PROJECT INFORMATION # 1

Project Title
Therapeutic Targeting of Long Noncoding RNA REG1CP for Colorectal Cancer Treatment
Hypothesis: Nanoparticles will be effective to deliver long noncoding RNA to colorectal cancer cells and supress cell proliferation

PROJECT ATTRIBUTES AND BENEFIT TO THE STUDENT

Brief description of project:

Despite the recent advance in the development of molecularly targeted therapy, curative treatment of metastatic colon cancer remains an unmet medical need. We have found in our preliminary study that the long noncoding RNA (lncR) REG1CP is frequently upregulated in colon cancer cells/tissues and that knockdown of REG1CP via RNA interference (RNAi) inhibits colon cancer cell proliferation and tumorigenicity. However, development of RNAi therapeutics has been challenging due to difficulties in delivering RNAi therapeutics to systemic targets. To address the challenge, we will develop novel nanoparticles that carry REG1CP siRNA and target to colorectal cancer cells specifically. Overall, this research will lead to novel targeted therapy at a lower dose and with fewer side effects. While this proposal is solely focused on the treatment of colorectal cancers, we envisage that our nanoparticle platform can be adapted to develop targeted therapies against many other types of cancer

Student's role in the project:

During the scholarship period, the student will use our state-of-the-art microfluidic platform to work on the formulation and characterization of novel delivery systems for RNA and plasmid DNA.

Student's benefit from their involvement:

The student will acquire fundamental laboratory techniques and skills for development of nanoparticles as drug delivery systems.

Research Location Information (where the project work will be conducted)

Campus: Callaghan

Building & room number: Medical Science Building MS114

Supervisor's Information	
Supervisor Name: Roger Liang	**Academic Appointment at UON: Senior Lecturer**
Preferred Phone:	29854959
E-mail Address:	**Roger.liang@newcastle.edu.au**

PROJECT INFORMATION # 2

Project Title: **Effects of omega-3 fatty acid status on sarcopenia**
Hypothesis: Higher omega-3 index is associated with improved clinical and biochemical measures of sarcopenia

PROJECT ATTRIBUTES AND BENEFIT TO THE STUDENT

Brief description of project:

Sarcopenia is the age related loss of muscle mass, strength and function that occurs over time, predisposing older adults to reduced quality of life, loss of independence and increased risk of falls and hospitalisation. While low protein intakes and sedentary lifestyle are key factors in the development of sarcopenia, the impact of 'inflammaging', or the development of chronic low-grade inflammation during aging may also play a role. Increased levels of inflammation have been shown to impact protein absorption, utilisation and muscle synthesis in older populations, increasing the risk of developing sarcopenia. Omega-3 fatty acids are known for their anti-inflammatory properties and may provide a unique target to reduce inflammation and therefore improve muscle synthesis, strength and function in older adults. This project will examine the relationship between omega-3 index and fatty acid status and relevant clinical and biochemical measures of sarcopenia such as body composition, systemic inflammation and hand grip dynamometry.

Student's role in the project:

To conduct laboratory analysis of erythrocyte membrane fatty acids and analyse body composition scans and strength and function measures such as handgrip dynamometry. To conduct statistical analysis to examine the relationship between omega-3 index and clinical and biochemical measures of sarcopenia.

Student's benefit from their involvement:

- Gain an understanding of clinical research methodology
- Gain an understanding of clinical data collection, eg DEXA analysis
- Learn a variety of lab techniques, including erythrocyte membrane fatty acid determination

Research Location Information (where the project work will be conducted)

Campus: HMRI Building
Building & room number: Level 2, West Wing

Supervisor's Information	
Supervisor Name: Lisa Wood	**Academic Appointment at UON: Professor**
Preferred Phone: 02 40420147	
E-mail Address: lisa.wood@newcastle.edu.au	

PROJECT INFORMATION # 3

Project Title:
How stressful is a virtual reality? The correlation of immersion, fidelity, performance and threat in mixed-reality applications to physiological arousal states.

Hypothesis: Increased level of fidelity within a mixed- reality experience correlates with an increased change in arousal state, measured as changes in heart rate, respiratory rate and skin conductance.

PROJECT ATTRIBUTES AND BENEFIT TO THE STUDENT

Brief description of project:

Our research group is currently developing multiple biofeedback enabled training tools using virtual reality technology. One particular application provides repeated practical training of stress management skills and utilises physiological alterations such as heart-rate, respiratory rate and skin conductance to assess changes in arousal states within the VR application. The work on this project has highlighted a current gap in the literature relating to the level of fidelity in a XR experience that is required to change the arousal and affective state of the user. There are numerous components that are believed to influence user engagement and immersion (level of realism, inclusion of personal threat, performance anxiety and cinematic techniques) however there is limited data available connecting these with physiological changes. Furthermore, it is unclear how these physiological changes within an XR application translate to the perception of the experience, e.g. the perceived level of stress, fear, excitement and/or fun. We are interested in how the level of fidelity within a virtual, augmented and 360 application effect an individual's state of arousal and their experience.

