



Biomedical Sciences,
School of Biomedical Sciences
University of Western Australia

BACHELOR OF BIOMEDICAL SCIENCES (HONOURS IN MEDICAL RESEARCH) HANDBOOK 2020 COURSE

This book includes an outline of the different components of the course and how they will be assessed, specific instructions on how to apply to enrol in Honours, advice for supervisors and examiners, and a list of Research Projects available.

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A Welcome from the Head of the School of Biomedical Sciences

This 2020 Handbook introduces the Honours in Medical Research in the School of Biomedical Sciences, Faculty of Health and Medical Sciences at the University of WA. This innovative research-based program provides the training and launching pad for a career in science or further postgraduate study, including medicine, dentistry and/or PhD research. Entry into Honours requires an average grade of 65 or better in a Major in Anatomy and Human Biology, Biochemistry and Molecular Biology, Biomedical Science, Genetics, Medical Sciences, Microbiology and Immunology, Pathology & Laboratory Science, Pharmacology, Neuroscience, Pathology, Physiology, Population Health, Psychological Sciences, Psychology and Zoology, or similar biomedical science discipline.



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 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 valuable whatever direction your life takes.

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!

Head of School, Professor Jeffrey Keelan, BSc Liv., MSc PhD Auck., FSRB

TABLE OF CONTENTS

| | |
|--|----|
| Introduction..... | 4 |
| Objectives | 4 |
| Entry Requirements for Honours in Medical Research..... | 4 |
| Outline of Honours in Medical Research Program | 5 |
| BMED4005-4008 (6 pts each for 24 pts) Biomedical Sciences Research Project Parts 1-4 | 5 |
| BMED4001 (6 pts) Biomedical Sciences Research Literature Review | 5 |
| BMED4002 (6 pts) Research Communication in Biomedical Sciences..... | 5 |
| BMED4003 (6 pts) Biomedical Sciences Research Design, Protocols and Analysis..... | 6 |
| Assessment..... | 6 |
| <i>Site-project specific training:</i> | 6 |
| Instructions for SAFETY training..... | 7 |
| I. Student safety induction: Online unit enrolment..... | 7 |
| II. Online Enrolments for Biohazard, Gene technology, and Biosafety Induction..... | 7 |
| III. Read the powerpoint presentation on local safety for L and M Blocks on LMS..... | 7 |
| BMED4004 (6 pts) Medical Research Ethics and Scientific Rationale | 8 |
| Structure of the Bachelor of Biomedical Sciences (Honours) program..... | 9 |
| Medical Research Design, Protocols and Analysis (BMED4003)..... | 9 |
| Medical Research Ethics and Clinical Rationale (BMED4004)..... | 9 |
| Research Communications in Biomedical Sciences (BMED4002)..... | 9 |
| 1. Preliminary Honours Seminar..... | 10 |
| 2. Journal Club/Seminars..... | 10 |
| 3. Poster Presentation with Interview | 10 |
| Biomedical Sciences Research Literature Review (BMED4001)..... | 11 |
| Biomedical Sciences Research Project (BMED4005, 4006, 4007 & 4008)..... | 12 |
| Requirements | 12 |
| MANUSCRIPT Assessment | 12 |
| General Assessment | 13 |
| Preparing Your Biomedical Sciences Honours Thesis | 14 |
| 2020 Biomedical Sciences Honours Schedule..... | 14 |
| Responsibilities of the Honours Student..... | 14 |
| Responsibilities of the Honours Supervisor..... | 15 |
| Responsibilities of the Honours Examiner | 15 |
| Responsibilities of the Honours Coordinator | 16 |
| Plagiarism..... | 16 |
| Definition | 16 |
| Procedures for handling a Suspected Case of Plagiarism..... | 16 |
| Appendix A: Marking Guides | 17 |
| Literature Review & Research Plan Grading Sheet | 17 |
| Examiner’s Comments and Evaluation of Manuscript..... | 18 |
| Supervisor’s Assessment..... | 20 |
| How Do I Enrol in Honours in Medical Research for 2020? | 21 |
| DECIDE ON AN HONOURS PROJECT | 21 |
| Identify the appropriate Entry Requirements | 21 |
| Students with a Biomedical Sciences or Biomedical Major:..... | 21 |
| Students without a Biomedical Sciences or Biomedical Major:..... | 21 |
| Submit an application..... | 21 |
| Step 1: Register your agreed project with the UWA Biomedical Sciences office..... | 21 |
| Step 2: Apply to the Honours Programme..... | 21 |
| Step 3: Enrol in the appropriate units..... | 21 |
| Application for Honours in Medical Research 2020 | 23 |
| What Honours Projects are Available in 2020? | 25 |

Introduction

The purpose of Honours in the School of Biomedical Sciences at the University of Western Australia is to introduce students to the processes involved in original scientific Research. The Honours course comprises an academic year of full-time Research under the supervision of a Researcher in the biomedical sciences, and, perhaps, other co-supervisors. It will foster enhanced observational skills, relevant practical skills, lateral thinking and problem solving, independent lab work, including time-management, literacy and communication skills, as well as professional responsibility and ethical conduct (BMED4004).

Each Honours student undertakes an individual Research project, the findings of which form the basis for a literature review, similar to a review paper in a journal (BMED4001), 'ready-for-publication' manuscript (BMED4008, 4005, 4006, 4007) and a 'conference-style' poster presentation (BMED4002). At the beginning of the year, students share some general training in use of Research infrastructure and safety. Specific students may be required to receive specific training for certain types of Research. For example, if you to a Research project in non-human animals, you are required to complete the PAWES training course offered by Animal Services, and if you work with radioactive isotopes, you must complete a radiation safety course, and similarly if you work with gene-modified organisms. Such general laboratory training, student-specific training in specific Research protocols, and instruction in Research design, results presentation and analysis will contribute to BMED4003. Training in Research Ethics and clinical rationale for projects will be covered in BMED4004.

Bachelor of Biomedical Sciences (Honours) provides an additional qualification that expands your employment opportunities and opens the way for postgraduate Research. We hope that you enjoy the year and embrace the challenges it will provide.

Objectives

Students who complete Bachelor of Biomedical Sciences (Honours) should:

- acquire the critical skills and attitudes necessary to
 - think, reason and analyse logically and creatively,
 - critique experiments and their findings, and question accepted wisdom,
 - be open to innovation in their literature review;
 - have an appreciation of the philosophy and practicalities of Research, and be able to formulate and write a literature review and Research proposal in a standard format;
 - acquire the skills needed to embrace rapidly changing technologies;
 - understand how to design experiments, analyse and present the results appropriately;
 - develop the skills required to learn, and to continue through life to learn, from a variety of sources and experiences, through the process of learning the scientific method of knowledge acquisition;
 - be conversant with published literature relevant to the field of study, and skilled in the retrieval of this information;
 - be experienced in Research methodology appropriate to their chosen field of study;
 - be able to collect, critically analyse, and interpret data;
 - communicate clearly, effectively and appropriately in a range of contexts;
 - write scientific work in a highly concise, informative and lucid fashion, suitable for submission for publication.
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Entry Requirements for Honours in Medical Research

A minimum weighted average mark of 65 per cent in the Level 3 units of a major in Biomedical Science, Cancer biology, Genetics, Neuroscience, Pathology, Microbiology and Immunology, or similar biomedical science discipline appropriate for the field of study within the School of Biomedical Science (e.g., anatomy, physiology, biology, psychology, public health, etc). In addition, a student must be accepted by at least one Academic supervisor from the School of Biomedical Sciences, UWA. Details of the enrolment process can be found on pages 22-23.

Outline of Honours in Medical Research Program

This program is a Research-based program, with the coursework directly related to Research or data analysis and presentation, comprising 8 six-point units, listed below. Four of these units constitute your experimental project. The other four units include the literature review, Research communication component, Research design, protocols and analysis, and Research Ethics and Clinical Rationale. You will begin with some training in general and specific Research protocols, the former for all students, the latter tailored to each student's requirements, and in Research ethics and rationale. You must also develop a preliminary honours seminar in which you describe the rationale, Research design and methodology of your project. This seminar will be followed some weeks later by a literature review. Prior to the seminar, you submit your Research design to the Coordinator of BMED 4003. The seminar is part of unit BMED 4002, and the literature review is BMED 4001. You will be required to attend your lab's seminars/journal club, and will be assessed on attendance and participation as part of BMED 4002. If these are not available in your Research lab, then you may attend the Friday morning Biomedical Sciences seminar run by Prof Fiona Pixley. Near the end of the second semester, you will present a Poster of your Research with an Interview by your examiners, as a component of BMED4002. Penultimately, you submit a 'ready-for-publication' Manuscript for the last assessable component of your Honours program. The ultimate task is to submit your final thesis, comprising a pdf of your preliminary seminar, literature review, a pdf of your poster, and your manuscript, plus any appendices containing additional methodology and results that were not included in your final poster and/or manuscript.

Students undertaking Bachelor of Biomedical Sciences (Honours) on a full-time basis will complete concurrently each of the following co-requisite units:

BMED4005-4008 (6 pts each for 24 pts) Biomedical Sciences Research Project Parts 1-4

Students carry out an individual Research project under the supervision of a member of the School of Biomedical Sciences, or with a primary supervisor in a cognate area along with a co-supervisor (who may be largely administrative) from the School. Students prepare and submit a 'ready-for-publication' style manuscript for assessment.

UNIT Coordinator: Professor Mathew Martin-Iverson

BMED4001 (6 pts) Biomedical Sciences Research Literature Review

Students will write a Literature Review and Research Plan outlining the principal Aims of the study and an overview of the approaches used to achieve the Aims. The purpose of the Literature Review and Research Plan is manifold, including (a) ensuring that the student is familiar with existing work in the field, (b) increasing her/his awareness of experimental approaches that can be used to investigate Research ideas, (c) heightening the relevance of their project, (d) identifying gaps in current knowledge and formulating aims addressing the identified gaps, and (e) focussing the student on the task ahead. The Literature Review and Research Plan must be between 4500 and 6000 words (not including references, include a word count at the end of the document). Assessed by the same examiners who assess the thesis.

UNIT Coordinator: Professor Mathew Martin-Iverson

BMED4002 (6 pts) Research Communication in Biomedical Sciences

A presentation to the Biomedical Sciences and the Honours supervisors and other honours students, of the proposal (an in-depth overview of the literature pertaining to his/her field of study, an outline of the principal Aims of the study and an overview of the approaches used to achieve the Aims), Laboratory-specific weekly seminar/journal club, in which journal articles are critiqued by students and staff in each Research group, and/or lab members present results obtained, and a poster presentation and defence on the Research. Assessment: Each of these is assessed by the thesis examiners and other attending staff,

except that the journal club activities are assessed by the supervisor(s) based on attendance and participation.

UNIT Coordinator: Professor Mathew Martin-Iverson

BMED4003 (6 pts) Biomedical Sciences Research Design, Protocols and Analysis

Between-subjects, within-subjects, mixed between-within subjects designs will be described, as will basic single-subject designs, time-series and formal qualitative design. The concepts of Bayesian and frequentist approaches to statistical analyses will be introduced, but specific methods from the classic frequentist approach will be taught (E.g., t-tests, ANOVAs, ANCOVAs, regression including correlations, methods of curve fitting, and nonparametric statistics), and when they should be used, including the concepts of power analysis and effect size. General laboratory safety and Research equipment care will be taught, as will Research specific required courses (E.g., PAWES, radiation safety, GMO handling, first-aid and aggressive incident management for those working with clinical samples) specific to each student.

Students who are using laboratory animals during their Honours Project must complete the PAWES course (Program in Animal Welfare, Ethics and Science) taught by the Office of Research Ethics and Animal Care at UWA. Please establish with your Supervisor whether you should complete this and other courses and indicate on the yellow "Intention to Apply for Bachelor of Biomedical Sciences (Honours) form". Please note that this course fills up quickly and you should reserve a space as early as possible, or you might not get enrolled. The course time-table on the Research website

(<http://www.Research.uwa.edu.au/staff/animals/pawes>) usually becomes available in January of the year of your honours.

In the event your Honours Project involves the use of radiolabelled drugs or reagents, you must also complete the Unsealed Radioisotope Handling Course run by the Safety and Health Office at UWA. Again, your Supervisor can advise whether you are required to complete the Radioisotopes course. If your Honours Project involves clinical Research with patients, you may need to do additional training (Eg. CPR, Defibrillation, Aggressive Incident Management, Manual Handling, How to obtain Informed Consent, etc, provided in your lab, hospital or health service).

The online Gene Technology Awareness Session is essential for students who work with gene technology. It is compulsory for all Researchers who work with Genetically Modified Organisms (GMOs), and for anyone who works within (or administrates) a facility certified by the Office of the Gene Technology Regulator (OGTR). Go to: <https://www.class2go.uwa.edu.au/enroll/3MHEFE>

A copy or screenshot of your badge of completion must be forwarded to your lab manager or supervisor. Please advise the Honours Coordinator of any such courses that you take, as assessment as pass/fail will apply to BMED4003. Three min 2 hour tutorials in week 1

Recommended Text Book: Bate and Clark's "The design and statistical analysis of animal experiments"
Cambridge University Press, 2014. Cheaper from Amazon, and there may be an online version.

Assessment

| | |
|--|------------|
| Online safety training. | 5% |
| Complete Chemistry for Researchers refresher online (LMS) module | 5% |
| Pitfalls in Research design and statistics. | 5% |
| Look at your data first: Graphing | 5% |
| ANOVA and T-tests. | 5% |
| Regression and ANCOVA. | 5% |
| Nonparametric tests. | 5% |
| Total assessments from lecture/tuts: | 35% |

Site-project specific training:

Please upload to the 4403 LMS copies of all training done and assessments for your lab work (e.g. PAWES, Gene technology (Biosafety 2 on LMS). In addition, please complete the UWA Biosafety 1 (Biohazards) unit online (LMS):

Instructions for SAFETY training

I. Student safety induction: Online unit enrolment

Use Mozilla Firefox, Google Chrome or Safari web browser

Go to [Blackboard](#) and log on

Click on the Units tab

Enter **UWA Health and Safety Induction - Non Staff** in the search box

Hover over unit title and click on the chevron (down arrow) to self-enrol

Should you require more information or if you experience difficulty go to [UWA Learning Management System \(LMS\)](#). Please work through the module and complete the quiz. You can then obtain your certificate of completion. Students who have a staff 8-digit staff number must use this entry to Elmo rather than the separate online health and safety induction for students (this is important for students, who are staff, to have verification of induction). Students will also be required to conduct a local workplace induction.

NOTE – Whilst UWA students do not have access to any workers compensation entitlements, they are able to access the following support:

UWA Medical Centre - The University Medical Centre is a fully equipped and accredited health service providing safe, high quality and confidential health care to the UWA community.

UWA Counselling and Psychological services - provides professional and confidential service free of charge to students of the University of Western Australia.

UniAccess - provides free services and support to UWA students who want to disclose a disability or a medical condition and request assistance.

Other services are accessible here - <http://www.student.uwa.edu.au/experience/health>

II. Online Enrolments for Biohazard, Gene technology, and Biosafety Induction

1. [Log on to www.lms.uwa.edu.au](http://www.lms.uwa.edu.au)
2. Go to the "Community" tab
3. Search under "Organizations" for "Biosafety"
4. Hover your cursor over the right of; 'UWA-Biosafety-Induction'. A grey down arrow will appear and you should click on the 'enrol' option.
5. You can now take the modules "Biosafety 1 (Biohazards)", "Biosafety 2 (Gene technology)" with the associated quizzes, and complete the Biosafety Induction signoff.
6. Your certificates should be saved and submitted to the Biosafety Office when applying for approvals. Your lab manager should also keep a copy.

Problems with your online enrolment? Please contact the IT Help Desk on ithelp-is@uwa.edu.au

III. Read the powerpoint presentation on local safety for L and M Blocks on LMS.

Assessment for all safety and additional onsite training (including PAWES etc): 25

Research Project Design & Statistics plan

Assessment: 40%

Research Design part of assignment

For this, you need a description of your planned research design for your honours project. You can and probably should get help from your supervisor. This description should include:

A very brief description of the general and specific aims of the project.

A description of what the experimental and observational units are.

A description of the independent and dependent variables.

What the known confounding variables are and how they will be controlled.

How you will deal with unknown confounding variables (E.g., through randomisation).

If you are counterbalancing (i.e. using a blocked design), it would be useful to show the

ezDesign graph indicating a fully balanced design.7. If you plan to use parametric statistics (i.e., ANOVA, t-tests, correlations or regressions) do a power analysis indicating the minimum number of observational units needed to achieve a power of 0.8, unless you have a specific rationale for choosing another power level.

Statistics Plan part of this assignment

This is the plan for the statistical analysis of the data that you expect to obtain for your honours thesis. It is best if you have some preliminary data to test the plan on, but if you don't have data, you can easily produce "dummy" data to test it on using R statistics. The plan then should include the example of the completed analysis. Examples of what could be included are below.

Some of you may be doing specialised statistics (E.g., genetic analysis, multivariate tests, test reliability tests), and then you just send in your plan of what stats you will be doing and why, and with examples. The purpose of this assessment is to ensure that your stats will be appropriate before your thesis manuscript is sent to the examiners, and that you can answer questions about the stats at your poster defense.

Examples: 1. Parametric statistics:

Multiple Linear Modelling, ANOVA, ANCOVA, or t-tests.

The number of factors (except for t-tests) of each type (between-subjects or within-subjects), levels per factor, one-sided or two-sided tests. How you plan to determine if the assumptions of these tests are violated (homogeneity of variance, normal distribution of the residuals, sphericity, lack of interactions between the factors and covariates), and how you plan to deal with significant departure from these assumptions. If a Linear modelling, ANOVA or ANCOVA approach is planned with more than 1 factor of 2 levels, how you plan to test for more detailed comparisons (E.g., one of the many orthogonal planned contrast approaches such as polynomial, repeated or Helmert contrasts, or your own specified contrasts) or which corrections for post-hoc multiple comparisons with t-tests).

2. Curve fitting

Correlations, 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, etc.

How you plan to fit your data, which formula you will use, how you will check for outliers that may bias the results, and which algorithm is used to fit the data. If you have multiple treatments or factors, how you will compare the coefficients statistically afterwards with parametric or nonparametric tests, and which ones (E.g., comparing ED₅₀'s from different groups).

3. Nonparametric statistics

Chi-Square, Fisher's exact test, Wilcoxon (paired or unpaired), Kruskal-Wallis ANOVA, Survival Analysis, etc

Which tests you will use, and why. How will you deal with multiple ties (if applicable)? If there are multiple levels of multiple factors, how will you deal with those?

