

RESEARCH AREAS

for

POTENTIAL HONOURS PROJECTS in 2010

Department of Medical and Molecular Biosciences (MMB)

& Institute for Biotechnology and Infectious Diseases (IBID)

Faculty of Science, UTS

Supervisor: Professor Ann Simpson, MMB, UTS

Location: UTS, Building 4.

Research Area: Diabetes

Project: Liver-directed gene therapy of diabetes; Characterisation of liver cell populations that undergo pancreatic transdifferentiation

Type I diabetes mellitus is caused by the autoimmune destruction of the beta cells of the pancreas that secrete insulin. We have shown that we can cure diabetes in spontaneously diabetic mice by delivery of the insulin gene to the liver using a non-pathogenic viral delivery system. Reversal of diabetes was seen within 2 days of vector administration, which was stable until the experimental endpoint (150 days), glucose response curves were normal and a process of pancreatic transdifferentiation occurred in areas of the liver tissue with the generation of hepatic insulin storage granules and expression of pancreatic beta cell transcription factors. There was no evidence of autoimmune reactions against insulin-producing hepatocytes.

The aim of the honours project(s) is to characterise the expression profiles of genes and proteins in rodent liver cells that are permissive to *in vivo* lentiviral transduction and subsequent transdifferentiation into insulin-secreting cells. This will be done by sampling liver tissue from diabetic mice treated with the empty vector of the insulin vector (these samples are already available). For expression profiling, microarrays will be performed. Total RNA will be isolated and sent to the Clive and Vera Ramaciotti Centre for Gene Function Analysis (University of New South Wales) where labelling reactions, hybridisation procedures, reading of the signals and normalisation will be performed. Comparison and statistical analysis of microarray data will then be conducted. Quantitative real time PCR validation of differentially expressed genes will be performed. Relative quantification will be calculated using the comparative threshold cycle (C_T) method. Protein analysis of selected genes will be followed up by western analysis.

Supervisor: Associate Professor Steve Djordjevic, IBID/MMB, UTS

Location: Building 4, Level 6, UTS

Email: steven.djordjevic@edu.au

Research Areas:

1. Microbial Pathogenesis

I have been interested in adhesin molecules and their role in pathogenesis for many years. Until recently, I have focussed on mycoplasmal pathogens of agriculturally-important domestic animal species but will increasingly be undertaking work with mycoplasmal pathogens of humans. Adhesin molecules typically play a role in binding to extracellular matrix components such as fibronectin, laminin and various glycosaminoglycans but may also target key receptors on host epithelial surfaces. My work has focussed on the molecular characterisation of mycoplasmal adhesins with an emphasis on identifying key domains that interact with host molecules. We have shown that many important adhesins of *Mycoplasma hyopneumoniae* (an important porcine pathogen) are posttranslationally cleaved into discrete functional domains that remain attached to the mycoplasmal cell surface. A subset of these adhesins has been shown to be modified chemically by the addition of various carbohydrate moieties and by phosphorylation. More recently I have begun to expand my research to include an analysis of surface adhesins of medically important Gram negative Enterobacterial spp such as Shiga toxin-producing *Escherichia coli* and *Campylobacter jejuni*.

Techniques used: Microbial imaging, cloning, sequencing, expressing and purifying adhesin domains, ligand-binding studies, proteomics, western/ligand blotting.

2. Molecular analysis of complex antibiotic resistance loci in the *Enterobacteriaceae*.

Class 1 integrons capture antibiotic resistance gene cassettes and are major contributors to the evolution of multiple antibiotic resistance (MR) in clinically important Gram-negative spp. Since most class 1 integrons in clinical environments are defective transposons they are often located within complex resistance loci comprising functional transposons, insertion elements and other horizontally acquired genetic material. These complex resistance loci can be found within genomic islands such as Salmonella Genomic Island 1 (SGI1) but more typically are located on conjugative or mobilizable plasmids. The co-localisation of virulence and resistance genes within mobile genetic elements represents an increasing challenge in the battle against MR- bacteria. I am interested in the detection and characterisation of complex resistance loci with an emphasis on mobile elements that carry clustered virulence and antibiotic resistance genes.

Techniques used: cloning and sequencing of complex resistance loci, plasmid sequencing and analysis, detailed bioinformatics, conjugation and transformation studies, and molecular epidemiology

Supervisor: Dr Meiya Sutisno, MMB, UTS

Location: Building 4, UTS

Research Area: Forensic Biology Research

Projects:

Forensic Face Mapping Research

Crimes of fraud, in particular identification theft, are a growing concern with more than half a million cases recorded in Australia between 2000 and 2006 (Australian Institute of Criminology 2007). Most common is the use of false credentials to verify identity for: [1] local transactions (e.g. RTA, banks, telecommunication companies, shops etc); [2] entry at customs check points; and [3] migrants' application for entry visas. Relevant to all these cases is the use of Identification Document (ID) photographs for establishing identity. Our research group is working to generate a large database of facial biometrics for the development of innovative systems of facial identification that are robust and accurate.

