

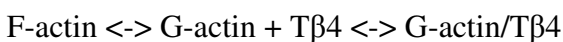
Name	Thymosin β4 Acetate
Cat #	PP-1780
Size	1 g, 10 g, 100, g and bulk custom packages
CAS#	77591-33-4
Mol. Mass	4963.49
Formula	C ₂₁₂ H ₃₅₀ N ₅₆ O ₇₈ S
Sequence	Ac-Ser-Asp-Lys-Pro-Asp-Met-Ala-Glu-Ile-Glu-Lys-Phe-Asp-Lys-Ser-Lys-Leu-Lys-Lys-Thr-Glu-Thr-Gln-Glu-Lys-Asn-Pro-Leu-Pro-Ser-Lys-Glu-Thr-Ile-Glu-Gln-Glu-Lys-Gln-Ala-Gly-Glu-Ser-OH
Purity	>95%

Thymosin β₄, is a member of a highly conserved family of actin monomer-sequestering proteins. β-thymosins are the primary regulators of unpolymerized actin, and are essential for maintaining the small cytoplasmic pool of free G-actin monomers required for rapid filament elongation and allowing for the flux of monomers between the thymosin-bound pool and F-actin.

Thymosin is an actin-binding protein in cells.

The predominant form of thymosin, thymosin β₄, is a member of a highly conserved family of actin monomer-sequestering proteins. β-thymosins are the primary regulators of unpolymerized actin, and are essential for maintaining the small cytoplasmic pool of free G-actin monomers required for rapid filament elongation and allowing for the flux of monomers between the thymosin-bound pool and F-actin (Dedova et al., 2006).

Thymosin β₄ sequesters actin, holding it in a form that is unable to polymerize. Due to its profusion in the cytosol and its ability to bind ATP G-actin but not F-actin, thymosin β₄ is regarded as the principal actin-sequestering protein. Tβ₄ binds ATP G- monomeric actin in a 1:1 complex where G-actin cannot polymerize. Thymosin β₄ (Tβ₄) functions like a buffer for monomeric actin as represented in the following reaction (Lodish et al., 2000):



Increase in cytosolic concentrations of thymosin β₄ increases the concentration of sequestered actin subunits and correspondingly decreases F-actin due to actin filaments being in equilibrium with actin monomers (Lodish et al., 2000).

Furthermore, the inhibitory thymosin which sequesters the actin competes for monomers with profilin.

Actin monomers preferentially bind to either ATP or ADP and both forms of G-actin are capable of polymerization. The affinities of ATP-G-actin and ADP-G-actin monomers for thymosin and profilin vary significantly. Both profilin and thymosin β₄ bind ATP monomers with higher affinity than ADP monomers; however, binding by thymosin is preferred over profilin-binding. This affinity for ATP monomers ensures that the pool of

unpolymerized actin consists almost entirely of ATP-G-actin with no significant amount of ADP-G-actin in the thymosin-sequestered pool (Atkinson et al., 2004).

Release of ATP-actin monomers from thymosin β 4 occurs as part of the mechanism that drives rapid actin polymerization in the normal function of the cytoskeleton in cell morphology and cell motility. Thymosin maintains the bulk of the monomer pool due to its abundance and high affinity for ATP monomers. Maintenance of a high concentration of available monomers at nuclei or filament barbed ends is necessary for rapid actin polymerization. The low affinity of the interaction between ADP monomers and thymosin is necessary to allow monomers to be handed on so that catalysis of nucleotide exchange by profilin regenerates ATP monomers for rapid addition onto filament barbed ends (Atkinson et al., 2004).

In Figure 1, thymosin β 4 and profilin serve complementary roles in regulating the polymerization of G-actin. (a) Profilin is bound to PIP2, a membrane lipid, at the cell membrane while the majority of G-actin is bound in a complex with thymosin β 4 and thus unable to polymerize. (b) In response to an extracellular signal, such as chemotactic molecules that stimulate actin assembly, profilin is released from the membrane by the hydrolysis of PIP2. The released profilin displaces thymosin β 4, forming profilin G-actin complexes that can assemble into filaments. (c) The profilin-actin complexes interact with proline-rich proteins in the membrane, where profilin adds actin monomers to the (+) end of actin filaments. (d) Eventually, the incorporation of monomers into filaments depletes the pools of profilin-actin and thymosin β 4 actin complexes. ADP G-actin subunits that have dissociated from a filament are converted into ATP G-actin by profilin, thus helping to replenish the cytoplasmic pool of ATP G-actin (Lodish et al., 2000).

In Figure 2, the effect of thymosin and profilin on actin polymerization is shown. When thymosin binds to an actin monomer it sterically prevents further binding to and elongation of the plus end of the actin filament. In contrast, when profilin binds to an actin monomer the filament is still capable of elongating. As thymosin and profilin cannot both bind to a single actin monomer at the same time, there is competition between the inhibitory thymosin and the profilin. Generally a majority of actin monomer is thymosin-bound, thus the activation of a small amount of profilin produces rapid filament assembly. Profilin binds to actin monomers that are temporarily released from the thymosin-bound monomer pool, shuttles them onto the plus ends of actin filaments, and is then released and recycled for further rounds of filament elongation (Alberts et al., 2002).

Therefore, the polymerization of actin is controlled by the give and take between thymosin and profilin. Thymosin basically acts in an inhibitory fashion and interacts with the G-actin monomer and interferes with conformations (ATP and ADP bound forms) to control the assembly of microfilaments.

Skin is the largest organ of the body, which makes up 16% of total body weight. It is also the largest organ that provides immune protection and plays a role in inflammation. Composed of specialized epithelial and connective tissue cells, skin is our major interface with the environment, a shield from the outside world and a means of interacting with it. As such, the skin is subjected to insults and injuries: burns from the sun's ultraviolet radiation that elicit inflammatory reactions, damage from environmental pollutants and wear and tear that comes with aging.

Thymosin beta 4 accelerated skin wound healing in a rat model of a full thickness wound where the epithelial layer was destroyed. When Tb4 was applied topically to the wound or injected into the animal, epithelial layer restoration in the wound was increased 42% by day four and 61% by day seven, after treatment, compared to untreated. Furthermore, Tb4 stimulated collagen deposition in the wound and angiogenesis. Tb4 accelerated keratinocyte migration, resulting in the wound contracting by more than 11%, compared to untreated wounds, to close the skin gap in the wound. An analysis of skin sections (histological observations) showed that the Tb4 treated wounds healed faster than the untreated. Proof of accelerated cell migration was also seen in vitro, where Tb4 increased keratinocyte migration two to threefold, within four to five hours after treatment, compared to untreated keratinocytes.

A critical step in wound healing is angiogenesis. New vessels are needed to supply nutrients and oxygen to the cells involved in repair, to remove toxic materials and debris of dead cells and generate optimal conditions for new tissue formation. Another important step is the directional migration of cells into the injured area, joining up to repair the wound. This requires an attractant that will direct the cells to the wound and propel them to the site. These critical steps in wound healing are regulated by beta 4, as seen in the following experiments