

CURRICULUM VITAE

NAME: Steven Marion Reppert
DATE OF BIRTH: September 4, 1946
PLACE OF BIRTH: Sioux City, IA
E-MAIL: Steven.Reppert@umassmed.edu
WEBSITES: <http://www.umassmed.edu/neurobiology/faculty/reppert.cfm>
<http://reppertlab.org/>

DEGREES:

1973 B.S. University of Nebraska, Omaha, NE
1973 M.D. University of Nebraska, College of Medicine, Omaha, NE
(with Distinction)
1993 M.A. Harvard University (Honorary)

POSTDOCTORAL TRAINING:

Internship and Residencies:

1973-1974 Pediatric Intern, Massachusetts General Hosp, Boston
1974-1976 Pediatric Resident, Massachusetts General Hosp, Boston

Fellowships:

1973-1976 Clinical Fellow, Harvard Medical School
1976-1979 Postdoctoral fellow in the Laboratory of David C. Klein, Section on Neuroendocrinology, National Institutes of Health, Bethesda, MD

LICENSURE AND CERTIFICATION:

1976 Massachusetts License Registration No. 39414

ACADEMIC APPOINTMENTS:

2001- Higgins Family Professor of Neuroscience, U Mass Medical School
2001- Professor & Chair, Dept of Neurobiology, U Mass Medical School
1993-2003 Professor, Harvard Medical School
1985-1993 Associate Professor, Harvard Medical School
1981-1985 Assistant Professor, Harvard Medical School
1979-1981 Instructor, Harvard Medical School

HOSPITAL APPOINTMENTS:

1983-2001 Director, Laboratory of Developmental Chronobiology,
Massachusetts General Hospital

VISITING APPOINTMENTS:

2001- Pediatrician, Massachusetts General Hospital
1989-1990 Visiting Scientist, Lab of Molecular Neurobiology, MGH

AWARDS AND HONORS:

- 2013 *Doctor honoris causa* (honorary doctorate) University of South Bohemia
- 2012 G.J. Mendel Honorary Medal for Merit in Biological Sciences from the Academy of Sciences of the Czech Republic
- 2011-2001- Fellow, American Association for the Advancement of Science
Higgins Family Professor of Neuroscience, UMass Med School
- 2002-2004 President, Society for Research on Biological Rhythms
- 1998 Chair, Gordon Conference on Pineal Cell Biology
- 1993 M.A. (honorary), Harvard University
- 1992-2002 NIH-NICHD MERIT Award
- 1989 E. Mead Johnson Award for distinguished research
- 1987- Member, American Association for Clinical Investigation
- 1985-1990 Established Investigator, American Heart Association
- 1981-1983 Basil O'Connor Early Scholar Award
- 1981-1984 Charles A. King Trust Research Fellow, Medical Foundation Inc
- 1980 Charles H. Hood Foundation Award
- 1973 M.D. with Distinction
- 1973 Alpha Omega Alpha Honor Medical Society

HONORIFIC LECTURES/LECTURESHIPS (since 2000)

- 2012 Presidential Symposium, Society for Research on Biological Rhythms
- 2012 Plenary Talk, 53rd Annual Drosophila Research Conference, Chicago
- 2012 Keynote Speaker, 2nd Annual Symposium in Brain, Behavior & Evolution, U of Texas at Austin
- 2011 The John G. Nicholls Endowed Lecture, Marine Biological Labs, Woods Hole
- 2010 UT San Antonio, Inaugural Keynote Lecture at graduate student retreat, Dept of Physiology
- 2010 Dupont Lecture on Invertebrate Neurobiology, U of Arizona
- 2010 Keynote Lecture, 15th Annual Symposium on Biotechnology Education, Museum of Science, Boston
- 2009 Inaugural Lecture, Mexican Society for Physiology, Morelia
- 2009 Plenary Lecture, European Pineal & Biological Rhythms Society Meeting, Strasburg
- 2006 NICHD Pioneer in Circadian Biology Lecture, NIH, Bethesda
- 2006 Mayer Lecture, Wellesley College
- 2005 Plenary Lecture, European Pineal & Biological Rhythms Society Meeting, Frankfurt
- 2005 Vanderbilt University MSTP Physician-Scientist Special Lecture
- 2004 Keynote Lecture, Behavior Club Symposium, Tufts University
- 2004 Featured Lecture, Hood Foundation Research Symposium, Boston
- 2004 Special Lecture, Society for Neuroscience Annual Meeting, San Diego

