Faculty of Pharmacy

Honours Research Project Areas

2015
Name of Primary Supervisor: Prof. Alan Boddy

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Email: alan.boddy@sydney.edu.au
Phone: 8627 0205

Name of other academic and research staff involved in the project and / or supervisory team:

How many students will this project be available for?
1

Project Title
Interactions between proton pump inhibitors and anti-cancer drugs

Project Summary
Many cancer patients take proton pump inhibitor, either prescribed or as over-the-counter medication. Although these drugs are known to be potential inhibitors and inducers of drug-metabolising enzymes, there has been little systematic work to evaluate the potential for such drug interactions to influence cancer chemotherapy.

The student will perform in vitro investigations of the metabolism of a selection of anti-cancer drugs, and evaluate the potential for inhibition by omeprazole and other drugs. Based on laboratory investigations, the student will use modelling software such as Simcyp to evaluate the likely magnitude in cancer patients of the observed inhibition.

Aim
To evaluate drug interactions between PPIs and cancer chemotherapy

Significance
Potential impact on cancer treatment.

Methods
Drug and metabolite analysis – HPLC or LCMS
In vitro metabolism – incubation with human liver microsomes
PBPK modelling – Simcyp software.

Feasibility
Materials are available, and access to HPLC and LCMS can be arranged. Access to the required software will be arranged under academic license. Further support through PhD student and Post-Doctoral fellow.

References


Faculty of Pharmacy Research Theme(s)
Cancer
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<th><strong>Name of Primary Supervisor:</strong></th>
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<tr>
<td>Prof. Andrew McLachlan</td>
<td>Email: <a href="mailto:andrew.mclachlan@sydney.edu.au">andrew.mclachlan@sydney.edu.au</a></td>
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<td>Phone: 9767 7373</td>
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<th><strong>Name of other academic and research staff involved in the project and / or supervisory team:</strong></th>
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<tr>
<td>Rosemary Burke</td>
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<td>Director of Pharmacy, Concord Hospital</td>
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**Project Title**

Medication management issues at a University teaching hospital

**Project Summary**

*This project is based at Concord Hospital*

**Aim**

This project will explore medication management issues at University Teaching Hospital based on process and outcome data.

The specific themes of the relate to the following topics:

- Outcomes from drug committee decisions individual approvals (e.g. rituximab)
- Patient case-series on anticoagulants & DOACS
- Weight based dosing & accuracy of weights
- Care transition medication management– post-discharge from ICU
- ADR reporting at CRGH
- Medication reconciliation
- Audit of medicines on hospital discharge summaries

**Significance**

The Drug and Therapeutics Committee has oversight of medication management in the hospital. The findings of this research will inform the design and evaluation of medication management services in the hospital with implications for public hospitals.

**Methods**

Retrospective and prospective research methods to gather clinical and laboratory data. This will include the use of clinical audits and surveys.

**Feasibility**

This project is supported the Director of Pharmacy in the Pharmacy Department at Concord Hospital. This project will require ethics approval [low or negligible risk], which will be obtained before the commencement of the project.

**References (if any)**


**Faculty of Pharmacy Research Theme(s)**

Health Services and Patients Safety
**Name of Primary Supervisor:**
Prof. Andrew McLachlan

**Contact details**
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**Phone:** 9767 7373

**Name of other academic and research staff involved in the project and/or supervisory team:**
Fiona Bournazos,  
Senior Pharmacist (Antimicrobial Stewardship)  
Pharmacy & Infectious Diseases/Microbiology Departments, Concord Hospital

**How many students will this project be available for?**
1

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**Project Title**
Investigating the impact of antimicrobial stewardship at a University Teaching Hospital

**Project Summary**
*This project is based at Concord Hospital*

**Aim**
This project will explore the impact of antimicrobial stewardship services at University Teaching Hospital based on process and outcome data.

The specific themes of the relate to the following topics:
- antimicrobial ADR reporting at CRGH
- Appropriate continuation of stress ulcer prophylaxis
- IV to oral switch of antimicrobial agents
- Continuous vs. intermittent infusions
- Assessing the impact of AMS ward rounds
- The use of antimicrobials for non-infectious conditions

**Significance**
AMS represents a new and important initiative to improve the quality use of antimicrobial agents. This project will generate evidence to support the impact of AMS service.

**Methods**
Retrospective and prospective research methods to gather clinical and laboratory data. This will include the use of clinical audits and surveys.

**Feasibility**
This project is supported the Senior Pharmacist (Antimicrobial Stewardship) and the Pharmacy & Infectious Diseases/Microbiology Departments. This project will require ethics approval [low or negligible risk], which will be obtained before the commencement of the project.

**References (if any)**

**Faculty of Pharmacy Research Theme(s)**
Health Services and Patients Safety
### Name of Primary Supervisor:
Dr Annette Gross  
Director, Ethnopharmacology, GSK R&D

### Contact details
**Email:** annette.s.gross@gsk.com  
**Phone:** 9684 0845

### Name of other academic and research staff involved in the project and / or supervisory team:
Dr Sophie Stocker, CPMS, GSK  
Dr Romina Nand, CPMS, GSK  
Dr Christine Clifton, CPMS, GSK  
Dr Fanfan Zhou (Faculty liaising supervisor)

### How many students will this project be available for?
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<th>Project Title</th>
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<td>Can clinical trial data obtained in Europe and North America inform drug development in Africa and South America?</td>
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<th>Project Summary</th>
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<td><em>The Ethnopharmacology Group in Clinical Pharmacology Modelling &amp; Simulation, GlaxoSmithKline Research &amp; Development is pleased to offer an Honours Project in 2015 for students in the Faculty of Pharmacy, University of Sydney. This project relates specifically to an important issue for the interpretation of the results of multiregional clinical trials performed during global drug development programmes.</em></td>
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Clinically significant inter-ethnic differences in drug response have been reported for a number of drugs [Bjornsson, 2003]. In particular different responses for drugs used in the treatment of some cardiovascular diseases have been reported in African American relative to European American subjects [Ref]. These differences in drug response have been related to inter-ethnic differences in drug pharmacokinetics, pharmacodynamics or the underlying biology of the disease being treated. Such inter-ethnic differences can in turn be attributed to differences between populations in the profile of the intrinsic factors (such as genetics and body weight) and extrinsic factors (such as environmental exposures) which contribute to inter-individual variation in drug response [Bjornsson, 2003]. Understanding these inter-ethnic differences is key to establishing appropriate doses of new drugs during global drug development.

In general, drug development in sub-Saharan Africa has focussed on infectious diseases which are a considerable burden in the local geographic region. For new drugs for non-communicable diseases, only limited dose response information is often available in subjects of African ancestry resident in Africa. In order to bridge this knowledge gap, the relevance of data collected in African Americans resident in North America to Africans resident in Africa warrants evaluation. This approach is considered because from a genetic perspective, African Americans most closely resemble the populations of western African countries, consistent with historical narratives [Bryc, 2010; Tishkoff, 2009]. Most African Americans have some non-African ancestry [Zakharia, 2009], with an average of 13% European ancestry reported by a recent genetic study [Tishkoff, 2009]. The diversity among the populations of Africa is also widely acknowledged from a linguistic, anthropological and genetic perspective [Bryc, 2010].
In addition to genetics, differences in extrinsic factors such as diet, environment and local medical practise may potentially influence the relevance of data from African American subjects to the populations of Sub-Saharan Africa. Even though these extrinsic factors will differ, information on the profile of important intrinsic ethnic factors, such as demographics, is not currently available in clinical trial participants. In particular some equations used to estimate glomerular filtration rate from serum creatinine include cofactors for African American subjects. The use of these equations in individuals in Africa in the context of global drug development has not been evaluated. In summary, it remains unclear whether clinical trial data collected in African Americans resident in the North America is relevant to subjects of African ancestry resident in Sub-Saharan Africa.

There is rich ethnic diversity in the population of South America. Although many individuals have only European, Native American or African ancestry, a considerable proportion of the South American population are of mixed geographic ancestry. Intrinsic ethnic factors in these groups of clinical trial participants will also be profiled relative to clinical trial participants in North America and Europe. This evaluation will inform conclusions regarding the relevance of clinical trial results obtained in South America to Western populations, as well as the relevance of Western data to South American populations.

Aim
To evaluate the profile of intrinsic ethnic factors in North American and European clinical trial populations relative to the diverse populations resident in Africa and South America as relevant to multiregional clinical trials.

Significance
This project will contribute to the evidence base evaluating the relevance of African American clinical trial data to populations in Africa as well as evaluating the relevance of European/North American clinical trial data to populations in South America. This project will also provide insight into the demographic heterogeneity within African and South American populations. Importantly this project will use demographic data from subjects included in global drug development programmes.

Methods
This project will use de-identified data obtained from GSK clinical trials which have been approved for secondary use i.e. appropriate ethics committee and subject informed consent have been obtained. Demographic data in specific populations of interest, for example in African Americans and subjects of African ancestry resident outside North America, will be compared as appropriate. A particular focus of the project will consider equations used to estimate renal function. Peer reviewed literature and other relevant data sources (e.g. WHO databases) will be referenced as required during this evaluation.

Feasibility
This project utilises internal GSK data which has previously been approved for secondary use.
and therefore additional ethics approval is not required. These databases are available for extraction of relevant data. Given the varying day-to-day work commitments of the Primary Supervisor, Dr Sophie Stocker and other members of the GSK Ethnopharmacology Group will be able to support the Honours student, as required.

References

Faculty of Pharmacy Research Theme(s)
Cardiovascular and Diabetes
Project Title
Spindles, drugs and memory – an exciting nexus

Project Summary
The project is suited for a highly motivated student who is willing to work with a high powered sleep research group, and interested in training for conducting sleep studies.

Sleep is an important part of human physiology, and plays a role in energy restoration and memory consolidation. Sleep is often mapped using a brain EEG (Electroencephalogram) along with other cardiovascular, respiratory and musculoskeletal markers in a test known as Polysomnography (PSG). Spindles are classic EEG manifestations occurring during ‘light sleep’. Recent evidence suggests that spindles are associated with sleep maintenance, and may be linked to memory and memory related performance. Interestingly, it is also known via experimental studies that certain drugs can influence sleep spindles. These initial data provide a rationale for further testing the hypothesis that pharmacological enhancement of sleep spindles may lead to improvements of sleep maintenance and daytime function in patients, particularly those with sleep disorders, who manifest deficits in spindle formation when asleep.

Aim: This project will explore the effect of select CNS active drugs such as benzodiazepines and non benzodiazepine GABA receptor agonists (zolpidem, zopiclone) on sleep spindles and declarative memory.

Methods: 5-10 volunteer healthy patients will be administered select drugs at clinical doses and their EEGs monitored via polysomnography in nap studies or full overnight PSGs. Sleep spindles will be detected and measured using an automated algorithm linked to EEG data. These volunteer participants will be asked to participate in specially designed declarative memory tasks. These data will allow the research team to explore associations between specific drugs,
their effect on sleep spindles and memory tasks.

**Feasibility:** Automated algorithms to detect spindles are being tested in one of the 2014 honours projects. The research team has combined experience in EEG and PSG conduct. The project will be housed at the Sleep labs in the Woolcock Institute of Medical Research; these facilities are world class, and research on biomarker mapping and drug effects on sleep is already being conducted at these facilities. An ethics application to conduct the project will be prepared by the end of the year. There will be clinician oversight of the protocol and participating patients.


**Significance:** This project has the potential for discovering a novel pharmacological way of enhancing memory by manipulating sleep biomarkers. Given the high prevalence of sleep disorders and conditions where memory is affected, this research can potentially have far reaching consequences.