All Assessments: Note that final mark will be a pass/fail, with pass being an $\geq 50\%$ overall.

| | |
|--|-----|
| Class assignments: | 35% |
| Site-project specific training: | 25% |
| Research Project Design & Statistics plan* | 40% |

*Uploaded together as one assignment, **maximum 4 pages**

Unit Coordinator: Professor Mathew Martin-Iverson

BMED4004 (6 pts) Medical Research Ethics and Scientific Rationale

Knowledge and understanding of medical research ethics is integral to research. Students participate in a face-to-face discussion of an interactive movie at the start of semester. In addition, students will complete an online Research Ethics Online Training modular course as well as the Good Clinical Practice short course provided by the Global Health Training Centre and. Students will also be required to submit a clinical OR SCIENTIFIC rationale for their thesis project.

Students are required to subscribe to the BMED4004 Discussion Forum on LMS and check their UWA emails every day for updates.

General research ethics, Human and/or Clinical Research Ethics, clinical and experimental rationale for thesis project.

Unit Coordinator: Dr Lynette Fernandes

[Summary of Requirements](#)

Students participate in a face-to-face discussion of an interactive movie at the start of semester. Students complete an online Research Ethics Online Training modular course and Good Clinical Practice short course provided by the Global Health Training Centre. Students are required to submit their clinical or scientific rationale prior to the Preliminary Honours Seminar. More details on the assessment of this unit will be provided by the beginning of the first semester of 2020.

Please note, students are required to pass each of the following components in order to pass BMED4004. Furthermore, failure in any or all of these components will result in failure in the entire Honours course.

1. Global Health Training Centre Research Ethics Online Training Modular course
2. Global Health Training Centre Good Clinical Practice short course
3. Clinical Rationale

Structure of the Bachelor of Biomedical Sciences (Honours) program

Obtaining Bachelor of Biomedical Sciences (Honours) involves the successful completion of the eight Biomedical Sciences units listed above. **Failing any one unit will fail the course.** Your overall mark will be the weighted average of 6 of the 8 units (excluding 4003 and 4004 which are pass/fail units), meaning each unit contributes 16.67% to the final mark. All units must be passed to pass the course.

Medical Research Design, Protocols and Analysis (BMED4003)

Students attend the School's lab safety and equipment protocols training, and complete the required additional training required for specific projects (E.g., PAWES, radiation safety training, GMO handling, Aggressive Incident Management, CPR, etc, depending on the Research lab that you are working in) at the start of the first semester. In addition, lectures on Research design, data presentation, and statistical analyses will be attended and assessed. Three weeks prior to the Preliminary Honours Seminar, the students' specific Research designs will be submitted and assessed by 4003 Unit Coordinator, and then discussed with the students, with any possible revisions incorporated. This unit is a pass/fail unit. Providing you pass, it will not influence your final mark. More details on the assessment of this unit will be provided by the beginning of the first semester of 2020.

Medical Research Ethics and Clinical Rationale (BMED4004)

Students complete the online CITI (Collaborative Institutional Training Initiative) course on biomedical ethics and participate in a face-to-face discussion of an interactive movie at the start of the first semester. One week prior to the Preliminary Honours Seminar, students will submit their clinical rationale as well as their completed animal or human ethics application as appropriate. This unit is a pass/fail unit. Providing you pass, it will not influence your final mark. More details on the assessment of this unit will be provided by the beginning of the first semester of 2020.

Research Communications in Biomedical Sciences (BMED4002)

This unit comprised three components: Preliminary Seminar (35%), specific engagement in weekly lab journal clubs/seminars (15%) and a Poster presentation and defence (50%).

1. Preliminary Honours Seminar

Seminars will be held in mid-April and should give an in-depth presentation (E.g., PowerPoint) of the literature pertaining to your field of study, an outline of the principal Aims of the study and an overview of the approaches used to achieve the Aims. Preliminary data may be included. Students can and should receive guidance from their Supervisor with respect to preparing this seminar. Typically, the seminar will consist of a 20-minute presentation followed by a 5-10 minute question and answer session. The Preliminary Seminar will count 35% of the Unit mark and will be assessed by all attending academics (except supervisors) using the following criteria:

| | |
|---|-----|
| (a) Clarity 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% |

2. Journal Club/Seminars

Students must attend either their specific lab weekly journal club/seminars with their supervisor providing the Unit Coordinator a record of attendance and participation OR the Biomedical Sciences seminar series probably being held on Friday mornings. The organiser of the Friday morning seminar series or the student's supervisor will provide the Unit Coordinator with a record of attendance and participation.

3. Poster Presentation with Interview

Students will prepare a 'conference-style' Poster, which provides an overview of the Research completed by the student during their Honours program. The poster will typically consist of a title that identifies the Research at the top of the poster (using large lettering of 4 cm or higher). Authors and their affiliations are included under the title. With respect to the organisation of the different sections of the poster (e.g. Introduction, Methods, Results, Conclusions, etc.), the key is to achieve clarity and simplicity – don't overload the poster. Use a coherent sequence (top to bottom then left to right) to guide the viewer through the poster. Keep text brief, and use figures, tables, graphs and photographs when appropriate. All materials should be legible from a distance. Avoid using abbreviations, acronyms and jargon. The size of the Poster should not exceed 1.0 m high by 1.2 m wide, e.g. 4 columns containing three A4 pages/column in portrait orientation, or 3 columns containing four A4 pages/column in landscape orientation. The poster may be composed of a single poster large piece or may be composed of individual A4 pages. If the student is presenting at a conference near the same time, the conference style poster may be followed so that they do not need to make two separate posters.

Please note that Uniprint may take 3 or more days to prepare a poster.

The poster should be ready for mounting and submitted to the Administrative staff in the Biomedical Sciences , Ground floor M-Block) the day before your presentation. At designated times during the Poster Presentation with interview, students will individually attend their Poster, with Examiners, Supervisors, Honours Coordinator and attending academics also present. Students will be allocated 5 minutes to explain the content of their posters to the Examiners before panel members have the opportunity to ask questions about the study. It is anticipated that the Interview (question and answer session) will last about 15 mins.

The Poster presentation will be assessed independently by the examiners using the following criteria:

| | |
|----------------------------------|-----|
| (a) Quality of Poster | 30% |
| (b) Quality of Oral presentation | 20% |
| (c) Quality of Q and A session | 50% |

As the questions may cover issues related to the manuscript as well as the Poster, please bring a copy of the manuscript for ready access during the Poster presentation and any other relevant material. You should be prepared to defend the methodology, results and interpretations expressed in your Poster and manuscript.

Your performance at the Interview will be assessed on:

- (a) how well you can get the answer across (try to speak fluidly and lucidly, avoid long and rambling answers, demonstrate some depth and breadth of understanding where possible), and
- (b) your ability to demonstrate an understanding and mastery of the Research area (answer questions correctly using references to the scientific literature, have an appreciation of the limitations of the study, be able to discuss alternative interpretations of the data).

Biomedical Sciences Research Literature Review (BMED4001)

Following on from the Preliminary Seminar, students will write a Literature Review and Research Plan outlining the principal Aims of the study and an overview of the approaches used to achieve the Aims.

The purpose of the Literature Review and Research Plan is manifold, including (a) ensuring that you are familiar with existing work in the field, (b) increasing your awareness of experimental approaches that can be used to investigate Research ideas, (c) heightening the relevance of your project, (d) identifying gaps in current knowledge and formulating aims addressing the identified gaps, and (e) focussing you on the task ahead.

Submissions must be in English, typewritten using 12 point, Times New Roman font, 1.5-spacing throughout. The style of the literature review followed should be from a standard journal in your specific area style for a review article. Search for the "*journal name* Instructions to authors" to determine stylistic features including in-text citation and reference style. State the name of the journal format on the title page. Your examiners are likely to detract marks if you do not follow the style consistently. **The use of figures and diagrams is encouraged to facilitate communication of your ideas, but any images or figures reproduced from published sources must be appropriately referenced (author, journal title, date, pages, etc.). Otherwise, you may face a plagiarism penalty.** Each page of your Literature review 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. The Literature Review and Research Plan for your Research topic must be between 4500 and 6000 words (not including references, include a word count at the end of the document). You will likely lose marks if you fail to number pages.

All students are required to formally seek input from Supervisors into the first draft of your Literature Review/Research Plan. To facilitate this process, please deliver the first draft of your Literature Review/Research Plan to your Primary Supervisor by the date stipulated in the 2020 Honours Schedule. Supervisors are encouraged to return your Lit Review (together with any suggested recommendations for improvements) within the week.

One copy of the Literature and Research Plan must be submitted in electronic format as a PDF to the Honours Co-ordinator and Administrative Assistant. The Literature Review and Research Plan will count 40% of the Unit mark (i.e. 20% of final Honours mark). A backup hard copy can be handed to the Administration Office, if you wish, but this is optional.

The Literature Review/Research Plan will be assessed by 2 examiners via 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 Literature Review summarise the current state of knowledge and identify gaps in that knowledge?
- (c) how clearly have the Hypotheses and Aims been stated?
- (d) does the Research Plan clearly establish how the Hypotheses will be tested and the Aims accomplished?
- (e) has the document been written in a clear, concise and logical manner?
- (f) is the manuscript well-organised (e.g., appropriate use of subheadings), succinct and clear? Is it of an appropriate length? Does the manuscript demonstrate an appropriate use of grammar? Has care been demonstrated to avoid spelling mistakes and typographical errors? Has the nominated journal style been followed consistently?

The importance of specifying a clear, well-written Hypothesis as well as Project Aims cannot be stressed too highly. Examiners are likely to grade a Literature Review poorly if such features are lacking.

They will also assess how well your Hypotheses and Project Aims are grounded in the preceding Literature Review (i.e. are the Aims directly addressing or “filling” any “knowledge gaps” identified in the Literature Review?). You should also ensure your Research Plan effectively describes the methods to be used in your project, clarifying how they will allow achievement of the Project Aims and testing of the relevant project Hypotheses.

Following assessment of your Lit Review/Research Plan, you’ll receive written comments from Examiners including typographical and stylistic changes to be made to the document before its final submission as part of your final Thesis. Those changes will not be re-assessed, and will not contribute to your final mark, but gives you a final chance to do minor editing before a permanent thesis is submitted.

Biomedical Sciences Research Project (BMED4005, 4006, 4007 & 4008) Requirements

The student prepares and submits a “ready-for-publication” scientific manuscript according the format used by a prototypic journal in your specific field of research. You must state the nominated journal format on the title page, and you must follow that style consistently throughout. However, word counts should follow the below limits, not the journal limits (as they vary widely across journals). This should be in format of an original research article, not a review. There is a strict word limit. Abstracts are limited to 250 words. Introduction is limited to 750 words. Methods is restricted to a maximum of 1500 words. Results are limited 1500 words, including figure legends. Discussion is also limited to 1500 words. References are limited to 40. The manuscript must be submitted as a pdf so that formatting will be software and platform independent. Additional data, methods and equipment may be placed in an appendix. This appendix will be available to examiners and will be included in the final bound thesis. However, it will not be marked by examiners. Supervisors can provide feedback before submission on the Introduction, Methods and Results but **NOT** the discussion, which is the student’s own work.

MANUSCRIPT Assessment

LATE PENALTIES: All late submissions will incur a 10% mark penalty per day.

The manuscript will be assessed by examiners according to specific descriptors (Appendix A). The examiners will also provide written feedback concerning any typographical and grammatical errors needing attention. These will be available for collection from the Unit’s Admin Office according to the dates in the 2020 Schedule. These changes should be made prior to lodging your Thesis. The primary supervisor will also provide a mark for the manuscript and for the student’s aptitude for Research as demonstrated throughout the Honours year (Appendix B), although this mark is not included in the final assessment submitted to Faculty. In the week following the Poster Defence session the Biomedical Sciences Honours Examiners, Coordinator (the latter as a representative of the student) will meet by email or in person as required for the examiners to agree on a consensus mark for each candidate.

The marks awarded for the manuscript will not depend on completion of all the experiments outlined in the Literature Review and Research Plan, as research plans sometimes go awry.

General Assessment

The marking bands for assessment are as follows:

90-100% (H1: HD+): An outstanding thesis in a challenging or difficult area, demonstrating excellence in terms of conceptualisation, theoretical framework or previous experimental Research leading to derivation of hypotheses as described in the introduction, the use of rigorous or innovative methodology, a mastery of statistical methods and presentation of results, the capacity to discuss the results in an analytic manner, skilful treatment of unexpected or inconsistent results, or a recognition of some limitation of the methodology, and integration of the findings within the theoretical framework or empirical background outlined in the introduction or an alternative framework if appropriate. Excellent written expression, organisation and format are consistent throughout the thesis.

80-89 (H1: HD-): As for 90-100 but with some trivial weakness, such as in the presentation or structure, or some minor inconsistency or oversight in the arguments, or a discussion that does not fully exploit the findings or links with theory or previous empirical Research.

75-79 (H2A: D+): For a thesis showing excellence in one or two aspects of conceptualisation, methodology, statistical analysis or discussion, but no particular strengths elsewhere, or for a generally good thesis with some weaknesses or flaws which are offset by some excellent features. Written expression, organisation and format are very good.

70-74 (H2A: D-): For a consistently good piece of work with well-structured arguments leading to development of the hypotheses, appropriate methodology and statistical treatments and an accurate interpretation of the results, but with no particular strengths elsewhere.

60-69 (H2B: CR): For a generally sound thesis with minor misconceptions, inconsistencies or omissions in one or more areas, or poor organisation or incorrect interpretation of the results, or an inability to recognise the limitations of the methodology, or limited evidence of independent thought or execution. The misconceptions are such that they do not affect the basic thrust of the thesis.

50 -59 (H3: Pass): For a thesis containing a number of misconceptions, inconsistencies or omissions, and/or unrecognised deficiencies in methodology, and/or misinterpretation of the statistical analysis and/or lack of integration with theoretical or empirical framework and/or inadequate evidence of independent thought or effort.

<50 (Fail: N+): For a thesis with major problems in conceptualisation or execution, or inability to present arguments coherently and with clarity.

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 10% mark penalty per day

Preparing Your Biomedical Sciences Honours Thesis

At the completion of the assessable components of the Honours program, students will be required to submit their Thesis for binding. The Thesis should include updated versions of the Literature Review and Final Manuscript which incorporate any typographical and grammatical corrections suggested by Examiners. The final content of the Thesis should be as follows:

1. Title page
2. A signed statement indicating that this work was solely performed by the student (unless otherwise indicated) as part of the requirement for a BSc Honours degree (a pro forma page will be provided)
3. Table of contents
4. List of acknowledgments – all those that contributed to the research should be acknowledged, and what work was not your own but was contributed by others should be clearly stated. Your examiners' must be able to ascertain what you did yourself. For PhD theses, all co-authors must sign off on what their contributions were.
5. Manuscript
6. The Poster presentation (as single PowerPoint slide)
7. Literature Review and Research Plan
8. Slides from Preliminary Seminar

The entire Thesis should be printed using A4 paper and single-sided printing. Formatting of thesis can include wider left margins for binding purposes than in the original manuscript. Students should submit *at least 4* copies of the Thesis to Ms Succorin Fernandes (Administration, School of Biomedical Sciences) for permanent binding. THREE of the permanently bound copies of the Thesis will be distributed as follows: 1 copy will be given to the student, 2 copies to the Supervisor(s) and 1 copy to the Department/Division of the primary Supervisor. Students who have more than one Supervisor will need to submit an extra copy for binding. Students will only be asked to pay for the permanent binding of any extra personal copies.

2020 Biomedical Sciences Honours Schedule

The Honours Schedule will be available early in 2020. The Honours program follows the standard two semesters, but without study breaks.

Responsibilities of the Honours Student

- One of the exciting challenges of the Honours year is that you will encounter many learning curves. The inevitable downside of this is that each task will take longer than anticipated, so it is important to be highly organised. 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, please ensure that this is kept to a reasonable level (less than 8 hours per week as a guide). If you are ill during the year you will need to obtain a Medical Certificate to receive due consideration.
- Ensure you are aware of Unit requirements particularly with respect to the safe and responsible usage of Unit facilities such as the Internet and core equipment, and security. If in doubt consult your Supervisor, the Honours coordinator or the Senior Technical Officer, Mr Richard Claudius.
- Document all your experimental work in a notebook and show it the Supervisor on a regular basis. Remember, it is a requirement that the notebook 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 and having copies saved on several different sites.

- You need to 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
- It is important that you arrange regular meetings with your Supervisor to discuss all aspects of your work.
- The role of the Supervisor is to guide, advise, help, constructively criticise, but not to push – it is your responsibility to be motivated to succeed in your work, and to assume ownership of the Research project.
- Attend your weekly journal club/seminar series in your Research lab OR the Biomedical Sciences Friday morning seminars..
- Be open to suggestions and advice from your Supervisor, but it is important that as the year progresses you develop signs of independence and initiative.
- Ensure that any conflicts that might develop with Supervisors or others are brought to the attention of the Honours Coordinator so that attempts can be made to resolve the matter quickly and amicably.
- It is important that you uphold the academic standards and good reputation of the Biomedical Sciences and Anaesthesiology Unit.

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 day-to-day running of the Research project
- 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 resources and ethics approvals
- be a good listener, and offer encouragement for good ideas and well-developed thoughts, but criticising where appropriate.
- keep the student informed about relevant regulations and administrative processes in the Unit, School and University
- to make arrangements for continuing supervision during periods while the Supervisor is away.
- provide advice and guidance on the preparation of the
 - Preliminary Seminar,
 - Literature Review & Research Plan,
 - Manuscript, and
 - Poster Presentation & Interview
- **ensure the integrity of the student's work and NOT read drafts of the Discussion section of the manuscript**
- 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 & Interview process
- attend an Examiners Meeting at end of year as student representative, if required for resolving major differences in thesis marking between examiners.

Responsibilities of the Honours Examiner

Each student will have 2 examiners with expertise in the general area. The Examiners are involved in all matters associated with the fair and equitable assessment of students. Specifically, the Examiners should:

- attend and assess the Preliminary Seminar (late April)
- read and assess the Literature Review & Research Plan and provide feedback on the work.
- assess the Manuscript (mid-to-late October)
- attend and participate in the Poster Presentation & Interview process (late October)
- attend Examiner's Meetings, as required (usually by email, except in complex cases, in early November).

Responsibilities of the Honours Coordinator

The Honours coordinator is responsible for organising and overseeing the entire Honours course.

Specifically, in preparation for next cohort of students, the Honours Coordinator will:

- call for Honours projects (July) and prepare the Honours booklet (September)
- coordinate Conditional enrolment of Honours students (from September onwards)

Specifically, for current cohort of Honours students, the Honours Coordinator will:

- ensure all students correctly enrolled (January/February)
- organise Honours Orientation program (for late-February)
- explain the Bachelor of Biomedical Sciences (Honours) course, especially assessment practices (late-February)
- organise welcome function for Honours students (late-February)
- assign Examiners to each student (late February)
- organise Preliminary Honours Seminars (early May)
- collect Literature Review/Research Plan from Students and distribute to Examiners (late May)
- informally check on students' progress (May to August)
- provide Students with instruction on writing the Discussion section of the manuscript (August)
- collect Manuscript from Students and distribute to Examiners (mid-October)
- organise and run Poster Presentation and Interview sessions (late October)
- arrange final assessment meetings between Examiners, Supervisors and Honours Coordinator.
- submit marks to Faculty (via Unit Administrative Officer)

Plagiarism

Definition

Plagiarism is defined as appropriating someone else's words or ideas without acknowledgment. There are many areas in society where plagiarism may be regarded as acceptable, for example the unacknowledged speech writer for a politician or a Commission Report which bears the name of the Chairman and not those who actually drafted the material.

