Author response to letter LIVint-17-00420.R1 "Low L-Ficolin associated with disease severity during sepsis in adult ICU patients" Kessler et al.

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Reply to "Low L-Ficolin associated with disease severity during sepsis in adult ICU patients"

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To the Editor:

We read with great interest the study of Dr. Kessler et al. [1] related to our article published in Liver International [2]. We thank the authors for their kind interest in our work and welcome their results that support our finding and also for giving a rational clue to further clarify the significance of ficolin molecules in cirrhosis-associated bacterial infections.

In our study low levels of L-ficolin (Liver ficolin, ficolin-2 [FCN-2]) and H-ficolin (Hakata ficolin, ficolin-3 [FCN-3] were associated with immune dysfunction in cirrhosis resulting in the development of clinically significant bacterial infections. Likewise, Ulf et al. found reduced L-ficolin levels in a non-cirrhotic patient population with sepsis. Stability of the L-ficolin in both patient populations supports the fact that low levels of the molecule precede the development of bacterial infections and are rather the cause than the

consequence of these episodes and associated complications. More interestingly, levels of L-ficolin were significantly lower in patients with severe sequential organ failure assessment (SOFA)-score that warrants further studies in patients with cirrhosis. It is worthy defining the role of ficolins in the development of acute-on-chronic liver failure (ACLF) directly during the acute decompensation episodes associated with bacterial infection [3]. This issue was not evaluated in our cohort.

In patients with cirrhosis, development of bacterial infections increases mortality by four-fold despite of proper and timely administered antibiotic therapy [4]. Besides preventive strategies, supportive non-antibiotic medication(s) during episodes with bacterial infections would be of clinical utility. Up to now no supplementary medical treatment is known that is able to improve survival in cirrhosis-related infections. In a recent randomized controlled trial, albumin infusion failed to improve short-term survival in cirrhotic patients with infections other than SBP [5]. If low levels of ficolins turn out to show association with the development of ACLF and infection-related mortality, the possible benefit of ficolin supplementation should be further investigated. Feasibility of this approach might be verified by the reported data that restoration of mannose binding lectin (MBL)-deficiency with MBL substitution either by plasma derived (pdMBL) or recombinant (rMBL) protein proved to be viable, safe and effective in both pre-clinical studies and early phase II trials in non-cirrhotic patient population [6].

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