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CJC-1295 (no DAC)

Modified GRF 1-29 — a 29-residue tetra-substituted analogue of growth hormone-releasing hormone, engineered for resistance to DPP-IV cleavage and Asn deamidation while retaining full agonism at the GHRH receptor in pituitary somatotroph preparations.

CAS REGISTRY	CATALOG REFERENCE	CLASS	DATE OF ISSUE
863288-34-0	BM-LYO-014	Synthetic peptide · 29 a.a.	May 2026

CJC-1295 without DAC — more accurately designated Modified GRF 1-29 or "Mod GRF" in the chemistry literature — is a 29-residue tetra-substituted analogue of growth hormone-releasing hormone (GHRH). It corresponds to the N-terminal 29 residues of human GHRH(1-44) with four targeted residue substitutions for chemical and pharmacological stabilisation: D-Ala at position 2 (blocking DPP-IV cleavage), Gln at position 8 (removing the deamidation-susceptible Asn), Ala at position 15 (modest helix stabilisation), and Leu at position 27 (removing the oxidation-susceptible Met). The C-terminus is amidated. The molecule is the chemistry scaffold onto which the DAC albumin-binding group was subsequently added to produce CJC-1295 with DAC (Monograph 016). Without DAC, the molecule retains GHRH-receptor pharmacology without albumin conjugation chemistry, behaving in preclinical pituitary preparations as a stabilised but short-acting GHRH analogue. ***This monograph summarises published preclinical findings for laboratory research reference only.***

01 Compound Profile

COMMON DESIGNATION	CJC-1295 (no DAC) · Modified GRF 1-29 · Mod GRF · tetrasubstituted GRF 1-29
PRIMARY SEQUENCE	Tyr-D-Ala-Asp-Ala-Ile-Phe-Thr-Gln-Ser-Tyr-Arg-Lys-Val-Leu-Ala-Gln-Leu-Ser-Ala-Arg-Lys-Leu-Leu-Gln-Asp-Ile-Leu-Ser-Arg-NH_2
MODIFICATIONS VS. NATIVE GHRH(1-29)	Ala2→D-Ala · Asn8→Gln · Gly15→Ala · Met27→Leu · C-terminal amide
CAS REGISTRY	863288-34-0
MOLECULAR FORMULA	$C_{152}H_{252}N_{44}O_{39}$
AVERAGE MOLECULAR MASS	3367.91 g · mol^{-1}
PRIMARY MOLECULAR TARGET	GHRH receptor (GHRHR), Class B GPCR — full agonist with binding affinity comparable to native GHRH in cell-line transfection systems[1]
PHYSICAL FORM	White lyophilised solid
SOLUBILITY (LAB RECONSTITUTION)	Soluble in sterile water and bacteriostatic water; reconstituted solutions report reasonable stability owing to the four protective substitutions[2]
STORAGE (RESEARCH HANDLING)	Lyophilised solid: −18 °C, desiccated; reconstituted solution refrigerated 2–8 °C short-term; aliquoted long-term at −18 °C with freeze–thaw minimised
ANALYTICAL SPECIFICATION	≥ 99 % purity by HPLC (BIOMOD Labs internal release specification)

02 Origin and Chemistry

The Modified GRF 1-29 scaffold was developed at ConjuChem Inc. in the early 2000s as the peptide backbone for the Drug Affinity Complex (DAC) albumin-binding technology programme. The four targeted residue substitutions address the principal chemical liabilities of native GHRH(1-29): the Tyr1-Ala2 bond is the major DPP-IV cleavage site (addressed by substituting D-Ala for the L-Ala at position 2); Asn8 undergoes spontaneous deamidation in aqueous solution (addressed by substituting Gln); Gly15 has been shown to contribute modestly to helical instability of the GHRH backbone (addressed by Ala substitution); and Met27 is susceptible to methionine oxidation in solution (addressed by Leu substitution). The C-terminal amide is retained from native GHRH and is required for receptor activity.[1]

The four substitutions together produce a peptide that retains full receptor pharmacology — receptor-binding affinity at GHRHR in cell-line transfection systems is comparable to native GHRH — while exhibiting substantially improved chemical stability in aqueous solution. Without the DAC albumin-binding modification, however, the molecule retains a relatively short duration of action in plasma (on the order of tens of minutes), characteristic of unconjugated peptides of this size. The "no DAC" form is therefore the appropriate research compound for studies designed to deliver pulsatile GHRH-like signalling with short signal duration; the "with DAC" form (Monograph 016) is the appropriate compound for sustained-signalling studies.[3]

03 Molecular Target and Cellular Signalling

The growth hormone-releasing hormone receptor (GHRHR) is a Class B G-protein-coupled receptor expressed on pituitary somatotrophs and in several extra-pituitary tissues. Receptor activation couples principally to Gαs, with downstream activation of adenylyl cyclase, elevation of cyclic AMP, activation of protein kinase A, and phosphorylation of CREB (cAMP response element binding protein). In somatotroph cell-culture preparations, GHRHR engagement produces both immediate exocytotic release of preformed growth hormone from secretory granules and longer-term effects on GH gene transcription.[4]