However, in science a much stricter view must be adopted. New ideas and findings which are crucial to the advancement of knowledge are published in international journals under particular authors' names, and credit for some contribution in the eyes of one's peers is probably the main factor driving scientists to struggle and persist with difficult Research questions (obviously curiosity, job prospects, promotion, tenure, Research funds, etc. are others). It is therefore extremely important that this credit be properly assigned for personal, and in the longer term, historical reasons. Because no one works in a vacuum and there will always be earlier work in an area, 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 another BSc Hons or other thesis constitutes plagiarism. If you are in doubt as to what constitutes plagiarism, make sure you consult your Supervisor or Honours Coordinator.

Procedures for handling a Suspected Case of Plagiarism

The DISCIPLINE is ultimately bound by University procedures (given in Part II - *Procedures for dealing with allegations of misconduct in Research*, approved by Senate and circulated to Disciplines, 12 December 1991) on the matter of a suspected case of plagiarism, as with all other cases of misconduct in Research. As indicated, a complainant may opt to approach the Head of Faculty directly with details of a case. However, the Discipline feels that in most cases it may be preferable to discuss the matter in the first instance with the Head of Discipline, who may then decide that it should proceed to the Head of Faculty, or that it is without substance or magnitude, or that it can be dealt with internally.

Appendix A: Marking Guides

UWA – Honours in Medical Research Literature Review & Research Plan Grading Sheet

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%)

| Assessment Criterion | Mark (/100) | Comments |
|--|-------------|----------|
| 1) <i>The document shows familiarity with relevant literature and a good understanding of central concepts in the field.</i> | | |
| 2) <i>The document identifies significant “knowledge-gaps” in the existing literature.</i> | | |
| 3) <i>The manuscript states clear Project Aims and Hypotheses that are well grounded in the Literature Review.</i> | | |
| 4) <i>The chosen Experimental Methods are well justified and are relevant to Project Aims.</i> | | |
| 5) <i>The document shows insight and critical analysis and arguments are supported by appropriate evidence.</i> | | |
| 6) <i>Is the manuscript well-organised (e.g., follows a coherent structure, appropriate use of sub-headings, etc), succinct and clear? Is it of an appropriate length? Does the manuscript demonstrate an appropriate use of grammar? Has care been demonstrated to avoid spelling mistakes and typographical errors? Has the nominated journal style been followed consistently</i> | | |

Examiner's Comments and Evaluation of Manuscript

BIOMEDICAL SCIENCES RESEARCH METHODOLOGY (BMED4005, BMED4006, BMED4007 AND BMED4008)

Student Name: Student Number:

Manuscript Title:

.....
** NOTE: When apportioning marks please take into account the grades used by UWA:

90% - 100% H1: HD+

80% - 89% H1: HD-

75% - 79% H2A: D+

70% - 74% H2A: D-

First class Honours

60% - 69% H2B: CR

50% - 59% H3: Pass

2A Honours

less than 50% Fail: N+

1. ABSTRACT, INTRODUCTION, AIMS AND HYPOTHESIS

[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 manuscript? Did the Introduction provide appropriate scientific background, as well as identify limitations of the literature and areas of controversy? Did the Introduction include the key articles within the scientific literature? Were the Aims and Hypotheses clear and valid?]

Comments:

2. MATERIALS AND METHODS

[Were the Materials and Methods clearly described and fully referenced? Were the Methods used appropriate and valid for the stated aims?]

Comments:

3. RESULTS

[Does the Results section represent an adequate body of work? Are the results presented clearly and accurately? Were appropriate choices of experimental conditions, such as doses, concentrations, time-points, etc. used? Were sufficient controls and replicates performed? Were appropriate numbers of observations performed? Was there sound and appropriate use of statistical analyses and tests? Was the presentation of results (Figures, Tables, etc.) clear and logical?]

Comments:

4. DISCUSSION

[Is the Discussion relevant to the Introduction, Methods and Results? Is it logical in presentation and content? Is there evidence of critical and creative analysis? Does it place the findings in the context of past studies? Are there suggestions for future studies? Is there evidence of over-interpretation of data? What is frequency and extent of bias in interpreting the data? Have unexpected or inconsistent results been fairly and skilfully discussed?]

Comments:

5. REFERENCES

[Is the in-text citation style appropriate and consistent? Is the reference list free from careless errors? Is the content of the manuscript supported with appropriate in-text primary research citations, or is there over-reliance on reviews?]

Comments:

6. STYLE AND PRESENTATION

[Is the manuscript well-organised (e.g. appropriate use of subheadings), succinct and clear? Is it of an appropriate length? Does the manuscript demonstrate an appropriate use of grammar? Has care been demonstrated to avoid spelling mistakes and typographical errors? Has the nominated journal style been followed consistently]

Comments:

GRADING OF THE MANUSCRIPT

Please provide an overall grade (as a percent) that most closely reflects your assessment of the work.

This grade should in general reflect the individual scores given for the descriptors. However, since each descriptor need not have the same weighting applied, the final mark may not be a simple arithmetic mean of the individual marks.

GRADE: _____%

Name of Examiner: _____

Signature of Examiner: _____ Date: _____

Supervisor's Assessment

Student Name: **Student Number:**

Manuscript Title:

.....
**** NOTE:** When apportioning marks please take into account the grades used by UWA:

90% - 100% H1: HD+

80% - 89% H1: HD-

75% - 79% H2A: D+

70% - 74% H2A: D-

60% - 69% H2B: CR

50% - 59% H3: Pass

less than 50% Fail: N+

1. Please comment on quality of the Discussion section in the manuscript

2. Please comment on the student's aptitude for Research

| Criteria | Comment |
|--|---------|
| <i>Motivation towards scientific Research</i> | |
| <i>Organisation skills</i> | |
| <i>Laboratory and related practical skills</i> | |
| <i>Data analysis and interpretation</i> | |
| <i>Scientific reading and writing skills</i> | |
| <i>Independence and capacity for original thought</i> | |
| <i>Social skills in relation to other work personnel</i> | |

GRADE: _____%

Name of Supervisor: _____

Signature of Supervisor: _____ Date: _____

How Do I Enrol in Honours in Medical Research for 2020?

DECIDE ON AN HONOURS PROJECT

A list of Honours projects for 2020 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 formally apply for entry to the Honours program

Identify the appropriate Entry Requirements

Students with a Biomedical Sciences or Biomedical Major:

If you have completed a Major in Biomedical Sciences, or a Biomedical Major with an average of 65% or better in third year Units contributing to the major (1), in the Biomedical major, or you are eligible to apply to the BSc (Hons) directly. *This Honours degree is administered and awarded by the Faculty of Health and Medical Sciences.*

Students without a Biomedical Sciences or Biomedical Major:

The key requirement is that both UWA- and non-UWA applicants can demonstrate an equivalent to a 65% average in third year major units in disciplines that are relevant to their proposed project, a major in biomedical science field. Supporting documentation uploaded must include a brief Research proposal with confirmation from the relevant 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, Handbook prior to enrolling so that the School of Biomedical Sciences 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) eight units shown below: BMED4001, BMED4002, BMED4003, BMED4004, BMED4005, BMED4006, BMED4007, BMED4008

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

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Application for Honours in Medical Research 2020

To be filled in by STUDENT:

Name: _____ Student No: _____

Primary Supervisor: _____

Biomedical Sciences Supervisor (if different from above): _____

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 |
|------|----------------------|---------------|
| | | |
| | | |

SUPERVISOR Contact Details:

Mailing address: _____

Email address: _____

Telephone: _____

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 2020.

Supervisor's signature: _____ Date: _____

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What Honours Projects are Available in 2020?

| Primary Supervisor(s) | Project Title | pp |
|-----------------------|--|----|
| Aleksandra Debowski | <i>Understanding the role of two putative β-lactamase genes in conveying resistance to β-lactams in Burkholderia cenocepacia</i> | 28 |
| Aleksandra Filipovska | <i>Characterizing the pathology of cardiovascular diseases and cancer</i> | 29 |
| Aleksandra Filipovska | <i>Mitochondrial RNA-binding proteins and their role in mitochondrial gene expression</i> | 30 |
| Mark Fear | <i>An exploration of the phenotype of heterogeneous populations of scar fibroblasts</i> | 31 |
| Mark Fear | <i>The impact of matrix stiffness on scar fibroblasts</i> | 32 |
| Asha Bowen | <i>SToP trial: Step One Analysis</i> | 33 |
| Belinda Guo | <i>Using genome editing technology to characterise gene(s) that are important for driving cancer progression in haematological malignancies.</i> | 34 |
| Belinda Guo | <i>Using platelet function analysis to assess bleeding and clotting risk in myeloproliferative neoplasms</i> | 35 |
| Kathy Fuller | <i>Using automated imaging flow cytometry to characterise chromosomal abnormalities in haematopoietic stem cells: Identifying blood-based markers for predicting cancer progression for haematological malignancies.</i> | 36 |
| Kathy Fuller | <i>Imaging flow cytometry analysis of multiple myeloma: towards improving diagnostic sensitivity and minimal residual disease monitoring</i> | 37 |
| Jeff Keelan | <i>Identification of resident placental bacteria using RNAscope visualisation</i> | 38 |
| Jonathan Chee | <i>Developing preclinical models of cancer immunotherapy induced side effects</i> | 39 |
| Lynette Fernandes | <i>Improve the student learning experience within the School of Biomedical Sciences</i> | 40 |
| Mitali Sarkar-Tyson | <i>Characterising the role of cyclophilins in Burkholderia thailandensis</i> | 41 |
| Mitali Sarkar-Tyson | <i>Assessment of the role of FK-506 binding proteins in N. meningitidis</i> | 42 |
| Nathan Pavlos | <i>Characterisation of New Lysosomal Membrane Proteins in Bone-digesting Osteoclasts</i> | 43 |
| Vanessa Fear | <i>Rapid diagnosis of rare genetic diseases in paediatric patients.</i> | 44 |
| Carla Mellough | <i>Modelling Microphthalmia using induced pluripotent stem cell-derived retinal organoids</i> | 45 |

| Primary Supervisor(s) | Project Title | Pp |
|-----------------------|--|----|
| Carla Mellough | <i>Modelling severe early onset retinitis pigmentosa using human retinal organoids</i> | 46 |
| Carla Mellough | <i>Investigating the role of insulin-like growth factor during human retinal development</i> | 47 |
| Carla Mellough | <i>Developing a human RPE platform to test a novel dual AAV approach for VEGF knockdown</i> | 48 |
| Gina Ravenscroft | <i>Extending diagnosis and gene discovery for neurogenetic diseases</i> | 49 |
| Livia Carvalho | <i>Cellular and molecular characterisation of cone photoreceptor migration in normal and degenerate retinas</i> | 50 |
| Livia Carvalho | <i>Investigating the genetic and environmental factors involved in early onset myopia</i> | 51 |
| Livia Carvalho | <i>Testing a dual AAV gene therapy approach for the treatment of Usher syndrome using human retinal organoids</i> | 52 |
| Livia Carvalho | <i>Evaluating neuroprotective treatments for vision loss</i> | 53 |
| Livia Carvalho | <i>Studying cone photoreceptor cell death mechanisms in inherited retinal disorders</i> | 54 |
| Livia Carvalho | <i>Investigating the correlation of myopia susceptibility with cone opsin gene variants</i> | 55 |
| Fred Chen | <i>Modelling inherited retinal disease to evaluate aberrant splicing using induced pluripotent stem cells and retinal organoids</i> | 56 |
| Fred Chen | <i>Modelling inherited retinal disease to develop splice interventions using induced pluripotent stem cells and retinal organoids</i> | 58 |
| Mark Nicol | <i>Interactions between bacteria colonizing the airways of young children</i> | 60 |
| Amelia Harray | <i>Impact of Food on Glycaemic Control in individuals with Type 1 diabetes</i> | 61 |
| Aveni Haynes | <i>How does mode of delivery influence risk of childhood type 1 diabetes in Western Australia?</i> | 62 |
| Aveni Haynes | <i>How is maternal Vitamin D sufficiency during pregnancy associated with the risk of islet autoimmunity development in children at risk of type 1 diabetes?</i> | 63 |
| Elizabeth Davis | <i>Using continuous glucose monitoring and a carbohydrate algorithm to manage blood glucose levels during exercise in adolescents with type 1 diabetes</i> | 64 |
| Paul Fournier | <i>Effect of hypoxia typical of high altitude on the accuracy of continuous glucose monitors and its impact on blood glucose management in individuals with type 1 diabetes mellitus</i> | 65 |

| Primary Supervisor(s) | Project Title | Pp |
|-----------------------|---|----|
| Paul Fournier | <i>Is the recommendation to decrease basal insulin dose pre-exercise conducive to severe hyperglycaemia during and after exercise?</i> | 66 |
| Paul Fournier | <i>Effect of swimming and head-out water immersion in cold water on the risk of hypoglycaemia in type 1 diabetes</i> | 67 |
| Paul Fournier | <i>Effect of high blood glucose levels on executive function, attention and driving performance on a driving simulator in people with type 1 diabetes</i> | 68 |
| Jenette Creaney | <i>Biological activity of mesothelin in malignant mesothelioma</i> | 69 |
| Kate Hammer | <i>Effects of extraction, processing and storage on the antimicrobial activity of Western Australian honeys</i> | 70 |
| Steven Mutsaers | <i>TILs and TAMs; therapeutically targeting cellular communication in lung cancer</i> | 71 |
| Steven Mutsaers | <i>The role of PD-1/PD-L1 in pulmonary fibrosis</i> | 72 |
| Steven Mutsaers | <i>Transfer RNA-derived fragments in malignant mesothelioma</i> | 73 |
| Cecilia Prele | <i>Modelling and regulating extracellular matrix deposition by inner ear cells</i> | 74 |
| Rhonda Taylor | <i>Investigating novel therapies for neurogenetic diseases</i> | 75 |
| Yuben Moodley | <i>Mechanism of anti-fibrotic treatments in slowing the progression of Idiopathic Pulmonary fibrosis (IPF)</i> | 76 |
| Charlene Kahler | <i>Cationic antimicrobial peptide hetero-resistance in commensal Neisseria species</i> | 78 |
| Charlene Kahler | <i>Examining the role of EptA in the colistin resistance in Neisseria gonorrhoeae.</i> | 80 |
| Charlene Kahler | <i>Polymyxin hetero-resistance in commensal Neisseria species</i> | 81 |
| Phil Burcham | <i>Testing the "Carbonyl Stress" Concept</i> | 83 |
| Peter Henry | <i>Exploring pharmacological approaches to inhibit mucus hypersecretion using ex vivo and in vivo murine models of airways disease</i> | 85 |
| Fiona Pixley | <i>Exploring the role of genes upregulated by CSF-1 during macrophage differentiation</i> | 86 |
| Fiona Pixley | <i>Examining the efficacy of a macrophage targeting drug in a mouse model of melanoma</i> | 87 |

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Dr Aleksandra Debowski (93463854, aleksandra.debowski@uwa.edu.au)
Marshall Centre for Infectious Disease Research and Training,
Room 2. 10, SBMS, L Block, QEII Medical Centre

School of Biomedical Sciences Coordinating supervisor

Same as primary? No

If No: Dr Mitali Sarkar-Tyson (93464872, mitali.sarkar-tyson@uwa.edu.au)
Marshall Centre for Infectious Disease Research and Training

| Other supervisor/s if any | Phone number, email address and location |
|---------------------------|--|
| 1. | Ms Clare Moran (clare.moran@research.uwa.edu.au) Marshall Centre for Infectious Disease Research and Training |
| 2. | A/ Prof Keith Stubbs, (6488 4479, keith.stubbs@uwa.edu.au) School of Molecular Sciences, Bayliss Building |

Project title **Understanding the role of two putative β -lactamase genes in conveying resistance to β -lactams in *Burkholderia cenocepacia*.**

Project location: Marshall Centre for Infectious Disease Research and Training,
Room 2. 10, SBMS, L Block, QEII Medical Centre

Project description

Several bacterial species within the *Burkholderia cepacia* complex (Bcc), including *Burkholderia cenocepacia*, *B. cepacia* and *B. multivorans*, are important opportunistic pathogens. These bacteria are widely distributed in the natural environment and have the capacity to cause severe lung infections in cystic fibrosis (CF) patients and infections in immunocompromised individuals. It is very difficult to treat Bcc infections as these organisms are naturally resistant to many different classes of antibiotics.

Cephalosporins are currently still effective for treating infections, however many Bcc species express various β -lactamases, like AmpC and PenB, which are capable of inactivating cephalosporins. AmpC and PenB have been characterised in *B. cenocepacia* and their expression has been linked to the peptidoglycan recycling pathway. However, a recent study involving whole genome sequencing of *B. cenocepacia* strain J2315 has revealed that this species in fact harbours four β -lactamase genes in its genome: *ampC*, *penB* and two putative Class A β -lactamases. The substrate specificity and the role of these two putative β -lactamases in conferring resistance to β -lactams is unknown.

The aim of this work is to generate Bcc mutants and to use heterologous gene expression to elucidate the role of these enzymes in conferring resistance to β -lactams in *B. cenocepacia*. This work will lead to a better understanding of the antibiotic resistance mechanisms employed by Bcc species and will help set the foundation toward identifying new therapeutic approaches for these infections.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Aleksandra Filipovska
6151 0736, aleksandra.filipovska@uwa.edu.au and Harry Perkins Institute of
Medical Research

Pharmacology Coordinating supervisor **Same as primary? Yes X No _____**

If No: Name Phone number, email address and location

Other supervisor/s Phone number, email address and location

Project title

Characterizing the pathology of cardiovascular diseases and cancer

Project location:

Harry Perkins Institute of Medical Research

Project description

Mitochondrial dysfunction plays a major role in the onset and progression of heart diseases as well as cancer. We have identified mutations in genes that code for mitochondrial proteins that can cause heart disease or cancer as a result of impaired gene expression and compromised energy metabolism.

We have established several animal models of cardiomyopathy and cancer and we use tissues from these mice to investigate the effects of mitochondrial dysfunction in heart and tumour formation. Furthermore we are investigating how specific proteins regulate gene expression and how lack of these genes can cause the disease pathologies in each of these diseases. This work is of great importance because it will elucidate the molecular mechanisms underlying the most common diseases that cause mortality in humans and provide new avenues for therapeutic interventions.

