

Romani L, Moretti S, Fallarino F, Bozza S, Ruggeri L, Casagrande A, Aversa F, Bistoni F, Velardi A, Garaci E. (2012) Jack of all trades: thymosin  $\alpha$ 1 and its pleiotropy. *Ann N Y Acad Sci.* 1269:1.

Thymosin  $\alpha$ 1 (T $\alpha$ 1), a thymosin-related 28-mer synthetic amino-terminal acetylated peptide, has gained increasing interest in recent years, due to its pleiotropy. The peptide has been used worldwide as an adjuvant or immunotherapeutic agent to treat disparate human diseases, including viral infections, immunodeficiencies, and malignancies. The peptide can enhance T cell, dendritic cell (DC), and antibody responses, modulate cytokine and chemokine production, and block steroid-induced apoptosis of thymocytes. Its central role in modulating DC function and activating multiple signaling pathways that contribute to different functions may offer a plausible explanation for its pleiotropic action. Additionally, the ability of T $\alpha$ 1 to activate the indoleamine 2,3-dioxygenase enzyme-which confers immune tolerance during transplantation and restrains the vicious circle of chronic inflammation-has been a turning point, suggesting a potential, specific function in immunity. Accordingly, T $\alpha$ 1 has recently been shown to promote immune reconstitution and improve survival of recipients of HLA-matched sibling T cell-depleted stem cell transplants in a phase I/II clinical trial. Thus, T $\alpha$ 1 continues to live up to its promises.