- 2004 Green College Thematic Lectureship, Images of the Cell, U of British Columbia
- 2004 Helen Jones Memorial Lecture, Massachusetts General Hosp
- 2002 Plenary Lecture, European Pineal & Biological Rhythms Society Meeting, Scotland
- 2002 Dolan Pritchett Memorial Lecture, U Penn, Dept Pharmacology
- 2000 Lecturer at Inaugural Symposium. Dept of Genetics, Dartmouth Medical School
- 2000 Plenary Lecture, FENS 2000, Brighton England

RESEARCH GRANTS (as Principal Investigator):

- 2010-2014 AFOSR FA9550-10-1-0480
- 2009-2011 NIH R01 GM086794-02S1
- 2008-2012 NIH R01 GM086794
- 2003-2008 NIH R01 NS047141
- 2003-2009 NIH R01 NS39303
- 1998-2001 NIH R01 GM55820
- 1997-2000 Research Grant of International Human Frontiers Science Program
- 1994-2000 Sponsored Research Agreement, Bristol-Myers Squibb
- 1993-1999 AFOSR F49620-97-1-004
- 1992-1993 Grant from Gensia Pharmaceuticals
- 1990-2000 NIH R01 DK42125
- 1990 Grant from Whitby Research
- 1986-1989 NIH R01 AM38116
- 1986-1987 Grant-In-Aid, American Heart Assoc
- 1985-1990 Established Investigatorship, American Heart Assoc
- 1984-1988 Basic Research Grants, March of Dimes
- 1983-1986 NIH R01 NS18755
- 1981-2002 NIH R01 HD14427 – converted to R27 MERIT Award last 10 yrs
- 1981-1985 Basil O'Connor Early Scholar Award, Natl Fnd March of Dimes
- 1981-1983 Charles King Trust Fellowship
- 1980 Milton Fnd
- 1980 Charles H. Hood Fnd

PATENTS (as Principal Inventor):

- Pat. no. 5,516,894 A2b-Adenosine Receptor and Related Molecules and Methods
- Pat. no. 5,856,124 DNA Encoding High-Affinity Melatonin Receptors
- Pat. no. 5,889,177 Melatonin 1A Receptor Gene Regulatory Regions and Uses Thereof
- Pat. no. 6,037,131 Melatonin 1a Receptor Gene Regulatory Regions and Uses Thereof
- Pat. no. 6,326,526 Melatonin Receptor-Deficient Mice and Uses Thereof
- Pat. no. 6,475,744 Methods for Identifying Compounds Which Modulate Circadian Rhythms
- Pat. no. 7,081,349 High-affinity melatonin receptor and uses thereof

INVITED SYMPOSIA/SEMINARS (Since 2000)

- 2000 Dept of Genetics, U of Utah
Dept of Biochemistry, McMaster U
Florida State University Rushton Symposium on Biological Clocks,
Keystone Symposium, Genetic Basis of Brain Development and
Dysfunction, Taos
Institute for Biomolecular Science, U South Florida,
GC Pineal Cell Biology, Cambridge
Royal Society Seminar on The Measurement of Time, London
Graduate Student Invited Speaker, Dept of Neurobiology, Yale
- 2001 Annenberg Center, Sleep Disorders Conference, Rancho Mirage, CA
UMass Boston, Dept of Biology Seminar
Keystone Symposium on Molecular Clocks, Tahoe City
- 2002 NIH Neuroscience Series, NINDS, Bethesda
Society for Research on Biological Rhythms, Amelia Island
GC Pineal Cell Biology, Ventura
- 2003 Baylor School of Medicine, Dept of Genetics
MBL lecture, Woods Hole
Mosbacher Kolloquium, The Rhythm of Life: Molecular
Mechanisms of Circadian Clocks, Mosbach Germany
GC Chronobiology, Barga, Italy
- 2004 St. Jude Children's Research Hospital, Basic Science Talk
UCSF, Program in Neuroscience Seminar
U of Providence, Biology Dept
Pineal Cell Biology GC, Oxford
- 2005 Massachusetts General Hosp, Dept Molecular Biology
Women's Health Research Institute at Wyeth Research,
Merck Research Laboratories, West Point, PA
Yale, Dept of Cellular and Molecular Physiology
RCMI Symposium on Molecular approaches to Brain Function, City
College, City University of NY, Dept of Biology
- 2006 International Symposium on Insect Genetics and Genomics,
Hyderabad, India
Pineal Cell Biology Gordon Conference, Buellton, CA
U of New Hampshire, Zoology Dept
Society for Research on Biological Rhythms, Invited speaker, Sandestin,
Tufts University, Neuroscience Seminar Series
UNC seminar, Dept Mol Biol