To gain a better understanding of the components that contribute to changes in arousal we propose to rate existing XR applications on their level of fidelity and the amount of immersive components and correlate their effect on physiological responses as well as the perceived experiences of the user. This knowledge will help with the future development of useful and effective training tools in XR.

Student's role in the project:

The key responsibilities of the student will be auditing of existing VR applications and the development of a rating matrix of fidelity and immersion of VR, AR and 360 content. The student will be involved in proof of concept testing and preliminary data sampling of physiological responses and psychometric data. The student will also be included in a literature search and review and preliminary data collection and analysis.

Student's benefit from their involvement:

The student will gain valuable experience and insights into the initial planning phases of a project and the practical application of a Question Answer Model as a research framework.
They will be trained in the collection and analysis of biometric data using the Equivital belt system and LabChart as well as how to scan the current literature to compile a short literature review.

Research Location Information (where the project work will be conducted)

Campus: Callaghan Campus
Building & room number: Medical Sciences Building 323

Supervisor's Information	
Supervisor Name: Rohan Walker	**Academic Appointment at UON: Professor**
Preferred Phone: 15012	
E-mail Address: rohan.walker@newcastle.edu.au	

PROJECT INFORMATION # 4

Project Title: Dietary modification of the microbiome as new therapies for respiratory diseases
Hypothesis: Modifying the diet (high fibre/high fat/high protein) will regulate the composition and function of the gut microbiome, which impacts the development and progression of respiratory diseases.

PROJECT ATTRIBUTES AND BENEFIT TO THE STUDENT

Brief description of project:

Chronic respiratory diseases (e.g. asthma, emphysema/chronic obstructive pulmonary disease (COPD), lung cancer, etc.) are a major cause of death globally, but are often poorly treated. These diseases are largely driven by dysfunctional immune responses, and we have recently shown that the microbiome (microorganisms residing in the gastrointestinal tract) are key drivers of immune responses and disease development in the lung. Diet is a key regulator of the microbiome and immune responses, and therefore we aimed to assess the effect of dietary interventions on disease development through regulation of the microbiome.

Diets were carefully designed to assess the role of different macronutrients (fibre, protein, fats) and were given to mice in experimental models of asthma and COPD. Samples collected from these mice will be analysed to assess changes in immune responses and the microbiome which may be correlated with disease development. We will also assess changes in human cell lines exposed to cigarette smoke and dietary components, and will analyse dietary data from human COPD patients to assess the impact on disease severity.

Student's role in the project:

Students will have the opportunity to assess disease pathology through analysis of histology samples collected from these experiments. They will also perform molecular analyses, such as assessment of gene expression (RNA extraction, reverse transcription, PCR) and protein abundance (ELISA) to characterise the immune responses in both lung tissue and the gastrointestinal tract. Students will also design and perform cell culture experiments to assess the impact of dietary components or microbial metabolites on immune responses. Finally, the student will be able to apply their findings to data from human patients to demonstrate how the research can be translated to clinical applications.

Student's benefit from their involvement:

Students will have the opportunity to observe how animal research is performed, and how these techniques can be applied to questions about human health. In addition to practical laboratory skills, they will gain valuable experience in how to design experiments. Student will be working in a successful group that has a great mix of PhD students and post-doctoral researchers who work collaboratively with a number of other research groups around the University (clinical and basic science) and in other institutes both in Australia and internationally. The group has a strong track-record for developing the careers of number of highly successful researchers.

Research Location Information (where the project work will be conducted)

Campus: Hunter Medical Research Institute (HMRI)
Building & room number: Level 2 East Wing

Supervisor's Information	
Supervisor Name: Dr Alexandra Brown (02) 4042 0201 Alexandra.brown@newcastle.edu.au	**Academic Appointment at UON:** Post Doctorate Researcher

PROJECT INFORMATION # 5

Project Title: The impact of life-style factors on lung aging and respiratory health
Hypothesis: Life-style factors such as alcohol consumption, high-fat diet/obesity and cigarette smoking accelerate lung aging and that is detrimental to lung health**.**

PROJECT ATTRIBUTES AND BENEFIT TO THE STUDENT

Brief description of project:

The lung is the crucial site of gas exchange. It matures during childhood and performs at optimal capacity when we reach early adulthood. However, lung function gradually declines thereafter with increasing age in all individuals. Lung aging is thought to be associated with a process known as senescence, whereby cells stop regenerating and being replenished. The accumulation of aging cells causes the gradual weakening of respiratory muscles, reduces lung elasticity and causes narrowing of airways. These events make breathing more difficult as we age. Whilst lung function declines naturally with increasing age, certain lifestyle factors have been shown to increase the risk of accelerated lung aging. These lifestyle factors include excessive alcohol consumption, high-fat diet and/or obesity (HFD) and cigarette smoking.

