

Summary of Proposal

Host institution	University of Tsukuba
Chief entire-project officer (Head of host institution)	Nobuhiro Yamada, President
Chief center-project officer	Masashi Yanagisawa, Center for Behavioral Molecular Genetics, Professor and Director
Center director	Masashi Yanagisawa, Center for Behavioral Molecular Genetics, Professor and Director
Center name	International Institute for Integrative Sleep Medicine
Project Summary	<p>Sleep is a remarkably universal phenomenon in the higher animal species, and its disturbances reduce mental and physical wellbeing. However, the function of sleep and the mechanism for sleep regulation still remain unknown; these questions are among the most important challenges in modern neuroscience. The proposed research center will gather the world prominent scientists from multiple research fields contributing to the neurobiology of sleep. We will aim at elucidating the fundamental mechanism of sleep/wake regulation by combining the cutting-edge methodologies of neurobiology, molecular genetics and physiology. We will induce the fusion of medicine, chemistry, pharmacology and biology in order to reveal the pathophysiology of sleep disorders and related diseases, and to develop methods for their treatment and prevention. Through these research efforts, we will strive to reduce sleep disorders and associated diseases, and to contribute to an improvement of physical and mental health in today's aging society with a dwindling birthrate.</p>
Mission statement and/or Center identity	<p>The mission of this WPI Center is to be a multidisciplinary, international hub for the research to elucidate the fundamental mechanism of sleep/wakefulness, to develop strategies to regulate sleep, and to contribute to enhancement of world health through the combat with sleep disorders and associated diseases.</p>
Target research field	<p><u>Name of the target research field</u> Sleep biomedicine</p> <p>Sleep biomedicine, as defined here, is an inherently interdisciplinary field in terms of methodology, spanning molecular genetics, cellular biology, neurophysiology, neurochemistry, pharmaceutical sciences, medicinal chemistry, and clinical and social medicine. While focusing on sleep, the field is also interdisciplinary with respect to its integral research targets, e.g., studying mood disorders as well as metabolic diseases that are closely associated with pathological variations in sleep/wake states.</p> <p><u>Importance of the target research field</u></p> <p>Sleep is a behavior that everyone experiences daily and it takes up as much as one third of one's entire lifetime. While sleep has been a black box stubbornly resisting scientists' challenges, its medical and social importance is very clear. Healthy sleep is necessary for maintaining our mind and body fitness; lack of sound sleep not only causes a reduction in higher brain functions including memory and decision making, but also increase the risk of mood disorders such as depression. The society demands the development of strategies to remedy sleep disorders and associated diseases.</p> <p><u>Research trend of this field</u></p> <p>As for the current trend of the field, triggered by the reports by Yanagisawa that a deficiency of the hypothalamic neuropeptide OREXIN is the root cause of the then-mysterious sleep disorder NARCOLEPSY, a consensus has been formed by most researchers in the field that orexin constitutes one of the centerpieces of the neural circuitry regulating sleep and wakefulness. Moreover, multiple pharmaceutical companies are currently focused on developing new classes of sleeping pills, indicating the consensus among the domestic and overseas pharmaceutical industries that this field is highly important for drug discovery.</p> <p><u>Reasons why the project fit for this call for proposals</u></p> <p>Japan has been producing a number of researchers who have made significant accomplishments in the field of sleep biomedicine. Masashi Yanagisawa and Takeshi Sakurai discovered the neuropeptide orexin and unraveled pathophysiological mechanisms of narcolepsy. This is arguably one of the most significant discoveries in the past 50 years of sleep research, which has created a new avenue of inquiry in the field: the two papers describing the discovery of orexin and the narcolepsy phenotype in orexin knockout mice have been cited more than 4,400 times combined. While primarily focusing on sleep, they have been conducting various behavioral studies that are related to sleep. Hiromasa Funato and Yanagisawa elucidated the potent role of orexin in basal metabolism and body weight regulation, uncovering the possibility of drug discovery for metabolic diseases. In part due to the wide recognition of these contributions, Yanagisawa has been selected as one of the Principal Investigators for the FIRST Program of the Cabinet Office of Japan, which has allowed him to intensively promote sleep research at his new Center hosted by the University of Tsukuba.</p>
Research objectives	<p>The research objectives that the proposed center seeks to achieve are: 1) elucidation of the fundamental mechanisms of sleep/wake, 2) elucidation of molecular pathogenesis of sleep disorders and related diseases, and 3) development of treatments for sleep disorders.</p>
Outline of management	<p>Establish a top-down administrative system headed by the Center Director by fully utilizing his long-term experience at an American university.</p> <p>Under the supervision of the Administrative Director who is thoroughly knowledgeable in both the research contents of the center and the administrative affairs of the national university corporation, the administrative staff will be composed of the Administrative Director, Assistant Administrative Director, and the following three sections. (General affairs section, Accounting section, Research fund section).</p>