**Faculty of Pharmacy Research Theme(s)**
Respiratory and Mental Health
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<th><strong>Name of Primary Supervisor</strong></th>
<th><strong>Contact details</strong></th>
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<tr>
<td>Dr Bandana Saini</td>
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<td>Phone: 02 93516789</td>
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<th><strong>Name of other academic and research staff involved in the project and / or supervisory team</strong></th>
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<tr>
<td>Ms Janet Cheung, Faculty of Pharmacy, University of Sydney (PhD candidate)</td>
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<tr>
<td>Dr Jason Ellis, Director, Sleep Research Centre Northumbria, UK.</td>
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<tr>
<td>Investigators from the CRC for Alertness, Safety and Productivity, Woolcock Instt of Medical Research, Sydney</td>
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<td>Sedatives, sleep and safety - stepping forward</td>
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<th><strong>Project Summary</strong></th>
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<td>The consumption of some psychotropic medicines has a negative effect on psychomotor and cognitive skills such as concentration, mood, coordination and reaction times. Sedative and hypnotic medications obviously fall in this category. A key area of focus in this regard is driving and use of heavy machinery. All psychoactive medications are legally required to have the dispensing pharmacist place the L1 cautionary label on the medication pack. This label states that the drug may cause drowsiness and that caution should be exercised when using heavy machinery or driving. However, there has been very little research on how consumers understand such warnings, and how they apply them to their personal lives/settings. Nor is there any information on how the risk is communicated to patients. These issues inform the aim of this study.</td>
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<th><strong>Methods:</strong></th>
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<td>The research will involve multiple focus groups with general consumers, who drive, professional drivers, pharmacists, clinicians (GPs and sleep physicians, psychiatrists). In this phase participants will be asked about the risk assessment undertaken before prescription and how the medication risk communication accompanying a prescription is conducted. In case of consumers and pharmacists this exploration will include over the counter medications such as antihistamines, pain killers and cold/flu tablets. Consumers will be asked how they understand and interpret standard warnings such as those on the cautionary Label 1. The focus group discussions will be recorded, transcribed and content analysed for key themes and issues. The information from this project will feed into larger projects.</td>
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<th><strong>Feasibility:</strong></th>
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<td>The research team has significant experience in the conduct of qualitative research. The ethics application will be prepared by the end of the year, and all materials to conduct the project will be readied. Facilities required for the conduct of the project are available in house (venues with facility of audio recording)</td>
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<th><strong>Significance:</strong></th>
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<td>Our vision for a large scale national project is to build better sources of information on the effect of medications on driving safety, and improved ways of communicating this information to drivers.</td>
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<td>Respiratory and Mental Health</td>
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**Name of Primary Supervisor:**
Dr. Betty Chaar  
**Contact details**  
**Email:** betty.chaar@sydney.edu.au  
**Phone:** 9036 7101

**Name of other academic and research staff involved in the project and / or supervisory team:** TBC  
**How many students will this project be available for?**  
1

**Project Title:**  
Medicine shortages in Australia

**Project Summary**  
Clinical and therapeutical healthcare cannot exist without medicines and therapeutic products. There has been a worldwide phenomenon of medicine shortages over the last few years, which has reached Australia. There are many reasons for shortages in medicines supplies: ranging from logistics, to lack of raw materials and reliance on limited resources or the occurrence of epidemics.

The impact of medicine shortages has been well documented, and includes potential harm and suffering for patients, inconvenience and increased costs related to treatment.

In Australia the manufacturing of medicines is limited, and we often rely on external importation of medicinal products. Thus we are as vulnerable as any other country to medicine shortages. The TGA has initiated a website for the monitoring of medicine supplies, providing notice for the imminent shortage of supply of any particular medicine.

The questions arising: is this initiative sufficient enough to prevent potential harm or lack of treatment for patients? What else can be done to promote awareness and try to prevent or lessen the incidence of medicine shortages? Can we trace the reason for shortages and address each case of shortages as they occur?

**Aim:**  
To explore the impact of the TGA’s initiative and the reasons behind some existing shortages of medicines in Australia

**Methods**  
This project involves researching the reason/s behind current shortages of medicines in Australia by exploring sources of medicines, management of shortages and possible prevention. This can be achieved by taking examples of shortages from the TGA webpage, and trace the production and supply chain of the medicines back to their origins to detect where the weakness in the chain is and how to address it. This research may be supplemented with semi-structured interviews with key stakeholders and managers in the pharmaceutical industry.

**Feasibility**  
This project will require ethics approval [low or negligible risk] for interviews to be conducted, which will be obtained before the commencement of the project; and all resources for investigating the production/ market chain are available within the faculty.

**References**  

**Faculty of Pharmacy Research Theme(s):** Health Services and Patient Safety
**Primary Supervisor:**  
Dr. Betty Chaar

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<td><strong>Email:</strong> <a href="mailto:betty.chaar@sydney.edu.au">betty.chaar@sydney.edu.au</a></td>
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<td><strong>Phone:</strong> 9036 7101</td>
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**Name of other academic and research staff involved in the project and / or supervisory team:** TBC

**Project Title**  
Medicines Use in the Elderly

**Project Summary**  
As people age there is an anecdotally observed tendency to increase medicine intake, and for long periods of time. There are studies which indicate no particular benefit to some medicines, such as statins, being taken for very long periods of time over a certain age. This project seeks to explore the nature of medicines being taken by residents of nursing homes, who will have either high level care or low level care, and for how long they have been taking these medicines. We hypothesise that there may be over-utilisation of some medicines, in the elderly stratification of our population.

**Aim**  
To investigate medicines use by aged care residents in nursing homes around Sydney.

**Significance**  
This project could highlight a gap in clinical decision making, which may be instigating a high cost in our healthcare expenditure. This project may provide some evidence for the recommendation to create guidelines for when to cease prescribing or what is now known as “deprescribing”.

**Methods**  
We will approach nursing homes for permission to access residents’ medical notes and gather data from their current medicines chart. All data will be stratified into high level care and low level care, and completely de-identified. Once we have achieved a significant data collection, we will analyse the data statistically and report any recommendations ensuing.

**Feasibility**  
This project will need ethics approval which we will start early in the year. The other resources needed are readily available in the faculty.

**Faculty of Pharmacy Research Theme(s)**  
Health Services and Patient Safety
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<th>Name of Primary Supervisor</th>
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<td>Dr Carl R Schneider</td>
<td>Email: <a href="mailto:carl.schneider@sydney.edu.au">carl.schneider@sydney.edu.au</a>&lt;br&gt;Phone: 93096015</td>
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<td>Esther Mier, Manager, Meditrax, A/Prof Tim Chen</td>
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**Project Title:**
Psychotropic medication monitoring in Australian aged care facilities.

**Project Summary**

**Background**
The frequent use of psychotropic medication in the residential care population is of concern.¹ Psychotropic medication is often used to treat challenging behaviour associated with dementia, however they are associated with significant side effects.² Despite the efforts of health professionals, care home staff and government agencies, overall use of these agents in this population has yet to decrease.³ However medication review has been shown to reduce psychotropic prescribing.⁴ Australian guidelines recommend treatment with benzodiazepines for no longer than two weeks and for antipsychotic therapy to be reviewed after no more than three months.⁵ However, nursing homes may have individual monitoring guidelines. You will be working with the Meditrax team of accredited consultant pharmacists to investigate the monitoring practices for psychotropic medication in Australian aged care homes. This is an extension of the research collaboration which started in 2014.

**Aim**
To determine the monitoring practices for psychotropic medication use in the care home population.

**Significance**
By establishing the current monitoring practices for psychotropic medication in aged care homes, practice improvement may be achieved via development of targeted interventions.

**Methodology**
The research methodology will consist of surveying aged care home monitoring practices and undertaking analysis of nursing home psychotropic audit data. It is expected that this research will result in publication/s.

**Feasibility**
This research project has been approved by the University of Sydney Human Research Ethics Committee.

3. Snowdon J, Galanos D, Vaswani D. Patterns of psychotropic medication use in nursing

Faculty of Pharmacy Research Theme(s)
Mental Health
Name of Primary Supervisor
Dr Carl R Schneider

Contact details
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Phone: 93096015

Name of other academic and research staff involved in the project and/or supervisory team
Dr Rebekah Moles

How many students will this project be available for?
1

Project Title
Walking in consumers’ shoes: Reshaping the pharmacy student placement curriculum via mystery shopping with feedback

Project Summary
We have conceived a novel approach to the pharmacy student placement curriculum that requires students to be active participants in work-integrated learning rather than passive observers. That is, third-year pharmacy students will assume the role of the consumer and request non-prescription medicines, allowing them to reflect on what it is like to be a consumer. They will also act as peer educators by providing feedback to pharmacy staff.

The aim of this trial is to determine whether learning outcomes, research engagement and clinical competence achieved by pharmacy students participating in mystery shopping with feedback placements are superior to the achievement of students undertaking the traditional pharmacy clinical placement curriculum. The specific objectives are to:

- Measure the impact of this trial on pharmacy student learning, research engagement and clinical competence.
- Investigate the feasibility and acceptability of pharmacy students acting as mystery shoppers and providers of feedback to pharmacy staff.

Pharmacy Student Evaluation (Deliverables):
- Student focus groups to investigate feasibility of the trial, perceived changes in professional identity and barriers and facilitators to implementation will occur in this project. Transcripts will be thematically analysed.
- To assess outcomes of student learning, all pharmacy students in third year will be requested to complete two voluntary questionnaires. Questionnaire 1 will measure students’ perceived clinical competency using Miller’s levels of competency, mapped to the National Competency Standards Framework for Pharmacists in Australia. This questionnaire has been designed with reference to the Pharmacy Experiential Placements Tool developed in the ALTC Experiential Placements in Pharmacy Project, 2010. Questionnaire 2 will measure students’ attitudes towards pharmacy practice research as this trial engages students in research enriched learning and teaching. Analysis of variance will be used to detect changes in scores within and between groups for both questionnaires. In anticipation of a biased sample (volunteer recruitment), adjustment of baseline differences may occur.
- Student OSCE examination marks will be retrieved and compared with those that were involved in the trial versus the standard cohort.
Value/Need for Project
This trial enables us to compare the traditional placement curriculum with a new method of student exposure to their profession. The methods employed encourage students to be active contributors to professional practice improvement, thereby acting as change agents. Benefits for students include improvement in communication skills, clinical competency, and research engagement. Students may also improve in their ability to reflect on their practice, gain confidence and enhance the development of their professional identity. This authentic work-integrated learning approach may revolutionise pharmacy education.

Feasibility
This research project has been approved by the University of Sydney Human Research Ethics Committee.

Faculty of Pharmacy Research Theme(s)
Health Services and Patient Safety
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<th><strong>Name of Primary Supervisor</strong></th>
<th><strong>Contact details</strong></th>
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| Dr. Claire O’Reilly         | **Email:** claire.oreilly@sydney.edu.au  
|                             | **Phone:** 9351 2729 |

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| A/Prof Timothy Chen  
Mental Health colleagues at RNSH | 1 |

**Project Title**
Carers and staff perspectives of discrimination and stigma in community mental health

**Project Summary**
The behavioural consequences of stigma (i.e. discrimination) can compound the disability of people with mental illness, and may lead to disadvantages in many aspects of life, including personal relationships, education and work. This can limit the life opportunities of those affected, through loss of income, unemployment, reduced access to housing or health care, and other important means of recovery. This project will investigate the experiences of stigma and discrimination from the perspective of those caring for consumers living with schizophrenia; carers and community mental health staff.

