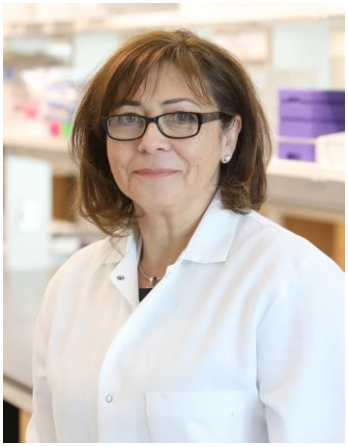
The Centre for Blood Research
VIRTUAL SEMINAR SERIES

Wednesday, March 31, 2021
11:15am - 12:15pm PST



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"Endothelial-Myeloid Collaborations in Hemostasis"

Vascular endothelial and hematopoietic cells hold a close relationship which is initiated during development, but that continuously broadens in the adult to include new functions aimed at maintaining homeostasis. We have identified a population of macrophages (MacAIRs) that takes permanent residency in the tunica intima of the aorta and that shares the luminal surface side-by-side with the endothelium. MacAIRs were found to be transcriptionally distinct from other macrophages and closely associated with the endothelium in the absence of pathology. Lineage tracing analysis indicated that adult MacAIRs were derived from definitive hematopoietic lineage precursors that migrated from the ductus arteriosus seeding the aorta immediately post-birth in areas of turbulent flow including the lesser curvature of the aortic arch and branch openings. These aortic resident macrophages expand via direct cell renewal and progressively expand in aged aortae to also populate regions of laminar flow. Binding of MacAIRs relied heavily on expression of endothelial ICAM that interacts with CD11c on macrophages. Genetic deletion of either ICAM or CD11c significantly impaired anchorage of MacAIRs to the endothelium. To clarify the biological significance of this population of macrophages, we used a dual diphtheria toxin induced-depletion system that efficiently eliminated MacAIRs in adult animals. Utilizing this model, we found that absence of MacAIRs leads to progressive fibrin accumulation and formation of microclots that, once dislodged, can cause blockade of vessels and organ failure. In fact, 40% of the animals with genetic-mediated depletion of MacAIRsdied within 2 weeks post-depletion suggesting that these macrophages were required to clear fibrin deposits in regions of turbulent blood flow. These findings advance our knowledge of how vascular endothelial cells profit from this unique interaction with macrophages to control hemostasis, prevent intravascular clotting, and ensure vascular health.

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