

Biographical Sketch

Hiroki R. Ueda

Dr. Hiroki R. Ueda was born in Fukuoka, Japan, in 1975. He graduated from the Faculty of Medicine, the University of Tokyo in 2000, and obtained his Ph.D in 2004 from the same university. He was appointed as a team leader in RIKEN Center for Developmental Biology (CDB) from 2003 and promoted to be a project leader at RIKEN CDB in 2009, and to be a group director at RIKEN Quantitative Biology Center (QBiC) in 2011. He became a professor of Graduate School of Medicine, the University of Tokyo in 2013. He is currently appointed as a team leader in RIKEN Center for Biosystems Dynamics Research (BDR), an affiliate professor in Graduate School of Information Science and Technology and an principle investigator in IRCN (International Research Center for Neurointelligence) in the University of Tokyo, an invited professor in Osaka University, and a visiting professor in Tokushima University.

He has an expertise in systems biology and focus on chronobiology by investigating mammalian circadian clocks and sleep/wake cycles. He determined a basic structure of a transcriptional circuit of mammalian circadian clocks and identified multiple delayed negative feedback motifs (Ueda et al, 2002, Ueda et al, 2005, Ukai-Tadenuma et al, 2008, Ukai-Tadenuma 2011). He also focused on long-standing and unsolved questions in chronobiology and found that a singularity behavior (i.e. temporal stopping of circadian clocks) is caused by desynchronization of multiple cellular circadian oscillators (Ukai et al, 2007), and that temperature-insensitive biochemical reactions underlie temperature compensation of mammalian circadian clocks (Isojima et al, 2009, Shinohara et al, 2017). He also invented molecular-timetable methods to detect the circadian time of the body by measuring a snapshot information of circadian clocks (Ueda et al, 2004, Minami et al, 2009, Kasukawa et al, 2012, Narumi et al, 2016). For sleep/wake cycles, he found that Ca^{2+} and CaMKII-dependent hyperpolarization pathways underlie sleep homeostasis (Tatsuki et al, 2016, Sunagawa et al, 2016, Tatsuki et al, 2017, Ode et al, 2017, Shi et al, 2017), and that muscarinic receptors, M1 and M3, as essential genes for REM sleep (Niwa et al, 2018). To accelerate these studies, he also invented whole-brain and whole-body clearing and imaging methods called CUBIC (Susaki et al, 2014, Tainaka et al, 2014, Susaki et al, 2015, Susaki et al, 2016, Tainaka et al, 2016, Kubota et al, 2017, Nojima et al, 2017, Murakami et al, 2018, Tainaka et al, 2018), as well as the next-generation mammalian genetics (Susaki et al, 2017) such as Triple-CRISPR(Sunagawa et al, 2016), ES-mice (Ode et al, 2017, Ukai et al, 2017) and SSS methods (Sunagawa et al, 2016) for one-step production and analysis of KO and KI mice without crossing.

He received awards, including Tokyo Techno Forum 21, Gold Medal (Tokyo Techno Forum 21, 2005), Young Investigator Awards (MEXT, 2006) and IBM Science Award (IBM, 2009), a Young Investigator Promotion Awards (Japanese Society for Chronobiology, 2007). He also received Tsukahara Award (Brain Science Foundation, 2012), Japan Innovator Awards (Nikkei Business Publications Inc. 2004), Yamazaki-Teiichi Prize (Foundation for Promotion of Material Science and Technology of Japan, 2015), Innovator of the Year (2017) and The Ichimura Prize in Science for Excellent Achievement (Ichimura Foundation for New Technology, 2018).

