

## 論文の内容の要旨

論文題目 Intestinal epithelial cell-based microRNA networking profile for gut inflammation  
(腸炎における腸上皮細胞マイクロRNAのネットワークプロファイルの関与)

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Inflammatory bowel diseases (IBDs) accompany a critical loss of the frontline barrier function that is achieved primarily by intestinal epithelial cells (IECs). Although the gene-regulation pathways underlying these host-defense roles of IECs presumably are deranged during IBD pathogenesis, the quantitative and qualitative alterations of posttranscriptional regulators such as microRNAs (miRNAs) within the cells largely remain to be defined. I aimed to uncover the regulatory miRNA-target gene relationships that arise differentially in inflamed small- compared with large-IECs. Whereas IBD significantly increased the expression of only a few miRNA candidates in small-IECs, numerous miRNAs were upregulated in inflamed large-IECs. These marked alterations might explain why the large, as compared with small, intestine is more sensitive to colitis and shows more severe pathology in this experimental model of IBD. In-depth assessment of the miRNA-mRNA expression profiles and the resulting networks prompts us to suggest that miRNAs such as miR-1224-5p, miR-3473a, and miR-5128 represent biomarkers that appear in large-IECs upon IBD development and co-operatively repress the expression of key anti-inflammatory factors. This study provides insight into gene-regulatory networks in IECs through which dynamic rearrangement of the involved miRNAs modulates the gene expression-regulation machinery between maintaining and disrupting gastrointestinal homeostasis.