The project will use a variety of techniques ranging from immunohistochemistry, molecular and cell biology, biochemistry, transcriptomics, animal handling and physiology.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Aleksandra Filipovska
6151 0736, aleksandra.filipovska@uwa.edu.au and Harry Perkins Institute of
Medical Research

Pharmacology Coordinating supervisor **Same as primary? Yes_X_ No_____**
If No: Name Phone number, email address and location

Other supervisor/s Phone number, email address and location

Project title
Mitochondrial RNA-binding proteins and their role in mitochondrial gene expression

Project location:
Harry Perkins Institute of Medical Research

Project description

Mitochondria play a fundamental role in cell and energy metabolism and consequently mitochondrial dysfunction can lead to severe multi-system disorders with wide range of clinical presentations that commonly include neurodegeneration, muscle defects and exercise intolerance. To understand these conditions better and identify therapeutic targets it is necessary to understand how gene expression is regulated within mitochondria, as some of the most significant gaps in our knowledge of mitochondrial function and disease are in the regulation of mitochondrial gene expression. Links between transcription and translation in mammalian mitochondria are not well understood.

Mitochondrial mRNAs are transcribed as part of long primary transcripts that generally encompass the entire mtDNA, therefore the ratios of the 13 mammalian mitochondrial mRNAs and their proteins are controlled post-transcriptionally. Little is known about how these 13 mRNAs are regulated in mammalian mitochondria. This is particularly important since tissue-, cell- and disease-specific variations in expression of the 13 different mtRNAs has been observed, but cannot be explained at present. The basic components and mechanisms of transcription have recently been discovered, however the control of mRNA processing, translation and stability remains unclear.

We are interested in identifying mammalian mitochondrial RNA-binding proteins and investigating their role in RNA metabolism in cells. Discovery of proteins and the RNAs they bind may shed light on the regulation of gene expression in mammalian mitochondria. In addition, we are developing new methods for the identification of mitochondrial RNAs bound by the mitochondrial RNA-binding proteins that may regulate their expression in health and in disease.

This project involves the use of a range of techniques in cell biology (such as cell culture, cell death assays, fluorescence microscopy, gel electrophoresis, western blotting), genomics (RNA sequencing), molecular biology (cloning, quantitative PCR) and biochemistry (protein purification, enzyme activity measurements).

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor: Dr. Mark Fear

Phone number, email address and location: 6488 8133, mark@fionawoodfoundation.com, Burn Injury Research Office, First Floor, CTEC, UWA main campus

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes No

If No: Name

Phone number, email address and location

Other supervisor/s if any

Phone number, email address and location

1. Dr. Andrew Stevenson, andrew@uwa.edu.au, Curnow Building, UWA
2. Prof Fiona Wood, Fiona.wood@health.wa.gov, Fiona Stanley Hospital

Project title

An exploration of the phenotype of heterogeneous populations of scar fibroblasts

Project location:

Curnow Building, UWA main campus

Project description

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 heterogeneity of scar cells. Although they are the main cell type that produces scar tissue during wound healing, dermal fibroblasts have been poorly characterised until recently and were once thought to be relatively homogenous. Work by our group and other groups have explored fibroblast heterogeneity using single cell RNA-seq, which sequences RNA from individual cells, differentiating identical looking cells into functionally distinct clusters based on their transcriptome, confirming that different populations have different function and contributions to the wound healing process in the skin. Although confirmed in by immunofluorescence in tissue, there has been no functional analysis of these subtypes. This project will focus on establishing the functional roles of the distinct subtypes identified. Fluorescence Activated Cell Sorting (FACS) will be carried out to sort these cells into separate populations, and a battery of phenotypic assays will be carried out on the subpopulations to examine properties such as collagen and ECM production, proliferation, cellular migration and ECM contraction. These experiments will determine whether truly distinct fibroblast phenotypes exist, their potential roles in scarring and fibrosis and the ability of subsets of fibroblasts to respond to environmental stimuli. The student will be integrated in a team of researchers from a variety of fields such as chemistry, molecular biology and medical practitioners.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor: Dr. Mark Fear

Phone number, email address and location: 6488 8133, mark@fionawoodfoundation.com, Burn Injury Research Office, First Floor, CTEC, UWA main campus

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes No

If No: Name

Phone number, email address and location

Other supervisor/s if any

Phone number, email address and location

1. Dr. Andrew Stevenson, andrew@uwa.edu.au, Curnow Building, UWA
2. Dr. Yu Suk Choi, yusuk.choi@uwa.edu.au, Anatomy Building, UWA
3. Prof Fiona Wood, Fiona.wood@health.wa.gov, Fiona Stanley Hospital

Project title

The impact of matrix stiffness on scar fibroblasts

Project location:

Curnow Building, UWA main campus

Project description

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 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 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.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
Dr Belinda Guo 64572744, belinda.guo@uwa.edu.au, M Block QEII

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes

Other supervisor/s if any Phone number, email address and location

1. A/Prof Kathy Fuller, 64573192, kathy.fuller@uwa.edu.au M block, QEII
2. A/Prof Matthew Linden, matthew.linden@uwa.edu.au M Block, QEII
3. Prof Wendy Erber, wendy.erber@uwa.edu.au M block, QEII

Project title

Using genome editing technology to characterise gene(s) that are important for driving cancer progression in haematological malignancies.

Project location:

Translational Cancer Pathology Laboratory, UWA, 1st Floor, M block, QEII Medical Centre

Project description

In this project, we will be using gene editing technology (CRISPR-Cas9) to assess the role of specific gene(s) in driving cancer progression in a group of haematological malignancies called myeloproliferative neoplasms (MPN). MPN are bone marrow cancers which lead to overproduction of blood cells. Each patient has up to 20% risk of progressing to a life-threatening stage of the cancer, where their bone marrow becomes scarred (fibrosis) and begins to fail (unable to produce new blood cells).

The pathological mechanisms underlying fibrotic progression in MPN are not understood, although megakaryocytes (large cells in the bone marrow) have been implicated in driving this process. Megakaryocytes are derived from CD34-positive haematopoietic stem cells and have features which are associated with fibrotic progression: dysregulated megakaryopoiesis resulting in distinct morphological changes, defective apoptotic machinery and aberrant release of pro-fibrogenic factors. We have previously identified mutations and transcriptomic changes in patients which are associated with the presence of bone marrow fibrosis. We hypothesise that these changes are responsible for driving fibrotic progression. In this project, we will use CRISPR-Cas9 technology to delete the gene(s) in haematopoietic stem cells in a megakaryocyte cell culture model and use imaging flow cytometry to characterise the changes in cell morphology and phenotype. This will allow us to determine whether loss of the gene(s) recapitulates the disease phenotype and identify potential new targets for therapeutic intervention.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
Dr Belinda Guo 64572744, belinda.guo@uwa.edu.au, M Block QEII

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes

Other supervisor/s if any Phone number, email address and location

1. A/Prof Matthew Linden, matthew.linden@uwa.edu.au M Block QEII
2. A/Prof Kathy Fuller, 64573192, kathy.fuller@uwa.edu.au M block, QEII
3. Prof Wendy Erber, wendy.erber@uwa.edu.au M block, QEII

Project title

Using platelet function analysis to assess bleeding and clotting risk in myeloproliferative neoplasms

Project location:

Translational Cancer Pathology Laboratory, UWA, 1st Floor, M block, QEII Medical Centre

Project description

In this project, we will characterise the function and protein expression profile of platelets from patients with myeloproliferative neoplasms (MPN) using a range of techniques, including whole blood flow cytometry, mass spectrometry, and Western blotting. MPN are bone marrow cancers which lead to overproduction of blood cells. Each patient has up to 20% risk of progressing to a life-threatening stage of the cancer, where their bone marrow becomes scarred (fibrosis) and begins to fail (unable to produce new blood cells). Approximately 40% of MPN patients suffer from blood clotting complications which is associated with significant morbidity (e.g. heart attack; stroke) and mortality. Little is known of the mechanisms which drive this risk. Our preliminary data shows that platelets from MPN patients with bone marrow fibrosis do not behave normally in response to signals. We hypothesise that this is responsible for the bleeding and clotting complications seen in patients. Understanding the platelet dysfunction in MPN could help improve treatment approaches for management of this risk in patients.

In this project, we will collect blood samples from prospectively recruited patients and analyse the platelets. Platelet function will be analysed by flow cytometry for a range of markers in response to stimulation with canonical platelet agonists. Platelets will also be isolated for platelet proteome analysis. These results will be correlated with clinico-pathological features to characterise how platelet dysfunction is related to bleeding and clotting risk in myeloproliferative neoplasms.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
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School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes

Other supervisor/s if any Phone number, email address and location

1. Dr Belinda Guo, 64572744, belinda.guo@uwa.edu.au, M Block QEII
2. Dr Henry Hui henry.hui@uwa.edu.au M block, QEII
3. Prof Wendy Erber, wendy.erber@uwa.edu.au M block, QEII

Project title

Using automated imaging flow cytometry to characterise chromosomal abnormalities in haematopoietic stem cells: Identifying blood-based markers for predicting cancer progression for haematological malignancies.

Project location:

Translational Cancer Pathology Laboratory, UWA, 1st Floor, M block, QEII Medical Centre

Project description

In this project, we will be using imaging flow cytometry (IFC) to detect chromosomal abnormalities and assess the potential of this approach as a blood test for predicting cancer progression. We will focus on a group of haematological malignancies called myeloproliferative neoplasms (MPN). These are bone marrow cancers which lead to overproduction of blood cells, including platelets. Each patient has up to 20% risk of progressing to a life-threatening stage of the cancer, either through development of bone marrow fibrosis (scarring) or leukaemic transformation to acute myeloid leukaemia. Treatment options are very limited once patients have progressed, and the current detection methods require sampling of the bone marrow, which is an invasive test and not acceptable for regular monitoring. Our aim is therefore to identify novel biomarkers for cancer progression in the blood which can be used as indicators or predictors to monitor a patient's risk of progressing.

IFC is a high-throughput instrument that uses the principles of standard flow cytometry with the addition of digital microscopy and extended depth of field capability. In the Translational Cancer Pathology Laboratory we have developed the Eureka Award winning "immuno-flowFISH" method to identify chromosomes in whole cells in suspension identified by their phenotype. We hypothesise that our immuno-flowFISH method will increase the sensitivity of detecting chromosomal abnormalities in haematopoietic stem cells, leading to improvements in risk stratifying patients at diagnosis and monitoring disease progression.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
A/Prof Kathy Fuller 64573192 / 0416085960 kathy.fuller@uwa.edu.au M block, QEII

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes

Other supervisor/s if any Phone number, email address and location

1. Dr Henry Hui henry.hui@uwa.edu.au M block, QEII
2. Prof Wendy Erber wendy.erber@uwa.edu.au M block, QEII

Project title

Imaging flow cytometry analysis of multiple myeloma: towards improving diagnostic sensitivity and minimal residual disease monitoring

Project location:

Translational Cancer Pathology Laboratory, UWA, 1st Floor, M block, QEII Medical Centre

Project description

Multiple myeloma is a plasma cell neoplasm characterised by genetic instability leading to a multitude of abnormalities such as chromosomal deletions, duplications and translocations. Cytogenetic abnormalities present at diagnosis have been established as powerful prognostic tools, leading to the ability to risk stratify patients into high, intermediate and standard risk categories. High risk myeloma patients demonstrating either 17p deletion, t(14;16) or t(14;20) have a median overall survival of 2-3 years as opposed to standard risk patients whose median overall survival currently stands at 6-7 years. The current established methods of cytogenetic analysis are conventional karyotyping and interphase fluorescence in situ hybridisation (FISH). Conventional karyotyping is successful in identifying abnormalities in only 30-40% of cases primarily as a consequence of the low proliferation rate of plasma cells. Interphase FISH is currently the most utilised method to assess cytogenetic changes in myeloma however most laboratories analyse only 100-200 plasma cells. The analysis is time consuming, requires significant technical expertise and is low in sensitivity.

Imaging flow cytometry (IFC) is a high-throughput instrument that uses the principles of standard flow cytometry with the addition of digital microscopy and extended depth of field capability. In the Translational Cancer Pathology Laboratory we have developed the Eureka Award winning "immuno-flowFISH" method to identify chromosomes in whole cells in suspension identified by their phenotype. We hypothesise that our immuno-flowFISH method will increase the sensitivity of detecting chromosomal abnormalities in multiple myeloma, leading to improvements in risk stratifying patients at diagnosis and assessing minimal residual disease. In this project we will assess the ability of immuno-flowFISH to detect chromosomal abnormalities in multiple myeloma bone marrow and blood samples and determine the sensitivity of detection.

School of Biomedical Sciences

Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
Jeffrey Keelan 6458 1889 Jeff.keelan@uwa.edu.au QEIIMC and KEMH

School of Biomedical Sciences Coordinating supervisor: **Jeffrey Keelan**

Project title
Identification of resident placental bacteria using RNAscope visualisation

Project location:
King Edward Memorial Hospital and QEII Medical Centre, School of Biomedical Sciences

Project description:

The reported existence of a placental microbiome has provoked enormous controversy in the obstetric research community. This year, four high profile publications have appeared which have polarised the debate even further, with two claiming to have proven the existence of low-abundance bacteria in normal healthy placentas and two concluding that the placenta is normally sterile. The controversy has focussed around the impact of external contamination, the difficulty in distinguishing between live cells and remnant DNA, and the immunological consequence of placental bacterial exposure on the fetus and its health and development after birth. In this one-year project we will use a highly-sensitive technique (RNAscope) to visualise metabolically-active bacteria within placental tissue and assess cellular immunological responses. We will use tissues from the WA Pregnancy Biobank for this study, including both the villous placenta and the extraplacental membranes (amnion, chorion and decidua). By visualising bacterial and human gene expression *in situ* we will be able to confirm the viability status of the bacteria and their impact on the host cells. We will study both normal term placentas and preterm placentas likely to be infected (chorioamnionitis) to validate the clinical relevance of the findings.

Aims:

1. Establish highly-sensitive in-situ hybridisation assays, using the RNAscope system, capable of detecting both bacterial and human genes in PFA fixed placental sections from the WA Pregnancy Biobank
2. Employ RNAscope to visualise the presence and cellular location of bacteria in human placentas from both term and preterm placentas
3. Correlate bacterial presence with inflammatory gene expression and histopathological inflammation score

Techniques:

- a) In situ hybridization visualisation of bacterial and placental gene expression using the proprietary method known as RNAscope, combined with super-resolution fluorescence microscopy (CMCA)
- b) Tissue histology and scoring of inflammation according to standard clinical criteria
- c) Statistical correlation analysis of gene expression, histological inflammation and the presence and abundance of bacteria

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Dr Jonathan Chee

jonathan.chee@uwa.edu.au

Location: 5th floor, Perkins Institute

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes

Other supervisor/s if any Phone number, email address and location

- 1.
- 2.

Project title

Developing preclinical models of cancer immunotherapy induced side effects

Project location:

Perkins Institute

Project Description:

Cancer immunotherapy such as blocking checkpoint inhibitors remove negative regulators of immune cells, unleashing them to target and kill cancer cells. However, unwanted side effects are collateral tissue damage caused by the immune system, which are termed immune related adverse events (IRAE). IRAE can affect different tissues and organs, and their immunopathology can be highly similar to some autoimmune diseases. Approximately 80% of treated patients develop some form of IRAE, and they vary in severity. In rare instances, they can be life changing or threatening. Understanding why IRAEs develop is important for the improvement of cancer immunotherapy, and will likely inform the aetiology of autoimmune diseases.

There is currently a lack of preclinical models to study both IRAE and tumour responses induced by immunotherapy. In this project we assess if checkpoint blockade immunotherapy induces autoimmune pathology in different mouse models, and if it associates with tumour responses to therapy. This project involves animal work, immunohistochemistry and basic immunology techniques such as flow cytometry.

Aim 1. To characterise immunopathology of tissues (heart, pancreas, colon, thyroid glands), and serum markers of autoimmunity induced by checkpoint blockade immunotherapy in different mouse models.

- BALB/c
- BALB/c x NOD F1
- BALBc.Foxp3DTR

Aim 2. To determine if tumour responses to cancer immunotherapy correlate with the severity of immunopathology in tissues.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

| | |
|----------------------|--|
| Primary supervisor | Phone number, email address and location |
| Dr Lynette Fernandes | 6457 4517, Lynette.Fernandes@uwa.edu.au , Room 1.33a, M Block, QEII Medical Centre |

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes No

If No: Name Phone number, email address and location

Other supervisor/s if any Phone number, email address and location

1. Dr Demelza Ireland 6457 2262 Demelza.Ireland@uwa.edu.au, Room 1.4G, M Block, QEII MC
2. Dr Ricky Chen 6457 4247, Ricky.Chen@uwa.edu.au, Room 1.27b, M Block, QEII MC
3. Dr Sonia Fernandez 6457 4657, Sonia.Fernandez@uwa.edu.au, Room 1.4E, M Block, QEII MC

Project title

Improve the student learning experience within the School of Biomedical Sciences

Project location:

M Block, QEII MC, School of Biomedical Sciences

Project description

This project will appeal to students with a passion for biomedical sciences education. Students will be invited to meet with and talk about their ideas to improve student learning in the School of Biomedical Sciences. Projects might include, but not be restricted to, creation of an online tool or resource, surveys of students and/or staff to determine their perceptions, development of a new “wet lab”, ePractical or learning activity for a unit within the School of Biomedical Sciences.

As such, students will be empowered to take real ownership of their project to improve the student learning experience for future biomedical science students.

Depending on the choice of project, supervisors may be selected from those listed above.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor

Dr Mitali Sarkar-Tyson; mitali.sarkar-tyson@uwa.edu.au, Marshall Centre for Infectious Diseases Research and Training, School of Biomedical Sciences, 2nd Floor L Block, QEII Medical Centre

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes X ____ No ____

If No:

Other supervisor/s if any Phone number, email address and location

Ms Nicole Bzdyl; nicole.bzdyl@research.uwa.edu.au, Marshall Centre for Infectious Disease Research and Training, L Block, QEII

Project title

Characterising the role of cyclophilins in *Burkholderia thailandensis*

Project location:

Marshall Centre for Infectious Diseases Research and Training, School of Biomedical Sciences, 2nd Floor L Block, QEII Medical Centre

Project description

Burkholderia pseudomallei is the causative agent of melioidosis, a disease endemic in South-East Asia and northern Australia. Mortality rates in these areas are high even with antimicrobial treatment, and there are few options for effective therapy. Therefore, there is a requirement to identify anti-bacterial targets for the development of novel treatments.

Cyclophilins are a class of enzymes which possess peptidyl-prolyl *cis-trans* isomerase activity which speeds up the rate of protein folding within the cell. We have recently shown that a cyclophilin from *B. pseudomallei*, *ppiB*, is important for maintaining proteome homeostasis and deletion of *ppiB* ultimately leads to *B. pseudomallei* being unable to cause infection in mice (Bzdyl et al. 2019).

