Animal-Free™ Recombinant Human Activin A

Catalog Number: BT-ACTA-AFL

DESCRIPTION

Source	*E. coli*-derived human Activin A protein Gly311-Ser426 Accession # P08476.2 Produced using non-animal reagents in an animal-free laboratory.
N-terminal Sequence Analysis	Gly311
Structure / Form	Disulfide-linked homodimer
Predicted Molecular Mass	13 kDa (monomer)

SPECIFICATIONS

SDS-PAGE	13 kDa, under reducing conditions. 23 kDa, under non-reducing conditions.
Activity	Measured by its ability to induce cytotoxicity using MPC-11 mouse B lymphocyte cells. The ED_{50} for this effect is <10.0 ng/mL. The specific activity of Animal-Free™ Recombinant Human Activin A is >1000 units/mg, which is calibrated against the human Activin A WHO reference standard (NIBSC code: 91/626).
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>97%, by SDS-PAGE with 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 at 500 µg/mL in water.
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.

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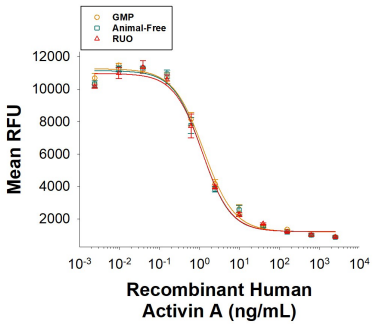
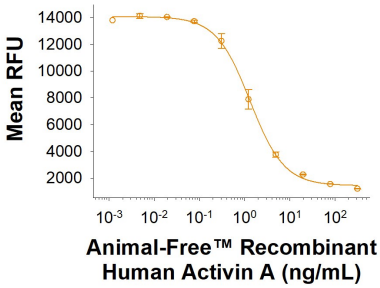
DATA

Bioactivity



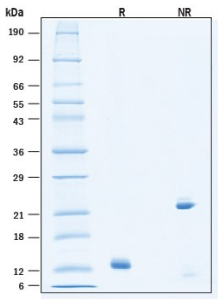
Equivalent Bioactivity of GMP, Animal-Free, and RUO grades of Recombinant Human Activin A. Equivalent bioactivity of GMP (Catalog # BT-ACTA-GMP), Animal-Free (Catalog # BT-ACTA-AFL), and RUO (Catalog # BT-ACTA) grades of Recombinant Human Activin A, as measured in a cytotoxicity assay using MPC-11 mouse B lymphocyte cells (orange, green, and red, respectively).

Bioactivity



Animal-Free™ Recombinant Human Activin A Protein Bioactivity. Animal-Free™ Recombinant Human Activin A Protein (Catalog # BT-ACTA-AFL) induces cytotoxicity in the MPC-11 mouse B-lymphocyte cell line.

SDS-PAGE



Animal-Free™ Recombinant Human Activin A Protein SDS-PAGE. 2 µg/lane of Animal-Free™ Recombinant Human Activin A Protein (Catalog # BT-ACTA-AFL) was resolved with SDS-PAGE under reducing (R) and non-reducing (NR) conditions and visualized by Coomassie® Blue staining, showing bands at 13 kDa and 23 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).

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MANUFACTURING SPECIFICATIONS

Animal-Free Manufacturing Conditions
Our dedicated controlled-access animal-free laboratories ensure that at no point in production are the products exposed to potential contamination by animal components or byproducts. Every stage of manufacturing is conducted in compliance with R&D Systems' stringent Standard Operating Procedures (SOPs). Production and purification procedures use equipment and media that are confirmed animal-free.

Production

- All molecular biology procedures use animal-free media and dedicated labware.
- Dedicated fermentors are utilized in committed animal-free areas.

Purification

- Protein purification columns are animal-free.
- Bulk proteins are filtered using animal-free filters.
- Purified proteins are stored in animal-free containers in a dedicated cold storage room.

Quality Assurance

- Low Endotoxin Level.
- No impairment of biological activity.
- High quality product obtained under stringent conditions.
- For *ex vivo* research or bioproduction, **additional documentation** can be provided.

Please read our complete Animal-Free Statement

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