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Thymosin α-1

A 28-residue N-terminally acetylated thymic peptide first isolated by Goldstein, Low and McAdoo in 1977 from calf-thymus thymosin fraction 5 — the founding peptide of the thymosin family, characterised in preclinical models as an immunomodulator acting through Toll-like receptors TLR2 and TLR9 on dendritic cells and macrophages.

CAS REGISTRY	CATALOG REFERENCE	CLASS	DATE OF ISSUE
62304-98-7	BM-LYO-005	Synthetic peptide · 28 a.a.	May 2026

Thymosin α-1 (Tα1, INN thymalfasin) is a 28-residue N-terminally acetylated peptide with sequence Ac-SDAAVDTSSEITTKDLKEKKEVVEEAEN, first isolated by Allan Goldstein, Teresa L. K. Low, and colleagues in 1977 from calf-thymus thymosin fraction 5. The molecule is the founding member of the thymosin α family and is biosynthetically derived from the N-terminal region of prothymosin-α (a 109-residue chromatin-remodelling protein) by cleavage by the lysosomal asparaginyl endopeptidase legumain. Across approximately five decades of subsequent investigation, Tα1 has been characterised in cell-culture and animal-model preparations as an immunomodulator acting through Toll-like receptors TLR2 and TLR9 on dendritic cells and macrophages, driving downstream IRF3 / NF-κB / p38-MAPK signalling, dendritic cell maturation, T-cell differentiation toward Th1 / cytotoxic phenotypes, and natural-killer-cell activation. ***This monograph summarises published cellular pharmacology and preclinical findings for laboratory research reference only.***

01 Compound Profile

COMMON DESIGNATION	Thymosin α-1 · Tα1 · Thymalfasin (INN)
SEQUENCE (28 RESIDUES)	Ac-Ser-Asp-Ala-Ala-Val-Asp-Thr-Ser-Ser-Glu-Ile-Thr-Thr-Lys-Asp-Leu-Lys-Glu-Lys-Lys-Glu-Val-Val-Glu-Glu-Ala-Glu-Asn
N-TERMINAL ACETYLATION	N-terminal serine is acetylated; the acetylation is preserved in both native and synthetic preparations
CAS REGISTRY	62304-98-7
MOLECULAR FORMULA	$C_{129}H_{215}N_{33}O_{55}$
AVERAGE MOLECULAR MASS	3108.30 g · mol^{-1}
BIOSYNTHETIC ORIGIN	Cleavage product of prothymosin-α (109 residues) by lysosomal asparaginyl endopeptidase legumain[2]
PRIMARY MOLECULAR TARGETS	Toll-like receptor 2 (TLR2) · Toll-like receptor 9 (TLR9) on dendritic cells and macrophages; additional reported interaction with TLR4[3]
PHYSICAL FORM	White lyophilised solid
SOLUBILITY (LAB RECONSTITUTION)	Highly water-soluble; the molecule is intrinsically disordered with no rigid secondary structure in solution; net acidic at physiological pH
STORAGE (RESEARCH HANDLING)	Lyophilised solid: −18 °C, desiccated; reconstituted solution refrigerated 2–8 °C; long-term aliquots at −18 °C with freeze–thaw minimised
ANALYTICAL SPECIFICATION	≥ 98 % purity by HPLC (BIOMOD Labs internal release specification)

02 Origin and Chemistry

Thymosin α-1 was originally isolated during work at Albert Einstein College of Medicine and George Washington University by Allan Goldstein and collaborators, who had been fractionating thymus-derived peptide preparations for immunomodulatory activity. Tα1 was the first peptide isolated to homogeneity from thymic tissue and was named for its activity in restoring immune function in thymectomised mice. Complete amino-acid-sequence determination was published in 1977; the synthetic peptide was made by Wang, Makofske, Bach, and Merrifield in 1980 and shown to be biologically equivalent to the natural product.[1, 2]

Chemically, Tα1 is an intrinsically disordered peptide — no rigid secondary structure in aqueous solution. The sequence is unusually rich in acidic residues (5 aspartate, 7 glutamate) and contains no cysteine (no disulfide consideration). The N-terminal serine is acetylated in both the native and synthetic forms; this acetylation is part of the parent prothymosin-α N-terminal sequence and is preserved in the cleaved Tα1 product. The molecule's net acidic character at physiological pH is similar to other intrinsically-disordered chromatin-associated proteins.

03 Molecular Targets and Cellular Signalling

Tα1 engages Toll-like receptors on dendritic cells and macrophages — principally TLR2 and TLR9, with additional interactions reported at TLR4 in some preparations. Receptor activation drives canonical TLR downstream signalling: NF-κB nuclear translocation, IRF3 activation, and p38 MAPK phosphorylation. In dendritic cell preparations, Tα1 exposure promotes maturation markers (CD80, CD86, MHC class II upregulation), interleukin-12 production, and the cytokine profile that drives Th1-skewed T-cell differentiation. Romani and colleagues additionally documented Tα1-mediated activation of dendritic cell tryptophan catabolism through indoleamine 2,3-dioxygenase (IDO), a pathway associated with immune tolerance and inflammation calibration.[3, 4] IN VITRO

The molecule's pharmacology is therefore distinctive: an immunomodulator with bidirectional calibration rather than a unidirectional immune stimulant. Th1 / cytotoxic-T-cell activation pathways and tolerogenic / regulatory pathways are both engaged, with the resulting net effect depending on cellular context and concurrent signalling.[5]

04 Preclinical Findings

SYSTEM	PREPARATION	REPORTED OBSERVATION	REF.
Dendritic cell biology	Murine bone-marrow-derived DCs	Promoted DC maturation; activation marker upregulation; T-cell-stimulatory capacity modulation	4
TLR signalling	TLR-transfected reporter cell lines	Engagement of TLR2, TLR9, with additional TLR4 activity reported	3
NK cell biology	NK preparations	Enhanced NK cell cytotoxic function in animal-model studies	5
Tryptophan catabolism	DC cultures, IDO assays	Romani 2006: induction of DC tryptophan catabolism via IDO pathway	3
Thymectomised mouse	Original characterisation	Restoration of immune function in thymectomised animals	1
Anti-viral models	Cell-culture viral infection preparations	Enhanced cytotoxic-T-cell and NK cell responses against viral targets	5

05 Research Synthesis & Limitations

METHODOLOGICAL NOTES

Tα1 has one of the deepest published preclinical literatures of any thymic peptide, with independent characterisation across multiple laboratories over nearly five decades. The TLR2/TLR9 engagement and downstream signalling architecture are well-replicated; the dendritic-cell IDO induction and Th1-skewing pharmacology characterised by Romani and colleagues add a tolerogenic-calibration dimension to the simpler immune-stimulation picture. For researchers, the principal handling considerations are (a) preservation of the N-terminal acetylation, which is part of the molecule's identity; (b) the intrinsically disordered nature of the molecule, which means there is no rigid fold to disrupt during reconstitution; and (c) the acidic side-chain richness, which can lead to unusual chromatographic behaviour on some HPLC columns.

06 Laboratory Handling, Reconstitution, and Storage

Lyophilised Ta1 is supplied under research-use specifications. Reconstitution in sterile water for injection, phosphate-buffered saline, or bacteriostatic water is standard practice; the peptide is highly water-soluble. Lyophilised storage at −18 °C, desiccated; reconstituted solutions held refrigerated 2–8 °C for short-term work; aliquoted long-term storage at −18 °C with strict minimisation of freeze–thaw. Working concentrations are determined by the investigator's experimental design.

07 References

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