BIOMOD LABS · RESEARCH PEPTIDE CO.

RESEARCH COMPOUND MONOGRAPH · SERIES 1 · NO. 008

Kisspeptin-10

A 10-residue C-terminal fragment of the KISS1-encoded kisspeptin family — the minimal receptor-binding pharmacophore engaging the KISS1 receptor (GPR54) and constituting the master upstream regulator of the hypothalamic-pituitary-gonadal axis.

CATALOG REFERENCE	FORM FACTOR	STRENGTH	DATE OF ISSUE
BM-LYO-008	Lyophilized vial	10 mg / vial	May 2026

Kisspeptin-10 is a 10-residue C-terminal fragment of the parent kisspeptin family of peptides encoded by the human KISS1 gene. The parent KISS1 gene product is a 145-residue prepropeptide proteolytically processed to yield kisspeptin-54 (the originally characterised secreted form, also called metastin), with further processing producing the shorter biologically active fragments kisspeptin-14, kisspeptin-13, and the most-studied kisspeptin-10. All four fragments share the conserved C-terminal decapeptide Tyr-Asn-Trp-Asn-Ser-Phe-Gly-Leu-Arg-Phe-NH_2, which constitutes the receptor-binding pharmacophore. Kisspeptin-10 engages the KISS1 receptor (KISS1R, also known as GPR54), a Class A G-protein-coupled receptor coupling principally to Gαq with downstream phospholipase C activation, IP_3 / DAG / Ca^{2+} signalling, and ERK / MAPK pathway engagement. The molecule is the master regulator of the hypothalamic-pituitary-gonadal (HPG) axis, with hypothalamic kisspeptin neurons driving gonadotropin-releasing hormone (GnRH) neuron pulsatile activity. ***This monograph summarises published cellular pharmacology and preclinical findings for laboratory research reference only.***

01 Compound Profile

COMMON DESIGNATION	Kisspeptin-10 · KP-10 · Metastin (10-54)
PRIMARY SEQUENCE (10 RESIDUES)	Tyr-Asn-Trp-Asn-Ser-Phe-Gly-Leu-Arg-Phe-NH_2 (YNWNSFGLRF-NH_2)
C-TERMINAL AMIDE	Essential for receptor binding; the Phe10-NH_2 is the key pharmacophore residue
CAS REGISTRY	374675-21-5
MOLECULAR FORMULA	$C_{63}H_{83}N_{17}O_{14}$
AVERAGE MOLECULAR MASS	1302.45 g · mol^{-1}
PRIMARY MOLECULAR TARGET	KISS1 receptor (KISS1R / GPR54) — Class A G-protein-coupled receptor, Gαq-coupled, expressed densely in GnRH neurons of the hypothalamic preoptic area and arcuate nucleus
FORM FACTOR	Lyophilized vial · 10 mg / vial
PHYSICAL FORM	White lyophilized solid
SOLUBILITY (LAB RECONSTITUTION)	Water-soluble; the molecule lacks rigid secondary structure in solution
STORAGE (RESEARCH HANDLING)	Lyophilized solid: −18 °C, desiccated, light-protected (Trp3 photo-oxidation susceptibility); reconstituted solution refrigerated 2–8 °C short-term; aliquoted long-term at −18 °C
ANALYTICAL SPECIFICATION	≥ 98 % purity by HPLC (BIOMOD Labs internal release specification)

02 Origin and Chemistry

The KISS1 gene was originally identified in 1996 by Lee, Welch and colleagues at the Pennsylvania State University College of Medicine as a metastasis-suppressor gene in melanoma (the name "kisspeptin" derives from this discovery context and from Hershey, Pennsylvania, where the laboratory was located). The 1996 paper characterised KISS1 expression in metastatic-suppressed melanoma cell lines and the gene's chromosomal localisation to 1q32. The orphan G-protein-coupled receptor GPR54 was subsequently identified as the kisspeptin receptor independently by multiple groups in 2001 (Ohtaki et al., Muir et al., Kotani et al.). The full clinical and physiological significance of the kisspeptin–GPR54 system emerged in 2003 when two independent groups (de Roux et al.; Seminara et al.) reported that loss-of-function mutations in GPR54 produce idiopathic hypogonadotropic hypogonadism in humans, establishing the kisspeptin system as the master upstream regulator of pubertal onset and reproductive HPG axis activity.

Chemically, kisspeptin-10 is the minimal C-terminal sequence retaining full receptor agonist activity. The C-terminal amide is essential — the free-acid analogue has dramatically reduced potency. The Trp3 residue is photo-oxidation susceptible. The molecule is rapidly cleaved by matrix metalloproteinases at the Gly7-Leu8 bond and other sites, contributing to a short plasma half-life of approximately 4 minutes in cell-free studies.

