Recombinant Human Activin A Hyperactive

Catalog Number: BT-ACTAH

DESCRIPTION

Source	Chinese Hamster Ovary cell line, CHO-derived human Activin A protein Gly311-Ser426, F368A Accession # P08476.2
N-terminal Sequence Analysis	Gly311
Structure / Form	Disulfide-linked homodimer
Predicted Molecular Mass	13 kDa

SPECIFICATIONS

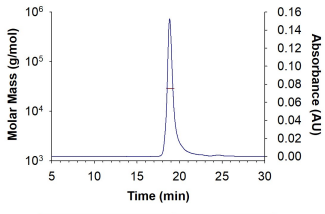
SDS-PAGE	12-14 kDa, under reducing conditions.
Activity	Measured by its ability to induce cytotoxicity using MPC-11 mouse B lymphocyte cells. The ED_{50} for this effect is < 5.00 ng/mL.
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>95%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.
Formulation	Lyophilized from a 0.2 µm filtered solution in Acetonitrile and TFA with Trehalose. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution	Reconstitute the 10 µg size at 100 µg/mL in sterile 4 mM HCl. Reconstitute all other sizes at 500 µg/mL in sterile 4 mM HCl.
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.

DATA

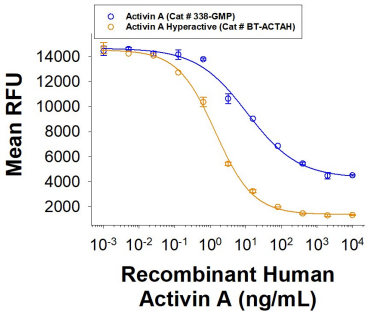
SEC-MALS



SEC-MALS Data	Result
Retention Time (Min)	18.5 - 19.4
MW - Predicted (Monomer)	13.0 kDa
MW - MALS	28.8 kDa
Polydispersity	1.000
System Suitability: BSA Monomer 66.4 ± 3.32 kDa	Pass

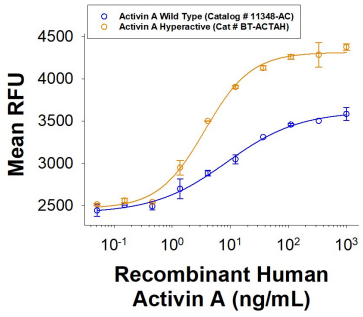
Recombinant Human Activin A Hyperactive Protein SEC-MALS. Recombinant Human Activin A Hyperactive (Catalog # BT-ACTAH) has a molecular weight (MW) of 28.8 kDa as analyzed by SEC-MALS, suggesting that this protein is a homodimer. MW may differ from predicted MW due to post-translational modifications (PTMs) present (e.g. Glycosylation).

Bioactivity



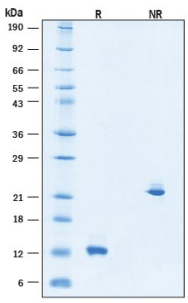
Recombinant Human Activin A Hyperactive Protein Bioactivity. Human Activin A Hyperactive Protein (Catalog # BT-ACTAH) induces cytotoxicity on MCP-11 cells. The ED_{50} for this effect is < 5.00 ng/mL. The hyperactive Activin A protein has greater bioactivity than Wild Type Activin A.

Bioactivity



Recombinant Human Activin A Hyperactive Protein Bioactivity. Human Activin A Hyperactive Protein (Catalog # BT-ACTAH) induces SBE (SMAD-binding element) reporter activity in HEK293 human embryonic kidney cells. The hyperactive Activin A protein has greater bioactivity than Wild Type Activin A.

SDS-PAGE



Recombinant Human Activin A Hyperactive Protein SDS-PAGE. 2 µg/lane of Recombinant Human Activin A Hyperactive Protein (Catalog # BT-ACTAH) was resolved with SDS-PAGE under reducing (R) and non-reducing (NR) conditions and visualized by Coomassie® Blue staining, showing bands at 12-14 kDa and 20-30 kDa, respectively.

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BACKGROUND

Activin and Inhibin are members of the TGF-β superfamily of cytokines and are involved in a wide range of biological processes including tissue morphogenesis and repair, fibrosis, inflammation, neural development, hematopoiesis, reproductive system function, and carcinogenesis (1-7). Activin and Inhibin are produced as precursor proteins. Their amino terminal propeptides are proteolytically cleaved and facilitate formation of disulfide-linked dimers of the bioactive proteins (8, 9). Activins are nonglycosylated homodimers or heterodimers of various β subunits (βA, βB, βC, and βE in mammals), while Inhibins are heterodimers of a unique α subunit and one of the β subunits. Activin A is a widely expressed homodimer of two βA chains. The βA subunit can also heterodimerize with a βB or βC subunit to form Activin AB and Activin AC, respectively (10). The 14 kDa mature human βA chain shares 100% amino acid sequence identity with bovine, feline, mouse, porcine, and rat βA. Activin A exerts its biological activities by binding to the type 2 serine/threonine kinase Activin RIIA which then noncovalently associates with the type 1 serine/threonine kinase Activin RIB/ALK-4 (7, 11). Signaling through this receptor complex leads to Smad activation and regulation of activin-responsive gene transcription (7, 11). The bioactivity of Activin A is regulated by a variety of mechanisms (11). BAMBI, Betaglycan, and Cripto are cell-associated molecules that function as decoy receptors or limit the ability of Activin A to induce receptor complex assembly (12-14). The intracellular formation of Activin A can be prevented by the incorporation of the βA subunit into Activin AC or Inhibin A (3, 10). And the bioavailability of Activin A is restricted by its incorporation into inactive complexes with α2-Macroglobulin, Follistatin, and FLRG (15, 16). Activin A is involved in the differentiation of various cell and tissue types. The induction of definitive endoderm by Activin A is required in differentiation protocols of induced pluripotent stem cells (iPSCs) (17, 18). *In vitro* models of human gametogenesis use prolonged Activin A supplementation to human embryonic stem cells for differentiation into human primordial germ cell-like cells (19). Activin A can also be used to maintain cells *in vitro*, as is the case for iPSC-derived nephron cells that can then be used in disease modeling, drug screening and in regenerative medicine (20). Activin A is an important factor for tumor cells to evade the immune system as Activin A can act on surrounding immune cells to decrease their antitumor activity (21). Activin A also promotes migration and growth of tumors, making it a target for cancer therapies (22). Specifically, research has shown that interfering with Activin A activity can assist in overcoming CD8 T-cell exclusion and immunotherapy resistance (23). In bone marrow-derived stem cell transplants for treatment of diabetes, Activin A enhances migration and homing of stem cells towards pancreatic lineage (24). With AI assisted designing, this engineered rhActivinA shows superior activity compared to the wild type.

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