

# Stanford Center for Sleep Sciences and Medicine

## FACULTY SPOTLIGHTS



### **Emmanuel Mignot, MD, PhD**

*An eminent sleep scientist who has transformed our understanding of narcolepsy and its origins, Dr. Mignot and his colleagues were the first to discover that narcolepsy is an autoimmune disease caused by loss of hypocretin. Dr. Mignot created a database made up of data from thousands of patients, providing an invaluable resource for study that has led to many breakthroughs. He heads the Stanford Technology Analytics and Genomics in Sleep study and is also the lead researcher in Kleine-Levin Syndrome, focusing on proteomics and genetics research.*



### **Clete Kushida, MD, PhD**

*Dr. Kushida is chief of the Division of Sleep Medicine and medical director of the Stanford Sleep Clinic. He is a neurologist who specializes in the diagnosis and management of sleep-related breathing disorders, sleep-related movement disorders, and parasomnias. Dr. Kushida's research focuses on the anatomic and physiologic changes associated with sleep apnea, the management of restless legs syndrome, and countermeasures for sleep loss.*

The pace of our lives has never been more intense. It seems our society has become permanently wired into the “on” position, with no dimmer switch in sight. We’re expected to keep up with the latest news, care for our families, stay connected with friends, and remain available to our employers. In this world of hyper-stress and information overload, sleep has become a precious and scarce commodity.

Sleep disorders impact more than 60 percent of adults at some point during their lifetime. The price we pay for our lack of sleep is high: it affects the mind as well as the body. Chronic sleep deprivation has enormous medical consequences for cardiovascular, metabolic, and psychiatric conditions. Sleep and circadian rhythm dysfunction are associated with pain and allergies, as well as neurodegenerative and neuromuscular disorders.

Stanford is recognized by the world as the birthplace of sleep medicine and a beacon in the field of sleep research. We coined the term “obstructive sleep apnea,” established gold-standard clinical evaluations such as the multiple sleep latency test, and discovered the cause of narcolepsy. Our researchers are continuing to uncover sleep’s hidden mysteries and are setting the highest standards of care globally.

### **THE STANFORD CENTER FOR SLEEP SCIENCES AND MEDICINE**

With a high level of collaboration among investigators across campus, the Stanford Center for Sleep Sciences and Medicine integrates research and treatment to advance our fundamental understanding of sleep and sleep disorders.

Investigators here are unraveling the mechanisms of sleep regulation at the molecular, cellular, and neural network levels, while also discovering the genetics and pathophysiology of sleep disorders. They are working to develop blood tests for sleep disorders such as sleep apnea and tests that can assess the extent of sleep deprivation or the circadian timing of individual patients. The team also aims to develop a new home sleep monitoring system to replace current cumbersome in-clinic nocturnal sleep polysomnography technology. A major goal is to empower patients through self-monitoring. These developments can revolutionize sleep medicine.

Under the leadership of Director Emmanuel Mignot, MD, PhD, and Chief of the Division of Sleep Medicine, Clete Kushida, MD, PhD, the Stanford Sleep Center includes basic researchers, psychiatrists, psychologists, neurologists, surgeons, internists, pediatricians, ENT specialists, and dentists, all of whom address a wide range of sleep disorders, including:

#### **Insomnia**

The inability to fall or stay asleep has negative daytime consequences such as poor concentration, low energy, and irritability. Recent genetic studies have led to new insights into the relationships between insomnia, hypersomnia (long sleep), and neuropsychiatric disorders. For example, results have shown that insomnia is not only a symptom of depression but also can contribute to depression. Treating insomnia to manage or prevent the development of depression is a promising area, especially in adolescents. Research at Stanford involves cognitive behavioral therapies, new uses for existing drugs, and light therapy.

## Apnea

Obstructive sleep apnea is a disorder where soft tissue in the airway repeatedly collapses, interrupting breathing during sleep. It prevents deep sleep, which leads to daytime sleepiness, causes cognitive problems, and induces repetitive low oxygenation, with cardiovascular consequences such as high blood pressure and increased risk of stroke. Stanford researchers have made great strides in understanding how this disorder develops and are creating novel methods of measurement so that eventually sleep apnea can be diagnosed, monitored, and treated at home. The work involves developing new biosensors and the use of machine learning to automatically detect and act on sleep disorder breathing events. The team has been able to create algorithms that can automatically score sleep stages, detect events such as autonomic arousals, and classify subtypes of sleep apneas that have various effects on sleepiness and the cardiovascular system. Yet much remains to be learned about the molecular mechanisms involved in apnea, so that treatment can be personalized based on its subphenotype and lead cause in each individual.

## Restless Legs Syndrome (RLS)

The hallmark of this neurological disorder is an uncomfortable, and in some cases, painful sensation in the legs, with the irresistible urge to move them. The symptoms occur mostly at night when at rest and are relieved by movement, causing sleep disturbances. It is strongly associated with a condition called periodic leg movements during sleep. Although we don't know what causes RLS, we now know its genetic basis and many of its mechanisms. RLS runs in families, with heredity accounting for about half of cases. Stanford researchers were the first to pinpoint the anatomical region in the brain where the programming takes place; it appears that alterations in the developing forebrain during the early embryonic stage may lead to a predisposition to RLS, which manifests later in life. A biomarker study is currently underway.

