DEVELOPMENT OF AN *IN VITRO* MICROVESSEL BLOOD FLOW PLATFORM

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Microvessels (≤100μm diameter) are embedded within living tissues for the purpose of nutrient delivery and gas exchange. Microvascular blood flow must be tightly regulated and dysfunction of flow regulation is implicated in a number of microvascular diseases, such as diabetes and malaria [1]. The properties of red blood cells (RBCs) are also altered in such conditions, which leads to changes in blood flow [1]. As flow-mediated vasomotor tone control by endothelial cells (ECs) [2] is a key mechanism of blood flow regulation, it is important to better understand the interactions between RBCs and endothelial cells in healthy and pathological conditions.

Unlike large vessels, blood flow in microvessels cannot be considered as a single-phase Newtonian fluid due to the unique mechanical properties of red blood cells and their complex flow behaviour. The role of RBC mechanical properties, such as their deformability [3] or the extent of their aggregation [4], on flow parameters (e.g. velocity profile) have been studied in various numerical and experimental models. While numerous studies have investigated the effect of shear stress using culture media, studies that incorporate both physiologically relevant RBC flows and EC studies are severely lacking.

To better understand how EC response is modulated by the mechanical properties of RBCs, we have developed a system that allows perfusion of human RBCs through a fully endothelialised PDMS-based microvessel (Fig. 1A and B). Human umbilical vein endothelial cells (HUVECs) cultured within the microfluidic device were subjected to an average wall shear stress of 30 dyn/cm^2 for 2 hr with either cell culture medium (EGM2) or healthy human RBCs suspended in EGM2 at 25% haematocrit (physiological for a large microvessel). Preliminary results show that after being perfused with the Newtonian EGM2, HUVECs have clear elongation and remodelling of the actin cytoskeleton (Fig. 1D), contrary to HUVECs perfused with the non-continuum RBC suspension (Fig. 1E). Ongoing work will elucidate difference between the ECs after perfusion with health vs chemically-stiffened human RBCs, and characterisation of key markers (i.e. activated eNOS and ET-1) involved in the endothelial vasodilation response.

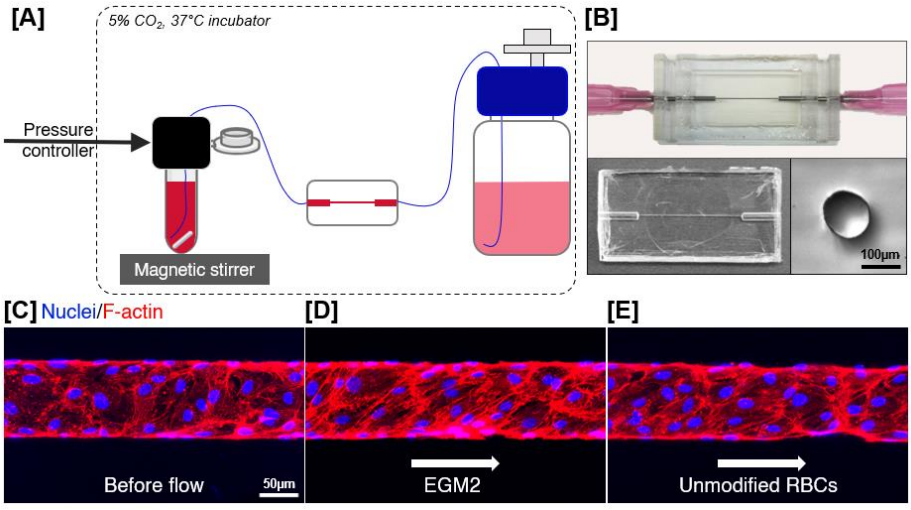

Fig. 1: (A) Schematic of pressure-based flow system. (B) PDMS-based microfluidic device with round cross-section. Scale bar = 100μm. (C) HUVEC morphology before flow, (D) after 2 hr flow with Newtonian cell culture medium EGM2 and (E) after 2 hr flow with healthy human RBC suspension at 25% Hct. Scale bar = 50μm.

References

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