

Characterisation of the kynurenine pathway and NAD⁺ metabolism in primary human skin cells

Supervisors: Dr Gilles Guillemin, Dr Ross Grant and Dr Nady Braidy

Suitable for: Honours studies

Project: The kynurenine pathway (KP) is a metabolic route that breaks down one of the essential amino acids, tryptophan. Over the years, our group has demonstrated that this pathway becomes deregulated in several inflammatory diseases. UV exposure, toxic chemicals and advancing age lead to oxidative stress and skin damage with an inflammatory component. It is likely that some KP metabolites may act as pro-inflammatory and anti-inflammatory mediators since the KP plays a crucial role in immune regulation. However, the KP components in human skin cells (keratinocytes, fibroblasts) are still unknown. We aim to characterize the KP metabolic profile in human skin and primary skin cells under both physiologic or inflammatory conditions using state of the art technology such as High performance Liquid chromatography (HPLC), Gas chromatography-mass spectrometry (GCMS), quantitative PCR, cell culture, tissue processing immunohistochemistry and immunocytochemistry.

Email contact: g.guillemin@unsw.edu.au, r.grant@unsw.edu.au or n.braidy@unsw.edu.au



Targeting tumour-stromal interactions in pancreatic cancer

Supervisor: Dr Phoebe Phillips

Suitable for: Honours, Masters and Post-graduate studies

Project: Pancreatic cancer claims five Australian lives every day and is one of the nation's most lethal diseases. Despite aggressive treatment regimes, there has been no improvement in patient survival in the last decade. Evidence suggests that targeting cancer cells alone is not enough. The intense stromal reaction inhibits drug delivery and increases the aggressiveness of the tumours. Thus, depletion of the stroma or pancreatic stellate cells (key mediators of pancreatic fibrosis) is a potential therapeutic target. The overall aim of my research is to therapeutically target tumour cells and stromal pancreatic stellate cells (PSCs) which both contribute to chemoresistance in pancreatic cancer. My research is at the forefront in identifying novel targets to treat pancreatic cancer and using relevant in vitro and in vivo models to study this disease. Students would gain experience in several techniques including: tissue culture, western blotting, real-time PCR, an in vivo mouse model of pancreatic cancer, immunohistochemistry, gene silencing using siRNA and fluorescent microscopy. This research program has the potential to develop novel therapies to target this drug-refractory disease and improve the long-term survival of patients with pancreatic cancer.

Email contact: p.phillips@unsw.edu.au



Evolutionary dynamics in infectious diseases

Supervisors: Dr Fabio Luciani and Prof Andrew Lloyd

Suitable for: Honours, Masters and Post-graduate studies



Project: Infectious diseases can be regarded as complex biological systems with ongoing interactions between pathogens and the immune system. Our overall research topic is to use computational biology and bioinformatics to describe and understand these complex interactions between host immune responses and pathogens. In particular we are interested in understanding the dynamics of hepatitis C virus. (HCV).

This virus causes chronic infections and mechanisms driving HCV chronic infections are still largely unknown and vaccines are not available. A number of projects are available, for both Honours and PhD candidate.

Students with strong interest in quantitative methods such as Bioinformatics, Statistics, and Mathematical models are encouraged to apply, even if their background is outside biology or Bioinformatics.

Email contact: Luciani@unsw.edu.au

Next generation sequencing to unravel the dynamics of hepatocellular carcinoma in liver transplant

Supervisor: Dr Fabio Luciani and David Bowen

Suitable for: Post-graduate studies

Project: Hepatocellular carcinoma (HCC) is third deadliest cancer in the world. The majority of HCCs are attributable to either hepatitis B virus or hepatitis C virus infection. HCC is a very heterogeneous cancer, which typically evolves from damaged liver tissues at different stages of cirrhosis. The evolutionary dynamics of HCC cells remains largely unknown. It is paramount to identify those events that characterize the evolution from an infected liver into cancer. Liver transplant offers a unique opportunity to study the evolutionary events that characterize the transformation from a damaged/infected liver tissue into a cancer. The major aim of this project is to apply next generation sequencing to study the genetic diversity of HCC from liver explants and to identify key factors driving evolution into cancer. This project is suitable for students seeking a PhD involving experimental and/or computational (next generation sequencing/bioinformatics).

