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Characterization of regulatory T cells in humans

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Keywords

Anergy, regulatory T cells, suppression

Context

Regulatory T cells with the ability to prevent or regulate autoimmune disease have been demonstrated in several different experimental systems (see Additional information [1]). Studies have shown that this potent $CD4^+$ immunoregulatory T-cell population can be defined by expression of the interleukin (IL)-2 receptor a chain (CD25). $CD4^+$ $CD25^+$ T cells are anergic to stimulation via T-cell receptors and suppress proliferation of $CD4^+CD25^-$ lymphocytes *in vitro*. This suppression was shown to be cytokine-independent but required cell-cell contact to be efficient. This study was undertaken to establish the existence of such T-cell populations in humans.

Significant findings

$CD4^+CD25^+$ T cells were purified from human thymus lymphocytes and peripheral blood lymphocytes (PBLs). As has been shown in mice, these cells proliferated poorly in response to mitogenic stimulation, and this defect was reversed by exogenous IL-2. $CD4^+CD25^+$ T cells expressed cytotoxic T lymphocyte associated antigen (CTLA)-4 and CD122 molecules, and suppressed proliferation of $CD4^+CD25^-$ T cells in a dose-dependent manner. This suppression required direct interactions between $CD4^+CD25^+$ and $CD4^+CD25^-$ T cells *in vitro*. Unstimulated thymic $CD4^+CD25^+$ T cells secreted IL-10 (not IL-2, IL-4 and interferon [IFN]-?), and suppressed secretion of IL-2, IL-4 and IFN-? by $CD4^+CD25^+$ T cells in co-culture experiments. Similar characteristics were found in $CD4^+CD25^+$ from PBLs, except that these cells produced similar levels of IL-4 when compared with $CD4^+CD25^+$ T cells.

Comments

This is the first description of regulatory $CD4^+CD25^+$ T cells with suppressive functions on $CD4^+CD25^-$ T cells in humans. One interesting point is that certain differences in cytokine production by $CD25^+$ lymphocytes were found in thymic versus PBL $CD4^+$ T cells. The authors proposed that this could be explained by a difference in the number and/or the type of antigen presenting cells present in these two sites. Another group recently reported the presence of $CD4^+CD25^+$ T cells in human PBLs and in tonsils (see Additional information [2]). They showed that suppression is cell contact dependent, but also demonstrated that it is not mediated via IL-4, IL-10 or transforming growth factor-?. They confirmed that these cells express high levels of CTLA-4. Further characterization of the function and development of these T cells may further our understanding of the cause and mechanism of autoimmune disease, and may help in developing new strategies for treatment.

Methods

T cell purification, FACS analysis, co-culture experiments

Additional information

1. Sakaguchi S: **Policing the regulators.**

   Nat Immunol 2001, **2**:283-284.

2. Taams LS, Smith J, Rustin MH, Salmon M, Poulter LW, Akbar AN: **Human anergic/suppressive $CD4^+CD25^+$ T cells: a highly differentiated and apoptosis-prone population.**

   Eur J Immunol 2001, **31**:1122-1131.

References

1. Stephens LA, Mottet C, Mason D, Powrie F: Human $CD4^{+}CD25^{+}$ thymocytes and peripheral T cells have suppressive activity *in vitro* . Eyr J Immunol. 2001, 31: 1247-1254. ,