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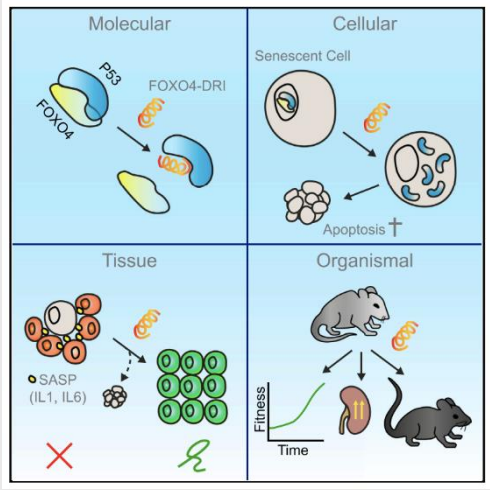
FOX04-DRI

Molecular Formula: C228H388N86O64

Molecular Weight: 5358.05 g/moil | Sequence: H-D-Leu-D-Thr-D-Leu-D-Arg-D-Lys-D-Glu-D-Pro-D-Ala-D-Ser-D-Glu-D-Ile-D-Ala-D-Gln-D-Ser-D-Ile-D-Leu-D-Glu-D-Ala-D-Tyr-D-Ser-D-Gln-D-Asn-D-Gly-D-Trp-D-Ala-D-Asn-D-Arg-D-Arg-D-Ser-D-Gly-D-Gly-D-Lys-D-Arg-D-Pro-D-Pro-D-Pro-D-Arg-D-Arg-D-Arg-D-Gln-D-Arg-D-Arg-D-Lys-D-Lys-D-Arg-D-Gly-OH

DESCRIPTION:

FOXO4-DRI is a peptide antagonist designed to perturb the interaction of FOXO4 and p53. Disrupting the p53-FOXO4 interaction causes p53 to be excluded from the nucleus and directed to mitochondria for induction of apoptosis in senescent cells, ultimately eliminating senescent fibroblasts through triggering apoptosis. It's found to decrease our bio-ages (biological age, what age you are in terms of health), and as a result to increase and restore the inner stability of our tissues. Buck Institute for Research on Aging has obtained a patent for its usage in cancerous and senescent cells in an experiment titled 'Targeting senescent and cancer cells for selective killing by interference with foxo4'.



This diagram shows FOXO4 being touched by FOXO4-DRI to avoid interacting with the p53 gene. It, as a result, initiates apoptosis in senescent cells. Over some time, the mice in this diagram became healthier because of the drop in senescent cells.

Researchers identify FOXO4 as a pivot in senescent cell viability. They designed a FOXO4 peptide that perturbs the FOXO4 interaction with p53.

In senescent cells, this selectively causes p53 nuclear exclusion and cell-intrinsic apoptosis. Under conditions where it was well tolerated in vivo, this FOXO4 peptide neutralized doxorubicin-induced chemotoxicity. Moreover, it restored fitness, fur density, and renal function in both fast aging XpdTTD/TTD and naturally aged mice. Thus, therapeutic targeting of senescent cells is feasible under conditions where loss of health has already occurred, and in doing so tissue homeostasis can effectively be restored.

PROTOCOL:

Content & Potency: Provided as a 10mg lyophilized vial

Vial reconstitution: 1ml sterile water for injection

Suggested dosage: Inject 100-400mcg/kg intravenously every other day 3 doses over 5 days

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CLINICAL RESEARCH:

Senolytic Peptide FOXO4-DRI Selectively Removes Senescent Cells From in vitro Expanded Human Chondrocytes

Autologous chondrocyte implantation (ACI) is a procedure used to treat articular cartilage injuries and prevent the onset of post-traumatic osteoarthritis. In vitro expansion of chondrocytes, a necessary step in ACI, results in the generation of senescent cells that adversely affect the quality and quantity of newly formed cartilage. Recently, a senolytic peptide, fork head box O transcription factor 4-D-Retro-Inverso (FOXO4-DRI), was reported to selectively kill the senescent fibroblasts. In this study, we hypothesized that FOXO4-DRI treatment could remove the senescent cells in the expanded chondrocytes, thus enhancing their potential in generating high-quality cartilage. To simulate the in vitro expansion for ACI, chondrocytes isolated from healthy donors were expanded to population doubling level (PDL) 9, representing chondrocytes ready for implantation. Cells at PDL3 were also used to serve as the minimally expanded control. Results showed that the treatment of FOXO4-DRI removed more than half of the cells in PDL9 but did not significantly affect the cell number of PDL3 chondrocytes. Compared to the untreated control, the senescence level in FOXO4-DRI treated PDL9 chondrocytes was significantly reduced. Based on the result from standard pellet culture, FOXO4-DRI pre-treatment did not enhance the chondrogenic potential of PDL9 chondrocytes. However, the cartilage tissue generated from FOXO4-DRI pretreated PDL9 cells displayed lower expression of senescence-relevant secretory factors than that from the untreated control group. Taken together, FOXO4-DRI is able to remove the senescent cells in PDL9 chondrocytes, but its utility in promoting cartilage formation from the in vitro expanded chondrocytes needs further investigation.

Huang, Y., He, Y., Makarcyzk, M. J., & Lin, H. (2021). Senolytic Peptide FOXO4-DRI Selectively Removes Senescent Cells From in vitro Expanded Human Chondrocytes. Frontiers in bioengineering and biotechnology, 9, 677576. https://doi.org/10.3389/fbioe.2021.677576

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