Homeodynamics in Clocks, Sleep and Metabolism

TOKYO TRANSLATIONAL THERAPEUTICS MEETING

Wednesday, September 24, 2014

at Ito Hall, Ito International Research Center,
The University of Tokyo

Organizing Committee

Hiroki R. Ueda
The University of Tokyo / RIKEN QBiC

Joseph T. Bass
Northwestern University

Masashi Yanagisawa
WPI-IIIS, University of Tsukuba

Main Speakers

Joseph T. Bass
Northwestern University

Yang Dan
University of California, Berkeley

Takashi Kadowaki
University of Tokyo

Emmanuel Mignot
Stanford University

Hitoshi Okamura
Kyoto University

John Renger
Merck Research Laboratories

Hitoshi Shimano
University of Tsukuba

Joseph S. Takahashi
UT Southwestern Medical Center

Hiroki R. Ueda
University of Tokyo / RIKEN QBiC

Masashi Yanagisawa
WPI-IIIS, University of Tsukuba

Discussants

Ravi Allada
Northwestern University

Michael Hastings
University of Cambridge

Samer Hattar
Johns Hopkins University

Yu Hayashi
WPI-IIIS, University of Tsukuba

Takao Kondo
Nagoya University

Kazuhiko Kume
Nagoya City University

Michael Lazarus
WPI-IIIS, University of Tsukuba

Akhilesh Reddy
University of Cambridge

Sue-Goo Rhee
Yonsei University

Michael Rosbash
Brandeis University

Amita Sehgal
University of Pennsylvania

Susumu Seino
Kobe University

Akihiro Yamanaka
Nagoya University

Takashi Yoshimura
Nagoya University

QBiC

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IIIS
INTERNATIONAL INSTITUTE FOR INTEGRATIVE SLEEP MEDICINE

Program

Wednesday, September 24, 2014

Opening Remarks			
9:20 - 9:40	Opening Address 1	**Hiroki R. Ueda**	The University of Tokyo / RIKEN QBiC
	Opening Address 2	**Nobutaka Hirokawa**	Fujihara Foundation of Science
	Opening Address 3	**Takashi Kadowaki**	The University of Tokyo
	Opening Address 4	**Toshio Kuroki**	WPI Program Director, Japan Society for the Promotion of Science (JSPS)

Session 1 - Sleep		Chair: Michael Lazarus	
9:40 - 9:45	Introductory Remarks	**Michael Lazarus**	WPI-IIIS, University of Tsukuba
9:45 - 10:15	Forward genetic analysis of sleep in ENU-mutagenized mice	**Masashi Yanagisawa**	WPI-IIIS, University of Tsukuba
10:15 - 10:45	Neural circuits controlling sleep and wakefulness	**Yang Dan**	University of California, Berkeley
10:45 - 11:15	Orexin/hypocretin receptor antagonist preclinical profile on sleep and arousability versus GABA modulators	**John Renger**	Merck Research Laboratories

Data Blitz		Chair: Samer Hattar	
11:20 - 11:50	Data blitz by poster presenters		

Luncheon Seminar		Chair: John Renger	
12:00 - 12:10	Lunch boxes distributed		
12:10 - 12:40	Immunogenetics of narcolepsy	**Emmanuel Mignot**	Stanford University
12:40 - 13:10	Break		

Session 2 - Rhythm & Metabolism		Chair: Akhilesh Reddy	
13:15 - 13:20	Introductory Remarks	**Akhilesh Reddy**	University of Cambridge
13:20 - 13:50	Bioenergetic regulation during the sleep-wake cycle by the molecular clock	**Joseph T. Bass**	Northwestern University
13:50 - 14:20	A new aspect of organ lipids in metabolic diseases, lessons from Elovl6	**Hitoshi Shimano**	University of Tsukuba
14:20 - 14:50	A small-molecule AdipoR agonist for type 2 diabetes and short life in obesity	**Takashi Kadowaki**	The University of Tokyo

Poster Session	
15:00 - 16:15	Poster Session (Poster awards presentation begins at 16:05, led by Michael Hastings)

Session 3 - Clock		Chair: Ravi Allada	
16:20 - 16:25	Introductory Remarks	**Ravi Allada**	Northwestern University
16:25 - 16:55	Molecular architecture to the circadian clock in mammals	**Joseph S. Takahashi**	University of Texas Southwestern Medical Center
16:55 - 17:25	New cellular regulations of the circadian clock	**Hitoshi Okamura**	Kyoto University
17:25 - 17:55	Systems and Synthetic Biology of mammalian circadian clocks	**Hiroki R. Ueda**	The University of Tokyo / RIKEN QBiC

Closing Remarks			
17:55 - 18:00	Closing Remarks	**Masashi Yanagisawa**	WPI-IIIS, University of Tsukuba

