Alpha-5 beta-1

Integrin α5β1was firstly reported in the 1992s and was the only known α5 integrin

Alpha-5 beta-1 (α5β1), also known as the fibronectin receptor, is an integrin that binds to matrix macromolecules and proteinases and thereby stimulates angiogenesis.

It is composed of α5 (ITGA5/CD49e) and β1 (ITGB1/CD29) subunits. It is the primary receptor for fibronectin. The interaction of VLA-5 with fibronectin plays an important role in regulating inflammatory cytokine production by human articular chondrocytes (From the Cell Migration Gateway ITGA5 ITGB1).

α5β1-integrin is transported inside the cell by the kinesin KIF1C, a kinesin-3 organelle transporter that walks along microtubules.

The interaction of urokinase-type plasminogen activator (uPA) with its cell-surface receptor (uPAR) is implicated in diverse biological processes such as cell migration, tissue remodeling, and tumor cell invasion. Recent studies indicated that uPAR can act as an extracellular matrix receptor during cell adhesion. Recently, we showed that transfection of the human glioma cell line SNB19 with antisense uPAR resulted in downregulation of uPAR at both the mRNA and protein levels. In this study, we used SNB19 to determine how the presence or absence of uPAR promotes cell spreading and associated changes in cell morphology. Microscopic analysis of cell spreading revealed that antisense uPAR-transfected cells were larger, remained round, and did not spread efficiently over extracellular matrix substrate type IV collagen and fibronectin, unlike parental SNB19 cells, which were smaller and spindle shaped. Biochemical studies showed that antisense uPAR-transfected cells, in addition to not spreading, exhibited increased expression of alpha 3 beta 1 integrin but not alpha 5 beta 1 integrin. However, we could not find a change in the expression of extracellular matrix components or altered growth rate in these cells. Furthermore, despite the increased alpha 3 beta 1 integrin expression, antisense uPAR-transfected cells failed to form an organized actin cytoskeleton when plated on type IV collagen or fibronectin, unlike parental SNB19 cells, which displayed an organized cytoskeleton. These findings show that the absence of uPAR in human glioma cells leads to morphological changes associated with decreased spreading and a disorganized cytoskeleton resulting in altered cell morphology, suggesting that coordinated expression of uPAR and integrin may be involved in spreading of antisense uPAR-transfected glioma cells [1)].

We have investigated the effect of integrin antibodies to a well-characterized alpha 5 beta 1 (fibronectin receptor) and to a multi-specific alpha 3 beta 1 (laminin, collagen, and fibronectin receptor), on the expression of matrix metalloproteases and the invasion ability of two human glioblastoma cell lines, SNB19 and U251. Cell adhesion assays indicated that both cell lines adhere to fibronectin, type IV collagen and laminin. Adhesion of cells to fibronectin was inhibited by a RGD peptide. Cells treated with anti-alpha 3 beta 1 or anti-alpha 5 beta 1 antibodies expressed increased levels of MMP-2. An in vitro matrigel assay also showed that the alpha 3 beta 1 antibody-treated cells had greater invasive ability than the controls. Immunofluorescence data showed that glioma cells treated with either anti-alpha 3 beta 1 or anti-alpha 5 beta 1 antibodies expressed diminished alpha 3 beta-1 and alpha 5 beta 1 integrins relative to the controls. The data show that treatment of cells with alpha 3 beta 1 antibody diminishes the integrin expression on the cell surface and increases the

MMP-2 activity and invasiveness [2].

We investigated glioblastoma multiforme (Glioblastoma) for a pattern of consistent alterations in cell adhesion molecules (CAM) expression that might distinguish tumor from normal autologous brain tissue. We used frozen section immunohistochemistry with anti-CAM and computerized image analysis to quantify staining intensity which we expressed as relative intensity units (RIU). Our results showed that normal brain tissue generally did not express alpha 1 beta 1, intercellular CAM-1 (ICAM-1), and sialylated Lewisx, slightly expressed alpha 2, alpha 4, alpha 5, alpha 6 beta 1, alpha v beta 3, lymphocyte function-associated antigen-3 (LFA-3), Lewisx, sialylated LewisLewisx, had a good expression of alpha 3 beta 1 and CD44, and strongly expressed neural CAM (NCAM). Glioblastoma expressed alpha 2, alpha 3, alpha 5, alpha 6 beta 1, alpha v beta 3, ICAM-1, LFA-3, CD44, Lewisx, sialylated Lewisx, and sialylated LewisLewisx significantly higher (2-11-fold RIU) than normal brain tissue. ICAM-1 and LFA-3 were the most distinctive markers of Glioblastoma. The small blood vessel endothelial cells of the normal brain and the Glioblastoma showed a few differences. The tumor endothelium expression of alpha 2 beta 1, alpha 4 beta 1, and LFA-3 RIU appeared twice higher than in normal endothelium and alpha 6 beta 1 showed an average of 40% RIU decrease in comparison to normal. These results show that the expression of several CAM is consistently altered in Glioblastoma and its microvasculature when compared with autologous normal brain tissue [3].

The migration of rIL-2-activated T and NK cells into the intercellular space of glioma tissue was studied using multicellular spheroids grown from the human H-2 glioblastoma cell line as targets. Lymphocytes of all analyzed subtypes migrated into the spheroids, but CD56+ cells were particularly migratory. Lymphocytes and the H-2 tissue expressed adhesion molecule subunits for the following potential cell-cell or cell-matrix interactions: alpha 3 beta 1 (VLA-3) to fibronectin, laminin, and collagen; alpha 4 beta 1 (VLA-4) and alpha 5 beta 1 (VLA-5) to fibronectin; alpha 6 beta 1 (VLA-6) to laminin; alpha 4 beta 1 to VCAM-1; alpha L beta 2 (Leu-CAMa/LFA-1) to CD54 (ICAM-1); CD44 to fibronectin, collagen, laminin, hyaluronate; CD2 to CD58 (LFA-3); and CD56 (N-CAM) to CD56. In the H-2 tissue, CD54 and VCAM-1 were expressed as a gradient. The expression of CD54 was weak in the peripheral zone and the expression was stronger in the quiescent deeper zone, whereas the distribution of VCAM-1 showed an inversed pattern. The low expression of CD54 was up-regulated along the frontier of migrating lymphocytes. The migration was almost totally prevented by the anti-CD18 (beta 2) mAb IB4 and TS1/18, and also strongly inhibited by the anti-CD54 mAb LB-2. Instead, mAb known to inhibit the binding of beta 1 integrins to fibronectin were not significantly inhibitory. However, a combination of the GPEILDVPST and GRGDS peptides, which compete for the binding of alpha 4 beta 1 and alpha 5 beta 1 to fibronectin and may also affect other adhesion systems, partially prevented migration [4].

1)
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