We believe our research would place UTS in a prime position to become a national resource (that can eventually grow into the Southeast/Pacific Region) for facial biometrics to use for legal basis for decades to come. The derivation of a large database in the field of Forensic Identification is equivalent to having a bank of fingerprints/DNA profiles that the INTERPOL can access. With such database researchers would be able to test legal/privacy/public needs for identification and not just the scientific issues. This would allow multiple collaborations for interchangeable use of the data not only with UTS-based IT and engineering colleagues on innovative Facial Identification projects but also with both national and international police, forensic and security agencies.

Forensic Body Mapping Research

Identification of "Persons of Interest" (POI) is crucial for conviction or exoneration in court. With the increased usage of CCTV surveillance cameras to monitor crime, identification of POI from CCTV images has become a topical issue in the criminal courts, particularly in Australia. One aspect of our

research is focussed on the anatomical analysis of the human body from the CCTV images using the principles of “Body Mapping”. In the Australian Criminal Courts, “Body Mapping” is not fully recognised as a field of specialised knowledge with the main argument stemming from the non-establishment of invariable uniqueness of different parts of the human body. Furthermore, it is also argued that there appears to be no body of knowledge on distinctive body movements or manner of walking that would support positive identification.

It is for this reason our research group aims to generate information that would eventually lead to the acceptance of “Body Mapping” evidence in the Criminal Courts. Primarily we will be examining the functional anatomy of the human body with respect to various body movements including gait. This is to generate data on invariable uniqueness between individuals based on their body movements. This research would also open up avenues for collaborations with UTS-based IT and engineering colleagues on innovative Body Identification projects including the police and security agencies.

Supervisor: Associate Professor Liz Harry, IBID/MMB, UTS

Location: Bldg 4, UTS

Project: Cell Cycle Control in Bacteria and Antibacterial Discovery

Cell division in bacteria is essential for survival and infection, and therefore represents an attractive antibacterial target for the development of new antibiotics. What are the cues that signal cells to divide at the right place and at the right time? How are the division proteins recruited to the division site and what is their function? Which division proteins make the best antibiotic targets? Research in my laboratory addresses these questions in bacteria to gain an understanding of the regulation of this vital process and to facilitate the design of novel antibiotics that target it. There are several honours projects available that are aimed at answering these questions in both model and antibiotic-resistant pathogenic bacteria that pose a significant threat in hospitals (*Staphylococcus aureus* and *Acinetobacter* spp.). Projects include (i) examining regulation of the first step in cell division: assembly of the cytokinetic Z ring (ii) the isolation of division protein complexes in pathogenic bacteria to identify new proteins and their function (iii) the application of our research to the development of antibacterials. This later project includes examining how natural antibiotics such as honey kill pathogenic bacteria and affect biofilm formation.

Experimental techniques will typically involve bacteriology, molecular biology, advanced fluorescence microscopy, and could also include proteomics, protein purification and mass spectrometry.

Supervisor: Dr Tony George, Institute for Biotechnology of Infectious Diseases (IBID) and MMB, UTS

Location: Building 4, UTS

Research Area: Infectious Diseases and Cancer

Projects:

1. Bacterial biofilms and Cystic Fibrosis infection control.

(in collaboration with Assoc Prof Cythia Whitworth and Dr Lynne Turnbull, IBID/UTS).

Cystic fibrosis is the most common lethal inherited disorder in Caucasians, affecting 1 in 2,500 births. Whilst median survival has increased from 1-2 years (1960) to a current 36-38 years, chronic suppurative lung disease still causes the majority of the mortality associated with this disease. Infection with *P. aeruginosa* and *B. cepacia* are important causes of morbidity and mortality in CF, progressively damaging the lungs and ultimately causing death from respiratory failure in the majority of patients. Most patients with CF are infected chronically with *P. aeruginosa*, the organism being sustained mainly in antibiotic-resistant biofilms. While non-mucoid strains are isolated initially, *P. aeruginosa* in the CF lung is soon seen to secrete a protective mucoid layer that limits host defences. Resistance to most chemotherapeutic antibiotics, or combinations of antibiotics, is commonplace, with estimates that 25-45% of adult CF patients are infected with mutiresistant bacteria within their airways. We have demonstrated striking clinical efficacy for the combination of an aminoglycoside antibiotic, tobramycin, and a diuretic agent, amiloride, against *B cepacia* in a small clinical pilot study. We have also shown *in vitro* activity for amiloride and related compounds against both *B. cepacia* and *P. aeruginosa*. This project will determine the extent to which this is generally true for these bacterial pathogens; and will determine feasibility for clinical trials.

