Response to the role of platelets on regenerating liver

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Response to the role of platelets on regenerating liver: Thoughts beyond parenchymal proliferation

As suggested by Moris and coworkers, although there is accumulating evidence that platelets stimulate liver regeneration in rodent models and in humans, there is a paucity of high-quality data to indicate by which mechanism(s) platelet exert their stimulating effect. Several mechanisms have been postulated including direct stimulatory effects of platelet-derived molecules on hepatocyte proliferation, functional transfer of platelet RNA to the hepatocyte, and platelet-mediated stimulation of influx of inflammatory cells, as we have reviewed recently. In addition, it has been suggested that platelet-endothelial cell interactions drive liver regeneration. Unfortunately, unequivocal evidence to support or refute any of these mechanisms in platelet-mediated liver regeneration in rodents and humans is lacking.

Moris and coworkers also point to data suggesting a role of platelets in improving liver fibrosis. However, platelets have been shown to have both stimulating and inhibitory roles in fibrosis, depending on the context and experimental models used. In addition, we studied liver regeneration in mice with otherwise healthy livers. We (and others) have not assessed proliferation of non-parenchymal cells in experimental models in which platelets were depleted, but this would be of definite interest.

Although I agree that liver function tests would nicely complement studies on platelet-mediated liver regeneration, I do note that the combination of liver-body weight ratio with ki67 immunostainings is compatible with functional liver regeneration in otherwise healthy livers.

To my knowledge, it is unknown whether platelet deposition in the liver remnant decreases portal flow by increasing vascular resistance or whether the number of platelets deposited within the liver remnant is too limited to cause a decrease in flow. The study by Starlinger does not address this specific question.

We showed that deficiency of VWF not only virtually abolishes platelet influx, but also substantially delays liver regeneration, suggesting that VWF is a key player in platelet-mediated stimulation of liver regeneration. This finding might be clinically relevant as VWF release can be stimulated by 1-desamino-8-D-arginine vasopressin (DDAVP).

I agree it would be of interest to assess which platelet receptors (e.g. the glycoprotein Ib/IX/V complex or αIIbβ3) facilitate VWF-mediated platelet influx in the liver remnant, but this may be less relevant in a therapeutic context.

In aggregate, I concur with Moris and coworkers that crucial details on the mechanisms by which platelets stimulate liver regeneration are as yet unknown. Future work should combine development of strategies to stimulate platelet-mediated liver regeneration in humans with in depth mechanistic studies.

CONFLICT OF INTEREST

The authors do not have any disclosures to report.

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REFERENCES


Cautious use of platelet as a relevant inducer of liver regeneration following partial hepatectomy in patients with metastatic hepatic carcinoma

To the Editor:

The article by Kirschbaum et al. shows that temporary von Willebrand factor-mediated platelet influx in the liver remnant drives platelet-mediated liver regeneration (LR) following partial hepatectomy. Indeed, there is mounting evidence that platelet and endogenous factors are beneficial to hepatocyte regeneration in patients with hepatocellular carcinoma (HCC). Furthermore, platelet-increasing therapy has been recommended to improve LR following partial hepatectomy. However,