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Wednesday, May 25, 2011
12:00pm
in LSC3

Life Sciences Centre
2350 Health Sciences Mall

“Unique Mechanisms by which Activated Platelets Regulate Thrombin Generation at their Membrane Surfaces”

Effective thrombin generation requires the formation of factor Va, a two subunit protein produced by the proteolytic conversion of its single chain procofactor, factor V. Factor Va functions as the obligate non-enzymatic cofactor of Prothrombinase, a supramolecular enzyme consisting of a 1:1 Ca²⁺-dependent complex of factor Va, and the serine protease, factor Xa, assembled on the surface of activated platelets. In addition to providing the membrane for Prothrombinase assembly, platelets also contain and release approximately 20-25% of the total factor V/Va found in blood. The platelet-derived factor Va pool is formed subsequent to megakaryocyte endocytosis of plasma-derived factor V. Endocytosed factor V is then phenotypically modified, proteolytically activated and packaged into α -granules to form the hemostatically relevant cofactor pool.

These phenotypic changes result in significant functional differences between the two cofactor pools, such that the platelet-derived factor Va expresses greater cofactor activity and is resistant to proteolytic inactivation. One such modification is evidenced by the observation that a significant fraction of the factor Va expressed on the activated platelet surface is covalently bound to the membrane via a GPI anchor on the C-terminus of the heavy chain subunit. However, not only is the retention of factor Va at their membrane surface a way in which activated platelets sustain procoagulant events, but the manner in which they regulate the activity of Prothrombinase ensures their procoagulant phenotype, as well. The platelet-bound enzyme first cleaves prothrombin at Arg271 to form the non-enzymatic intermediate prethrombin-2, followed by a second cleavage at Arg320 to yield thrombin. As a result procoagulant activity is optimized hemostatically, since the initial cleavage at Arg320, to form the meizothrombin intermediate, a protease with substantial anticoagulant activity, is avoided. Thus, platelet-derived factor Va and the activated platelet membrane work in concert to contribute significantly to sustaining and regulating the generation of thrombin on the surfaces of activated platelets.

This Seminar is sponsored by:



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

