receptors (GPCRs) are critically important targets for pharmaceuticals due to their crucial role in responding to hormonal, neurotransmitter and environmental stimuli. We are looking to develop the next generation of medicines targeting these receptors that are not only more effective, but also have fewer side effects. This requires improved understanding of how GPCRs function at the molecular and cellular level, in terms of ligand binding, signalling, regulation, and cellular trafficking. Aim: to investigate various novel aspects of GPCR molecular pharmacology Design/Techniques: Receptor pharmacology will primarily be monitored using bioluminescence resonance energy transfer (BRET) and other cell-based assays. Receptors and interacting biomolecules (protein and ligands) will be labelled with BRET tags and transfected or added to cells, with resulting interactions monitored using BRET. Outcomes: The results will aide in future drug discovery efforts for the GPCRs under investigation.

Research Project Proposal 2024

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Conflict of Interest	None
Project title:	**The Expression of Chemokines in Premalignant to Advanced Oral Cancer**
Project location:	Dental School
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Cancers involving the lip, oral cavity, and oropharynx (OSCC) have the 13th highest incidence and death rate among all cancers globally, accounting for 475 855 new cases and 225,900 deaths. The individual and societal burden of OSCCs are high, with a significant impact on the quality of life in afflicted patients. Additionally, there are significant economic costs, both at the patient and societal level, which escalate with advancing disease. As such, early detection and management of OSCC are paramount. Of particular use, is the identification of biomarkers that can act as prognostic predictors for early detection and screening of these cancers. A range of potential molecular prognostic biomarkers has been identified for OSCC. However, more research is required to validate many of these biomarkers. Novel proteins that remain to be explored are chemokines. They are overexpressed in OSCC compared with normal mucosa. Early evidence shows the disruption of chemokines has been implicated in the progression of dysplasia, and consequently the development of malignancy. This study will explore the role of chemokines in the microenvironment of oral carcinogenesis and their contribution to its progression.

Research Project Proposal 2024

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Conflict of Interest	n/a
Project title:	**Development of a human cell model to study rare bone diseases**
Project location:	(1) Bone Biology & Disease Laboratory, UWA School of Biomedical Sciences and ; (2) Translation Genetics, Precision Health, Genetic and Rare Diseases, Telethon Kids Institute
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background:** Paradoxically, rare diseases are common. Hundreds of millions of lives are globally affected by ~10,000 unique rare genetic diseases. In Australia alone, two million individuals suffer with a rare disease, a figure that is similar to the proportion of people living with diabetes or asthma. Despite this, people with rare diseases face disproportionate and longstanding inequity in care, including gruelling diagnostic delays and lack of treatment. Development of new diagnostics and treatments for patients with rare diseases ultimately requires a better understanding of the mechanisms underlying disease pathobiology. Autosomal Recessive Osteopetrosis (ARO) is a rare (1:250,000 births) but devastating high bone mass disease that occurs in children and is fatal unless a suitable bone marrow transplant is performed.

Children suffering ARO commonly exhibit bone fractures, poor growth, absence of a bone marrow cavity and vision loss due to optic nerve compression. Currently, very little is known about the pathogenesis of ARO, partly due to the rarity of ARO and limited patient samples available to study ARO pathobiology in depth. ARO is typically associated with dysfunction of osteoclasts, giant bone-digesting cells that regulate bone turnover and homeostasis. Osteoclasts are multinucleated cells derived from the fusion of mononuclear macrophage precursors (**Figure 1**).

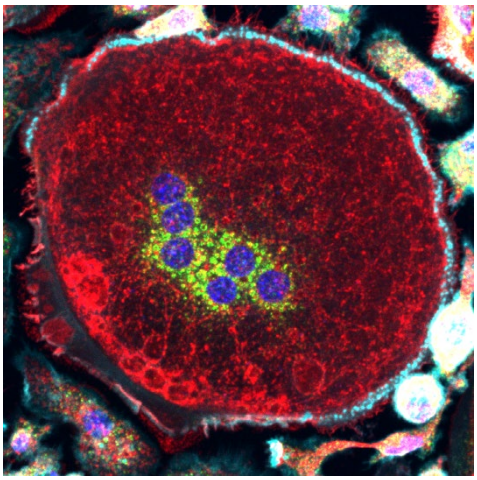

Figure 1: Morphology of an osteoclast

Presently, we lack suitable cellular models of human osteoclasts that can be manipulated genetically to introduce ARO disease causing mutations and thus be used as a testbed to study the mechanisms underpinning osteoclast dysfunction in ARO patients.

Aim:

This project aims to develop a new cellular model of ARO using osteoclasts derived from human inducible Pluripotent Stem (iPS) cells carrying ARO-disease causing gene mutations.

Techniques:

Students will become familiar with the following key methods: stem cell and osteoclast culture, immunofluorescence confocal microscopy, CRISPR gene editing, sequencing, bone resorption assays etc.

Outcomes:

(i) Optimise and characterise the differentiation of human iPS cell into functional osteoclasts (hiPSdOCs).

(ii) Introduce an ARO causing genetic mutation in hiPSdOCs.

Research Project Proposal 2024

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Conflict of Interest	None to declare
Project title:	**Interactions between antimicrobial components and physicochemical parameters in honey**
Project location:	Lab 1.4 L block, QEII Medical Centre
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Honey is a complex mixture containing sugars, water, phenolic compounds, proteins, minerals and vitamins, produced largely by the European honeybee *Apis mellifera*. Honey has antibacterial and antifungal activity, which varies according to the specific floral source, and is largely attributed to osmotic activity (since it is essentially a saturated sugar solution), low pH, production of hydrogen peroxide and the activity of plant-derived phenolic compounds. Although antibacterial activity can be attributed to these factors described above, the contribution of each component has not actually been well characterised. In addition, the possibility that the various antimicrobial factors within honey are acting synergistically is often hypothesised, but has also not been systematically investigated. Therefore, this project aims to investigate the contribution of components (such as sugars) or conditions (such as pH) that are universally present in honeys to total antimicrobial activity. This will be achieved by investigating each component or condition in isolation, as well as combined. Activity will be assessed against a range of microorganisms, including Gram positive and negative bacteria, to ensure that a broad and representative understanding of the relationship between each component and activity is obtained. Interactions between components and conditions will be investigated using checkerboard assays in 96-well microtitre trays. A series of dilutions of

	each agent in prepared and then each is dispensed into the tray to create a wide range of combinations (a checkerboard). If interesting relationships are identified in the checkerboard assays, time permitting these may be followed up with time kill assays, with bacterial viability determined using viable counting techniques. Kwakman PHS, Zaat SAJ. Antibacterial components of honey. IUBMB life. 2012;64(1):48-55. doi: 10.1002/iub.578. Masoura, M., Passaretti, P., Overton, T.W. et al. Use of a model to understand the synergies underlying the antibacterial mechanism of H2O2-producing honeys. Sci Rep 10, 17692 (2020).

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**Harnessing viruses to combat cancer.**
Project location:	5th Floor Harry Perkins Building
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background**. Pleural mesothelioma (PM) is incurable and has limited sensitivity to standard forms of therapy, with median survival of only 12 months. The ability of the immune system to recognise and control cancer has been known for more than 100 years, and has been harnessed in modern immunotherapies. These immunotherapies, such as immune checkpoint blockade (ICB), have revolutionized cancer treatment. However, ICB only works in a small subset of patients and is not curative in PM. Therefore, alternative or synergistic strategies are required. **Design**. In this project you will use a virotherapy approach that combines the activation of natural killer (NK) cells with tumour specific vaccination to prime anti-cancer T cell responses. **Aim 1** to use a modified virus to retarget NK cells to PM. **Aim 2** to use a modified virus as a cancer vaccine. **Techniques**. This project is laboratory based and will include a range of techniques such as; virology, flow cytometry and animal models. **Outcomes**. This study will determine if a virus can be used to enhance NK cell and T cell activation and promote effective control of MM.

Research Project Proposal 2024

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Conflict of Interest	
Project title:	Developing a novel T cell biomarker of islet pathology
Project location:	School of Biomedical Science, Perkins Level 5
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Type 1 Diabetes (T1D) is an organ-specific autoimmune disease in which T cells destroy insulin producing beta cells within the pancreatic islets. There is no cure for T1D, and the disease is managed by insulin injections. Islet pathology occurs before clinical disease, and this project seeks to develop novel blood biomarkers of islet pathology based on T cells. T cells that target islet antigens can be detected in the blood of patients that developed T1D. However, a bottleneck is the identification of T cells that are actually specific for islet antigens. The current approach involves isolating islet-reactive T cell clones from patient blood or islets, but the process is technically challenging. We propose the use of deep learning on T cell receptor sequencing (TCR) data to identify islet-specific TCRs in the peripheral blood and pancreatic islets. Each unique TCRβ sequence is a tag for a unique T cell clone, sequence based profiling of T cells is a useful tool for monitoring antigen-specific T cells In this project, we will apply a published deep learning algorithm on TCR data in a well characterised model of autoimmune diabetes (NOD mouse). In this model, we were the first to describe that the frequency of CD8+ T cells specific for an islet antigen (IGRP) in the

	peripheral blood increased with the severity of islet pathology. We have extensively characterised the TCRs of IGRP specific CD8+ T cells. In this project, we will isolate blood and islets from NOD mice at different stage of disease, sequence TCRβs and apply deep learning algorithms to identify TCRs that are predictive of islet pathology. We hypothesize that this approach will be able to identify a peripheral blood TCR signature predictive of islet pathology, and that this signature will consist of IGRP reactive clones. There are promising immunomodulatory agents that can delay diabetes onset by targeting T cells. This project is important for developing novel, non-invasive strategies to monitor islet autoimmunity.