**Aim**
To describe the experiences of stigma and discrimination among people living with schizophrenia from the perspective of carers and community mental health staff. The specific objectives are to explore:

- the level of unfair treatment experienced due to mental health problems (experienced discrimination)
- the level of discrimination experienced when seeking health care
- times people have stopped doing things due to mental health problems (anticipated discrimination)
- how people have overcome stigma and discrimination experienced due to mental health problems
- the level of positive discrimination experienced due to mental health problems

**Significance**
The expected outcomes from this study include:

- In-depth understanding of experiences of anticipated and experienced stigma and discrimination among clients of community mental health services in NSW from the perspective of carers and mental health staff.
- This study will provide important baseline data on the type and levels of discrimination experienced by clients of community mental health services which will help the development of an intervention with service-users families & key primary health care staff to counter any significant experienced stigma and discrimination.
Methods
This will be use a cross-sectional study design and will follow on from work conducted as part of an honours project in 2014. In 2014 a cross sectional study of consumers living with schizophrenia (through the Assertive Outreach Team (AOT) at Royal North Shore Hospital) was conducted using the Discrimination and Stigma Scale (DISC-12). Early results from this project indicate the experiences of stigma and discrimination from the consumer themselves may differ from what carers and mental health staff notice while providing care to consumers living with schizophrenia. Community mental health staff and carers of clients of AOT will be invited to participate in a face-to-face interview that will last approximately one hour. This interview consists of 32 questions that surround the participant’s experiences of discrimination in key areas of everyday life such as accessing health care, work, relationships and housing. Results will be compared with the consumer’s experience from the 2014 results.

Feasibility
Ethics has been approved for five years from April 2014 through Northern Sydney Local Health District and this proposed project will only need a minor ethics modification. The project only requires a small amount of consumables such as printing and postage. Depending on the findings from this research, it may be submitted for publication in a scientific journal. If considered appropriate, an open access journal with a publication fee may be selected.

References (if any)

Faculty of Pharmacy Research Theme(s)
Mental Health
**Project Title**
Resolution X-ray Crystallography: Pharmaceutical Co-crystals by Design

**Project Summary**
Over the last decade, the importance of the design and characterisation of pharmaceutical co-crystals has become an area of primary interest to both industry and academia. Co-crystals incorporate pharmaceutically acceptable guest molecules into a crystal lattice along with the Active Pharmaceutical Ingredient (API) and improve physicochemical properties such as poor dissolution rate, solubility, chemical stability and most importantly, improve the therapeutic efficacy of many pharmaceuticals, and significantly lower the market value of the drug. Multi-component crystals, e.g., solvates, hydrates, co-crystals, and salts have an important role in new formulations that address these issues particularly in the pharmaceutical area.

Finally, using the information gained, we will produce new co-crystal forms with targeted properties. This stream embodies a substantial research program exploring both the structural and electronic nature in the construction of assemblies that are fundamental to crystal formation, enzyme catalysis, and receptor binding. Possible combinations for study are given below in table 1.

<table>
<thead>
<tr>
<th>API1</th>
<th>API2</th>
<th>Indication</th>
<th>API1</th>
<th>API2</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel</td>
<td>Aspirin</td>
<td>Anticoagulant</td>
<td>Thiazide</td>
<td>CCB’s</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Risedronate</td>
<td>Calcium</td>
<td>Osteoporosis</td>
<td>Levodopa</td>
<td>Carbidopa</td>
<td>Parkinsonism</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>Salmeterol</td>
<td>Asthma</td>
<td>Budesonide</td>
<td>Eformeterol</td>
<td>Asthma</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Esomeprazole</td>
<td>Pain/GERD</td>
<td>Cacipotiene</td>
<td>Corticosteroids</td>
<td>Psoriasis</td>
</tr>
</tbody>
</table>

Table 1 Combination Treatments that could form co-crystals

**Aim**
This project seeks to design API co-crystals that can be used as novel formulations.

**Significance**
This research proposal brings together three major research streams grouped under the common theme of the understanding of non-bonded interactions of known co-crystals using X-ray crystallography, and how these interactions may be specifically tailored, aiding the development of new drugs and formulations. The first involves the application of this methodology to a study of the intermolecular interactions of small molecules with predefined intermolecular binding modes, in an attempt to discern the individual contributions of the interactions mentioned above. Stream two concentrates on the use of Electron Density methods in the study of co-crystals that contain far larger host-guest complexes, so that greater numbers of interactions can be determined in a single experiment, and will advance this powerful tool to a level where they can...
be used routinely for API/co-former construction.

**Methods**
The methodology will involve computational design and synthesis co-crystals, as well as X-ray diffraction methods to determine the impact of potential inhibitors on NDM-1 uptake.

**Feasibility**
All tools and expertise are available. The concept of designing co-crystals that contain more than one API is feasible, with applications in drug discovery.

**References**
**Name of Primary Supervisor**  
Prof. Dai Hibbs

**Contact details**  
**Email:** david.hibbs@sydney.edu.au  
**Phone:** 02 9351 6005

**Name of other academic and research staff involved in the project and / or supervisory team**  
Prof Paul Groundwater  
Prof John Perry (UK)

**How many students will this project be available for?**  
1

**Project Title**  
Design and synthesis of small molecules for NDM-1 inhibition

**Project Summary**  
New Delhi metallo-β-lactamase (NDM-1) is a recent addition to the antibiotic resistance weaponry of Enterobacteriaceae. It has been found to confer resistance to most β-lactam antibiotics, including carbapenems. Since its discovery in 2008, NDM-1 producing bacteria have disseminated globally, facilitated predominantly by gut colonisation and the conjugation of plasmids carrying the \textit{bla}_{NDM-1} gene. NDM-1 producers are involved in infections in both hospital and community settings and have also been isolated from water sources in India. With few effective antibiotics against NDM-1 producers, and resistance developing to those remaining, there has been a push to develop new treatments effective against NDM-1 producers.

**Aim**  
This project seeks to design small molecules that inhibit NDM-1.

**Significance**  
The rapid spread of broad spectrum antibiotic resistance conferred by NDM-1 makes it a very real threat to current antimicrobial approaches. This calls for the prioritisation of drug design attempts to find effective antibiotics against NDM-1. The development of increasingly sophisticated virtual compound library screening techniques in recent years may hold great potential in the search for NDM-1 inhibitors. Coupled with high resolution NDM-1 crystal structures, these approaches are able to rapidly and accurately assess binding interactions between NDM-1 and extensive libraries of chemical compounds; thus enabling the identification of better inhibitors.

**Methods**  
The methodology will involve computational design and synthesis of small molecules, as well as cell-based assays to determine the impact of potential inhibitors on NDM-1 uptake.

**Feasibility**  
All tools and expertise are available. The concept of designing small molecules that inhibit NMD-1 interactions is feasible, with applications in drug discovery.
References


**Faculty of Pharmacy Research Theme(s)**
Cardiovascular and Diabetes
**Name of Primary Supervisor**
Dr Danijela Gnjidic

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Phone: 02 9351 2298

**Name of other academic and research staff involved in the project and / or supervisory team**
Collaborators from Concord and Royal North Shore Hospitals

**How many students will this project be available for?**
1

<table>
<thead>
<tr>
<th><strong>Project Title</strong></th>
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<tbody>
<tr>
<td>What are the predictors of deprescribing preventative and high risk medicines in older patients?</td>
</tr>
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<table>
<thead>
<tr>
<th><strong>Project Summary</strong></th>
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<tr>
<td>Older people consume the most medicines with approximately 50% of older Australians being exposed to polypharmacy. Exposure to high risk medicines such as those with anticholinergic and sedative effects is associated with adverse health outcomes in older people. To minimise drug-related symptoms in older people, pharmacological treatments should be prioritised and rationalised. Continuing preventative treatments in older people requires the consideration of the expected treatment effects within the context of the estimated life expectancy, potential harms associated with preventative treatments, patients clinical characteristics and individuals health preferences.</td>
</tr>
</tbody>
</table>

**Aim:** The aim of this study is to describe the deprescribing patterns of preventive medicines (Student 1) and high risk medicines (Student 2) according to major clinical characteristics, individuals’ health preferences and estimated life expectancy in older people.

**Significance:** This study will provide the first evidence on the major predictors associated with deprescribing of preventative and high risk medicines in older patients.

**Methods:** A prospective observational study of patients aged ≥65 years admitted to Concord (Student 1) and Royal North Shore (Student 2) Hospitals, Sydney will be conducted. Data will be collected from patient notes, medical charts and patient interviews using a standardised questionnaire, developed by the student. The student will collect data over 3 months, depending on the recruitment rate. As per previous studies, it is envisaged that approximately 100-150 patients will be enrolled during the recruitment period. Data on socio-demographic characteristics, multimorbidity (e.g. number of chronic diseases), and geriatric syndromes (e.g. dementia, frailty) will be obtained from the medical notes. Validated tools will be used to measure frailty (e.g. the Reported Edmonton Frail Scale), patients’ health preferences and estimated life expectancy.

**Feasibility:** The ethical approval will be obtained by the primary supervisor early next year. The students will work on the literature review, research proposal and data collection questionnaire in Semester 1. Data collection and data analysis will occur in Semester 2.

<table>
<thead>
<tr>
<th><strong>Faculty of Pharmacy Research Theme(s)</strong></th>
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<tr>
<td>Health Services and Patient Safety</td>
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<table>
<thead>
<tr>
<th>Name of Primary Supervisor</th>
<th>Contact details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Danijela Gnjidic</td>
<td>Email: <a href="mailto:danijela.gnjidic@sydney.edu.au">danijela.gnjidic@sydney.edu.au</a></td>
</tr>
<tr>
<td></td>
<td>Phone: 02 9351 2298</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Name of other academic and research staff involved in the project and / or supervisory team</th>
<th>How many students will this project be available for?</th>
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<tbody>
<tr>
<td>A/Prof Sallie Pearson</td>
<td>1</td>
</tr>
</tbody>
</table>

**Project Title**
Development and validation of a Frailty Claims Score (FCS) using routinely collected health data

**Project Summary**
Frailty is a clinical syndrome that occurs commonly in older people. It is an important predictor of health outcomes and drug therapy in old age. When assessing the patterns and effects of drugs in large observational pharmacoepidemiologic studies of older people it is important to measure and account for frailty.\(^1\)

**Aim:** The aim of this study is to develop and validate a Frailty Claims-data Score (FCS) for application in pharmacoepidemiologic studies of older adults using administrative claims data.

**Significance:** Development of frailty scores for administrative claims data has a great potential to improve the validity of pharmacoepidemiologic studies in older adults.

**Methods:** Observational study of community-dwelling enrolled in the Concord Health and Ageing in Men (CHAMP) study\(^2\) and linked to administrative datasets will be conducted. The student will calculate the FCS index and will compare it the gold standard frailty index using the sensitivity and specificity analysis. Data on a range of clinical outcomes (e.g. mortality, nursing home admission) will be obtained to test and compare the associations of the FCS and other frailty scores with important health in the CHAMP study.

**Feasibility:** The ethical approval for the study will be obtained by the primary supervisor early next year. The student will work on the literature review and research proposal in Semester 1. Data analysis and interpretation, guided by supervisors and other team members (eg. CHAMP study investigators) will occur in Semester 2.

**References:**

**Faculty of Pharmacy Research Theme(s)**
Health Services and Patient Safety
Name of Primary Supervisor: Dr. Dong Fu

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Phone: 9351 4444

Name of other academic and research staff involved in the project and / or supervisory team: How many students will this project be available for?
1

Project Title: Investigation of AMPK activation in reverse mitochondrial dysfunction and damage during drug induced liver injury.

Project Summary: Drug induced liver injury (DILI) is responsible for many cases of acute liver failure, and is the most common reason for withdrawing new agents during drug development or after approval. Substantial evidence suggested that hepatotoxic drugs target mitochondria and cause hepatocyte damage, revealing the central mechanism for DILI involves mitochondria. Thus, minimizing mitochondrial damage and/or enhancing mitochondrial function may be an important determinant for hepatocyte survival and clinical outcome in DILI. To date, few strategies have focussed on mitochondrial damage for treatment of DILI.

