Recombinant Human Agrin N-terminal

Catalog Number: 8909-AG

DESCRIPTION

Source	Chinese Hamster Ovary cell line, CHO-derived Thr30-Arg1102, with a C-terminal 6-His tag Accession # O00468
N-terminal Sequence Analysis	Thr30
Predicted Molecular Mass	113 kDa

SPECIFICATIONS

SDS-PAGE	138-181 kDa, reducing conditions
Activity	Measured by its ability to inhibit neurite outgrowth of E16-E18 rat embryonic cortical neurons on a Laminin α4 coated plate. Able to significantly inhibit neurite outgrowth when immobilized as a 3 µL droplet containing 50 ng of protein.
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>95%, by SDS-PAGE with silver 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 with polar packs. 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

Agrin is a 400-600 kDa heparan sulfate proteoglycan component of the extracellular matrix. The N-terminal half of human Agrin, which mediates ECM interactions, contains a Laminin-binding NtA domain, nine Follistatin-like/Kazal-type protease inhibitor domains, two Laminin EGF-like domains, and one SEA domain. The C-terminal half contains four EGF-like repeats and three Laminin globular G domains. Rat Agrin lacks the NtA domain, and mouse and chick Agrin include the NtA domain only by the use of an alternate promoter. Additional isoforms are generated by alternative splicing at sites Y and Z in the C-terminal half of rat Agrin (known as A and B, respectively in chick). Agrin isoforms that contain an insert at site Z (Z^+ forms) are known as neural Agrin and are selectively produced by motoneurons. Other isoforms are known as muscle Agrin and are additionally expressed in non-neuronal tissues, particularly in basement membranes of the lung and kidney (1-3). In addition, multiple proteolytic fragments of Agrin are produced by Neurotrypsin, MMP-1, -7, -12, and -14 (4, 5). This recombinant protein consists of the N-terminal region of human Agrin (up to the Neurotrypsin α-cleavage site upstream of the SEA domain) (4). It shares 80% amino acid sequence identity with comparable regions of mouse and rat Agrin. The N-terminal region binds to BMP-2, BMP-4, and TGF-beta, and it blocks BMP-induced signaling through BMPR1A (6). The C-terminal half of Z- and Z^+ Agrin binds to α-Dystroglycan and mediates adhesion between motoneurons and myotubes at the neuromuscular junction (NMJ) (7-9). In contrast, only Z^+ Agrin is effective at inducing clustering of the postsynaptic Acetylcholine Receptor (AChR) and presynaptic motoneuron differentiation (10, 11). Agrin-induced AChR clustering requires a myotube receptor complex that contains α-Dystroglycan, MuSK, and LRP4 (7, 12-14). Agrin exhibits many functions in addition to NMJ development. It is enriched in senile Alzheimer's disease plaques where it binds the Aβ (1-40) peptide and promotes amyloid fibril formation (15). It regulates neuronal excitability by binding and inhibiting the α3 subunit of the neuronal Na/K ATPase (16). It functions as an epithelial cell attachment receptor for HIV-1 through interactions with the gp41 coat protein (17). During T cell activation, Agrin contributes to formation of the immunological synapse and regulates the threshold of T cell activation (18). Agrin is up-regulated in hepocellular carcinoma, where it enhances cell proliferation and tumor progression (19).

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