Author	Cytokine	Study	Result
Experimental administration of cytokines			
Shoham 1987[1]	TNF	Intravenous and intraventricular injection into rats	Increases SWS
	IL-1B		Increases SWS
Fang 1997[2]	TNF	Intraperitoneal injection in mice	Increases NREM sleep
	IL-1B		Increases NREM sleep
Takahashi 1999[3]	TNF inhibitor	Intraventricular injection into rabbits	Decreases IL-1-induced NREM sleep
	IL-1 inhibitor		Decreases TNF-induced NREM sleep
Dickstein 1999[4]	TNF	Intraventricular injection in sheep	Increases SWS
Obal 1995[5]	IL-1	Intraventricular injection into rats	Increases NREM sleep and SWS
	GHRH antibodies		Decreases IL-1-induced NREM sleep and SWS
Krueger 1987[6]	IFN alpha	Intraventricular or intravenous injection into rabbits	Increases SWS
Kubota 2001[7]	IL-2	Intraventricular injection into rabbits	Increased NREM sleep; some decreases in REM sleep
Kushikata 1998[8]	IL-4	Intraventricular injection into rabbits	Decreases NREM sleep; some decreases in REM sleep
Spath-Schwalbe 1998[9]	IL-6	Intravenous injection into humans	Decreases REM sleep, but variable effects on SWS
Hogan 2003[10]	IL-6	Intraventricular injection into rats	Increases then decreases NREM sleep; no effect on REM
Benedict 2009[11]	IL-6	Intranasal administration to humans	Increases SWS
Opp 1995[12]	IL-10	Intraventricuar injection into rats	Decreases NREM sleep
Kushikata 1999[13]	IL-10	Intraventricuar injection into rabbits	Decreases NREM sleep
	IL-15		Increases NREM sleep; some decreases in REM sleep
Kubota 2000[14]	IL-13	Intraventricular injection into rabbits	Decreases NREM sleep
	TGFB		Decreases NREM sleep
Kubota 2001[15]	IL-18	Intraventricular injection into rabbits	Increases NREM sleep
Kubota 2000[16]	NFKB inhibitor	Intraventricular injection into rats and rabbits	Decreases IL-1B-induced sleep
Endogenous levels of cytokines			
Fang 1997[2]	TNF	Knockout mice for TNF receptor compared with controls	Decreased baseline NREM sleep

Fang 1998[17]	IL-1	Knockout mice for IL-1 receptor compared with controls	Decreased baseline NREM sleep
Opp 1994[18]	Anti-IL-1B	Intraventricular injection into rats after sleep deprivation	Reduces sleep
Takahashi 1995[19]	Anti-TNF antibody	Intraventricular injection into rats and rabbits	Decreases NREM sleep
Moldofsky 1986[20]	IL-1	Measurement in plasma of humans during sleep/wake cycle	Increase at onset of SWS
Gudewill 1992[21]	IL-1B	Measurement in plasma of humans during sleep/wake cycle	Some increases during sleep
	TNF		No change
	IL-6		Some increases during sleep
Lissoni 1998[22]	IL-2	Measurement in humans during sleep/wake cycle	Peaks during sleep
Redwine 2000[23]	IL-2	Measurement in plasma of humans during sleep/wake cycle	No change with sleep
	IL-6		Increase at sleep onset
Dimitrov 2006[24]	IL-6R	Measurement in plasma of humans during sleep/wake cycle	Increased during sleep
Hogan 2003[10]	Anti-IL-6 antibodies	Intraventricular injection into rats	No effect on spontaneous sleep
Thomas 2010[25]	IL-6	Measurement after stimulation of human monocytes during sleep/wake cycle	Increased IL-6 associated with decreased SWS and increased REM sleep, and fatigue the next day
Benedict 2007[26]	IL-7	Measurement in plasma of humans during sleep/wake cycle	Increases during REM sleep
Kubota 2000[16]	NFKB inhibitor	Intraventricular injection into rats and rabbits	Decreases REM and NREM sleep
Dimitrov 2004[27]	IL-2, IL-4, TNF, IFN gamma	Flow cytometry analysis of blood cells in humans during sleep/wake cycle	Increased Th1 activity in early sleep, shift to Th2 dominance in late sleep
Sleep deprivation and cytokines			
Born 1997[28]	TNF	Measurement in plasma after 24 h sleep deprivation in humans	No change
	IL-1B	Production by T cells after 24 h sleep deprivation in humans	No change
	IL-2		Decreased
	IL-6		No change
Mackiewicz 1996[29]	IL-1B	Quantitative gene expression after 24 h sleep deprivation in rats	Increase in expression
Shearer 2001[30]	TNFR-1	Measurement in plasma after 88 hours total compared to partial sleep deprivation in humans	Increased
	IL-6		Increased

