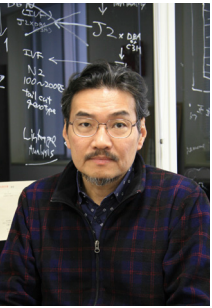


# THE SCIENCE OF SLEEP

## PROFESSOR MASASHI YANAGISAWA DIRECTS THE INTERNATIONAL INSTITUTE FOR INTEGRATIVE SLEEP MEDICINE




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**MARTIN LEROUX**

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**T**HE necessity of sleep is a unifying factor: every existing individual requires a certain amount of it. Yet changes in our lifestyle have brought with them a rise in sleep disorder, posing a threat to productivity in society. Sleep disorder has been linked to various mental conditions and lifestyle diseases, giving greater cause for worry. What was once an essential regimen appears to have become more of a privilege amid escalating pressures of life in the 21<sup>st</sup> century.

So how can we regulate sleep? And why is it necessary in the first place? The answers to these questions are surprisingly still unknown. “There are lots of mysteries regarding sleep,” states Professor Masashi Yanagisawa, MD, PhD. “In sleep, you lose consciousness and become vulnerable to danger. That should pose a major evolutionary risk, yet all mammalian species sleep. This means that sleeping has to have great benefits that surpass those risks.”

Yanagisawa directs the University of Tsukuba’s World Premier International Research Center Initiative International Institute for Integrative Sleep Medicine (WPI-IIIS), a world-class collective of scientists from various fields that studies

the neurobiology of sleep, aiming to better understand sleep mechanics in order to cure sleep disturbances and related disorders.

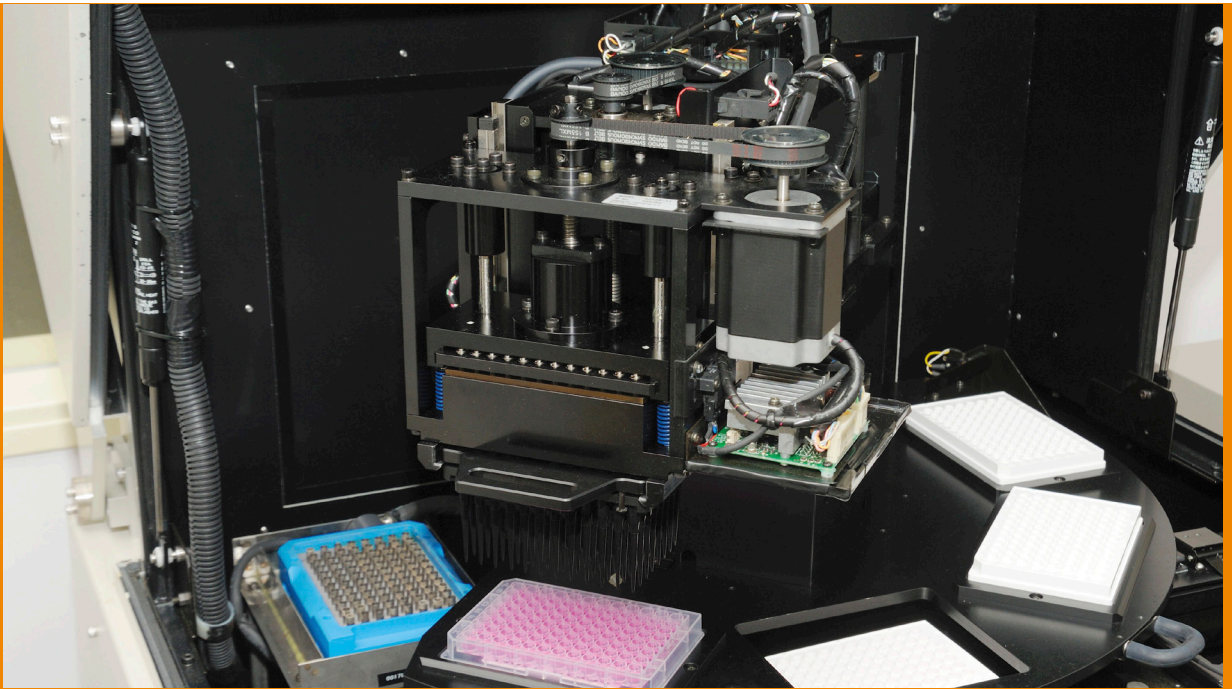
The WPI-IIIS was launched following the discovery of the correlation between sleep and orexin, a chemical in the brain that manages wakefulness. Orexin functions as a wake-inducing substance, the lack of which causes a difficulty in keeping oneself awake.

The conventional sleep process involves transitioning from wakefulness into non-REM sleep, the obligatory initial stage of sleep. This leads to REM sleep, a deeper state of physical rest where the body muscles remain flaccid to prevent the physical enacting of dreams.

In his earlier research, Yanagisawa discovered that orexin deficiency caused mice to instantly transition from consciousness to REM sleep, completely skipping the primary non-REM stage.

“We observed bizarre behavior in laboratory mice, where they would run around and suddenly just collapse - as if dead - and then run around again a minute later. We concluded that these mice suffered from narcolepsy.”

Narcolepsy is a sleep disorder stemming from abnormal sleep-wake transitions, manifesting in humans as either chronic fatigue and sleepiness during the day due to irregular sleep regulation; or cataplexy, a condition where the patient maintains



Investigating candidate substances for pharmaceutical applications


consciousness but loses control of muscles, usually triggered by surges of positive emotion like laughing.

“Researchers learned that more than 95 percent of human narcolepsy patients are orexin-deficient,” Yanagisawa explains. “If we can somehow replace orexin, it will be fundamentally cured. Unfortunately, orexin has to be delivered directly into the brain, which is difficult to do. What we need here is an orexin receptor agonist - a drug that can mimic the functions of orexin receptor - to wake a person up in a completely natural way. That’s what we’re aiming to make.”

The development of an orexin receptor agonist would aid in sleep regulation and could treat various physical and mental conditions stemming from sleep disorder such as depression, obesity and metabolic syndrome.

On the other hand, orexin antagonists - drugs that block the effects of orexin - would

make one sleeper. While current commercial drugs are merely sedative, orexin antagonists induce a natural state of sleep that would remedy everything from depression to jet lag - and they could be hitting the market soon.

“Orexin antagonists are on the verge of being approved as sleeping medication by around June or July this year,” says Yanagisawa. “So it’s a very exciting time.” It seems we may well indeed be on the cusp of unraveling the mysteries of the science of sleep. 



Mouse sleep measurement