‘Melatonin promotes sleep by activating the BK channel’

by

Dr. Bojun Chen at University of Connecticut School of Medicine (USA) on the 30th Oct. 2020 (14:00 CET via zoom https://uio.zoom.us/j/8863743687)

The NO-Age and NO-AD Seminar Series 011

“Melatonin promotes sleep by activating the BK channel”

by

Bojun Chen, Ph.D.

University of Connecticut School of Medicine, USA

at

14:00-15:00 (CET), Friday on the 30th Oct. 2020

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Speaker: Bojun Chen, Ph.D.

Name: Bojun Chen
Institute: University of Connecticut School of Medicine
Email: bochen@uchc.edu

Title: "Melatonin promotes sleep by activating the BK channel"

Abstract:
Melatonin is a natural hormone that plays an important role in the sleep-wake cycle. It is synthesized mainly by the pineal gland and promotes sleep through G protein-coupled receptors. However, the downstream molecular target(s) of melatonin's sleep-promoting action is unknown. Through an unbiased genetic approach with the nematode *C. elegans*, we identified the BK channel SLO-1, a key negative regulator of neurotransmitter release, as a molecular target of the melatonin receptor PCDR-1. Knockout of *pcdr-1*, *slo-1*, or *homt-1* (a gene required for melatonin synthesis) causes substantially increased neurotransmitter release and shortened sleep duration, and these effects are non-additive in the double knockouts. Exogenous melatonin inhibits neurotransmitter release and promotes sleep in wild-type and *homt-1* knockout worms, but not in *pcdr-1* and *slo-1* knockout worms. In a heterologous expression system, we found that melatonin activates the human BK channel (hSlo1) in a membrane-delimited manner in the presence of the melatonin receptor MT1 but not MT2. A peptide acting to release free Gβγ from heterotrimeric G proteins also activates hSlo1 in a MT1-dependent and membrane-delimited manner, whereas a Gβλ inhibitor abolishes the stimulating effect of melatonin. Our results suggest that melatonin activates the BK channel through a specific melatonin receptor and Gβλ, and that BK channels may play an evolutionarily conserved role in mediating the sleep effect of melatonin.

Biography:
Dr. Bojun Chen is an Assistant Professor in the Department of Neuroscience at University of Connecticut School of Medicine, USA. He received his Ph.D in 2003 from Peking University in China, where he studied molecular mechanisms of drought-resistance in plants with Professor Zhongping Lin. In 2004, he joined Dr. Zhao-Wen Wang's lab at University of Connecticut School of Medicine as a postdoc to study the regulation of BK channels and gap junctions in *C. elegans*. Since he became an independent investigator in 2013, his research has focused on Slo2 potassium channels, which are paralogs of BK channels existing in both mammals and invertebrates with important roles in the nervous system. He has made important contributions to understanding the regulation of BK and Slo2 channels by novel proteins, and has published over 30 peer-reviewed papers.