

Melatonin Edition References

Gottfried, Sara. **“The Hormone Cure.”** (Scribner, March 12, 2013).

Farez, Mauricio F.; Mascanfroni, Ivan D. ; Méndez-Huergo, Santiago P.; Yeste, Ada; Murugaiyan, Gopal; Garo, Lucien P. ; Aguirre, María E. Balbuena; Patel, Bonny; Ysraelit, María C. ; Zhu, Chen ; Kuchroo, Vijay K.; Rabinovich, Gabriel A.; Quintana, Francisco J.; Correale, Jorge. **“Melatonin Contributes to the Seasonality of Multiple Sclerosis Relapses.”** Farez et al., 2015, Cell 162 , 1338–1352, September 10, 2015 ©2015 Elsevier Inc. 1339.

Abstract:

Interleukin-10 (IL-10)-secreting T regulatory type 1 (Tr1) cells are defined by their specific cytokine production profile, which includes the secretion of high levels of IL-10 and transforming growth factor-beta (TGF-beta), and by their ability to suppress antigen-specific effector T-cell responses via a cytokine-dependent mechanism. In contrast to the naturally occurring CD4⁺ CD25⁺ T regulatory cells (Tregs) that emerge directly from the thymus, Tr1 cells are induced by antigen stimulation via an IL-10-dependent process in vitro and in vivo. Specialized IL-10-producing dendritic cells, such as those in an immature state or those modulated by tolerogenic stimuli, play a key role in this process. We propose to use the term Tr1 cells for all IL-10-producing T-cell populations that are induced by IL-10 and have regulatory activity. The full biological characterization of Tr1 cells has been hampered by the difficulty in generating these cells in vitro and by the lack of specific marker molecules. However, it is clear that Tr1 cells play a key role in regulating adaptive immune responses both in mice and in humans. Further work to delineate the specific molecular signature of Tr1 cells, to determine their relationship with CD4⁺ CD25⁺ Tregs, and to elucidate their respective role in maintaining peripheral tolerance is crucial to advance our knowledge on this Treg subset. Furthermore, results from clinical protocols using Tr1 cells to modulate immune responses in vivo in autoimmunity, transplantation, and chronic inflammatory diseases will undoubtedly prove the biological relevance of these cells in immunotolerance.

Obayashi, K., K. Saeki, et al. **“Physiological Levels of Melatonin Relate to Cognitive Function and Depressive Symptoms: The HEIJO-KYO Cohor.”** *J Clin Endocrinol Metab.* 2015 June 8:jc20151859.

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Paredes, S.D., K.A. Forman, et al. **“Protective actions of melatonin and growth Hormone on the aged cardiovascular system.”** *Horm Mol Biol Clin Investig.* 2014 May;18(2):79-88.

Sánchez-Hidalgo M; Guerrero JM; Villegas I; Packham G; de la Lastra CA. **“Melatonin, A Natural Programmed Cell Death Inducer in Cancer.”** *Immunol Rev.* 2006 Oct;213:257.

Abstract:

Melatonin, an indolamine derived from the amino-acid tryptophan, participates in diverse physiological functions and has great functional versatility related to the regulation of circadian rhythms and seasonal behavior, sexual development, retinal physiology, tumor inhibition, as an antioxidant, immunomodulatory and anti-aging properties. In relation to its oncostatic properties, there is evidence that tumor initiation, promotion or progression may be restrained by the night-time physiological surge of melatonin in the blood or extracellular fluid. In addition, depressed nocturnal melatonin concentrations or nocturnal excretion of the main melatonin metabolite, 6-sulfatoxymelatonin, were found in individuals with various tumor types. In the majority of studies, melatonin was shown to inhibit development and/or growth of various experimental animal tumors and some human cell lines in vitro. Many tumors do not respond to drug treatment due to their resistance to undergo apoptosis thereby contributing to the development of cancer. Thus, given the importance of the apoptotic program in cancer treatment, the role of melatonin in influencing apoptosis in tumor cells attracted attention because it seems that it actually promotes apoptosis in most tumor cells, in contrast to the obvious inhibition of apoptotic processes in normal cells. Thus, this paper is also intended to provide to the reader an up-date of all the researches that have been carried out to date, which investigate the pro-apoptotic effects of melatonin in experimental preclinical models of cancer (in vitro and in vivo) and the underlying proposed action mechanism of this effects. If melatonin uniformly induces apoptosis in cancer cells, the findings could have important clinical implications to improve the quality of live while preventing the appearance of cancer.

Sarlak, G., A. Jenwitheesuk, et al. **“Effects of melatonin on nervous system Aging: neurogenesis and neurodegeneration.”** *J Pharmacol Sci.* 2013 September 20;123(1):9-24.

Scheer, F.A., G.A. Van Montfrans, et al. **“Daily nighttime melatonin reduces blood pressure in male patients with essential hypertension.”** *Hypertension.* 2004 February;43(2):192-7.

Silvestri, M., and G.A Rossi. **“Melatonin: It’s possible role in the management Of viral infections--a brief review.”** *Ital J Pediatr.* 2013 October 3;39:61.

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