CBR
Canadian Blood Services
Société canadienne du sang

The Centre for Blood Research Seminar Series

Dr. Athan Kuliopulos

Professor of Medicine, Tufts University

Wednesday, March 13th, 2013
LSC 3 - Life Sciences Centre
2350 Health Sciences Mall

12-1pm

"PARticipating in Metalloprotease Signaling in Blood Vessels"

When plaques coating blood vessel walls rupture and expose collagen, platelets spring into action to form a blood clot at the damaged site. Dr. Kuliopulois reveals how those life-threatening clots get an early grip. The discovery might offer a new way to fight clot formation before it can even begin. Compared to other diseases, blood clotting has been very well understood, nevertheless, many people still suffer from heart attacks, ischemic stroke and death as a result of clot formation. Scientists have known that a protein called thrombin plays an important role in clot formation as a potent activator of platelets. It also cuts fibrinogen into fibrin, a fibrous protein that works together with platelets to form a clot. But thrombin isn't the whole story. Enzymes known as matrix metalloproteases have recently emerged as important players in platelet function, sepsis, and the biology of blood vessels. In cancer cells too, MMP-1 activates a receptor known as PAR1 – the same PAR receptor that is also responsible for receiving the thrombin signal on human platelets. They show that exposure of platelets to collagen activates MMP-1, which in turn directly cut PAR1 on the surface of platelets. Collagen is the first thing a platelet "sees" when a blood vessel ruptures or is cut. The MMP-1-PAR1 pathway activates another set of molecular players known to be involved in early clot formation. Those activated platelets change their shape, sending out spikes and membrane sheets. Within seconds, they become more sticky, adhering to the vessel surface and then other platelets. Moreover, treatments that block the MMP1-PAR1 pathway prevent blood clots from forming in the presence of collagen, suggesting that drugs, such as the PZ-128 pepducin, that target this metalloprotease-receptor system could offer a new way to treat patients with acute coronary syndromes.

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