Integrin beta 1

Integrin beta-1 (ITGB1), also known as CD29, is a cell surface receptor that in humans is encoded by the ITGB1 gene. This integrin associates with integrin alpha 1 and integrin alpha 2 to form integrin complexes which function as collagen receptors. It also forms dimers with integrin alpha 3 to form integrin receptors for netrin 1 and reelin. These and other integrin beta 1 complexes have been historically known as very late activation (VLA) antigens.

Stretch injury of the facet capsular ligament is a cause of neck pain, inducing axonal injury, neuronal hyperexcitability, and upregulation of pain neuromodulators. Although thresholds for pain and collagen reorganization have been defined and integrins can modulate pain signaling with joint trauma, little is known about the role of integrin signaling in neuronal dysfunction from tensile loading of the innervated capsular ligament. Using a well-characterized biomimetic collagen gel model of the capsular ligament's microstructure and innervation, a study evaluated extrasynpatic expression of N-Methyl-D-Aspartate receptor subtype 2B (GRIN2B) as a measure of neuronal dysfunction following tensile loading and determined mechanical thresholds for its upregulation in primary sensory neurons, with and without integrin inhibition.Collagen gels with dissociated dorsal root ganglion neurons (n = 16) were fabricated; a subset of gels (n = 8) was treated with the β1 integrin subunit inhibitor, TC-I15. Gels were stretched to failure in tension and then immunolabeled for axonal NR2B. Inhibiting the integrin subunit does not change the failure force ($p = 0.12$) or displacement ($p = 0.44$) but does reduce expression of the β1 subunit by 41% ($p < 0.001$) and decrease axonal NR2B expression after stretch ($p = 0.018$). Logistic regressions estimating the maximum principal strain threshold for neuronal dysfunction as evaluated by Analysis of Covariance determine that integrin inhibition increases ($p = 0.029$) the 50th percentile strain threshold (7.1%) above the threshold for upregulation in untreated gels (6.2%). These results suggest that integrin contributes to stretch-induced neuronal dysfunction via neuron-integrin-collagen interactions [1)]

Combined inhibition of the adhesion receptor β1 integrin and the stress-mediator c-Jun N-terminal kinase (JNK) induces radiosensitization and blocks invasion in stem-like and patient-derived Glioblastoma cultures as well as in Glioblastoma cell lines. In vivo, this treatment approach not only significantly delays tumor growth but also increases median survival of orthotopic, radiochemotherapy-treated Glioblastoma mice. Both, in vitro and in vivo, effects seen with β1 integrin/JNK co-inhibition are superior to the monotherapy. Mechanistically, the in vitro radiosensitization provoked by β1 integrin/JNK targeting is caused by defective DNA repair associated with chromatin changes, enhanced ATM phosphorylation and prolonged G2/M cell cycle arrest. Our findings identify a β1 integrin/JNK co-dependent bypass signaling for Glioblastoma therapy resistance, which might be therapeutically exploitable [2)].

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Singh S, Winkelstein BA. Inhibiting the β1integrin subunit increases the strain threshold for neuronal dysfunction under tensile loading in collagen gels mimicking innervated ligaments. Biomech Model Mechanobiol. 2022 Mar 12. doi: 10.1007/s10237-022-01565-6. Epub ahead of print. PMID: 35279768.
2)
Vehlow A, Klapproth E, Storch K, Dickreuter E, Seifert M, Dietrich A, Bütof R, Temme A, Cordes N. Adhesion- and stress-related adaptation of glioma radiochemoresistance is circumvented by β1 integrin/JNK co-targeting. Oncotarget. 2017 Apr 27. doi: 10.18632/oncotarget.17480. [Epub ahead of

print] PubMed PMID: 28514757.