- 2007 U Illinois Urbana, Dept Entomology
 Boston U, Biology Dept
 WWF forum on monarch butterfly conservation, Morelia, Mexico
 HHMI Janelia Farms Symposium on Visual Processing in Insects
 Cold Spring Harbor Symposium on Clocks and Rhythms
 UC Irvine, Dept of Ecology and Evolutionary Biology
- 2008 Society for Research on Biological Rhythms, Invited speaker, Sandestin,
 GC Neuroethology, Breaking news in insect neuroethology talk, Oxford
 McGuire Center for Lepidoptera and Biodiversity, Gainesville, FL
 UMass Medical School Research Retreat, Plenary talk, Woods Hole
 Yale University, Dept of Ecology and Evolutionary Biology
 U Virginia, Dept Biology, Grad Student invited speaker
- 2009 Royal Society Special Lecture on magnetoreception, London
 The 11th International Symposium on Spin and Magnetic Field
 Effects in Chemistry and Related Phenomena, Ontario
 UMass Amherst, Entomology Departmental Seminar
 Evolution of vision workshop, Fondation des Treilles, France
- 2010 Clark University, Dept of Biology seminar
 Brandeis University, Dept Biology Seminar
 NIH/NIDDK Circadian Workshop, Bethesda
 CIG Symposium on "Sensing the environment", Lausanne
 GC on Visual System Development, Barga, Italy.
 Program in Gene Function and Expression, UMass Med School
 Harvard Brain Science Center
 Washington University St. Louis, Dept Biology seminar.
 CANMove Centre and Vision Group, U of Lund, Sweden
- 2011 Dept of Biology, U of North Carolina, Chapel Hill
 CANMove talk, U Lund, Sweden
 Stanford Institute for Neuro-Innovation&Translational Neuroscience
- 2012 GC on Photosensory Receptors & Signal Transduction, Galveston, Texas
 Program in Molecular Medicine, UMass Med School
 U of Texas at Austin, Section on Integrative Biology
 Baylor Medical Center, Houston, Neuroscience
 U of Notre Dame, Dept of Biological Sciences
 Cambridge Neuroscience, U of Cambridge, UK
 European Clock Club, Keynote speaker, U of Edinburgh, UK
 U of Leicester, Genetics Dept, UK
 Small brains, Big ideas, Santiago, Chile (Outreach & Seminar Talks)
 Case Western Reserve, Neuroscience & Biology
 North Carolina State Keck Center Distinguished Speaker

- 2013 SICB Symposium, San Francisco
 Cell Biology Seminar, UMass Medical School
 UC Davis, Dept Entomology Seminar
 Vienna BioCenter Seminar, Vienna
 Faculty of Science, U of South Bohemia
 Czech Academy of Sciences, Institute of Organic Chemistry and
 Biochemistry of the Academy of Sciences, Prague
 Czech Academy of Sciences, Institute of Physiology, Prague
 Physics-Biology Colloquium, U of Miami
 Janelia Conference: Sensory Signaling in Model Organisms
 Champalimaud Neuroscience Symposium, Lisbon, Portugal
 Evolution of vision workshop, Fondation des Treilles, France
 Peking University School of Life Sciences, Beijing
 Chinese Academy of Sciences, Shanghai
 Vanderbilt U, Dept of Biology
 Cornell U, Dept of Ecology and Evolutionary Biology
- 2014 U of Washington, Dept of Pharmacology
 IUSSI Meeting, Cairns, Australia

SYNOPSIS OF MAJOR RESEARCH CONTRIBUTIONS

- Defined the field of fetal circadian clocks using physiological, metabolic and molecular techniques.

