

Reactivity of intestinal CD4 T cells to bacterial antigens in Crohn's disease patients.

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Abstract

Crohn's disease (CD) is a chronic granulomatous inflammation of the intestine. The etiology is unknown, but an excessive immune response to bacteria in genetically susceptible individuals is probably involved. The response is characterized by a strong Th1/Th17 response, but the relative importance of the various bacteria is not known. In an attempt to address this issue, we made T-cell lines from intestinal biopsies of patients with CD (n=11), ulcerative colitis (UC) (n=13) and controls (n=10). The T-cell lines were tested for responses to *Escherichia coli*, *Bacterioides thetaiotaomicron*, *Bifidobacterium bifidum*, *Lactobacillus gasseri* and *Mycobacterium avium* subsp. *paratuberculosis*. A majority of the CD patients with active disease had a dominant response to *Mycobacterium avium* subspecies *paratuberculosis* (MAP). The T cells from CD patients also showed higher proliferation in response to MAP compared to UC patients (p<0.025). MAP reactive CD4 T-cell clones (n = 28) were isolated from four CD patients. The T-cell clones produced IL-17 and/or IFN- γ , while minimal amounts of IL-4 were detected. To further characterize the specificity, the responses to antigen preparations from different mycobacterial species were tested. One T-cell clone responded only to MAP and the very closely related *M. avium* subspecies *avium* (MAA) while another responded to MAP, MAA and *M. intracellulare*. A more broadly reactive T-cell clone reacted to MAP1508 which belongs to the *esx* protein family and the epitope was determined. The presence of MAP reactive T cells with a Th1 or Th1/Th17 phenotype may suggest a possible role of mycobacteria in the inflammation seen in CD. The isolation of intestinal T cells followed by characterization of their specificity is a valuable tool to study the relative importance of different bacteria in CD.