

Wednesday, March 21, 2012
12:00pm
in LSC3



Dr. Heyu Ni

*Canadian Blood Services and St. Michael's Hospital
Associate Professor
Department of Laboratory Medicine and Pathobiology,
Department of Medicine, and Department of Physiology
University of Toronto*

Life Sciences Centre
2350 Health Sciences Mall

“Thrombosis and Thrombocytopenia: Lessons from animal models and human patients”

Platelets play key roles in hemostasis and thrombosis. Recent studies found that platelets contain significant amounts of P-selectin, TLRs, CD40/CD40L, TGF- β and other inflammatory factors. They also contain both pro- and anti-angiogenic factors. Thus, platelets are versatile cells and significantly contribute to inflammation, immune responses, and angiogenesis.

It has been documented for more than 4 decades that fibrinogen is required for platelet aggregation. However, using an intravital microscopy thrombosis model, we found that platelet aggregation and thrombus formation occurred in mice lacking either fibrinogen or both fibrinogen and von Willebrand factor (Fg/VWF $^{-/-}$). We further demonstrated that Fg/VWF-independent platelet aggregation can be induced in vitro under more physiological conditions (i.e. non-anticoagulated blood) and that β 3 integrin (GPIIb/IIIa) is the platelet receptor required for this non-classical mechanism of platelet aggregation. To examine whether plasma fibronectin (pFn) is the alternative β 3 integrin ligand mediating this novel platelet aggregation pathway, we generated Fg/VWF/pFn $^{-/-}$ triple knock-out mice. Surprisingly, platelet aggregation and thrombus formation in Fg/VWF/pFn $^{-/-}$ mice were not abolished but were enhanced, as compared with Fg/VWF $^{-/-}$ mice. Our data demonstrate that pFn is a supportive factor in hemostasis but a regulatory factor in thrombosis.

The platelet fibrinogen receptor (GPIIb/IIIa) and VWF receptor (GPIb complex) are also the major target antigens in immune-mediated thrombocytopenia. We established several animal models of auto- and alloimmune thrombocytopenia. We found that anti-GPIb antibody-mediated thrombocytopenia has significant differences from anti-GPIIb/IIIa-mediated thrombocytopenia with regards to both pathogenesis and response to therapies.

This Seminar is sponsored by:

Baxter

Host: Dr. Ed Prydzial, Clinical Professor Pathology and Laboratory Medicine & Centre for Blood Research



Refreshments will be served 10 minutes before the seminar
Seminar information: 604 822 7407