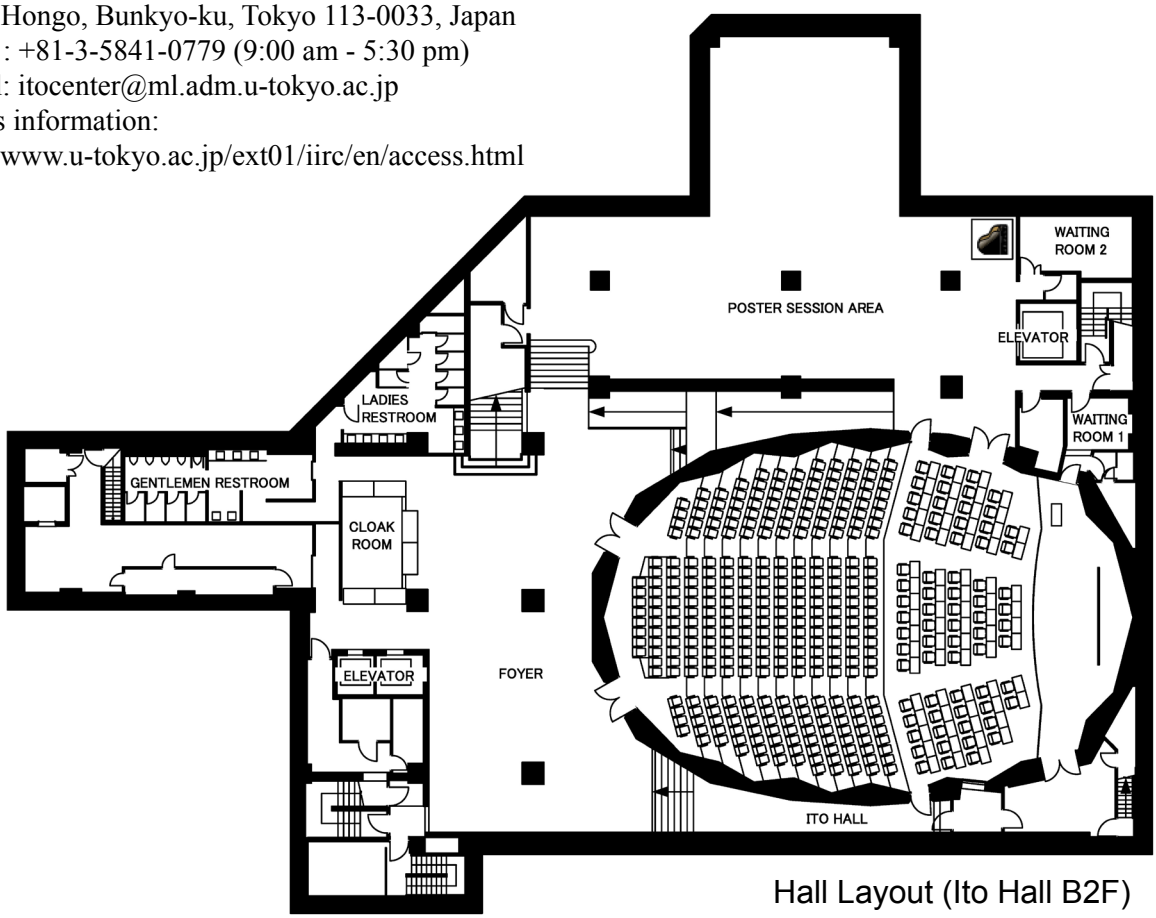
Reception / Mixer	
18:30 - 21:00	The reception/mixer will commence after a short duration upon the close of the symposium

General Information

Wednesday, September 24, 2014

Venue

Ito International Research Center
7-3-1, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan
Phone : +81-3-5841-0779 (9:00 am - 5:30 pm)
E-mail: itocenter@ml.adm.u-tokyo.ac.jp
Access information:
http://www.u-tokyo.ac.jp/ext01/iirc/en/access.html



Hall Layout (Ito Hall B2F)

Notes

1. No power outlets are available nearby audience seats
2. Eating and drinking are prohibited in the Ito Hall (except for luncheon seminar period)
3. No smoking on the premises
4. Wireless LAN is available;

Network ID: iirc-hall	Password: %01-2012-guest

Lunchbox

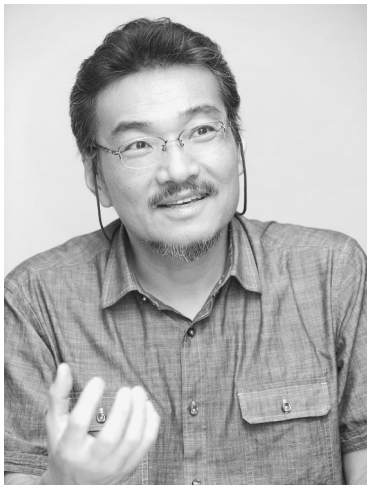
Free lunchboxes will be provided for pre-registered participants. Extra may be distributed to non-pre-registered participants on a first-come-first-served basis (will be announced).