Professional Appointments

2013-present: Professor, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo

2011-present: Laboratory Head, Laboratory for Synthetic Biology, RIKEN

2017-present: Principle Investigator, International Research Center for Neurointelligence, The University of Tokyo

2016-present: Affiliate Professor, Graduate School of Information Science and Technology, The University of Tokyo
2011-present: Invited Professor, Graduate School of Frontier Biosciences, Osaka University
2005-present: Visiting Professor, Tokushima University
2012-2013: Visiting Professor, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo
2010-2013: Visiting Professor, National Institute of Genetics
2009-2013: Invited Professor, Department of Mathematics, Kyoto University
2006-2014: Invited Professor, Department of Biology, Osaka University
2005- 2006: Visiting Professor, Tohoku University
2004-2013: Laboratory Head, Functional Genomics Unit, RIKEN Center for Developmental Biology
2003-2014: Laboratory Head, Laboratory for Systems Biology, RIKEN Center for Developmental Biology
2002-2004: Group Leader, Systems Biology Group, NEDO project, Yamanouchi Pharmaceutical Co., Ltd.
2000-2002: Research Scientist, Yamanouchi Pharmaceutical Co., Ltd.
1999-2000: Technical Staff, Yamanouchi Pharmaceutical Co., Ltd.
1999-2000: Research Assistant, ERATO Kitano Symbiotic Project
1998-1999: Research Assistant, Sony Computer Science Laboratories

Professional Preparation

The University of Tokyo, Faculty of Medicine, M. D., 2000
The University of Tokyo, Graduate School of Medicine, Department of Pharmacology, Ph. D., 2004

Awards

15 Awards for 13 years, including The Ichimura Prize (2018), Innovator of the Year (2017), Yamazaki-Teiichi Prize (2015), Tsukahara Nakaakira Memorial Award (2012), Nagase Award (2011), Changemaker of the year 2011 (2011), JSPS Award (2010), IBM Science Award (2009), Young Scientist Award (MEXT) (2006), Tokyo Techno-Forum 21 Gold medal (2005), Japan Innovator Award (2004).

Other Activities

Founded Japanese Society of Cell Synthesis Research (2005-)
Scientific Editors for EMBO Journal (2011-), and Genes to Cells (2010-)
Research Supervisor, PREST Control and Design of Cellular Functions (2011-)
Organizer of 10 symposiums over 5 years.
Associate Editor for IEEE Life Sciences Letters (2014-)
Associate Editor for NPJ Systems Biology and Applications (2014-)
Member Science Council of Japan (SCJ) (2014-)
The representative of Young Academy of Japan (2015-2018)
International Advisory Board for Advanced Biosystems (2016-)
iScience, Scientific Advisory Board (2018-)

Professional Societies

Society for Research on Biological Rhythms (SRBR)
Society for Neuroscience (SfN)
European Sleep Research Society (ESRS)

European Biological Rhythms Society (EBRS)
Japanese Society for Cell Synthesis Research
The Molecular Biology Society of Japan
The Japanese Biochemical Society
The Japanese Pharmacological Society
The Japanese Society of Sleep Research
The Biophysical Society of Japan
Japan Society for Marmoset Research
Japanese Society of Anti-aging Medicine
The Japan Neuroscience Society

Publication (Original Paper)

Sumiyama K, Matsumoto N, Garçon-Yoshida J, Ukai H, Ueda HR, Tanaka Y. Easy and efficient production of completely embryonic-stem-cell-derived mice using a micro-aggregation device. *PLoS One.* 2018 Sep 19;13(9):e0203056.

Yoshida K, Shi S, Ukai-Tadenuma M, Fujishima H, Ohno RI, Ueda HR. Leak potassium channels regulate sleep duration. *Proc Natl Acad Sci U S A.* 2018 Sep 17.

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Tainaka K, Murakami TC, Susaki EA, Shimizu C, Saito R, Takahashi K, Hayashi-Takagi A, Sekiya H, Arima Y, Nojima S, Ikemura M, Ushiku T, Shimizu Y, Murakami M, Tanaka KF, Iino M, Kasai H, Sasaoka T, Kobayashi K, Miyazono K, Morii E, Isa T, Fukayama M, Kakita A, Ueda HR. Chemical Landscape for Tissue Clearing Based on Hydrophilic Reagents. *Cell Rep.* 2018 Aug 21;24: 2196–2210.

