

# MicroRNAs: A New Understanding of Platelet Physiology and Pathology

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Platelets have roles in both health and disease beyond their role in haemostasis. As platelets are anucleate and do not perform transcription, micro-ribonucleic acids (miRNAs) are in the spotlight as post-transcriptional regulators of their protein content. Through discoveries that have partly emanated from our group,<sup>1,2</sup> it has now become apparent that miRNAs are relevant to platelet biology. Using human megakaryocytes in addition to mouse models enables mechanistic insights on how miRNAs regulate platelet protein content, but also platelet protein release. For example, miR-21 has recently been shown to attenuate the platelet release of transforming growth factor  $\beta$  1, a master regulator of fibrosis.<sup>2</sup> In this issue, Garcia et al<sup>3</sup> address the role of miR-126-3p, an important miRNA in platelets. While miR-126-3p is highly abundant in endothelial cells and was long considered endothelial specific, it is also expressed in megakaryocytes, and its potential role in platelet function has been overlooked. Garcia et al<sup>3</sup> demonstrate that miR-126-3p is involved in the regulation of platelet activation using a relevant human cell type. The authors transfected CD34 + - derived megakaryocytes with miR-126-3p and differentiated the megakaryocytes into platelet-like structures. Next, the authors performed platelet aggregation tests in a fibrinogen-coated flow chamber. They were able to show that miR-126-3p over-expression in megakaryocytes resulted in increased platelet activation. This is consistent with our previous findings in mice showing reduced platelet

function upon treatment with a pharmacological inhibitor (antagomiR) against miR-126-3p.<sup>1</sup> Moreover, the authors confirmed that miR-126-3p targets ADAM9 in megakaryocytes.<sup>1</sup> ADAM9 has been shown to affect collagen-induced platelet aggregation. They also identified plexin-B2 as a new target of miR-126-3p. Plexin-B2 is involved in regulating platelet signalling. In summary, this article provides further evidence for a role of miR-126-3p in regulating platelet function. This finding should now be followed up in more detail using an appropriate model system.

## Conflict of Interest

M. Mayr filed and licensed patent applications on miRNAs as biomarkers (EP15193448.6, EP2776580 B1, DE112013006129T5, GB2524692A, EP2576826 B, JP2013-513740).

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