AMP activated kinase (AMPK) is a cellular energy sensor. An important consequence of AMPK activation is promotion of mitochondrial biogenesis and function. AMPK also confers cellular protection by eliminating damaged mitochondria through activation of autophagy. Using collagen sandwich culture of well-differentiated, non-dividing primary hepatocytes, the most useful culture system for study of drug metabolism and testing of DILI, the current project investigates the detail insights of role of mitochondria in DILI and how activation of AMPK prevents liver injury in DILI.

Aim: 1) Examine how hepatotoxic drugs affect mitochondrial function, fusion/fission morphology and mitophagy.
2) Investigate the effect of AMPK activation on reversing/prevention of mitochondrial dysfunction/damage.

Significance: DILI is responsible for 50% of all acute liver failures. DILI is also the main reason for withdrawing drug candidates pre- or post-market. It is difficult to study mechanisms of DILI, particularly ‘idiosyncratic reactions’ in vitro. To date, one of the biggest challenges is to define the cellular mechanisms and pathways through which drugs initiate and produce liver injury. This uncertainty impedes prevention and timely treatment of liver damage. This project defines cellular pathways causing DILI, and unveils novel cellular targets for treating DILI. It will provide fundamental insights into the molecular basis of liver injury that have major implications for treatment, prevention and management of DILI.

Methods: Immunofluorescence for morphological studies; Western blot for protein expression...
and activation examinations; basic cell culture technique; images analysing.

**Feasibility:** All the methods are well established in the lab of Dr. Dong Fu. Dr. Dong Fu will directly supervise the student to ensure the sufficiency and quality of training as well as the progress of the project.

**References:**

Name of Primary Supervisor
Dr Fanfan Zhou

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Name of other academic and research staff involved in the project and/or supervisory team

How many students will this project be available for?
1

Project Title
To investigate the regulatory effect of AMPK on the function and expression of Organic Anion Transporters (OATs/OATPs)

Project Summary
Organic anion transporters (OATs/OATPs) are membrane proteins responsible for cellular entry of a wide range of substances including hormones, toxins and many drugs. They are widely expressed in human key organs including the liver and kidney. They play critical roles in drug absorption, distribution and elimination, therefore, greatly impact on drug performance in body. The function and expression of OATs/OATPs have been found to be altered in diseases, which is often mediated through the regulation of cellular factors such as protein kinases.

5' AMP-activated protein kinase (AMPK) is an enzyme that plays a fundamental role in cellular energy homeostasis and has been confirmed to be closely related to many human diseases including diabetes mellitus and cancer (1-4). Our recent findings indicated that AMPK inhibitors have pronounced regulatory effect on the function and expression of OATs/OATPs. Because OATs/OATPs are responsible for the cellular entry of drugs administered to treat the relevant diseases (eg. diabetes and cancers), the down-regulation of OATs/OATPs caused by the AMPK inhibitors could not only significantly impact on disease progression but also influence the therapeutic outcome of drugs in patients through limiting the drug access to the target cells. Noteworthy, the regulation of OATs/OATPs through AMPK has never been reported before. The AIM of this honors project in 2015 is to investigate the molecular mechanisms involved in the AMPK induced regulation of OATs/OATPs. The SIGNIFICANCE of this project is to form the basis to understanding how OATs/OATPs function will be modulated in diseases and how altered transporter function will feedback to the disease progression as well as drug performance in patients. The research METHODS involved in this project mainly include transporter function assay and western blot analysis. The project is FEASIBLE since similar methods were published by this group before (5-6). There are senior post-graduate students to facilitate the research on a day-to-day base, while Dr. Zhou will directly supervise the honors student in technical training and monitoring the project progress.

REFERENCES:


**Faculty of Pharmacy Research Theme(s)**

Cancer
**Name of Primary Supervisor**  
Dr George Li

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Phone: 9351 4435

**Name of other academic and research staff involved in the project and / or supervisory team**  
Dr Kong Li (Medical School); Dr Jun-Lae Cho; Dr Sunny Kim

**How many students will this project be available for?**  
1

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**Project Title**  
Development of a cellular metabolomics approach for natural product drug discovery against diabetes and cardiovascular disease

**Project Summary**  
Metabolomics is an emerging set of technologies, based on mass spectrometry, enables the monitoring of hundreds of metabolites from biological samples. Metabolites are the terminal downstream products of the genome, and are thus likely to provide useful disease biomarkers. An emerging body of data suggests that metabolites may participate in human physiology in unanticipated ways. Our recent work on endothelial cell lines found amino acid homocysteine caused cell death when used in combination with adenosine and TNF-α. We have also established the great potentials of botanical medicines, pomegranate, kudzuvine, propolis, and centella, for drug discovery for the management of diabetes and cardiovascular diseases. *Therefore, we hypothesise that metabolite perturbations induced by high glucose concentrations, in cellular assays, can be used for drug discovery and mechanistic studies of natural products.*

**Aims**  
The project aims are to:  
1. *To establish a cellular platform to identify metabolites which are perturbed in cell lines exposed to high glucose media.*  
2. *To test the effects of anti-diabetic drugs and natural products on the above metabolite biomarkers.*

**Significance**  
The cellular assay and lead compounds will contribute to drug discovery and development. Ultimately the public health significance of this research will be to improve health outcomes and reduce the financial burden of cardiovascular disease and diabetes. The project will contribute to the National Health Priorities of cardiovascular disease and stroke and to the National Research Priority goals of ‘Ageing well, ageing productively’ and ‘Preventative healthcare’ under ‘Promoting and Maintaining Good Health’.

**Methods**  
These studies will be performed in the following cells with high glucose: adipocyte cells 3T3 L1, liver cells HepG2, Huh7; Monocytes RAW 246.7, THP-1; human-derived cardiovascular (EA.hy926) and cerebrovascular (HBEC-5i) endothelial cells;
The effects of antidiabetic drugs metformin, rosiglitazone, and natural products on the cellular metabolomics profile will be examined. In particular, the effects on metabolites known to be perturbed in diabetes, such as branched-chain and aromatic amino acids, will be explored.

**Feasibility**  
Our research team has the expertise and experience required for this project in analytical chemistry and cell biology. We have extensive publications on natural products and the team members have both national and international ongoing collaborations. Excellent facilities for analytical chemistry and cell biology are at our disposal in the Faculty of Pharmacy, and Charles Perkins Centre (The Mass Spectrometry Core Facility).

**References**


**Faculty of Pharmacy Research Theme(s)**

Cardiovascular and Diabetes
**Name of Primary Supervisor**
Dr George Li

**Contact details**
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*Phone:* 9351 4435

**Name of other academic and research staff involved in the project and / or supervisory team**
Prof Gareth Denyer (School of Molecular Bioscience); Dr Kong Li (Medical School); Dr Sunny Kim; Dr Jun-Lae Cho

**How many students will this project be available for?**
1

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**Project Title**
The pharmacological activities of herbal medicines in metabolic syndrome through regulation of adipocytes

**Project Summary**
Function of the adipose tissue is now prospective issue to study pathophysiology of metabolic syndrome. Herbal medicines have been traditionally used to treat metabolic syndrome, like diabetes. This project will investigate the potential effects of traditional herbs as pharmacotherapeutical agents against metabolic syndrome. The objectives are to identify active chemical compounds in the selected herbal medicines and their effects in the macrophage-adipocyte interaction *in vitro*. The priority herbs are Australian centella, propolis, and Chinese herbs.

**Aims**
1. To perform quality analysis of the *Centalla spp.*, propolis using TLC/HPLC using reference compounds.
2. To separate extracts into fraction and pure compounds and identify their chemical structures.
3. To screen these active constituents for the anti-metabolic syndrome effects (the macrophage-adipocyte interaction) in the established cell lines (eg. 3T3-L1 and macrophage).

**Significance**
The cellular assay and lead compounds will contribute to drug discovery and development. Ultimately the public health significance of this research will be to improve health outcomes and reduce the financial burden of cardiovascular disease and diabetes. The project will contribute to the National Health Priorities of cardiovascular disease and stroke and to the National Research Priority goals of ‘Ageing well, ageing productively’ and ‘Preventative healthcare’ under ‘Promoting and Maintaining Good Health’.

This research will contribute to the urgent need for preclinical and clinical research on complementary medicines, a need voiced by the Australian Expert Committee’s recommendations in 2003.

**Methods**
The herbal samples will be collected and extracted with ethanol; partition with chloroform, butanol, and water; separation and isolation of pure compounds and fraction with silica gel column, finger printing and quantitative analysis with HPLC, LCMS, HPTLC.
To screen the biological effects, enzyme assays, microscopic analyses (fluorescent and confocal microscopy), and molecular analyses (RT-PCR and western blot) will be applied.

**Feasibility**

Our research team has the expertise and experience required for this project in analytical chemistry and cell biology. We have extensive publications on natural products and the team members have both national and international ongoing collaborations. Excellent facilities for analytical chemistry and cell biology are at our disposal in the Faculty of Pharmacy.

**References**


**Faculty of Pharmacy Research Theme(s)**

Cardiovascular and Diabetes
### Project Summary

**Aim**
Respiratory infections especially those caused by multiple drug resistant (MDR) Gram-negative bacteria have become one of the major priorities for the Australian healthcare system (1). While bacterial resistance emerges quickly, no new drugs have yet reached advanced stages of development for infections caused by the ‘superbugs’ (2). Bacteriophages (‘bacteria eaters’) – viruses which attack and destroy bacteria with stunning efficiency and are harmless to human have been proposed as an alternative to traditional antibiotics because they are not affected by MDR. This project aims to formulate bacteriophages in the dry powder form for respiratory delivery to provide a more efficacious solution for the treatment of MDR respiratory infections.

**Significance**
The success of this project will result in new pharmaceutical therapies which will benefit those patients who are suffering from respiratory infections. Also, it will advance the knowledge base of inhalation aerosol delivery of biologics as the concept of inhaled phage therapy is in its infancy.

**Methods**
Clinically relevant bacteriophages (e.g. those against *A. baumannii*) and chemicals generally regarded as safe which have been used in protein-based formulations will be employed in this project. Spray-freeze drying (SFD) combining the spraying with freeze-drying process to eliminate the heat stress normally encountered in spray-drying will be used to prepare inhalable phage powders with controlled porosity (3). Phage viability and structural integrity will be assessed by phage enumeration tests and transmission electron microscopy (TEM), respectively. The physical properties of the phage powders will be examined using state-of-the-art characterisation tools such as scanning electron microscopy (SEM), X-ray powder diffraction (XRD), differential scanning calorimetry (DSC) and dynamic vapour sorption (DVS). The *in vitro* aerosol performance and powder stability will also be evaluated.

**Feasibility**
The proposed project is feasible as significant resources, in both equipment and intellectual aspects, are available to support the project which aligns closely with the strength of our research group in advanced drug delivery.
References (if any)

Faculty of Pharmacy Research Theme(s)
Respiratory Disease
**Name of Primary Supervisor:**
Prof Hak-Kim Chan

**Contact details**
**Email:** kim.chan@sydney.edu.au
**Phone:** 93513054

**Name of other academic and research staff involved in the project and/or supervisory team:**
Dr Qi Tony Zhou

**How many students will this project be available for?**
1

**Project Title**
Inhaled nano-formulations of antibiotics for respiratory infections

**Project Summary**

**Aim**
This study aims to develop inhaled nano-formulations of antibiotics with controlled drug-release profiles.

**Significance**
Respiratory infections are expected to be one of the major priorities for the Australian healthcare system [1]. Lower respiratory infections are the third leading cause of death worldwide [2]. Systemic administration of many high-dose anti-microbials can cause severe adverse effects; while inhaled formulation can deliver antibiotics directly to the infection sites in the respiratory tracts, with superior efficacy and reduced systemic side effects [3]. However, many inhaled antibiotics are rapidly absorbed into blood circulation and cleared. Therefore, nano-formulations may prolong the drug action in lungs by controlling its drug release and reducing clearance by encapsulation of drugs in liposomes or polymeric materials.