Mixer (7:00 - 9:00 pm, September 24)

Capo PELLICANO
7-3-1, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan
Phone : +81-3-5841-1527
*Reception starts at 6:30 pm
*We will welcome walk-in participants. Please pay the participation fee in advance (industry 7,000 JPY; academic 5,000 JPY; students 3,000 JPY) at the reception desk of the symposium to receive a ticket.

Session 1 | 9:45 – 10:15

Forward genetic analysis of sleep in ENU-mutagenized mice



Masashi Yanagisawa

International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba, Japan

ABSTRACT

Unbiased forward genetic analysis can be a powerful approach to crack open biological black boxes where a meaningful hypothesis is unavailable. The neural substrate for "sleepiness," as well as its regulatory pathways, remains one such black box in behavioral neuroscience. Although genetic and chemical screening for the sleep/wake phenotype has been intensively carried out in fruit flies and zebra fish, the behavioral readout used in these screens has been the animal's locomotor activity, a surrogate marker for sleep/wake.

We set out to perform a forward genetic screen of sleep/wake traits in ENU-mutagenized mice based on true EEG/EMG-based somnography, the gold standard for sleep assessment in mammals. Through the streamlining of surgical procedures for implanting EEG/EMG electrodes and development of semi-automatic sleep staging software that is optimized for genetic screens, we achieved a sustained throughput of 80 mice/week, with each mouse sleep-monitored for 5 days. The tight distribution of EEG/EMG-based quantitative parameters for sleep/wake behavior (relative standard deviation of 5-10%) ensured a robust screen, which we expected would yield a spectrum of mutations distinct from that found in flies.

We have so far screened >7,000 heterozygous ENU-mutagenized founders, and established >10 pedigrees exhibiting heritable and specific sleep/wake abnormalities. Linkage analysis in N2 backcrosses between inbred strains highly close to each other (C57BL/6J versus C57BL/6N) ensured no interference from inter-strain phenotypic differences. By combining linkage analysis and the whole-exome deep sequencing, we have so far molecularly identified at least three mutations: *Dreamless*, causing short and highly fragmented REM sleep; *Sleepy-1* and *Sleepy-2*, each causing a significant hypersomnia (increased non-REM sleep). Genetic, biochemical and neurophysiological analyses of these mutations are underway. Since these dominant mutations cause quite strong phenotypic traits, we expect that the mutated genes are at or nearby the core of the elusive pathway regulating sleep/wake amounts.

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Session 1 | 10:15 – 10:45

Neural circuits controlling sleep and wakefulness

Yang Dan

University of California,
Berkeley, USA

ABSTRACT

The neural circuits controlling sleep and wakefulness are distributed in the basal forebrain/preoptic area, hypothalamus, and brainstem. Each brain region contains a diversity of cell types with intricate synaptic interactions through both local and long-range connections, but the specific roles played by each neuronal type remains unclear. Using optogenetic manipulation, behavioral measurements, electrophysiological recording, imaging, and virus tracing, we define the functional properties and connectivity of different cell types in both the basal forebrain and brainstem underlying wake, rapid-eye-movement (REM) sleep, and non-REM sleep.

Session 1 | 10:45 – 11:15

Orexin/hypocretin receptor antagonist preclinical profile on sleep and arousability versus GABA modulators

John Renger

Neuroscience Discovery,
Merck Research Laboratories,
USA

ABSTRACT

Orexin (hypocretin) receptor antagonists (ORAs) promote sleep onset and maintenance by transiently inhibiting wake signaling, a very different mechanism of action from $GABA_aR$ modulators which induce sleep through globally inhibiting the CNS via enhancing inhibitory neurotransmission. Compounds that increase physiological sleep should preserve the animal's ability to wake to relevant auditory cues signaling critical information (salience) while maintaining sleep during ambient (non-salient) noise. Moreover, sleep inducing compounds which cause impairment of cognitive function can be of concern. Here we examine DORA's and $GABA_aR$ modulators for the ability to impair arousability and/or cognitive performance after drug administration. Rhesus monkeys, and dogs, implanted with EEG, EMG and EOG telemetry were assessed for sleep/wake activity. Stimulus-evoked arousability gating was evaluated by conditioning to acoustic stimuli with reward (CS+), or neutral (CS-) tones. Once conditioned, stimuli were presented near T_{max} and cognition was examined via psychomotor vigilance task (PVT) testing. Eszopiclone/diazepam dosed monkeys showed significant performance deficits, reductions in trials performed, and elevated response latencies. In contrast, animals receiving DORAs had task engagement and response latencies that were unchanged. Furthermore, administration of $GABA_aR$ modulators increased NREM with significant reductions in REM. In contrast, administration of DORA's increased all sleep stages; similar to normal sleep. Examination of spectral EEG following drug administration revealed that $GABA_aR$ modulators produced significant, dose-related changes in stage-specific EEG spectral profiles compared to vehicle. DORA showed little change in the power spectrum, with small changes observed only with super-therapeutic doses. In conclusion, DORA's are able to promote sleep while preserving the ability to wake to salient stimuli and generally not interfere with normal EEG activity, suggesting a clear difference between the activities of DORA's and $GABA_aR$ modulators and their impact on the CNS during sleep induction.

