Longitudinal Study of Circulating miRNA Biomarkers in Inflammatory Bowel Disease

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Background: Inflammatory bowel diseases (IBDs) are chronic and progressive inflammatory disorders of the gastrointestinal tract. The current serum biomarkers for IBD are limited by low specificity and poor predictive power. Serological assessments of IBD activity and early-stage diagnosis could be markedly improved through the use of a non-invasive serological biomarker signature, such as miRNA and the use of mouse model for IBD for longitudinal investigation. Here, we hypothesized that the time-course of the disease and its lesions can be correlated with specific miRNA profiles.

Methods: Serum samples were collected from wild-type (WT), IL10-/- and TLR5-/- mice once a week for 15 weeks, and miRNA profiles were analyzed using high-throughput technology. IL10-/- mice were treated with anti-TNF-α antibody in order to prevent the development of intestinal inflammation and miRNA profiles were analyzed.

Results: Among the 104 miRNAs tested, mmu-miR-29b, -122, -150, -192, -194, -146a and -375 were found to increase with disease progression, while mmu-miR-335-5p, -148a, -152, -140, -331-3p, -195, -140* and -199b were observed to decrease in IL10-/- mice developing intestinal inflammation. Statistical analyses revealed that among the miRNAs that were differentially expressed in colitic versus non-colitic mice, six could be used as a profiling set that could efficiently determine the inflammation status of the intestinal mucosa. Moreover, the miRNA profiles were not identical between IL10-/- colitic mice, DSS-induced colitis model, or TLR5-/- mice developing low grade intestinal inflammation, suggesting that miRNA signatures could be a powerful tool for discriminating among various types of intestinal inflammation. Finally, the treatment of IL10-/- mice with anti-TNF-α antibody was sufficient to abrogate the development of intestinal inflammation as well as perturbation of miRNA profile. These murine data may help establish miRNA patterns that can be used to assess the diagnosis, prognosis, and therapeutic responses of IBD patients.

Conclusion: We used a mouse model to establish a putative miRNA signature of colitis that could be a useful tool for following the evolution of intestinal inflammation in mice. Future work is warranted to adapt this concept to human serum samples and identify IBD specific miRNA patterns in human patients.