Email contact: Luciani@unsw.edu.au or d.bowen@centenary.usyd.edu.au

Optimising drug therapies through clinical pharmacokinetics and pharmacodynamics

Supervisors: Prof Ric Day, A/Prof Ken Williams and Prof Garry Graham

Suitable for: Honours, Masters and Post-graduate studies

Project: Rheumatic disorders, diabetes and psychotic illness are prevalent chronic illnesses that demand high quality pharmacotherapy. We are researching powerful techniques for individualising pharmacotherapy using pharmacokinetic/pharmacodynamic models. Our aim is safe yet effective therapy. Allopurinol used in gout, metformin used in diabetes and clozapine used in psychotic illness are currently being studied. Also we are investigating the mechanisms of paracetamol actions in association with the Heart Research Institute. We are examining genetic factors that predict serious adverse drug reactions and also explain variation in response to medicines, especially transporter molecules and their controlling genes. The effects of electronic medication management and decision support tools in a teaching hospital on the rate of adverse events occurring is a new and exciting research interest.

Email contact: r.day@unsw.edu.au, ken.williams@unsw.edu.au or g.graham@unsw.edu.au



Do pain and movement restriction cause sensory and perceptual changes?

Supervisors: Dr James H McAuley, Prof G. Lorimer Moseley, Dr Tasha Stanton and Dr Ben Wand

Suitable for: Honours studies

Project: People with low back pain have perceptual deficits and sensory changes related to their back. These perceptual deficits and sensory changes are associated with increased symptoms, such as pain intensity. It is unknown whether these deficits/changes are caused by the onset of pain, and whether other factors, such as restricted movement have a role. Our primary hypothesis is that low back pain causes sensory and perceptual changes of the back and our secondary hypothesis is that immobilisation of the back increases the magnitude of these changes. We will recruit 40 healthy participants and randomise them to one of four experimental groups: pain induced by delayed onset muscle soreness (DOMS) with immobilisation, DOMS and sham immobilisation, sham DOMS and immobilisation, and sham DOMS and sham immobilisation. After 5 days we compare the sensory and perceptual changes between the groups.

Email contact: j.mcauley@neura.edu.au



Cannabinoids – a risk factor for schizophrenia?

Supervisor: Dr Tim Karl

Suitable for: Honours studies



Project: Schizophrenia is a chronic and disabling mental disorder that affects 1% of the world's population. Importantly, cannabis use may be a risk factor in the development of this disease but its role in schizophrenia is not straightforward. This might be due to the opposing effects of the two major cannabis components, delta9-tetrahydrocannabinol (THC) and cannabidiol (CBD). Furthermore, only a small proportion of cannabis users (<10%) develop schizophrenia suggesting that a genetic predisposition (i.e. susceptibility) may interact with cannabis abuse to "cause" the disorder. This proposal aims to investigate this potential interaction between the gene neuregulin 1 and the environmental risk factor cannabis by treating a mouse model for this gene [i.e. the heterozygous Nrg1 Type III mutant mouse (Nrg1 HET)] with THC and CBD. This project is a continuation of a earlier project in which we investigated how another mouse model for neuregulin 1 (i.e. transmembrane domain neuregulin 1) responds to acute and chronic treatment with different components of cannabis (those mutant mice have been more susceptible to the effects of cannabis). The difference between the two mouse models is the type of peptide affected by the mutation. Both forms exist in humans so it is important to distinguish between these two forms of neuregulin 1.

We will use acute and chronic treatment designs for THC (which can induce psychosis in humans) and CBD (which has antipsychotic-like potential) and will also administer a combination of both cannabinoids to investigate the interactive relationship of these compounds. Behavioural paradigms relevant for schizophrenia will be carried out in our laboratory at Neuroscience Research Australia.

Email contact: t.karl@neura.edu.au

Effects of laboratory housing conditions on schizophrenia animal models

Supervisor: Dr Tim Karl

Suitable for: Honours studies

Project: Several studies have shown that an animal's neurobiology and behaviour are positively affected by multifaceted living conditions - so-called environmental enrichment (EE). Importantly, environmentally enriched laboratory housing is more comparable to the living conditions experienced by humans than standard housing, which can be seen as an impoverished or deprived environment. Consequently it is important to test potential animal models for human diseases such as schizophrenia when housed under the comparable enriched conditions. The importance of the environment on the aetiology of schizophrenia has been shown e.g. in a schizophrenia-related CA1-specific NMDA receptor 1 subunit knockout mouse model, in which daily exposure to EE led to a reduction of deficits in object recognition, olfactory discrimination, and contextual fear memory relative to standard housing of animals. Thus, we intend to investigate the behavioural phenotype of an animal model for the schizophrenia candidate gene neuregulin 1 as a response to different housing conditions (e.g. standard laboratory housing *versus* EE) using a battery of behavioural investigations into anxiety, cognition and other schizophrenia-relevant tasks.

Email contact: t.karl@neura.edu.au