2. Preventing asbestosis – a new approach.

When asbestos is mined or pulverized, small dust balls become suspended in the air as “parachutes”, and it is this propensity that leads to inhalation into the lungs where it can induce both fibrosis (asbestosis) and malignancy (mesothelioma). Once inside lung cells, asbestos-bound or released metal ions, especially iron, generate cytotoxic reactive oxygen radicals that cause most of the cellular and DNA damage that leads to asbestosis or mesothelioma. The presence of other heavy metals from exogenous sources, for example, cadmium from smoking, and mercury, aluminium, zinc, copper and tungsten from industry and mining, exacerbate the lung problems. We have made a serendipitous discovery for ameliorating the adverse effects of asbestos fibres that we now want to test in lung cell cultures, and then in animal trials. Our hypothesis is based on the premise that Compound ‘M’ will entrap the iron as it is released from asbestos particles. Iron sequestered in this way is effectively rendered chemically inert. “M” is harmless to humans, having been approved for human use for other conditions. After achieving proof-of-concept, we will forge a commercial partnership to conduct animal trials with a nebulizer formulation to reverse the effects of inhaled asbestos fibres. If these trials are successful, human clinical trials will be possible.

3. ABC transporters and cancer – functional and structural studies.

(in collaboration with Dr Richard Callaghan, University of Oxford, UK; Dr Ian Kerr, University of Nottingham, UK; and Dr Megan O’Mara, University of QLD).

ATP-Binding Cassette (ABC) transporters couple hydrolysis of ATP to vectorial translocation of substrates across cellular membranes. These integral membrane proteins are involved in diverse cellular processes including, maintenance of osmotic homeostasis, nutrient uptake, resistance to cytotoxic drugs, antigen processing, cell division, pathogenesis, cholesterol transport, and stem cell

biology. ABC transporters are found in all phyla and form one of the largest protein families. The ability of some ABC transporters to efflux diverse cytotoxic compounds is a crucial problem in human medicine - cancer cells, pathogenic microbes and parasites employ this mechanism to evade chemotherapeutic drugs. Inhibition of these proteins will improve the efficacy of primary drug treatment and render these ABC proteins as targets for new drugs. We will address key mechanistic questions about ABC transporters, using recent atomic structures as the basis for molecular dynamics calculations, homology modelling, and cross-linking experiments designed to identify regions crucial to the functioning of ABC transporters, thereby enabling us to identify and test small molecules that interfere with the normal modes of movement of critical regions in these proteins.

Supervisors: Associate Professor Cynthia Whitchurch and Dr Lynne Turnbull, IBID/MMB, UTS

Location: UTS, Building 4

Phone: 9514 4144

Project: Bacterial biofilms and host-pathogen interactions

It is now increasingly appreciated that bacteria usually live as communities of bacteria that are organized into matrix-encased structures known as biofilms, rather than as free-living (planktonic) forms. The transition from a free-living, independent existence to a biofilm lifestyle in the disease setting can be devastating as biofilms notoriously resist killing by host defence mechanisms and have elevated resistance to antibiotics. The overall research objectives of our group include the study of bacterial biofilms formed by a number of different human pathogens, analysing multicellular collective behaviours, and studying how bacteria interact with host cells and tissues to cause disease. Several Honours projects are available in these areas. Experimental techniques will typically include bacteriology, tissue culture, biofilm culture, molecular biology and advanced microscopy techniques including fluorescence and time-lapse microscopy.

Supervisor(s)—Dr Sara Lal, and / or Ms Jennifer Wyndham , Dr Tamara Sztynka, MMB, UTS

Location: UTS, Building 4

Research Area: Understanding physiological associations (brain, cardiac, etc.) with parameters such as: clinical, cognitive function, lifestyle, fatigue, anxiety, depression etc.

Studies into physiological associations for identifying biomarkers (e.g. for fatigue, anxiety, depression etc.) and/or clinical associations (diabetes, hypertension, cognitive activity, cardiac risk factors etc.) are continuously underway. There is lack of information in the literature in many such areas of physiological and neurophysiological associations.

Such studies can help identify neurophysiological and lifestyle factors in samples that make them more predisposed to particular states such as fatigue, cardiac risk factors, cognitive decline, disease states, anxiety, depression etc. The impact of these states on a variety of physiological changes can be investigated.