Due to the hazards of working with *B. pseudomallei*, the closely related organism *Burkholderia thailandensis* is often used as a model to understand *B. pseudomallei* infection. The aim of this project would be to construct cyclophilin mutants in *B. thailandensis* and characterise their role in *in vitro* virulence and persistence in human cell lines. Determination of intracellular folding partners can be done by reinsertion of a tagged-cyclophilin protein and pull-down studies can be used to identify proteins which are being interacted with, allowing us to be one step closer to knowing precisely what cyclophilins are folding within a bacterial cell.

Reference: Bzdyl NM, Scott NE, Norville IH, Scott AE, Atkins T, Pang S, Sarovich DS, Coombs G, Inglis TJ, Kahler CM, Sarkar-Tyson M. Peptidyl-prolyl isomerase, *ppiB*, is essential for proteome homeostasis and virulence in *Burkholderia pseudomallei*. *Infection and immunity*. 2019 Jul 22;IAI-00528.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location

Dr Mitali Sarkar-Tyson, mitali.sarkar-tyson@uwa.edu.au, Marshall Centre for Infectious Disease Research and Training, L Block, QEII

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes X ____ No

If No:

Other supervisor/s if any Phone number, email address and location

1. Emily Kibble, emilyalice.kibble@murdoch.edu.au, Marshall Centre for Infectious Disease Research and Training, L Block, QEII
2. Associate Professor Dr Charlene Kahler, charlene.kahler@uwa.edu.au, Marshall Centre for Infectious Disease Research and Training, L Block, QEII

Project title

Assessment of the role of FK-506 binding proteins in *N. meningitidis*.

Project location:

Marshall Centre for Infectious Disease and Training, L Block, QEII

Project description

Neisseria meningitidis is the bacterial causative agent of invasive meningococcal disease (IMD). While *N. meningitidis* is carried asymptotically by 10% of the adult human population, pathogenic strains can invade through the nasopharyngeal mucosa, causing meningococcal meningitis and sepsis. In order to cause infection, *N. meningitidis* encodes for a wide range of virulence factors. Of particular interest are enzymes involved in protein-folding pathways. The PPlase protein superfamily catalyse the *cis-trans* isomerisation of peptide bonds to proline residues, which is known to be a rate-limiting reaction in the process of bacterial protein folding. This superfamily includes three subsets: the cyclophilins, the parvulins, and the FK-506 binding proteins (FKBPs). Within the FKBP family, proteins SlyD and Trigger Factor are believed to be involved in the virulence of pathogenic bacteria. While some knowledge exists, the role of these proteins in the pathogenesis of *N. meningitidis* is yet to be elucidated.

This project will involve the creation and characterisation of mutant strains of *N. meningitidis*. This project will incorporate molecular biology techniques such as DNA cloning and manipulation, advanced microbiology and genetic manipulation, and tissue culture and cell infection models to meet these aims.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
A/Prof Nathan Pavlos 6457-2085 nathan.pavlos@uwa.edu.au
Bone Biology & Disease Laboratory, Rm 2.36 2nd Floor M Block, School of Biomedical Sciences

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes

If No: Name Phone number, email address and location

Other supervisor/s if any Phone number, email address and location
Dr Pei Ying Ng 6457-2085 peiying.ng@uwa.edu.au
Bone Biology & Disease Laboratory, Rm 2.36 2nd Floor M Block,
School of Biomedical Sciences

Project title
Characterisation of New Lysosomal Membrane Proteins in Bone-digesting Osteoclasts

Project location:
Bone Biology & Disease Laboratory, Rm 2.36 2nd Floor M Block, School of Biomedical Sciences

Project description

Osteoclasts are giant multinucleated cells exclusively responsible for the physiological digestion (resorption) of bone. Excessive osteoclast formation and activation is a hallmark of metabolic bone diseases like osteoporosis and localised tumour-mediated bone lysis. Osteoclasts resorb bone via a specialised lysosome-related organelle called the ruffled border. The ruffled border is formed upon the fusion of 'secretory lysosomes' with the bone-apposed plasma membrane. Fusion of secretory lysosomes with the ruffled border releases osteolytic enzymes (e.g. cathepsin k) into the underlying resorptive space. At the same time, it equips the ruffled border with sets of lysosomal membrane proteins that are essential for bone resorptive function. Despite its crucial importance, our understanding of the molecular anatomy of the ruffled border and its secretory lysosomal progenitors remains limited. In particular, we still lack elementary information on the protein composition of the ruffled border, including the numbers and identities of lysosomal membrane residents that collectively participate in bone resorption. To extend the molecular inventory of lysosomal membrane proteins operating at the ruffled border, we have recently combined biochemical isolation methods with high-resolution tandem mass spectrometry (LC-MS/MS) to unbiasedly survey the osteoclast lysosomal membrane proteome. Using this approach, we identified several candidate lysosomal membrane proteins whose involvement in osteoclast function and bone homeostasis remain to be ascribed.

Aim: The major goal of this project is to characterise the expression, localisation and function of newly identified lysosomal membrane proteins in osteoclasts and other surrogate cell models (e.g. RAW 264.7 cells and HEK293 cells).

Methods: Students will become familiar with qPCR, immunoblotting, biochemical isolation methods, cell culture, live cell confocal microscopy and gene interfering technologies (siRNA, CRISPR-Cas9 etc)..

School of Biomedical Sciences

Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
Dr Vanessa Fear 63191022 vanessa.fear@telethonkids.org.au Telethon Kids Institute

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes ___ No **X**

Dr Joost Lesterhuis willem.lesterhuis@uwa.edu.au

Other supervisor/s if any Phone number, email address and location
1. Dr Genevieve Syn. Genevieve.syn@telethonkids.org.au

Project title

Rapid diagnosis of rare genetic diseases in paediatric patients.

Project location:

Telethon Kids Institute

Project description

Rare diseases collectively affect more than 190,000 Western Australians, including 63,000 paediatric patients, and accordingly have been identified as a public health priority. Around 80% of all rare diseases have a genetic basis. The advent of Next Generation Sequencing has allowed high speed, affordable sequencing, with Whole Exome Sequencing (WES) now implemented in WA as the diagnostic method of choice for rare diseases. However, diagnosing a child with a rare disease requires that the genetic variant has previously been functionally characterised, validated and reported. This means that many children with rare diseases present with previously unseen single nucleotide variants (SNVs) that are of uncertain significance. Even in cases where the new mutation is localised to a region known to be important to gene function, providing the patient with a diagnosis requires validation of the effects of the new variant. This means that many patients and their families endure months or even years of not knowing the cause and best treatment for their disease, with the psychological burden this entails.

CRISPR technology provides a new way to rapidly validate the effects of rare variants found in patients. This project will use CRISPR homology directed repair, with click chemistry, and CRISPR base editing to mutate human inducible pluripotent stem cells (iPSCs) with the SNV of interest. The impact of these SNVs on relevant mesoderm, endoderm, ectoderm differentiation pathways in iPSCs will then be investigated using RNAseq, flow cytometry and protein analysis.

This project will contribute to our genetic and rare disease studies that aim to reduce the time to paediatric patient diagnosis. This is highly valuable as an early, accurate diagnosis may alleviate disease progression, reduce complications and co-morbidities, and improve patient quality of life.

School of Biomedical Sciences

Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
Dr Carla Mellough +61 8 9381 0799, CarlaMellough@lei.org.au

This project is available at the LEI Research Laboratories (based at Perkins, QQ Block, QEII), Nedlands, Perth WA.

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes ___ No x ___

If No: Prof Mathew Martin-Iverson: (m) +61 4 14186393 (mobile); (Office) +61 8 6457 2982; mathew.martin-iverson@uwa.edu.au; 1.41, M Block, QE II Medical Centre, Nedlands, 6009.

Other supervisor/s if any Phone number, email address and location

1. Dr Samuel McLenachan; SamuelMcLenachan@lei.org.au; LEI
 2. Dr Fred Kanfau Chen; fredchen@lei.org.au; LEI
-

Project title

Modelling Microphthalmia using induced pluripotent stem cell-derived retinal organoids

Project location:

LEI Research Laboratories (based at Perkins, QQ Block, QEII), Nedlands, Perth WA.

Project description:

Microphthalmia is a developmental disorder of the eye where one or both of the eyes are abnormally small or have anatomic malformations. Chromosomal, monogenic and environmental causes of microphthalmia have been identified. Of monogenic causes, only SOX2 has been identified as a major causative gene. Other linked genes include PAX6, OTX2, CHX10 and RAX. OTX2, CHX10 and RAX have retinal expression and may result in microphthalmia through failure of retinal differentiation, but the underlying pathophysiological mechanisms remain unknown. Three-dimensional miniature versions of the human retina, called retinal organoids, can be made from iPSCs and studied entirely in the laboratory. In this project, the student will utilise iPSCs generated from a patient harbouring a mutation in the OTX2 gene to generate a personalised in vitro model of microphthalmia. Patient and unaffected control iPSC lines will be differentiated into retinal tissue to elucidate the consequences of this mutation on human retinal development and function, and identify potential therapeutic targets.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
Dr Carla Mellough +61 8 9381 0799, CarlaMellough@lei.org.au

School of Biomedical Sciences Coordinating supervisor

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Other supervisor/s if any Phone number, email address and location

1. Dr Samuel McLenachan; SamuelMcLenachan@lei.org.au; LEI
2. Dr Fred Kanfau Chen; fredchen@lei.org.au; LEI

Project title

Modelling severe early onset retinitis pigmentosa using human retinal organoids

Project location:

LEI Research Laboratories (based at Perkins, QQ Block, QEII), Nedlands, Perth WA.

Project description:

Retinitis Pigmentosa (RP) is a hereditary retinal disease which afflicts 1 in 3000 Australians and causes the progressive loss of the rod and cone photoreceptor cells. SNRNP200, linked to Retinitis Pigmentosa type 33 (RP33), is a gene which encodes for a component of the spliceosome. The spliceosome is a complex molecular machine which edits the genetic sequences that are translated into proteins. By removing introns (intervening sequences in the genetic code) and 'splicing' together exons (expressed sequences), a single gene can encode for multiple proteins depending on which exons are included/excluded from the final processed messenger RNA. It remains unknown how mutations in the SNRNP200 gene cause the pathophysiology seen in the retina. In this project, the student will utilise iPSCs generated from a young patient with severe early-onset RP33. The patient was found to have compound heterozygous SNRNP200 mutations, which is thought to be a first case report of autosomal recessive RP. Using patient and unaffected control iPSC lines, the student will generate retinal organoids to elucidate the effects of this mutation on retinal development and function and evaluate potential therapeutic approaches in this personalised in vitro model of RP33.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
Dr Carla Mellough +61 8 9381 0799, CarlaMellough@lei.org.au

School of Biomedical Sciences Coordinating supervisor

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Other supervisor/s if any Phone number, email address and location

1. Prof. Alan Harvey; alan.harvey@uwa.edu.au; ANHB, UWA
 2. Dr Livia Carvalho; LiviaCarvalho@lei.org.au; LEI
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Project title

Investigating the role of insulin-like growth factor during human retinal development

Project location:

LEI Research Laboratories (based at Perkins, QQ Block, QEII), Nedlands, Perth WA.

Project description: Insulin-like growth factor 1 (IGF-1) is a primary mediator of the effects of growth hormone, meaning that it has growth-promoting effects on almost every cell in the body. IGF-1 also plays an important role in eye formation during development, and high expression of the IGF-1 receptor (IGF-1R) has been identified in the developing outer nuclear layer of the retina where the light-sensitive photoreceptor cells reside. The mechanisms underlying the action of IGF-1 in the retina, however, remain unknown. In this project, the student will investigate the role of IGF-1 during human retinal development by generating retinal organoids derived from control human embryonic stem cells (hESCs) and iPSC lines already available in-house. By transducing human retinal organoids during defined stages of development with adeno-associated vector 9 (AAV9) expressing IGF-1, the effects of IGF-1 expression on retinal development and histogenesis can be examined and potential actions of IGF-1 uncovered.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
Dr Carla Mellough +61 8 9381 0799, CarlaMellough@lei.org.au

School of Biomedical Sciences Coordinating supervisor

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Other supervisor/s if any Phone number, email address and location

1. Dr Livia Carvalho; LiviaCarvalho@lei.org.au; LEI
2. Prof. Ian Constable; ian.constable@lei.org.au; LEI

Project title

Developing a human RPE platform to test a novel dual AAV approach for VEGF knockdown

Project location:

LEI Research Laboratories (based at Perkins, QQ Block, QEII), Nedlands, Perth WA.

Project description: Wet age-related macular degeneration (AMD) causes a rapid loss of vision and is currently treated with frequent intensive and intrusive injections of drugs into the eye that limit the activity of the rogue protein responsible for causing the disease. Although monthly injections preserve and, in some cases, restore vision, it is a burden to the patient and the healthcare system. A long-term, single-administration of a safe therapeutic gene that would produce a natural inhibitor of the rogue protein was trialled at the LEI (led by Profs. Rakoczy and Constable) and showed very promising results. Data from the clinical trial, however, showed that not all patients respond to this therapeutic approach. The development of an approach which could circumvent the short term activity and repetitive intravitreal delivery of current therapeutic agents would be highly beneficial. In this project, the student will develop a human VEGF-upregulated retinal pigmented epithelial (RPE) platform that will be characterised and used to test the efficiency of a novel dual AAV approach for VEGF knockdown. This approach allows the investigation of VEGF expression levels and testing of advanced constructs on human tissue in real time, giving this platform important industrial, pharmaceutical and clinical relevance.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor

Phone number, email address and location

Dr Gina Ravenscroft, gina.ravenscroft@uwa.edu.au, 6151 0740, Harry Perkins Institute of Medical Research and CMR/HMS

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes ___ No X

If No: Name

Phone number, email address and location

Prof Nigel Laing, nigel.laing@uwa.edu.au, Harry Perkins Institute of Medical Research and CMR/HMS

Project title

Extending diagnosis and gene discovery for neurogenetic diseases

Project location:

Harry Perkins Institute of Medical Research, QE II Medical Centre

Project description: The Laing laboratory has a strong track record of gene discovery for neurogenetic diseases. An accurate genetic diagnosis is the crucial step for the affected individual and their families and allows for gold standard clinical management in line with their disease, inclusion in clinical trials where available and networking with other families with the same rare genetic disease. For couples who have had a severely affected baby, knowledge of the genetic cause of the disease can inform family planning decisions into the future. Most couples do not want to have another severely affected baby.

In recent years our team has relied on next generations sequencing in the form of targeted gene panels and whole exome sequencing for the diagnosis and identification of novel human disease genes. We have a focus on neurogenetic fetal akinesias: a group of diseases that present in utero with reduced or absent fetal movements and associated abnormalities. These conditions are often fatal in the prenatal or antenatal period. Through international and national collaborations, we have access to DNA from hundreds of families that are yet to receive a genetic diagnosis, despite extensive genetic testing. These families are enriched for gene discovery since many of the known disease genes have already been excluded.

This project will include analysis, filtering and interpretation of whole exome and/or genome sequencing data from families with severe and rare neurogenetic disease. Primers will be designed for candidate variants and Sanger sequencing will be performed. Novel candidate genes will be entered into GeneMatcher for facilitation of gene matching with other families with variants in the same candidate gene. Functional studies will be performed to confirm the likely pathogenicity of candidate variants/genes and may include: cDNA and protein studies (western blotting and immunohistochemistry) from patient tissues and/or cell lines, over-expression studies in cultured cells, mini-gene assays to look at splicing defects where appropriate.

This project has to potential to result in immediate impact for the affected families, through accurate genetic diagnosis and will allow the candidate to collaborate nationally and internationally with expert clinical and research teams and thus built their network.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

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|--------------------|---|
| Primary supervisor | Phone number, email address and location |
| Dr Livia Carvalho | Lions Eye Institute (LEI), 4 th floor Harry Perkins Medical Research Building 9381 0712 liviacarvalho@lei.org.au |

School of Biomedical Sciences Coordinating supervisor

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If No: Name Phone number, email address and location

| | |
|---------------------------|---|
| Other supervisor/s if any | Phone number, email address and location |
| 1. Dr Carla Mellough | 9381 0712; carlamellough@lei.org.au , Lions Eye Institute |

Project title

Investigating the genetic and environmental factors involved in early onset myopia

Project location:

Lions Eye Institute, 4th floor Harry Perkins Medical Research Building

Project description

The growing incidence of myopia (short-sightedness) in children indicates that childhood is a critical period for intervention. Uncorrected refractive errors are the most common causes of visual impairment and, the earlier the onset, the higher the risk of related visual complications. In addition to environmental factors, genetic factors predispose children to myopia. The CREAM study has now identified over 100 genes associated with myopia. In this project, the student will establish an easily accessible zebrafish animal model pipeline for screening myopia-associated factors during eye development and correlate the influence of environmental factors on the different genetic variants with how these affect the severity of myopia. This project will be the first to combine results of genome-wide association studies, cutting edge CRISPR-Cas9 gene editing techniques and the use of the vertebrate zebrafish model to study the mechanisms of early onset myopia. This project will facilitate a deeper understanding of childhood myopia which could inform future policy and practice.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

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| Primary supervisor | Phone number, email address and location |
| Dr Livia Carvalho | Lions Eye Institute (LEI), 4 th floor Harry Perkins Medical Research Building 9381 0712 liviacarvalho@lei.org.au |

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| 1. Dr Carla Mellough | 9381 0712; carlamellough@lei.org.au , Lions Eye Institute |

Project title

Testing a dual AAV gene therapy approach for the treatment of Usher syndrome using human retinal organoids

Project location:

Lions Eye Institute, 4th floor Harry Perkins Medical Research Building

Project description

Usher syndrome is a rare genetic disorder that results in a combination of hearing loss and visual impairment. For some forms of Usher syndrome, the gene carrying the disease-causing mutation is too large for traditional gene therapy approaches to be used. This project will explore a split gene treatment, called a dual adeno-associated vector (AAV) approach, to test its therapeutic potential in Usher type 1F. In this study, the student will derive iPSCs from skin fibroblasts harvested from an Usher 1F patient and generate patient-specific retinal organoids to evaluate the dual AAV treatment approach. The data generated from this work will demonstrate the scientific value of a directly relevant human patient-specific disease modelling platform for the evaluation of potential treatment approaches in disorders caused by mutations in larger genes.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

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| Primary supervisor | Phone number, email address and location |
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| Other supervisor/s if any | Phone number, email address and location |
| 1. Dr Carla Mellough | 9381 0712; carlamellough@lei.org.au , Lions Eye Institute |
| 2. Prof David Hunt | 9381 0712; david.hunt@uwa.edu.au , Lions Eye Institute |

Project title

Evaluating neuroprotective treatments for vision loss

Project location:

Lions Eye Institute, 4th floor Harry Perkins Medical Research Building

Project description

There are two types of photoreceptors, the rods and cones; rods are active in dim light/night vision, whereas cones are critical for some of the most essential aspects of vision like facial recognition, colour, high acuity vision fine processing and contrast detection. Interestingly, cone photoreceptors appear to be remarkably sensitive and will undergo degeneration even when the genetic lesion is present only in rod-specific genes. When considering potential treatment strategies for vision loss, the most crucial aspect is how can we prolong survival of cones and therefore preserve day light vision in patients. This project will determine whether cone death can be reduced, delayed, or prevented after treatment with different neuroprotective factors. Using different mouse models of cone loss, this project will explore the effects of a clinically approved HDAC inhibitor on cone survival in vivo. This project will use a broad-range of molecular, histological and cell biology techniques. More specifically, the student's role includes tissue collection and sample preparation, immunohistochemistry experiments, microscopy imaging, extraction of high quality nucleic acids; real-time qPCR and analysis of gene expression.