Reppert SM, Schwartz WJ. Maternal coordination of the fetal biological clock in utero. ***Science*** 1983; 220:969-971.

Reppert SM, Schwartz WJ. The suprachiasmatic nuclei of the fetal rat: Characterization of a functional circadian clock using [¹⁴C]-labeled deoxyglucose. ***J Neurosci*** 1984; 4:1677-1682.

Reppert SM, Schwartz WJ. The maternal suprachiasmatic nuclei are necessary for maternal coordination of the developing circadian system. ***J Neurosci*** 1986; 6:2724-2729.

Weaver DR, Rivkees SA, Reppert SM. D1-dopamine receptors activate c-fos expression in the fetal biological clock. ***Proc Natl Acad Sci USA*** 1992; 89:9201-9204.

- Cloned a family of G-protein coupled receptors for the pineal hormone melatonin in mice, humans, birds and zebrafish. Designed gene targeting strategies for the two mouse receptors and reported results of functional studies. Melatonin has been used to treat jet lag and sleep disorders to which the cloning of the mammalian receptors has contributed.

Ebisawa T, Karne S, Lerner MR, Reppert SM. Expression cloning of a high-affinity melatonin receptor for *Xenopus* dermal melanophores. ***Proc Natl Acad Sci USA*** 1994; 91:6133-6137.

- Reppert SM, Weaver DR, Ebisawa T. Cloning and characterization of a mammalian melatonin receptor that mediates reproductive and circadian responses. **Neuron** 1994; 13:1177-1185.
- Reppert SM, Godson C, Mahle CD, Weaver DR, Slaugenhaupt SA, Gusella, JF. Molecular characterization of a second melatonin receptor expressed in human retina and brain: The Mel_{1b}-melatonin receptor. **Pro Natl Acad Sci USA** 1995; 92, 8734-8738.
- Reppert SM, Weaver DR, Godson C, Cassone VM, Kolakowski, LF. Melatonin receptors are for the birds: Molecular analysis of two receptor subtypes differentially expressed in chick brain **Neuron** 1995; 15, 1003-1015.
- Reppert SM, Weaver DR, Mahle CD, Kolakowski, LF. Cloning of a melatonin-related receptor from human pituitary. **FEBS Lett** 1996; 386, 219-224.
- Roca AL, Godson C, Weaver DR, Reppert SM. Structure, characterization and expression of the gene encoding the mouse Mel_{1a} melatonin receptor. **Endocrinology** 1996; 137, 3469-3477.
- Weaver DR, Liu C, Reppert SM. Nature's knockout: The Mel_{1b} melatonin receptor is not necessary for reproductive and circadian responses in the Siberian hamster **Mol Endocrinol** 1996; 10, 1478-1487.
- Liu C, Weaver DR, Jin X, Shearman LP, Pieschl RL, Gribkoff VK, Reppert SM. Molecular dissection of two distinct actions of melatonin on the suprachiasmatic circadian clock. **Neuron** 1997; 19, 91-102.

- Discovered that the circadian clock mechanism in the mammalian suprachiasmatic nucleus (SCN), the site of the master brain clock, is cell autonomous (i.e., contained within single cells), using clever electrophysiological approach for monitoring individual neurons in culture.

- Welsh DK, Logothetis DE, Meister M, Reppert SM. Individual neurons dissociated from rat suprachiasmatic nucleus express independently phased circadian firing rhythms. **Neuron** 1995; 14:697-706.
- Liu C, Weaver DR, Strogatz SH, Reppert SM. Cellular construction of a circadian clock: period determination in the suprachiasmatic nuclei. **Cell** 1997; 91, 855-860.
- Liu C, Reppert SM. GABA synchronizes clock cells within the suprachiasmatic circadian clock. **Neuron** 2000; 25, 123-128.

- Presented the "breakout" sequence of the clock gene period in silkworm, which aided the initial cloning of mammalian Period homologs.

- Reppert SM, Tsai T, Roca A, Sauman I. Cloning of a structural and functional homolog of the circadian clock gene *period* from the giant silkworm *Antheraea pernyi*. **Neuron** 1994; 13:1167-1176.