These types of studies can lead to development of human state indicators or countermeasures, identification of biomarkers and early clinical intervention in some cases. If interested a specific or focussed project should be discussed with the supervisor.

Laboratory studies will include attaching non-invasive electrodes such as electroencephalogram (brain) for measuring EEG or ERP, electrocardiogram (ECG), electro-oculogram (eye), respiration etc.

Cognitive tests may be performed. The study will enable you to interpret physiological data as well as administer and interpret psychophysiological questionnaires.

Supervisors: Dr Najah Nassif, Dr Bronwyn O'Brien, MMB, UTS

Location: Building 4, UTS

Effect of Cancer-Associated *PTEN* Mutations on *PTEN* Subcellular Localisation

Colorectal cancer constitutes the second most common cause of cancer death in Australia and many other Western countries. We have described a high frequency (41%) of *PTEN* gene alterations (mutation and/or deletion) in primary sporadic (non-familial) colorectal cancer. This data redefines the role of this important tumour suppressor gene in colon cancer. We have detected 12 mutations of which approximately half alter *PTEN* function. Although *PTEN* interacts with its major substrate, and the enzyme phosphoinositide 3-kinase (PI3-K), at the cytoplasmic membrane, its substrate, and PI3-K, have also been found in the nucleus but their role there is unknown. *PTEN* localisation to the nucleus may be significant in the control of the cell cycle. Interestingly, cancer-associated mutations appear to disrupt the subcellular localisation of *PTEN*. Inappropriate cellular compartmentalisation of *PTEN* has now been proposed as another epigenetic mechanism of *PTEN* inactivation. The current project aims to study the effect of our newly-described *PTEN* mutations on the subcellular distribution of *PTEN* in human cancer cells by introducing these mutations into appropriate cancer cell lines. These cell lines will be transiently transfected with GFP-tagged wild type (WT) and mutant *PTEN* constructs. After transfection, cells will be visualised by fluorescence and confocal microscopy and the subcellular localisation of C-terminal GFP-tagged *PTEN* will be determined. To confirm the subcellular localisation, nuclear and cytoplasmic extracts will be prepared from transfected cells and western analysis will be used to detect *PTEN* in the cellular fractions.

Supervisor: Dr. Bronwyn O'Brien, Dr Mark Robinson, MMB, UTS

Location: Building 4, UTS

Research Area: Immunology

Project: Prevention of autoimmune disease using novel parasite-derived immunomodulatory molecules.

Type 1 Diabetes (T1D) develops when the insulin-producing pancreatic beta cells are destroyed by the body's own immune system; it is an autoimmune disease. One of the foremost therapeutic goals in T1D research is to identify potential points in the disease pathway at which to intervene and prevent disease development. With this perspective we have studied the immuno-modulatory properties of secretions from invasive helminth parasites. To prevent their expulsion from the host, these parasites secrete molecules that stimulate innate immune cells to activate a potent Th2 immune response and induce the proliferation of regulatory T-cells (Treg). We have isolated two novel compounds from the excretions of *Fasciola hepatica* and have shown that these molecules exhibit potent immune-modulatory properties and prevent diabetes development. We hypothesise that these helminth-derived immune-modulatory molecules represent a novel approach to understanding the immune mechanisms of T1D and offer potential for the development of therapeutic interventions to prevent beta cell destruction. The goals of this project are to elucidate the immune mechanisms by which parasite molecules prevent the initiation of autoimmunity. To address these goals this project will adopt a proteomic approach.

Bionanotechnology Research

Supervisors: Dr Stella Valenzuela (UTS) & Dr Bruce Cornell (Surgical Diagnostics P/L)

Project description:

To participate in the development of new high throughput screening techniques to identify "hits and leads" for potential ligand gating compounds that target membrane associated ion channels. The project would involve preparing ion channel protein samples, proteoliposomes, developing novel techniques for their incorporation into tethered lipid membranes and screening by automated impedance spectroscopy a library of compounds directed against ion channels. Familiarity with data fitting software, with the biochemistry of biological membranes and with the operation of software driven electronic equipment an advantage but not essential. A successful outcome would be co-authorship on a publication describing the work and experience in a novel field of drug discovery directed towards the difficult but high value targets of membrane associated ion channels.