Murakami TC, Mano T, Saikawa S, Horiguchi SA, Shigeta D, Baba K, Sekiya H, Shimizu Y, Tanaka KF, Kiyonari H, Iino M, Mochizuki H, Tainaka K, Ueda HR. A three-dimensional single-cell-resolution whole-brain atlas using CUBIC-X expansion microscopy and tissue clearing. *Nat Neurosci.* 2018 Apr;21(4):625-637.

Udagawa T, Harita Y, Miura K, Mitsui J, Ode KL, Morishita S, Urae S, Kanda S, Kajiho Y, Tsurumi H, Ueda HR, Tsuji S, Saito A, Oka A. Amnionless-mediated glycosylation is crucial for cell surface targeting of cubilin in renal and intestinal cells. *Sci Rep.* 2018 Feb 5;8(1):2351.

Yamamoto J, Imai J, Izumi T, Takahashi H, Kawana Y, Takahashi K, Kodama S, Kaneko K, Gao J, Uno K, Sawada S, Asano T, Kalinichenko VV, Susaki EA, Kanzaki M, Ueda HR, Ishigaki Y, Yamada T, Katagiri H. Neuronal signals regulate obesity induced β-cell proliferation by FoxM1 dependent mechanism. *Nat Commun.* 2017 Dec 5;8(1):1930.

Hughes ME et al, Guidelines for Genome-Scale Analysis of Biological Rhythms. *J Biol Rhythms.* 2017 Oct;32(5):380-393.

Ukai H, Kiyonari H, Ueda HR. Production of knock-in mice in a single generation from embryonic stem cells. *Nat Protoc.* 2017 Nov;12(12):2513-30.

Shinohara Y, Koyama YM, Ukai-Tadenuma M, Hirokawa T, Fujishima H, Umehara T, Tainaka K, Ueda HR. Temperature-Sensitive Substrate and Product Binding Underlie Temperature-Compensated Phosphorylation in the Clock. *Molecular Cell.* 2017 Sep 7;67(5): 783-798

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Kubota SI, Takahashi K, Nishida J, Morishita Y, Ehata S, Tainaka K, Miyazono K, Ueda HR. Whole-Body Profiling of Cancer Metastasis with Single-Cell Resolution. *Cell Rep.* 2017 Jul 5;20(1):236-250.

Sugai SS, Ode KL, Ueda HR. A Design Principle for an Autonomous Post-translational Pattern Formation. *Cell Rep.* 2017 Apr 25;19(4):863-874.

Hosoya M, Fujioka M, Sone T, Okamoto S, Akamatsu W, Ukai H, Ueda HR, Ogawa K, Matsunaga T, Okano H. Cochlear Cell Modeling Using Disease-Specific iPSCs Unveils a Degenerative Phenotype and Suggests Treatments for Congenital Progressive Hearing Loss. *Cell Rep.* 2017 Jan 3;18(1):68-81.

Ode KL, Ukai H, Susaki EA, Narumi R, Matsumoto K, Hara J, Koide N, Abe T, Kanemaki MT, Kiyonari H, Ueda HR. Knockout-Rescue Embryonic Stem Cell-Derived Mouse Reveals Circadian-Period Control by Quality and Quantity of CRY1. *Mol Cell.* 2017 Jan 5;65(1):176-190.

Narumi R, Shimizu Y, Ukai-Tadenuma M, Ode KL, Kanda GN, Shinohara Y, Sato A, Matsumoto K, Ueda HR. Mass spectrometry-based absolute quantification reveals rhythmic variation of mouse circadian clock proteins. *Proc Natl Acad Sci U S A.* 2016 Jun 14;113(24):E3461-7.