Research Project Proposal 2024

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Conflict of Interest	N/A
Project title:	**Repurposing anti-copper drugs to improve mesothelioma immunotherapy**
Project location:	National Centre for Asbestos Related Diseases, Harry Perkins Institute of Medical Research
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background** Mesothelioma is an incurable cancer. While new therapies that increase anti-cancer immune responses have shown promise, most patients do not benefit from immunotherapy. Metals such as copper accumulate in mesothelioma, are essential for tumour growth and help cancers evade the immune response. Using copper-binding drugs, we aim to reduce the copper available to the cancer and understand how it improves the function of anti-cancer immune cells. We will investigate the changes in gene and protein expression of tumour cells in response to copper and copper chelation therapy. Additionally, we will characterise the effect of treatments on immune cell (T cells and macrophages) activity in-vitro. We will assess T cell mediated killing of tumour

	cells using in-vitro coculture assays in the presence of copper chelation therapies. Finally, we will determine the activity of copper chelation therapies in-vivo, and their effect on the tumour microenvironment. As these copper-binders are clinically approved for use in other diseases, they are novel drugs that can be repurposed to improve immunotherapies for patients with mesothelioma. **Aims** To understand how copper chelation improves immune cell function To determine whether copper chelation therapy improves anti-tumour immune responses **Design** **Techniques** Animal models Cell Culture Flow cytometry Drug repurposing **Outcomes** Chance to travel to Sydney to work with UNSW collaborators.

Research Project Proposal 2024

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Conflict of Interest	Nill
Project title:	**Immunostimulatory effect of respiratory bacteria on respiratory epithelium to inform development of novel therapies**
Project location:	Telethon Kids Institute-PCH
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background:** Bacterial respiratory infections are mostly caused by *Streptococcus pneumoniae*, Non-typeable *Haemophilus influenzae* (NTHi) and *Moraxella catarrhalis.* NTHi and *M. catarrhalis* currently have no approved vaccines. A novel approach for preventing these infections could utilise respiratory commensals as an immunostimulant to provide protection against pathogen colonisation. There are several projects available that will investigate the interplay and immunostimulatory effects of commensal and pathogenic bacteria on the respiratory epithelium. **Aims:** • Establish bacterial exposure to epithelium assays. • Screen commensal bacterial strains of interest. • Define immunostimulatory signatures. • Assess impact of epithelial viability and integrity.

	Techniques: Aseptic technique and working in BSL-2 cabinets, tissue culture (cell line maintenance and experimental infections), Microbiology, flow cytometry, immunological assays, microscopy. **Outcomes:** These projects will directly contribute to the understanding of respiratory pathogens and potentially contribute to the development of novel therapeutics that could prevent or treat millions of respiratory infections globally. **References:** Pickering *et al. Haemophilus haemolyticus* Interaction with Host Cells Is Different to Nontypeable *Haemophilus influenzae* and Prevents NTHi Association with Epithelial Cells. Front. Cell. Infect. Microbiol. 2016, 6:50. Granland *et al.* Nasal Delivery of a Commensal *Pasteurellaceae* Species Inhibits Nontypeable *Haemophilus influenzae* Colonization and Delays Onset of Otitis Media in Mice. Infect Immun. 2020 Mar 23;88(4):e00685-19.

Research Project Proposal 2024

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Conflict of Interest	None.
Project title:	**Investigating causative factors of early-onset myopia in zebrafish as a model of refractive error.**
Project location:	Lions Eye Institute.
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background:** Myopia, or near-sightedness has rapidly become one of the world's leading causes of distant visual impairment. Following excessive axial elongation of the eye, myopia results in refractive error, the second leading cause of disability in the world, as light entering the eye is focused in front of, rather than on the neural retina. Left untreated, high myopia (>-5.00 diopters) can lead to other visual disorders such as retinal detachment, retinal atrophy, myopic maculopathy, glaucoma, and cataracts. Prevalence rates are as high as 97% in some countries (namely within East Asia) and at 25% here in Australia. However, the World Health Organisation has predicted approximately 3.36 billion people worldwide will become myopic by the year 2030 and this is expected to increase to 50% by the year 2050, with 10% of those developing into high myopia. Therefore, it is a condition that is forecast to increasingly burden the healthcare system globally. Sadly, the fastest rise in prevalence is occurring in school-aged children as young as 6 years of age, whereby early-onset or juvenile myopia develops. There are several contributing factors attributed to the development of myopia, including both genetics and environmental determinants such as near-work (reading, screen time and schoolwork) and time spent outdoors. The rise in myopia prevalence, however, is occurring at a rate too rapid to be attributed to genetic variance or environmental factors alone, suggesting a compelling association between complex genetic interactions and environmental risk factors, yet the fundamental causal mechanisms remain unknown.

Aims: This project aims to help understand the mechanisms associated with developing early-onset myopia with the intention of implementing preventative measures across multidisciplinary fields including policy makers and government, medical research, clinicians, and educational institutions.

Design: This project will utilise a morpholino anti-sense oligonucleotide knockdown approach in zebrafish embryos within our established, robust, and rapid myopia-associated gene screening platform. By utilising the rapid, *ex vivo* development of the zebrafish embryo and larvae, genes of interest were chosen from large human Genome Wide Association Studies (GWAS) and identified in our group as contributing to increased axial length, the greatest contributing factor leading to refractive error, and diagnostic metric used in humans. This project aims to characterise the role of these identified genes through a range of both structural and functional analyses as well as molecular techniques such as qPCR and gene expression.

Techniques: Single cell microinjection of morpholino oligomers (MO); live imaging microscopy (fluorescence; confocal; optical coherence tomography (OCT); zebrafish handling and husbandry; RNA extraction; generation of cDNA; RT-PCR; qPCR; gel electrophoresis; gene sequencing; and functional optokinetic response.

Outcomes: The potential significance emerging from the outcomes of this project are anticipated to contribute considerably to the framework of understanding the biological pathways and links between genetic and environmental factors in the development of myopia and in particular early-onset myopia. Given the sharpest rise in myopia prevalence is among children as young as 6 years of age, elucidating the mechanisms involved in disease progression and determining factors that modulate its severity, will be imperative in mitigating an increasingly global socio-economic burden as these children age.

References:

Holden, B. A., Fricke, T. R., Wilson, D. A., Jong, M., Naidoo, K. S., Sankaridurg, P. *et al.* (2016). Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology **123**, 1036-42.

Baird, P. N., Saw, S., Lanca, C. *et. al.* (2020). Myopia. Nat Rev Dis Primers. **6**, 99.

Hysi, P. G., Choquet, H., Khawaja, A. P., Wojciechowski, R. and Tedja, M. S. *et al.* (2020). Meta-analysis of 542, 934 subjects of European ancestry identifies new genes and mechanisms predisposing to refractive error and myopia. Nat Genet **52**, 401-407.

Research Project Proposal 2024

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Project title:	**Identifying fibroblasts subtypes in skin and investigating their role in skin repair, scar formation and fibrosis**
Project location:	Level 5, Harry Perkins North
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	The Burn Injury Research Unit aims to reduce or eliminate the scarring that occurs after burn injury. One area we are examining is the heterogeneity of skin and scar fibroblasts. Recent studies have suggested distinct populations of fibroblasts exist in the skin, with some subtypes promoting scar formation or fibrosis and others driving a more regenerative repair process. CD26 has been postulated to be a cell surface marker that identifies pro-fibrotic subsets of fibroblasts and can therefore be used to identify and potentially target fibrosis. Preliminary work in our lab has shown that CD26+ and CD26- fibroblasts showed differences in phenotype, however we also found that the expression of CD26 on cells could change over time. This project will analyse the expression of CD26 as well as investigate other potential cell surface markers to stratify fibroblasts and develop a greater understanding of fibroblast heterogeneity in normal and scar skin. In addition, we will investigate the role of these different fibroblast subtypes in wound healing and scarring using functional assays. This project will involve flow cytometry, cell sorting, collagen and ECM production assays and in vitro wound healing assays using primary human fibroblasts in cell culture. The project will further our understanding of fibroblast subtypes, fibroblast fluidity, and their roles in wound repair and scarring, providing important insight into possible therapeutic approaches to promote regeneration rather than scar formation after injury.

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**The impact of matrix stiffness on skin fibroblasts**
Project location:	Harry Perkins North Level 5 and Anatomy Building
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	The Burn Injury Research Unit aims to reduce or eliminate the scarring that occurs after burn injury, and one of the areas we are examining is the effect of the stiffness of the extracellular matrix on the phenotype of the scar and normal skin cells. Scars have a stiffer matrix than normal skin, and cells can sense this through a process called mechanotransduction. This 'abnormal' stiffness can cause the cells to proliferate and may prevent the cells from returning to a 'normal' phenotype. This project will examine the effects of different stiffness matrices on different types of scar and normal skin cells, using a variety of cell culture models such as polyacrylamide gels, and measure changes using molecular biology and image analysis techniques. The student will be integrated in a team of researchers from a variety of fields such as chemistry, molecular biology and medical practitioners. The project will further our understanding of skin fibroblasts subtypes, providing important insight into possible therapeutic approaches to promote regeneration rather than scar formation after injury.