- Defined the functions of clock genes which encode PERIOD2 and PERIOD3 in the mouse clockwork.

Shearman, LP, Zylka MJ, Weaver DR, Kolakowski Jr LF, Reppert SM. Two *period* homologs: Circadian oscillations and photic regulation in the suprachiasmatic nuclei. *Neuron* 1997; 19, 1261-1269.

Zylka MJ, Shearman LP, Weaver DR, Reppert SM. Three period homologs in mammals: Differential light regulation in the suprachiasmatic circadian clock and oscillating transcripts outside of brain. *Neuron* 1998; 20, 1103-1110.

Bae K, Jin X, Maywood ES, Hastings MH, Reppert SM, Weaver DR. Differential functions of mPer1, mPer2 and mPer3 in the SCN circadian clock. *Neuron* 2001; 30, 525-536.

- Defined a general molecular mechanism used for regulating clock-controlled genes in mammals.

Jin X, Shearman LP, Weaver DR, Zylka MJ, De Vries GJ, Reppert SM. A molecular mechanism regulating rhythmic output from the suprachiasmatic circadian clock. *Cell* 1999; 96, 57-68.

- Discovered the function of CRYPTOCHROMES, as essential clock genes, within the mammalian circadian clock.

Kume K, Zylka MJ, Sriram S, Shearman LP, Weaver DR, Jin X, Maywood ES, Hastings MH, Reppert SM. mCRY1 and mCRY2 are essential components of the negative limb of the circadian clock feedback loop. *Cell* 1999; 98, 193-205.

- Defined interlocking transcriptional feedback loops in the mouse clockwork.

Shearman LP, Sriram S, Weaver DR, Maywood ES, Chaves I, Zheng B, Kume K, Lee CC, van der Horst, GTJ, Hastings MH, Reppert SM. Interacting molecular loops in the mammalian circadian clock. *Science* 2000; 288, 1013-1019.

- Described post-translational mechanisms that regulate the mammalian circadian clock by developing specific antibodies against the major mouse clock proteins and performing chromatin immunoprecipitation experiments.

Lee C, Etchegaray J-P, Cagampang FRA, Loudon ASI, Reppert SM. Post-translational mechanisms regulate the mammalian circadian clock. *Cell* 2001; 107, 855-867.

Lee C, Weaver DR, Reppert SM. Direct association between mouse PERIOD and CKIε is critical for a functioning circadian clock. *Mol Cell Biol* 2004; 24, 584-594.

- Defined the importance of rhythmic histone acetylation in the mammalian clockwork and proposed the existence of a “histone code” for the clockwork. A cottage industry of chromatin regulation of clock gene expression has sprung from this study.

Etchegaray JP, Lee C, Wade PA, Reppert SM. Rhythmic histone acetylation underlies transcription in the mammalian circadian clock. *Nature* 2003; 421, 177-182.

- Showed that CLOCK and NPAS2 have overlapping roles in the suprachiasmatic circadian clock but that peripheral oscillators require CLOCK only.

DeBruyne JP, Noton E, Lambert CM, Maywood ES, Weaver DR, Reppert SM. A clock shock: mouse clock is not required for circadian oscillator function. *Neuron* 2006; 50, 465-477.

DeBruyne JP, Weaver DR, Reppert SM. CLOCK and NPAS2 have overlapping roles within the suprachiasmatic circadian clock. *Nature Neurosci* 2007; 10, 543-545.

DeBruyne JP, Weaver DR, Reppert SM. Peripheral circadian oscillators require CLOCK. *Curr Biol* 2007; 17, R538-R539.

- Discovered and characterized a family of vertebrate-like CRYPTOCHROMES in insects, revolutionizing the function of CRYs in non-drosophilid insects.

Zhu H, Yuan Q, Briscoe AD, Froy O, Casselman A, Reppert SM. The two CRYs of the butterfly. *Curr Biol* 2005; 15, R953-R954.

Yuan Q, Metterville D, Briscoe AD, Reppert SM. Insect cryptochromes: Gene duplication and loss define diverse ways to construct insect circadian clocks. *Mol Biol Evol* 2007; 24, 948-955.

- Defined components of time-compensated sun compass orientation in migrating monarch butterflies.