Irwin 2006[31]	TNF	Measurement after monocyte stimulation after 1 night partial sleep deprivation in humans	Increased
	IL-6		Increased
Redwine 2000[23]	IL-6	Measurement after 4 hours sleep loss	Regular increase at sleep onset delayed by deprivation
Haack 2007[32]	IL-6	Measurement in plasma after 8 nights partial sleep deprivation in humans	Increased
Frey 2007[33]	IL-1B, IL-1RA	Measurement in plasma after 24 h sleep deprivation in humans	Increased
	IL-6		Decreased
Yehuda 2009[34]	IL-1B, TNF, IL-6, IL-17	Measurement in plasma after 72 h sleep deprivation in rats	Increased
Rosa Neto 2010[35]	TNF	Measurement in adipose tissue after 96 h paradoxical sleep deprivation in rats	Decreased
	IL-6		Increased
	IL-10		No change
Chennaoui 2011[36]	TNF	Measurement in plasma after 24 h sleep deprivation in humans	Increased
	TNFR1, IL-6		No change
Ruiz 2010[37]	IL-1B, IL-2, IL-4, IL-6, IL-10, TNF, IFN gamma	Measurement in plasma after 48 h sleep deprivation in humans	No change
Moller-Levet 2013[38]	IL-6	Gene expression after 7 nights partial sleep loss	Increased IL-6 expression
Moller-Levet 2013[38]	IL-1R	Gene expression after 7 nights partial sleep loss	Increased IL-1R expression

SWS – slow wave sleep, NREM – non rapid eye movement, REM - rapid eye movement, TNF – tumor necrosis factor, TNFR – TNF receptor, IL – interleukin, IL-1R – interleukin-1 receptor, IFN – interferon,TGFB – transforming growth factor beta

References

1. Shoham S, Davenne D, Cady AB, Dinarello CA, Krueger JM. Recombinant tumor necrosis factor and interleukin 1 enhance slow-wave sleep. *Am J Physiol* 1987;253(1 Pt 2):R142-9.
2. Fang J, Wang Y, Krueger JM. Mice lacking the TNF 55 kDa receptor fail to sleep more after TNFalpha treatment. *J Neurosci* 1997;17(15):5949-55.
3. Takahashi S, Kapas L, Fang J, Krueger JM. Somnogenic relationships between tumor necrosis factor and interleukin-1. *Am J Physiol* 1999;276(4 Pt 2):R1132-40.
4. Dickstein JB, Moldofsky H, Lue FA, Hay JB. Intracerebroventricular injection of TNF-alpha promotes sleep and is recovered in cervical lymph. *Am J Physiol* 1999;276(4 Pt 2):R1018-22.

5. Obal F, Jr., Fang J, Payne LC, Krueger JM. Growth-hormone-releasing hormone mediates the sleep-promoting activity of interleukin-1 in rats. *Neuroendocrinology* 1995;61(5):559-65.
6. Krueger JM, Dinarello CA, Shoham S, Davenne D, Walter J, Kubillus S. Interferon alpha-2 enhances slow-wave sleep in rabbits. *Int J Immunopharmacol* 1987;9(1):23-30.
7. Kubota T, Brown RA, Fang J, Krueger JM. Interleukin-15 and interleukin-2 enhance non-REM sleep in rabbits. *Am J Physiol Regul Integr Comp Physiol* 2001;281(3):R1004-12.
8. Kushikata T, Fang J, Wang Y, Krueger JM. Interleukin-4 inhibits spontaneous sleep in rabbits. *Am J Physiol* 1998;275(4 Pt 2):R1185-91.
9. Spath-Schwalbe E, Hansen K, Schmidt F, Schrezenmeier H, Marshall L, Burger K, et al. Acute effects of recombinant human interleukin-6 on endocrine and central nervous sleep functions in healthy men. *J Clin Endocrinol Metab* 1998;83(5):1573-9.
10. Hogan D, Morrow JD, Smith EM, Opp MR. Interleukin-6 alters sleep of rats. *J Neuroimmunol* 2003;137(1-2):59-66.
11. Benedict C, Scheller J, Rose-John S, Born J, Marshall L. Enhancing influence of intranasal interleukin-6 on slow-wave activity and memory consolidation during sleep. *FASEB J* 2009;23(10):3629-36.
12. Opp MR, Smith EM, Hughes TK, Jr. Interleukin-10 (cytokine synthesis inhibitory factor) acts in the central nervous system of rats to reduce sleep. *J Neuroimmunol* 1995;60(1-2):165-8.
13. Kushikata T, Fang J, Krueger JM. Interleukin-10 inhibits spontaneous sleep in rabbits. *J Interferon Cytokine Res* 1999;19(9):1025-30.
14. Kubota T, Fang J, Kushikata T, Krueger JM. Interleukin-13 and transforming growth factor-beta1 inhibit spontaneous sleep in rabbits. *Am J Physiol Regul Integr Comp Physiol* 2000;279(3):R786-92.
15. Kubota T, Fang J, Brown RA, Krueger JM. Interleukin-18 promotes sleep in rabbits and rats. *Am J Physiol Regul Integr Comp Physiol* 2001;281(3):R828-38.
16. Kubota T, Kushikata T, Fang J, Krueger JM. Nuclear factor-kappaB inhibitor peptide inhibits spontaneous and interleukin-1beta-induced sleep. *Am J Physiol Regul Integr Comp Physiol* 2000;279(2):R404-13.
17. Fang J, Wang Y, Krueger JM. Effects of interleukin-1 beta on sleep are mediated by the type I receptor. *Am J Physiol* 1998;274(3 Pt 2):R655-60.
18. Opp MR, Krueger JM. Anti-interleukin-1 beta reduces sleep and sleep rebound after sleep deprivation in rats. *Am J Physiol* 1994;266(3 Pt 2):R688-95.
19. Takahashi S, Kapas L, Fang J, Krueger JM. An anti-tumor necrosis factor antibody suppresses sleep in rats and rabbits. *Brain Res* 1995;690(2):241-4.
20. Moldofsky H, Lue FA, Eisen J, Keystone E, Gorczynski RM. The relationship of interleukin-1 and immune functions to sleep in humans. *Psychosom Med* 1986;48(5):309-18.
21. Gudewill S, Pollmacher T, Vedder H, Schreiber W, Fassbender K, Holsboer F. Nocturnal plasma levels of cytokines in healthy men. *Eur Arch Psychiatry Clin Neurosci* 1992;242(1):53-6.
22. Lissoni P, Rovelli F, Brivio F, Brivio O, Fumagalli L. Circadian secretions of IL-2, IL-12, IL-6 and IL-10 in relation to the light/dark rhythm of the pineal hormone melatonin in healthy humans. *Nat Immun* 1998;16(1):1-5.
23. Redwine L, Hauger RL, Gillin JC, Irwin M. Effects of sleep and sleep deprivation on interleukin-6, growth hormone, cortisol, and melatonin levels in humans. *J Clin Endocrinol Metab* 2000;85(10):3597-603.
24. Dimitrov S, Lange T, Benedict C, Nowell MA, Jones SA, Scheller J, et al. Sleep enhances IL-6 trans-signaling in humans. *FASEB J* 2006;20(12):2174-6.