**Methods**
Antibiotics will be encapsulated in liposomes or polymeric materials using dry film or emulsion methods. Effect of production conditions and excipients on encapsulation efficiency and drug release rate will be evaluated using the established approaches. Stability will be tested after nebulisation via various nebuliser devices.

**Feasibility**
All production equipments including the high-speed homogenizer and particulate characterisation tools such as nano-sizer and spraytech are available in the lab.

**References (if any)**

**Faculty of Pharmacy Research Theme(s)**
Respiratory diseases
Name of Primary Supervisor:  
Prof Ines Krass

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Email: ines.krass@sydney.edu.au
Phone: 9351 3507

Name of other academic and research staff involved in the project and / or supervisory team:
RPAH Diabetes Centre team led by Professor Stephen Twigg

How many students will this project be available for?
1

Project Title
Medication safety – Clinical significance of Medication discrepancies in transferring type 2 diabetes (T2DM) patients from Australian primary care to tertiary ambulatory care

Project Summary

Study 1:
A study to identify, classify and determine factors associated with medication discrepancies for type 2 diabetes patients (T2DM), referred from primary care to a tertiary ambulatory clinic was conducted by retrospective audit of outpatient clinic records of 300 randomly selected adult T2DM patients who attended the Diabetes Centre between 01 January 2010, and 31 December 2011. Over 80% of referral letters contained at least one discrepancy with a median of 2 discrepancies per referral. Of a total of 744 discrepancies, the majority of were omissions (58.9%). Insulins had the highest discrepancy rate. Factors independently associated with medication discrepancies were GP referral letter type, total number of medications and medication regimen type. However, the clinical significance of the discrepancies was not determined, neither was the method for identifying and classifying medication discrepancies validated.

Objectives:
1. To validate the system for determining medication discrepancies through a follow-up retrospective audit of the same patient cohort used for the period January 2012- December 2013.
2. To determine the clinical significance of the medication discrepancies identified in the both studies.
3. To examine the relationship between medication discrepancies and glycaemic, blood pressure and lipid control.

Methods:
The study will be conducted using a retrospective audit of outpatient clinic medical records of 300 patients included in the previous study for clinic visits between January 2012 and December 2013. The study will compare information provided by the GP referral with that collected by nurses in the RPAH Diabetes clinic during routine clinic visits. Medication discrepancies and factors influencing discrepancies will be compared to data from the 2011-2012 study.

Data collection:
Data has been obtained already, which include the following; patient demographics, clinical data, complications, medication regimen, GP and GP practice characteristics.
Data Analysis
The de-identified data will be entered into a spreadsheet and SPSS used to generate descriptive statistics. McNemar’s test will be used to compare discrepancy rates between the 2 time periods. Multivariate analysis will be used to explore predictors of medication discrepancies and relationship with clinical outcomes. Clinical significance will be determined using an expert panel including an endocrinologist, GP, clinical pharmacist, diabetes nurse practitioner. Discrepancies will be classified according to potential for and severity of harm using a 6-point confidence scale whether the medication discrepancy had the potential to cause patient harm if the discrepancy was not intercepted and corrected. Secondly, the reviewers will determine the potential severity of harm, if it were to occur, on a 3 point scale (significant, serious, and life-threatening). Level of agreement between members of the expert panel will be examined with Kappa statistic.

Feasibility:
The required ethical approval was obtained already.

Name of Primary Supervisor: Prof Ines Krass

Contact details
Email: ines.krass@sydney.edu.au
Phone: 9351 3507

Name of other academic and research staff involved in the project and / or supervisory team: Dr Bandana Saini

How many students will this project be available for? 1

Project Title: Pharmacy Culture and Practice Change

Project Summary

Background
There is consensus that community pharmacy roles have evolved from the basic supply of medicines to much more sophisticated clinical care, patient and public health centred models. Future pharmacy practice in Australia needs to embrace these newer models, particularly as new entrants into the profession are trained to participate in advanced clinical practice, but often find limited opportunity to practice what they are now trained for. This is because, community pharmacists have been slow to adopt new practices; neither are they integrated into primary health care teams. This is despite the high level evidence of health benefits of pharmacists’ interventions (much of it generated by our research group).

Besides the ideology of newer professional practice, the ageing of the population highlights the need to build capacity in the primary care sector to better manage patients with multiple chronic diseases. Clearly, pharmacy is part of the primary care system that is largely untapped. While previous research has focused on practitioner-perceived barriers to implementation, the missing link may be an understanding the underlying context, i.e., the culture of pharmacy and how this relates to the cultures of other health care professionals in primary care. Obtaining a better understanding of pharmacies organisational culture are key ingredients to improving the success of Knowledge Translation initiatives directed at optimizing the care provided by pharmacists to patients.

Objectives:
1. To characterize the professional culture of pharmacies and pharmacists within NSW.
2. To characterize the services provided by pharmacists to patients and their understanding of evidence for pharmacist interventions
3. To characterize the professional culture of general practice and compare it with the culture of pharmacy to identify barriers to integration.

The honours project will address objectives 1 and 2

Methods: A cross-sectional survey will be distributed to a random sample of 500 pharmacies within NSW. A list of pharmacies will be obtained from the Pharmacy Board of NSW. The survey will comprise
a. Modified version of the Organizational Culture Profile (OCP)\(^1\), a validated tool designed to measure cultural values.
b. Questions about the types of professional services provided by pharmacists within their respective practices, how much time they dedicate to these services and their understanding on the evidence of pharmacist interventions.
c. Attitudes to potential integration with general practice
d. Pharmacy and pharmacist demographics

**Data Analysis:**
The survey data will be analysed using SPSS® version 22. Descriptive statistics, ANOVA and chi-square analysis will be applied to the questions as appropriate. With respect to the OCP confirmatory factor analysis will be used to analyse the data using the procedures. Central tendency measures will be calculated for each domain.

**Feasibility:**
The required ethical approval will be obtained before the commencement of the project.


**Faculty of Pharmacy Research Theme(s)**
Health Services and Patient Safety
Name of Primary Supervisor: Dr Ingrid Gelissen

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Email: Ingrid.gelissen@sydney.edu.au
Phone: 02-86270357

Name of other academic and research staff involved in the project and / or supervisory team:

How many students will this project be available for?
1

Project Title:
Unravelling the role of the ABCG4 transporter in neuronal lipid homeostasis

Project Summary
ABCG4 is an ABCG-half transporter that is highly expressed in the brain and eye. Existing studies using animal models have reported observations of involvement by ABCG4 in cellular cholesterol, cholesterol precursors and oxysterol metabolism in neuronal cells. In addition, a new role for ABCG4 was also recently discovered with high expression identified in megakaryocyte progenitor cells, a bone marrow cell type from which platelets are formed. Currently, very little is known about the basic cell biology of this transporter, including its exact substrates and its transcriptional regulation. This project aims to investigate aspects of the function and regulation of the ABCG4 transporter in neuronal lipid homeostasis, in order to further our understanding of its role in the development of conditions such as Alzheimer’s disease.

Aim
To study aspects of the function and transcriptional regulation of ABCG4 in neuronal cells.

Significance:
This project will help our understanding of the function and regulation of an important lipid transporter protein, ABCG4. Understanding how this transporter is regulated and what its lipid export function entails will give us a better understanding of how this transporter could potentially be modulated in the future. Furthermore, it will provide better understanding of its potential role in Alzheimer disease and platelet lipid homeostasis.

Methods:
This is a basic cell biology project and will involve the use of cell culture models that are relevant to the disease state such as neuronal cell lines. Methodology includes measurement of cellular protein expression, the use of silencing RNAs as well as transporter activity studies.

Feasibility:
All methods needed for this project are in place in the laboratory of Dr Gelissen

References
Kerr ID, Haider AJ and Gelissen IC. “The ABCG family of membrane-associated transporters: you don’t have to be big to be mighty” Br. J. Pharmacol. 2011:164:1767-1779

Faculty of Pharmacy Research Theme(s)
Cardiovascular and Diabetes
Name of Primary Supervisor:  
Professor Iqbal Ramzan

Contact details:  
Email: pharmacy.dean@sydney.edu.au  
Phone: 9351 2831

Name of other academic and research staff involved in the project and / or supervisory team:  
Dr. Dong Fu

How many students will this project be available for?  
1

Project Title  
Examination of the Hepatotoxicity of Kava Alkaloid, Pipermethystine (PMS).

Project Summary:  
Kava (Piper methysticum) is a perennial plant which has been used for centuries by South Pacific communities for medicinal, social and cultural purposes. The rhizome is traditionally macerated with water and coconut milk to produce a beverage with relaxant and psychoactive properties; however, many commercial kava products are extracted using organic solvents. Although kava extracts are known to be generally well tolerated, kava-mediated hepatotoxicity and cases of liver failure were reported, which has raised concerns in regulatory authorities. Therefore, many countries have totally banned all kava-containing products or have issued a warning [1].

Studies suggest that the aqueous extracts of kava are less cytotoxic than organic solvent fractions [2]. Using liver cancer cell line, a study showed that pipermethystine (PMS), an alkaloid in kava organic extractions, significantly decreased cell viability while kavalactones such as 7,8-dihydromethysticin and desmethoxyyangonin, did not affect cell viability, revealing the potential role of PMS in kava medicated hepatotoxicity [3, 4]. However, little is known about hepatotoxic effect of PMS and the detailed mechanism is unclear.

The Aim of this study is to investigate the toxicity of kava alkaloid, pipermethystine (PMS) in liver cells using an in vitro sandwich culture of primary hepatocytes, and to elucidate the cellular mechanism by studying its effect mitochondria, a cellular organelle is shown to play a central role in drug induced liver injury [5].

The specific aims of this project are:
1. Examine the effect of PMS on primary hepatocytes viability and morphology.
2. Elucidate the mechanisms by which PMS interferes with mitochondrial function.

Methods:  
Immunofluorescence for morphological studies; Western blot for protein expression and activation examinations; basic cell culture technique; images analysing.

Feasibility:  
Prof. Iqbal Ramzan and Dr. Dong Fu will directly supervise the student. All the methods are well established. Dr. Dong Fu will directly train the student for all the techniques.

References:


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**Faculty of Pharmacy Research Theme**

Cancer
**Name of Primary Supervisor:**
A/Prof. Jane Hanrahan

**Contact details**
**Email:** jane.hanrahan@sydney.edu.au
**Phone:** 9351 2078

**Name of other academic and research staff involved in the project and / or supervisory team:**
Prof. Mary Collins, Raja Vizwas, VJ Tallapragada

**How many students will this project be available for?**
1

**Project Title:**
Development and biological activity of *cis*-aminocrotonic acid (CACA) analogues as sub-type selective GABA agonists.

**Project Summary**
*cis*-Aminocrotonic acid (CACA) is a conformationally restricted non-selective GABA agonist at GABA-A and GABA-C receptors, however the current synthesis of CACA is problematic and requires a difficult chromatographic separation from *trans*-aminocrotonic acid (TACA). We have developed a new simple four-step synthesis of CACA that avoids the need for the chromatographic separation. This new synthetic route is also amenable to the synthesis of N-substituted CACA derivatives that will then be studied to obtain a greater understanding the structural requirements of each receptor subtype through structure activity relationships.