	<p>Decision-making system In order to facilitate efficient and flexible administration of the research center, the Center Director will have the sole authority of decision-making related to the personnel and management matters within the Center, except for the removal of himself and the determination of his own salary. Regardless of the position, anyone who is participating in this Center can offer his/her opinions regarding the management or treatment directly to the Center Director.</p> <p>Allocation of authority between the center director and host institution The President of the University has the authority to elect or dismiss the Center Director, The Center Director has a wide range of authorities regarding the general management and internal administration of the research center.</p>												
Researchers and other center staffs, satellites, partner institutions	Principal Investigators: 15 (foreigners 5) (Achieved by October, 2013), Total Researchers: 115 (foreigners 35) (Achieved by March, 2015), Total Staff at Core-Center: 169 (Achieved by March, 2015), Main principal investigators: Masashi Yanagisawa, Hiromasa Funato, Takeshi Sakurai, Yoshihiro Urade, Robert Greene, Qinghua Liu, Hiroshi Nagase, Ichiyo Matsuzaki, Hitoshi Shimano, Junichi Hayashi, Akiyoshi Fukamizu, Satoru Takahashi, Tetsuo Shimizu, Carla Green, Joseph Takahashi, Satellite: University of Texas Southwestern Medical Center, Akita University, Collaboration: RIKEN BioResource Center												
Administrative director	Katsutoshi Goto, Professor Emeritus, University of Tsukuba												
Outline of research environment	(1) Establish a strong supportive organization in order to decrease the burden of administrative obligations of scientists so that they concentrate on their research. (2) Reduce the burden of administrative obligations of researchers and allow them to devote themselves exclusively to their research. (3) Take advantage of Tsukuba as a research city in providing living support for researchers. (4) Provide a sufficient amount of startup research funding and strong administrative support when applying for external funding through the entire application process for the independent researchers. (5) Conduct International recruitment to hire post-doctoral fellows. (6) English will be used as an official language at the research center. (7) Adopt a system for evaluating research and merit-based compensation. (8) Provide appropriate equipment and facilities, office and animal center (space exceeding 5000m ²) as a top world-premier research center. (9) Hold international symposia once a year, and invited seminar series twice a month. And hold a retreat once a year for the development of students and young researchers, promotion of collaborative researches, and also an increased sense of a family-like unity of the Center. Provide workshops at overseas Satellites to increase the visibility of the research center overseas.												
Outline of indicators for evaluating a center's global standing	i) Criteria and methods to be used for evaluating the center's global standing in the subject field 1. Number of citations of published papers in the medium to long term. 2. Positions and scientific accomplishments of the alumni (trainee) of the research center. 3. Funding ii) Results of current assessment made using said criteria and methods 1. The number of citations for the article that reported the discovery of orexins is 2668 and for the article describing narcolepsy episodes in orexin-deficient mice, the number of citations are 1660. 2. Many researchers who received trainings as post-doctoral fellows in Yanagisawa Lab have become professors and assistant professors of domestic and overseas universities, working in responsible positions in research institutions and corporate settings. 3. The prospective Center Director, has attained domestic funding worth 1.8 billion yen (US\$22,500,000,) over five years as the Core Researcher of the FIRST project. In addition, he secured an average of US\$1,260,556 per year of competitive funding in the U.S. in the last 5 years. iii) Goals to be achieved through the project (at time of interim and final evaluations) (at time of interim) 1. The citation indices of our publications surpass those at other premier research centers for sleep biomedicine, such as the Stanford Center for Sleep Sciences and Medicine. 2. It would be too early to evaluate graduate students and post-doctoral fellows who are alumni of the research center. (at time of final evaluations) The citation indices of our publications surpass those at other premier research centers for sleep biomedicine, such as the Stanford Center for Sleep Sciences and Medicine. 2. More senior alumni of the research center have attained independent positions in the academia and in the industry, both domestic and overseas												
Securing research funding	The total amount of competitive research funding raised by the prospective Principal Investigators in the past five years is \$44,316,704 averaging at \$8,863,341/year. The University of Tsukuba will be responsible for the labor costs for the scientists who are full-time Principal Investigators or researchers at the University before participating in this research center, and for the full-time University staffs who were appointed to the administrative division of this research center. The University will provide support for securing sufficient research space and for moving into new space, and will be partially responsible for providing research funding. By providing the funding, the University will support the installation of equipment and facilities, renovation of research laboratories, and the administrative management of the research center.												
Exploiting the results of previously-initiated center-building efforts	Program name: Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST Program) Project title: Molecular Mechanism and Control of Complex Behavior Representative's name: Masashi Yanagisawa Funding period: 2010-2014 <p><u>The reason why we believe that this WPI based on our existing FIRST program will succeed</u> Our forward genetic screening of mutagenized mice for sleep/wake abnormalities, which is enabled by the FIRST program, has been going on smoothly with promising positive results. Our suite of cutting-edge equipment and experimental systems developed under the FIRST program constitute an ideal environment where the prospective top Principal Investigators of this WPI Center can productively explore their research ideas.</p> <p><u>Our prospects after the FIRST program</u> Use the Health and Medical Science Innovation Laboratory as the core facility of the Center.</p>												
Appropriations plan (Exchange Rate: JPY/USD=80)	FY	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Total (\$ millions)	
	WPI grant	3,127	5,770	7,020	7,020	7,020	7,020	7,020	7,020	7,020	7,020	65,057	

	Funding for previously-initiated center-building efforts (if any)	1,008	1,730	1,730	1,730	1,730	1,730	1,730	1,730	1,730	1,730	16,578
	Total	4,135	7,500	8,750	8,750	8,750	8,750	8,750	8,750	8,750	8,750	81,635
Summary of host institution's commitment	<p><u>How positioned within the host institution's mid-to-long-term strategy plan</u> The Midterm Goals states: "strive for deep specialized expertise, open up new cross-disciplinary fields, and achieve research results which are outstanding by international standards," and "ambitiously open up new cross-disciplinary fields." The WPI is in complete agreement with the University's Midterm Goals and Midterm Plan. We will specify "International Institute for Integrative Sleep Medicine" for a Midterm Plan in the near future.</p> <p><u>Concrete Measures</u></p> <ol style="list-style-type: none"> 1) Provide at least the same level of resources as funded by this project. 2) Enable top-down decisions by the Center Director regarding personnel affairs and budgets. 3) Make necessary adjustments to assemble persons from other institutes of the University. 4) Amend the regulations, if necessary, to accommodate the new system of management. 5) Provide >5,000m² of floor space that a "globally visible" premier research center deserves. 6) Support to sustain the Center after this program ends. 											