Jetté and colleagues, in a 2005 study published in *Endocrinology*, examined modified-GHRH(1-29) analogues including the Mod GRF 1-29 scaffold and their albumin-bioconjugated derivatives in rat pituitary preparations. The unconjugated form (the "no DAC" molecule) was shown to activate the GHRH receptor on rat anterior pituitary cells with potency comparable to native GHRH and to stimulate GH release from somatotrophs in culture. This work established the receptor-pharmacology equivalence of the modified scaffold to its native parent.[1] PRECLINICAL · RAT

04 Preclinical Findings

SYSTEM	PREPARATION	REPORTED OBSERVATION	REF.
Receptor activation	Rat anterior pituitary cells	Full GHRHR agonism; GH release from somatotrophs in culture	1
Cellular signalling	GHRHR-transfected cell lines	Gαs coupling → ↑ cAMP → PKA / CREB activation	4
Chemical stability	Aqueous solution stability studies	Improved stability vs. native GHRH(1-29) — DPP-IV, Asn deamidation, Met oxidation all addressed	1, 3
GH-releasing potency	GHRH-knockout mouse	Once-daily administration of CJC-1295 normalises growth in GHRH-knockout animals	5

05 Research Synthesis & Limitations

METHODOLOGICAL NOTES

The "no DAC" Mod GRF 1-29 scaffold has been less independently characterised than its DAC-bioconjugated derivative in the published animal literature, because the original ConjuChem development programme was focused on the long-acting DAC form. Most cited rat-pituitary and GHRHR receptor data come from the originating laboratory and its collaborators. Researchers designing studies with the no-DAC compound should be aware that observed effects will reflect short, GHRH-like pulses rather than sustained albumin-tethered signalling — and that the literature pool specific to the no-DAC form is smaller than for native GHRH or the DAC-bioconjugated form.

06 Laboratory Handling, Reconstitution, and Storage

Lyophilised Mod GRF 1-29 is supplied under research-use specifications and is conventionally held at −18 °C, desiccated. Reconstitution in sterile water for injection or bacteriostatic water is the standard practice in cited methodology. The four protective residue substitutions confer substantial chemical stability relative to native GHRH(1-29) — DPP-IV cleavage of the Tyr1-Ala2 bond is blocked, Asn8 deamidation is eliminated, and Met27 oxidation is no longer possible. Reconstituted solutions are held refrigerated 2–8 °C for short-term work; long-term aliquoted storage at −18 °C with minimised freeze–thaw is standard. Working concentrations are determined by the investigator's experimental design.

07 References

1. Jetté L, Léger R, Thibaudeau K, Benquet C, Robitaille M, Pellerin I, Paradis V, van Wyk P, Pham K, Bridon DP. Human growth hormone-releasing factor (hGRF)1-29-albumin bioconjugates activate the GRF receptor on the anterior pituitary in rats: identification of CJC-1295 as a long-lasting GRF analog. *Endocrinology.* 2005;146(7):3052–3058. PMID: 15817669. pubmed.ncbi.nlm.nih.gov/15817669
2. Frohman LA, Downs TR, Heimer EP, Felix AM. Dipeptidylpeptidase IV and trypsin-like enzymatic degradation of human growth hormone-releasing hormone in plasma. *J Clin Invest.* 1989;83(5):1533–1540. pubmed.ncbi.nlm.nih.gov/2495303
3. Ionescu M, Frohman LA. Pulsatile secretion of growth hormone (GH) persists during continuous stimulation by CJC-1295, a long-acting GH-releasing hormone analog. *J Clin Endocrinol Metab.* 2006;91(12):4792–4797. PMID: 17018654. pubmed.ncbi.nlm.nih.gov/17018654
4. Mayo KE, Miller TL, DeAlmeida V, Zheng J, Godfrey PA. The growth-hormone-releasing hormone receptor: signal transduction, gene expression, and physiological function in growth regulation. *Ann N Y Acad Sci.* 1996;805:184–203. pubmed.ncbi.nlm.nih.gov/8993402
5. Alba M, Fintini D, Sagazio A, Lawrence B, Castaigne JP, Frohman LA, Salvatori R. Once-daily administration of CJC-1295, a long-acting growth hormone-releasing hormone (GHRH) analog, normalizes growth in the GHRH knockout mouse. *Am J Physiol Endocrinol Metab.* 2006;291(6):E1290–E1294. pubmed.ncbi.nlm.nih.gov/16822960
6. Frohman LA, Kineman RD. Growth hormone-releasing hormone and its receptor: signaling and physiology. In: *Endocrinology: Adult and Pediatric.* Elsevier; 2016. doi.org/10.1016/B978-0-323-18907-1.00012-3

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