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Macrophage-derived angiogenin maintains epithelial barrier integrity to prevent colitis

Desen Sun[1], Rongpan Bai[1], Wei Zhou[1], Muxiong Chen[1], Xiaoliang Shi[1], Liang Luo[1], Zhengrong Yao[1], Xiangwei Gao[1], Guo-fu Hu[2], Jinghao Sheng[1], Zhengping Xu[1]

[1]Zhejiang University School of Medicine, China
[2]Molecular Oncology Research Institute, USA

Statement of the Problem: Communications between macrophages and epithelium play critical roles in maintaining epithelial barrier integrity. Macrophages orchestrate intestinal epithelial cell (IEC) homeostasis by producing various mediators. Current challenges faced in inflammatory bowel disease (IBD) treatment suggest the existence of new mediators. Angiogenin (ANG) is a secreted ribonuclease and participates in cell-cell crosstalk and promotes cell growth and survival. We aimed to determine the protective role of macrophage-derived ANG in IBD.

Methodology & Theoretical Orientation: We characterized ANG expression in IBD patients and in dextran sodium sulfate (DSS)-induced colitis mice. The functional role of ANG in intestinal inflammation was addressed in the experimental colitis model with wild-type, Ang-deficient or bone marrow reconstituted mice. The underlying mechanism was investigated at animal and cellular levels by administrating ANG protein and its enzymatic or receptor-binding site variant, by blocking its interaction with receptor plexin B2 (PLXNB2) or by knocking down PLXNB2.

Findings: Expression of ANG was significantly down-regulated in IBD patients and in colitis mice. Functional studies showed that deficiency of Ang in myeloid cells caused high susceptibility to DSS-induced experimental colitis and impaired epithelial barrier integrity. Mechanistically, macrophage-derived ANG promoted IEC survival and proliferation through Plxnb2-mediated tRNA-derived stress-induced small RNA (tiRNA) production, and ribosomal RNA (rRNA) transcription, respectively. Importantly, treatment with recombinant ANG significantly attenuated the severity of mouse experimental colitis.

Conclusion & Significance: We have, for the first time, identified macrophage-derived ANG as a contributor in maintaining epithelial barrier integrity during intestinal inflammation, suggesting that ANG may serve as a new preventive or therapeutic target for IBD.

Biography

Desen Sun, Ph.D student, biochemistry and molecular biology, Zhejiang University School of Medicine. Desen focuses on using the is a Ph.D student majoring in biochemistry and molecular biology. He is good at using molecular and cellular biology tools and experimental animal models to study the pathogenesis of iIntestinal diseases. He is also interested in the roles of Recently, he mainly focuses on studying how antibacterial peptides in maintaining the intestinal microbiota and protect against inflammatory bowel disease.regulate microbiota and protect against IBD.

sdscm2510@zju.edu.cn

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