In this issue of *Thrombosis and Haemostasis*, Alrehani et al. (1) use human embryonal kidney 293 cells expressing the recombinant αIIbβ3-integrin to investigate the role of different isoforms of protein phosphatase 1 (PP1) in αIIbβ3-mediated outside-in signalling. PP1 is a serine/threonine phosphatase that is involved in a wide variety of cellular functions. Three isoforms of this enzyme have been identified (PP1α, PP1β/δ and PP1γ). In previous work by the authors and others an association of PP1 with the cytoplasmic tails of αIIbβ3 has been demonstrated. In this issue’s manuscript the authors aimed to elucidate the specific roles of the individual isotypes of PP1. A pharmacological approach was not possible as the available phosphatase inhibitors are not specific for the individual PP1 isoforms and also potentially inhibit other serine/threonine phosphatases as well. Specific subtype knockout mice were also not available and therefore the authors used an alternative genetic approach: siRNA-mediated downregulation in αIIbβ3-expressing HEK 293 cells. Interestingly and unexpectedly, outside in signalling as measured by αIIbβ3-mediated cell adhesion and clot retraction was affected in a highly differential and isoform-specific manner: PP1γ knockdown did not affect outside-in signalling at all, PP1β knockdown reduced and unexpectedly, PP1α knockdown increased outside-in signalling. The latter effect could be further shown to involve mitogen-activated protein kinase (MAPK) p38. Therefore, using the genetic tools of heterogeneously expressed αIIbβ3 and siRNA knockdown, the authors could elucidate a complex and highly differentiated regulatory mechanism in integrin αIIbβ3 outside-in signalling.

The authors’ approach is a good example for the valid use of platelet surrogate cells. As platelets are anucleated cells they are not amendable to standard genetic manipulation, a hurdle that hampers platelet research substantially. However, cells expressing recombinant αIIbβ3 have been instrumental early on in the functional evaluation of inside-out as well as outside-in signalling (2, 3). Further progress in genetic manipulation of platelets has been achieved by the generation of platelets from CD34+ progenitor cells in cell culture (4). For *in vivo* experiments, genetic manipulation of platelets has been recently elegantly performed by targeting of stem cells via mouse bone marrow stem cell isolation and transplantation into irradiated C57/BL6 mice (5). Four to six weeks after transplantation, nearly all platelets isolated from recipient mice were derived from transplanted and genetically manipulated stem cells (5). Besides the time-consuming and costly traditional way of creating knockout or transgenic mice, very recently another genetic tool has emerged as a new tool in platelet research. The zebrafish Danio rerio model, which has nucleated thrombocytes instead of anucleated platelets, is easily amendable to genetic manipulation and thus holds great promise for fast and high throughput screening of any protein function in platelet biology (6). Finally, the use of platelet surrogate cells has substantially contributed to the understanding and development of various strategies towards pharmacological αIIbβ3 inhibition (7).

Although some caution has to be applied in regards to transferability to human platelet biology, in all of these approaches of using surrogates for human platelets the contribution towards platelet research has been and will foreseeably continue to be considerable.

**Conflicts of interest**
None declared.

**References**