Supervisors: Dr Stella Valenzuela, Dr Hui Chen, MMB, UTS

Co-supervisor: Prof Michael Cortie, UTS Institute for Nanoscale Technology

Location: Bldg 4, UTS

Project: Gold Nanoparticles for Regulating Cells of the Immune System

Gold nanoparticles (GNPs) possess a number of interesting physical and chemical properties which are of value for use in therapeutic applications. These attributes have recently been exploited to target and destroy selected live cells. In particular, photothermal cancer therapy using GNPs activated by near-infrared laser has generated significant interest, with a rapidly increasing number of publications demonstrating targeted killing of cancer cells both *in vitro* and *in vivo*. There has also been some interest in targeting infectious diseases in this manner, with schemes to target bacteria and the protozoan parasite *Toxoplasma gondii*, recently reported.

This project aims to develop the use of gold nanoparticles as a platform to regulate the activity of macrophage cells of the body's immune system. In particular, the special chemical and physical properties of gold nanoparticles will be exploited to deliver genetic material and other active molecules in order to either destroy or down-regulate macrophage cell function. The project is also envisaged to generate new and fundamental understanding of the distribution and elimination of GNPs via different administration approaches, and how the response of the immune system to various dosages of nanoparticles. This project will build the foundation for the application of GNPs in several serious diseases, such as rheumatoid arthritis, or in the reducing of insulin resistance in obesity and diabetes, via the modification of immune system, particularly macrophage activity to guide the development of critical therapeutic strategies.

Supervisor: Dr David van Reyk, MMB, UTS

Location: UTS, Bldg 4

Project: The potential protective action of carnosine in a murine model of diabetes-induced kidney disease

With regard to the complications of diabetes, the kidneys are one of the major targeted organs. Evidence supports a major contribution to pathology of diabetic nephropathy from reactions between glucose (and its reactive metabolites) and cell and tissue components (glycation/glycooxidation reactions). Carnosine (beta-alanyl-L-histidine) is an endogenous dipeptide which can also be derived from food and health supplements. It is of great interest because of its demonstrated action to block glycation/glycooxidation reactions. However, this has not been well demonstrated in whole animal studies. In this project we have collected the kidneys and urine from diabetic and non-diabetic mice. Half of the mice from each group received carnosine in their drinking water. We are interested in whether carnosine can impede the development of diabetic nephropathy in these animals. Experimental techniques will involve: preparation of tissue samples for light microscopy, analysis of pathological changes to the kidney using histological staining techniques and clinical chemistry.

Supervisors: Dr Maurice Labbatte and Professor Hatch Stokes, IBID/MMB, UTS

Location: UTS, Bldg 4

Project: Evolution of vibrio pathogens through lateral gene transfer

Vibrio bacteria are abundant microorganisms in the marine environment that have a significant role in the natural ecosystem and a devastating role in human pathogenesis. *Vibrio parahaemolyticus* and *Vibrio vulnificus* are amongst the most notable pathogenic vibrios. *Vibrio cholerae* however, is perhaps one of the worst pathogens in human history, responsible for numerous pandemics causing hundreds of thousands of deaths. Lateral gene transfer (LGT) is the ability for bacteria to acquire and transfer genes amongst themselves and is one of the major driving forces in the evolution of bacteria with some bacterial species having obtained up to 25 % of their gene content via LGT. This wholesale sharing of genetic resources allows bacteria to colonize new niches, and with regard to pathogens, facilitates the emergence of novel pathogenic strains and the evasion of host defense mechanisms. In *V. cholerae* and all other vibrios, a specific region of the chromosome called the integron is a 'hot spot' for the acquisition of genes from other bacteria and from the environment. This region makes up 1-3% of the vibrio chromosome carrying genes of which a staggering 75% are of unknown function. Despite this, studies into a handful of these genes has led to the view that this area of the chromosome is a significant tool in the adaptability and continuing evolution of vibrio bacteria. We have created large deletions in the integron of a model vibrio to create four mutants. The Honours project involves the use of these deletion mutants to identify how the integron affects vibrio physiology and ultimately host colonization and pathogenesis. The project will involve the use of techniques such as molecular biology, proteomics and bacterial bioassays.

Supervisor: Dr Tamara Sztzynda, MMB, UTS and Affiliated Institutions

Location: Building 4, UTS

Project: Behavioural feature recognition in video sequences – forensic, security, and surveillance implications.

A. UTS

Co-supervisors: Dr M Sutisno

Location: Medical and Molecular Biosciences Research

Research Area: Forensic Anatomy

Project: 1. Characterisation of the Mongoloid Eye

Identification of ethnicity of a skull can be divided into four main categories; Caucasoid, Australoid, Negroid and Mongoloid. All four have unique anthropological features of, and not limited to, the nasal area, zygomatic arches, mandible, palate, skull sutures, teeth and orbital openings. These unique features of the bony structure underlying the soft tissues gives rise to certain facial features of an individual which can be used in identification. The Mongoloid orbital openings of the skull are rounded and do not slope downwards. The eyes show an epicanthic fold, a double fold of fat of the upper eyelid from the nose to the inner eyebrow, producing an eye that appears almond shaped.