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**Next-generation sequencing of platelets to monitor blood cancers**
Project location:	Translational Cancer Pathology Laboratory, UWA, M block, QEII Medical Centre
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Myelofibrosis is an aggressive bone marrow cancer that can ultimately lead to bone marrow failure due to scar tissue (fibrosis) forming in the bone marrow which prevents production of blood cells. This can be highly debilitating with increased infections, bleeding, and anaemia and risk of developing acute myeloid leukaemia. The only possibility of cure is with a bone marrow transplant and this treatment is offered in WA. Work from our group has demonstrated that platelets in patients with myelofibrosis have altered gene expression. The aim of this project is to determine whether the abnormal expression can be reversed and return to normal following a bone marrow transplant. If this is proven, then monitoring platelet gene expression may provide a practical method to assess patient outcome. In this project, you will take a world-first approach, using our new genomic techniques, to address this problem by studying gene expression in blood platelets of patients who have received a transplant for myelofibrosis. You will use research methods pioneered in our Translational Cancer Pathology Laboratory at UWA. This includes handling patient samples, blood cell isolation, RNA extraction and next generation sequencing as well as bioinformatics. Keywords: haematology, cancer, next-generation sequencing, biomarkers, bioinformatics

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**Identification of probiotic bacteria to prevent mastitis in breastfeeding women.**
Project location:	The Marshall Centre of Infectious Diseases, School of Biomedical Sciences, The University of Western Australia
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Mastitis is an inflammatory breast condition that affects up to 33% of breastfeeding women worldwide. This distressing condition is one of the primary reasons for early, undesired weaning which negatively impacts the infant's health [1]. Despite the prevalence of mastitis, there is still much that we do not know about this condition, including its aetiology and pathogenesis, and thus treatment options are considerably limited. Dysbiosis (the imbalance of the normal bacterial composition) in human milk has been associated with mastitis, with pathobionts, such as *Staphylococcus aureus*, more frequently isolated from the milk of women suffering from mastitis. Recent literature on the human milk microbiome, has also shown that certain species of *Corynebacterium* and *Acinetobacter* have been associated with health while *Propionibacterium acnes* and *Staphylococcus hominis* have been found to be more abundant in milk after resolution of mastitis-associated symptoms [2]. The current standard treatment for mastitis is antibiotics, however with rising antibiotic-resistance as well as the recognition that exposure to antibiotics in early life can be harmful for infants, there is a need to identify alternative therapeutic options, or interventions which could

prevent mastitis. Bacteriotherapy or bacterial interference is where commensal bacteria are used to counteract pathogens to prevent infections. Studies from gut, nasal and skin microbiome suggest that microbial species-specific interactions can affect colonization by opportunistic pathogens [3]. Our hypothesis is that the presence of protective bacterial species in human milk can prevent dysbiosis. Commensal bacteria compete for nutrients and binding sites and kill pathogens by producing metabolites or bacteriocins. This study will focus on identifying human milk bacterial species which could potentially contribute to health conditions by inhibiting mastitis-associated pathogens. Large numbers of bacterial strains have been isolated from healthy as well as mastitis milk samples. In this project several commensal bacterial species will be tested in co-culture-based competition assays as well as agar overlay assays for identification of bacteria with inhibitory potential against mastitis-causing pathogens.

Aims:

1. Bioinformatics analysis of our existing human milk microbiome dataset to identify commensals which are negatively associated with mastitis causing pathogens.
2. Identify a panel of commensal milk bacteria to challenge against mastitis-associated bacteria, based on bioinformatics analysis.
3. Identify bacterial species isolated from milk samples by MALDI-ToF mass spectrometry.
4. Design and optimise agar overlay assays for high-throughput screening of bacteria with inhibitory potential against mastitis associated pathogens.
5. Design and optimise liquid media based *in vitro* assays to study interactions between bacterial species of interest.
6. Determine the nature of interaction between bacteria: contact-independent or contact-dependent.

Techniques:

Bioinformatics and associated statistics (no prior skills needed), bacterial culture, MALDI-ToF mass spectrometry, agar disk-diffusion assay, liquid media co-culture assays, conditioned media assays.

Reference(s): (2 or 3 is sufficient)

1. Contreras, G.A. and J.M. Rodriguez, *Mastitis: comparative etiology and epidemiology*. J Mammary Gland Biol Neoplasia, 2011. **16**(4): p. 339-56.
2. Boix-Amoros, A., et al., *Human milk microbiota in sub-acute lactational mastitis induces inflammation and undergoes changes in composition, diversity and load.* Sci Rep, 2020. **10**(1): p. 18521.
3. Ramsey, M.M., et al., *Staphylococcus aureus Shifts toward Commensalism in Response to Corynebacterium Species.* Front Microbiol, 2016. **7**: p. 1230.

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**Development of next-generation probiotics to prevent childhood pneumonia.**
Project location:	The Marshall Centre of Infectious Diseases, School of Biomedical Sciences, The University of Western Australia And Wal-yan Respiratory Research Centre, Telethon Kids Institute Northern Entrance, Perth Children's Hospital, 15 Hospital Ave, Nedlands WA 6009
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	We have recently been awarded Wesfarmers Seed grant funding to carry out this research work to identify beneficial respiratory bacterial species. The "microbiome" has emerged as a new frontier for the treatment and prevention of human disease[1,2]. Strategies range from use of probiotic species (*Lactobacillus* and *Bifidobacterium*) for gut health to fecal transplants to cure severe antibiotic-resistant intestinal infections with *Clostridium difficile*. Despite success with these approaches, probiotic development for extra-intestinal sites is in its infancy. Our preliminary work has identified two commensal (or friendly) bacterial genera found in the upper respiratory trac that are associated with reduced incidence of respiratory tract infections and reduced admission to paediatric intensive care units. In this project, we will undertake a novel laboratory approach to mimic the in vivo respiratory environment[3,4] and dissect the ability of novel beneficial bacteria to inhibit the growth of pneumonia-causing pathogens. This study will aim to identify novel potential probiotic

bacterium to prevent pneumonia or a novel therapeutic compound (produced by this bacterium) to treat pneumonia. We aim to promote respiratory health and provide a novel pathway forward to prevent pneumonia and the associated antibiotic use.

Aims:

Research questions:

1. What are the biomechanisms governing the protective associations observed for *Corynebacterium* and *Dolosigranulum* against NTHi in the nasopharynx?
2. Do these beneficial bacteria alter the host inflammatory response to NTHi?
3. Does inhibition involve secreted bioactive molecules that can be developed into therapeutic compounds?

Techniques:

Microbiology culturing, co-culture assays, quantitative real time PCR, cell culture of human nasal cells, fractionation, liquid chromatography–mass spectrometry (LC-MS), High-performance liquid chromatography (HPLC), bioinformatics.

<u>Objective 1: To identify protective bacterial isolates with direct inhibitory activity against pneumonia-causing pathogens.</u>

We will carry out solid agar side-by-side spot co-culture assays and cell-free conditioned media-based competition assays using methods established by team members at the UWA Marshall centre.

<u>Objective 2: To establish and validate the protective effects of the beneficial bacteria in an *in vitro* model that closely replicates human nasal tissue.</u>

To increase confidence that inhibitory activity will be demonstrated *in vivo* and these beneficial bacteria do not harm human nasal tissue, we will carry out bacteria-human epithelium co-culture experiments. We will use primary nasal epithelial cells (pNEC) obtained from a WA cohort of children aged 2-3 years from the WA Epithelial Research program.

Methodology:

pNECs will be differentiated for four weeks at air-liquid interphase (ALI) into nasal tissue using methods established by team members at Telethon Kids Institute (ethics approvals have been obtained).

(A) We will Investigate interactions between bacterial communities (up to three strains, including inhibitory beneficial and pathogenic strains) and nasal epithelium. Microbial growth will be measured using species-specific qPCR on DNA extracted from the apical wash (adhesion) and basal media (invasion) on days 0, 2, 4, and 6 post-infection. Cytotoxicity will be measured by lactate dehydrogenase assay.

(B) We will investigate the immunostimulatory capacity of

each strain using Bio-plex pro-human cytokine release panel) in monoculture and co-culture infection scenarios. Using Bio-plex will allow high-performance screening of modulation of infection-associated inflammatory cytokines such as IL-8 (CXCL8), IL-6, TNF - α, and IL-1β in addition to other biologically-relevant collections of adaptive immunity cytokines, pro-inflammatory cytokines, and anti-inflammatory cytokines.

Objective 3: To discover the mechanism of action underlying competitive inhibition of pathogenic strains.

We will carry out whole genome sequencing and comparative genomic analysis to identify the presence of any specialized genetic regions, called secondary metabolite biosynthetic gene clusters (BGC) in our beneficial isolates. Secondary metabolites are small molecules produced by bacteria that have proven beneficial to human health. These molecules include antibiotics such as penicillin, antimicrobial peptides, cholesterol-lowering statins, and immunosuppressive cyclosporins.

We will also carry out assays to characterize the active components involved in inhibition, using bioassay guided fractionation, liquid chromatography–mass spectrometry (LC-MS) and high-performance liquid chromatography (HPLC).

Reference(s):

1. Claassen-Weitz S, Gardner-Lubbe S, Xia Y, Mwaikono KS, Mounaud SH, Nierman WC, et al. Succession and determinants of the early life nasopharyngeal microbiota in a South African birth cohort. Microbiome. 2023;11(1):127.

2. Claassen-Weitz S, Lim KYL, Mullally C, Zar HJ, Nicol MP. The association between bacteria colonizing the upper respiratory tract and lower respiratory tract infection in young children: a systematic review and meta-analysis. Clin Microbiol Infect. 2021;27(9):1262-70.

3. Martinovich KM, Iosifidis T, Buckley AG, Looi K, Ling KM, Sutanto EN, et al. Conditionally reprogrammed primary airway epithelial cells maintain morphology, lineage and disease specific functional characteristics. Sci Rep. 2017;7(1):17971.

4. Laucirica DR, Schofield CJ, McLean SA, Margaroli C, Agudelo-Romero P, Stick SM, et al. Pseudomonas aeruginosa modulates neutrophil granule exocytosis in an in vitro model of airway infection. Immunol Cell Biol. 2022.

Research Project Proposal 2024

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Conflict of Interest	None
Project title:	**Defining the surface-ome of mucosal tissue-resident memory B cells**
Project location:	Telethon Kids Institute
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background:** Antibodies are produced by antigen-activated memory B cells, a cell type that is pivotal for vaccine-induced immunity. For protection against respiratory pathogens, a vaccine that can specifically induce airway resident memory B cells is sought after. However, evaluating and identifying promising mucosal vaccine candidates remains challenging, as robust and highly specific markers to characterise airway mucosa-bound B cells are lacking. This project aims to discover specific markers of airway tissue resident memory B cells with spectral flow cytometry and computational methods. **Techniques:** This project will utilise a specialised application of flow cytometry using marker arrays to screen ~250 surface receptors on B cells from cryopreserved Tonsils, Adenoids and Peripheral Blood Mononuclear Cells collected by the Vaccine Trials Group. Techniques will involve magnet-assisted cell separation, spectral flow cytometry and computational cytometry/data science. It is ideal for prospective students who have a background in Biomedical Science and Computer Science or related fields.

	Aims: 1. To Identify the composition of tonsillar and adenoid B cells with an established (28-colour) Spectral Flow Cytometry panel. 2. To compare two different computational pipelines for analysing cytometric marker array data. 3. To identify core markers uniquely expressed by tissue resident memory B cells. **Hypothesis:** A set of surface markers will uniquely identify mucosal resident memory B cells.

