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| Name |  | Organisation | Research Project Name | Project short  summary (100 words) |  |  |  |  | Willing to act as a Supervisor Indicate Honours or PhD | Request for supervisor/co-supervisor |
| Freda Passam, MD, PhD |  | Senior Lecturer in Medicine  St George Clinical School VMO in Haematology Dept of Haematology, St George Hospital | Control of thrombus formation by S-nitrosylation.  Regulation of integrin function by thiol isomerases in haemostasis and thrombosis. |  |  |  |  |  | yes |  |
| Genia Burchall, |  | RMIT University | Haemostatic system in PCOS | ; |  |  |  |  |  | interested in someone suitable to co-supervise my project |
| Murray Adams |  | Senior Lecturer in Haematology Biomedical Science | School of Health Sciences | Faculty of Health University of Tasmania | Inhibition of Platelet Aggregation by Vanilloid-Like Agents  Effect of antiphospholipid antibodies on platelet function  Haemostasis in the elite athlete | <http://www.utas.edu.au/human-life-sciences/people/Murray-Adams> |  |  |  |  | Yes |  |
| Ass. Prof Robert K. Andrews |  | Australian Centre for Blood Diseases ,  The Alfred Hospital | Human platelet receptors in vascular systems: laboratory studies and clinical evaluation | Robert K. Andrews Human platelet receptors in vascular systems: laboratory studies and clinical evaluation The aim of this project is to provide new approaches for evaluating bleeding risk in people with normal or low platelet count. Platelet-related disorders are heterogeneous, and consequences with respect to platelet function and bleeding are unpredictable. Novel flow cytometry and ELISA based assays will be used to profile expression and function of platelet-specific receptors, glycoprotein (GP)Ib-IX-V and GPVI, critical for thrombus formation at arterial shear rates. This will provide experience in diagnosis, laboratory analysis and experimental systems. |  |  |  |  | yes |  |
| Natalie Pecheniuk |  | Lecturer, School of Biomedical Sciences  Head, Blood Coagulation and Thrombosis Research  Institute of Health and Biomedical Innovation  Queensland University of Technology | Modelling the effect of procoagulant phospholipid and microparticles in stored red blood cells during blood transfusion | : Recent evidence has suggested that RBCs may actively stimulate thrombin generation, and that procoagulant activity increases with storage age. The current storage time frame for RBCs is 0 to 42 days; however procoagulant activity has been detected much earlier than this expiry date. Current studies have postulated a multitude of mechanisms for how RBCs increase procoagulant activity, including exposure of phosphatidylserine. We aim to investigate the impact of stored PRBCs on coagulation and adherence properties across the time course and donor-related variation. In vitro whole blood transfusion and flow perfusion models will investigate the procoagulant properties across the storage duration of donor packed RBCs. |  |  |  |  | yes |  |
| Natalie Pecheniuk |  |  | Properties of blood coagulation following reversal of acute coagulopathy in haemorrhagic shock using Adenosine, Lidocaine and Magnesium. | Storage conditions and current liquid preservatives fail to effectively prevent the storage lesion of RBCs, and in some cases have been shown to increase coagulation activation. There is currently no known solution available to increase the viability of stored RBCs. Recently it has been shown that adenosine, lidocaine and magnesium (ALM) has resuscitative and protective abilities in rat models of trauma and haemorrhagic shock, cardiac arrest and sepsis. Individually, lidocaine has been shown to inhibit the haemolysis of RBCs and can act as a free radical scavenger. It has also shown protective effects on RBCs stored for seven days. Our studies will elucidate the mechanisms by which this resuscitation therapy restores the beneficial coagulation properties. |  |  |  |  |  |  |
| Natalie Pecheniuk |  |  | High Density Lipoproteins (HDL) are beneficial for anticoagulant activity | Changes to normal lipoprotein levels, as illustrated by deficiency of high density lipoprotein (HDL), in particular deficiency of the larger HDL subclasses, is associated with a hypercoagulable state and with venous thromboembolism. Also, patients with VTE recurrence have a reduced risk when HDL apolipoprotein, ApoAI, levels are elevated. Anticoagulant activity mediated by activated protein C and protein S is enhanced by HDL (and not LDL) resulting in the down-regulation of thrombin. It is yet unclear if the molecular components of specific HDL subclasses, such as apolipoproteins, contribute to anticoagulant activity or the relative risk of hypercoagulation observed in VTE. The proposed experiments will characterise the HDL subfractions with enhanced anticoagulant activity and apolipoproteins identified will be assessed using coagulation assays. |  |  |  |  |  |  |