Luncheon Seminar | 12:10 – 12:40

Immunogenetics of narcolepsy

Emmanuel Mignot

Stanford Center for Sleep Sciences and Medicine, School of Medicine, Stanford University, USA

ABSTRACT

Narcolepsy is a neurological disorder characterized by excessive daytime sleepiness, cataplexy, hypnagonic hallucinations, sleep paralysis, and disturbed nocturnal sleep patterns. Narcolepsy is caused by the loss of hypocretin (orexin)-producing neurons in the lateral hypothalamus. Evidence, such as a strong association with HLA DQB1*06:02, strongly suggests an autoimmune basis targeting hypocretin neurons. Genome-wide association studies have strengthened the association between narcolepsy and immune system gene polymorphisms, including the identification of additional polymorphisms in the HLA (notably DP), polymorphisms in the T cell receptor alpha and beta loci, TNFSF4 (also called OX40L), Cathepsin H (CTSH) the purinergic receptor P2RY11, and the DNA methyltransferase DNMT1. Recently, attention has been raised regarding a spike in cases of childhood narcolepsy in 2010 following the 2009 H1N1 pandemic (pH1N1) in China and vaccination with Pandemrix, an adjuvanted H1N1 vaccine that was used in Europe. Interestingly, the association with other vaccines, including Arepandrix, a similar vaccine produced in Quebec instead of Germany using a slightly different protein extraction procedure, has not been associated with large increased risks. Differences in protein composition and effects on molecular mimicry are being explored. How the immune system may be involved in disease initiation and/or progression remains a challenge to researchers. Potential immunological pathways that could lead to the specific elimination of hypocretin producing neurons include molecular mimicry or bystander activation, and are likely a combination of genetic and environmental factors, such as upper airway infections.

Funding: NIH NS23724 and grants from GSK and Jazz Pharmaceuticals

Session 2 | 13:20 – 13:50

Bioenergetic regulation during the sleep-wake cycle by the molecular clock

Joseph T. Bass

Northwestern University, USA

ABSTRACT

Circadian clocks are biologic oscillators with 24 hr periodicity (from *circa diem*, about a day) that can be traced in geologic time to the oxygen expansion of the atmosphere and emergence of photosensitive organisms. These intrinsic clocks are now recognized to be present in all forms of terrestrial life and central to bioenergetics processes. Genetic studies first revealed that cellular clocks are encoded by an autoregulatory transcription feedback loop that, in the Metazoa, is organized hierarchically with master pacemaker neurons in the hypothalamus entrained by sunlight, in turn synchronizing circadian clocks within nearly every peripheral cell and tissue. Molecular analysis has shown that over 10% of the transcriptome in tissues such as liver exhibit marked 24 hr variation, although our understanding of the functional links between circadian rhythm and physiology remains in its infancy. Circadian mutant animals have demonstrated a central role of the clock system in metabolism and energetics and reveal that inter-tissue clock communication is necessary for constancy across the daily feeding/fasting cycle. Indeed animals with conditional clock gene ablation in endocrine pancreas develop hypoinsulinemic diabetes mellitus and post-prandial hyperglycemia; in contrast, clock deletion in liver and skeletal muscle results in profound hypoglycemia and energetic collapse upon fasting. A central question is how does the clock transcription network orchestrate metabolic tissue function? Our recent studies have uncovered a role of the clock in the metabolism of nicotinamide adenine dinucleotide (NAD+), a central electron shuttle in glycolysis and oxidative-phosphorylation, and a co-factor for the class III histone deacetylase enzymes (silencer of information regulators, SIRTS), that play a primary role in energy production during caloric restriction and aging. Integrated biochemical and genetic studies demonstrate that the CLOCK-NAD+ pathway produces rhythmic fluctuation in the activity of the mitochondrial-localized enzyme SIRT3, producing daily cycles in the acetylation and activity of rate-limiting enzymes in lipid oxidation and carbon delivery to the TCA cycle. An emerging portrait reveals that the circadian system exerts dynamic effects on organismal physiology that varies according to the phase of the light-dark cycle and underlies bioenergetics homeostasis during alternating periods of sleep and wakefulness.

