HHS Public Access

Author manuscript

Platelets. Author manuscript; available in PMC 2018 July 01.

Published in final edited form as:

Platelets. 2017 July ; 28(5): 425–426. doi:10.1080/09537104.2017.1325187.

Utility and development of microfluidic platforms for platelet research

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The formation of a hemostatic plug to staunch blood loss at sites of vascular injury relies on the dynamical processes of platelet recruitment and activation of the coagulation cascade in the setting of the biorheology of blood flow.[1–3] Thus, elucidation of the molecular mechanisms of thrombus formation has relied on the use of engineering principles to design platforms to study platelet cell biology under physiologically relevant shear flow conditions. Historically this necessitated the use of custom-made parallel-plate flow chambers coupled with fluorescent or phase-contrast microscopy, restricting these studies to cell biology or biochemistry laboratories that collaborated with engineering and physics departments.[4–6] Recent advances in fabrication, standardization and commercialization of microfluidics has now allowed for the widespread distribution of microfluidic platforms amongst the platelet research community. Moreover, the silos or cell biology, biochemistry, engineering and physics are rapidly dissolving, with the composition of research teams now spanning data science, quantitative biology, and translational medicine. This review series presents an overview of the history, current use and future applications of microfluidic platforms for platelet research.

The shear-dependent binding of the platelet receptor glycoprotein (GP)Ib to von Willebrand Factor (VWF) is requisite for the initial step of platelet recruitment to exposed subendothelial extracellular matrix proteins under flow.[7,8] The review by Hastings *et al.* describes the use of microfluidic devices for the study of biophysics of platelet biology under shear, with the review of Zhang *et al.* focusing on the utility of microfluidics to study GPIb-VWF interactions. Concomitant with platelet recruitment is activation of the coagulation cascade to generate thrombin and form fibrin. The review by Nagy *et al.* describes the use of microfluidic platforms to study the role of the platelet surface as a site of catalysis for thrombin generation under physiologically relevant shear flow conditions. The review by Zilberman-Rudenko *et al.* then explores the use of endothelialized microfluidic platforms to combine the study of platelet recruitment and activation of the coagulation cascade in the physiological context of vascular cells and shear.

Declaration of interest

The authors report no declaration of interest.

It has been shown that transfusion of platelets during resuscitation drastically improves trauma patient survival.[9–11] Inversely, increased platelet counts and activity is deleterious in the setting of cardiovascular disease or cancer.[12–14] Yet, standard clinical tests provide incomplete guidance for selecting patients who might benefit from platelet transfusion or anti-platelet therapy, balancing safety with efficacy.[15–19] Herein the reviews by Li *et al*. and Schoeman *et al*. discuss the utility of microfluidic technologies which mimic the biorheology of the vasculature to interrogate platelet response to therapy, assess hemostasis and diagnose clinical bleeding defects. Finally, the review by Thon *et al*. introduces the use of microfluidic platforms as an organ-on-the-chip bioinspired approach to generate platelets *ex vivo*, with potential applications in transfusion medicine.

Taken together, the goal of this series of reviews is to provide the readership of *Platelets* a state-of-the-art overview of the development and use of microfluidic platforms to study and assess the function of platelets in health and disease.

Acknowledgments

This work was supported by grants from the National Institutes of Health (R01HL101972 and R01GM116184 to O.J.T.M. and F31HL13623001 to J.Z.-R.). O.J.T. McCarty is an American Heart Association Established Investigator (13EIA12630000).

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