| Shaun Jackson, Simone Schoenwaelder |  | Heart Research Institute and Charles Perkins Centre ,  The University of Sydney | Investigating  the  role  of  cell  death  pathways  in  regulating  the  proinflammatory  function  of  platelets  and  leukocytes  during  ischaemia--‐  reperfusion  injury | Ischemia reperfusion (I/R) injury is an important  complication of a wide range of human diseases,  including acute myocardial infarction (AMI),  ischaemic stroke, cardiac arrest, sickle cell crisis  and solid organ transplantation. I/R injury is  characterised by microvascular dysfunction and  hypoperfusion, leading to tissue ischemia and  extensive platelet and leukocyte recruitment to the microcirculation. A growing body of  evidence suggests a key role for platelet-leukocyte adhesive interactions in exacerbating  tissue injury by promoting microvascular obstruction, tissue hypoperfusion and inflammation  however the underlying mechanisms regulating these processes remain ill-defined.  Recent studies from our laboratory have made the unexpected observation that a specific  form of platelet cell death, termed programmed necrosis, plays a major role in promoting  leukocyte recruitment and tissue damage following I/R injury. Notably, this pathway is  resistant to the inhibitory effects of conventional anti-platelet and anti-inflammatory agents.  In collaboration with Dr Ben Kile’s group at WEHI, we plan to examine the thromboinflammatory  response of mice that are resistant to apoptotic cell death (Bak:Bax knock-out  mice) or necrosis (Cyclophilin D knock-out mice), in *in vivo* models of inflammation and  ischaemia-reperfusion injury. Our aim is to investigate the role of specific cell death  pathways in regulating platelet proinflammatory function and leukocyte recruitment, with the  ultimate aim of identifying new therapeutic targets to improve microvascular perfusion and  reduce inflammation and organ injury. This project utilises a range of techniques including  detailed cell biology and signalling assays, *in vitro* perfusion assays, flow cytometry,  confocal microscopy and *in vivo* models of thrombosis, inflammation and ischaemia  reperfusion injury. |  |  |  |  |  |  |
| Shaun Jackson, Simone Schoenwaelder |  |  | Identifying  new  pathways  regulating  platelet  hyperactivity  and  thrombosis  in  diabetes | Atherothrombosis is a major healthcare  problem that affects >40% of the adult  population. In particular, the development of  arterial thrombosis in the coronary or  cerebral circulation (causing acute myocardial infarction and ischaemic stroke, respectively)  is responsible for more deaths in the community than any other disease process. Despite  intense investigation over the last 40 years into the discovery and development of more  effective anti-platelet drugs, the impact of these therapies on mortality rates has remained  disappointingly low, with less than 1 and 6 patients taking anti-platelet therapies avoiding a  fatal thrombotic event. This situation is likely to worsen in the future due to the rapidly  growing incidence of obesity, diabetes and the metabolic syndrome. These diseases are  typically more resistant to the benefits of anti-platelet therapy, thus there is a pressing need  for the identification and development of more effective approaches.  Our laboratory has recently defined a new pathway promoting platelet aggregation and  thrombus development that involves biomechanical platelet activation. More recently, we  have identified that this pathway is dysregulated in diabetes and leads to enhanced plateletendothelial  interaction through a molecular process that is linked to atherogenesis. In this  project we aim to identify the molecular mechanisms by which hyperglycemia leads to  enhanced biomechanical platelet activation, and the relevance of this pathway to plateletendothelial  and platelet-platelet adhesive interactions linked to atherothrombosis. This  collaborative project with Prof. Mark Cooper’s group at the Baker Institute, involves the  study of platelet function from genetically-manipulated mouse models of diabetes as well as  patients with Type I and II diabetes. The role of platelet scavenger receptors, including CD36  and SR-BI, receptors for advanced glycation end-products (AGEs) and key components of  the oxidative stress pathways in platelets will be examined for their ability to promote  biomechanical platelet activation. This project utilises a broad range of techniques including  detailed cell biology and signalling assays, *in vitro* perfusion assays, flow cytometry,  confocal microscopy and *in vivo* models of endothelial dysfunction and thrombosis. |  |  |  |  |  |  |
