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Diabetes and Thrombosis: The Dark Side of the Force

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Abstract: Thrombotic diseases where platelets form clots and obstruct blood vessels remains the leading cause of death and disability in the world. Despite intense investigation over the last 40 years into the discovery and development of more effective drugs, less than 1 in 6 patients taking anti-thrombotic therapies avoid a fatal event. This situation is likely to worsen in younger generations due to the rapidly growing incidence of diabetes, which makes people more prone to thrombosis and resistant to existing anti-thrombotics with unknown reasons.

To investigate this, I have developed the 'Biomembrane Force Probe' as the first-of-its-kind. This nanotool represents a significant departure from traditional biological studies of protein-protein and cell-cell interactions after prolonged incubation, uniquely suitable for studying these transient interactions in rapidly circulating blood under mechanical force. I have identified a previously unrecognised force-sensing mechanism utilised by platelets during blood clotting (Nature Materials 2019). This mechanism is dysregulated in diabetes, leading to shear-specific enhancement in platelet thrombus formation. Importantly, my studies defined a new therapeutic approach to reduce platelet shear force-sensing function – through inhibition of PI3-Kinase 110beta (Nature Communications 2018). This may ultimately lead to a new treatment to combat the fatal thrombotic disease for patients with diabetes.

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