

**DESCRIPTION**

<b>Source</b>	<i>E. coli</i> -derived human IGF-I/IGF-1 protein	
	MFPAMPLSSLFVN	Human LR3 IGF-I/IGF-1 (Gly49-Ala118 (Glu51Arg)) Accession # P05019
	N-terminus	C-terminus
Produced using non-animal reagents in an animal-free laboratory. Manufactured and tested under cGMP guidelines.		
<b>N-terminal Sequence Analysis</b>	Met-Phe-Pro-Ala-Met-Pro-Leu-Ser-Ser-Leu	
<b>Predicted Molecular Mass</b>	9 kDa	

**SPECIFICATIONS**

<b>SDS-PAGE</b>	8 kDa, reducing conditions
<b>Activity</b>	Measured in a serum-free cell proliferation assay using MCF-7 human breast cancer cells. Karey, K.P. <i>et al.</i> (1988) Cancer Research 48:4083. The ED <sub>50</sub> for this effect is 0.3-1.5 ng/mL. IGFBP-3 does not inhibit its activity.
<b>Endotoxin Level</b>	<0.01 EU per 1 µg of the protein by the LAL method.
<b>Purity</b>	>95%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.
<b>Mass Spectrometry</b>	The result of the major peak from mass spectrometry analysis is 9111 Da, which corresponds to the calculated molecular mass of 9118 Da.
<b>Host Cell Protein</b>	<0.1 ng per µg of protein when tested by ELISA.
<b>Mycoplasma</b>	Negative when tested in a ribosomal RNA hybridization assay.
<b>Host Cell DNA</b>	<0.0015 ng per µg of protein when tested by PCR.
<b>Formulation</b>	Lyophilized from a 0.2 µm filtered solution in Acetic Acid. See Certificate of Analysis for details.

**PREPARATION AND STORAGE**

<b>Reconstitution</b>	Reconstitute at 100-200 µg/mL in sterile 100 mM Acetic Acid
<b>Shipping</b>	The product is shipped with polar packs. Upon receipt, store it immediately at the temperature recommended below.
<b>Stability &amp; Storage</b>	Use a manual defrost freezer and avoid repeated freeze-thaw cycles. <ul style="list-style-type: none"> <li>• A minimum of 12 months when stored at ≤ -20 °C as supplied. Refer to lot specific COA for the Use by Date.</li> <li>• 1 month, 2 to 8 °C under sterile conditions after reconstitution.</li> <li>• 3 months, ≤ -20 °C under sterile conditions after reconstitution.</li> </ul>

**DATA**

<p><b>Bioactivity</b></p> <p><b>Recombinant Human LR3 IGF-I/IGF-1 GMP Protein Bioactivity</b> GMP-grade Recombinant Human LR3 IGF-I/IGF-1 (Catalog # 8335D-GMP) stimulates cell proliferation in a serum-free assay using the MCF-7 human breast cancer cell line. The ED<sub>50</sub> for this effect is 0.3-1.5 ng/mL.</p>	<p><b>SDS-PAGE</b></p> <p><b>Recombinant Human LR3 IGF-I/IGF-1 GMP Protein SDS-PAGE</b> 2 µg/lane of GMP-grade Recombinant Human LR3 IGF-I/IGF-1 (Catalog # 8335D-GMP) was resolved with SDS-PAGE under reducing (R) and non-reducing (NR) conditions and visualized by Coomassie® Blue staining, showing R and NR bands at 8 kDa.</p>
--	--

**BACKGROUND**

Insulin-like Growth Factor 1 (IGF-1 or IGF-I), also known as Somatomedin C, is the dominant effector of Growth Hormone (GH) and is structurally homologous to Proinsulin. Human IGF-1 is synthesized as two precursor isoforms with N- and alternative C-terminal propeptides (1). These isoforms are differentially expressed by various tissues (1). The 7.6 kDa mature IGF-1 is identical between isoforms and is generated by proteolytic removal of the N- and C-terminal regions. Mature human IGF-1 shares 94% and 96% amino acid (aa) sequence identity with the mouse and rat orthologs, respectively (2). GH stimulates the production of IGF-1 in most tissues (3). Hepatocytes produce circulating IGF-1, while local IGF-1 is produced by many other tissues in which it has paracrine effects (1). IGF-1 induces the proliferation, migration, and differentiation of a wide variety of cell types during development and postnatally (4, 5). IGF-1 regulates glucose, fatty acid, and protein metabolism, steroid hormone activity, and cartilage and bone metabolism (6-11). It plays an important role in muscle regeneration and tumor progression (1, 12, 13). IGF-1 binds IGF1R, IGF2R, and the Insulin Receptor, although its effects are mediated primarily by IGF1R (14). IGF-1 also binds with strong affinity to IGF binding proteins (IGFBPs), which regulate the availability and biological activities of IGF-1 (15, 16).

