Recombinant Human Dystroglycan

Catalog Number: 6868-DG

DESCRIPTION

Source	Mouse myeloma cell line, NS0-derived human Dystroglycan protein Met1-Val749, with a C-terminal 6-His tag Accession # NP_004384
N-terminal Sequence Analysis	Gln313 (blocked) of alpha chain and Ser654 of beta chain
Structure / Form	Noncovalently-linked heterodimer
Predicted Molecular Mass	67.8 kDa (α subunit) & 11.3 kDa (β subunit)

SPECIFICATIONS

SDS-PAGE	65-90 kDa & 20 kDa, reducing conditions
Activity	Measured by the ability of the immobilized protein to enhance the adhesion of H4 human neuroglioma cells. The ED_{50} for this effect is 1.5-6.0 µg/mL. Optimal dilutions should be determined by each laboratory for each application.
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>95%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.
Formulation	Lyophilized from a 0.2 µm filtered solution in PBS. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution	Reconstitute at 500 µg/mL in PBS.
Shipping	The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	**Use a manual defrost freezer and avoid repeated freeze-thaw cycles.** • 12 months from date of receipt, -20 to -70 °C as supplied. • 1 month, 2 to 8 °C under sterile conditions after reconstitution. • 3 months, -20 to -70 °C under sterile conditions after reconstitution.

BACKGROUND

Dystroglycan, also called DAG-1 (dystrophin-associated glycoprotein 1) or DG, is a heterodimeric adhesion molecule that links the extracellular matrix (ECM) to the cell cytoskeleton (1-4). Human preproDAG-1 is an 895 amino acid (aa) type I transmembrane protein that contains a 27 aa signal sequence and an 868 aa proform. Autocatalysis of the proform produces two fragments that remain noncovalently-linked. The first fragment (or α-chain) is 626 aa in length (aa 28-653) and contains a mucin-like region, while the second fragment (or β-chain) is a 42-44 kDa, 242 aa N-glycosylated protein with an extracellular (aa 654-749), transmembrane, and cytoplasmic domain (5). Over aa 28-749, human DAG-1 shares 93% aa sequence identity with mouse DAG-1. It is widely expressed but differentially O-glycosylated on skeletal muscle and epithelia (which contain a 160 kDa α-chain) as compared to cardiac muscle, smooth muscle, fibroblasts, keratinocytes, lymphocytes, and hematopoietic stem cells (which contain a 100 - 140 kDa α-chain) (1-3, 6-9). DAG-1 binding of ECM molecules is influenced by its α-chain O-glycosylation (2, 6-10). In addition to skeletal muscle and neuromuscular junctions in which DAG-1 binds several ECM molecules, DAG-1 is important for neuronal migration (through neurexin interactions), keratinocyte attachment to the ECM (through laminin), and adhesion at the immunological synapse and in the hematopoietic stem cell niche (through agrin) (3, 6-11). In muscle, the β-chain cytoplasmic domain connects with the cytoskeleton via formation of the dystrophin-glycoprotein complex with isoforms of dystrophin, sarcoglycan, syntrophin, and sarcospan (3). This complex is critical for skeletal muscle viability and regeneration (3, 4, 10, 11). MMP9 cleavage of the 44 kDa β-chain creates a 30 kDa transmembrane form that causes dissociation of the heterodimer and a down-regulation of ECM interactions (6, 12). Dystroglycanopathies, a group of congenital muscular dystrophies affecting the brain, eye and skeletal muscle, are caused by either abnormalities in glycosyltransferases, or their accessory proteins, or rare DAG-1 polymorphisms. All result in DAG-1 hypoglycosylation, especially of O-mannosyl forms, and affect DAG-1 binding to ECM proteins (2, 3, 10, 13, 14).

References:

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