## Narcolepsy

A chronic neurological disorder that affects the brain's ability to control sleep-wake cycles, narcolepsy is a lifelong problem. Its symptoms include severe sleepiness, cataplexy (muscle tone weakness triggered by emotions), sleep paralysis, dream-like hallucinations, fragmented sleep, insomnia, and autonomic behavior. The center is the academic world leader in narcolepsy research. Researchers here have established that the cause of the disorder is an autoimmune disease caused by a loss of hypocretin/orexin neurons in the hypothalamus. Besides testing new therapies, researchers are now using machine learning on sleep recording signals to diagnose the condition at home instead of in a sleep laboratory. They are also making strides in their understanding of how the immune system destroys hypocretin neurons to cause narcolepsy. Findings indicate that the flu can trigger an abnormal immune response in some predisposed individuals, which then cross-react with hypocretin. Research in this area has far-reaching applications, not only for narcolepsy but for the understanding of other autoimmune diseases and for the development of safer flu vaccines. New hypocretin/orexin drugs have been developed for insomnia and narcolepsy thanks to this discovery.

## FACULTY SPOTLIGHTS



### William Dement, MD, PhD

*Known as the “father of sleep medicine,” Dr. Dement helped discover and describe rapid eye movement (REM) sleep as one of several distinct phases in the sleep cycle. He established the Stanford Sleep Medicine Clinic, the world's first accredited sleep center, which sparked the development of the sleep medicine specialty. He and his close associate, Christian Guilleminault, MD, went on to conduct the first major research studies on sleep disorders. He documented the shift in circadian rhythms in early adolescence, showing sleep deprivation as a major factor in teen mood disorders and drug use. As the founder of the American Academy of Sleep Medicine and the American Board of Sleep Medicine, and with the creation by Congress of the National Center of Sleep Disorders Research, Dr. Dement's impact on the field and national sleep research has been incalculable.*



### Rafael Pelayo, MD

*Dr. Pelayo is a Stanford sleep expert in adult and pediatric sleep disorders who has advocated for a California bill aiming for later middle- and high-school starting times to address sleep deprivation, car accidents, and mood disorders that can occur at this age. He leads high-school and undergraduate sleep education programs, which are preventive medicine at heart, establishing prioritization of healthy practices at an early age.*

## Kleine-Levin Syndrome (KLS)

Although rare, Kleine-Levin Syndrome is teaching us much about the relationships between mood disorders and sleep. KLS is characterized by sudden, one- to two-week episodes of extreme sleep—for example, 20 hours a day—associated with behavioral/cognitive disturbances (being in a fog, disconnected from reality). Stanford is now the leading institution conducting research on this enigmatic disorder. Following a study of 700 patients from all continents, researchers found that predisposition to KLS involves a combination of circadian abnormalities and genetic factors predisposing to bipolar disorder. This is transforming our understanding of the condition, which we are now treating using mood stabilizers and light therapy. Molecular studies of the condition also promise to reveal mechanisms that may explain the complex relationships that exist between hypersomnia and mood disturbances.

## Sleep Homeostasis and Circadian Regulation of Sleep

Our propensity to sleep at any moment is regulated by two processes: sleep “homeostasis,” which represents a need to catch up on lost sleep (also called sleep debt), and the circadian clock, an effect of the time of the day that is independent of any prior sleep debt. These two processes interact constantly to optimize wakefulness during the day and sleep during the night.

We are learning more every day about the circadian control of sleep, including the specific genes within the molecular clock that alter the timing of sleep, creating “early birds” and “night owls.” Every cell in the body has some measure of what time of day it is, and the entire body is synchronized to the proper time zone by a complex array of hormonal and cellular connections. The center is currently using new technology that can measure thousands of proteins at once in a small blood sample to establish blood tests for sleep debt and circadian timing.

