

DESCRIPTION

Source	<i>E. coli</i> -derived Asn299-Ser407, with an N-terminal Met Accession # O95390 Manufactured and tested under cGMP guidelines.
N-terminal Sequence Analysis	Met-Asn ₂₉₉ -Leu-Gly-Leu-Asp-(Cys)-Asp-Glu-His
Structure / Form	Disulfide-linked homodimer
Predicted Molecular Mass	12.6 kDa (monomer)

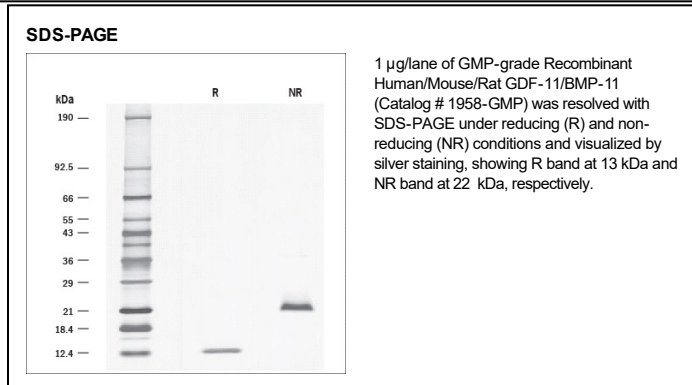
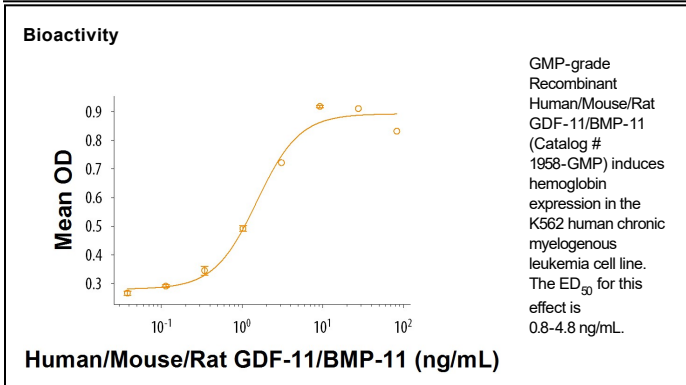
SPECIFICATIONS

SDS-PAGE	12 kDa, reducing conditions
Activity	Measured by its ability to induce hemoglobin expression in K562 human chronic myelogenous leukemia cells. Schwall, R.H. <i>et al.</i> (1991) <i>Method Enzymol.</i> 198 :340. The ED ₅₀ for this effect is 0.8-4.8 ng/mL.
Endotoxin Level	<0.01 EU per 1 µg of the protein by the LAL method.
Purity	>95%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.
Host Cell Protein	<0.5 ng per µg of protein when tested by ELISA.
Mycoplasma	Negative when tested in a ribosomal RNA hybridization assay.
Formulation	Lyophilized from a 0.2 µm filtered solution in Acetonitrile and TFA. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution	Reconstitute at 100 µg/mL in 4 mM HCl.
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"> • A minimum of 12 months when stored at ≤ -20 °C as supplied. Refer to lot specific COA for the Use by Date. • 1 month, 2 to 8 °C under sterile conditions after reconstitution. • 3 months, ≤ -20 °C under sterile conditions after reconstitution.

DATA



BACKGROUND

Growth Differentiation Factor 11 (GDF-11), also known as BMP-11, is a member of the TGF- β superfamily and is highly related to GDF-8. GDF-11 encodes a 407 amino acid (aa) prepropeptide which contains a signal sequence for secretion and an RXXR proteolytic processing site to yield a 109 aa residue carboxy-terminal mature protein (1). Mature GDF-11 contains the canonical 7-cysteine motif common to other TGF- β superfamily members; however, like the TGF- β s, Activins and GDF-8, GDF-11 also contains one extra pair of cysteine residues. At the amino acid sequence level, mature human, mouse, rat and chicken GDF-11 are 99-100% identical. GDF-11 and GDF-8 share 90% amino acid sequence identity within the mature protein. As detected by in situ hybridization, GDF-11 is expressed in diverse regions of the mouse embryo: tailbud, somitic precursors, limbs, mandibular and branchial arches, dorsal neural tube, odontoblasts, nasal epithelium, and particular regions of the brain (1, 2). Targeted deletion of GDF-11, in mice, results in a spectrum of abnormalities including palatal malformation, vertebral defects, elongated trunks with a reduced or absent tail, missing or malformed kidneys, and an increased number of neurons in the olfactory epithelium (2-5). GDF-11 signals through the Activin type II receptors and induces phosphorylation of Smad2 to mediate axial patterning (6). Systemic GDF-11 levels decline with age and administration of higher levels of GDF-11 can reverse age-related cardiac hypertrophy (7). In addition, systemic administration of recombinant GDF-11 protein restores genomic integrity and health of muscle stem cells, neurovasculature and enhances neurogenesis (8, 9). R&D Systems recombinant GDF-11 preparations have been shown to act similarly to GDF-8 in both the Xenopus animal cap and the K562 assays.

References:

1. Gamer, L.W. *et al.* (1999) *Dev. Biol.* **208**: 222.
2. Nakashima, M. *et al.* (1999) *Mech. Dev.* **80**:185.
3. Gad, J.M. and P.P.L. Tam (1999) *Curr. Biol.* **9**:R783.
4. McPherron, A.C. *et al.* (1999) *Nat. Genet.* **22**:260.
5. Esquela, A.F. and S.J. Lee (2003) *Dev. Biol.* **257**:356.
6. Oh, S.P. *et al.* (2002) *Genes & Dev.* **16**:274.
7. Loffredo, F.S. *et al.* (2013) *Cell.* **153**:828.
8. Katsimpardi, L. *et al.* (2014) *Science* (ahead of print).
9. Sinha, M. *et al.* (2014) *Science* (ahead of print).