School of Biomedical Sciences

Honours in Medical Research 2020
Research Project Proposal

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|--------------------|---|
| Primary supervisor | Phone number, email address and location |
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| Other supervisor/s if any | Phone number, email address and location |
| 1. Dr Carla Mellough | 9381 0712; carlamellough@lei.org.au , Lions Eye Institute |
| 2. Prof David Hunt | 9381 0712; david.hunt@uwa.edu.au , Lions Eye Institute |

Project title

Studying cone photoreceptor cell death mechanisms in inherited retinal disorders

Project location:

Lions Eye Institute, 4th floor Harry Perkins Medical Research Building

Project description

Inherited retinal degeneration (IRD) is a major contributor to early onset blindness worldwide. Currently there is no definite treatment to cure or delay disease progression and restore vision, leaving patients with a poor visual prognosis. The retina is quite unique in the number of different mutations that can cause vision loss, with >250 different disease genes now identified. Amongst the different neuronal cell types in the retina, the photoreceptor cells, which are critically important for light detection, are one of the main targets for mutations leading to vision loss. There are two types of photoreceptors, the rods and cones; rods are active in dim light/night vision, whereas cones are critical for some of the most essential aspects of vision like colour detection, high acuity vision and fine processing. Interestingly, cone photoreceptors appear to be remarkably sensitive and will undergo degeneration even when the genetic lesion is present only in rod-specific genes. Thus, cone loss in IRD can be divided into either primary or secondary cone death depending on whether the mutation is present in a cone- or rod-specific gene, respectively. Using different mouse models of IRDs as our primary tools, we hypothesize that primary and secondary cone death are driven by separate molecular pathways. The overall goal of this project is to combine gene and protein expression profiles with a method for following cone fate in the retina of mouse models of inherited retinal degeneration. This project will also provide a parallel study of different cone degeneration models of primary and secondary cone death and will thereby enable the exact pathways behind cell death to be identified, together with the identification of the common and differential factors involved in each type of inherited retinal degeneration.

School of Biomedical Sciences

Honours in Medical Research 2020
Research Project Proposal

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| Primary supervisor | Phone number, email address and location |
| Dr Livia Carvalho | Lions Eye Institute (LEI), 4 th floor Harry Perkins Medical Research Building 9381 0712 liviacarvalho@lei.org.au |

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If No: Name _____ Phone number, email address and location _____

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| Other supervisor/s if any | Phone number, email address and location |
| 1. Prof David Hunt | 9381 0712; david.hunt@uwa.edu.au , Lions Eye Institute |

Project title

Investigating the correlation of myopia susceptibility with cone opsin gene variants

Project location: Lions Eye Institute, 4th floor Harry Perkins Medical Research Building

Project description

Refractive errors are the most common cause of visual impairment in humans, with elongation of the eye - myopia - the most prevalent form. The frequency of myopia is increasing, reaching epidemic proportions in some countries, with a lack of exposure to daylight cited as a major environmental factor. The process of emmetropization, eye lengthening, is regulated by visual experience to match the eye's optics and to compensate for variation in corneal/lens curvature and power. The signals that guide this process are initiated largely by light absorption of the photopigments found in L and M cones. Changes in the pattern of light and dark in the retinal image that characterizes blurred versus sharply focused images are monitored to stop eye growth when the correct length for coordinated plano (neutral) optics is reached. In the absence of sufficient daylight, this process malfunctions, resulting in myopia. This project will examine the link between myopia and changes in the expression of the cone visual pigment (opsin) genes. The approach will be two-fold. Firstly, we will expand our previous study of opsin gene sequences in myopic individuals and secondly, we will use the zebrafish as a model system to study the effect of opsin gene variants on the development of the eye. The first part of this project will use a broad-range of molecular techniques including quantitative and long-range PCRs, cloning, DNA sequencing, site-directed mutagenesis and in vitro expression studies. The second part of this study will use CRISPR-Cas9 technology in the zebrafish to evaluate the effect of sequence variants of the M/L opsin gene on eye development and morphology and its contribution to refractive errors like myopia.

School of Biomedical Sciences

Honours in Medical Research 2020
Research Project Proposal

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| Primary supervisor | Phone number, email address and location |
| Dr Fred K Chen | 9381 0817, fredchen@lei.org.au The UWA Centre for Ophthalmology and Visual Science, Lions Eye Institute, 4 th Floor Perkins Research Building, 6 Verdun Street, Nedlands |

School of Biomedical Sciences Coordinating supervisor

Same as primary? No

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| If No: Name | Phone number, email address and location |
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| | |
|---------------------------|--|
| Other supervisor/s if any | Phone number, email address and location |
| 1. | Dr Samuel McLenachan |
| 2. | Dr Dan Zhang |
| 3. | Dr Carla Mellough |

Project title

Modelling inherited retinal disease to evaluate aberrant splicing using induced pluripotent stem cells and retinal organoids.

Project location:

The UWA Centre for Ophthalmology and Visual Science, Lions Eye Institute, 4th Floor Perkins Research Building, 6 Verdun Street, Nedlands

Project description

Inherited retinal disorders (IRDs), such as Stargardt disease and retinitis pigmentosa (RP), are a major cause of blindness in Australian children. The Ocular Tissue Engineering Laboratory is developing patient cell derived models of IRDs for the elucidation of disease mechanisms and evaluation of therapeutic approaches. Our lab has established a cell bank containing dermal fibroblasts from hundreds of patients with a wide range of IRDs. Our patients receive comprehensive clinical examinations and genetic screening. To generate personalized models of IRDs, skin cells harvested from patients with retinal disease-causing mutations are reprogrammed to produce induced pluripotent stem cells (iPSC). These iPSCs can be differentiated to produce many different cell types in the laboratory, enabling the reproduction of a patient's retinal, neural and cardiac organoids (miniature organs) in a cell culture dish.

Patient-iPSC and iPSC-retinal organoids provide an ideal platform for characterizing the molecular pathophysiology of novel or poorly understood gene mutations. For example, some missense mutations may cause splicing defects that can be examined in iPSC-retinal organoid. Moreover these lines can be used to screen for treatments that can correct the molecular defect. To date, several

iPSC disease models have been generated in our laboratory from patients with mutations in genes including *ABCA4*, *CLN3*, *RP1*, *CRB1*, *USH2A*, *PRPF31*, *OTX2* and *SNRNP200*. Available projects for honours students are listed below.

In this project, the student will reprogram patient fibroblasts to pluripotency to produce a personalized iPSC model of the selected IRD. Patient-iPSC lines will be differentiated into retinal organoid and retinal pigment epithelium. Mutant transcripts (mRNA) of the selected genes will be characterized in these tissues to examine the effect of the specific mutation on splicing.

School of Biomedical Sciences

Honours in Medical Research 2020
Research Project Proposal

Primary supervisor

Dr Fred K Chen

Phone number, email address and location

9381 0817,

fredchen@lei.org.au

The UWA Centre for Ophthalmology and Visual Science, Lions Eye Institute, 4th Floor Perkins Research Building, 6 Verdun Street, Nedlands

School of Biomedical Sciences Coordinating supervisor

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If No: Name

Phone number, email address and location

Other supervisor/s if any

Phone number, email address and location

1. Dr Samuel McLenachan
2. Dr Dan Zhang
3. Dr Carla Mellough

Project title

Modelling inherited retinal disease to develop splice interventions using induced pluripotent stem cells and retinal organoids.

Project location:

The UWA Centre for Ophthalmology and Visual Science, Lions Eye Institute, 4th Floor Perkins Research Building, 6 Verdun Street, Nedlands

Project description

Inherited retinal disorders (IRDs), such as Stargardt disease and retinitis pigmentosa (RP), are a major cause of blindness in Australian children. The Ocular Tissue Engineering Laboratory is developing patient cell derived models of IRDs for the elucidation of disease mechanisms and evaluation of therapeutic approaches. Our lab has established a cell bank containing dermal fibroblasts from hundreds of patients with a wide range of IRDs. Our patients receive comprehensive clinical examinations and genetic screening. To generate personalized models of IRDs, skin cells harvested from patients with retinal disease-causing mutations are reprogrammed to produce induced pluripotent stem cells (iPSC). These iPSCs can be differentiated to produce many different cell types in the laboratory, enabling the reproduction of a patient's retinal, neural and cardiac organoids (miniature organs) in a cell culture dish.

Patient-iPSC and iPSC-retinal organoids provide an ideal platform for characterizing the molecular pathophysiology of novel or poorly understood gene mutations. For example, some missense mutations may cause splicing defects that can be examined in iPSC-retinal organoid. Moreover these lines can be used to screen for treatments that can correct the molecular defect. To date, several

iPSC disease models have been generated in our laboratory from patients with mutations in genes including *ABCA4*, *CLN3*, *RP1*, *CRB1*, *USH2A*, *PRPF31*, *OTX2* and *SNRNP200*. Available projects for honours students are listed below.

In this project, the student will utilise an established iPSC model of retinitis pigmentosa or Stargardt disease to characterize molecular pathophysiology and evaluate treatment strategies. iPSC carrying splice altering mutations in any of the IRD genes and control-iPSC will be differentiated into retinal organoids. Gene expression and protein level will be characterized using RT-PCR, transcript sequencing and western blot. Splicing correction or exon skipping will be induced by personalised splice intervention therapy (antisense oligonucleotide) to restore transcript production. Functional impact will be assessed through morphology and metabolic assays.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Dr Amelia Harray – Telethon Kids Institute 08 6456 4616,
Amelia.Harray@health.wa.gov.au
Perth Children’s Hospital, Telethon Kids Institute,
15 Hospital Avenue, Nedlands

School of Biomedical Sciences Coordinating supervisor
Name: Professor Paul Fournier –
The University of Western Australia, Ph. 6488 1356,
paul.fournier@uwa.edu.au

Other supervisor/s if any: Prof Elizabeth Davis
Ph. 6456 5031 elizabeth.davis@telethonkids.org.au,
Perth Children’s Hospital/Telethon Kids Institute

Project title:
Impact of Food on Glycaemic Control in individuals with Type 1 diabetes

Project location:
Perth Children’s Hospital, Telethon Kids Institute, 15 Hospital Avenue, Nedlands

Project description: The Children’s Diabetes Centre is an integrated clinical and research centre conducting research into Type 1 diabetes (T1DM) and childhood onset Type 2 diabetes. The Children’s Diabetes Centre includes researchers at the Telethon Kids Institute’s Diabetes Research Team and researchers and clinicians within the Diabetes Service at Perth Children’s Hospital as part of the Western Australian Department of Health. Type 1 Diabetes is a 24/7 disease that requires constant management and vigilance. Blood glucose is affected by every mouthful of food and exercise — even sleeping, stress, fatigue, puberty, time of the day, time of the year, illness and temperature can affect blood glucose levels.

The goal of the Children’s Diabetes Centre is to improve the lives of children, adolescents and young adults living with diabetes and their families by improving outcomes, both now and into the future. Our primary objective is to generate significant new knowledge that will lead to tangible improvements in care. We do this by focused research studies across 6 research themes including food and nutrition and our research involves clinical investigations, clinical trials, epidemiological studies and qualitative research projects and we translate the results of these studies into the clinic and the community.

Our food and nutrition theme aims to better understand the impact of food on glycaemic control – that will be progressively translated into clinical practice and guidelines. Specific studies are dependent on the interest of the prospective student. The Centre offers PhD and Honours scholarships to competitive students. Start date January 2020.

Suitable for Honours, PhD

Essential skills & Qualifications:

- Outstanding academic record in relevant discipline
- First class honours in a relevant discipline
- Interest in clinical dietetics/nutrition
- Good communication skills

Ethics Approval not obtained

Funding:

- Top-up scholarship offered by project group
- Full scholarship could be available to outstanding student

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor

Dr Aveni Haynes, Children's Diabetes Centre
6456 4622, aveni.haynes@telethonkids.org.au,
Telethon Kids Institute, 15 Hospital Avenue, Nedlands

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1. Ph. 6488 1356, Prof Paul Fournier, paul.fournier@uwa.edu.au, The University of Western Australia, School of Human Science

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2. 6456 4609 grant.smith@telethonkids.org.au, Children's Diabetes Centre, Telethon Kids Institute
3. 6456 5031 elizabeth.davis@telethonkids.org.au Diabetes & Endocrinology, Perth Children's Hospital

Project title:

How does mode of delivery influence risk of childhood type 1 diabetes in Western Australia?

Project location:

Perth Children's Hospital/Telethon Kids Institute, 15 Hospital Avenue, Nedlands

Project description:

Childhood type 1 diabetes (T1D), thought to be the result of environmental and genetic factors, continues to increase in Western Australia (WA) but the cause of this increase unknown. Birth by Caesarean-section delivery has been shown to increase the risk of childhood T1D by 20%, but the mechanism for this association remains unclear. Technological and methodological advances in the burgeoning area of microbiome research have provided evidence that mode of delivery is a significant modifier of the infant gut microbiome, and importantly, that the infant gut microbiome has an important influence on early immune system development and maturation. Therefore, there is now a biologically plausible mechanism via which birth by Caesarean section may influence risk of later onset T1D.

In WA, >99% of children diagnosed with T1D <15 years of age are managed by the diabetes team at Perth Children's Hospital (PCH) and their data are stored in the Western Australian Children's Diabetes Database (WACDD). In addition, data are available on all births in WA from the Midwives' Notification System (MNS), a statutory data collection maintained by the Department of Health.

This project aims to better define the relationship between mode of delivery and risk of childhood T1D using a case-control study design and data linkage. Cases will be identified from the WACDD and defined as all children with T1D diagnosed <15 years, born in WA between 1995 and 2017. Perinatal variables to be analysed will include e.g. gestational age, infant birth weight, maternal age, parity, maternal pre-existing diabetes, complications of pregnancy and labour, labour onset and mode of delivery. Start date January 2020.

Suitable for Masters/PhD

Essential skills & Qualifications:

- Use of SPSS/STATA/R or other statistical package

Ethics Approval obtained

Funding:

- Top-up scholarship offered by project group
- Full scholarship could be available to outstanding student

For more information, please contact Tanyana Jackiewicz, tanyana.jackiewicz@health.wa.gov.au,
Ph. 6456 4616

Honours in Medical Research 2020

Research Project Proposal

Primary supervisor

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Telethon Kids Institute, 15 Hospital Avenue, Nedlands

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1. Ph. 6488 1356, Prof Paul Fournier, paul.fournier@uwa.edu.au, The University of Western Australia, School of Human Science

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2. Ph. 6456 4609 grant.smith@telethonkids.org.au, Children's Diabetes Centre, Telethon Kids Institute
3. Ph. 6456 5031 elizabeth.davis@telethonkids.org.au Diabetes & Endocrinology, Perth Children's Hospital

Project title:

How is maternal Vitamin D sufficiency during pregnancy associated with the risk of islet autoimmunity development in children at risk of type 1 diabetes?

Project location: Perth Children's Hospital/Telethon Kids Institute, 15 Hospital Avenue, Nedlands

Project description: Early environmental determinants of pancreatic islet autoimmunity: a pregnancy to early life cohort study (ENDIA) in children at risk of type 1 diabetes (T1D) is a multi-centre study involving researchers in South Australia, Victoria, New South Wales, Western Australia and Queensland. (www.endia.org.au). Over 1,300 pregnant women who have T1D or where their unborn child has a first degree relative with T1D have been recruited to the study and the children are being followed up from birth to 10 years of age.

There are numerous observational epidemiological studies reporting an association between low Vitamin D levels with increased risk of childhood T1D. ENDIA has the unique opportunity to further examine the influence of vitamin D levels on the development of islet autoimmunity by analysing the association between prenatal vitamin D levels and modifiable environmental factors such as dietary intake during pregnancy and infancy, compliance with supplementation or treatment if vitamin D deficiency is diagnosed, and the risk of islet autoimmunity in children at risk of T1D. Start date March 2020. This study aims to:

1. Determine the prevalence of vitamin D deficiency during pregnancy in the ENDIA study cohort
2. Investigate the association between vitamin D deficiency and antecedent factors being evaluated in the ENDIA study cohort
3. Investigate the association between vitamin D deficiency during pregnancy and the development of persistent islet autoimmunity in the ENDIA study cohort

Suitable for Honours/Masters

Essential skills & Qualifications:

- Outstanding undergraduate in Health Science, Public Health
- Use of SPSS/STATA/R or other statistical package
- Good communication and organisational skills

Ethics Approval obtained

Funding:

- Top-up scholarship offered by project group
- Full scholarship could be available to outstanding student

For more information, please contact Tanyana Jackiewicz, tanyana.jackiewicz@telethonkids.org.au,
Ph. 6456 4616

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Prof Elizabeth Davis
Perth Children's Hospital/Telethon Kids Institute
Ph. 6456 4622, elizabeth.davis@telethonkids.org.au
15 Hospital Avenue, Nedlands

School of Biomedical Sciences Coordinating supervisor

Same as primary? No _____

1. Ph. 6488 1356, Prof Paul Fournier, paul.fournier@uwa.edu.au, The University of Western Australia,
School of Human Science

Other supervisor/s if any: Phone number, email address and location

Project title:

Using continuous glucose monitoring and a carbohydrate algorithm to manage blood glucose levels during exercise in adolescents with type 1 diabetes

Project location:

Perth Children's Hospital/Telethon Kids Institute, 15 Hospital Avenue, Nedlands

Project description:

Physical exercise can cause both low and high blood glucose levels in children and adolescents with type 1 diabetes mellitus. Due to the immediate and potentially serious consequences of untreated low blood glucose levels, it is often being regarded as the main barrier to a physically active lifestyle.

In recent years, there has been an increase in the use of real-time continuous glucose monitoring (rtCGM) technology to better manage glucose levels. However, studies have not yet demonstrated the optimal use of rtCGM to reduce the time spent with low and high blood glucose levels during physical activity.