Research Project Proposal 2024

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Conflict of Interest	N/A
Project title:	**Exploring the role of macrophages in response to tumour irradiation**
Project location:	The National Centre for Asbestos Related Diseases, Harry Perkins Institute for Medical Research
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Recent work in our lab has examined how radiotherapy is able to modulate the immune system in ways that could potentially improve anti-tumour responses. Results from gene expression analysis has suggested that low doses of tumour-targeting radiation can alter the types of macrophages that are found within the tumour. We wish to examine this phenomenon in more detail, with a particular focus on detailed phenotypic changes, mechanisms of action, and how these cells interact with T cells with respect to immune checkpoint inhibitors. This project will primarily use tissue staining immunofluorescence from sectioned mouse tumours, plus flow cytometry, to gather these data.

Research Project Proposal 2024

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Conflict of Interest	N/A
Project title:	**Influence of mesothelioma cell plasticity in clinical outcomes**
Project location:	The National Centre for Asbestos Related Diseases, Harry Perkins Institute of Medical Research
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background** Asbestos-induced mesothelioma is an aggressive and fatal cancer. There are two types of mesothelioma; epithelioid and sarcomatoid, which have different clinical characteristics. Epithelioid mesothelioma is more common, and untreated has a significantly better prognosis than the sarcomatoid sub-type. Interestingly however, sarcomatoid mesothelioma appears more resistant to chemotherapy and more sensitive to immune-checkpoint blockade treatments than epithelioid tumours. However, most treatment responses are transient. We have shown using patient derived cell-lines that it is possible, in the laboratory, to change the phenotype of mesothelioma cells from epithelioid-like to sarcomatoid-like, and that some cell lines exist in a hybrid phenotypic state between the two. The ability therefore to alter the phenotype of mesothelioma cells offers the possibility of increasing

	treatment options for patients. **Aim 1** Integrate in-house and publicly available mesothelioma patient RNA sequence data sets **Aim 2** Perform bioinformatic analysis to identify factors associated with phenotype-switching **Aim 3** Evaluate the effect of targeting factors identified in Aim 2 in a panel of human cell lines. **Design** In this project we will perform a bioinformatic analysis of both cell line and patient derived RNA data to characterise changes associated with phenotype-switching. The aim is to identify the drivers of phenotype-switching that could be targeted. There is the potential to validate findings in either in vitro cultured human cell lines established from clinical samples, or in biospecimens from our extensive patient tumour biobank. **Techniques** Bioinformatics, mammalian tissue culture, molecular biology **Outcomes** This study will increase knowledge of the determinants of mesothelioma histology and could lead to the development of new treatment approaches.

Research Project Proposal 2024

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Conflict of Interest	N/A
Project title:	**Exploring mechanisms of mesothelioma chemotherapy resistance**
Project location:	The National Centre for Asbestos Related Diseases, Harry Perkins Institute of Medical Research
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background** Mesothelioma is a rare, asbestos induced cancer and in Australia there are approximately 700 people diagnosed each year. Like many other cancers, immunotherapy has recently been approved for use in mesothelioma. However, the majority of patients do not respond to this treatment and chemotherapy remains an important option for treating patients. Despite decades of chemotherapy usage, little is known about which mesothelioma patients will benefit most from this treatment. The availability of large data sets across multiple cancer types provides our research team with an opportunity to leverage our own data generated from the Western Australian mesothelioma patient cohort to identify biomarkers to predict which patients will respond and equally important, not respond to a given chemotherapy agent. We have developed a model system in which mesothelioma cells have, by

	being exposed to increasing quantities of drug, become resistant to some chemotherapy agents. In these resistant cells we have preliminary evidence of alterations in some of the cellular pathways involved with cellular metabolism and cell death pathways. **Aim 1** Integrate in-house and publicly available mesothelioma patient genomic data sets **Aim 2** Perform bioinformatic analysis to identify pathways associated with chemotherapy response in mesothelioma **Aim 3** Validate pathways identified in Aim 2 in a panel of human cell lines. **Design** In this project bioinformatic analysis of DNA and RNA sequence data will identify mechanisms of chemotherapy resistance in mesothelioma. There is the potential to validate findings in either in vitro cultured human cell lines established from clinical samples, or in biospecimens from our extensive patient tumour biobank. **Techniques** Bioinformatics, mammalian tissue culture, molecular biology **Outcomes** This study will identify biomarkers associated with response to chemotherapy, it could lead to the more effective selection of treatments for individual patients.

Research Project Proposal 2024

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Conflict of Interest	N/A
Project title:	**A combined radiotherapy and ferroptotic approach to treating mesothelioma**
Project location:	The National Centre for Asbestos Related Diseases, Harry Perkins Institute of Medical Research
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background** Cancer cells have developed many strategies to avoid being killed by both the host immune system and by cytotoxic assaults, such as chemotherapy and radiotherapy. Many studies have examined how cancer cells develop resistance to programmed cell death pathways such as apoptosis, and to the newly described ferroptopic pathway. Ferroptosis is a form of regulated cell death caused by reactive oxygen species and associated with iron accumulation and lipid peroxidation. Ferroptosis is precisely regulated at multiple levels, including epigenetic, transcriptional, posttranscriptional and posttranslational layers. Recently, it was shown that ferroptosis plays a crucial role in radiotherapy-induced cell

	death. Radiotherapy kills tumour cells by both directly inducing DNA damage and by generating reactive oxygen species (ROS). Thus resistance to ferroptosis and insensitivity to radiotherapy are intrinsically linked. Our laboratory at the National Centre for Asbestos Related disease focuses on mesothelioma, a uniformly fatal malignancy associated with asbestos exposure. The median survival for patients following diagnosis is approximately 12 months with only 5% surviving to 5 years. Mesothelioma is well recognised as being refractory to treatment and even the majority of patients do not respond to the recently adopted checkpoint inhibitor (ICI) immunotherapy. In this project we will use our established and well characterised mesothelioma models to investigate the therapeutic implications of targeting ferroptosis to overcome tumour radioresistance, the possibility of using ferroptosis regulators as potential predictive markers for radiotherapy efficacy, and the relevance of ferroptosis to radiotherapy combined with immunotherapy. **Aims** 1. To characterise the ferroptopic response of mesothelioma cell lines exposed to clinical relevant radiation doses 2. To evaluate the synergistic effects of inducing ferroptosis with tumour cell irradiation. **Design:** In vitro laboratory studies **Techniques:** Mammalian tissue culture, flow cytometry, RT-PCTR **Outcomes:** This study could lead to more effective treatment strategies for mesothelioma patients. **References:** Chang et al 2022. Immune marker expression of irradiated mesothelioma cell lines. Front Oncol. 12:1020493

Research Project Proposal 2024

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SBMS Coordinating supervisor (for non-SBMS supervisors)	
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Conflict of Interest	N/A
Project title:	**Understanding T cell diversity to cancer antigens**
Project location:	The National Centre for Asbestos Related Diseases, Harry Perkins Institute of Medical Research
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background**. The ability of the immune system to recognise and control cancer has been known for more than 100 years and is the basis of recent successful cancer immunotherapies. Whilst, these immunotherapies, such as immune checkpoint blockade, have revolutionized cancer treatment, they work in only a small subset of patients. Therefore, alternative or synergistic strategies are required. Our laboratory is seeking to use cancer vaccines to treat patients either as a stand-alone therapy or as an adjunct to conventional immunotherapies. Cancer vaccines target altered proteins (neoantigens) that are derived from tumour specific mutations. Therefore, cancer vaccines turn a cancer's strength, it's mutations, into a weakness, as targets for immune cells.

	Design. In this project you will use human samples to understand the T cell responses to neoantigens in lung cancer and mesothelioma patients. **Aim 1** Determine the diversity of the anti-cancer T cell response. **Aim 2** Define the T cell receptors used to recognise mutated human proteins. **Techniques.** Single cell TCR sequencing, bioinformatics, TCR cloning. T cell reporter assays. **Outcomes**. This study will define the diversity of the TCR usage in cancer patients and will use TCR cloning to verify the specificity of these TCRs allowing for latter 3-dimensional crystal structure analysis. From these studies we may be able to design novel, more effective cancer vaccines.

Research Project Proposal 2024

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Conflict of Interest	N/A
Project title:	**The impact of T cell exhaustion on cancer vaccination**
Project location:	The National Centre for Asbestos Related Diseases, Harry Perkins Institute of Medical Research
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background**. The ability of the immune system to recognise and control cancer has been known for more than 100 years and is the basis of recent successful cancer immunotherapies. Whilst, these immunotherapies, such as checkpoint blockade (CPB), have revolutionized cancer treatment, they work in only a small subset of patients. Therefore, alternative or synergistic strategies are required. Our laboratory is seeking to use cancer vaccines to treat patients either as a stand-alone therapy, or as an adjunct to conventional immunotherapies. During cancer progression the T cells that recognise cancer antigens become increasingly “exhausted”. This T cell exhaustion is reversed by CPB, however we do not know if vaccination also reverses T cell exhaustion **Design**. We have shown that precursor non-exhausted (stem-like) T cell frequency correlates with positive outcomes in lung cancer and mesothelioma patients. This finding will be investigated in this study. **Aim 1** Determine the antigen specificity of stem-like T cells in

	cancer patients. **Aim 2** In an animal model determine if vaccination can reverse T cell exhaustion. **Techniques.** Tetramer staining, ELISpot assays, mouse models vaccine studies. **Outcomes**. This study will determine the antigen specificity of exhausted and stem-like T cells in cancer patients. And in an animal model determine under what conditions T cell exhaustion can be reversed. It could lead to more effective vaccines for cancer patients.