MANUFACTURING SPECIFICATIONS

GMP Proteins

R&D Systems, a Bio-Techne Brand's GMP proteins are produced according to relevant sections of the following documents: WHO TRS, No. 822, 1992 Annex 1, Good Manufacturing Practices for Biological Products; USP Chapter 1043, Ancillary Materials for Cell, Gene and Tissue-Engineered Products and USP Chapter 92, Growth Factors and Cytokines Used in Cell Therapy Manufacturing.

R&D Systems' quality focus includes:

- Manufactured and tested under an ISO 9001:2015 and ISO 13485:2016 certified quality system
- Documented processes and QA control of documentation and process changes
- Personnel training programs
- Raw material testing and vendor qualification/monitoring
- Fully validated equipment, processes and test methods
- Equipment calibration schedules using a computerized calibration program
- Facility maintenance, safety programs and pest control
- Material review process for variances
- Monitoring of stability over product shelf-life

R&D Systems strives to provide our customers with the analytical characteristics of each product so that customers may determine whether our products are appropriate for their research. The Certificate of Analysis provided contains the following lot specific information:

- N-terminal amino acid analysis, SDS-PAGE analysis, and endotoxin level (as determined by LAL assay) performed on each bulk QC lot, not on individual bottlings of each QC lot
- Post-bottling lot-specific bioassay results (compliance with an established range) and results of microbial bioburden testing (using broth culture, Sabourand's dextrose and blood agar plates with results reported at 3 days and at 7 days)
- Host Cell Protein testing performed by ELISA
- Mycoplasma testing by ribosomal RNA hybridization assay

Additional testing and documentation requested by the customer can be arranged at an additional cost. Testing may include, but is not limited to, USP< 61> bioburden testing, positive identity testing, testing for adventitious agents and testing for residual host cell content.

Production records and facilities are available for examination by appropriate personnel on-site at R&D Systems in Minneapolis, Minnesota USA.

R&D Systems sells its GMP grade recombinant protein products for research use or further manufacturing use in *ex vivo* cell therapy applications. They are not for *in vivo* use or for use as therapeutic or other drugs, biologic products or devices. Please read the following End User Terms prior to using this product.

PRODUCT SPECIFIC NOTICES

END USER TERMS OF USE OF PRODUCT

The following terms are offered to you upon your acceptance of these End User Terms of Use of Product. By using this product, you indicate your acknowledgment and agreement to these End User Terms of Use of Product. If you do not agree to be bound by and comply with all of the provisions of these End User Terms of Use of Product, you should contact your supplier of the product and make arrangements to return the product.

We suggest you print and retain a copy of these End User Terms of Use of Product for your records.

The End User is aware that R&D Systems, Inc. sells its GMP products for research use only or further manufacturing and not for *in vivo* use, the production of therapeutics or other drugs or for biologic products or devices. The End User further agrees, as a condition of the sale of R&D Systems' GMP products that: a) the End User will not use this GMP Product in any procedure wherein the product may be directly or indirectly administered to humans, unless the End User has obtained, or prior to their use will have obtained, an Investigational New Drug (IND) exemption from the FDA and will use the product only in accordance with the protocols of such IND and of the Institutional Review Board overseeing the proposed research, or b) the End User will use the products outside of the United States in accordance with the protocols of research approved by the Institutional Review Board or authorized ethics committee and regulatory agencies to which the End User is subject to in their territory.

R&D Systems, Inc. has the right, at its sole discretion, to modify, add or remove any terms or conditions of these End User Terms of Use without notice or liability to you. Any changes to these End User Terms of Use are effective immediately following the printing of such changes on this product insert. The most recent version of these End User Terms of Use of Product may be found at: RnDSystems.com/Legal.

You agree to review these End User Terms of Use of Product to ensure any subsequent use by you of R&D Systems' GMP Products following changes to these End User Terms of Use of Product constitutes your acceptance of all such changes.

TERMS AND CONDITIONS

The following limitation applies to R&D Systems' warranty and liability for damages: All products are warranted to meet R&D Systems' published specifications when used under normal laboratory conditions.

R&D SYSTEMS DOES NOT MAKE ANY OTHER WARRANTY OR REPRESENTATION WHATSOEVER, WHETHER EXPRESS OR IMPLIED, WITH RESPECT TO ITS PRODUCTS. IN PARTICULAR, R&D SYSTEMS DOES NOT MAKE ANY WARRANTY OF SUITABILITY, NONINFRINGEMENT, MERCHANTABILITY OR FITNESS FOR ANY PARTICULAR PURPOSE.

NOTWITHSTANDING ANY OTHER PROVISIONS OF THESE TERMS AND/OR ANY OTHER AGREEMENT BETWEEN R&D SYSTEMS AND PURCHASER FOR THE PURCHASE OF THE PRODUCTS, R&D SYSTEMS' TOTAL LIABILITY TO PURCHASER ARISING FROM OR IN RELATION TO THESE TERMS, AN AGREEMENT BETWEEN THE PARTIES OR THE PRODUCTS, WHETHER ARISING IN CONTRACT, TORT OR OTHERWISE SHALL BE LIMITED TO THE TOTAL AMOUNT PAID BY PURCHASER TO R&D SYSTEMS FOR THE APPLICABLE PRODUCTS. IN NO EVENT WILL R&D SYSTEMS BE LIABLE FOR THE COST OF PROCUREMENT OF SUBSTITUTE GOODS.

Full details of R&D Systems' Terms and Conditions of Sale can be found online at: RnDSystems.com/Legal.