

Identification & Characterization of Liver-Derived Hematopoietic Factors in Healthy & Diseased Livers

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Introduction: Chronic liver disease (CLD) is associated with disrupted hematopoiesis, contributing to hepatic and systemic inflammation. While the liver regulates immune function, its role in modulating hematopoiesis through liver-derived factors remains poorly understood. We hypothesize that healthy and diseased livers produce distinct hematopoietic factors that can influence bone marrow (BM) function and immune responses. This study aims to identify and characterize liver-derived hematopoietic factors and define their potential role in liver-BM crosstalk during health and disease. **Methods:** A curated panel of hematopoietic factors was selected based on established roles in hematopoietic stem/progenitor cell maintenance, differentiation, mobilization, and immune cell development from the published literature. Image-based screening using the Human Protein Atlas (HPA) identified liver-expressed factors and their localization within hepatocytes, non-parenchymal cells, or both. Candidate factors were evaluated for differential expression across stages of CLD using publicly available Gene Expression Omnibus (GEO) datasets. **Results:** Thirty hematopoietic factors were curated and evaluated for hepatic expression. Of these, 18 hematopoietic factor probes were identified in the HPA. One factor was exclusively expressed by hepatocytes, eight by non-parenchymal cells, and nine by both cell populations. Analysis of normalized GEO expression data showed that most liver-derived hematopoietic factors remained relatively stable throughout CLD progression. In contrast, JAG1 and SPP1 were consistently and significantly upregulated in advanced stages of CLD while being expressed within the liver. These findings identify JAG1 and SPP1 as potential mediators of liver-BM communication and regulators of hematopoiesis during chronic liver injury. Ongoing studies are evaluating their hepatic expression and secretion in mouse models of liver fibrosis, alcohol-associated liver disease, and metabolic dysfunction-associated steatotic liver disease. **Conclusions:** Our findings identify a panel of liver-derived hematopoietic factors and suggest that the hepatic secretome may contribute to the regulation of BM hematopoiesis during CLD. Disease-associated upregulation of JAG1 and SPP1 highlights these factors as potential mediators of liver-BM crosstalk and systemic immune dysregulation. Further studies are underway to validate their role in altered hematopoiesis and inflammation during CLD.