Currently, facial identification involves the use of biometric systems, 2D and 3D facial superimposition and facial mapping, all of which require further research and supporting data. Forensic reporting in a court of law is there to assist the court in decision making, and this is weighted favourably by producing a meaningful value from data using a Bayesian approach and forming a likelihood ratio. For this reason, further data needs to be gained through research to add to the current body of knowledge.

With this in mind, a research project focusing on the characterization of the Mongoloid eye is proposed. This may assist, amongst other data, with the process of facial identification. Data will be collected using morphological measurements of width, height and epicanthic fold size taken from a database of 2D Mongoloid and Caucasoid, male and female subjects. This data will then be plotted. It is postulated that a correlation may then be made between the eye measurements of test subjects of mixed ethnicity and the area of the curve under which they fall. Further examination of male and female subjects and the differences in measurements may then allow for further categorization.

Co-supervisors: Dr S Lal

Location: Medical and Molecular Biosciences Research

Research Area: Forensic Image analysis and identification of intent in human behaviour

Project:2. Behavioural feature recognition in video sequences: implications for counter terrorism and criminology

The use of technology for human behaviour recognition has implications for counter-terrorism. The application of video cameras in surveillance systems is very popular within the security agencies and most of the analysis is done offline. Studies have demonstrated success in real-time tracking of multiple objects in video capture. Video image analysis is a reliable tool for understanding human behaviour and characteristics such as facial tone, eyelid motion and other mannerisms such as rubbing, fidgeting and acting suspiciously. Facial patterns of fatigue and the levels of stress can be classified through video signal processing to determine the mind-set of a subject. However this is still a new area of research and human behaviour needs to be studied further to understand behaviour

during different emotional states. The information on the state of mind of a would-be criminal or terrorist is often neurological in nature, reflected by behaviours such as stress, anxiety and nervousness. Most surveillance systems deployed in public places simply record and but fail to distinguish neurological signals of criminals. However, these signals could present direct markers of the intentions. Video activity can be used to differentiate between emotional and human functional states. Assessing eye activity, facial characteristics or fingerprints can provide information about a person's identity and behavioural status, especially when used together. These forms of subject recognition and identifications can be used in a variety of applications, including controlled access to secure sites, making financial transactions, access to networked computers, in criminology and recognising a potential terrorist in a public place.

Existing facial recognition technology from video sources is becoming a practical tool for application in criminology, security, and counter-terrorism. Facial recognition has been implemented in limited applications, but has not been studied during specific emotional states. The current study aims to understand human mannerisms and psychophysiology for application in such environments. Moreover, this study will examine the influence of some of the following such as; variations in facial expressions, eye activity, mannerisms, posture and psychophysiology, and the significance between different emotional behaviour with respect to factors such as ethnicity, age, gender and psychological status.

B. Westmead Hospital

Co-supervisors: Drs H Medbury & A Guiffre, Vascular Biology Research Centre, Dept of Surgery,

Location: Westmead Hospital

Research Area: Atherosclerosis

Project: 3. Macrophages subsets in atherosclerosis

Atherosclerosis continues to be a major cause of morbidity and mortality in Australia. With ruptures more likely to occur in unstable atherosclerotic plaques (ones that have a relatively thin fibrous cap and large fatty core), the therapeutic goal is thus to convert unstable plaques to stable plaques. We propose that atherosclerotic plaque stability can be promoted by modulating monocyte/macrophage transformation. While monocytes have traditionally been known to play a detrimental role in cardiovascular disease by their transformation into macrophage (M) foam cells, we have recently shown (in clinical samples) that monocytes contribute to the formation of the atherosclerotic cap by transforming into a macrophage subtype called a fibrocyte – a cell that exhibits both macrophage (expresses CD68, CD163 and presents antigen) and smooth muscle cell (SMC) characteristics, such as expression of SMC α -actin and production of collagen – factors which promote plaque stability. With macrophages known to adopt various functional phenotypes (inflammatory, immune regulation and wound healing subgroups) that can be sequentially converted from one phenotype to another, it may be possible to stabilise atherosclerotic plaques through modulating monocyte/macrophage transformation. It is thus crucial to understand the differing roles of macrophage subtypes in atherosclerosis and their relationship to plaque stability.

This project has two aims: firstly, flow cytometry will be used to determine whether circulating monocyte subsets are polarised towards an M1/M2 phenotype relative to cholesterol levels and, secondly, immunohistochemistry will be used to identify different M1/M2 macrophage phenotypes in the carotid atherosclerotic plaque and assess their association with plaque stability.