Session 2 | 13:50 – 14:20

A new aspect of organ lipids in metabolic diseases, lessons from Elovl6

Hitoshi Shimano

Department of Internal Medicine, Endocrinology and Metabolism, Faculty of Medicine, University of Tsukuba, Japan

ABSTRACT

Obesity and excess lipid accumulation in the organs following excess energy balance have been thought to be the primary metabolic state linking to diabetes, dyslipidemia, atherosclerosis, inflammation, fibrosis, and recently even cancer, justifying control of obesity. However, through the study of SREBPs, key transcription factors for lipid synthesis, we realize that not only quantity, but also quality of organ lipids matter in disease and health issues. Along with the well-known issue: desaturation of fatty acids (animals fat vs. fish oil), we have proposed that the chain length of fatty acids is another novel aspect of lipid quality. Elovl6 is a long fatty acid elongase and regulates tissue fatty acid composition around C16-C18. When fed a high-fat diet or mated to genetic obese mice, mice deficient for Elovl-6 develop obesity, fatty liver and hyperlipidemia with the similar levels to the controls. However, they exhibited marked protection from insulin resistance, diabetes, atherosclerosis and non-alcoholic steatohepatitis (NASH) that control animals developed. Tissue-specific KO experiments suggest that Elovl6 in responsible organs contributed to pathological signaling pathways by different molecular mechanisms. Meanwhile, Elovl6 is necessary for normal functions in other organs. Lung Elovl6 is important for surfactant with unique fatty acid composition, leading its absence to lung fibrosis. Furthermore, Elovl6 KO mice have increased brain and hippocampus weights accompanying abnormalities in behaviors including depression, anxiety, and sucrose preference in food intake. Brain Elovl6 seems important for normal functions of glia cells and neurons.

Diversity of fatty acid composition in different tissues and cells is now revealed by metabolome analysis. This unique enzyme is involved in a variety of biological functions in the body reflecting complex roles of fatty acids: signaling through receptors, membrane phospholipid remodeling, fluxes from storage lipids, and can be a new therapeutic target in various disorders and organs.

Session 2 | 14:20 – 14:50

A small-molecule AdipoR agonist for type 2 diabetes and short life in obesity

Takashi Kadowaki

Department of Diabetes and Metabolic Diseases, Graduate School of Medicine, The University of Tokyo, Japan

ABSTRACT

Adiponectin secreted from adipocytes binds to adiponectin receptors AdipoR1 and AdipoR2, and exerts antidiabetic effects via activation of AMPK and PPAR-α pathways, respectively. Levels of adiponectin in plasma are reduced in obesity, which causes insulin resistance and type 2 diabetes. Thus, orally active small molecules that bind to and activate AdipoR1 and AdipoR2 could ameliorate obesity-related diseases such as type 2 diabetes. Here we report the identification of orally active synthetic small-molecule AdipoR agonists. One of these compounds, AdipoR agonist (AdipoRon), bound to both AdipoR1 and AdipoR2 in vitro. AdipoRon showed very similar effects to adiponectin in muscle and liver, such as activation of AMPK and PPAR-α pathways, and ameliorated insulin resistance and glucose intolerance in mice fed a high-fat diet, which was completely obliterated in AdipoR1 and AdipoR2 double-knockout mice. Moreover, AdipoRon ameliorated diabetes of genetically obese rodent *db/db* mice, and ameliorated neointimal foundation induced by cuff-injury. Finally, AdipoRon prolonged the shortened lifespan of *db/db* mice on a high-fat diet. Thus, orally active AdopoR agonists such as AdipoRon are promising therapeutic approach for the treatment of obesity-related diseases such as type 2 diabetes and cardiovascular disease.

Co-authors:
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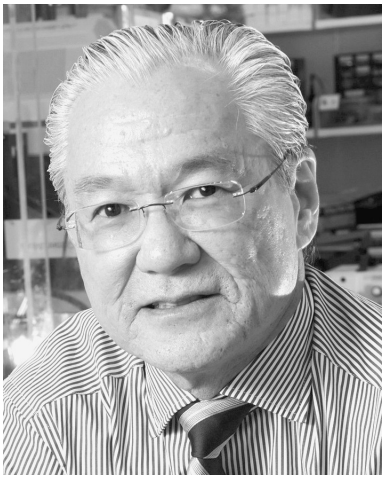
The University of Tokyo

