Thymosin beta-4

Background

Thymosin beta-4 is a small peptide that is a water-soluble G-actin–sequestering protein associated with anti-inflammatory, antioxidant, and wound healing properties. According to Sosne & Kleinman (2015), the multifunctional protein supports cell migration, stem cell recruitment and differentiation, and the expression of multiple regulatory genes such as antioxidative enzymes (as cited in Goldstein et al., 2012). [6,7] The primary method of biological action is through the promotion of angiogenesis. [1] Additionally, this peptide may be on the forefront of new perspectives in anti-aging science, e.g., adaptable molecules capable of reactivating the embryonic development of target organs, e.g., regenerative ability that is more universal and freer of environmental and genetic effects. [2]

Research

Xing et al. (2021) states that Thymosin β4 (Tβ4) is an adaptable peptide that serves important functions in multiple physiological processes, primarily promoting angiogenesis (the formation of new blood vessels) and reducing inflammation. [1] The authors sought to build on existing frameworks and illuminate progress on additional applications of Tβ4. [1] Some additional positive findings associated with the natural endogenous repair factor are, a protective effect on the heart in cases of myocardial infarction, amelioration of corneal injury and dry eye syndrome, accelerated skin wound healing, and proliferation of hair growth. [1] Maar et al. (2021) believe Tβ4 and other special molecules that remain undiscovered in the body may hold important clues to anti-aging strategies. [2] The researchers offer a fresh perspective on anti-aging science, e.g., instead of preventing age-related processes (cellular decay, tissue damage, widespread inflammation, mitochondrial mutations, breakdown of protein networks, etc.), rather transmit the adult organ back towards its embryonic development. [2] In other words, adaptable peptides like Tβ4 may serve a contributory role in reactivating the embryonic development of target organs, e.g., regenerative ability that is more universal and freer of environmental and genetic effects. [2]

Su et al. (2022) examined the role of Thymosin β4 (Tβ4) on endothelial function, e.g., cells that are pivotal in multiple functions in cardiovascular homeostasis, namely modulation of vascular tone. [3] Applying diabetic human induced pluripotent stem cells derived endothelial cells (dia-hiPSC-ECs) in a mouse model (600 ng/mL Tb4) of type 2 diabetes mellitus (T2DM) in vivo, the researchers found evidence of increased human induced pluripotent stem cells capability, and, by extension, decrease in senescence and enhancement of angiogenesis in diabetes. [3] Bock-Marquette et al. (2023) employ a similar theoretical framework as Maar et al. (2021) [2] in that anti-aging strategy is better suited fusing knowledge of aging and embryonic development targeting the individual organ level. [4] Utilizing the heart as a model system to examine developmental expression of TB4 in mouse embryos, the researchers found evidence that intravenous injections of TB4 in the adult heart supported reactivation of the embryonic program as evidenced by proliferation of cardiac vessels and a gene expression signature representative of an embryonic heart. [4] Finally, Zhang et al. (2020) suggest Thymosin β4 (Tβ4) may have additional treatment

applications, e.g., traumatic and neurological brain injuries. [5] The authors state that Tβ4 regulates neurogenesis and tissue growth during the development of the central nervous system (CNS). [5] Their review finds support for the function of Tβ4 as treatment potential in neurodegenerative diseases through angiogenesis and modulation of brain inflammatory processes, even possibly through a role in stem/progenitor cell differentiation. [5]

Conclusion

Thymosin-β4 (Tβ4) is a forty-three amino acid peptide considered to be the main intracellular G-actin sequestering peptide. Among its prominent roles in multiple biological activities, promoting angiogenesis (the formation of new blood vessels) and reducing inflammation are widely known. [1] Furthermore, Tβ4 shows promise to reactivate the embryonic program in organ development, initiating a new wave of anti-aging science; instead of preventing age-related processes, refreshing the target organ to its original developmental patterns. [2]

References

[1] Xing Y, Ye Y, Zuo H, Li Y. Progress on the Function and Application of Thymosin β4. Front Endocrinol (Lausanne). 2021 Dec 21;12:767785. doi: 10.3389/fendo.2021.767785. PMID: 34992578; PMCID: PMC8724243.

[2] Maar K, Hetenyi R, Maar S, Faskerti G, Hanna D, Lippai B, Takatsy A, Bock-Marquette I. Utilizing Developmentally Essential Secreted Peptides Such as Thymosin Beta-4 to Remind the Adult Organs of Their Embryonic State-New Directions in Anti-Aging Regenerative Therapies. Cells. 2021 May 28;10(6):1343. doi: 10.3390/cells10061343. PMID: 34071596; PMCID: PMC8228050.

[3] Su, L., Kong, X., Loo, S. *et al.* Thymosin beta-4 improves endothelial function and reparative potency of diabetic endothelial cells differentiated from patient induced pluripotent stem cells. *Stem Cell Res Ther* **13**, 13 (2022). https://doi.org/10.1186/s13287-021-02687-x

[4] Ildiko Bock-Marquette, Klaudia Maar, Szabolcs Maar, Balint Lippai, Gabor Faskerti, Ferenc Gallyas Jr, Eric N. Olson, Deepak Srivastava, Thymosin beta-4 denotes new directions towards developing prosperous anti-aging regenerative therapies, International Immunopharmacology, Volume 116, 2023, 109741, ISSN 1567-5769, https://doi.org/10.1016/j.intimp.2023.109741.

[5] Zhang G, Murthy KD, Binti Pare R, Qian Y. Protective effect of Tβ4 on central nervous system tissues and its developmental prospects. European Journal of Inflammation. 2020;18. doi:10.1177/2058739220934559

[6] Gabriel Sosne, Hynda K. Kleinman; Primary Mechanisms of Thymosin β4 Repair Activity in Dry Eye Disorders and Other Tissue Injuries. *Invest. Ophthalmol. Vis. Sci.* 2015;56(9):5110-5117. https://doi.org/10.1167/iovs.15-16890.

[7] Goldstein AL, Hannappel E, Sosne G, et al. Thymosin beta 4: a multi-functional regenerative peptide. *Expert Opin Biol*. 2012; 12: 37–51.