Project: 4. Redefining the role of monocytes in atherosclerosis

It is well recognised that the clinical significance of an atherosclerotic plaque is dependent more on its composition than its overall size as it is the composition that determines the likelihood of plaque rupture. Plaques with a relatively large fatty core and thin fibrous cap are unstable whilst those with a relatively small fatty core and a thick fibrous cap are reasonably stable. In order to develop treatments to promote plaque stability it is crucial to understand the processes involved in the formation of both the core and fibrous cap. Monocytes have traditionally been known to play a detrimental role in cardiovascular disease by transforming into macrophage foam cells which contribute to the development of the fatty core. However, monocytes can also contribute to the formation of the atherosclerotic cap by transforming into a fibrocyte – a cell that exhibits both macrophage (expresses CD68, CD163 and presents antigen) and smooth muscle cell (SMC) characteristics, such as expression of SMC α -actin and production of collagen – factors which promote plaque stability.

This project will use fluorescent-activated cell sorting (FACS), cell culture and immunocytochemistry to determine: the subgroup of monocytes that produce fibrocytes (CD14⁺/CD16⁻ or CD14⁺/CD16⁺); whether macrophages can produce collagen; and whether, once a monocyte transforms into a fibrocyte can it further differentiate to form a foam cell or vice versa.

Supervisors: Dr H Medbury, Vascular Biology Research Centre, Dept of Surgery, Westmead Hospital & Assoc Prof A Holland, Burns Research Institute Department of Academic Surgery, Westmead Children's Hospital

Location: Westmead Hospital

Research Area: Hypertrophic Scarring in Paediatric Burns

Project: 5. Monocyte contribution to hypertrophic scar formation in the healing of paediatric burns

Each year in Australia, 6000 children present to emergency centres due to a burn; with 10% of these being admitted to hospital. At our unit alone, over 2000 children presented in 2007 with a burn. It is known that up to 35% of children who are hospitalised with a scald burn will subsequently develop severe scarring, known as a hypertrophic scar (HTS). In addition to considerable cosmetic and psychological sequelae, scars are often inflamed, itchy, and can result in functional impairment that may permanently disable the child. Even children that appear to heal well at a young age may develop functional sequelae later as they grow. In spite of continuous improvements in the management of acute burns, therapeutic strategies to treat HTS remain limited and we are basically left with supportive management and delayed reconstructive surgery. It is thus imperative that the process of HTS be understood so that its formation can be prevented.

We have recently shown that the presence of monocyte-derived fibrocytes in the paediatric burn wound is associated with the subsequent development of HTS. This project will now use flow cytometry to determine whether fibrocyte levels in the blood are also associated with HTS and, therefore, might be used to predict its subsequent development. In addition, flow cytometry will also be used to examine whether monocyte sub populations are polarised towards an M1/M2 phenotype post burn injury.

C. Royal North Shore Hospital

Supervisors: Dr A Gill Surgical Pathologist and Clinical Senior Lecturer Anatomical Pathology, PaLMS RNSH & Dr L Tan, Anatomical Pathology, PaLMS RNSH
<<http://www.cancerresearch.med.usyd.edu.au/members/profiles/affgill.php>>

Location: Royal North Shore Hospital

Research Area: Gastrointestinal Histopathology

Project: 6. Archival histological investigation examining mitochondrial cytopathy associated with gastrointestinal disease.

Supervisor: Dr Lisa Sedger, Institute for the Biotechnology of Infectious Diseases (IBID) and Department of Medical and Molecular Biosciences (MMB), UTS.

Location: Building 4, UTS.

Project 1: Poxviral inhibition of TNF-mediated inflammation.

Tumour Necrosis Factor- α (TNF α) is one of the most pleiotropic cytokines produced in mammals in response to infection, acting to induce inflammation and to directly kill virus-infected cells. It is not surprising therefore that most viruses have evolved strategies to evade TNF. For this same purpose Poxviruses encode a TNF-receptor homologue, first described in Myxoma virus as "T2" protein. Secreted T2 binds and sequesters TNF α , and intracellular T2 physically associates with the cells own TNF-Rs rendering the cellular receptors incapable of transmitting apoptotic cell death of the virus-infected cells.

On the other hand, patients with recurrent episodes of fever and multi-systemic inflammation frequently have an autosomal dominantly inherited periodic fever syndrome known as TNFR-associated periodic syndrome (TRAPS). Many of these patients have been shown to encode point mutations in their germline TNFR1 genes that result in the constitutive signaling of their TNF-Rs and hence these patients experience frequent inflammation and fever syndromes.