| Shaun Jackson, Simone Schoenwaelder |  |  | Identifying  novel  approaches  to  facilitate  blood  clot  dissolution | Blood platelets play a critical in the development of  occlusive arterial blood clots (thrombi), precipitating  diseases such as heart attack and ischaemic stroke. The  rapid reperfusion of occluded blood vessels to  minimise tissue death is a key treatment goal in patients  suffering heart attack and stroke, with the administration of thrombolytic therapy an  important means of establishing reperfusion. This is usually achieved through administration  of fibrinolytic agents modelled on tissue-type plasminogen activator (tPA). However,  thrombolytic therapy is not without its limitations, with lysis resistant blood clots, as well as  hemorrhage presenting as major complications.  One of the main factors delaying reperfusion and increasing the risk of reocclusion of  cerebral vessels is the presence of platelets in arterial thrombi. Platelets inhibit thrombolysis  through multiple mechanisms and numerous preclinical and clinical studies have  demonstrated the benefits of adjunctive anti-platelet therapy to enhance cerebral reperfusion  and reduce reocclusion following thrombolysis. Unfortunately in stroke patients, the benefits  of combined antiplatelet and thrombolytic therapy are partially offset by the increased risk of  life-threatening intracerebral bleeding, limiting the widespread use of this approach.  Our laboratory has recently demonstrated that inhibitors of PI 3-kinase (PI3K), when  adminsitered alone or with tPA, are highly effective at promoting thrombus dissolution,  without markedly increasing tail bleeding times. These results raise the possibility that PI3K  inhibitors may represent a safe and effective adjuvant therapy for the treatment of stroke.  This project will examine the potential use of PI3Kinhibitors as adjuvant therapy for stroke  and compare their safety and efficacy with that of currently used anti-platelet agents. Studies  will involve the use of *in vivo* models of thrombosis and thrombolysis, *in vitro* flow-based  assays, genetic mouse models and state-of-the-art imaging systems (confocal microscopy,  intravital microscopy), complemented with *in vitro* analysis of platelet function. These  studies will not only provide important insight into our understanding of blood clot  formation, but may also lead to new approaches to regulate the size and stability of blood  clots forming in the body, providing major clinical benefit in the delivery of thrombolytic  therapy (blood clot removal). |  |  |  |  |  |  |
| Matthew Linden |  | University of WA | Platelet induced signal transduction in immune cells | Platelets are anuclear blood elements with well characterised functions in haemostasis and an emerging role immunity. Platelets execute their function through complex intra- and extra- cellular signalling pathways which allow conformational changes, release of thromboinflammatory mediators, and aggregation in response to stimulation. Evidence is accumulating that there are complex interactions, or “cross talk,” between platelets and other haemopoeitic cells (particularly leukocytes) which influence the functional state of these cells. However, little is known of the interaction of platelet-leukocyte signalling transduction and its relationship to haemostatic and immune function. Dr Linden and others have previously shown that platelets communicate monocytes through expression of adhesion receptors (such as P-selectin) and release of soluble thromboinflammatory chemokines and soluble CD40L. These platelet-derived signals result in a pro-adhesive and pro-atherogenic monocyte phenotype, and have been suggested to play a role in the progression of inflammatory diseases, including atherogensis. Therapeutic interventions which target the platelet-monocyte nexus have shown promising in slowing the progression of these diseases. Recent advances in cytometry now allow researchers to examine the platelet mediated signal transduction and the functional impact of platelet interactions not limited to monocytes, but across the entire haemopoeitic lineage at once. By using an innovative systems biology approach the candidate will address these important questions with the following specific aims. 1. Analyse signal transduction of platelets in response stimulation. 2. Analyse the time course of signal transduction pathways initiated by activated platelets in a variety of cell lines. 3. Analyse the time course of signal transduction pathways and functional changes initiated by activated platelets across the entire haemopoeitic lineage on a cell-by-cell basis. 4. Measure changes in platelet and platelet-mediated signal transduction with age. The supervisor for this project is Dr Matthew Linden. All work will be conducted in the Platelet Biology Laboratory, School of Pathology and Laboratory Medicine and at the Centre for Microscopy, Characterisation and Analysis, QEII Medical Centre. If you would like additional information regarding this project, please email matthew.linden@uwa.edu.au or call (+61 8) 9346 1050. If you have questions about how to apply to become a PhD student at UWA, please email pghelp@postgraduate.uwa.edu.au or call (+61 8) 6488 2807. |  |  |  |  |  |  |