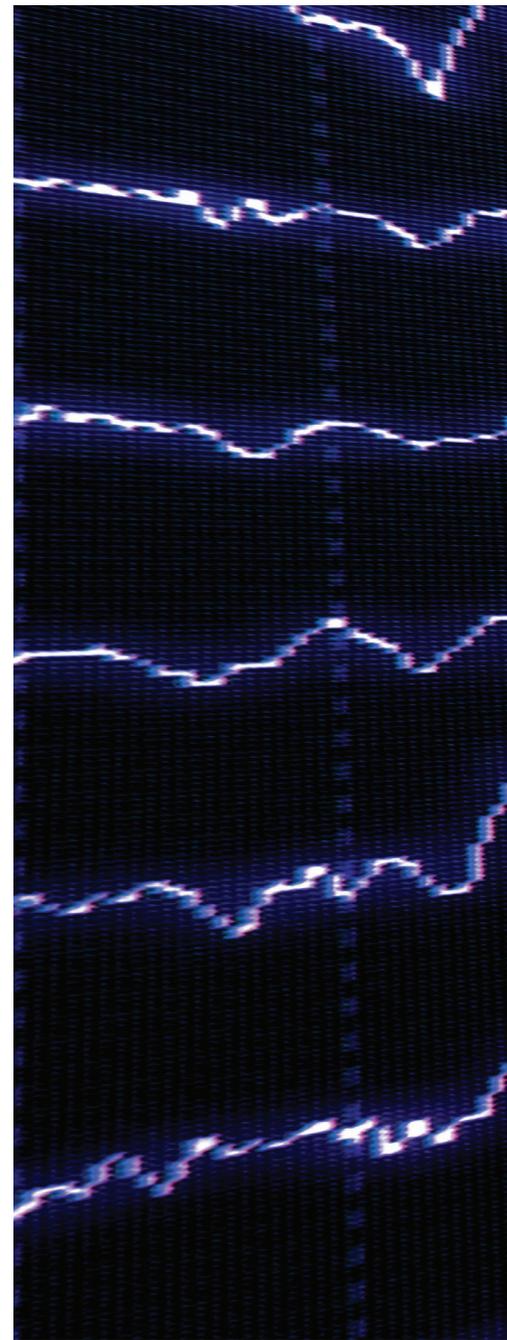
## STANFORD TECHNOLOGY ANALYTICS AND GENOMICS IN SLEEP (STAGES)

Sleep clinics around the world currently evaluate patients using nocturnal polysomnography recordings, composed of multiple digital signals recorded during the night. Surprisingly, analysis of the rich data gathered has not been standardized nor connected with genetics and proteomics on a large scale. In the largest sleep study to date, the STAGES study will investigate the genetics of objective sleep measures in 30,000 people, providing novel insights into sleep and all types of sleep disorders.

## OUR VISION FOR THE FUTURE

This is a unique moment in the history of sleep medicine—the field is poised to benefit greatly from accelerating progress in hardware, software, genetics and proteomics, “big data,” and the development of wearable devices.

At the Stanford Center for Sleep Sciences and Medicine, our goal is to transform the field, building upon our world-renowned sleep research program. We are getting closer every day to creating a more complete picture of sleep and sleep disorders. With your help, there is good reason to expect that our discoveries, strategies, and effective treatments will continue to improve the lives of people around the world.



COVER: Brain waves (alpha, beta, gamma) showing REM-sleep moving into consciousness

## CONTACT US

For questions or more personalized conversation around your philanthropic interests, please contact:

**Ariel Korn**, Senior Associate Director  
Medical Center Development  
650.850.1859 | [ariel.korn@stanford.edu](mailto:ariel.korn@stanford.edu)

To make a gift online, go to [medicalgiving.stanford.edu](https://medicalgiving.stanford.edu) and designate Sleep Medicine in the special instructions.



# Stanford Center for Sleep Sciences and Medicine

## **OPPORTUNITIES TO INVEST IN SLEEP MEDICINE RESEARCH AT STANFORD**

With your philanthropic partnership, we will develop a more comprehensive understanding of the circuitry that regulates sleep, including its molecular, genetic, and neurobiological basis. We aim to discover blood biomarkers that will help to diagnose sleep disorders. And, with advanced sensor technology, our goal is to create a new non-intrusive at-home sleep monitoring tool that records multiple biosignals, allowing for a highly accurate interpretation of normal and abnormal sleep.

### **Professorship Honoring William Dement, MD, PhD | \$4 million**

Endowed professorships help Stanford attract and retain top faculty. They are the highest honor the university can bestow upon its most distinguished faculty. As a pioneer in sleep medicine and one of the founders of the field, William Dement, MD, PhD, has made extraordinary contributions to our knowledge of sleep and sleep disorders. The establishment of this named professorship would honor his legacy in perpetuity.

### **Professorship | \$4 million**

Established as permanent funds that provide an annual payout, this endowment would play a vital role in recruiting and retaining a world-renowned leader to help make major advances in the field. The endowment supports a portion of the holder's salary in perpetuity and helps defray research costs, making it possible to focus on rapidly translating laboratory research into improved diagnosis, treatments, and prevention.

### **Postdoctoral Training Fellowships | \$1.2 million (endowed) or \$100,000 per year (expendable)**

Postdoctoral fellows play a vital role in the execution of research. Named fellowships help Stanford to attract the most talented graduate students and post-graduate trainees. Nurturing the research of young investigators allows the center to recruit and train the next generation to the field of sleep medicine.

### **Sleep Sciences Research Funds | Gifts of any size**

These funds are designed to jumpstart the most creative research ideas, allowing investigators to pursue promising avenues of inquiry and ultimately develop effective new diagnostic techniques and therapies. These funds will fuel innovative early-stage research projects that don't yet have the preliminary data to receive federal grants in today's conservative funding environment.

*For questions or more personalized conversation around your philanthropic interests, please contact:*

*Ariel Korn | Senior Associate Director | Medical Center Development | 650.850.1859 | [ariel.korn@stanford.edu](mailto:ariel.korn@stanford.edu)*

*To make a gift online, go to [medicalgiving.stanford.edu](https://medicalgiving.stanford.edu) and designate Sleep Medicine in the special instructions.*