CD25+/Foxp3+ T cells regulate gastric inflammation and Helicobacter pylori colonization in vivo.

BACKGROUND & AIMS: Helicobacter pylori infects more than half of the world's population. In contrast to most other pathogens, the microbe persists for the virtual life of its host. It is unclear why the immune system is unable to eliminate the infection, but recent studies suggested that CD4+/CD25+/Foxp3+ regulatory T cells may be involved in this process.

METHODS: By using a mouse model of infection and gastric biopsies from 108 patients, we performed a detailed descriptive and functional characterization of the Helicobacter-induced CD25+/Foxp3+ T-cell response. RESULTS: In C57BL/6 mice, H. pylori induced a marked gastric Foxp3+ T-cell response, which increased over several months together with the severity of inflammation, until a stable homeostatic situation became established. Accordingly, in Helicobacter-infected patients, but not in uninfected individuals, large numbers of gastric Foxp3+ T cells were detected immunohistochemically. To define the functional in vivo relevance of this response, CD25+ cells were depleted systemically in mice by using an anti-CD25 monoclonal antibody (PC61). Already 4 weeks after infection, PC61-treated mice, but not untreated animals, developed a severe gastritis with heightened cytokine expression and increased...
numbers of mucosal T cells, B cells, and macrophages. This was accompanied by increased titers of H pylori-specific IgG1 and IgG2c antibodies in the sera of PC61-treated mice. This increased gastric inflammatory response in CD25-depleted mice was associated with reduced bacterial loads.

CONCLUSIONS: CD25+/Foxp3+ T cells actively participate in the immune response to H pylori. In vivo depletion of these cells in infected mice leads to increased gastric inflammation and reduced bacterial colonization.