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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 MedicineSt George Clinical SchoolVMO in HaematologyDept 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 HaematologyBiomedical Science | School of Health Sciences | Faculty of HealthUniversity of Tasmania | Inhibition of Platelet Aggregation by Vanilloid-Like AgentsEffect of antiphospholipid antibodies on platelet functionHaemostasis 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 SciencesHead, Blood Coagulation and Thrombosis ResearchInstitute of Health and Biomedical InnovationQueensland 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 | Investigatingtheroleofcelldeathpathwaysinregulatingtheproinflammatoryfunctionofplateletsandleukocytesduringischaemia--‐reperfusioninjury | Ischemia reperfusion (I/R) injury is an importantcomplication of a wide range of human diseases,including acute myocardial infarction (AMI),ischaemic stroke, cardiac arrest, sickle cell crisisand solid organ transplantation. I/R injury ischaracterised by microvascular dysfunction andhypoperfusion, leading to tissue ischemia andextensive platelet and leukocyte recruitment to the microcirculation. A growing body ofevidence suggests a key role for platelet-leukocyte adhesive interactions in exacerbatingtissue injury by promoting microvascular obstruction, tissue hypoperfusion and inflammationhowever the underlying mechanisms regulating these processes remain ill-defined.Recent studies from our laboratory have made the unexpected observation that a specificform of platelet cell death, termed programmed necrosis, plays a major role in promotingleukocyte recruitment and tissue damage following I/R injury. Notably, this pathway isresistant 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 thromboinflammatoryresponse of mice that are resistant to apoptotic cell death (Bak:Bax knock-outmice) or necrosis (Cyclophilin D knock-out mice), in *in vivo* models of inflammation andischaemia-reperfusion injury. Our aim is to investigate the role of specific cell deathpathways in regulating platelet proinflammatory function and leukocyte recruitment, with theultimate aim of identifying new therapeutic targets to improve microvascular perfusion andreduce inflammation and organ injury. This project utilises a range of techniques includingdetailed cell biology and signalling assays, *in vitro* perfusion assays, flow cytometry,confocal microscopy and *in vivo* models of thrombosis, inflammation and ischaemiareperfusion injury. |  |  |  |  |  |  |
| Shaun Jackson, Simone Schoenwaelder |  |  | Identifyingnewpathwaysregulatingplatelethyperactivityandthrombosisindiabetes | Atherothrombosis is a major healthcareproblem that affects >40% of the adultpopulation. In particular, the development ofarterial thrombosis in the coronary orcerebral circulation (causing acute myocardial infarction and ischaemic stroke, respectively)is responsible for more deaths in the community than any other disease process. Despiteintense investigation over the last 40 years into the discovery and development of moreeffective anti-platelet drugs, the impact of these therapies on mortality rates has remaineddisappointingly low, with less than 1 and 6 patients taking anti-platelet therapies avoiding afatal thrombotic event. This situation is likely to worsen in the future due to the rapidlygrowing incidence of obesity, diabetes and the metabolic syndrome. These diseases aretypically more resistant to the benefits of anti-platelet therapy, thus there is a pressing needfor the identification and development of more effective approaches.Our laboratory has recently defined a new pathway promoting platelet aggregation andthrombus development that involves biomechanical platelet activation. More recently, wehave identified that this pathway is dysregulated in diabetes and leads to enhanced plateletendothelialinteraction through a molecular process that is linked to atherogenesis. In thisproject we aim to identify the molecular mechanisms by which hyperglycemia leads toenhanced biomechanical platelet activation, and the relevance of this pathway to plateletendothelialand platelet-platelet adhesive interactions linked to atherothrombosis. Thiscollaborative project with Prof. Mark Cooper’s group at the Baker Institute, involves thestudy of platelet function from genetically-manipulated mouse models of diabetes as well aspatients with Type I and II diabetes. The role of platelet scavenger receptors, including CD36and SR-BI, receptors for advanced glycation end-products (AGEs) and key components ofthe oxidative stress pathways in platelets will be examined for their ability to promotebiomechanical platelet activation. This project utilises a broad range of techniques includingdetailed 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 |  |  | Identifyingnovelapproachestofacilitatebloodclotdissolution | Blood platelets play a critical in the development ofocclusive arterial blood clots (thrombi), precipitatingdiseases such as heart attack and ischaemic stroke. Therapid reperfusion of occluded blood vessels tominimise tissue death is a key treatment goal in patientssuffering heart attack and stroke, with the administration of thrombolytic therapy animportant means of establishing reperfusion. This is usually achieved through administrationof fibrinolytic agents modelled on tissue-type plasminogen activator (tPA). However,thrombolytic therapy is not without its limitations, with lysis resistant blood clots, as well ashemorrhage presenting as major complications.One of the main factors delaying reperfusion and increasing the risk of reocclusion ofcerebral vessels is the presence of platelets in arterial thrombi. Platelets inhibit thrombolysisthrough multiple mechanisms and numerous preclinical and clinical studies havedemonstrated the benefits of adjunctive anti-platelet therapy to enhance cerebral reperfusionand reduce reocclusion following thrombolysis. Unfortunately in stroke patients, the benefitsof combined antiplatelet and thrombolytic therapy are partially offset by the increased risk oflife-threatening intracerebral bleeding, limiting the widespread use of this approach.Our laboratory has recently demonstrated that inhibitors of PI 3-kinase (PI3K), whenadminsitered 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 strokeand compare their safety and efficacy with that of currently used anti-platelet agents. Studieswill involve the use of *in vivo* models of thrombosis and thrombolysis, *in vitro* flow-basedassays, genetic mouse models and state-of-the-art imaging systems (confocal microscopy,intravital microscopy), complemented with *in vitro* analysis of platelet function. Thesestudies will not only provide important insight into our understanding of blood clotformation, but may also lead to new approaches to regulate the size and stability of bloodclots forming in the body, providing major clinical benefit in the delivery of thrombolytictherapy (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.   |  |  |  |  |  |  |