Abstract

Disruption of gut microbiota, altered mucosal defense, inappropriate immune response and gut barrier damage are all typical features in the pathogenesis of both necrotizing enterocolitis (NEC) and inflammatory bowel disease (IBD). Despite of intensive research, the exact pathogenesis of both diseases remains unclear and the diagnostics and outcome prediction are still problematic. Therefore, we analyzed the role of gut-associated and inflammatory biomarkers, with respect to different aspects of gut barrier dysfunction in the pathogenesis of both disease, with the aim to improve the diagnostics and to predict the disease course and outcome.

Using ELISA, we found that patients who will later develop NEC have significantly higher intestinal fatty acid-binding protein (I-FABP) than infants who will later develop sepsis already in first hours after NEC suspicion. Urinary I-FABP had high sensitivity (81%) and specificity (100%) and its addition to currently used gold standard for NEC diagnosis increased its sensitivity and negative predictive value. We found that serum amyloid A (SAA) was the strongest factor for prediction of the most severe stage of NEC. The combination of intestinal and liver FABP with SAA predicted the length of hospitalization in NEC patients and the low level of SAA predicted short achievement of full enteral feeding.

Using protein array, ELISA and flow cytometry we performed the broad spectrum analysis of serum biomarkers and specific anti-microbial B and T cell response to gut commensal microbiota. We found that proteins of matrix metalloproteinase system were the strongest factors discriminating IBD patients from healthy subjects. The osteoprotegerin was the strongest factor discriminating the patients with UC and PSC-IBD and in the combination with I-FABP, CXCR-1 and TIMP-1 it discriminated the UC from CD. IBD patients responded mostly similarly to selected commensal bacteria as healthy subject, but in CD patients we found lower antibody response, with significant decrease in IgA to *Faecalibacterium* and *Bacteroidetes*. Furthermore, we found increase in T cells response to these bacteria in CD patient.

Thus, we found that I-FABP is capable to distinguish NEC from sepsis and its combination with other biomarkers may be useful in NEC management. Our results stress the importance of gut barrier function and immune response to commensal bacteria and point at the specific differences in the pathogenesis between the different forms of IBD.