

# **Sleep Medical Center, West China Hospital**

## **Institute: Sleep Medical Center, West China Hospital**

West China Hospital sleep medicine center is mainly aimed at all kinds of common sleep disorders, such as snoring, sleep apnea, sleep hypoventilation, insomnia, sleep, circadian rhythm abnormalities, sleep related movement disorders, REM sleep behavior disorder and narcolepsy disease comprehensive examination and treatment platform. With the help of team “SCU-WestChina”, we made a contact with Professor Tang Xiangdong and his postdoctor Doctor Zhang Ye, and interviewed them about some questions in our project design.

## **Interviewee: Professor Tang Xiangdong & Doctor Zhang Ye**

Professor Tang Xiangdong received his M.D. in West China Medical University in 1996. Then he completed postdoctoral training in sleep medicine at the University of Pennsylvania during 1998-2008. When he worked in sleep room on the Eastern Virginia Medical School, he served as an associate professor and assistant professor. He is the responsible leader for 7 research projects of the National Institutes of health, the American Sleep Research Society, the National Science Foundation of China and the Ministry of health. In 2008, he returned to China and began to work as a special professor of Sichuan University. He has 37 papers published in SCI which are cited more than 500 times. There are 8 papers published on "SLEEP (sleep, IF 5.2)", the international and authoritative academic journal of sleep medicine. He is the director of the China Sleep Research Association and vice chairman of the Specialized Committee for Sleep and Mental Health currently.

Doctor Zhang Ye is a postdoc of Professor Tang Xiangdong's lab.

## **Interviewer:**

Liu Tian, Qiu Qinling, Wang Caiqin, and Yang Yuanhan, who are all the reserve players of SCU\_China

## **West China sleeping center interview**

As we know, melatonin is a sleep aid. But in what extent would melatonin influence our sleeping? As there are so many different claims about this question, we decided to interview professors of West China sleeping center as an authority to confirm the effect that melatonin has on sleep. The sleeping center once carried on a project about developing a melatonin sustained release tablets. Also, lots of researches have been done by the sleeping center on melatonin. Thus, we believed West China sleeping center would give us the authoritative answer we want.

Before we began this interview, we talked about our iGEM project with Dr. Zhang Ye. He showed a great interest in clinical treatment of sleep disorder. Then we asked Dr. Zhang several questions and he showed us some papers to answer our questions. Dr. Zhang stressed, “My answers to your questions must be valid and showing you papers is the most scientific way to answer your question.”

**Q: Compared to other drugs helping people sleep, what are the advantage and disadvantage of melatonin?**

He showed us a paper (Auld F, Maschauer E L, Morrison I, et al. Evidence for the efficacy of melatonin in the treatment of primary adult sleep disorders.[J]. Sleep Medicine Reviews, 2016.) and answered: The advantage of melatonin is apparent. In terms of pharmacological management of sleep disorders, drugs with a short half-life are preferable due to their smaller 'hangover' effects on the following morning. It's also strongly recommended that long term drug therapy should be avoided, as there is a great possibility that dependence and tolerance will develop. Previous studies have highlighted the potential use of melatonin to treat primary and secondary sleep disorders. Oral melatonin can decrease sleep onset latency and increase total sleeping time, thus improving sleep quality overall. Exogenous melatonin doesn't have reported tolerance, dependence, or 'hangover' effect. Also, it doesn't have side effect on alertness or mood on the following day, if administered at a low dose. Melatonin has a short half-life, only 30-50 minutes, and can induce phase shifts in the circadian timing system, reduce body temperature and suppress alertness when administered acutely, which encourage sleep propensity.

But we cannot ignore the disadvantage of melatonin. Melatonin could be easily brought in any drug store. But not everyone knows how to use it properly. If not administered according to the individual patient's circadian timing, melatonin and other treatments may not only be ineffective but also result in contrary effects. What's more, the overall quality of evidences was very low due to potential publication bias, heterogeneity, and imprecision. Meta-analysis was only achievable for sleep quality. Therefore, existing papers were weakly against melatonin's efficacy in improving sleep onset, maintenance, or quality.

**Q: According to present situation, there are some problems inhibiting clinical treatment of sleep disorders. Do you have any opinions on solving these problems?**

**A:** It is true that there are some problems on giving medicine to cure the sleep disorders. For example, drug abuse is a common problem when someone gets into significant sleep disorders. It is so easy for patients to get drug in drug store. What's more, drug usage is not well instructed by doctors sometimes. Let's see what the paper says "Although the Pharmacopoeia and the European Food Safety Agency recommend taking melatonin 1 to 2 hours before bedtime, several studies have shown that melatonin taken in the way of the recommendation is not always effective. The use of melatonin should be associated with the individual's circadian rhythm. Otherwise, it may even cause opposite effects. The current feasible solution is to collect saliva from patients and measure endogenous melatonin levels. We can use the fixed threshold to calculate the DLMO. By assessing the individual circadian rhythm of DLMO, it is possible to improve the diagnosis and

treatment of circadian rhythm insomnia. In this case, melatonin treatment of sleep problems can become more feasible."

**Q: Do you have any suggestion for our project?**

**A:** Yes. For safety purposes, a safer bacterial strain is recommended and it would also need to be tested in live mice. In addition, I suggest you to fully understand REM sleep, NREM sleep and arousal related neural circuits. You need to consider the relationship of melatonin expression and the sleep associated neural circuits. In addition, the differences between *Escherichia coli* treatment and oral sedative hypnotic drugs are supposed to take in to consideration. And then, you need to figure out whether melatonin in the gut can affect the central nervous system. Finally, you may also consider the use of light genetics and other techniques to stimulate brain regions associated with abnormal rhythm. Generally speaking, I think your project is meaningful, and it has great significance for practical problems and clinical treatment. I think your method, using microorganism to produce the melatonin, is very creative. And the cost of your method is much lower than chemical method usually used. If you can finish your project, it will have great economic value.

We received an email of Dr.Zhang before long after our interview that day. We were honored to be invited to the fourth China Sleep Research Association Youth Academic Forum and Sichuan Medical Association Sixth Session of Sleep Medicine academic conference. Lots of professors in Sichuan province gave a presentation on their projects. Some of these projects illustrate how melatonin worked in our sleeping process. We have learned a lot about most recent melatonin research. Attending the conference, we realized some of the points we didn't consider before. We are supposed to adjust the rhythmic expression in *Escherichia* to human's bio-clock.