Galectin-8 binds specific β1 integrins and induces polarized spreading highlighted by asymmetric lamellipodia in Jurkat T cells

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Abstract

Integrin-mediated encounters of T cells with extracellular cues lead these cells to adhere to a variety of substrates and acquire a spread phenotype needed for their tissue incursions. We studied the effects of galectin-8 (Gal-8), a β-galactoside binding lectin, on Jurkat T cells. Immobilized Gal-8 bound α1β1, α3β1 and α5β1 but not α2β1 and α4β1 and adhered these cells with similar kinetics to immobilized fibronectin (FN). Function-blocking experiments with monoclonal anti-integrin antibodies suggested that α5β1 is the main mediator of cell adhesion to this lectin. Gal-8, but not FN, induced extensive cell spreading frequently leading to a polarized phenotype characterized by an asymmetric lamellipodial protrusion. These morphological changes involved actin cytoskeletal rearrangements controlled by PI3K, Rac-1 and ERK1/2 activity. Gal-8-induced Rac-1 activation and binding to α1 and α5 integrins have not been described in any other cellular system. Strikingly, Gal-8 was also a strong stimulus on Jurkat cells in suspension, triggering ERK1/2 activation that in most adherent cells is instead dependent on cell attachment. In addition, we found that patients with systemic lupus erythematosus (SLE), a prototypic autoimmune disorder, produce Gal-8 autoantibodies that impede both its binding to integrins and cell adhesion. These are the first function-blocking autoantibodies reported for a member of the galectin family. These results indicate that Gal-8 constitutes a novel extracellular stimulus for T cells, able to bind specific β1 integrins and to trigger signaling pathways conducive to cell spreading. Gal-8 could modulate a wide range of T cell-driven immune processes that eventually become altered in autoimmune disorders.