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$CD4^{+}CD25^{+}$regulatory T cells directly act on antigen-presenting cells by downregulation of CD80/CD86 costimulatory molecules

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Keywords

$CD4^+$ $CD25^+$, co-stimulation, immunoregulation, regulatory T cell

Context

Elimination of $CD4^+CD25^+$ T cells, which constitute 5-10% of peripheral $CD4^+$ T cells in normal naive mice, leads to spontaneous development of various autoimmune diseases. When stimulated, these regulatory T cells suppress the proliferation of the $CD4^+CD25^-$ T cells, resulting in reduced IL-2 production by $CD4^+CD25^-$ T cells. Suppression depends on cellular interactions with APCs. The effector functions of regulatory T cells still remain unclear. Identifying the molecules involved in the interaction between regulatory cells and the naive T cells would contribute to our understanding of the causes and mechanisms involved in autoimmune diseases. To further elucidate the mechanism of $CD4^+CD25^+$ T cell suppression on $CD4^+CD25^-$ T cells.

Significant findings

$CD4^+CD25^+$ T cells suppress responses of $CD4^+CD25^-$ T cells stimulated with anti-CD3 antibody and cultured with either B cells (100% suppression with 1:4 ratio of $CD25^+/CD25^-$) or DCs (100% suppression with 9:1 ratio of $CD25^+/CD25^-$). The expression of costimulatory molecules (both CD80 and CD86) on DCs was decreased when graded numbers of $CD4^+CD25^+$ T cells were added to the coculture, even if DCs were first stimulated with anti-CD40 antibody. Surprisingly, $CD4^+CD25^+$ cells downregulate CD80 mRNA levels on DCs, whereas levels of CD86 mRNA were not significantly decreased. This suggests that the expression of these two molecules is regulated by different mechanisms. The down regulation of CD80 and CD86 molecules on DCs depends on direct interaction between $CD4^+CD25^+$ T cells and DC interaction, and no decreased expression was observed when DC were separated from $CD4^+CD25^+$ cells by a cell permeable membrane.

Comments

Recently, the ability of $CD4^+CD25^+$ T cells to regulate $CD4^+CD25^-$ T cells has been described. These regulatory T cells are able to inhibit both proliferation and interleukin (IL)-2 secretion of activated $CD4^+CD25^-$ T cells, and prevent the induction of autoimmune disease. It remains unclear whether this suppression mechanism is mediated by direct T cell-T cell interactions or requires antigen presenting cells (APCs) as well. In this study, the authors show that the $CD4^+CD25^+$ regulatory T cells can directly act on APCs (B and dendritic cells[DCs]), and can influence their presentation functions by downregulating costimulatory molecules such as CD80 and CD86. This article is very interesting because the data clearly demonstrate the influence of regulatory $CD4^+CD25^+$ T cells on the performance of APCs, and could have many implications in explaining persistence of tolerance. It would be very interesting to study this T cell population in an autoimmune context, and verify if this regulatory pathway is not deficient in autoimmune conditions.

Methods

$CD4^+$ T cell populations were recovered by negative selection, and $CD4^+CD25^+$ and $CD4^+CD25^-$ subpopulations were then separated by magnetic cell sorting (MACS technology). Splenic B cells and DCs were enriched with B220-antibody-congugated beads and CD11c conjugated beads, respectively. Suppressor cell activity was assessed by coculturing various numbers of $CD4^+CD25^+$ T cells with $CD4^+CD25^-$ T cells and various numbers of B cells or DCs in 96-well plates, and stimulating with anti-CD3 antibodies. Proliferation was measured after 3 days of culture. For flow cytometric analysis, cells were cocultured 48 h in 24-well plates. mRNA levels for CD80 and CD86 were determined by RT-PCR with specific primers for CD80, CD86, and hypoxanthine guanine phosphoribosyltransferase (HPRT) as internal control.

References

1. Cederbom L, Hall H, Ivars F: $CD4^+$ $CD25^+$regulatory T cells down-regulate co-stimulatory molecules on antigen-presenting cells. Eur J Immunol . 2000, 30: 1538-1543.