

# Macrophages and Thrombin—Another Link between Inflammation and Coagulation

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Macrophages are highly versatile cells of the innate immune system with a high degree of plasticity. In response to their respective tissue environment they can adopt various functionally different phenotypes or polarization states. In response to inflammatory stimuli macrophages polarize into proinflammatory M1 cells whereas anti-inflammatory stimuli induce alternative polarization into anti-inflammatory, reparative M2 macrophages. Accumulating evidence supports the notion that macrophages represent a cellular link between inflammation and cardiovascular pathologies such as atherogenesis and thrombosis.<sup>1</sup> On the other hand, thrombin is not only the central protease in the coagulation cascade but among various other functions also modulates inflammatory processes.<sup>2</sup> In this issue of *Thrombosis and Haemostasis*, López-Zambrano et al have revealed yet another link between the coagulation system and inflammation modulated by cells of the innate immune system.<sup>3</sup> The authors show in vitro that thrombin induces macrophages to polarize toward an M1 phenotype that is characterized by the expression of proinflammatory cytokines and chemokines. This effect of thrombin was at least in part mediated via protease activated receptor-1 (PAR-1). Interestingly, heat denatured, enzymatically inactive thrombin was still effective in inducing a proinflammatory response in macrophages suggesting a pathway independent of PAR-1, which has to be proteolytically cleaved to induce signal transduction. Taken together, this study provides evidence that in a prothrombotic microenvironment, formed thrombin is not only able to

promote thrombus formation but also can shift the setting toward inflammation by affecting the polarization state of macrophages. Interestingly, proinflammatory M1 macrophages in contrast to anti-inflammatory M2 macrophages are proteolytically highly active.<sup>4</sup> The kinetics and dynamics of macrophage polarization toward a particular phenotype have mainly been assessed in in vitro studies. Thus, future investigations addressing these research questions in vivo are highly relevant.

#### Conflict of Interest

None declared.

#### References

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