Insight | Extracellular RNA also triggers leukocyte extravasation and inflammatory responses

Inflaming attraction by RNA

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Recent findings indicate that naturally occurring polyphosphates, like nucleic acids and inorganic compounds, share the ability to trigger blood coagulation (1). The release of DNA or RNA by tissue damage can thus represent a first line of haemostatic defence against vascular injury. This view is further corroborated by the observation that extracellular RNA binds and activates factors XII and XI in vitro and in vivo. On the other hand, inorganic polyphosphates are stored in platelet granules, and their secretion triggers contact activation of factor XII (2). This is of clinical relevance because scavenging these polyanionic surfaces can be exploited to limit thrombosis (3).

Given the well-known intimate association between coagulation and immune system modulation, whether natural polyphosphates can regulate leukocyte function has remained unclear thus far. In this issue of *Thrombosis and Haemostasis*, Fischer et al. (4) show that extracellular RNA is not only involved in coagulation but also in triggering leukocyte extravasation and inflammatory responses. Using intravital microscopy technology, they report that extracellular RNA but neither DNA nor hydrolysed RNA induced mononuclear leukocyte adhesion to postcapillary venules as well as extravasation into the cremaster muscle. Interestingly, they provide a non-cell autonomous mechanism that involves leukocyte/endothelial interaction control. First, extracellular RNA triggers the nuclear factor-κB signalling cascade and the tumour necrosis factor (TNF)-α converting enzyme (TACE), leading to TNFα release from monocyctic cells. This evokes an inflammatory response and induces endothelial cells to express the adhesive molecule intravascular cell adhesion molecule-1 which eventually favours leukocyte recruitment.

While this suggests potential new avenues to control inflammation by reducing extracellular RNA, questions remain as to how TACE is triggered inside monocytes and how cells can sense and respond to extracellular RNA. Studies of natural polyphosphates role in coagulation and haemostasis show increasing popularity and future studies are expected to provide in depth comprehension of these processes.

Conflicts of interest
None declared.

References