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# Targeting Basic Leucine Zipper Transcription Factor ATF-Like Mediated Immune Cells Regulation to Reduce Crohn's Disease Fistula Incidence

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**Abstract :** Crohn's disease (CD) is a chronic gastrointestinal segment inflammation encompassing immune dysregulation in a genetically susceptible individual in response to the environmental triggers and interaction between the microbiome and immune system. Uncontrolled inflammation leads to long-term complications, including fibrotic strictures and enteric fistulae. Increased production of Th1 and Th17-cell cytokines and defects in T-regulatory cells have been associated with CD. Th17-cells are essential for protection against extracellular pathogens, but their atypical activity can cause autoimmunity. Intrinsic defects in the control of programmed cell death in the mucosal T-cell compartment are strongly implicated in the pathogenesis of CD. The apoptosis defect in mucosal T-cells in CD has been endorsed as an imbalance of the Bcl-2 and the Bax. The immune system encounters foreign antigens through microbial colonization of mucosal surfaces or infections. In addition, FOSL downregulated IL-26 expression, a cytokine that marks inflammatory Th17-populations in patients suffering from CD. Furthermore, the expression of IL-23 is associated with the transcription factor primary leucine zipper transcription factor ATF-like (Batf). Batf-deficiency demonstrated the crucial role of Batf in colitis development. Batf and IL-23 mediate their effects by inducing IL-6 production. Strong association of IL-23R, Stat3, and Stat4 with IBD susceptibility point to a critical involvement of T-cells. IL-23R levels in transfer fistula were dependent on the AP-1 transcription factor JunB that additionally controlled levels of RORγt by facilitating DNA binding of Batf. T lymphocytes lacking JunB failed to induce IL-23- and Th17-mediated experimental colitis highlighting the relevance of JunB for the IL-23/ Th17 pathway. The absence of T-bet causes unrestrained Th17-cell differentiation. T-cells are central parts of immune-mediated colon fistula. Especially Th17-cells were highly prevalent in inflamed IBD tissues, as RORγt is effective in preventing colitis. Intraepithelial lymphocytes (IEL) contain unique T-cell subsets, including cells expressing RORγt. Increased activated Th17 and decreased T-regulatory cells in inflamed intestinal tissues had been seen. T-cells differentiate in response to many cytokines, including IL-1β, IL-6, IL-23, and TGF-β, into Th17-cells, a process which is critically dependent on the Batf. IL-23 promotes Th17-cell in the colon. Batf manages the generation of IL-23 induced IL-23R+ Th17-cells. Batf is necessary for TGF-β/IL-6-induced Th17-polarization. Batf-expressing T-cells are the core of T-cell-mediated colitis. The human-specific parts of three AP-1 transcription factors, FOSL1, FOSL2, and BATF, are essential during the early stages of Th17 differentiation. BATF supports the Th17 lineage. FOSL1, FOSL2, and BATF make possession of regulatory loci of genes in the Th17 lineage cascade. The AP1 transcription factor Batf is identified to control intestinal inflammation and seems to regulate pathways within lymphocytes, which could theoretically control the expression of several genes. It shows central regulatory properties over Th17-cell development and is intensely upregulated within IBD-affected tissues. Here, we demonstrated that targeting Batf in IBD appears as a therapeutic approach that reduces colitogenic T-cell activities during fistula formation while aiming to affect inflammation in the gut epithelial cells.

**Keywords :** immune system, Crohn's Disease, BATF, T helper cells, Bcl, interleukin, FOSL
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