
Product Data Sheet

Animal models	ApoE-deficient mice
Preparation Method	Mice were fed a high cholesterol diet and received daily intraperitoneal injections of the HN analogue HNGF6A (0.4mg/kg/day) for 16 weeks. Vascular function, plaque size, and molecular markers in the aorta were analyzed at the end of the treatment period.
Dosage form	0.4mg/kg/day; i.p.; 16 weeks.
Applications	Chronic administration of HNGF6A preserved endothelium-dependent vasorelaxation in response to acetylcholine, significantly decreased atherosclerotic plaque size in the proximal aorta, and reduced nitrotyrosine immunoreactivity (a marker of oxidative stress) and apoptosis within the plaques. HNGF6A also preserved the expression of endothelial nitric oxide synthase (eNOS).

References:

- [1] Zhu X, Zhao Z, Zeng C, et al. HNGF6A Inhibits Oxidative Stress-Induced MC3T3-E1 Cell Apoptosis and Osteoblast Phenotype Inhibition by Targeting Circ_0001843/miR-214 Pathway. *Calcif Tissue Int.* 2020 May;106(5):518-532.
- [2] Oh YK, Bachar AR, Zacharias DG, et al. Humanin preserves endothelial function and prevents atherosclerotic plaque progression in hypercholesterolemic ApoE deficient mice. *Atherosclerosis.* 2011 Nov;219(1):65-73.

Background

HNGF6A is a synthetic polypeptide belonging to the Humanin analogue class^[1-2]. HNGF6A improves glucose metabolism and inhibits the production of reactive oxygen species (ROS). HNGF6A is used in research related to diabetes, atherosclerosis, and osteoarthritis^[3].

In vitro, meniscus cells were pretreated with HNGF6A (5–100ng/ml) for 48 hours and were then stimulated with TBHP (50µM) or IL-1β (10ng/ml). HNGF6A significantly restored the expression of extracellular matrix synthesis-related genes (COL1A1, COL3A1, ACAN) and inhibited the expression of degradation-related genes (MMP1, MMP3, ADAMTS5), while maintaining mitochondrial redox homeostasis, reducing ROS levels, and decreasing cell apoptosis^[4]. Murine osteoblastic cell line MC3T3-E1 cells were pretreated with HNGF6A (5–50ng/mL) for 3 days and were then exposed to H₂O₂ (400µM) for 4 hours. HNGF6A significantly inhibited apoptosis, downregulated the expression of pro-apoptotic proteins (Caspase-3, Cyto C, Bax), and upregulated the expression of the anti-apoptotic protein (Bcl-2). HNGF6A also promoted the expression

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of osteoblast phenotype-related proteins (ALP, BMP-2, OCN, RUNX2), enhanced alkaline phosphatase (ALP) activity, and increased mineralization nodule formation^[5].

In vivo, three-month-old Sprague-Dawley rats were treated with HNGF6A (0.07mg/kg/h) via continuous intravenous infusion for 2 hours. HNGF6A significantly increased the glucose infusion rate during a hyperglycemic clamp and caused a sustained increase in plasma insulin levels. C57BL/6N mice received a single intravenous injection of HNGF6A (2mg/kg) 10 minutes before a glucose tolerance test, which showed a trend toward increased first-phase insulin secretion^[6]. Apolipoprotein E (ApoE)-deficient mice fed a high-cholesterol diet were treated with HNGF6A (0.4mg/kg/day) via daily intraperitoneal injection for 16 weeks. HNGF6A significantly improved acetylcholine-induced endothelium-dependent vasodilation, reduced atherosclerotic plaque size in the proximal aorta, decreased nitrotyrosine immunoreactivity and apoptosis within the plaques, and preserved endothelial nitric oxide synthase expression^[7].

References:

- [1] Ding Y, Feng Y, Zhu W, et al. [Gly14]-Humanin Prevents Lipid Deposition and Endothelial Cell Apoptosis in a Lectin-like Oxidized Low-density Lipoprotein Receptor-1-Dependent Manner. *Lipids*. 2019 Nov;54(11-12):697-705.
- [2] Chin YP, Keni J, Wan J, et al. Pharmacokinetics and tissue distribution of humanin and its analogues in male rodents. *Endocrinology*. 2013 Oct;154(10):3739-44.
- [3] Peña Agudelo JA, Pidre ML, et al. Mitochondrial Peptide Humanin Facilitates Chemoresistance in Glioblastoma Cells. *Cancers (Basel)*. 2023 Aug 11;15(16):4061.
- [4] Liu R, Du X, Chen Y, et al. HNGF6A ameliorates oxidative stress-mediated mitochondrial dysfunction in degenerative meniscus. *Bone Joint Res*. 2025 Apr 7;14(4):318-330.
- [5] Zhu X, Zhao Z, Zeng C, et al. HNGF6A Inhibits Oxidative Stress-Induced MC3T3-E1 Cell Apoptosis and Osteoblast Phenotype Inhibition by Targeting Circ_0001843/miR-214 Pathway. *Calcif Tissue Int*. 2020 May;106(5):518-532.
- [6] Kuliawat R, Klein L, Gong Z, et al. Potent humanin analog increases glucose-stimulated insulin secretion through enhanced metabolism in the β cell. *FASEB J*. 2013 Dec;27(12):4890-8.
- [7] Oh YK, Bachar AR, Zacharias DG, et al. Humanin preserves endothelial function and prevents atherosclerotic plaque progression in hypercholesterolemic ApoE deficient mice. *Atherosclerosis*. 2011 Nov;219(1):65-73.

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