References:
1) Nature Medicine 7:941-946, 2001, 2) Nature Medicine 8: 856-863, 2002, 3) Nature 423: 762-769, 2003, 4) J.Clin.Invest. 116: 1784-1792, 2006, 5) Nature Medicine 13: 332-339, 2007, 6) Cell Metabolism 6: 49-64, 2008, 7) Nature (Article) 464: 1313-1319, 2010, 8) Proc. Natl. Acad. Sci. USA 108: 5753-5758, 2011, 9) Cell Metabolism 13: 123-124, 2011, 10) Cell Metabolism 13: 401-412, 2011, 11) Cell 148:624, 2012, 12) Cell 148:834, 2012, 13) Cell Metabolism 17:185-196, 2013, 14) Nature (Article) 503: 493-499, 2013, 15) The Lancet Diabetes and Endocrinology 2: 8-9, 2014

Session 3 | 16:25 – 16:55

Molecular architecture to the circadian clock in mammals



Joseph S. Takahashi

Howard Hughs Medical Institute, University of Texas Southwestern Medical Center, USA

ABSTRACT

The circadian clock mechanism in animals involves an autoregulatory transcriptional feedback loop in which CLOCK and BMAL1 activate the transcription of the Period and Cryptochrome genes. The PERIOD and CRYPTOCHROME proteins then feedback and repress their own transcription by interaction with CLOCK and BMAL1. We have studied the biochemistry of the CLOCK:BMAL1 transcriptional activator complex as well as the genomic targets of CLOCK and BMAL1 using ChIP-seq methods. We describe the dynamics of the core circadian clock transcriptional system. CLOCK and BMAL1 interact with the regulatory regions of thousands of genes. The gene network and dynamics of the system will be discussed. A mechanistic description of the core circadian clock mechanism should promote our understanding of how the circadian clock system influences behavior, physiology and behavioral disorders.

References:
1. Bass, J. and J.S. Takahashi. 2010. Circadian integration of metabolism and energetics. Science 330: 1349-1354. PMCID: 3756146.
2. Huang, N., Y. Chelliah, Y. Shan, C.A. Taylor, S.-H. Yoo, C. Partch, C.B. Green, H. Zhang and J.S. Takahashi. 2012. Crystal structure of the heterodimeric CLOCK:BMAL1 transcriptional activator complex. Science 337: 189-194. PMCID: 3694778.
3. Koike, N., S.H. Yoo, H.C. Huang, V. Kumar, C. Lee, T.K. Kim and J.S. Takahashi. 2012. Transcriptional architecture and chromatin landscape of the core circadian clock in mammals. Science 338: 349-354. PMCID: 3694775.

Session 3 | 16:55 – 17:25

New cellular regulations of the circadian clock

Hitoshi Okamura

Kyoto University, Japan

ABSTRACT

The unique feature of mammalian system is the gene expression in the suprachiasmatic nucleus (SCN) determines behavioral and physiological rhythms perfectly, further supported by multilayered regulations strengthening the stability of the clock: transcriptional and posttranscriptional regulation (DNA methylation, histone modification, RNA methylation, protein modification including phosphorylation and acetylation,…). Moreover, intercellular communication via gap junctions and neurotransmitter/hormones signaling coupled to G-protein-coupled receptors are now recognized as necessary for rhythm generation, and are themselves clock-controlled. In addition, critical cell events such as the cell cycle and cellular metabolism are also regulated by the circadian clock.

After rhythmic transcription of clock genes, what molecular process is involved in rhythm generation? We recently demonstrated the clock is regulated at the level of RNA processing. Methylation of internal adenosine residues (m6A) within mRNA was described in the 1970s, but its physiological significance remained unknown until now. We identified m6A methylation sites within several clock genes transcripts, thereby revealing RNA methylation as a potential new regulator of the circadian clock. Indeed, inhibiting m6A using pharmacological inhibitors and gene silencing of the m6A methylase Mettl3 resulted in the elongation of the circadian period, while overexpression of Mettl3 led to period shortening. These observations demonstrated the physiological relevance of m6A methylation.

Interconnection of cell rhythms also affects each cell rhythm. Particularly, SCN cells forms dense networks inside the nucleus. To identify candidate signaling molecules that might contribute to jet-lag, we extended a screening strategy called SCN Gene Project, in which we sought to identify genes whose expression is enriched in the mouse SCN, generate mutant mice lacking these genes of interest, to find the molecules important for jet-lag. We found that circadian rhythms of behavior, body temperature and clock gene expression of mice lacking both vasopressin receptors V1a and V1b ($V1a^{-/-}V1b^{-/-}$) rapidly re-entrained to a new light-dark cycles. Experiments with SCN slices in culture suggested that vasopressin-mediated interneuronal communication in the SCN has a key role of the jet-lag.

Session 3 | 17:25 – 17:55

Systems and Synthetic Biology of mammalian circadian clocks

Hiroki R. Ueda

The University of Tokyo, / RIKEN Quantitative Biology Center (QBiC), Japan

ABSTRACT

The logic of biological networks is difficult to elucidate without (1) comprehensive identification of network structure, (2) prediction and validation based on quantitative measurement and perturbation of network behavior, and (3) design and implementation of artificial networks of identified structure and observed dynamics.

