Gastroenterology and Hepatology From Bed to Bench

EDITORIAL

IL23 as a novel serum based biomarker in ulcerative colitis- an editorial

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IL23 is a heterodimeric member of the IL-12 cytokine family composed of two subunits, IL12p40 and IL23p19. It is produced by antigen presenting cells and has been shown to promote the production and survival of a distinct lineage of T-cells called T_H17 cells (1). Studies have revealed that naive T cells when stimulated by TGFβ and IL-6 are differentiate into T_H17 cells. However, this is inhibited by the presence of IFN-γ and IL-4. Once committed to the T_H17 lineage, the T_H17 cells remain committed even in presence of cytokines that stimulate other T cell lineages. Once activated, T_H17 cells release several cytokines (including IL-6, IL-17A, IL-17F, GM-CSF, TNF, CXCL1 and CCL7) that have been shown to be involved in immune mediated diseases including Inflammatory bowel disease (IBD), rheumatoid arthritis, psoriasis and multiple sclerosis (1). Studies in knockout mice models have revealed that lack of the IL23p19 subunit (but not the p40 subunit) makes the mice resistant to IBD. Further, administration of anti-IL23p19 or anti-IL12p40 mAbs significantly inhibited the production of cytokines downstream of T_H17 activation including IL-17, IL-6 and TNF. IL23p19 mRNA was shown to be significantly upregulated in the biopsies from inflamed areas of the intestine of patients with IBD (Crohn's disease > Ulcerative colitis) (2). Further, the T_H17 cytokine TNF was also shown to be elevated in these biopsies. IL-23 dependent T cells have been shown to be a key factor for the development of autoreactive CD4+ T cells that are associated with autoimmunity in the CNS. These studies suggest an important role for the IL-23/T_H17 axis in autoimmune diseases including IBD (2). However, it is not known whether serum IL23 levels have any correlation with disease severity and could be useful in the clinical management of IBD. Mirsattari and colleagues in this issue of GHFBB have investigated this question by comparing the level of IL23 in the serum of 85 patients with UC with that of 40 healthy controls. They observed that the level of IL-23 in serum measured by an electrochemiluminiscence assay was significantly higher in patients with UC compared to healthy controls (3). Further, they observe a significant positive correlation between serum IL-23 levels and disease severity, being higher in those with severe UC than in those with moderate or mild UC. Interestingly, there was a positive correlation between serum IL23 levels and duration of UC, suggesting that IL23 could potentially be useful in following the progression of UC.

The potential implications of this study include further exploration of the role of IL23 in

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UC and other IBDs. It also suggests the significance of the IL23/Th17 axis in the therapy of autoimmune diseases including IBD. Further, IL23 could be explored as a prognostic marker in those with moderate-severe UC and for immunolocalization of sites of active inflammation in those patients who are on therapy for UC and CD.

References

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