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Cross-talk between T cells and airway smooth muscle cells in airway responsiveness

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Andrea Heinzmann,[Aff1]
Corresponding Affiliation: Aff1

Aff1 Wellcome Trust Centre for Human Genetics, Oxford, UK

Keywords

Airway responsiveness, airway smooth muscle cell, T lymphocytes

Context

Over recent years many different cell types have been implicated in the pathophysiology of allergic asthma. Among these, much attention has been focused on the $CD4^+$ T lymphocytes, and their role in the development of asthma has been extensively investigated. The airway smooth muscle (ASM) cell itself has recently been found to have a variety of proinflammatory effects on the atopic asthmatic state. The authors of this study were interested in a possible interaction between resting/activated T cells and resting/activated ASM cells in mediating proasthmatic changes in airway response

Significant findings

In contrast to resting human T cells, anti-CD3-activated T cells significantly enhanced the constrictor response to acetylcholine and impaired the relaxation response to isoproterenol in isolated rabbit ASM tissue. In addition, the incubation of anti-CD3-activated T cells with naive human ASM cells evoked distinctive adhesive clustering. Comparably, exposure of resting T cells to ASM cells prestimulated with IgE immune complexes reciprocally elicited T-cell adhesion. Extended studies showed that the expression of the cell adhesion molecules (CAMs)/costimulatory molecules CD25, CD40, CD40L, CD80, CD86 and CD54, but not CD11a was upregulated by activating naive human ASM cells with anti-CD3-activated T cells. In accordance, resting T cells exposed to activated ASM cells showed a markedly increased expression of the same CAMs/costimulatory molecules. Pretreatment of resting ASM cells with neutralising monoclonal antibodies directed against CD40 and CD86 or against CD11a alone completely abrogated both the activated-T-cell-induced increase in expression of the adhesion molecules and the altered ASM tissue responsiveness to acetylcholine and isoproterenol. Similar effects were seen by pretreating resting T cells with the same mAbs before incubation with activated ASM cells.

Comments

The study provides new evidence for the existence of a bidirectional cross-talk between activated T cells and ASM cells. The interaction involves coligation of CAMs/costimulatory molecules and thereby mediates the induction of proasthmatic-like changes in ASM responsiveness. However, the ASM cells used in this study were derived from healthy nonasthmatic humans and rabbits. Thus it still has to be proved whether the same mechanisms are involved in the airway responsiveness of asthmatic humans. Besides, it would be of interest to investigate the release of proinflammatory cytokines during the interaction of these two cell types.

Methods

Flow cytometry, RT-PCR, isolation and culture of ASM and T cells, pharmacodynamic studies, microscopy.

Additional information

References

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