Mammalian circadian clock system is such a complex and dynamic system consisting of complicatedly integrated regulatory loops and displaying the various dynamic behaviors including i) endogenous oscillation with about 24-hour period, ii) entrainment to the external environmental changes (temperature and light cycle), and iii) temperature compensation over the wide range of temperature. In this symposium, I will take a mammalian circadian clock as an example, and introduce the systems- and synthetic-biological approaches for understanding of biological timings.

References:
1. Ueda, H.R. et al, Nature 418, 534-539 (2002).
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3. Sato T. K. et al, Nat Genet. 38, 312-9 (2006).
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9. Ukai-Tadenuma M et al. Cell 144(2):268-81 (2011).
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11. Jolley Cc, Ode KL, Ueda H.R. Cell Reports 2(4):938-50 (2012).
12. Sasagawa et al. Genome Biol. 14(4):R31 (2013).

Poster Titles at a Glance

No.	Title	Authors	Affiliation
P01	Neuronal basis of resting state functional connectivity investigated with wide field intrinsic and calcium imaging	Teppei Matsui, Tomonari Murakami, Kenichi Ohki	Kyushu University
P02	Establishment of new experimental methods to analyze cooperative roles of Per1 and Per2	Hiroyuki Tamiya, Rikuhiro G. Yamada, Hideki Ukai, Sumito Ogawa, Masahiro Akishita, Hiroki R. Ueda	Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo
P03	The role of adult born neurons during sleep	Masanori Sakaguchi[1*], Michael Lazarus[1], Lily Maei Yu[2], Thomas J. McHugh[2] and Takeshi Sakurai[1,3]	[1]International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba, [2]RIKEN BSI, [3]Kanazawa University
P04	A novel schizophrenia mouse model with NMDA receptor hypofunction in intralaminar thalamic cells	Kosuke Yasuda[1, 2], Yu Hayashi[3], Mika Tanaka[4], Shigeyoshi Itohara[1]	[1]Grad. Sch. of Agric. and Life Sci., University of Tokyo, [2]Lab. for Behavioral Genetics, RIKEN BSI, [3]WPI-IIIS, University of Tsukuba
P05	Regulation of Rgs4 in the islet of mutant cryptochrome1 transgenic mice	Satoshi Okano[1], Akira Yasui[2], Kiyoshi Hayasaka[3], Masahiko Igarashi[4], Osamu Nakajima[1]	[1]Yamagata University Faculty of Medicine, [2]IDAC, Tohoku University, [3]Miyuki-Kai Hospital, [4]Yamagata City Hospital Saiseikan
P06	Zinc promotes non-rapid eye movement sleep in mice	Yoan Cherasse[1], Hitomi Saitou[2], Yoshihiro Urade[1]	[1]International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba, [2]Fujifilm Corporation, Tokyo
P07	Crocin, a carotenoid pigment of saffron, promotes non-rapid eye movement sleep.	Kosuke Aritake, Nanako Itoh, Yukihiro Shoyama, Yoshihiro Urade	International Institute for Integrative Sleep Medicine (WPI-IIIS) University of Tsukuba, Molecular Sleep Biology
P08	Sleep quality affects glucose homeostasis in a mouse model	Sachiko Chikahisa, Saki Harada, Noriyuki Shimizu, Tetsuya Shiuchi, Hiroyoshi Sei	Department of Integrative Physiology, Institute of Health Biosciences, The University of Tokushima Graduate School
P09	Electrophysiological and anatomical development of hypothalamic orexin-producing neurons from embryonic to early postnatal stage	Yukino Ogawa, Masashi Yanagisawa	International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba
P10	Modulation of non-REM sleep delta power after exercise	Mari Hondo[1], Hiromasa Funato[1], Yoan Cherasse[1], Takashi Matsui[2], Hideaki Soya[2], Masashi Yanagisawa[1]	[1]International Institute for Integrative Sleep Medicine (WPI-IIIS), [2]Exercise Biochemistry and Neuroendocrinology, University of Tsukuba

