Insight … inflammatory pathways activated within unstable plaques which promote a pro-inflammatory M1 macrophage polarisation

M1 signature mediators in atheroma-derived single cell secretome of symptomatic plaques

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Atherosclerosis is a systemic lipid-driven inflammatory disease characterised by arterial wall lesions. It starts in childhood and usually takes decades to develop advanced atherosclerotic lesions responsible for clinical symptoms. Although clinical complications of atherosclerosis can arise from plaques causing flow-limiting critical stenosis, the most severe events arise from acute thrombotic occlusion due to plaque rupture, resulting in myocardial infarction or stroke (1).

Pathological studies have highlighted that the occurrence of acute athero-thrombotic events rather depends on the composition of the plaque than the degree of stenosis. Vulnerable plaques prone to rupture are characterised by thin fibrous caps, a large lipid core and increased inflammation. Large cohort studies with human carotid endarterectomy samples have confirmed that features of carotid plaque vulnerability are predictors of future cardiovascular events (2).

The implication of macrophages in atherosclerosis development has been intensively studied over the past decades, revealing their crucial implication in all stages from lesion initiation to plaque growth and clinical events, to potential resolution and regression of atherosclerotic lesions. In particular, major advances have been made in understanding the heterogeneity and function of macrophage subsets within atherosclerotic plaques (3). Most of these findings are based on experimental evidence resulting from mouse studies. There is clearly need for more clinical studies aimed at clarifying the relevance of proposed mechanisms underlying the development and progression of atherosclerosis for human pathophysiology. A better knowledge of local inflammatory mediators promoting leukocyte recruitment and inflammatory macrophage polarisation within vulnerable plaques may help developing new therapeutic drugs for plaque stabilisation.

In this issue of Thrombosis and Haemostasis, Shalhoub et al. (4) provide novel insights into inflammatory pathways activated within unstable plaques which promote a pro-inflammatory M1 macrophage polarisation. The study is based on a human carotid plaque-derived ex vivo single cell secretome analysis of symptomatic and asymptomatic plaque homogenates. This novel approach of cultured atheroma-derived single cell suspensions, in which the cells retain their inflammatory phenotype and secretory capacity, is certainly valuable for future investigations in larger patient cohorts with possibly testing of ≥100 factors in a small sample volume, which is facilitated by recent developments in analytical tools such as the multiplex technology. It may also provide the basis for proteomics-based screening approaches of yet even unknown local players potentially involved in plaque stability (5). In addition, it might be of interest to correlate these local inflammatory markers and pathways with systemic parameters, in search for the identification of circulating biomarkers for prevention, diagnosis as well as risk prediction of acute cardiovascular events.

Conflicts of interest
None declared.

References