03 Molecular Target and Cellular Signalling

KISS1R / GPR54 is a Class A G-protein-coupled receptor that couples principally to Gαq, with downstream phospholipase C-β activation, hydrolysis of PIP_2 to IP_3 and DAG, IP_3-mediated calcium release from intracellular stores, and DAG-mediated PKC activation. Downstream ERK / MAPK pathway engagement is also documented. In hypothalamic GnRH neurons, KISS1R activation drives membrane depolarisation and increased GnRH neuronal firing, which in turn drives pulsatile GnRH release into the hypophyseal portal system and consequent pulsatile LH and FSH release from anterior pituitary gonadotropes. Kisspeptin neurons in the arcuate nucleus (so-called KNDy neurons co-expressing kisspeptin, neurokinin B, and dynorphin) generate the GnRH pulse that drives downstream gonadal steroidogenesis.

04 Preclinical Findings

SYSTEM	PREPARATION	REPORTED OBSERVATION	REF.
KISS1R activation	HEK293 cells transfected with KISS1R	Full agonism; Gαq coupling; IP_3 / Ca^{2+} release	1
GnRH neuron activation	Mouse hypothalamic slice electrophysiology	Membrane depolarisation; increased GnRH neuronal firing	2
Gonadotropin release	Rodent pituitary preparations	LH and FSH release secondary to GnRH stimulation	3
HPG axis regulation	GPR54 knockout mice	Hypogonadotropic hypogonadism; absent pubertal onset	4
Plasma stability	Cell-free plasma incubation	Short plasma half-life (~4 min) due to matrix metalloproteinase cleavage	5

05 Research Synthesis & Limitations

METHODOLOGICAL NOTES

Kisspeptin-10 is the most extensively studied member of the kisspeptin family in published preclinical research. The molecule's short plasma half-life is a significant experimental design consideration — bolus administration in cell-culture or in-vivo preparations produces transient receptor engagement rather than sustained pathway activation, and observed effects are commonly compared between bolus and continuous-infusion paradigms. Longer-acting kisspeptin analogues (kisspeptin-54, kisspeptin-112-121, MVT-602) have been developed to address this limitation. The Trp3 photo-oxidation susceptibility requires light protection during handling. The C-terminal amide is essential — care should be taken to confirm amide preservation in supplied material via mass spectrometry where appropriate.

06 Laboratory Handling, Reconstitution, and Storage

Lyophilized Kisspeptin-10 is supplied under research-use specifications at 10 mg / vial. Reconstitution in sterile water for injection or bacteriostatic water at neutral pH is standard practice. **The Trp3 residue is photo-oxidation susceptible** — light protection is recommended throughout. Lyophilized storage at −18 °C, desiccated, light-protected; reconstituted solutions held refrigerated 2–8 °C for short-term work; aliquoted long-term storage at −18 °C with minimised freeze–thaw. Working concentrations are determined by the investigator's experimental design.

07 References

1. Lee JH, Miele ME, Hicks DJ, Phillips KK, Trent JM, Weissman BE, Welch DR. KiSS-1, a novel human malignant melanoma metastasis-suppressor gene. *J Natl Cancer Inst.* 1996;88(23):1731–1737. PMID: 8944003
2. Ohtaki T, Shintani Y, Honda S, Matsumoto H, Hori A, Kanehashi K, Terao Y, Kumano S, Takatsu Y, Masuda Y, Ishibashi Y, Watanabe T, Asada M, Yamada T, Suenaga M, Kitada C, Usuki S, Kurokawa T, Onda H, Nishimura O, Fujino M. Metastasis suppressor gene KiSS-1 encodes peptide ligand of a G-protein-coupled receptor. *Nature.* 2001;411(6837):613–617. PMID: 11385580
3. Seminara SB, Messager S, Chatzidaki EE, Thresher RR, Acierno JS Jr, Shagoury JK, Bo-Abbas Y, Kuohung W, Schwinof KM, Hendrick AG, Zahn D, Dixon J, Kaiser UB, Slaugenhaupt SA, Gusella JF, O'Rahilly S, Carlton MB, Crowley WF Jr, Aparicio SA, Colledge WH. The GPR54 gene as a regulator of puberty. *N Engl J Med.* 2003;349(17):1614–1627. PMID: 14573733
4. Han SK, Gottsch ML, Lee KJ, Popa SM, Smith JT, Jakawich SK, Clifton DK, Steiner RA, Herbison AE. Activation of gonadotropin-releasing hormone neurons by kisspeptin as a neuroendocrine switch for the onset of puberty. *J Neurosci.* 2005;25(49):11349–11356. PMID: 16339030
5. Kotani M, Detheux M, Vandenbogaerde A, Communi D, Vanderwinden JM, Le Poul E, Brézillon S, Tyldesley R, Suarez-Huerta N, Vandeput F, Blanpain C, Schiffmann SN, Vassart G, Parmentier M. The metastasis suppressor gene KiSS-1 encodes kisspeptins, the natural ligands of the orphan G protein-coupled receptor GPR54. *J Biol Chem.* 2001;276(37):34631–34636. PMID: 11457843