**Aim**
To syntheise the constrained GABA analogue CACA and CACA derivatives using a new simple new four step synthetic route and investigate the activity of the CACA analogues on different sub-types of GABA-A receptors.

**Significance**
GABA-A receptors are pentameric structures made up of α1-6, β1-3, γ1-3, δ, ε, θ, π subunits, most commonly two α, two β and one other sub-unit.¹ The complexity and number of potential subunit combinations require the development of sub-type selective agents to enable the study of the physiological function of different receptor sub-types and provide potential leads for new drugs.

GABA receptors form one of the major inhibitory neurological pathways in the central nervous system and have been implicated in a number of disorders including insomnia, epilepsy, myopia and memory impairment.¹,³ Most recently, increased GABA levels and over expression of the α5 subunit GABA-A receptor have been found in brain from Alzheimer’s disease patients and also in mouse models of Alzheimer’s disease, and it has been suggested that these receptors may be a target to prevent the development of the disease.²

**Methods**
Synthetic organic chemistry and two-electrode voltage-clamped electrophysiology on specific GABA-A receptor sub-types expressed in *Xenopus laevis* oocytes.

---

**Synthetic Scheme**

![Synthetic Scheme Diagram]

i) BzOH, Tol, 110 °C 11) THF:BH$_3$. THF, 10 °C iii) PPh$_3$. DIAD, HN$_2$. 0 °C-RT, iv) NaHSO$_4$.SiO$_2$.Tol v) Dowex 50 H$^+$ vi) R-Cl (R= Me, Bu, Bz)

**Feasibility**

All tools and expertise are available, the chemistry has been carried out on very similar molecules. Additional support will also be provided by two post-doctoral researchers, R. Viswas (chemistry) and VJ Tallapragada (electrophysiology).

**References (if any)**


**Faculty of Pharmacy Research Theme(s)**

Neuroscience and Mental Health
**Name of Primary Supervisor:** Prof. Lisa Bero  
**Contact details**  
**Email:** lisa.bero@sydney.edu.au  
**Phone:** 86271881

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**Project Title**  
Implementation of WHO Clinical Practice Guidelines

**Project Summary**  
World Health Organization (WHO) clinical practice guidelines are required to include an implementation plan. However, the types of implementation plans included and the evidence on which these plans are based have not been studied. In this project, we will access the database of WHO Clinical Practice Guidelines, characterize the types of implementation plans recommended and determine if the plans are based on evidence. The implementation plans will be characterized according to the classification scheme used by the Cochrane Collaboration Effective Practice and Organization of Care Group.

**Aim**  
To determine whether the implementation plans in WHO clinical practice guidelines are based on evidence of effective implementation interventions.

**Significance**  
WHO is in the process of revising their handbook for developing clinical practice guidelines and the results of this project will provide guidance on the types of implementation plans that can be used.

**Methods**  
Systematic review to identify effective implementation strategies. Descriptive study of types of strategies recommended in WHO guidelines.

**Feasibility**  
All data are readily accessible and publicly available.

**References (if any)**

**Faculty of Pharmacy Research Theme(s)**  
Health services and patient safety
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<th><strong>Name of Primary Supervisor:</strong></th>
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<tr>
<td>Prof. Lisa Bero</td>
<td>Email: <a href="mailto:lisa.bero@sydney.edu.au">lisa.bero@sydney.edu.au</a></td>
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**Project Title**  
Communicating the trade-off between risks and benefits of medicines

**Project Summary**

**Aim**  
To categorize how the trade-off between risks and benefits for approved medicines in Australia (2009-2014) for cardiovascular disease and diabetes has been described and to compare the reporting of risks and benefits to reports available from EMA and FDA.

**Significance**  
Accurate and understandable data on the risks and harms of medicines is essential for decision making. The reporting of the trade-off between risks and benefits of new medicines has not been consistent and important information is often missing (Schroll, et al). This study will analyse data from medicines approved in Australia (by the TGA and PBAC) to identify differences and similarities with how the data have been reported in Europe and the United States. The pros and cons of different templates for reporting benefits and harms will be discussed.

**Methods**  
Review of publically available reports from PBAC and TGA:  
The reporting of risks and benefits will be categorized according to different methods available for such reporting (eg, quantitative, summary of findings tables, qualitative, etc.)

**Feasibility**  
All data are readily accessible and publicly available.

**References**  
Schroll J, Abdel-Sattar M, Bero L. FDA reports provide more data but are more difficult to use than EMA reports. J Clin Epidemiol, in press.

**Faculty of Pharmacy Research Theme(s)**  
Health services and patient safety
Project Title
Cannabinoids, GABA-A receptors and pain

Project Summary
Our group has shown that certain non-psychotic cannabinoids can modulate GABA via GABA-A receptors. Enhancing GABA activity at peripheral sites in the dorsal root ganglia reduces pain perception. This project seeks to determine whether cannabidiols such as O-1602 and O-1921 mediate, in part, their pain alleviating effects via enhancing GABA-A receptors located in the dorsal root ganglia.

Aim
To evaluate whether cannabidiols enhance GABA at human recombinant GABA-A receptors.

Significance
Chronic pain is estimated to cost the Australian economy $34.3 billion each year with 20% of adult Australians suffering chronic pain that leads to poor quality of life. Few treatments exist that do not cause addiction and dependence. Thus new treatments for pain are highly sought after.

Methods
A variety of human GABA-A receptor subtypes will be expressed in the Xenopus oocyte cell expression system. Firstly mRNAs of the subunits that make up the GABA-A receptor are synthesised. The mRNA will then be injected into the Xenopus cell expression. Two to three days later, the effect of GABA with and without O-1602 and O-1921 can be tested using a technique called two-electrode voltage clamp. This technique measures chloride flux through the GABA-A channel i.e. as an electrical current. The amount of current is directly proportional to the potency of the ligand being studied.

Feasibility
All methods are up and running in the laboratory. Training will be provided by NH&MRC senior research associates and/or PhD students.

References (if any)

Faculty of Pharmacy Research Theme(s)
Mental Health
Project Title
Menthol, extrasynaptic GABA-A receptors and pain

Project Summary
Menthol, a major constituent of mint, can modulate GABA via GABA-A receptors. Enhancing GABA activity at peripheral sites in the dorsal root ganglia may be one pathway that reduces pain perception. This project seeks to determine which GABA-A receptor subtype mediates the pain alleviating effect of menthol.

Aim
To evaluate the effects of menthol on human recombinant extrasynaptic GABA-A receptors.

Significance
Chronic pain is estimated to cost the Australian economy $34.3 billion each year with 20% of adult Australians suffering chronic pain that leads to poor quality of life. Few treatments exist that do not cause addiction and dependence. Thus new treatments for persistent pain are highly sought after.

Methods
A variety of human extrasynaptic GABA-A receptor subtypes will be expressed in the Xenopus oocyte cell expression system. Firstly mRNAs of the subunits that make up the GABA-A receptor are synthesised. The mRNA will then be injected into the Xenopus cell expression. Two to three days later, the effect of GABA with and without menthol can be tested using a technique called two-electrode voltage clamp. This technique measures chloride flux through the GABA-A channel ie as an electrical current. The amount of current is directly proportional to the potency of the ligand being studied.

Feasibility
All methods are up and running in the laboratory. Training of methods will be conducted by NH&MRC senior research associates and/or PhD students.


Faculty of Pharmacy Research Theme(s)
Mental Health
**Project Title**
Nano-targeted molecular capsule drug delivery of a platinum drug via active tumour targeting

**Project Summary**
Platinum-based anticancer drugs, like cisplatin, carboplatin and oxaliplatin, suffer from chemical degradation inside cancer cells and deactivation through protein binding in the blood stream. Preventing this from occurring means more drug reaches its cellular target intake, making the drug more effective. As such, research into suitable drug delivery vehicles remains ongoing. In my research group we have extensively studied macrocycle based delivery vehicles, including cucurbiturils, cyclodextrins and calixarenes as well as nanoparticles. In this project the student will build a multi-layered nano-targeted molecular capsule.

**Aim**
To produce a nano-targeted molecular capsule for the delivery of a platinum anticancer drug to solid tumours.

**Methods**
The student will use physical chemistry to encapsulate the drug within the molecular capsule and attach it to a dendrimer. The student will use organic chemistry to attach cancer targeting groups to the surface of the dendrimer. The entire nano-targeted molecular capsule will be characterised by a variety of chemical and physical spectroscopic techniques and the anticancer activity will be examined using in vitro growth assays.

The student will be taught all techniques and skills needed during the project and will be supervised directly by Dr Wheate. The resources to undertake this project are available within the Faculty.

**References (if any)**


**Faculty of Pharmacy Research Theme(s)**
Cancer
Project Title
Enhancement of the Specificity of Fluorogenic Media for the Identification of Pathogenic Bacteria Through the Use of Dual Enzyme Substrates

Project Summary
Aim
The synthesis and testing, as pathogenic bacterial-specific detection agents, of fluorogens which are dual enzyme substrates.

Significance
Chromogenic media for the detection of pathogenic bacteria are simple to use, but a limiting factor in their use in a surveillance method which could be applied to all patients on admission to hospital is the time taken for the development of the indicative colour (typically 24-48 hours). Fluorogenic media, (Varadi et al., 2012) like chromogenic media, are simple, easy to use, cost-effective, and reliable, with the added advantages of the reduced time for bacterial detection and the possibility of enhanced specificity. The use of media which contain fluorogens that rely upon the activity of two enzymes (which are both expressed only by a specific bacterium) for the generation of fluorescence would be expected to produce fewer false positives than those which rely on a single enzymatic activity, and should thus have significant advantages in terms of specificity.

Methods
The synthesis and characterisation of fluorogens will be performed in the Faculty of Pharmacy and fluorogens will be assessed in agar media as part of an ongoing collaboration with the Freeman Hospital, Newcastle, UK.

Feasibility
Synthetic routes to fluorogens will be based upon those developed in the Faculty of Pharmacy as part of an NHMRC grant and previous Honours projects. For example, the chalcone analogue 1 will be coupled to 2 different amino acids (AA1 and AA2) thereby acting as a substrate for 2 different aminopeptidase activities. Only pathogenic bacteria which exhibit both of these aminopeptidase activities will be capable of releasing the fluorescent chalcone 2, and thus be detected.
References

Faculty of Pharmacy Research Theme(s)
Cancer
### Project Title
Attitudes of Australian practicing pharmacists to patient-centred care

### Project Summary

**Aim**
To assess Australian community pharmacists’ attitudes to patient-centred care; and investigate changes in attitudes over the last decade.

**Significance**
Patient-centred care (or concordance) is recognised as the philosophical concept underpinning effective delivery of pharmaceutical and health-related services by all healthcare professionals, including community pharmacists. It is believed that healthcare services which are delivered with the patient at their core, and include informed treatment decision making and self-care, have a more positive impact on overall patient health and humanistic outcomes.

Effective implementation of patient-centred care by community pharmacists requires appropriate knowledge of, positive attitudes towards, and effective skills in delivering, all components which constitute patient-centred care. In 2004, a national study was conducted to determine Australian community pharmacists’ attitudes towards the concept of concordance (a term more commonly used then compared to patient-centred care). Whilst attitudes were generally positive, there does not appear to have been an overwhelming surge in the delivery of patient-centred pharmaceutical care by community pharmacists. This study therefore aims to investigate the attitudes of community pharmacists to patient-centred care (and concordance), and investigate whether there have been changes over the last decade.

