

Background

Müllerian inhibiting substance (MIS), also named anti-Müllerian hormone (AMH), is a tissue-specific TGF- β superfamily growth factor. Its expression is restricted to the Sertoli cells of fetal and postnatal testis, and to the granulosa cells of postnatal ovary (1). The human MIS gene encodes a 553 amino acid residue (aa) prepropeptide containing a signal a sequence (1 - 24), a pro-region (25 - 455), and the carboxyl-terminal bioactive protein (446 - 553) (2 - 4). MIS is synthesized and secreted as a disulfide-linked homodimeric pro-protein. Proteolytic cleavage is required to generate the N-terminal pro-region and the C-terminal bioactive protein, which remain associated in a non-covalent complex. Recombinant C-terminal MIS has been shown to be bioactive. However, the complex with the N-terminal pro-region showed enhanced activity (3, 5). The C-terminal region contains the seven canonical cysteine residues found in TGF- β superfamily members. These cysteine residues are involved in inter- and intra-molecular disulfide bonds, which forms the cysteine knot structure. Human and mouse MIS share 73% and 90% aa sequence identity in their pro-region and C-terminal region, respectively. MIS induces Mullerian duct (female reproductive tract) regression during sexual differentiation in the male embryo (6). Postnatally, MIS has been shown to regulate gonadal functions (1). MIS inhibits Leydig cell proliferation and is a regulator of the initial and cyclic recruitment of ovarian follicles. MIS has also been found to have anti-proliferative effects on breast, ovarian and prostate tumor cells (7 - 9).

Like other TGF- β superfamily members, MIS signals via a heteromeric receptor complex consisting of a type I and a type II receptor serine/threonine kinase. Depending on the cell context, different type I receptors (including Act RIA/ALK2, BMP RIA/ALK3, and BMP RIB/ALK6) that are shared by other TGF- β superfamily members, have been implicated in MIS signaling (10 - 12). In contrast, the type II MIS receptor (MIS RII) is unique and does not bind other TGF- β superfamily members. Upon ligand binding, MIS RII recruits the non-ligand binding type I receptor into the complex, resulting in phosphorylation the BMP-like signaling pathway effector proteins Smad1, Smad5 and Smad 8 (10 - 12).

References:

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Description

Source	<i>E. coli</i> -derived Ala453 - Arg560 Accession # Q6GTN3
N-terminal Sequence Analysis	Ala453
Structure / Form	Disulfide-linked homodimer
Predicted Molecular Mass	11.7 kDa (monomer)

Specifications

Activity	Measured by its ability to inhibit growth of OVCAR-3 human ovarian carcinoma cells. Measured by its binding ability in a functional ELISA. Immobilized rhMIS at 3 μ g/mL (100 μ L/well) will bind rrMIS RII/Fc Chimera with a linear range of 1.6 - 100 ng/mL.
Endotoxin Level	<1.0 EU per 1 μ g of the protein by the LAL method.
Purity	>97%, by SDS-PAGE under reducing conditions and visualized by silver stain.
Formulation	Lyophilized from a 0.2 μ m filtered solution in Acetonitrile and TFA with BSA as a carrier protein. See Certificate of Analysis for details.

Preparation and Storage

Reconstitution	Reconstitute at 10 μ g/mL in sterile PBS containing at least 0.1% human or bovine serum albumin.
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. <ul style="list-style-type: none"> ● 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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