Poster Titles at a Glance

No.	Title	Authors	Affiliation
P11	Role of the pontomedullary tegmentum GABAergic neurons in the states of sleep and wakefulness.	Daiki Nakatsuka, Takeshi Kanda, Masashi Yanagisawa	International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba
P12	Next-generation high-throughput sleep phenotyping for mice	Genshiro A Sunagawa, Hiroki R Ueda	RIKEN QBiC
P13	Feeding rhythm during active phase influences hypothalamic regulation of energy metabolism in skeletal muscle	Tetsuya Shiuchi, Airi Otsuka, Noriyuki Shimizu, Sachiko Chikahisa, Hiroyoshi Sei	Department of Integrative Physiology, The University of Tokushima Graduate School
P14	Chronobiology meets Big Data: Humans 'in the wild'	Dimitri Perrin, Craig C. Jolley, Hiroki R. Ueda	RIKEN QBiC
P15	Multi-site unit recording revealed ON and OFF periods during NREM sleep in mice	Kaoru Ohyama[1], Robert W. Greene[1], Yuichi Makino[2], Thomas J. McHugh[2], Masashi Yanagisawa[1]	[1]International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba, [2]RIKEN BSI
P16	Orexin regulates glucose metabolism under the control of circadian system	Hiroshi Tsuneki, Tsutomu Wada, Toshiyasu Sasaoka	Department of Clinical Pharmacology, University of Toyama, Japan
P17	Prostaglandin D2 is crucial for seizure suppression and postictal sleep	Kaushik MK, Aritake K, Kamauchi S, Hayaishi O, Huang ZL, Lazarus M, and Urade Y	International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba
P18	Spontaneous calcium dynamics in the sleeping cortex.	Takeshi Kanda, Natsuko Tsujino, Ryo Ishii, Masashi Yanagisawa	International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba
P19	Phosphorylation and electron transfer pathway of mCRY1 regulate mammalian circadian rhythmicity.	Koji L. Ode[1,2], Ryohei Narumi[2], Hiroki R. Ueda[1,2]	[1]Dept. of Systems Pharmacology, Grad. Sch. of Med., The University of Tokyo, [2]Lab. for Synthetic Biology, RIKEN QBiC
P20	Spaciotemporal gene expression profiling with efficient brain clearing cocktails and computational analysis	Etsuo A. Susaki[1,2], Kazuki Tainaka[1,2], Dimitri Perrin[2], Hiroki R. Ueda[1,2]	[1]Dept. of Systems Pharmacology, Grad. Sch. of Med., The University of Tokyo, [2]Lab. for Synthetic Biology, RIKEN QBiC
P21	Whole-organ, whole-body imaging with single-cell resolution using chemical cocktails 1	Kazuki Tainaka[1,2], Shimpei I. Kubota[1], Hiroki R. Ueda[1,2]	[1]Dept. of Systems Pharmacology, Grad. Sch. of Med., The University of Tokyo, [2]Lab. for Synthetic Biology, RIKEN QBiC
P22	Whole-organ, whole-body imaging with single-cell resolution using chemical cocktails 2	Shimpei I. Kubota[1], Kazuki Tainaka[1,2], Hiroki R. Ueda[1,2]	[1]Dept. of Systems Pharmacology, Grad. Sch. of Med., The University of Tokyo, [2]Lab. for Synthetic Biology, RIKEN QBiC

Poster Titles at a Glance

No.	Title	Authors	Affiliation
P23	Circadian clock regulation by electrochemically-controlled extracellular electron transfer via redox-active mediator	Pornpitra Tunanunkul[1], Yue Lu[1], Koichi Nishio[1], Seiichiro Izawa[1], Hiroshi Ito[2], Taeko Nishiwaki-Ohkawa[3], Soichiro Kato[4,5,6], Kazuhito Hashimoto[1,4], Shuji Nakanishi[1]	[1]Department of Applied Chemistry, The University of Tokyo, [2]Faculty of Design, Kyushu University, [3]Institute of Transformative Bio-Molecules (WPI-ITbM), Nagoya University, [4]Research Center for Advanced Science and Technology, The University of Tokyo, [5]Bioproduction Research Institute, National Institute of Advanced Industrial Science and Technology, [6]Graduate School of Agriculture, Hokkaido University
P24	Whole-brain imaging of neural activity in the sleep/wake cycle with single cell resolution.	H. Yukinaga, E. Susaki, G. Sunagawa, D.Perrin, J. Hara, H. Ueda	Laboratory for Synthetic Biology, RIKEN QBiC
P25	Phase-mapping the mouse brain with a CRY1::mCherry fluorescent reporter	Arthur Millius, Rikuhiro Yamada, Junko Yoshida, Hideki Ukai, and Hiroki Ueda	Laboratory for Synthetic Biology, RIKEN QBiC
P26	Long-term recording of suprachiasmatic nucleus's field action potential using micro electrode array	Hitoshi Iuchi, Rikuhiro G. Yamada, Hiroki R. Ueda	Laboratory for Synthetic Biology, RIKEN QBiC
P27	Biochemical analysis of CLOCK-containing protein complex in the mouse liver	Kentaro Hirose[1], Yasunori Sugiyama[1], Hikari Yoshitane[1], Hiroko Hata[2], Hiroaki Oyama[2], Yoshitaka Fukada[1]	[1]Department of Biological Science, Graduate School of Science, The University of Tokyo, [2]Medical Proteomics Laboratory, Institute of Medical Science, The University of Tokyo