**Methods**
A survey of a random sample of community pharmacists in Australia will be conducted. The questionnaire used will include a previously validated “attitude to concordance” scale and additional questions on patient-centred care, informed decision making and delivery of pharmaceutical care. The “attitudes to concordance” scale is a modified version of the LATCon scale (Raynor et al., 2001, IJPP, 9:81-4), consisting of 14 items on a Likert scale ranging from 1 (Strongly Agree) to 5 (Strongly Disagree). The construct validity and internal consistency of the scale have been evaluated previously (Kansanaho et al., 2004, Ann Pharmacother, 38:1946-1953).

The Honours student will be involved in finalisation of the questionnaire; mail-out of the questionnaire to the national sample of community pharmacists (include three reminders); day entry and analysis.

**Feasibility**
Supervisor will seek HREC approval for the project prior to student commencing the project.

### Faculty of Pharmacy Research Theme(s)
Health Services and Patient Safety
| **Name of Primary Supervisor** | **Dr Ramin Rohanizadeh** |
| **Contact details:** | **Email:** ramin.rohanizadeh@sydney.edu.au  
**Phone:** 9351 2355 |
| **Name of other academic and research staff involved in the project and / or supervisory team** | **Prof. Kim Chan** |
| **How many students will this project be available for?** | **1** |

**Project Title**  
Treatment of smoke inhalation injury in burn-victim patients

**Project Summary**

**Background:** Smoke injury in the respiratory system is a major cause of morbidity and mortality in burns (fire) victims. Current treatments for smoke inhalation injury consist of mechanical intubation, positive pressure ventilation, fluid resuscitation, bronchial lavage to remove airway secretions, and antibiotics for established infection. These treatments are mostly supportive and there are no specific therapies for smoke inhalation injury.

The project will develop a novel curative method to accelerate healing in damaged lung tissue. The method will achieve greater efficacy by administrating anti-inflammatory drugs in the form of inhalable aerosol particles. Inhalable drugs in the form of micro-size particles have good stability and can be delivered in a wide range of doses. Such particles deliver a controllable and prolonged drug dose directly to injured lung tissue causing a local rapid onset of therapeutic action, even in deep and inaccessible areas.

**Material and Methods:** The project will fabricate stable aerosol formulated from heparin and pentoxifylline particles. The *in vitro* functionality and activity of human lung epithelial (Calu-3) cells and alveolar macrophages (AM) cultured in the presence of various doses of Heparin and Pentoxifylline solid aerosol particles will be determined in this project.

**Feasibility:** The student will be supervised by Dr. Rohanizadeh directly. The required facilities to carry out this project are available in the laboratory.
Name of Primary Supervisor  
Dr Rebekah Moles

Contact details  
Email: rebekah.moles@sydney.edu.au  
Phone: 93515968

Name of other academic and research staff involved in the project and / or supervisory team  
Dr Carl Schneider

How many students will this project be available for?  
1

Project Title  
Pharmacy students as mystery shoppers: Improving the supply of non-prescription medicines

Aim  
The aim of this research is to improve the performance of pharmacy staff responses to a variety of non-prescription medication requests via pharmacy students acting as mystery shoppers and providing associated feedback.

Background  
Community pharmacies in Australia are a frequent destination for patients seeking healthcare advice and medication supply. Owing to the accessibility of non-prescription medicines, they are often considered safer than prescription medicines; however, to truly be safe, they need to be used judiciously and appropriately, with the benefits and harms associated with use accounted for. The non-prescription sector of the Australian pharmaceutical industry is estimated to be between 1.7 and 3 billion AUD per annum, accounting for a large proportion of pharmacy turnover. Therefore, with the large market for these products, it is important to determine how they are being used.

Several researchers have captured evidence that current pharmacy practice has room for improvement when it comes to the supply of non-prescription medicines and their associated advice. A series of studies by Schneider and colleagues in Western Australia, have demonstrated that pharmacists and their staff would provide appropriate referral advice in a minority of non-prescription medication requests. These studies used mystery shoppers as a tool to observe and assess current pharmacy practice behaviour. This observation method can also be used as an intervention to improve practice behaviour when feedback is provided.

Methods  
Pharmacy recruitment  
Third year pharmacy students will recruit pharmacies in the Sydney metropolitan region. Each pharmacist and their staff members will be distributed participant information statements (PIS) and consent forms for completion and subsequent collection by the pharmacy student.

Mystery Shopper training  
Mystery shopping students receive training in how to perform mystery shopping for 10 non-prescription medicine requests (scenarios) and the delivery of feedback to pharmacy staff. Scenario topics will cover common non-prescription medication requests as follows: Paediatric cough/cold, Heartburn, Asthma, Diarrhoea, Red Eye, Headlice, Adult cough/cold, Pain (muscular) with hypertension, Allergic rhinitis, Headache, Insomnia.
**Mystery Shopping and Pharmacy Evaluation**
Each recruited pharmacy will be visited by a different student nine times over nine weeks. They will receive a similar scenario over nine visits (i.e. if a pharmacy is randomized to receive the cough and cold scenario, they will receive a cough cold scenario nine times). The scenario will however contain slight variations in the specific brands requested or the details of the patient (male, female etc.), in order to mimic the genuine variation in patient presentations. The performance of pharmacy staff will be scored via a scenario-specific assessment sheet at each visit. Key clinical and communication aspects will be scored as YES/NO or PARTIAL. For example if the scenario involves a request for medication for a child, the assessment form will state, “Did the staff member find out the medication was for a 4 year old?” and this is scored as either yes (2 points) or no (zero points) with partial (1 point) awarded if they found out it was for a child but not the specific age. A self-assessment form that mimics that of the researcher will be used when feedback is provided, in order to get the staff member involved in the visit to reflect on their performance. Scores at baseline and at various time points will be compared to track improvements over time via paired t-tests.

One to one semi-structured interviews with pharmacy staff will also take place at the end of each visit. In these the student will ask a series of questions to explore the thoughts of the pharmacy staff member with respect to the scenario delivered. As well as this data collection, a further follow-up interview with the pharmacy manager at the end of each semester will occur. These interviews conducted by the researchers (not the student participants), will assess the pharmacy manager’s thoughts on the feasibility of students providing mystery shopping visits, the quality of the feedback provided by students and strategies for improvement, the quality of the scenarios and the benefits and barriers to the methods being employed as an ongoing QA activity (until saturation, maximum n=60).

**Significance**
This research is a novel strategy to monitor and improve professional performance surrounding the provision of non-prescription medicines to the public.

**Feasibility**
The required ethical approval on this project has already been obtained.

**Faculty of Pharmacy Research Theme(s)**
Health Services and Patient Safety
**Name of Primary Supervisor:**
Dr Rebecca Roubin

**Contact details**
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**Phone:** +612 9036 7104

**Name of other academic and research staff involved in the project and / or supervisory team:**
A/Prof Jane Hanrahan

**How many students will this project be available for?**
2

**Project Title**
Pharmacological Targeting of Oncogenic Signalling Pathways using Novel Therapeutics

**Project Summary**

**Aim**
To examine the antitumour effects and mechanism of action of new lead compounds identified from “natraceuticals”, or natural products derived from plant and herb sources.

**Significance**
Aggressive tumours adapt quickly, finding a way to develop resistance against chemotherapies. A new approach to cancer treatment is to develop new drugs that can utilise multi-targeting pathways. One way forward is to examine the signalling pathways of cancer, in particular the role of oncogenic enzymic intracellular transport. Our research previously identified potential new lead compounds identified from “natraceuticals”, or natural products derived from plant and herb sources. The selective anticancer activity of these compounds have been demonstrated in metastatic colon, cervical, liver, leukaemia and prostate cancer cells, and whilst they were active against these cancer cells, they did not harm healthy immune cells. This project will form the basis for future studies on elucidating the cancer signalling pathways involved in different types of cancers and the development of novel anticancer therapeutics. In addition, it is becoming increasingly clear that these enzymic intracellular transport have many critical roles in health and disease.

**Methods**
This project will use a combination of techniques that are used in biochemistry, cell biology, molecular biology and pharmacology, and will involve growing human tumour cells in tissue culture and assessing the effects of novel compounds on oncogenic enzymic intracellular transport. This will be done using a wide variety of techniques including anti-proliferative activity, and intracellular enzyme activity. One student can focus on metastatic colon, cervical, liver cancer and one on leukaemia and prostate cancer cells in this project.

**Feasibility**
This project will build upon work developed in the Faculty of Pharmacy and previous Honours projects, supervised by Dr Roubin, as part of an NHMRC application ongoing collaboration with A/Prof Hanrahan.

**References**

**Faculty of Pharmacy Research Theme(s)**
Cancer
**Project Title:**  
Using video/audio diaries to explore the concept of treatment burden among patients who use multiple medicines.

**Project Summary**  
The population is ageing and the burden of chronic disease and co-morbidity is growing. Multiple medicines are often used to manage common chronic diseases, resulting in complex medication regimens. For some time researchers have focussed on the burden of diseases and how disease influences patients’ quality of life. There is however, increasing recognition that patients experience a degree of burden as a result of treatment. In this setting, treatment burden may be defined as patients’ subjective experiences related to maintaining treatment with multiple medicines for chronic diseases. Among Australian patients who use multiple medicines there is qualitative data which shows that patients experience financial burden, time and travel burden, access problems and medication-related burden. The qualitative data obtained in that study was obtained during focus groups and telephone interviews. While this type of data collection method is valuable, it is recognised that obtaining data using video/audio of a person in their natural setting (while attending to medication-related tasks in the home) in their own time, may provide unique and previously unexplored perspectives. Participation in diary recording or responding to electronic messaging may allow for the capture of data from patients with disabilities who may have difficulty attending “focus groups” or responding in a timely manner to telephone calls.

**Aim**  
The aims of this study are to: (i) use video/audio diaries and electronic-prompted video/audio interviews to explore the concept of treatment burden among patients who use multiple medicines; and (ii) conduct an evaluation of the impact of the new, evidence-based ‘living-with-multiple-medicines’ website hosted by the National Prescribing Service (http://www.nps.org.au/topics/living-with-multiple-medicines) on patient experiences of multiple medicines use.

**Significance**  
The importance of treatment burden – as a new target for quality improvement initiatives, is highlighted with a recently released Mayo Clinic Grand Rounds presentation. At present, there is no validated patient-reported outcome measure (PROM) to estimate the burden of treatment on multiple medicines-users. Having such a PROM would be a valuable tool for researchers interested in understanding how a health–care intervention such as for example, Home Medicines Review influences patients’ subjective experiences of burden. Access to such a PROM could help clinicians to understand more about how best to tailor their prescriptions to suit the individual thereby improving adherence and outcomes. The development of such a PROM requires a good grounding in qualitative research. At present there is a dearth of
qualitative information regarding treatment burden. In particular, to the knowledge of the lead researcher, there is no study which has obtained video qualitative data from multiple medicines users during their daily lives. This study has the potential to influence the direction of research in this area for some time to come.

**Methods**

Study #1: It is intended that patients who use multiple medicines will be recruited by community pharmacists. Using V+ Mobile Qualitative app for smartphone, and other devices, participants will be prompted to log-in to the app at pre-agreed times (as often as daily) and asked to record their experiences of taking medicines, thoughts and concerns about medicines, interacting with health professionals and purchasing medicines. The questions asked will be defined during the study to explore the concept of treatment burden. In a sense this is a pilot project and the number of patients to be recruited will have to be determined. N-vivo will be used to assist the analytical process.

Study #2: A 4 week, repeated measures control versus intervention group design will be employed to evaluate the impact of an evidence-based multiple medicines use website. Outcome measures will be taken at baseline and 4 weeks, and will include treatment burden, self-management practices, self-efficacy, and quality of life.