Froy O, Gotter AL, Casselman AL, Reppert SM. Illuminating the circadian clock in monarch butterfly migration. *Science* 2003; 300, 1303-1305.

Reppert SM, Zhu H, White R. Polarized light helps monarch butterflies navigate. *Curr Biol* 2004; 14, 155-158.

Merlin C, Gegear RJ, Reppert SM. Antennal circadian clocks coordinate sun compass orientation in migratory monarch butterflies. *Science* 2009; 325: 1700-1704.

Heinze S, Reppert SM. Sun compass integration of skylight cues in migratory monarch butterflies. *Neuron* 2011; 69, 345-358.

Heinze S, Reppert SM. Anatomical basis of sun compass navigation I: The general layout of the monarch butterfly brain. *J Comp Neurol* 2012; 520:1599-1628.

- Guerra PA, Merlin C, Gegear RJ, Reppert SM. Discordant timing between antennae disrupts sun compass orientation in migratory monarch butterflies. **Nat Commun** 2012; 3:958.
- Heinze S, Florman J, Asokaraj S, el Jundi B, Reppert SM. Anatomical basis of sun compass navigation II: The neuronal composition of the central complex of the monarch butterfly. **J Comp Neurol** 2013; 521:267-298.
- Guerra P, Reppert SM. Coldness triggers northward flight in re-migrant monarch butterflies. **Curr Biol** 2013; 5:419-423.

- Discovered and defined a novel circadian clock mechanism in lepidopterans.

- Sauman, I., Reppert SM. Circadian clock neurons in the silkworm *Antheraea pernyi*: Novel mechanisms of *period* protein regulation. **Neuron** 1996; 17, 889-900.
- Sauman I, Briscoe AD, Zhu H, Shi D, Froy O, Stalleicken J, Yuan Q, Casselman A, Reppert SM. Connecting the navigational clock to sun compass input in monarch butterfly brain. **Neuron** 2005; 46, 457-467.
- Zhu H, Sauman I, Yuan Q, Casselman A, Emery-Le M, Emery P, Reppert SM. Cryptochromes define a novel circadian clock mechanism in monarch butterflies that may underlie sun compass navigation. **PLoS Biol.** 2008; 6, e4.

- Produced a brain expressed sequence tag database for monarch butterflies, performed expression profiling between summer and migratory monarchs, and initiated sequencing of monarch butterfly genome.

- Zhu H, Casselman A, Reppert SM. Chasing migration genes: A brain expressed sequence tag resource for summer and migratory monarch butterflies (*Danaus plexippus*). **PLoS One** 2008; 3, e1293.
- Zhu H, Gegear RJ, Casselman A, Kanginakudru S, Reppert SM. Defining behavioral and molecular differences between summer and migratory monarch butterflies. **BMC Biol** 2009; 7:14.

- Provided first genetic evidence that cryptochrome is essential for magnetosensitivity in any animal and that both the Drosophila-type CRY and vertebrate-type CRY can mediate light-sensitive magnetosensitivity using transgenic Drosophila.

- Gegear R, Casselman A, Waddell S, Reppert SM. Cryptochrome mediated light-dependent magnetosensitivity in *Drosophila*. **Nature** 2008; 454, 1014-1018.
- Gegear RJ, Foley LE, Casselman, A, Reppert SM. Animal cryptochromes mediate magnetoreception through an unconventional photochemical mechanism. **Nature** 2010; 463, 804-807.

- Presented the draft sequence of the monarch butterfly genome, the first genome of a butterfly and of a long-distance migrating species.

Zhan S, Merlin C, Boore JL, Reppert SM (2011). The monarch butterfly genome yields insights into long-distance migration. *Cell* 147:1171-1185.

Zhan S, Reppert SM (2013). MonarchBase: the monarch butterfly genome database. *Nucl Acid Res* doi: 10.1093/nar/gks1057.

- Developed a high efficiency gene targeting strategy in the Monarch butterfly using zinc finger nucleases that is applicable to other lepidopterans.

Merlin C, Beaver LE, Taylor OR, Wolfe SA, Reppert SM (2013). Efficient targeted mutagenesis in the monarch butterfly using zinc finger nucleases. *Genome Res* 23:169-180.

OUTREACH/NEWS ITEMS (since 2003)

See: <http://reppertlab.org/newsoutreach/>