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Tatsuki F, Sunagawa GA, Shi S, Susaki EA, Yukinaga H, Perrin D, Sumiyama K, Ukai-Tadenuma M, Fujishima H, Ohno R, Tone D, Ode KL, Matsumoto K, Ueda HR. Involvement of Ca(2+)-Dependent Hyperpolarization in Sleep Duration in Mammals. *Neuron.* 2016 Apr 6;90(1):70-85.

Sunagawa GA, Sumiyama K, Ukai-Tadenuma M, Perrin D, Fujishima H, Ukai H, Nishimura O, Shi S, Ohno R, Narumi R, Shimizu Y, Tone D, Ode KL, Kuraku S, Ueda HR. Mammalian Reverse Genetics without Crossing Reveals Nr3a as a Short-Sleeper Gene. *Cell Rep.* 2016 Jan 26;14(3):662-77.

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Harumoto T, Ito M, Shimada Y, Kobayashi TJ, Ueda HR, Lu B, Uemura T. Atypical cadherins Dachsous and Fat control dynamics of noncentrosomal microtubules in planar cell polarity. *Dev Cell*. 2010 Sep 14;19(3):389-401.

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AK-AH76, regulates mammalian circadian clock. *J Antibiot* (Tokyo). 2008 Dec;61(12):756-8.

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Ukai-Tadenuma M, Kasukawa T, Ueda HR. Proof-by-synthesis of the transcriptional logic of mammalian circadian clocks. *Nat Cell Biol*. 2008 Oct;10(10):1154-63.

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Kiyohara YB, Nishii K, Ukai-Tadenuma M, Ueda HR, Uchiyama Y, Yagita K. Detection of a circadian enhancer in the mDbp promoter using prokaryotic transposon vector-based strategy. *Nucleic Acids Res*. 2008 Mar;36(4):e23.

Ukai H, Kobayashi TJ, Nagano M, Masumoto KH, Sujino M, Kondo T, Yagita K, Shigeyoshi Y, Ueda HR. Melanopsin-dependent photo-perturbation reveals desynchronization underlying the singularity of mammalian circadian clocks. *Nat Cell Biol*. 2007 Nov;9(11):1327-34.

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Yamada R, Ueda HR. Microarrays: statistical methods for circadian rhythms. *Methods Mol Biol*. 2007;362:245-64.

Uno K, Ueda HR. Microarrays: quality control and hybridization protocol. *Methods Mol Biol*. 2007;362:225-43.

Ueda HR. Systems biology flowering in the plant clock field. *Mol Syst Biol*. 2006;2:60.

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Kiyohara YB, Tagao S, Tamanini F, Morita A, Sugisawa Y, Yasuda M, Yamanaka I, Ueda HR, van der Horst GT, Kondo T, Yagita K. The BMAL1 C terminus regulates the circadian transcription feedback loop. *Proc Natl Acad Sci U S A*. 2006 Jun 27;103(26):10074-9.

Kurimoto K, Yabuta Y, Ohinata Y, Ono Y, Uno KD, Yamada RG, Ueda HR, Saitou M. An improved single-cell cDNA amplification method for efficient high-density oligonucleotide microarray analysis. *Nucleic Acids Res*. 2006 Mar 17;34(5):e42.

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Publication (Review)

Shi S, Ueda HR. Ca(2+) -Dependent Hyperpolarization Pathways in Sleep Homeostasis and Mental Disorders. *Bioessays.* 2018 Jan;40(1).

Ode KL, Ueda HR. Design Principles of Phosphorylation-Dependent Timekeeping in Eukaryotic Circadian Clocks. *Cold Spring Harb Perspect Biol.* 2017 Oct 16. pii: a028357.

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Tainaka K, Kuno A, Kubota SI, Murakami T, Ueda HR. Chemical Principles in Tissue Clearing and Staining Protocols for Whole-Body Cell Profiling. *Annu Rev Cell Dev Biol.* 2016 Oct 6;32:713-741.

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