Reply to: “Circulating platelet derived microparticles are not increased in patients with cirrhosis”

To the Editor:

We thank Dr. Rautou et al. for their interest in our Snapshot review (in which we sought to summarize the important role that platelets play in mediating coagulation and thrombosis in patients with cirrhosis) [1]. We proposed that microparticles could have important effects on coagulation and thrombosis in these clinical settings. We mentioned the possibility of circulating cell-derived, and by inference (given the current state of the field), platelet microparticles as possible mediators of inflammation. Rautou and colleagues correctly point out that they and other groups have recently published data in this area [2]. In acute and chronic liver diseases, circulating microparticle levels have consistently been shown to be increased, albeit previous studies have shown variable levels of platelet-derived microparticles in these settings [3–7]. Importantly, Rautou et al. also found that “the severity of cirrhosis and systemic inflammation were major determinants of the levels of leuko-endothelial and hepatocyte microparticles” [2]. Specifically, after correcting for the circulating concentrations of platelets, the levels of platelet-derived microparticles in this study are lower in cirrhotic patients when compared to controls [2]. Other investigators have suggested increased levels of platelet microparticles in cirrhosis [3] or that no differences are associated with increasing levels of hepatic fibrosis [6].

The origins of circulating microparticles, whether platelet-derived or not, remain a point of contention. In truth, this is a field in evolution where critical elements of methodology are yet to be determined. For example, Rautou et al. and other groups have measured static microparticle levels. It is not clear if such static values are pathophysiologically relevant, in relation to a given stimulus, or whether the rapidity of changes in concentration levels and fluxes over time are more important [5]. Nor is it clear whether determination of CD41 labeling is sufficient to describe platelet versus megakaryocyte-derived microparticles – in either health or disease states [8–10]. While Rautou et al. utilize CD41 as a marker of platelet microparticles, the article that we had cited utilized the related marker CD61 to measure platelet microparticles and infer that these may vary with inflammatory insults as during and after an alcoholic binge [3].

Finally, Rautou et al. suggest tissue factor expressing microparticles may be more relevant as prothrombotic mediators in liver disease and not platelet microparticles per se. Tissue factor expression, typically thought to be distinct from platelet-derived microparticles, can be readily found co-expressed with CD41 in plasma microparticles using whole blood analyses and modified techniques [8]. Clearly, microparticles can co-express a variety of surface proteins (e.g., CD39), likely with unique biological properties depending on both source and target interaction [11]. Further, one might speculate that microparticles from platelets and other cellular sources could function as transport and delivery systems for bioactive molecules in vivo, participating not only in hemostasis and thrombosis but also in inflammation, angiogenesis, tissue remodeling, and cellular transformation [11].

As this field matures and more data is available, the controversies that uncertainty brings will likely settle. Future studies are needed to understand the respective roles of static/dynamic changes in concentrations, to standardize methodology for the quantification process and to delineate not only the absolute levels but also, importantly, any qualitative differences in microparticle populations.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

References


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