Reviewer's report

Title: Th17-related cytokines: new players in the control of chronic intestinal inflammation

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Reviewer: Stephan Brand

Reviewer's report:

General Comments

This review gives a good overview about recent developments in the field of Th17 cytokines. The paper is well written and I have only a few suggestions.

Major Comments

(1) Given the recent insights into IBD genetics, which demonstrated a number of Th17 related genes as major IBD susceptibility genes, a few sentences should be given about the recent progress in Th17-related IBD susceptibility genes (e.g., IL23R, JAK2, TYK2, STAT3, CCR6). In particular, the two recent meta-analyses of genome-wide association studies and related papers should be mentioned:


Anderson CA et al. Meta-analysis identifies 29 additional ulcerative colitis risk loci, increasing the number of confirmed associations to 47. Nat Genet. 2011 Mar;43(3):246-52.


(2) Recent findings on how IL23R variants modulate Th17 secretion should be added:


(3) The direct anti-inflammatory effects of IL-22 on the intestinal epithelium should be mentioned:

a) by increasing mucin production and goblet cell restitution (Sugimoto K et al. IL-22 ameliorates intestinal inflammation in a mouse model of ulcerative colitis. J Clin Invest. 2008 Feb;118(2):534-44.)

b) by increasing epithelial cell migration/wound healing and increasing defensin expression (Brand S et al. IL-22 is increased in active Crohn's disease and promotes proinflammatory gene expression and intestinal epithelial cell migration. Am J Physiol Gastrointest Liver Physiol. 2006 Apr;290(4):G827-38.)

(4) The Th17 chemokine CCL20 should be mentioned. Several studies demonstrated an increased expression in active IBD. Moreover, CCL20 is chemotactic for CCR6+ Th17 cells:


(5) Recent clinical applications such as ustekinumab (Certify trial; see DDW 2011 abstract) and the lack of efficacy of an anti-IL-17 antibody (AIN457 by Novartis) in Crohn's disease (see abstract of this year's ECCO meeting / Journal of Crohn’s & Colitis 2011) compared to response in other Th17-mediated diseases should be mentioned (Hueber W et al. Effects of AIN457, a fully human antibody to interleukin-17A, on psoriasis, rheumatoid arthritis, and uveitis. Sci Transl Med. 2010 Oct 6;2(52):52ra72.)

Minor Comments

(6) Page 4: Write „gamma delta T cells“ instead of „gamma lambda T cells“

(7) Add „IL-22“ to the keywords

(8) Figure 1: The quality of Figure 1 could be improved. APCs and not Th17 cells are the main producers of IL-23. IL-12 (and not IL-23) mediates development of Th1 cells, while IL-23 mediates differentiation/stabilization of Th17 cells. IL-21 is an autocrine mediator of Th17 cell function (Korn T et al. IL-21 initiates an alternative pathway to induce proinflammatory T(H)17 cells. Nature. 2007 Jul 26;448(7152):484-7.)

(9) Figure 1: Antigen sampling CD11b+CX3CR1+ DCs may be added to the figure; see also:


Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests