BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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NAME	POSITION TITLE
Siegel, Jerome M.	Professor of Psychiatry & Biobehavioral Sciences
eRA COMMONS USER NAME SIEGEL2	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
City College of New York, New York, NY	B.S.	1968	Psychology
University of Rochester, Rochester, NY	Ph.D.	1973	Neuroscience
University of California, Los Angeles, CA	Postdoctoral	1975	Postdoctoral

A. Personal Statement

Our group and the group at Stanford found in 2000 that human narcolepsy with cataplexy was caused by a loss of hypocretin (Hcrt) cells. Subsequently, we found a localized loss of Hcrt in human narcolepsy without cataplexy and a generalized loss in Parkinson's patients. We conducted the only study of Hcrt release within the human brain, using subjects implanted with microdialysis probes. We found that Hcrt release was maximal during pleasure and minimal during pain. In parallel with our human studies, we made the first unit recordings of sleep and waking activity of Hcrt neurons, using the rat. We followed this up with a comprehensive study of the behavioral deficits in the narcoleptic (Hcrt KO) mouse and Fos expression in their normal littermates. We find that unit activity and Fos expression in Hcrt neurons is not related to arousal *per se*, but rather to arousal linked to positive reward. KO animals are only deficient on positively rewarded tasks. The reward relation combined with the serendipitous discovery of the brain of a human heroin addict with abnormalities of Hcrt morphology and the development of the new DTA-orexin mouse model for narcolepsy lead to the current proposal and a potential treatment for narcolepsy with implications for furthering understanding and treatment of depression and addiction.

B. Positions and Honors.

Professional Positions

7/78-6/84	Assistant Professor of Psychiatry & Biobehavioral Sciences, UCLA, School of Medicine
1980-present	Chief, Neurobiology Research, Sepulveda VAMC
7/84-5/89	Associate Professor of Psychiatry & Biobehavioral Sciences, UCLA, School of Medicine
5/90-present	Professor of Psychiatry & Biobehavioral Sciences, member Brain Research Institute, UCLA School of Medicine
5/90-present	Deputy Editor Sleep
1993-1999	Chair, Program Committee, APSS (Association of Professional Sleep Societies)

Awards and Other Professional Activities

1980	V.A. Clinical Investigator Award
1992-1995	President-Elect, President, Past-President Sleep Research Society
2001	Special Award for Research Leading to the Discovery of the Cause of Human Narcolepsy, Sleep Research Society
2002	Distinguished Scientist Award, Sleep Research Society
2005	Dement Award, American Academy of Sleep Medicine
1994-2004	M.E.R.I.T. Award, NHLBI
1999-2006	Jacob Javits Neuroscience Investigator Award, NINDS
2011	William S. Middleton Award; for Outstanding Achievement in Biomedical Research, Department of Veterans Affairs (the national award of the VA for research excellence)
2013	Narcolepsy Researcher of the Year, The Narcolepsy Network (The main US patient group)

C. Most relevant publications

1. Siegel JM. Narcolepsy: A key role for hypocretins (orexins). Cell 98: 409-412, 1999.

2. Thannickal TC, Moore RY, Nienhuis R, Ramanathan L, Gulyani S, Aldrich M, Cornford M, Siegel JM. Reduced number of hypocretin neurons in human narcolepsy. Neuron 27: 469-474, 2000.
3. Mileykovskiy BY, Kiyashchenko LI, Kodama T, Lai YY and Siegel JM. Activation of pontine and medullary motor inhibitory regions reduces discharge in neurons located in the locus coeruleus and the anatomical equivalent of the midbrain locomotor region. J. Neuroscience 20: 8551-8558, 2000.
4. Kiyashchenko LI, Mileykovskiy BY, Maidment N, Lam HA, Wu M-F, John J, Peever J, Siegel JM. Release of hypocretin (orexin) in waking and sleep states. J. Neuroscience 22: 5282-5286, 2002.
5. John, J. Wu, M.F., Boehmer, L.B. and Siegel, J.M Cataplexy-active neurons in the posterior hypothalamus:: Implications for the role of histamine in sleep and waking behavior. Neuron 42, 619–634, 2004.
6. Blouin, M., Thannickal, T.C. Worley, P.F. Baraban, J.M, Reti, I.M. Siegel, J.M. Narp immunostaining of human hypocretin (orexin) neurons: loss in narcolepsy. Neurology 65: 1189-1192, 2005.
7. Mileykovskiy, B.Y., Lyudmila I Kiyashchenko, L.I. and Siegel, J.M. Behavioral correlates of activity in identified hypocretin (orexin) neurons. Neuron, 46:787-798, 2005.
8. Siegel JM, Boehmer LN (2006) Narcolepsy and the hypocretin system-where motion meets emotion. Nature Reviews Neurology 2:548-556.
9. Thannickal, TC, Lai, Y.Y. and Siegel, J.M. (2007) Hypocretin (orexin) cell loss in Parkinson's disease. Brain. 130, 1586-1595.
10. McGregor, R. and Siegel, J.M. Illuminating the locus coeruleus: control of posture and arousal. Nature Neuroscience 13 (12):1448-1449 (2010). PMID: 21102568
11. Scammell, T.E., Matheson, J.K , Honda, M., Thannickal, T.C. and Siegel, J.M. Co-existence of narcolepsy and Alzheimer's disease. Neurobiology of Aging. 2012 Jul;33(7):1318-9. Epub 2011 Jan 22.PMID: 21257235
12. Wu, M.F., Nienhuis, R., Maidment, N., Lam H.A. and Siegel,J.M. Role of the hypocretin (orexin) receptor 2 (Hcrtr2) in the regulation of hypocretin level and cataplexy. J. Neuroscience 31: 6305-6310 (2011).
13. McGregor, R. Wu, M.F. Barber, G. Ramanathan, L., Siegel, J.M Highly specific role of hypocretin (orexin) neurons: differential activation as a function of diurnal phase, operant reinforcement vs. operant avoidance and light level. J. Neuroscience 31:15455-15467 (2011).
14. Blouin AM, Fried I, Wilson CL, Staba RJ, Behnke EJ, Lam HA, Maidment NT, Karlsson KÆ, Lapierre JL, Siegel JM. Human hypocretin and melanin-concentrating hormone levels are linked to emotion and social interaction. Nature Communications. 2013 Mar 5;4:1547. doi: 10.1038/ncomms2461. PMID: 23462990
15. John J, Thannickal TC, McGregor R, Ramanathan L, Ohtsu H, Nishino S, Sakai N, Yamanaka A, Stone C, Cornford M, Siegel JM, Greatly increased numbers of histamine cells in human narcolepsy with cataplexy. Annals of Neurology, 2013 (in press). Accepted Article, doi: 10.1002/ana.23968

All published articles available at: http://www.npi.ucla.edu/sleepresearch

D Research Support

MH064109 (Siegel PI) 7/9/12-4/30/17
Behavioral role of hypocretin
This is a study of the effects of operant reinforcement on hypocretin release. No overlap.

VA0007 Siegel (PI) 4/1/11 – 3/31/14
Department of Veterans Affairs (annual funding 125,000)
Effects of morphine on the morphology of the hypocretin and MCH systems
This grant supported the pilot data presented here and will not be renewed. It will end before the earliest start date of the present grant.

NS069640 (Siegel PI) 6/1/10-5/31/14
Unihemispheric sleep: implications for mechanisms of sleep control and function in mammals
This is a study of sleep in fur seals aimed at localizing mechanisms for sleep control universal to mammals. This study is conducted at our laboratory on the Black Sea in Russia. No overlap.