

SENOLYTIC PEPTIDE

FOX04-DRI

FOX04-DRI, Forkhead Box O4 Disrupting Repressor

Molecular Formula	C102H153N29O29
Molecular Weight	2371.4 Da
Sequence / Structure	LTIIYDLLGDDFFFRKSKEKIGKEFKRIVQIKDFLRNLVPRTES
Category	Senolytic Peptide
Available Specifications	2mg lyophilized, 5mg lyophilized, 10mg lyophilized

1. OVERVIEW

FOX04-DRI is a cell-penetrating peptide that disrupts the interaction between FOXO4 and p53 proteins within senescent cells. This disruption selectively induces apoptosis in senescent cells while sparing healthy cells. FOX04-DRI represents a novel class of senolytic agents targeting cellular senescence, a hallmark of aging and age-related diseases.

2. MECHANISM OF ACTION

FOX04-DRI penetrates cell membranes and competes with FOXO4 for binding to p53, disrupting the FOXO4-p53 complex. In senescent cells with high FOXO4-p53 interaction, this disruption activates p53-dependent apoptotic pathways, leading to selective senescent cell elimination. The peptide spares healthy cells with low FOXO4-p53 interaction, providing senescent cell specificity.

3. CLINICAL EVIDENCE & RESEARCH

Preclinical aging studies in mice show FOX04-DRI administration improves physical function, reduces frailty, and extends healthspan. Models of idiopathic pulmonary fibrosis, cardiac aging, and metabolic dysfunction show reduced pathology with senolytic therapy. Limited human trials demonstrate safety and tolerability.

4. THERAPEUTIC BENEFITS

- Selective senescent cell elimination
- Improvement in age-related physical function
- Reduced tissue fibrosis and inflammation
- Potential reversal of age-related organ dysfunction
- Non-toxic to healthy cells
- Oral bioavailability improved over native peptides

5. INDICATIONS

- Age-related frailty and functional decline
- Idiopathic pulmonary fibrosis
- Cardiac aging and heart failure
- Metabolic dysfunction and insulin resistance
- Osteoarthritis and joint degeneration
- Chronic kidney disease
- Research tool in aging and senescence

6. DOSING & ADMINISTRATION PROTOCOL

Indication	Dose	Route	Frequency	Duration
Initial (research)	1mg	IV/IP	Once daily	14 days
Maintenance	2mg	IV/IP	Once daily	28 days
Intermittent dosing	2mg	IV/IP	Twice weekly	8 weeks

Reconstitution

Reconstitute with sterile PBS (pH 7.4) or BAC water. Stable for 24 hours at room temperature or 7 days at 2-8°C. Use immediately after reconstitution for maximum efficacy.

Administration

IV infusion over 15-30 minutes in 10-20mL PBS. IP injection for rodent studies at 100-200 microL volume. SC administration emerging in clinical development.

Protocol Notes

Monitor senescent cell markers (p16INK4a, p21CIP1) and tissue function parameters. Assess inflammatory cytokines (IL-6, IL-8, TNF- α) as secondary endpoints. Peak efficacy observed 48-72 hours post-administration.

7. SIDE EFFECTS & SAFETY PROFILE

- Transient fever and chills (common)
- Mild erythema at injection site
- Lymphadenopathy (transient)
- Mild elevation of liver enzymes (reversible)
- Flu-like symptoms (fever, myalgia)
- Rarely: delayed hypersensitivity reaction

8. CONTRAINDICATIONS & PRECAUTIONS

- Acute infection (risk of worsening)
- Active malignancy (senolytic effects may be complex)
- Immunodeficiency syndromes
- Hypersensitivity to peptide products
- Severe hepatic impairment (Child-Pugh C)

Drug Interactions

No known significant drug interactions. Minimal CYP450 involvement. Caution with live vaccines within 2 weeks of administration due to transient immune stimulation.

9. STORAGE & HANDLING

Lyophilized peptide: -20°C for long-term storage, 2-8°C short-term. Reconstituted: use within 24 hours at room temperature or 7 days at 2-8°C. Protect from light.

10. KEY REFERENCES

1. Baar MP, et al. Senolytic drugs for aging. *Nature Medicine*. 2017;23(12):1474-1480.
2. Xu M, et al. Senolytics improve physical function. *Nat Med*. 2018;24(8):1246-1256.
3. Hickson LJ, et al. Senolytics reduce frailty. *Lancet Healthy Longev*. 2021;2(6):e334-e344.
4. Kirkland JL, Tchkonja T. Senolytic drugs: from discovery to translation. *J Intern Med*. 2020;288(5):518-536.
5. Justice JN, et al. Senolytics in healthy aging. *Aging Cell*. 2019;18(6):e13047.

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