This project will assess if viral TNFR-like molecules from human-tropic poxviruses Variola virus (Smallpox) and monkeypox virus are able to inhibit constitutive TNFR signaling of TRAPS mutants TNF-Receptors.

The project utilizes the following techniques: plasmid cloning and transfection, tissue culture, antibody-immunoprecipitation, Western immunoblotting, and confocal cell imaging.

Project 2: TNF-family molecules as key factors controlling lymphocyte homeostasis and autoimmunity.

The Tumour Necrosis Factor-(TNF) family of cytokines are capable of inducing both apoptotic cell death as well as cell survival and cell proliferation. In vivo, this translates to control of lymphocyte homeostasis and autoimmunity. The use of gene knock-out mice has revealed that many of these molecules act in a co-operative manner, yet precisely how they interact in a physiological sense remains largely unknown. This project aims to define how TNF family molecules TRAIL and FasL co-operatively control lymphocyte homeostasis, and how this might influence autoimmune diseases such as Multiple Sclerosis.

The project utilizes the following techniques: In vitro culture of mouse lymphocytes, antibody-immunoprecipitation, Western immunoblotting, intracellular signaling (phosphorylation and caspase-activation), and multi-colour flow cytometry.

Supervisor: Dr Alison Heather, MMB

Location: Building 4, UTS

Research Project #1: Investigating the ability of the good cholesterol, HDL, to suppress liver inflammation and thereby block the development of insulin resistance

Recent lifestyle changes have resulted in an obesity epidemic. Weight gain and obesity are accompanied by activation of inflammatory pathways in the liver that increases the production of inflammatory mediators that leads to insulin resistance. Insulin resistance is an important state as unchecked it can lead to the development of type 2 diabetes and cardiovascular disease. These chronic diseases are major health burdens in the Australian economy with cardiovascular disease alone killing one Australian nearly every 10 minutes. The association between low levels of high density lipoprotein (HDL – the good cholesterol) and insulin resistance suggests a link between the two conditions. This current proposal will determine whether the good cholesterol, HDL, can stop inflammation and therefore stop insulin resistance. This project will provide experience in molecular biology, cellular biology and mouse animal work.

Research Project #2: The atheroprotective role of DHCR24

Dr Alison Heather's laboratory has recently discovered novel, potentially atheroprotective mechanisms with regard to intracellular stress mechanisms for the protein 3 β -hydroxysteroid- Δ^{24} -reductase (DHCR24), suggesting its potential as a therapeutic target to inhibit vascular inflammation and prevent atherosclerosis (H10). This research proposal now seeks to investigate the biological role of DHCR24, and how it is regulated, and whether elevated DHCR24 activity in endothelial cells protects them against cellular damage from atherosclerotic insults. It is hypothesised that increased expression of DHCR24 in vascular endothelial cells is anti-inflammatory, antioxidant, anti-apoptotic, thereby anti-atherogenic. This project will provide experience in molecular biology, cellular biology and mouse animal work.

Projects in Environmental Microbiology

There are also projects available in Environmental Microbiology and are suited to both MMB and DES students:

Supervisor: Josie Lategan

Location: Building 4, UTS

1. *Heavy metal toxicity on groundwater microbial and macroinvertebrate communities.* This projects investigates the effects on Chromium/Arsenic on microbial communities and macroinvertebrates that inhabit groundwater systems. The activity of microbial communities as measured by Fluorescein diacetate and ATP and, mortality of macroinvertebrates will be assessed against a range of heavy metal concentrations to determine the extent of toxicity and the dynamics of the response microbial to exposure.

2. *Effects of heavy metal contamination on groundwater microbial community diversity.*
This project examines changes in microbial community diversity as a result of heavy metal exposure. Diversity will be measured by the analysis of the 16S r DNA, using TRFLP.

3. *Rhodotorula sp, a potential bioindicator of groundwater health*
Rhodotorula is yeast which we have isolated from 4 different aquifers. Its wide distribution in aquifers that differ in geology, land use and which are geographically separated indicate that the organism might be a suitable bioindicator. The project will assess the organism against a variety of toxicants at various concentrations, using ATP as a measure of viability, in order to determine its suitability as a bioindicator.

4. *Stress responses of groundwater microbial communities exposed to heavy metals –a source of potential biomarkers.*
This project will screen established groundwater cultures exposed to heavy metals for stress proteins using 2 D gels. The project runs an initial assessment for potential biomarkers to be used in the detection of contamination of groundwater.

These projects will be presented and discussed at the DES Honours Information session on Wednesday 16:30 on level 5 seminar room. Come along to the session to find out more about the projects.