# **Product** Data Sheet

D-(Leu-Thr-Leu-Arg-Lys-Glu-Pro-Ala-

Ser-Glu-Ile-Ala-Gln-Ser-Ile-Leu-Glu-Ala-

Tyr-Ser-Gln-Asn-Gly-Trp-Ala-Asn-Arg-Arg-Ser-Gly-Gly-Lys-Arg-Pro-Pro-Pro-

Arg-Arg-Arg-Gln-Arg-Arg-Lys-Lys-Arg-

## FOXO4-DRI

Cat. No.: HY-P4157
CAS No.: 2460055-10-9

Molecular Formula:  $C_{228}H_{388}N_{86}O_{64}$ 

Molecular Weight: 5358.06

Sequence: D-(Leu-Thr-Leu-Arg-Lys-Glu-Pro-Ala-Ser-Glu-Ile-Ala-Gln-Ser-Ile-Leu-Glu-Ala-Tyr-Ser-G

ln-Asn-Gly-Trp-Ala-Asn-Arg-Arg-Ser-Gly-Gly-Lys-Arg-Pro-Pro-Pro-Arg-Arg-Arg-Gln-Arg-

Arg-Lys-Lys-Arg-Gly)

Sequence Shortening: D-(LTLRKEPASEIAQSILEAYSQNGWANRRSGGKRPPPRRRQRRKKRG)

Target: MDM-2/p53; Apoptosis

Pathway: Apoptosis

Storage: Sealed storage, away from moisture

Powder -80°C 2 years -20°C 1 year

\* In solvent: -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)

## **SOLVENT & SOLUBILITY**

In Vitro

H<sub>2</sub>O: 100 mg/mL (18.66 mM; Need ultrasonic) DMSO: 50 mg/mL (9.33 mM; Need ultrasonic)

| Preparing<br>Stock Solutions | Solvent Mass<br>Concentration | 1 mg      | 5 mg      | 10 mg     |
|------------------------------|-------------------------------|-----------|-----------|-----------|
|                              | 1 mM                          | 0.1866 mL | 0.9332 mL | 1.8663 mL |
|                              | 5 mM                          | 0.0373 mL | 0.1866 mL | 0.3733 mL |
|                              | 10 mM                         | 0.0187 mL | 0.0933 mL | 0.1866 mL |

Please refer to the solubility information to select the appropriate solvent.

# **BIOLOGICAL ACTIVITY**

**Description** FOXO4-DRI is a cell-permeable peptide antagonist that blocks the interaction of FOXO4 and p53. FOXO4-DRI is a senolytic

peptide that induces apoptosis of senescent  $\operatorname{cells}^{[1]}$ .

In Vitro FOXO4-DRI (25 mM; 3 days) causes nuclear exclusion of active p53 and induces apoptosis in senescent TM3 Leydig cells<sup>[1]</sup>.

FOXO4-DRI (25  $\mu$ M; 5 days) significantly reduces the senescence level in PDL9 cells<sup>[2]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay<sup>[1]</sup>

Cell Line: Senescent Leydig cells

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| Concentration:                       | 25 mM  |  |  |  |
|--------------------------------------|--|--|--|--|
| Incubation Time:                     | 3 days   |  |  |  |
| Result:                              | Reduced the viability of senescent as compared to normal TM3 Leydig cells.                     |  |  |  |
| Apoptosis Analysis <sup>[1]</sup>    |  |  |  |  |
| Cell Line:                           | Senescent Leydig cells   |  |  |  |
| Concentration:                       | 25 mM  |  |  |  |
| Incubation Time:                     | 3 days   |  |  |  |
| Result:                              | The apoptosis rate increased from 10% to 27%.  |  |  |  |
| Western Blot Analysis <sup>[2]</sup> |  |  |  |  |
| Cell Line:                           | PDL9 cells   |  |  |  |
| Concentration:                       | 25 μΜ  |  |  |  |
| Incubation Time:                     | 5 days   |  |  |  |
| Result:                              | Decreased the protein levels of representative senescent markers, including p16, p21, and p53. |  |  |  |
| RT-PCR <sup>[2]</sup>                |  |  |  |  |
| Cell Line:                           | PDL9 cells   |  |  |  |
| Concentration:                       | 25 μΜ  |  |  |  |
| Incubation Time:                     | 5 days   |  |  |  |
| Result:                              | Enhanced SOX9 expression, and reduced MMP12 and MMP13 expression.                              |  |  |  |

### In Vivo

FOXO4-DRI (5 mg/kg; i.p.; every other day for three administrations) alleviates testosterone secretion insufficiency and improves the testicular microenvironment in naturally aged  $mice^{[1]}$ .

 $\label{eq:mce} \mbox{MCE has not independently confirmed the accuracy of these methods. They are for reference only.}$ 

| Animal Model:   | Naturally aged male C57BL/6 mice (20-24 months old) <sup>[1]</sup>   |  |  |
|-----------------|--|--|--|
| Dosage:         | 5 mg/kg  |  |  |
| Administration: | Intraperitoneal injection, every other day for three administrations   |  |  |
| Result:         | Increased serum testosterone levels. Increased levels of both 3β-HSD and CYP11A1.  Decreased interstitial SA-β-gal activity and lowered levels of senescence-associated proteins p53, p21, and p16. Decreased the levels of IL-1β, IL-6 and TGF-β. |  |  |

### **REFERENCES**

[1]. Zhang C, et al. FOXO4-DRI alleviates age-related testosterone secretion insufficiency by targeting senescent Leydig cells in aged mice. Aging (Albany NY). 2020 Jan 20;12(2):1272-1284.

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| 2]. Huang Y, et al. Senolytic Peptide FOXO4-DRI Selectively Removes Senescent Cells From in vitro Expanded Human Chondrocytes. Front Bioeng Biotechnol. 2021 Apr 9;9:677576. |                            |                              |                                    |          |  |  |  |
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|  | Caution: Product has not h | peen fully validated for med | ical applications. For research us | se only. |  |  |  |
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