**Feasibility**

Ethical approval will be sought prior to the student beginning the project. Analysing video/audio recordings is a sophisticated and growing methodology in social research. Given the exploratory nature of the study, and the proliferation of smart-phone technology, among increasingly broader demographics, it is not anticipated that there will be difficulty obtaining sufficient patients to participate.

**References**


**Faculty of Pharmacy Research Theme(s)**

Healthy Aging
Name of Primary Supervisor: A/Prof Sallie-Anne Pearson

Contact details
Elin Lehnbom
Email: e.lehnbom@unsw.edu.au
Phone: 9385 1465

Name of other academic and research staff involved in the project and / or supervisory team:
Dr Elin Lehnbom
Prof Johanna Westbrook

How many students will this project be available for?
1

Project Title
The impact of an electronic medication management system on pharmacists' workflow: a time and motion study

Project Summary
Electronic medication management systems (eMMS) are being implemented in hospitals to reduce medication errors [1]. Research shows that eMMS reduce prescribing errors [2] and there is a growing body of research demonstrating how electronic systems impact on doctors’ and nurses’ work and communication patterns [3-9]. However, few studies [10] have examined the impact of eMMS on pharmacists’ work patterns.

Aim
To quantify the time pharmacists spend on specific work tasks before implementation of an electronic medication management system.

Significance
This project will provide baseline data on pharmacists’ work patterns when using paper charts. Data will be collected again once the eMMS has been implemented. This will increase our understanding of the impact of electronic medication management systems on pharmacists’ work patterns.

Methods
The student will be taught how to use an electronic data collection tool called the WOMBAT - Work Observational Method by Activity Timing. This is a method of collecting multi-dimensional data about work and communication patterns [11]. The student will able to quickly and accurately record tasks being performed by the observed pharmacist by selecting categories using a touch screen on a tablet. The categories include what the pharmacist is doing (chart review, history taking, etc), with whom they are doing it (patient, doctor, etc), how they are doing it (using paper charts, face-to-face, etc) and where they are doing it (on or off the ward, in the pharmacy department, etc).

The student will shadow consenting pharmacists performing their usual work tasks. A pharmacist will be observed for a maximum of two hours at a time. The observer will record all tasks performed during this period using the WOMBAT tool.
Feasibility
This is a feasible study for an independent and highly motivated honours student. The student will work with a research team, specialising in e-Health and medication safety research, based at Macquarie University. The student will collect data during normal business hours at Prince of Wales Hospital, Randwick. Ethics approval will be sought before the student commences. The student will need to comply with NSW Health vaccination guidelines, provide a police check and sign a confidentiality agreement before commencing data collection.

References

Faculty of Pharmacy Research Theme(s)
Health Services & patient safety
### Name of Primary Supervisor
A/Prof Timothy F Chen

### Contact details
**Email:** timothy.chen@sydney.edu.au  
**Phone:** 93514440, 0414 91 71 50

### Name of other academic and research staff involved in the project and / or supervisory team
Dr Claire O’Reilly, Dr Thomas Balle & Prof Mary Collins

### How many students will this project be available for?
1

### Project Title
Does smoking influence the efficacy of antidepressant medicines in consumers with depression?

### Project Summary
Consumers with depression are more likely to smoke than those without depression. Often, consumers with depression mention that smoking helps alleviate symptoms of anxiety and depression; however there is some evidence that cigarette smoking may exacerbate negative affect.\(^1\) It is hypothesised that neuronal nicotinic acetylcholine receptors are mediating this effect. In 2014 we conducted an exploratory qualitative study of consumers with depression, stratified by their cigarette smoking status. In 2015 we want to build on these qualitative findings by conducting a quantitative study, with the **Aim** of exploring relationship and impact of cigarette smoking on the effectiveness of antidepressant medicines used for the treatment of unipolar depression, stratified by the antidepressant medicine’s relative potency to inhibit nAchR. **Methods:** The quantitative survey will be developed based on a comprehensive review of the literature and the qualitative findings from the Honours project conducted in 2014. The survey instrument will be tested for at least face and content validity prior to the data collection phase. It is envisaged that an online platform will be used (eg SurveyMonkey) and administered to a cohort of consumers with unipolar depression. To facilitate data collection, we plan to work with relevant consumer organisations such as Consumer Health Forum and or BeyondBlue. A specific sample size calculation will be computed in semester 1, 2015, taking into consideration response rate, numbers required for multivariate analyses such as regression or factor analyses. **Significance:** This study is important as cigarette smoking status is not always considered in efficacy trials of antidepressant medicines. This study may provide preliminary evidence and an explanation for the differences in effectiveness of antidepressant medicines based on an individual’s smoking status. **Feasibility:** The resources needed for this project include: consumables for conducting the quantitative survey including postage and printing, if not conducted online. An incentive (eg prize) for participation will be offered to facilitate response rate, in accordance with ethical principles. A biostatistician may be consulted if needed. Depending on the findings from this research, it may be submitted for publication in a scientific journal. If considered appropriate, an open access journal with a publication fee may be selected.

### References:

**Faculty of Pharmacy Research Theme(s)**  
Mental Health
Project Title
Small molecules targeting cardiovascular benefits of PCSK9 inhibition

Project Summary
Inhibition of proprotein convertase subtilisin/kexin type 9 (PCSK9), which binds and promotes degradation of LDL receptor (LDLR), has become an alternative or adjunct to statin therapy\(^1,6-8\). PCSK9 inhibition elevates LDLR levels effectively lowering LDL-C. Small molecules inhibiting PCSK9 for oral administration are lacking\(^1,6\). Annexin A2 (AnxA2), a member of the annexin family inhibits PCSK9-mediated LDLR degradation and is one of only two currently known natural PCSK9 inhibitors\(^9,10\). Our preliminary genetic analysis of large patient cohorts, and cell-based studies support AnxA2 as a therapeutic target to inhibit PCSK9.

Aim
This project seeks to develop small molecules that enhance PCSK9/AnxA2 interaction to inhibit PCSK9 and elevate LDLR levels.

Significance
Cardiovascular diseases (CVD) are the leading cause of death in the developed world, affecting ≈14 million individuals/year worldwide. Elevated LDL is the most important risk factor for atherosclerosis, myocardial infarction and stroke. Statins, inhibitors of hydroxymethylglutaryl coenzyme A reductase (HMG-CoA-R), effectively lower lipoprotein cholesterol (LDL-C) and are a cornerstone to prevent and treat cardiovascular events. However, although considered safe and well tolerated, statins have limitations\(^1-5\): (1) The majority of (high-risk) CVD patients do not achieve currently recommended LDL-C levels, even at high-dose. Some patients are resistant or respond poorly to statins, such as FH. (2) Even with statins, significant risk for CVD events remains. (3) Adverse side effects like myopathies are common. Hence, new therapies that provide an alternative to or potentiate statin therapy, should ideally act via molecular mechanism distinct from statins (via HMG-CoA-R).

Methods
The methodology will involve computational design and synthesis of small molecules, as well as cell-based assays (tissue culture, ELISA, SDS-PAGE, western blotting) to determine the impact of potential PCSk9 inhibitors on LDL uptake.
Feasibility
All tools and expertise are available. The concept of designing small molecules that stabilize protein-protein interactions is feasible, with applications in drug discovery. 1 PhD student (Sung Choi, Supervisors D. Hibbs, T. Grewal) has commenced on this project and will support the Honours student.

References

Faculty of Pharmacy Research Theme(s)
Cardiovascular and Diabetes
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Name of other academic and research staff involved in the project and/or supervisory team

How many students will this project be available for?
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Project Title
Developing a Novel Biophysical Assay to Test Formulation Stability of Influenza Vaccine.

Project Summary
This project is sponsored by the largest vaccine manufacturer in the world and involves developing experimental-based novel assay(s) to test the stability of influenza vaccines. A variety of experimental tools ranging from high-resolution microscopes (e.g., TEM and optical) to spectroscopic methods (fluorescence, absorbance, light scattering) will be employed to aid in the design of new methods for vaccine preparations by way of fundamental understanding at the molecular level. The long-term goal is to develop a predictive tool for the degradation, in particular aggregation of hemagglutinin (HA) and neuraminidase (NA) proteins, in influenza vaccines during manufacturing processes. This will streamline the development of strategies for vaccine stabilization, moving beyond the trial and error approaches towards rational approaches.

Specific Objectives:
Determining surfactant induced split ratios in the influenza vaccine:

Currently there is no reliable and quick method to determine the split ratios of the virus upon Triton treatment. We hypothesize that information regarding amount of split virus can be probed by external-dye-binding via fluorescence spectroscopy. Preliminary experiments revealed that we could identify split ratios in the samples by following changes in the fluorescence properties of certain dyes.

For this purpose we use hydrophobic dyes whose fluorescence properties are expected to change with the amount of vaccine degradation. In viral vaccines, change of local viscosity of the sample is expected due to splitting or aggregate formation. Samples showing high potency loss tend to contain more whole viruses. Consequently, a stand-alone technique can be developed in order to determine the split ratios of the vaccine. This method would be especially useful for comparison of similar samples, before / after splitting and samples containing different amounts of Triton.

Studies will focus on the differences such as aggregation and degradation products. For this purpose, biophysical methods such as DLS, TEM, UV-Vis, 2nd derivative spectroscopy, and fluorescence spectroscopy (both intrinsic tryptophan fluorescence as well as external dye binding methods) will be used.

The specific aims of this study would include:

a. Development of a characterization method in order to determine the split ratio of the virus to be used especially in the early phases of vaccine development.

b. Characterization of the type of aggregates (sub-viral and protein) formed in the final products in both vaccines.

Feasibility: All required resources are available in the lab. Other senior students in the lab will support the Honours student.

Faculty of Pharmacy Research Theme(s)
Respiratory diseases
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Name of other academic and research staff involved in the project and / or supervisory team

How many students will this project be available for?
1

Project Title
Developing a Microparticle Delivery System for Encapsulation of Biotherapeutic Proteins

Project Summary
Biotherapeutics are the most rapidly expanding area of research in biotechnology. Very high costs ($1000-600,000) and a market value of ~$55 billion give a large incentive for the development of novel versions of therapeutic proteins. Specifically, the research focuses on developing:

1. Biotherapeutic formulations of proteins with enhanced stability
2. Novel microparticles for encapsulation of biotherapeutics
   1. Biotherapeutic formulations with enhanced stability
   2. Novel microparticles for encapsulation of biotherapeutics

   We plan to develop formulations of biotherapeutics with enhanced stability in appropriate form that is suitable for encapsulation in microparticles. This step requires assessing and improving therapeutic protein stability via elucidating protein folding and aggregation pathways and studying protein structural dynamics in detail to ensure that protein structure is indeed intact and no degradation due to processing steps occurred. Protein aggregation occurs in almost all phases of drug development and it is our objective to find ways of hindering aggregation to such an extent that these molecules are in the stable form required after encapsulation in the particles.

   Identifying protein-protein and protein-particle interactions would also be beneficial and we will attempt to decipher these interactions. A selected group of biotherapeutics will be studied in this project with the aim of developing biotherapeutic products stabilized against protein aggregation through rational formulation design. Formulation-screening, accelerated aggregation studies and stability predictions will be performed via various biophysical methods.

2. Novel microparticles for encapsulation of biotherapeutics

   The second phase of the study will involve designing and generating novel microparticles. Formulating protein particles for aerosol or parenteral delivery is a challenge as it requires biochemical stability of the protein molecules. We will prepare microparticles of the proteins by freeze-drying, with the presence of carbohydrates (e.g., mannitol, trehalose etc.) as both protein stabilizer and bulking agent. The performance and properties of the particles such as particle size distribution, morphology and crystallinity will also be characterized.

Feasibility: All required resources are available in the lab. Other senior students in the lab will support the Honours student.

Faculty of Pharmacy Research Theme(s)
Cancer