The Centre for Blood Research Seminar Series

Wednesday, October 10, 2018

LSC 3 | 12:00 - 1:00PM

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"ADAMTS13 deficiency in thrombotic thrombocytopenic purpura"

Von Willebrand Factor (VWF) plays an important role in recruiting platelets to sites of vessel injury. Its multimeric size is regulated by the enzyme ADAMTS13. A deficiency in ADAMTS13 can lead to the accumulation of ultra-large VWF multimers within the circulation and to the development of the disease thrombotic thrombocytopenic purpura (TTP) characterised by the uncontrolled formation of platelet-rich thrombi in the microcirculation and subsequent life threatening vessel occlusion. Approximately 5% of TTP patients have a congenital deficiency due to mutations within the ADAMTS13 gene which reduce the secretion and activity of ADAMTS13. The remaining 95% of TTP patients have an acquired, immune mediated deficiency due to the presence of anti-ADAMTS13 IgG antibodies. We have recently shown that the binding of these autoantibodies is dependent upon the conformation of ADAMTS13 (which can exist in 'open' and 'closed' forms). Anti-ADAMTS13 antibodies can exert their pathogenic effects by inhibiting ADAMTS13 function and/or inducing its clearance from the circulation. Antibody-mediated clearance is an important pathogenic disease mechanism but the mechanism by which this occurs is unknown and is currently under investigation.

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