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Collagen type I stimulates T cells

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Keywords

?-1 integrins, collagen, T cells

Context

T lymphocytes interact with extracellular matrix proteins (ECMPs) through the ?-1 or very late antigen (VLA) integrins. VLA integrins comprise a common ? chain with different a-subunits that influence ECMP-binding specificity. They are costimulatory molecules, involved in adhesion and cellular migration. Reports on the role of the ECMP fibronectin in costimulating T cells have described therapeutic effects of VLA antibodies or peptide ligands in inflammatory/autoimmune disease models or transplantation. In contrast, the ECMP type I collagen has inconsistent effects on T cell activation, with most reports finding that resting peripheral blood (PB) T cells do respond. However, here the authors suggest that resting PB T cells are not representative of populations of extravascular, activated, effector cells that encounter immobilised ECMPs and that are involved in the pathogenesis of inflammatory/ autoimmune diseases. To address this they have investigated the costimulatory effects of ECMPs on both freshly isolated human PB $CD4^+$ and $CD8^+$ T cells, and antigen- or mitogen-stimulated $CD4^+$ and $CD8^+$T cell lines used as models of the extravascular effector cells encountered in disease.

Significant findings

This work is largely based on *in vitro* proliferation assays using triplicate cultures, but no error bars are shown. As shown previously, PB $CD4^+$ and $CD8^+$ T cells proliferated in response to co-immobilised anti-CD3 and fibronectin, but not other ECMPs. In contrast, $CD4^+$ and $CD8^+$ T-cell lines proliferated in response to co-immobilised anti-CD3 with type I collagen, type III collagen, laminin or fibronectin. Similarly, immobilised type I collagen and fibronectin were costimulatory for antigen-induced T-cell line proliferation, using model antigen tetanus toxoid. However, type I collagen did not affect tetanus toxoid stimulation of fresh PB T cells. FACS analyses showed enhanced expression of a-1, 2 and 3 integrins on T cell lines. Experiments with blocking monoclonal antibodies to VLA-1 or VLA-2 or ?-1 integrins inhibited the response to type I collagen. Data suggested that the main T cell costimulatory activity was contained within the a-1 chain of type I collagen. Taken together these results demonstrate

the costimulatory effect of type I collagen on both $CD4^+$ and $CD8^+$human T-cell lines, but not fresh PB T cells. The data show the type I collagen effect is mediated via VLA-1 and VLA-2 integrins.

Comments

The authors use $CD4^+$ and $CD8^+$ T cell lines as models of extravascular effector cells, although it is not clear that such lines are true representatives of activated effector T cells. However, the results demonstrate the potential importance of type I collagen, a very abundant extracellular matrix protein. The authors suggest that type I collagen is a more potent stimulus than the other ECMPs studied here (on a ?g/ml basis), although it is not clear if this is true at molar equivalents. The data suggest that therapeutic interventions targeted at interactions between T cells and ECMPs should include blockade of collagen.

Methods

Proliferation assays, FACS analysis, human T-cell preps, HPLC, SDS-PAGE, amino acid sequencing

Additional information

References

1. Rao WH, Hales JM, Camp RD: Potent costimulation of effector T lymphocytes by human collagen type I. J Immunol. 2001, 165: 4935-4940..