

Role of macrophages in pathomorphogenesis of alcoholic liver disease

Burganova G., Deev R., Kiyasov A.

Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

Alcoholic liver disease combines various structural and functional impairments of liver caused by excessive alcohol consumption. Alcohol, as a direct hepatotoxic agent, is metabolized in the liver and affects both resident cells and their microenvironment. These changes are reflected in the resulting imbalance of pro- and anti-inflammatory mediators synthesized by the liver macrophages. To date, it is known about the polarization and phenotypic diversity of this cell population, and about macrophages and monocytes involvement in the development of alcoholic hepatitis. These facts allow us to consider macrophages as potential therapeutic targets. However, the available data do not fully disclose the mechanisms of inter- and intradiferon interactions in the human body. The review discusses the results of current studies on the involvement of liver macrophages in the pathomorphogenesis of alcoholic liver disease and the potential for their use in the treatment of this disease.

<http://dx.doi.org/10.23868/201703005>

Keywords

Alcoholic liver disease, Kupffer cell, Liver cirrhosis, Macrophage, Monocyte

References

- [1] Suraweera D.B., Weeratunga A.N., Hu R.W. et al. Alcoholic hepatitis: the pivotal role of Kupffer cells. *World J. Gastrointest. Pathophysiol.* 2015; 6(4):90-8.
- [2] Langevoort H.L. The mononuclear phagocyte system: a new classification of macrophages, monocytes, and their precursor cells. *Bull. World Health Organ.* 1972; 46:845-52.
- [3] Sell S. Heterogeneity and plasticity of hepatocyte lineage cells *Hepatology* 2001; 33(3):738-50.
- [4] Kmieć Z. Cooperation of liver cells in health and disease. *Adv. Anat. Embryol. Cell Biol.* 2001; 161:III-XIII, 1-151.
- [5] Wynn T.A., Barron L. Macrophages: master regulators of inflammation and fibrosis. *Semin. Liver Dis.* 2010; 30(3):245-57.
- [6] Vernon M.A., Mylonas K.J., Hughes J. Macrophages and renal fibrosis. *Semin. Nephrol.* 2010; 30(3):302-17.
- [7] Hardie W.D., Glasser S.W., Hagood J.S. Emerging concepts in the pathogenesis of lung fibrosis. *Am. J. Pathol.* 2009; 175(1):3-16.
- [8] Duffield J.S., Forbes S.J., Constandinou C.M. et al. Selective depletion of macrophages reveals distinct, opposing roles during liver injury and repair. *J. Clin. Invest.* 2005; 115(1):56-65.
- [9] Gibbons M.A., MacKinnon A.C., Ramachandran P. et al. Ly6Chi monocytes direct alternatively activated profibrotic macrophage regulation of lung fibrosis. *Am. J. Respir. Crit. Care Med.* 2011; 184(5):569-81.
- [10] Fallowfield J.A., Mizuno M., Kendall T.J. et al. Scar-associated macrophages are a major source of hepatic matrix metalloproteinase-13 and facilitate the resolution of murine hepatic fibrosis. *J. Immunol.* 2007; 178(8):5288-95.

- [11] Ju C., Mandrekar P. Macrophages and alcohol-related liver inflammation. *Alcohol Res.* 2015; 37(2):251-62.
- [12] Zeng T., Zhang C.L., Xiao M. Critical roles of Kupffer cells in the pathogenesis of alcoholic liver disease: from basic science to clinical trials. *Front. Immunol.* 2016; 7:538. eCollection 2016.
- [13] Hersoug L.G., Moller P., Loft S. Gut microbiota-derived lipopolysaccharide uptake and trafficking to adipose tissue: implications for inflammation and obesity. *Obes. Rev.* 2016; 17(4):297-312.
- [14] Sica A., Mantovani A. Macrophage plasticity and polarization: in vivo veritas. *J.Clin. Invest.* 2012; 122(3):787-95.
- [15] Louvet A., Teixeira-Clerc F., Chobert M.N. et al. Cannabinoid CB2 receptors protect against alcoholic liver disease by regulating Kupffer cell polarization in mice. *Hepatology* 2011; 54(4): 1217-26.
- [16] Wan J., Benkdane M., Teixeira-Clerc F. et al. M2 Kupffer cells promote M1 Kupffer cell apoptosis: a protective mechanism against alcoholic and nonalcoholic fatty liver disease. *Hepatology* 2014; 59(1):130-42.
- [17] Kiliaritskaia I.L., Stilidi E.I. Pathogenetic importance of proinflammatory cytokines in the formation and progression of fibrosis in alcoholic hepatitis. *Eksp.Klin.Gastroenterol.* 2013; (4):13-20.
- [18] Hanck C., Rossol S., Böcker U. et al. Presence of plasma endotoxin is correlated with tumour necrosis factor receptor levels and disease activity in alcoholic cirrhosis. *Alcohol* 1998; 33:606-8.
- [19] McClain C.J., Barve S., Deaciuc I. et al. Cytokines in alcoholic liver disease. *Semin. Liver Dis.* 1999; 19:205-19.
- [20] Uesugi T., Froh M., Arteel G.E. et al. Toll- like receptor 4 is involved in the mechanism of early alcohol-induced liver injury in mice. *Hepatology* 2001; 34:101-8.
- [21] Yin M., Bradford B.U., Wheeler M.D. et al. Reduced early alcohol-induced liver injury in CD14-deficient mice. *J.Immunol.* 2001; 166:4737-42.
- [22] Adachi Y., Bradford B.U., Gao W. et al. Inactivation of Kupffer cells prevents early alcohol-induced liver injury. *Hepatology* 1994; 20:453-60.
- [23] Szabo G., Mandrekar P., Dolganiuc A. Innate immune response and hepatic inflammation. *Semin. Liver Dis.* 2007; 27:339-50.
- [24] Karlmark K.R., Weiskirchen R., Zimmermann H.W. Hepatic recruitment of the inflammatory Gr1+ monocyte subset upon liver injury promotes hepatic fibrosis. *Hepatology* 2009; 50:261-74.
- [25] Galastri S., Zamara E., Milani S. et al. Lack of CC chemokine ligand 2 differentially affects inflammation and fibrosis according to the genetic background in a murine model of steatohepatitis. *Clin.Sci. (Lond).* 2012; 123:459-71.
- [26] Heymann F., Hammerich L., Storch D. et al. Hepatic macrophage migration and differentiation critical for liver fibrosis is mediated by the chemokine receptor C-C motif chemokine receptor 8 in mice. *Hepatology* 2012; 55: 898-909.
- [27] Ramachandran P., Pellicoro A., Vernon M.A. et al. Differential Ly-6C expression identifies the recruited macrophage phenotype, which orchestrates the regression of murine liver fibrosis. *PNAS USA* 2012; 109(46):E3186-95.
- [28] Duffield J.S., Forbes S.J., Constandinou C.M. Selective depletion of macrophages reveals distinct, opposing roles during liver injury and repair. *J.Clin. Invest.* 2005; 115(1):56-65.
- [29] Holt M.P., Cheng L., Ju C. Identification and characterization of infiltrating macrophages in acetaminophen-induced liver injury. *J.Leu. Biol.* 2008; 84(6):1410-21.
- [30] Mosser D.M., Edwards J.P. Exploring the full spectrum of macrophage activation. *Nat. Rev.Immunol.* 2008; 8(12): 958-69.
- [31] Hongl.H., Han S.Y., Ki M.R. et al. Inhibition of Kupffer cell activity improves transplantation of human adipose-derived stem cells and liver functions. *Cell Transplant.* 2013; 22(3):447-59.