Gliadin-specific type 1 regulatory T cells from the intestinal mucosa of treated celiac patients inhibit pathogenic T cells.


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Celiac disease (CD) results from a permanent intolerance to dietary gluten and is due to a massive T cell-mediated immune response to gliadin, the main component of gluten. In this disease, the regulation of immune responses to dietary gliadin is altered. Herein, we investigated whether IL-10 could modulate anti-gliadin immune responses and whether gliadin-specific type 1 regulatory T (Tr1) cells could be isolated from the intestinal mucosa of CD patients in remission. Short-term T cell lines were generated from jejunal biopsies, either freshly processed or cultured ex vivo with gliadin in the presence or absence of IL-10. Ex vivo stimulation of CD biopsies with gliadin in the presence of IL-10 resulted in suppression of Ag-specific proliferation and cytokine production, indicating that pathogenic T cells are susceptible to IL-10-mediated immune regulation. T cell clones generated from intestinal T cell lines were tested for gliadin specificity by cytokine production and proliferative responses. The majority of gliadin-specific T cell clones had a Th0 cytokine production profile with secretion of IL-2, IL-4, IFN-gamma, and IL-10 and proliferated in response to gliadin. Tr1 cell clones were also isolated. These Tr1 cells were anergic, restricted by DQ2 (a CD-associated HLA), and produced IL-10 and IFN-gamma, but little or no IL-2 or IL-4 upon activation with gliadin or polyclonal stimuli. Importantly, gliadin-specific Tr1 cell clones suppressed proliferation of pathogenic Th0 cells. In conclusion, dietary Ag-specific Tr1 cells are present in the human intestinal mucosa, and strategies to boost their numbers and/or function may offer new therapeutic opportunities to restore gut homeostasis.

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