Research Project Proposal 2024

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Conflict of Interest	No
Project title:	**Towards finding new cures for childhood leukaemia**
Project location:	Telethon Kids Institute – Cancer Centre
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Leukaemia is the most common type of cancer in children. Remarkable therapeutic advances have been made over the past sixty years. Despite this success, it remains the second cause of death by Cancer in Australia. Current therapeutic approaches have reached their maximum potential and specific subtypes of leukaemia continue to have a poor prognosis due to treatment toxicity and relapses. This highlights the need for new efficacious treatments. These poor clinical features are exemplified for Down syndrome children that developed acute lymphoblastic leukaemia (named DS-ALL). Indeed, treatment intensification is limited for these DS children due to a high rate of treatment-related morbidity. As a result, there is a nearly two-fold increased risk of developing relapses in DS-ALL compared to other type of childhood ALL.

	Our group is focused on finding new key vulnerabilities in the leukaemia cells and in the tumour microenvironment to develop novel and less toxic targeted therapies. To achieve this, we are using sophisticated models of childhood leukaemia to reproduce the setting seen in primary patients. Using those, our projects are focused on 1- understanding the molecular bases of leukaemia development and response to standard of care treatments to, 2- develop new approaches that target key weaknesses of the tumour cells. During this project, the student will be introduced to: - Flow cytometry, - Animal handling, tissue preparation and drug testing, - Tissue culture and molecular biology, - CRISPR/Cas9 technology and screening strategies. Ultimately, our goal is to develop new strategies to improve prevention, diagnosis, long-term survival and quality of care for children with leukaemia.

Research Project Proposal 2024

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Conflict of Interest	No
Project title:	**A novel vaccine to prevent Group A *Streptococcus* attachment to the tonsils**
Project location:	Telethon Kids Institute
Project Description: Aims; Design; Techniques; Outcomes;	Group A *Streptococcus* (GAS) is responsible for over 500,000 deaths each year due to invasive infections and autoimmune sequelae. Underlying these severe diseases is GAS infection of the tonsils, commonly called "Strep throat". Globally, there are more than 600 million cases of Strep throat each year. The World Health Organization has declared development of a GAS vaccine

References (optional):	a global priority to reduce mortality and morbidity from GAS infections and associated antibiotic use. Current GAS vaccine approaches are aimed at preventing symptomatic disease, yet asymptomatic GAS infections are immunologically significant and potentially trigger autoimmune diseases and seed GAS infections in sterile sites (invasive infections). To combat the burden of GAS diseases, we are developing a pre-clinical vaccine candidate to stop the initial attachment of GAS to healthy tonsils, which is the first step in a Strep throat infection. As part of this vaccine development, this project aims to: 1. Identify targets of antibodies that can block diverse GAS strains. 2. Develop a multi-valent vaccine against GAS. This project will involve bacterial culturing, molecular cloning, tissue culture and protein expression and purification.

Research Project Proposal 2024

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Project title:	**Detection of deletions of chromosome 13 in chronic lymphocytic leukaemia by immuno-flowFISH**
Project location:	Translational Cancer Pathology Laboratory, UWA, M block, Queen Elizabeth II Medical Centre. Nedlands 6009
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Chronic lymphocytic leukemia (CLL) is the most common leukemia in adults. Chromosomal changes are associated with clinical behaviour and deletions of chromosome 13 being the most common, detected in up to 50% of patients. There are different types of abnormalities in chromosome 13 depending on the location of the breakpoint and the size of the deletion. The ”short” deletion of 13(q14) breaks close to the miR16/15a locus. The larger deletion includes the *RB1* gene and is associated with greater genomic complexity and a more aggressive course with shorter time to commencement of treatment and reduced overall survival. In addition, these deletions may be heterozygous (monoallelic) or homozygous (biallelic). Our team has invented a fast automated method that quantifies proteins to determine cell identity (immunophenotype) and can simultaneously detect chromosomal changes to diagnose blood cancers. This method, called “immuno-flowFISH”, is exquisitely sensitive and a major diagnostic advance. The aim of this project is to assess the ability of the immuno- flowFISH method to detect these del(13q) subtypes in CLL, and determine whether these are monoallelic or biallelic. In this project, you will use research methods pioneered in our Translational Cancer Pathology Laboratory at UWA. This includes handling patient samples, immuno-flowFISH processing, imaging flow cytometry and data analysis. Keywords: haematology, chronic lymphocytic leukaemia, cytogenetics, fluorescence *in situ* hybridisation, imaging flow cytometry

Research Project Proposal 2024

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Project title:	**Identifying the protein-protein interaction of the Macrophage infectivity potentiator (Mip) of *B. pseudomallei.***
Project location:	Marshall Centre for Infectious Disease Research and Training, Room 2. 04, School of Biomedical Sciences, L Block, QEII Medical Centre
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background**: The macrophage infectivity potentiator (Mip) is a member of the FK506-binding proteins, shown to be important for the virulence of the multi-drug resistant bacterium *Burkholderia pseudomallei.* Targeting or inhibiting this protein using novel Mip inhibitors reduced the virulence of the bacteria *in vitro,* making it a good target for therapeutic intervention. Currently, Mip is involved in the survival of *B. pseudomallei* within macrophage cells and the bacterial resistance to host-killing mechanisms, however, the exact mechanism of action is unknown. Proximity labelling is a new method that can help identify the protein-protein interactions of Mip, thereby helping to uncover the exact mechanism of action of Mip. This new methodology uses biotin to tag and identify the protein interaction and, in some instances, even the weak transient interactions which has been a problem with the older methods.

Aims:

The aim of this work is to construct plasmids to use in the proximity labelling experiment to identify the protein-protein interactions of Mip protein in *B. pseudomallei.*

a) Generate plasmid constructs that can be used to tag the protein interactors of Mip.

b) Confirm the expression of the plasmid construct and the tagging of the proximal proteins using Western Blots.

c) Identify the protein interactors of Mip.

Techniques:

a) Molecular biology techniques including DNA cloning and manipulation.

b) Aseptic techniques and working with bacterial cultures

c) Protein work including SDS-PAGE and western blotting

Outcomes:

This project will help uncover the exact function of Mip in *B. pseudomallei* which will help the development of new treatment options for this multi-drug resistant bacterium.

References:

1. Norville IH, Harmer NJ, Harding SV, Fischer G, Keith KE, Brown KA, et al. A *Burkholderia pseudomallei* macrophage infectivity potentiator-like protein has rapamycin-inhibitable peptidylprolyl isomerase activity and pleiotropic effects on virulence. *Infect Immun*. **2011**;79(11):4299-307.

2. Iwasaki J, Lorimer DD, Vivoli-Vega M, Kibble EA, Peacock CS, Abendroth J, et al. Broad-spectrum in vitro activity of macrophage infectivity potentiator inhibitors against Gram-negative bacteria and Leishmania major. *J Antimicrob Chemother*. **2022**;77(6):1625-34.

3. Santin YG. Uncovering the In Vivo Proxisome Using Proximity-Tagging Methods. *Bioessays.* **2019**;41(12):e1900131.

Research Project Proposal 2024

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Project title:	**Characterisation of a novel folate biosynthesis fusion gene in *Burkholderia pseudomallei***
Project location:	Marshall Centre for Infectious Disease Research and Training, Room 2.04, School of Biomedical Sciences, L Block, QEII Medical Centre
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Background**: *Burkholderia pseudomallei* is a soil-dwelling bacterial pathogen capable of infecting humans and animals, and is responsible for causing the often-fatal disease melioidosis. Per annum globally, there are approximately 165,000 human cases of melioidosis resulting in 89,000 deaths. *B. pseudomallei* infection can be difficult to identify, as symptoms mimic that of other pneumonia diseases, such as tuberculosis. Antibiotic treatment of melioidosis is harsh and involves extensive intravenous and oral therapy, but as current antibiotics are not very efficacious, mortality rates are still seen at up to 37% in some countries (1). *B. pseudomallei* is a Gram-negative bacterium, able to survive and replicate proficiently in its tropical environmental niche, and within eukaryotic host cells. The folate biosynthesis pathway has been extensively studied in many pathogenic organisms, and is the target of one of the most successful and longest-standing antibiotics, trimethoprim. However, this pathway has not yet been fully investigated in *B. pseudomallei*. Interestingly, *B. pseudomallei* appears to possess a unique folate biosynthesis fusion gene, *bpsl2825*, which encodes for a dual-function enzyme (BPSL2825-B-C) not seen in most other clinically relevant pathogens. Novel proteins such as these have proven great targets to

develop species-specific and efficacious therapeutics to help combat disease and the ever-growing threat of antimicrobial resistance.

Aims:

The aim of this project is to characterise a unique and novel dual-functioning folate biosynthesis protein in *B. pseudomallei*, and to investigate its essential role in one of the most important intermediary metabolic pathways of bacteria. Specific experimental aims:

- Construction of individual domain deletion vectors for both *bpsl2825-B* and *bpsl2825-C* in *B. pseudomallei*
- Expression and purification of *B. pseudomallei* BPSL2825-B and BPSL2825-C protein domains
- Investigation of the crucial role BPSL2825-B and BPSL2825-C play in folate metabolism in *B. pseudomallei*

Techniques:

General molecular biology techniques, bacterial culturing, aseptic technique, protein expression and purification, SDS-PAGE and Western blot analysis, protein characterisation.

Outcomes:

This project will unveil the role of the unique folate biosynthesis fusion gene *bpsl2825* in *B. pseudomallei*, contributing a greater understanding of critical bacterial metabolic pathways in the pursuit of novel antibiotic development.

References:

1. Limmathurotsakul D, Golding N, Dance DA, Messina JP, Pigott DM, Moyes CL, Rolim DB, Bertherat E, Day NP, Peacock SJ, Hay SI. Predicted global distribution of Burkholderia pseudomallei and burden of melioidosis. Nat Microbiol. 2016 Jan 1;1(1):15008. doi: 10.1038/nmicrobiol.2015.8. PMID: 26877885; PMCID: PMC4746747.