Alcohol consumption occupies a significant place in Australian culture and a wide range of social events. In 2017-2018, ~80% of young Australians (≥18 years) had consumed alcohol in the past year. Of which, 1 in 6 over-consumed (excessive consumption) more than two standard drinks per day on average. Previous studies have shown that excessive alcohol consumption had detrimental effects on the airways and lung. High concentrations of alcohol vapor in the lungs may disrupt normal cellular functions, induce inflammation/oxidative stress and impair healing. Alcohol consumption, particularly excessive drinking, has been linked with reduced lung function, which is a sign of accelerated lung aging.

A HFD is known to shorten lifespan and to increase risk of several aging-related diseases such as cardiovascular disease and type 2 diabetes. Interestingly, a recent study demonstrated that HFD exacerbates aging-induced lung inflammation and oxidative stress in young mice. The same study also showed that caloric/fat restriction diet reversed aging/HFD-induced lung inflammation and oxidative stress.

Cigarette smoking is also widely regarded as an important factor in causing lung aging. Long-term cigarette smoking causes debilitating lung diseases, like chronic obstructive pulmonary disease (COPD), which is are associated with premature lung aging. COPD is the 3rd leading cause of death worldwide (5th in Australia). In Australia, one in seven people over the age of 40 are affected (~1.45 million). COPD patients experience a progressive decline in their condition, even after smoking cessation. There is no effective treatment for COPD. Recent studies in humans and mice suggest lung aging may play a role in COPD. However, the underlying mechanisms remain poorly understood.

Taken together, these lifestyle factors have detrimental effects on lung health. However, the underlying mechanisms in causing accelerated lung aging and its role in respiratory disease remain poorly understood. This project aims to explore the influence of alcohol, HFD and cigarette smoking on lung aging or order to elucidate the role of lifestyle factors in lung aging in clinically important respiratory diseases.

Student's role in the project:

Students will look at key markers of aging in experimental models of excessive alcohol consumption, HFD and cigarette smoke exposure. The students will be involved in assessing lung aging factors using a variety of techniques (see below).

Student's benefit from their involvement:
Students will gain experience in developing and managing experimental models. In addition, they will have the opportunity to learn and perform various laboratory techniques such as lung function assessment, DNA/RNA extraction, reverse transcription, qPCR, protein extraction/quantification, western blot, ELISA and assessment of lung pathology.

Research Location Information (where the project work will be conducted)

Campus: HMRI
Building & room number: Lvl 2 east wing

Supervisor's Information	
Supervisor Name: **1) Tatt Jhong Haw** 2) **Jay Horvat**	**Academic Appointment at UON:** **1) Research Associate (Tatt Jhong)** **2) Associate Professor (Jay)**
Preferred Phone: **1) 0240420193 (Tatt Jhong)** **2) 0240420220 (Jay)**	
E-mail Address: **1) TattJhong.Haw@newcastle.edu.au** **2) Jay.Horvat@newcastle.edu.au**	

PROJECT INFORMATION #6

Project Title: Does amniotic (pro)renin receptor regulate fetal membrane integrity?
Hypothesis: Inhibiting the (pro)renin receptor will reduce pro-fibrotic factors and tissue homeostasis

PROJECT ATTRIBUTES AND BENEFIT TO THE STUDENT

Brief description of project:

We are investigating the role of the (pro)renin receptor ((P)RR) in maintaining the strength of fetal membranes during pregnancy. Male babies are more likely to be born preterm compared with female babies and this can be attributed to an increased disposition for early rupture of the fetal membranes (particularly the amnion). (P)RR signalling in the kidneys and eyes can stimulate fibrosis and regulate tissue homeostasis. Amnion from pregnancies carrying males have significantly less (P)RR than pregnancies carrying female babies. We propose that (P)RR in the amnion stimulates cell growth and fibrosis in the amnion to produce a strong amnion. As amnion from pregnancies carrying male babies have less (P)RR, we predict that this predisposes them to premature rupture of the membranes and preterm birth. We have knocked down the (P)RR in primary amnion cells from both male and female pregnancies and examined gene expression effects. We will now look at protein levels and enzyme activity in the samples.

Student's role in the project:

The student will assist in immunoblotting protocols as well as optimising protocols for measuring protease activity.

Student's benefit from their involvement:

The student will learn multiple techniques from their role in the project and experience a supportive environment where they will be encouraged to work independently.

Research Location Information (where the project work will be conducted)

Campus: HMRI
Building & room number
Level 3 East Wing

Supervisor's Information	
Supervisor Name: Dr Sarah Delforce	**Academic Appointment at UON:** Research Associate
Preferred Phone: (02) 4042 0343	
E-mail Address: Sarah.delforce@newcastle.edu.au	