25. Thomas KS, Motivala S, Olmstead R, Irwin MR. Sleep depth and fatigue: role of cellular inflammatory activation. *Brain Behav Immun* 2010;25(1):53-8.
26. Benedict C, Dimitrov S, Marshall L, Born J. Sleep enhances serum interleukin-7 concentrations in humans. *Brain Behav Immun* 2007;21(8):1058-62.
27. Dimitrov S, Lange T, Tieken S, Fehm HL, Born J. Sleep associated regulation of T helper 1/T helper 2 cytokine balance in humans. *Brain Behav Immun* 2004;18(4):341-8.
28. Born J, Lange T, Hansen K, Molle M, Fehm HL. Effects of sleep and circadian rhythm on human circulating immune cells. *J Immunol* 1997;158(9):4454-64.
29. Mackiewicz M, Sollars PJ, Ogilvie MD, Pack AI. Modulation of IL-1 beta gene expression in the rat CNS during sleep deprivation. *Neuroreport* 1996;7(2):529-33.
30. Shearer WT, Reuben JM, Mullington JM, Price NJ, Lee BN, Smith EO, et al. Soluble TNF-alpha receptor 1 and IL-6 plasma levels in humans subjected to the sleep deprivation model of spaceflight. *J Allergy Clin Immunol* 2001;107(1):165-70.
31. Irwin MR, Wang M, Campomayor CO, Collado-Hidalgo A, Cole S. Sleep deprivation and activation of morning levels of cellular and genomic markers of inflammation. *Arch Intern Med* 2006;166(16):1756-62.
32. Haack M, Sanchez E, Mullington JM. Elevated inflammatory markers in response to prolonged sleep restriction are associated with increased pain experience in healthy volunteers. *Sleep* 2007;30(9):1145-52.
33. Frey DJ, Fleshner M, Wright KP, Jr. The effects of 40 hours of total sleep deprivation on inflammatory markers in healthy young adults. *Brain Behav Immun* 2007;21(8):1050-7.
34. Yehuda S, Sredni B, Carasso RL, Kenigsbuch-Sredni D. REM sleep deprivation in rats results in inflammation and interleukin-17 elevation. *J Interferon Cytokine Res* 2009;29(7):393-8.
35. Rosa Neto JC, Lira FS, Venancio DP, Cunha CA, Oyama LM, Pimentel GD, et al. Sleep deprivation affects inflammatory marker expression in adipose tissue. *Lipids Health Dis* 2010;9:125.
36. Chennaoui M, Sauvet F, Drogou C, Van Beers P, Langrume C, Guillard M, et al. Effect of one night of sleep loss on changes in tumor necrosis factor alpha (TNF-alpha) levels in healthy men. *Cytokine* 2011;56(2):318-24.
37. Ruiz FS, Andersen ML, Martins RC, Zager A, Lopes JD, Tufik S. Immune alterations after selective rapid eye movement or total sleep deprivation in healthy male volunteers. *Innate Immun* 2010;18(1):44-54.
38. Moller-Levet CS, Archer SN, Bucca G, Laing EE, Slak A, Kabiljo R, et al. Effects of insufficient sleep on circadian rhythmicity and expression amplitude of the human blood transcriptome. *Proc Natl Acad Sci U S A* 2013.