The aim of this study is to trial a carbohydrate algorithm based on rtCGM readings during 60 minutes of moderate intensity cycling, in 14-16 year old adolescents with T1DM. Participants will complete a familiarisation visit with a VO₂ peak test followed by two testing sessions. One session will use the carbohydrate algorithm based on the rtCGM and the other will give carbohydrates based on the standard guidelines. Start date January 2020.

Suitable for Honours

Ethics Approval obtained

Essential skills & Qualifications:

- Undergraduate in Health Sciences, Public Health, Exercise Science or other relevant area
- Good communication skills

For more information, please contact Tanyana Jackiewicz, tanyana.jackiewicz@telethonkids.org.au,
Ph: 6456 4616

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Professor Paul Fournier, School of Human Sciences,
The University of Western Australia, Ph. 6488 1356,
paul.fournier@uwa.edu.au

School of Biomedical Sciences Coordinating supervisor
Same as primary? Yes

Other supervisor/s if any Phone number, email address and location

1. Ph. 6456 5031 elizabeth.davis@telethonkids.org.au, Perth Children's Hospital/Telethon Kids Institute

2. Ph. 6456 5033 tim.jones@telethonkids.org.au, Perth Children's Hospital/Telethon Kids Institute

Project title:

Effect of hypoxia typical of high altitude on the accuracy of continuous glucose monitors and its impact on blood glucose management in individuals with type 1 diabetes mellitus

Project location: The University of Western Australia

Project description:

Regular self-monitoring of blood glucose levels using continuous glucose monitors (CGM) provides an effective means to minimise both hypoglycaemia risk and the magnitude of the glycaemic excursions experienced by people with type 1 diabetes. One potential limitation with this technology relates to the glucose sensors they use to measure glucose levels as some of these sensors maybe affected by the levels of ambient oxygen. Indeed, meters that use a glucose oxidase-based enzyme reaction may misread glucose levels under conditions of low blood oxygen tension. Although this may have been a limitation with the first generation of glucose-oxidase-based sensors because their electrochemical detection of glucose was dependent on ambient oxygen levels, current CGMs rely on oxygen-independent glucose-oxidase-based sensors, thus implying that these devices may not be affected by ambient oxygen levels. Whether this is the case remains to be determined. This is an important clinical issue to address given the popularity of high-altitude destinations and activities (e.g. trekking, skiing) associated with low oxygen levels. Our primary aim is to examine the extent to which the accuracy of current CGMs is affected by the hypoxic conditions found at high altitude and thus evaluate whether these devices provide reliable blood glucose management tools for individuals with type 1 diabetes. Start date February/July 2020.

Suitable for Honours, Masters, PhD

Essential skills & Qualifications:

- Initiative and dedication
- High level of written communication skills
- High level of organisation and time management skills
- Ability to complete projects on time
- Willingness to learn new skills
- Excellent ability to work independently and as part of a team
- Good interpersonal skills
- Good communication skills

Ethics Approval obtained Yes

Funding:

- Top-up scholarship offered by project group
- Full scholarship could be available to outstanding student

For more information, please contact Tanyana Jackiewicz, tanyana.jackiewicz@telethonkids.org.au,
Ph: 6456 4616



School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Professor Paul Fournier, School of Human Sciences,
The University of Western Australia, Ph. 6488 1356,
paul.fournier@uwa.edu.au

School of Biomedical Sciences Coordinating supervisor
Same as primary? Yes

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1. Ph. 6456 5031 elizabeth.davis@telethonkids.org.au, Perth Children's Hospital/Telethon Kids
Institute
2. Ph. 6456 5033 tim.jones@telethonkids.org.au, Perth Children's Hospital/Telethon Kids Institute

Project title:

Is the recommendation to decrease basal insulin dose pre-exercise conducive to severe hyperglycaemia during and after exercise?

Project location:

The University of Western Australia

Project description: Current guidelines recommend that people with type 1 diabetes (T1D) should reduce their basal insulin dose by 25-50% prior to exercise to minimise their risks of hypoglycaemia both during and after exercise. However, these recommendations are challenged by our recent findings that when exercise is performed under basal insulin conditions, with no prior insulin dose adjustments, blood glucose levels remain stable or change little. These findings suggest that reducing basal insulin levels prior to a bout of high intensity exercise might be conducive to a marked increase in blood glucose levels, and thus be detrimental to blood glucose management. For this reason, our aim is to test the hypothesis that the recommendation to reduce basal insulin dose by 25 or 50% prior to engaging in a bout of high intensity exercise is conducive to a high increase in blood glucose levels in people with T1D.

Suitable for Honours, Masters

Essential skills & Qualifications:

- Initiative and dedication
- High level of written communication skills
- High level of organisation and time management skills
- Ability to complete projects on time
- Willingness to learn new skills
- Excellent ability to work independently and as part of a team
- Good interpersonal skills
- Good communication skills

Ethics Approval obtained Yes

Funding:

- Top-up scholarship offered by project group
- Full scholarship could be available to outstanding student

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School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Professor Paul Fournier, School of Human Sciences,
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School of Biomedical Sciences Coordinating supervisor
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1. Ph. 6456 5031 elizabeth.davis@telethonkids.org.au, Perth Children's Hospital/Telethon Kids Institute
2. Ph. 6456 5033 tim.jones@telethonkids.org.au, Perth Children's Hospital/Telethon Kids Institute

Project title:

Effect of swimming and head-out water immersion in cold water on the risk of hypoglycaemia in type 1 diabetes

Project location: The University of Western Australia

Project description:

Physical activity increases the risk of hypoglycaemia in individuals with type 1 diabetes (T1D), with the associated increased fear of hypoglycaemia contributing to their lower participation rates in regular exercise and lower than average fitness levels. For this reason, a number of recommendations have been published to reduce such risks of hypoglycaemia. Unfortunately, one major limitation with these recommendations is that they generally overlook the impact that some environmental conditions may have on blood glucose response to exercise. Since cold water immersion increases glucose oxidation rate and may inhibit the production of glucose by the liver, this raises the issue of whether upright immersion or swimming in cold water increases hypoglycaemia risk in people with T1D. This is a clinically important issue given the increased risk of drowning associated with hypoglycaemia. Since this issue has not been investigated before, the primary aims of this proposed research project are to test the hypotheses that (a) head out of water immersion in cold (20°C) compared to thermoneutral water (32°C) is associated with a faster rate of fall in blood glucose level; and (b) exercising in cold water causes a greater rate of fall in blood glucose level compared to exercising under thermoneutral conditions.

Suitable for Honours, Masters

Essential skills & Qualifications:

- Initiative and dedication
- High level of written communication skills
- High level of organisation and time management skills
- Ability to complete projects on time
- Willingness to learn new skills
- Excellent ability to work independently and as part of a team
- Good interpersonal skills
- Good communication skills

Ethics Approval obtained Yes

Funding:

- Top-up scholarship offered by project group
- Full scholarship could be available to outstanding student

For more information, please contact Tanyana Jackiewicz, tanyana.jackiewicz@telethonkids.org.au,
Ph: 6456 4616



School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Professor Paul Fournier, School of Human Sciences,
The University of Western Australia, Ph. 6488 1356,
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School of Biomedical Sciences Coordinating supervisor
Same as primary? Yes

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1. Ph. 6456 5031 elizabeth.davis@telethonkids.org.au, Perth Children's Hospital/Telethon Kids
Institute
2. Ph. 6456 5033 tim.jones@telethonkids.org.au, Perth Children's Hospital/Telethon Kids Institute

Project title:
**Effect of high blood glucose levels on executive function, attention and driving performance on a
driving simulator in people with type 1 diabetes**

Project location:
The University of Western Australia

Project description:

It is well established that several years of exposure to high blood glucose levels in people with type 1 diabetes mellitus (T1D) can be detrimental to the central and peripheral nervous systems. In particular, reaction time, cognitive function (e.g. executive function and attention), and driving performance have been reported to be adversely affected by T1D. What is still unclear, however, is the impact that an acute increase in blood glucose levels (e.g. after a meal) may have on driving performance and cognitive function. Although a small number of studies have investigated the effects of acute hyperglycaemia on cognition, some cognitive abilities essential to everyday tasks, such as driving, have not been thoroughly assessed; namely, executive functions, attention, and driving ability. For these reasons, the primary aim of this proposed project is to test the hypothesis, in people with T1D, that an acute exposure to high blood glucose levels will impair their driving performance in a driving simulator. We also hypothesise that both attention and executive function will be impaired upon exposure to acute hyperglycaemia.

Suitable for Honours, Masters

Essential skills & Qualifications:

- Initiative and dedication
- High level of written communication skills
- High level of organisation and time management skills
- Ability to complete projects on time
- Willingness to learn new skills
- Excellent ability to work independently and as part of a team
- Good interpersonal skills
- Good communication skills

Ethics Approval obtained Yes

Funding:

- Top-up scholarship offered by project group
- Full scholarship could be available to outstanding student

For more information, please contact Tanyana Jackiewicz, tanyana.jackiewicz@telethonkids.org.au,
Ph: 6456 4616

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor: Associate Professor Steven Mutsaers

Phone number, email address and location: : 6151 0891, steven.mutsaers@uwa.edu.au, Institute for Respiratory Health (IRH), Tissue Repair Group, Fifth Floor, Harry Perkins Inst for Medical Research Building, QQ Block, QEII Medical Centre, Nedlands WA 6009.

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes No

If No: Name

Phone number, email address and location

Other supervisor/s if any Phone number, email address and location

1. A/Prof Fiona Pixley, fiona.pixley@uwa.edu.au, Pharmacology, UWA
2. A/Prof Cecilia Prêle, Cecilia.prele@uwa.edu.au, Ear Sciences Institute Australia, UWA

Project title

TILs and TAMs; therapeutically targeting cellular communication in lung cancer

Project location:

5th Floor Harry Perkins Building and 1st floor M Block, QEII Medical Centre

Project description

Non small cell lung cancer (NSCLC) tumours are composed of 13 immune cell types; 47 % T cells, 16 % B cells and 4.7% tumour-associated macrophages (TAMs). Our laboratory focus is on determining the role of B and T cells (tumour infiltrating lymphocytes, TILs) and TAMs in solid tumours. Infiltrating B and T cells are the most abundant cell in the virgin mammary gland. However, we have shown that TAMs act to exclude B and T cells from the breast tumour microenvironment. We have also shown that reducing TAM proliferation, differentiation and migration by inhibiting CSF1R activation reduces Py8119 mammary adenocarcinoma cell tumour size by ~80 %. In this study we will investigate the relationship between TILs and TAMs in NSCLC. Larger numbers of B cells were detected within the NSCLC tumour than the distal lung. In autoimmunity, B cells work in concert with T cells to enhance T-cell mediated responses through local cytokine, chemokine and autoantibody production. However, in the tumour microenvironment, B cell subsets have been reported to have both pro and anti-tumorigenic roles, raising questions as to their specific role. While B-TILs and increased plasma cells have been associated with improved outcome, suggesting a protective role for B cells, they can also produce lymphotoxin to promote tumour cell survival and cancer progression. In this study we will determine the role of TILs and TAMs in NSCLC growth.

Aim: To determine if TAM reprogramming alters the growth of the NSCLC Lewis lung carcinoma (LLC) cells in vivo. LLC cells will be transplanted into the hind flank of mice and CSF1R signalling will be inhibited using a potent and selective Src family inhibitor RK20449. We will determine the effect of RK20449 on LLC growth in vivo. We predict that, similar to other solid tumours, RK20449 will reprogram TAMs and reduce tumour burden. Using single cell RNASeq, we will confirm that, similar to breast cancer, RK20449 selectively targets CSF1R signalling in NSCLC to reprogram TAMs and reduce tumour growth. These data will provide proof-of-concept that TAM-driven mechanisms promoting tumour growth are similar in solid cancers. We will also determine the effect of altered TAM expression and activity on the tumour microenvironment with a focus on B-TILs. LLC tumours will be dissociated and cellular composition determined using multicolour flow cytometry. The distribution of B-TILs and other immune cells within the tumour will be determined by immunohistochemistry.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor: A/Prof Steven Mutsaers

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School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes No

If No: Name

Phone number, email address and location

Other supervisor/s if any Phone number, email address and location

1. A/Prof Cecilia Prêle, cecilia.prele@uwa.edu.au, Ear Science Inst Australia
2. Prof Gerard Hoyne, gerard.hoyne@nd.edu.au, Notre Dame University

Project title

The role of PD-1/PD-L1 in pulmonary fibrosis

Project location:

5th Floor Harry Perkins Building, QEII Medical Centre

Project description

Idiopathic pulmonary fibrosis (IPF) is an aggressive interstitial lung disease with no cure and a mean survival of three years from diagnosis. The drugs Pirfenidone and Nintedanib have improved the quality of life for a small proportion of patients with IPF but has had little effect on survival. Our group has pioneered studies identifying the Programmed Death-1 (PD-1) and its ligand (PD-L1) as key drivers of fibrosis. We have also shown the importance of the transcription factor STAT3 in PD-1/PD-L1-induced fibrosis but how they interact is unclear. PD-1 and PD-L1 inhibitors have revolutionised cancer immunotherapy with most successful treatments using combinations of PD-1/PD-L1 inhibitors with inhibitors of growth factor and cytokine signalling. In this study we will use human IPF and control cells and a mouse lung fibrosis model to examine 1. How PD-1/PD-L1 interact with STAT3 to drive fibrosis and 2. Determine if pirfenidone or nintedanib (inhibitors of growth factor and cytokine signalling) combined with PD-1/PD-L1 inhibitors will be more effective in reducing lung fibrosis than pirfenidone and nintedanib alone.

This study will use cell and molecular assays including tissue culture, proliferation and cytotoxicity assays, real time PCR, western blot analysis and animal models to address these aims.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor: A/Prof Steven Mutsaers

Phone number, email address and location: 6151 0891, steven.mutsaers@uwa.edu.au, Institute for Respiratory Health (IRH), Tissue Repair Group, Fifth Floor, Harry Perkins Inst for Medical Research Building, QQ Block, QEII Medical Centre, Nedlands WA 6009.

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes No

If No: Name

Phone number, email address and location

Other supervisor/s if any Phone number, email address and location

Prof Jenette Creaney, Jenette.creaney@uwa.edu.au, National Centre for Asbestos Related Disease and IRH

Project title

Transfer RNA-derived fragments in malignant mesothelioma

Project location:

5th Floor Harry Perkins Building, QEII Medical Centre

Project description

Malignant Mesothelioma (MM) is an aggressive and fatal cancer that is primarily caused by asbestos exposure. There is no cure and a 5 year survival rate of <1%. This project aims to determine the role of small non-coding RNAs called transfer RNA-derived fragments (tRFs) in MM. We have previously shown that tRF^{LysA}, tRF^{LysB}, tRF^{ThrA} and tRF^{LeuA} are highly expressed in this cancer. How these tRFs function and the role of tRFs in disease biology is yet to be fully elucidated. It appears that some tRFs may be involved in the regulation of gene expression and may have microRNA-like activity (another type of small non-coding RNA). However, tRF biogenesis is distinct from that of the miRNA pathway. Therefore, tRFs may also have important roles in the regulation of a wider variety of biological functions. **We hypothesise that these novel tRFs play important roles in the growth of MM.**

Aim 1. Determine the expression of tRF^{LysA}, tRF^{LysB}, tRF^{ThrA} and tRF^{LeuA} in a variety of MM and control cell lines. TRFs will be measured using qRT-PCR.

Aim 2. Determine the effect of downregulating TRFs on cell proliferation and cell death. MM cell lines and controls will be transfected with antisense oligonucleotides (AS-ODN; specifically designed to match and inhibit each tRF) to block tRF function in cells with relatively high tRF expression.

This study will use cell and molecular assays including tissue culture, proliferation, cytotoxicity and migration assays, real time PCR, western blot analysis and animal models to address these aims.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location

Associate Professor Cecilia Prêle 6151 0958 cecilia.prele@uwa.edu.au

Ear Science Institute Australia, 3rd Floor RR Block, QEII Medical Centre, 8 Verdun Street, Nedlands WA 6009

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes

If No: Name Phone number, email address and location

Other supervisor/s Phone number, email address and location

Prof Rodney Dilley, Ear Science Institute Australia, rodney.dilley@earscience.org.au

Dr Jafri Kuthubutheen, Ear Science Institute Australia, Jafri.Kuthubutheen@health.wa.gov.au

Project title

Modelling and regulating extracellular matrix deposition by inner ear cells

Project location:

Ear Science Institute Australia, 3rd Floor Sarich Neuroscience Research Institute, QEII Medical Centre, 8 Verdun Street, Nedlands

Project description:

Fibrosis in the inner ear can occur following surgery and as a complication of infection. Local tissue responses to cochlear implants can result in the formation of a fibrotic barrier between the electrode and the target neurons, causing loss of residual hearing and function of the implant. In patients with meningitis, cochlear fibrosis and subsequent ossification profoundly limits the capacity for cochlear implantation, which can also adversely affect hearing outcomes.

In this study we will examine the efficacy of the anti-fibrotic drugs in regulating extracellular matrix protein deposition by inner ear fibroblasts. Dose response curves will be performed and effects on TGFB-induced smad2/3 and p38 pathway activation will be confirmed by western blot. The effects of drug treatment on inner ear fibroblast cell proliferation, differentiation and ECM protein deposition by inner ear fibroblasts confirmed using in vitro assays.

Techniques: Immunocytochemistry, real time PCR, ELISA, Western blot analysis, confocal laser scanning microscopy, tissue culture.

Please note that several potential projects exist within this broad programme of research and we welcome all enquires.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location

Dr Rhonda Taylor, rhonda.taylor@uwa.edu.au, 6151 0740, Harry Perkins Institute of Medical Research and CMR/HMS

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes No

If No: Name

Phone number, email address and location

Other supervisor/s if any Phone number, email address and location

1. Prof Nigel Laing, nigel.laing@uwa.edu.au, Harry Perkins Institute of Medical Research and CMR/HMS
 2. Dr Joshua Clayton, joshua.clayton@perkins.org.au, Harry Perkins Institute of Medical Research and CMR/HMS
-

Project title

Investigating novel therapies for neurogenetic diseases

Project location:

Harry Perkins Institute of Medical Research, QE II Medical Centre

Project description

The Laing laboratory has a long history in both genetic diagnosis and investigation of treatment options for patients suffering from neuromuscular disorders. Neuromuscular disorders are a group of heterogeneous conditions that affect the function of the voluntary muscles (trunk, limbs, face) via a defect in the muscle itself, the neuromuscular junction, or the motor neuron (nerve). These disorders are rare and are frequently severe and life limiting. Unfortunately, adequate treatment options are not yet available for most patients.

We are currently investigating various gene editing strategies as novel treatment options for a subset of severe neuromuscular disorders. These include allele-specific deletion of dominant disease genes, modulation of enhancer activity, and upregulation studies on alternative isoforms or modifier genes.