Research Project Proposal 2024

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Project title:	**Interference patterns between Neisseria species.**
Project location:	Marshall Center, L block, QE II
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Description of Research Project:** **Background:** *Neisseria meningitidis* is a Gram-negative diplococcus that resides exclusively in humans and is the causative agent of invasive meningococcal disease (IMD). The population of *N. meningitidis* is structured into stable clonal complexes by limited horizontal recombination in this naturally transformable species. *N. meningitidis* is an opportunistic pathogen, with some clonal complexes, such as cc53, effectively acting as commensal colonisers; while other genetic lineages, such as cc11, are rarely colonisers but are over-represented in IMD and are termed hypervirulent. To understand how these lineages evolved, we examined the abundance and association of genomic islands (GIs) from genetic lineages representing commensal colonisers and hypervirulent lineages. We identified a sub-set of GIs from the accessory meningococcal pan-genome which are present in variable and unique combinations associated with genetic lineages of meningococci. Hypervirulent lineages were enriched for GIs encoding functions associated with meningococcal survival in phagocytic cells. In contrast, commensal colonising lineages such as cc53 have not acquired GIs associated with survival in phagocytic cells but have accumulated 13 unique loss-of-function loci and seven unique GIs suggesting a pathway of

	adaptive evolution for the trait of commensalism. Two of these islands encoded a putative bacteriocin and a CRISPR array, respectively. In this study, we will examine whether these pathways are functional. **Aims:** 1. To clone the bacteriocin genes into expression vectors in E. coli. 2. To construct mutants of these bacteriocin encoding islands in commensal Neisseria sp. 3. To conduct phenotypic assays to determine if these pathways are functional. These assays include transformation of methylated and unmethylated DNA and contact independent competition assays. **Techniques:** 1. Bacterial culture 2. Bioinformatic analysis of WGS datasets 3. Cloning and mutation **Reference:** 1. Rafael Custodio, Errin Johnson, Guangyu Liu, Christoph M. Tang, Rachel M. Exley. Commensal *Neisseria cinerea* impairs *Neisseria meningitidis* microcolony development and reduces pathogen colonisation of epithelial cell. https://doi.org/10.1371/journal.ppat.1008372

Research Project Proposal 2024

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Project title:	**Ceftriaxone resistance in Neisseria meningitidis**
Project location:	Marshall Center, L block, QE II
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Description of Research Project:** **Background:** *Neisseria meningitidis* is a Gram-negative diplococcus that resides exclusively in humans and is the causative agent of invasive meningococcal disease (IMD). The population of *N. meningitidis* is structured into stable clonal complexes by limited horizontal recombination in this naturally transformable species. N. meningitidis is typically not considered to be very antimicrobial resistant. However, isolates with elevated resistance to ceftriaxone have been observed in IMD cases from China. We have also observed an isolate with decreased resistance to ceftriaxone from a traveller from South east Asia. We are interested in understanding how frequently decreased resistance to ceftriaxone occurs in carriage isolates. We have a collection of 200 isolates which have been collected from carriage studies in which people had no disease. In this study, you will culture these organisms and perform antibiograms to determine their antibiotic resistance profiles. We will also perform whole genome sequencing so that we can examine the relatedness of these isolates with those lineages that display resistance profiles of interest.

	Aim: 1. To examine the prevalence of antimicrobial resistance in carriage isolates of N. meningitidis **Techniques:** 1. Bacterial culture 2. Bioinformatic analysis of WGS datasets **Reference:** 1. Antibiotic resistance among invasive *Neisseria meningitidis* isolates in England, Wales and Northern Ireland (2010/11 to 2018/19). PLoS One. 2021; 16(11): e0260677.

Research Project Proposal 2024

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Project title:	**Understanding MisR regulation in N. meningitidis**
Project location:	Marshall Center, L block, QE II
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Description of Research Project:** **Background:** *Neisseria meningitidis* is a Gram-negative diplococcus that resides exclusively in humans and is the causative agent of invasive meningococcal disease (IMD). *N. meningitidis* expresses a lot of virulence determinants during invasive disease. One of the most important regulators is the two-component regulator, MisR-S. We have recently found that MisR-S may be involved in regulating numerous essential genes including cell wall biosynthesis. However, we do not know if this is a direct or indirect effect via another regulator. To determine if MisR binds directly or indirectly to the promoter region, we can use mobility shift assays where we test whether the protein binds to the promoter or not. In this project, you will test up to four potential promoters for interactions with the MisR protein to help further characterise the regulon. **Aim:** 1. To characterise the regulon of the MisRS in *N. meningitidis*

	Techniques: 1. Bacterial culture 2. Purification of MisR protein 3. RT-PCR on genes of interest that may be regulated by misR 4. Mobility shift assays **Reference:** 1. MisR/MisS Two-Component Regulon in *Neisseria meningitidis.* Infect Immun. 2008 Feb; 76(2): 704–716.

Research Project Proposal 2024

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Conflict of Interest	Nil
Project title:	**Optimising a new method of heart storage – gas persufflation**
Project location:	HLRI WA Lab within Harry Perkins (South Campus)
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Our group is developing a new method of storing hearts for transplant. Oxygen gas alone may be delivered into the blood vessels of hearts during storage allowing later transplantation. We have already shown that oxygen is superior to conventional heart storage. If successful, this method may allow many more hearts to be retrieved and transplanted into patients. Your project will involve testing other gases as additives to oxygen to further improve heart performance. You will work in our fully equipped lab on our rodent isolated heart model, delivering anaesthesia, explanting rat hearts, using operating microscopes, a langendorff apparatus, echocardiography probes as well as performing fluid and tissue analysis for molecular markers of health and damage. You will have the opportunity to spend time with clinicians and witness human heart transplantation as part of the orientation process. You will be fully supervised by our team of scientists, doctors and nurses.

	Previous honours students with our group have had their work presented at the International Society of Heart & Lung Transplant meeting in the USA.

Research Project Proposal 2024

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Conflict of Interest	Nil
Project title:	**Mapping allospecific T cells in transplantation**
Project location:	UWA Medical School Level 5, Harry Perkins Institute of Medical Research
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Description of Research Project: Solid organ transplantation is the final treatment option for many end-stage diseases; however it is not a lifelong cure. Depending on the organ transplanted, 30-80% of organs fail within 10 years. This is primarily due to rejection, which is caused by the recipient's immune response against the grafted organ. Current treatments to suppress this rejection response, while effective short-term, are unable to prevent long-term chronic rejection and convey serious side effects including increased rates of infection and cancer. New targets for treatments to suppress the anti-graft or allo-response are therefore urgently needed. Our approach to addressing these issues is to improve the understanding of the anti-graft or allo-response using mouse models of liver, kidney, and heart transplantation(1). While CD8 T cells are known to be involved in alloresponses, their mechanisms of action are not well understood, which is needed to develop new

	targeted therapies. Allospecific T cells are those cells which have a TCR specific for an antigen derived from the grafted organ. These allospecific cells drive the alloresponse and can cause the tissue damage which results in graft rejection. Until recently, accurate identification of allospecific cells has been difficult. However, recent advances in identifying the peptides stimulating the alloresponse means allospecific CD8 T cells can now be detected(2). In this project, we will use these peptides to identify alloreactive CD8 T cells in our models of transplantation and characterise the cells using flow cytometry to potentially identify new targets for immunosuppression. **Aims:** 1. Set up ELISpot assays to identify alloreactive CD8 T cells after transplantation in mice 2. Validation of CD8 T cell alloreactivity by flow cytometry **Techniques:** Mouse work – handling, monitoring, euthanasia, tissue harvesting. Lab work - cellular isolation from mouse tissue, aseptic technique, cell culture, ELISpot, flow cytometry **Reference(s):** 1. Prosser A, Huang WH, Liu L, Dart S, Watson M, de Boer B, Kendrew P, Lucas A, Larma-Cornwall I, Gaudieri S, Jeffrey GP, Delriviere L, Kallies A, Lucas M. Dynamic changes to tissue-resident immunity after MHC-matched and MHC-mismatched solid organ transplantation. Cell Rep. 2021;35(7):109141. 2. Son ET, Faridi P, Paul-Heng M, Leong ML, English K, Ramarathinam SH, Braun A, Dudek NL, Alexander IE, Lisowski L, Bertolino P, Bowen DG, Purcell AW, Mifsud NA, Sharland AF. The self-peptide repertoire plays a critical role in transplant tolerance induction. J Clin Invest. 2021;131(21).

Research Project Proposal 2024

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Conflict of Interest	
Project title:	**Taste masked microparticles for formulating bitter drugs into acceptable medicines for young children**
Project location:	206 Curnow building, UWA
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	A leading cause of therapeutic non-compliance in young children is the lack of appropriate formulations that cater to their specific medication needs. The paediatric population is highly diverse, and while the adolescents may be able to take tablets and capsules designed for adults, younger children, in particular the pre-schoolers will require more age-appropriate formulations. Despite recent innovations, many oral formulations are still not able to provide the accurate and flexible dosing, as well as effective taste masking of bitter drugs that are required to meet the medication needs of this patient group. To address these challenges, our laboratory has developed several taste-masking platforms for formulating bitter drugs into oral solid formulations that are appropriate for administration to children aged 3 – 16 years. One of these platforms utilises the principle of polyelectrolyte complexation to produce taste masked microparticles of bitter drugs. The polyelectrolyte complex formation is a spontaneous reaction driven by entropy when a drug applied as sodium salt is reacted with a fatty acid in the presence of a cationic polymer. Proof of concept has been obtained with sodium flucloxacillin, a highly bitter antibiotic that has extremely poor therapeutic compliance among young paediatric patients.

	The aim of this project is to ascertain the universality of application of the polyelectrolyte complex platform by determining whether it is able to also produce taste masked microparticles of other bitter drugs available as sodium salts. In this regard, sodium docusate and sodium diclofenac will be used as the model drugs. The project requires the production of drug-loaded microparticles using a solvent evaporation technique that has been optimised for sodium flucloxacillin, palmitic acid and Eudragit EPO. The weight ratios of drug:fatty acid:polymer for manufacturing the microparticles will be calculated for each combination based on stoichiometric considerations. The second objective of the project is to assess the robustness of the polyelectrolyte complex platform. This will be accomplished by determining whether the formulation and manufacturing method are applicable to various fatty acids. The fatty acids to be investigated include lauric, myristic, palmitic, and stearic acids. The cationic polymer used, Eudragit EPO, is unique in that it is not soluble in neutral saliva pH but becomes soluble in gastric pH. Additionally, it is soluble in the same solvent as the fatty acids. The drug-loaded microparticles will be evaluated for drug content, in vitro drug dissolution profile in simulated saliva and gastrointestinal fluids, and stability at specified storage conditions. Validated HPLC assays will be used to quantify sodium docusate and sodium diclofenac. Effectiveness of the microparticles in achieving taste masking of the bitter drugs will be assessed using a trained human taste panel.

