Cell Biology

EFFECT OF *IN VIVO* ADMINISTRATION OF ANTI-CTLA-4 mAb AND/OR ANTI-MCP-1 mAb ON TH1 CELL ORAL TOLERANCE

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Oral tolerance is defined as antigen specific immune hyporesponsivness. The type of mechanism involved in generating oral tolerance is thought to depend on the dose and frequency of antigen feeding. Generally, a high dose of antigen results in T cell anergy and deletion while a low does would result in suppressive cytokine secretion. In a normal immune response, $CD4^+$ T cells are activated by the binding of CD28 on their surface to the B7 receptor on an antigen presenting cell (APC); $CD4^+$ cells will then proliferate and differentiate into either Th1 cells (characterized by IFN-γ and IgG2a production) or Th2 cells (characterized by IL-4 and IgG1 production). Results from previous studies have suggested that binding of B7 to cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4), rather than CD28, prevents activation of $CD4^+$ cells and may, in part, be responsible for oral tolerance. In addition, it has been suggested that a decrease in gut monocyte chemotactic protein (MCP-1) expression may be involved in oral tolerance induction at the Th1 cell level. In the present study, the effects of administering anti-MCP-1 mAb and/or anti-CTLA-4 mAb *in vivo* on the induction of oral tolerance were investigated. Controls were administered only rabbit serum and/or rat IgG. Administration of anti-MCP-1 mAb to fed mice appeared to have no effect on the suppression of humoral titers (IgGAM, IgG1, IgG2a) or cytokine levels (IL-4, IFN-γ). However, proliferation of splenic cells in mice fed OVA and administered anti-MCP-1 mAb were no longer suppressed. Co-administration of anti-MCP-1 mAb and anti-CTLA-4 mAb, along with fed antigen, prevented the suppression of IgG2a titers but not that of IgGAM or IgG1. In addition, this treatment in fed mice prevented suppression in cell proliferation, IFN-γ levels and IL-4 levels in the spleen. These results suggest that administering anti-MCP-1 mAb alone had little effect on the induction of oral tolerance while co-administration of anti-MCP-1 mAb and anti-CTLA-4 mAb may prevent the induction of Th1 cell oral tolerance.