This project would involve CRISPR-Cas9 gRNA design and delivery to a range of human and/or murine cell cultures, followed by analysis of the effect of gene editing/engineering at the gene, mRNA and protein levels. This will result in generating data on the feasibility of these strategies for treating neuromuscular disorders, which would be a significant step forward in this field. Further, this project will provide the student with a broad range of key laboratory skills including cell culture, RNA and DNA extraction, PCR, real-time PCR and western blotting.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
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School of Medicine, University of Western Australia
Level 2, Harry Perkins Institute of Medical Research,
Fiona Stanley Hospital Campus,
5 Robin Warren Drive, Murdoch 6150 WA

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes ___ No X

If No: Dr Dino Bee Aik Tan Phone number, email address and location
0433877779
dino.tan@uwa.edu.au
Level 2, MRF Building, Royal Perth Hospital,
Rear 50 Murray Street, Perth 6000 WA

Project title

Mechanism of anti-fibrotic treatments in slowing the progression of Idiopathic Pulmonary fibrosis (IPF)

Project location:

Level 2, MRF Building, Royal Perth Hospital

Project description:

Idiopathic pulmonary fibrosis (IPF) is a chronic lung disease characterised by progressive decline in pulmonary function and irreversible scarring of the lungs with median survival of only 2-5 years. The rate of decline can vary, with some patients remaining stable over longer periods of time and others undergoing rapid progression. The highly heterogeneous nature of this disease makes it difficult to elucidate the pathways involved in the initiation and progression of IPF. Anti-fibrotic medications which may slow the progression of disease were recently made available on the Pharmaceutical Benefits Scheme (PBS). However, not all IPF patients will meet these criteria or antifibrotic medication may not be suitable for them. Those who receive anti-fibrotic medications may not respond to treatment. Hence, understanding the mechanism of IPF pathogenesis and the impact of anti-fibrotic treatment on biological pathways in IPF patients is important to help improve the treatment of IPF.

This project aims to investigate the biomarker profile of blood samples collected from IPF patients 4 times over 12-month period. The disease history of patients who received treatment and those who do not will be compared and the impact of anti-fibrotic medication on disease course and outcomes for these patients will be investigated. Biomarkers that were associated with the progression of IPF will be investigated include circulating proteins (e.g. osteopontin, MMP-7) or RNA (e.g. TAF2 and NT52C)

measured by ELISA or ddPCR respectively. Furthermore, circulating extracellular vesicles (EV) that contain important regulatory proteins and miRNA have been proven to be excellent biomarkers for diseases (e.g in cancers) and the characterisation of their profile has led to the elucidation of disease pathophysiology.

Hypothesis: There are changes in circulating protein, RNA and EVs in plasma samples of IPF patients that respond versus those that do not respond to treatment.

Aims:

1. Measure the concentration of circulating proteins by ELISA.
2. Quantify the levels of RNA transcripts by ddPCR.
3. To isolate and characterise the contents of EV.

Anticipated outcome: This project will find biomarkers to predict the progression of IPF, as well as response to therapy. Upon identifying these biomarkers, functional studies using *in vitro* lung fibroblasts cell cultures from IPF patients and healthy controls will be performed to investigate their potential as therapeutic targets.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location

Associate Professor Dr Charlene Kahler, charlene.kahler@uwa.edu.au, Marshall Centre for Infectious Disease Research and Training, L Block, QEII

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes No

If No: Name

Phone number, email address and location

Project title

Cationic antimicrobial peptide hetero-resistance in commensal *Neisseria* species

Project location:

Marshall Center, QEII L block

Project description

Description of Research Project:

Neisseria meningitidis is a respiratory pathogen which cause invasive meningitis and sepsis. However, recently a new pathotype has emerged which causes transmissible urethritis. These isolates belong to the genetic lineage of clonal complex 11 which is usually a serogroup W isolate. These urethritis isolates are different in that they now have acquired the ability for facultative anaerobic respiration through uptake of genes from *Neisseria gonorrhoeae* and have switched off capsule production by inversion of the genome. A separate phenotype is hetero-resistance to cationic antimicrobial peptides (CAMPs) in macrophages. These mutants appear sporadically in culture and are the result of numerous indels and point mutations. It is not clear that this feature is unique to this uropathotype or more widespread amongst *Neisseria* species.

We have tested a panel of 33 *Neisseria* commensal species and have shown that these species also have hetero-resistance to CAMPs. However, we do not know what the molecular basis of this mechanism is in these species.

Our hypothesis: CAMP hetero-resistance is a necessary phenotype for commensalism with the human host.

Aims:

1. To isolate and purify CAMP-resistant and sensitive isogenic strains from multiple *Neisseria* species
2. Perform whole genome sequencing and characterise the indels and point mutations that could be associated with the phenotype of hetero-resistance
3. To confirm the association of the hetero-resistance phenotype with a mutation by genetic modification
4. Examine the phenotype of hetero-resistance in survival in macrophages

Techniques:

1. Culture commensal *Neisseria* species
2. Whole genome sequencing and bioinformatics
3. Culture of macrophages and macrophage killing assays

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

Tzeng et al. Emergence of a new *Neisseria meningitidis* clonal complex 11 lineage 11.2 clade as an effective urogenital pathogen. <https://doi.org/10.1073/pnas.1620971114>

Tzeng et al. Heteroresistance to the model antimicrobial peptide polymyxin B in the emerging *Neisseria meningitidis* lineage 11.2 urethritis clade: mutations in the *pilMNOPQ* operon. Mol Microbiol. 2019 Jan;111(1):254-268

School of Biomedical Sciences
Honours in Medical Research 2019
Research Project Proposal

Primary supervisor Phone number, email address and location

Associate Professor Dr Charlene Kahler, charlene.kahler@uwa.edu.au, Marshall Centre for Infectious Disease Research and Training, L Block, QEII

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes No

If No: Name Phone number, email address and location:

Other supervisor/s Phone number, email address and location

Dr Mitali Sarkar-Tyson mitali.sarkar-tyson@uwa.edu.au, Marshall Centre for Infectious Disease Research and Training, L Block, QEII

Ms Emily kibble Emily.kibble@uwa.edu.au

Project title

Examining the role of EptA in the colistin resistance in *Neisseria gonorrhoeae*.

Project location:

Marshall Centre for Infectious Disease and Training, L Block, QEII

Project description

Neisseria gonorrhoeae is the bacterial causative agent of sexually transmitted gonorrhoea. *N. gonorrhoeae* has increasingly become multi-drug resistant strains becoming resistant to all off-the shelf therapies. Therefore, there is a requirement to look at novel avenues for drug therapy. Of particular interest are enzymes involved in protein-folding pathways and decoration of lipooligosaccharide (LOS). We have previously shown in *N. meningitidis*, that oxidoreductases are important for the stability of the enzyme, LOS phosphoethanolamine transferase (EptA) (1). EptA is considered an excellent target for intervention as it is essential for virulence in infectious models (2).

This project will examine we will test novel compounds for anti-EptA activity and assess their function in macrophages. We will aim to develop an assay using the ANMIS flow cytometer to measure bacterial survival in macrophages.

Skills in the project will be: culture of macrophages and bacteria, flow cytometry and LDH assays.

1. Piek, S., et al., 2014 The role of oxidoreductases in determining the function of the neisserial lipid A phosphoethanolamine transferase required for resistance to polymyxin. PLoS One, 2014. 9(9): p. e106513.
2. Kahler, C.M., et al., 2018 Structure-Function Relationships of the Neisserial EptA Enzyme Responsible for Phosphoethanolamine Decoration of Lipid A: Rationale for Drug Targeting. Front Microbiol, 2018. 9: p. 1922.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location

Associate Professor Dr Charlene Kahler, charlene.kahler@uwa.edu.au, Marshall Centre for Infectious Disease Research and Training, L Block, QEII

School of Biomedical Sciences Coordinating supervisor

Same as primary? Yes No

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Phone number, email address and location

Other supervisor/s if any

Phone number, email address and location

1. Professor Mark Nicol

mark.nicol@uwa.edu.au

2. Dr Shakeel Mowlaboccus

shakeel.mowlaboccus@murdoch.edu.au

Project title

Polymyxin hetero-resistance in commensal *Neisseria* species

Project location:

Marshall Center, QEII L block

Project description

Description of Research Project:

Over the last three years, Western Australia has steadily recorded an increase in invasive meningococcal disease (IMD) cases which now number about 44 cases annually. Approximately 50% of these cases are in children under the age of 4 and are the result of serogroup W isolates. The Department of Health recently introduced an ACYW vaccine for children and young adults (15-19 yr olds) in 2017 in an effort to stem the number of cases, however, there has been no reduction in the overall rate of disease in 2018. To understand the dynamics of the effect of vaccination on nasopharyngeal carriage, the Kahler lab has collected 1500 nasopharyngeal swabs from young adults and examined the prevalence of *N. meningitidis* in these samples. From this study the carriage rate in young adults is approximately 16% in domestic students during the winter period consistent with the higher rate of IMD during the year.

Two recent publications have reported that commensal *Neisseria sp.* are able to directly kill *N. meningitidis* and *N. gonorrhoeae* (Aho et al., 2018)(So et al, 2018). We are interested in determining whether the carriage of commensal species of *Neisseria species* is protective against IMD. To do this, we need to develop a PCR assay to detect *Neisseria sp.* In our recent publication on an essential gene, *dsbD*, we have shown that the *dsbD* gene which is present in all *Neisseria* species, is highly conserved in *N. meningitidis* and *N. gonorrhoeae* but variable in the commensal species (Smith et al., 2018) .

Our hypothesis: The *dsbD* gene can be used as a target to develop a *Neisseria* species specific PCR for surveys of nasopharyngeal swabs.

Aims:

1. Design a multi-plex PCR for *dsbD* that are specific for the *Neisseria sp.* found in humans.
2. Create a RT-PCR detection assay for use with clinical samples.
3. Screen 100 nasopharyngeal swabs (50 containing *Neisseria meningitidis*, 20 with known *Neisseria* commensals and 20 unknown samples) to determine the sensitivity and specificity of the detection assay

Techniques:

1. Primer and Fluorescent probe design
2. Real-time PCR analysis
3. Culture and characterization of commensal *Neisseria sp.*

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

AHO, E., FINK, A., and OGKE, J. 2018. *Neisseria mucosa* displays inhibitory activity against other *Neisseria* species. 21st International Pathogenic *Neisseria* Conference (San Fransico, 2018)

SO, M., KIM, W., HIGASHI, D., GOYTIA, M., PILLGUA-LUCAS, M., RENDON, M.A., BRONNIMAN, M., DUNCAN, J., and ANN JERSE. 2018. Tribal warfare: commensal *neisseria* kills *N. gonorrhoeae* via its DNA. 21st International Pathogenic *Neisseria* Conference (San Fransico, 2018)

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor Phone number, email address and location
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School of Biomedical Sciences Coordinating supervisor

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Project title

Testing the “Carbonyl Stress” Concept

Project location:

Pharmacology unit, M-block, QE2 Medical centre

Project description

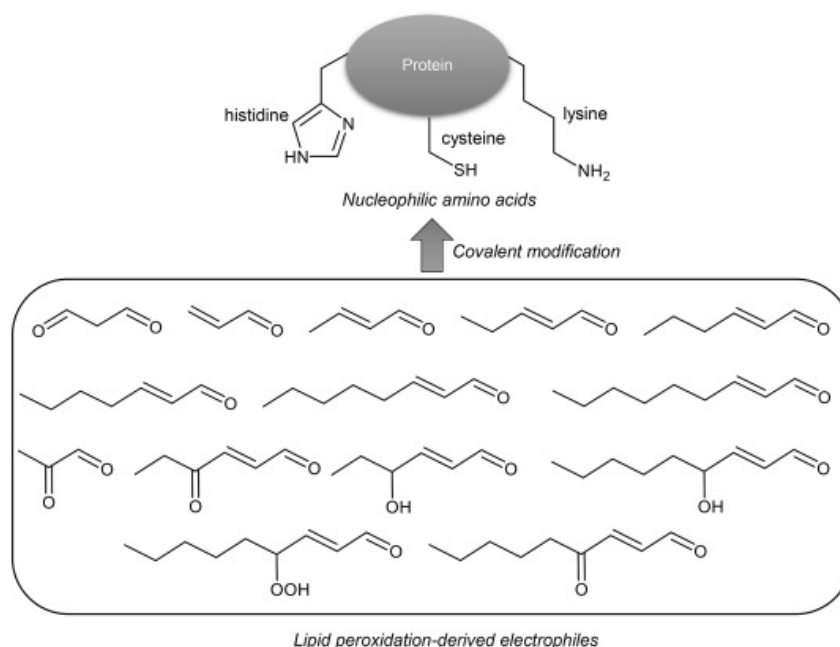
An increase in free radical formation during oxidative stress causes damage to many cell constituents, with polyunsaturated lipids in cell membranes among the most vulnerable targets. The oxidation of methylene bridges within unsaturated lipids triggers an autocatalytic cascade that fragments the hydrocarbon tail of fatty acids, releasing a variety of toxic “lipid-derived electrophiles” or LDEs. The most important of these are α,β -unsaturated compounds such as acrolein, malondialdehyde and 4-hydroxynonenal. The possession of two electrophilic centres (carbonyl and double bond) in close proximity within unsaturated LDEs confers high toxicological relevance due to their ability to attack cell macromolecules to form adducts that are drivers of various biochemical changes, transcriptional responses and even cell death. Although they can attack many targets, the thiol group (-SH) possessed by cysteine groups is preferred on chemical grounds (see image below).

Although LDE’s are widely implicated in many pathological conditions, much of the literature that implicates these agents in human disease involves “single compound” studies in which researchers investigate LDE involvement one compound at a time, such as acrolein or 4-hydroxy-nonenal. In tissues that are experiencing oxidative stress however, it is likely that multiple LDEs are generated simultaneously, creating a condition known as “carbonyl stress.” Since these unsaturated LDEs share a common mechanism of toxic action (i.e. all promote adduction of cell proteins), these compounds might be expected to induce greater damage when they are formed as part of a “LDE soup” than when cells are exposed to each compound in isolation. Accordingly, although a single LDE might be present at subtoxic concentrations, yet in conjunction with other LDEs might actually exert a greater toxic effect than we might expect. Somewhat surprisingly the evidence base of research data to support or refute this expectation is surprisingly thin.

This project will explore the hypothesis that combined exposure to multiple LDEs results in additive or synergistic toxicity.

The project will involve the use of a yeast model of carbonyl toxicity to seek evidence for toxicological interactions between multiple toxic carbonyl compounds. The experiments will involve the use of straightforward chemical, biochemical and immunochemical methods. The project will also involve the testing of carbonyl scavenger drugs such as edaravone to see if these agents can protect against the toxicity that accompanies exposure to multiple endogenous LDEs.

The project would be well suited to candidates with majors in pharmacology, biochemistry or chemistry who have a strong interest in toxicology.



Protein damage during carbonyl stress likely involves multiple LDEs (from Shibata and Uchida, 2019)

Some papers for further reading:

Golla U, Bandi G, Tomar RS (2015) Molecular cytotoxicity mechanisms of allyl alcohol (acrolein) in budding yeast. *Chem Res Toxicol.* 28: 1246-64.

Shibata T, Uchida K (2019) Protein adductomics: A comprehensive analysis of protein modifications by electrophiles. *Free Radic Biol Med.* S0891-5849(18)32648-0.

Zhang L, Geohagen BC, Gavin T, LoPachin RM (2016) Joint toxic effects of the type-2 alkene electrophiles. *Chem Biol Interact.* 254:198-206.

School of Biomedical Sciences

Honours in Medical Research 2020
Research Project Proposal

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Project Title

Exploring pharmacological approaches to inhibit mucus hypersecretion using *ex vivo* and *in vivo* murine models of airways disease

Project location:

Respiratory Pharmacology – Rms 1.30-1.34, M block QEII

Project Description

Accumulation and retention of airway mucus contributes to airway obstruction in patients with many chronic airway diseases including asthma, chronic obstructive pulmonary disease (COPD) and cystic fibrosis. Excessive airway mucus causes persistent symptoms including coughing and expectoration of phlegm, which can be socially and physically disabling. The presence of excessive amounts of airway mucus reflects an increased capacity to synthesise mucins (increased numbers of mucus-producing epithelial cells and larger submucosal glands) and increased secretion of mucins.

The principal aim of the project(s) will be to determine the extent to which selected pharmacologic agents can inhibit mucus hypersecretion in murine airways. In these studies, mucus hypersecretion will be induced by exposing murine airways, either *in vivo* or *ex vivo*, to various pro-inflammatory stimuli (e.g. house dust mite allergens, bacterial wall products). Hypersecretory airways will then be exposed to agents that stimulate mucus secretion (e.g. allergen, ATP, mAChR agonist, substance P, acrolein) in the presence and absence of putative inhibitors of mucus secretion (e.g. azithromycin, mAChR antagonists, NK receptor antagonists, TRPA1 antagonists). The effects of these agents on mucin hypersecretion will be quantitated using histological, biochemical and immunochemical approaches.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor

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Pharmacology Coordinating supervisor **Same as primary? Yes No**

If No: Name Phone number, email address and location

Other supervisor/s Phone number, email address and location

Jay Steer jay.steer@uwa.edu.au, M Block G.30

Project title

Exploring the role of genes upregulated by CSF-1 during macrophage differentiation

Project location:

Pixley lab, G.32, M Block, QEII MC

Project description

Macrophages infiltrate tumours to help cancer cells grow and invade. High levels of the macrophage growth and migration factor, CSF-1, correlate with a poor prognosis in many cancers, including breast cancer.

CSF-1 signals through its receptor, CSF-1R, to stimulate differentiation and migration in macrophages. Since macrophages infiltrate tissues to carry out their normal functions as well as their disease promoting activities, studies in the Pixley laboratory are aimed at identifying the specific CSF-1 pathways that control how macrophages move in and through tissues. Understanding these signalling pathways is helping us to develop therapies that inhibit macrophage migration to disease sites.

School of Biomedical Sciences
Honours in Medical Research 2020
Research Project Proposal

Primary supervisor

A/Prof Fiona Pixley 64574047; Fiona.pixley@uwa.edu.au

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Other supervisor/s Phone number, email address and location

Steve Mutsaers steven.mutsaers@uwa.edu.au, Institute of Respiratory Health, Perkins

Project title

Examining the efficacy of a macrophage targeting drug in a mouse model of melanoma.

Project location:

Pixley lab, G.32, M Block, QEII MC & Mutsaers lab, 7th floor, Perkins Building

Project description

Macrophages infiltrate tumours to help cancer cells grow and invade. Increased numbers of these tumour associated macrophages correlate with a poor prognosis in many cancers, including breast cancer and melanoma.

We have tested a drug that targets macrophages but not tumour cells and shown that it produces a striking reduction in tumour growth in a mouse model of breast cancer. We would now like to test this drug in a mouse model of melanoma.

This project will be shared between the Mutsaers lab, which has experience with the melanoma model, and the Pixley lab, which has experience in analysis of tumour associated macrophages.