Research Project Proposal 2024

Primary supervisor (name):	Dr Shaun Teo (Telethon Kid's Institute)
Contact details (phone; email; location)	Please contact the Children's Diabetes Centre, Senior Program Manager, Rebecca Pavlos for further information. Rebecca.Pavlos@health.wa.gov.au
Other supervisor/s if any (name):	Professor Elizabeth Davis (Telethon Kid's Institute, Perth Children's Hospital) Dr Vinutha Shetty (Telethon Kid's Institute, Perth Children's Hospital) Dr Craig Taplin (Telethon Kid's Institute, Perth Children's Hospital)
Contact details (phone; email; location)	
SBMS Coordinating supervisor (for non-SBMS supervisors)	N/A
Contact details (phone; email; location)	N/A
Conflict of Interest	Nil
Project title:	**Developing educational resources to improve awareness and knowledge of Type 1 Diabetes within community sport settings**
Project location:	Telethon Kids Institute
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Physical activity (PA) is a key factor in T1D management to help improve glycaemic control and cardiovascular health. Despite its well reported health benefits, children with T1D are engaging in less PA than their healthy peers due to barriers such as a fear of hypoglycaemia or inadequate information on diabetes management around exercise. Previous research by our team at the Children's Diabetes Centre found that one of the main challenges identified by adolescents and youth is the lack of knowledge and awareness around T1D by the community, particularly in community sport settings. Community sport is one of the most common settings in which youth exercise. Currently, there are a lack of educational exercise resources available in Western Australia, therefore, community sport coaches feel they lack the knowledge, confidence and understanding to provide adequate support for youth with T1D. Our current research is working on bridging this gap to

	provide support to both coaches and players with T1D. We have completed semi-structured interviews to determine the essential information our youth with T1D want and need their sport coaches to know, and from our community sport coaches and parents, what T1D information is needed for them to safely and respectfully support their players. As such, by building on our previous research findings, the overarching aims of the proposed work are to: i) develop a series of educational resources based on the needs of the T1D and sporting community, ii) explore the acceptability and usability of our educational resources and iii) implement the educational resources in community sport settings through a nationwide launch.

Research Project Proposal 2024

Primary supervisor (name):	Dr Aveni Haynes (Telethon Kids Institute)
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Other supervisor/s if any (name):	Mr Grant Smith (Telethon Kids Institute) Dr Matthew Cooper (Telethon Kids Institute) Adult Endocrinologist supervisor TBD
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SBMS Coordinating supervisor (for non-SBMS supervisors)	N/A
Contact details (phone; email; location)	N/A
Conflict of Interest	Nil
Project title:	**What is the burden of cardiovascular disease in Western Australian children and adolescents diagnosed with type 1 and type 2 diabetes?**
Project location:	Telethon Kids Institute
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Childhood diabetes is associated with significant long term health complications and an average 14-year reduced life expectancy. Major cardiovascular complications including heart disease and stroke are a significant contributor to the high morbidity and mortality associated with childhood diabetes. Previous research from our group, led by Dr Cooper, investigated the incidence of hospitalisations and risk factors for vascular complications experienced during early adulthood in children diagnosed with type 1 diabetes in Western Australia between 1992-2012, reporting a higher incidence in women and those with higher average glycaemic control in childhood. This project aims to determine the incidence of major cardiovascular outcomes and premature mortality in children diagnosed with type 1 and type 2 diabetes in Western Australia from 1992 to 2022, including an additional 10 years of new onset cases and follow-up period for those included in the previous study. Children with diabetes will be identified from the Western Australian Children's Diabetes Database (WACDD) maintained at

	Perth Children's Hospital and record linkage conducted by the Western Australian Data Linkage Unit (https://www.datalinkage-wa.org.au/) to the Hospitalisations and Morbidity Data System (HMDS) and Mortality Register to determine the incidence of cardiovascular outcomes in this cohort (Cooper et al, J Diabetes Complications (2017) 31(5):843-849). The findings of this study will be not only be novel but also make a significant impact on informing future models of care for children diagnosed with diabetes which aim to minimise the risk of long-term adverse effects for individuals affected by this lifelong condition so that they can be prevented in future generations.

Research Project Proposal 2024

Primary supervisor (name):	Dr Aveni Haynes (Telethon Kids Institute)
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SBMS Coordinating supervisor (for non-SBMS supervisors)	N/A
Contact details (phone; email; location)	N/A
Conflict of Interest	Nil
Project title:	**Investigating geospatial patterns in the occurrence of childhood onset type 1 diabetes in Western Australia**
Project location:	Telethon Kids Institute
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Childhood type 1 diabetes remains one of the commonest chronic conditions of childhood, affecting over 600,000 children aged <15 years worldwide. Type 1 diabetes is an autoimmune condition, with a peak age of onset in 10-14 year olds, requiring daily insulin replacement therapy in order to survive. Despite intense efforts, the cause of type 1 diabetes remains unknown. In Western Australia, all children newly diagnosed with type 1 diabetes are admitted to hospital for commencement of insulin therapy and diabetes related education and are then routinely followed by the diabetes team at Perth Children's Hospital in metropolitan and State-wide outpatient clinics every 3 months until the age of 18 years. Data on these children are available from the Western Australian Chidlren's Diabetes Database (WACDD) maintained at Perth Children's Hospital, which has an estimated case ascertainment rate of >99.9%. This population-based complete data provide a unique opportunity for investigating the incidence and trends in type 1 diabetes in Western Australia and identify potential environmental risk factors involved in its cause. This project aims to investigate the association between newly available covariates from the "digital WA" project, led by A/Prof Cameron and the incidence of type 1 diabetes in the State,

	which has been shown to have spatial and temporal patterns which have yet to be explained. Examples of such area level covariates now available include traffic flux, number of playgrounds/ovals or fast food outlets, amount of greenspace. These factors have previously been associated with either type 1 diabetes in other populations e.g Finland/Scandinavia or immune-mediated conditions (asthma/atopy), as well as the microbiome and hence there is sufficient rationale for conducting exploratory analyses.

Research Project Proposal 2024

Primary supervisor (name):	A/Prof Mary Abraham
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Conflict of Interest	Nil
Project title:	**Exploring management of hypoglycaemia in day-to-day life in children with Type 1 diabetes.**
Project location:	Telethon Kids Institute
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Hypoglycaemia is an inevitable occurrence of Type 1 diabetes. All familes are provided hypoglycaemia education at diagnosis, aligning with the recommendations of international guidelines. However, in clinical practice, a wide variation in treatment plans are observed. This project aims to revist the understanding of how families concur and adapt the current hypoglycaemia education. This includes reviewing the cut-off used for hypoglycaemia treatment and the treatment options. This provides an opportunity to learn from families their experiences and what works best for them. To address this aim, we will administer an on-line questionnaire with open-ended questions to help families voice their opinion on the current management guidelines.

Research Project Proposal 2024

Primary supervisor (name):	Dr Craig Taplin (Telethon Kid's Institute, Perth Children's Hospital)
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Other supervisor/s if any (name):	Professor Elizabeth Davis (Telethon Kid's Institute, Perth Children's Hospital) Dr Vinutha Shetty (Telethon Kid's Institute, Perth Children's Hospital) Dr Shaun Teo (Telethon Kid's Institute)
Contact details (phone; email; location)	
SBMS Coordinating supervisor (for non-SBMS supervisors)	N/A
Contact details (phone; email; location)	N/A
Conflict of Interest	Nil
Project title:	**The impact of early morning exercise performance on acute post-prandial glucose time in range and 24h glycaemic control in youth with Type 1 Diabetes**
Project location:	Telethon Kids Institute
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Although regular physical activity (PA) is a key recommendation for the management of Type 1 Diabetes (T1D), participation in exercise presents unique challenges for children living with T1D. These challenges result in them having significant barriers towards exercise-related diabetes management, with the most frequently reported barrier being fear of hypoglycaemia. Consequently, previous research has focused on the manipulation of exercise variables such as: i) exercise type; ii) intensity and; iii) duration, to provide the evidence needed to address the concerns relating to PA and T1D management. However, despite the availability of these evidence, PA levels in children remain lower than their non-T1D peers. As such, new contemporary methods of manipulating exercise variables are needed to help improve upon exercise prescription for children and adolescents living with T1D.

	The diurnal timing of exercise could be an important factor that has started to gain attention in recent times and may play a crucial role in T1D management during exercise performance. Hence, the overarching aim of the project is to explore the effect of a morning exercise session on acute glycaemic control measures when compared to a no-exercise control session in youth with T1D. This study will involve working with the team to recruit participants, supervise participants during in-clinic exercise sessions, and collect and analyse data.