Long R3 IGF-1 (LR3 IGF-1) is a 9.2 kDa synthetic analog of IGF-1 that is generated by modifying the aa sequence for mature human IGF-1. These modifications include the substitution of an Arg for Glu at position 3 of the mature IGF-1 sequence and the addition of a thirteen aa N-terminal extension, which is derived from methionyl porcine Growth Hormone (17). These aa changes generate a protein that is still capable of binding to IGF-1 and Insulin receptors, but shows considerably lower affinity binding to IGFBPs compared to wild-type IGF-1 (17, 18). As a result, LR3 IGF-1 has an increased half-life and displays increased biological potency compared to IGF-1 (17-22).

**References:**

1. Philippou, A. *et al.* (2007) *In Vivo* **21**:45.
2. Sandberg-Nordqvist, A.C. *et al.* (1992) *Brain Res. Mol. Brain Res.* **12**:275.
3. Berryman, D.E. *et al.* (2013) *Nat. Rev. Endocrinol.* **9**:346.
4. Guvakova, M.A. (2007) *Int. J. Biochem. Cell Biol.* **39**:890.
5. Sadagurski, M. and M.F. White (2013) *Endocrinol. Metab. Clin. North Am.* **42**:127.
6. Clemmons, D.R. (2006) *Curr. Opin. Pharmacol.* **6**:620.
7. Bluher, S. *et al.* (2005) *Best Pract. Res. Clin. Endocrinol. Metab.* **19**:577.
8. Garcia-Segura, L.M. *et al.* (2006) *Neuroendocrinology* **84**:275.
9. Malemud, C.J. (2007) *Clin. Chim. Acta* **375**:10.
10. Ling, P.R. *et al.* (1995) *Am. J. Clin. Nutr.* **61**:116.
11. Sheng, M.H. *et al.* (2014) *J. Bone Metab.* **21**:41.
12. Samani, A.A. *et al.* (2007) *Endocrine Rev.* **28**:20.
13. Gallagher, E.J. *et al.* (2010) *Endocr. Pract.* **16**:864.
14. LeRoith, D. and S. Yakar (2007) *Nat. Clin. Pract. Endocrinol. Metab.* **3**:302.
15. Denley, A. *et al.* (2005) *Cytokine Growth Factor Rev.* **16**:421.
16. Duan, C. and Q. Xu (2005) *Gen. Comp. Endocrinol.* **142**:44.
17. Francis, G.L. *et al.* (1992) *J. Mol. Endocrinol.* **8**:213.
18. Voorhamme, D. and C.A. Yandell (2006) *Mol. Biotechnol.* **34**:201.
19. Tomas, F.M. *et al.* (1993) *Biochem. J.* **291**:781.
20. Tomas, F.M. *et al.* (1996) *J. Endocrinol.* **150**:77.
21. Tomas, F.M. *et al.* (1997) *J. Endocrinol.* **155**:377.
22. von der Thüsen, J.H. *et al.* (2011) *Am. J. Pathol.* **178**:924.

## 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 testing according to USP
- 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.

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 GMP grade products for preclinical or clinical *ex vivo* cell therapy applications. They are not for *in vivo* use. Please read the following End User Terms prior to using this product.

### Animal-Free Manufacturing Conditions

Our dedicated controlled-access animal-free laboratories ensure that at no point in production are the products exposed to potential contamination by animal components or byproducts. Every stage of manufacturing is conducted in compliance with R&D Systems' stringent Standard Operating Procedures (SOPs). Production and purification procedures use equipment and media that are confirmed animal-free.

### Production

- All molecular biology procedures use animal-free media and dedicated labware.
- Dedicated fermentors are utilized in committed animal-free areas.

### Purification

- Protein purification columns are animal-free.
- Bulk proteins are filtered using animal-free filters.
- Purified proteins are stored in animal-free containers in a dedicated cold storage room.

### Quality Assurance

- Low Endotoxin Level.
- No impairment of biological activity.
- High quality product obtained under stringent conditions.

[Please read our complete Animal-Free Statement.](#)

**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 GMP products for preclinical or clinical *ex vivo* use and not for *in vivo* use. 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](http://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](http://RnDSystems.com/Legal).