Research Project Proposal 2024

Primary supervisor (name):	Steven Mutsaers
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Conflict of Interest	Nil
Project title:	**Examining the efficacy of the Hck inhibitor RK-20449 in a mouse lung fibrosis model**
Project location:	Inst for Respiratory Health, Perkins building north
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	**Project description:** Idiopathic pulmonary fibrosis (IPF) is a fatal disease of unknown aetiology that is unresponsive to current therapy. It is characterised by excessive deposition of extracellular matrix (ECM) proteins within the pulmonary interstitium, leading to impaired gas transfer, a loss of lung function and death. What drives the development of IPF is unknown but a widely accepted hypothesis is that repeated injury to the epithelium leads to dysregulated healing, initiating a cascade of processes resulting in fibroblast/myofibroblast accumulation and overproduction and deposition of collagen.Tissue-resident macrophages are versatile cells that express a high degree of plasticity represented by classically activated M1 (pro-inflammatory) or alternatively activated M2 (anti-inflammatory/profibrotic) macrophages. Macrophages are part of the immune system's initial response to injury and are important in the normal repair process by promoting the activation of fibroblasts, which are cells responsible for producing collagen and other proteins needed for regeneration. However, in chronic lung disease like IPF, macrophages can become dysregulated and contribute to the pathogenesis of fibrosis. Prolonged inflammation and the

	continuous recruitment of macrophages to the lungs can lead to the release of pro-inflammatory cytokines and growth factors that stimulate activation and proliferation of fibroblasts which are responsible for excessive collagen production leading to the formation of fibrotic tissue. While macrophages play a critical role in tissue repair and immune defence, their migration and activation must be tightly regulated to prevent excessive inflammation and fibrosis in the lungs. This study will investigate the effect of selectively inhibiting macrophage migration on lung fibrosis in a mouse model. More specifically, this study aims to: 1. Investigate the effect of the selective macrophage motility inhibitor, RK-20449, on the development of lung fibrosis using the bleomycin mouse model. 2. Determine whether RK-20449 affects fibroblast function. The project will involve the following activities. • Preparation of cells and tissues for immunocytochemistry/histochemistry • Preparation of cells for RNA isolation and real time PCR • Preparation of cells for protein isolation and western blot • Cell function assays • Animal models of lung injury and fibrosis

Research Project Proposal 2024

Primary supervisor (name):	Associate Prof Chris Bundell
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SBMS Coordinating supervisor (for non-SBMS supervisors)	
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Conflict of Interest	Nil
Project title:	Anti MDA5 antibodies: are they important,can we improve our diagnostics approach.
Project location:	Immunology, PathWest Laboratory Medicine
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Idiopathic inflammatory myopathies (IIM) are chronic multisystem autoimmune conditions which cause muscle inflammation (myositis), skin manifestations and interstitial lung disease. An expanding number of myositis specific and myositis associated antibodies are recognised which are important for accurate diagnosis and providing prognostic information. Increasingly, clinico-serologic associations are recognised that guide management of patients with IIM. MDA5 antibodies are associated with severe & rapidly progressive respiratory disease. Early recognition and accurate diagnosis of this

	subtype of dermatomyositis is vital to instituting timely and intensive immunosuppression. The QE2 Immunology Laboratory of PathWest Laboratory Medicine is a major testing centre for myositis autoantibodies and uses an immunoblot assay. The proposed study aims to assess existing immunoblot assay performance in regard to optimisation of reference ranges and determining whether there are significant associations with other autoantibody tests that can improve diagnostic performance. To further investigate the sensitivity and specificity of the MDA5 and TIF 1 gamma antibody testing, positive samples and disease controls will be rerun on an alternative commercially available ELISA method. Published data on novel myositis specific antibodies will be reviewed and the possibility of developing supplemental assays will be explored. The aims of this project are to: • review the frequency and concordance of positive myositis antibodies using local and manufacturer's reference ranges; correlation of ANA indirect immunofluorescence patterns with various myositis autoantibodies and review of the clinical details of the positive cases where available. • Investigate the sensitivity and specificity of commercial MDA 5 and TIF1 gamma antibody ELISAs relative to the immunoblot. The methods involve • literature review relating to the above stated aims, • reviewing antinuclear antibody patterns from Hep2000 indirect immunofluorescence • frequency and concordance analysis of myositis data collected through PathWest myositis autoantibody testing • Perform ELISA testing on myositis patient samples for assay evaluation and verification

Research Project Proposal 2024

Primary supervisor (name):	A/Prof Phil Burcham ([Pharmacy [SAH] and Pharmacology & Toxicology [BMS], UWA).
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Other supervisor/s if any (name):	
Contact details (phone; email; location)	
SBMS Coordinating supervisor (for non-SBMS supervisors)	
Contact details (phone; email; location)	
Conflict of Interest	
Project title:	A Novel Fluorescence Quenching Microplate Assay for Rapid Caffeine Estimation in Human Saliva
Project location:	Lab 1:20, M-block QE2 Medical Centre
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Caffeine is a widely consumed psychostimulant due to the high popularity of coffee and energy beverages. Significant interindividual variability is seen in human responses to caffeine, partly due to differences in the liver's capacity to metabolise this drug. The main catalyst of hepatic caffeine clearance, CYP1A2, shows significant variation at the gene level. Although often used as a phenotypic CYP1A2 "probe drug" in drug cocktails during pharmacogenomics studies, methods used to quantify caffeine are expensive, making their deployment in class labs difficult. Since caffeine levels in saliva parallel those in plasma, this non-invasive biofluid is a popular alternative, yet the assays used to measure caffeine in saliva samples are also complex. This project builds upon a successful trial of a novel fluorescent microplate assay for rapid estimation of salivary caffeine that was developed in 2023 by UWA M- Pharmacy students. **AIMS:** 1) To further optimise and validate a rapid fluorescence microplate assay for salivary caffeine estimation.

2) To use the assay to estimate caffeine levels in volunteer saliva samples collected after controlled oral doses of caffeine.

3) To use PCR-RFLP to assess the prevalence of CYP1A2*F alleles in volunteers to see if they influence salivary caffeine levels estimated with the fluorescence microplate assay.

DESIGN:

After obtaining HEC Approval, the student will recruit volunteers for a small-scale trial. After donating a "baseline" saliva sample, subjects will ingest 200 mg caffeine and then will donate saliva samples at hourly intervals for 3 h. A buccal cavity swab will be performed to permit DNA extraction for genotyping.

TECHNIQUES:

Fluorometric assay design and validation; small scale human trial design; processing human samples; use of multiwell plate fluorescence imager; DNA extraction; restriction digests; agarose gel electrophoresis; statistical analysis, etc.

OUTCOMES:

1) Candidate will gain skills in the design and conduct of small-scale human trials, processing of human biofluid samples, and use of basic analytical methods including multiwell plate assays and PCR-RFLP.

2) Project will reveal the suitability of a fluorescence quenching-based assay for rapid estimation of salivary caffeine levels following ingestion of an oral dose.

3) Project will reveal any association between AA, AC and CC CYP1A1*1F genotypes and salivary caffeine levels in human volunteers.

4) Project will reveal the suitability of the fluorescence microplate assay for use in pharmacogenomics lab classes in the pharmacology curriculum.

REFERENCES:

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Du, C et al (2020) Fluorescence sensing of caffeine in tea beverages with 3,5-diaminobenzoic acid. Sensors, 20, 819. C Sachse et al (1999) Functional significance of a C-->A polymorphism in intron 1 of the cytochrome P450 CYP1A2 gene tested with caffeine. Br J Clin Pharmacol, 47, 445-9.

THE UNIVERSITY OF WESTERN AUSTRALIA

School of Biomedical Sciences

Honours in Medical Research

Research Project Proposal 2024

Primary supervisor (name):	Anthony Akkari
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Conflict of Interest	None to declare
Project title:	Evaluating strategies to improve the awareness of pharmacogenetics in youth.
Project location:	The Perron Institute for Neurological and Translational Science
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Through our ongoing research and evaluation of the current literature evaluating the barriers and facilitators to pharmacogenetic testing in primary psychiatric care, we have found that there is a lack of awareness surrounding the use of pharmacogenetics in the youth population. This project aims to evaluate the most effective strategies to improving the awareness of pharmacogenetics in tailoring and personalising the treatment of antidepressants in young people (>25yrs) with a lived experience of depression and/or anxiety. Youth participants will be recruited for focus groups and/or interviews where they will be asked a series of questions pertaining to answering this research. Participation will be regarded based on the following inclusion criteria: • Aged between 18-24years, • Have a lived experience of anxiety and/or depression, • Fluent in English, • Ability to sign consent.

	Random sampling and snowball recruitment will be achieved through UWA. Focus groups will be recorded and transcribed and thematic analysis techniques will be used to determine themes and subthemes arising from discussions. The outcomes of this project will help build a campaign to promote the use of pharmacogenetic testing to aid in personalising antidepressant prescription in young people. Pharmacogenetics has the ability to inform practitioners on safer and more effective medication and dosage per individual patient, increasing patient pharmacotherapy outcomes and reducing the potential for medication-related side effects and hospitalisation. With mental health rates in young Australian's increasing in recent years, along with the prescription and use of antidepressants, more effect prescription models are required. Pharmacogenetics is another tool in a clinicians toolbelt to provide more effective care to a population in desperate need.

THE UNIVERSITY OF WESTERN AUSTRALIA

School of Biomedical Sciences

Honours in Medical Research

Research Project Proposal 2024

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SBMS Coordinating supervisor (for non-SBMS supervisors)	
Contact details (phone; email; location)	
Conflict of Interest	None
Project title:	Multi-omic immunophenotyping of KIR+CD8+ T cells in Multiple Sclerosis
Project location:	Perron Institute, RR Block 8 Verdun Street, QE11 Medical Centre, Nedlands 6008
Project Description: Aims; Design; Techniques; Outcomes; References (optional):	Dysregulation of immune responses is a key feature in autoimmune diseases including Multiple Sclerosis. Killer Immunoglobulin-like receptors (KIRs) are expressed on natural killer cells and certain T cell subsets that play a crucial role in modulating immune responses. The KIR family is complex and highly polymorphic, which poses challenges in accurately assessing KIR expression using traditional methods such as short-read RNA sequencing (RNA-seq) and consequently, the intricacy of the KIR repertoire is vastly underrepresented. Our project establishes a novel multi-omic, deep immunophenotyping pipeline to characterize the KIR repertoire expressed by CD8+ T cells. We will combine multi-parameter flow cytometry for protein expression and paired short-read and targeted long-read RNA-seq with high-resolution KIR allelic genotyping to provide a comprehensive, unbiased analysis of KIR expression on CD8+ T cell subsets. This innovative approach challenges the current understanding of KIR expression and improves our knowledge of the balance between inhibitory and activating KIR subsets. A greater understanding of KIR expression on CD8+ T cells will have significant implications in further understanding the immune

	response in health and disease with the goal of direct translation into improved, targeted immunotherapies for immune-mediated diseases. Techniques: Blood processing, flow cytometry, RNA-sequencing (bulk and single cell), RNA-seq analysis. Genotyping. Primary cell culture.