CURRICULUM VITAE

John Ewer
Instituto de Neurociencia
Facultad de Ciencias,
Universidad de Valparaiso
Pasaje Harrington 287
Casilla 5047, Correo 4. Playa Ancha,
Valparaiso, CHILE

Tel: (56)(32) 250-8187
Fax: (56)(32) 250-8027
e-mail: john.ewer@uv.cl
Website: https://www.ewerlab.org/ and. https://cinv.uv.cl/members/jewer/

EDUCATION / TRAINING

Year	Degree	Institution
1984	B.A./B.S.	University of Chile, Santiago, Chile
1984	M.S.	University of Chile, Santiago, Chile
1990	Ph.D.	Brandeis University, Waltham, MA

PROFESSIONAL EXPERIENCE:

1991-96	Postdoctoral fellow, Zoology Department, University of Washington, Seattle, Washington, USA. Jim Truman, Ph.D., Principal Investigator.
1996	Postdoctoral fellow, Neuroscience Institute, University of Oregon, Eugene, Oregon, USA. Janis Weeks, Ph.D., Principal Investigator.
1996-98	Postdoctoral fellow, Biology Department, York University, North York, Ontario, Canada. Marla Sokolowski, Ph.D. Principal Investigator.
1998-2004	Department of Entomology. Cornell University, Ithaca, NY, USA. Assistant Professor.
2004- 2006	Department of Entomology. Cornell University, Ithaca, NY, USA. Associate Professor.
2006-present	Instituto de Neurociencia, Universidad de Valparaiso, Valparaiso, Chile; Professor
2012-2014	NIH/NINDS; Special volunteer, Lab Dr. Miguel Holmgren.

SCIENTIFIC EDITORIAL BOARDS

Journal of Insect Science (Associate Editor); Insect Biochemistry and Molecular Biology (Editorial Board); Current opinions in Insect Science (Editorial Board); PLoS Genetics (Associate Editor); Current Research in Insect Science (Editorial Board); eLife (Reviewing Editor).

AWARDS AND HONORS

University of Valparaíso Medal (2016)
Member of DANA Alliance for Brain Initiatives (DABI) (2019)

PERSONAL STATEMENT

I am generally interested in the control of behavior by neuropeptides and by the circadian (biological) clock. Thus, my scientific contributions have centered on understanding how neuropeptides regulate complex behaviors and how the circadian clock imposes a daily rhythmicity to behavior. Most of my research has been done using the fruit fly, *Drosophila melanogaster*, as this model offers an opportunity to study the behavior of animals in which very precise manipulations of gene expression have been effected. More recently, I have become interested in exploring in Drosophila the impact on behavior and development of mutations which in humans are associated with neural diseases.

PUBLICATIONS:

Refereed journal articles

Wegener, C., E. Amini, J. Cavieres-Lepe and J. Ewer (2024). Neuronal and endocrine mechanisms underlying the circadian gating of eclosion: insights from *Drosophila*. Curr Opin Insect Sci 66: 101286. DOI: 10.1016/j.cois.2024.101286.

Cavieres-Lepe, J., E. Amini, M. Zabel, D. R. Nassel, R. Stanewsky, C. Wegener and J. Ewer (2024). Timed receptor tyrosine kinase signaling couples the central and a peripheral circadian clock in *Drosophila*. Proc Natl Acad Sci U S A 121(11): e2308067121. DOI: 10.1073/pnas.2308067121.

Palacios-Muñoz, A., D. de Paula Moreira, V. Silva, I. E. García, F. Aboitiz, M. Zarrei, G. Campos, O. Rennie, J. L. Howe, E. Anagnostou, P. Ambrozewic, S. W. Scherer, M. R. Passos-Bueno and J. Ewer (2022). Mutations in *trpγ*, the homologue of TRPC6 autism candidate gene, causes autism-like behavioral deficits in *Drosophila*. Mol Psychiatry. doi: 10.1038/s41380-022-01555-1

Piñeiro, M., W. Mena, J. Ewer and P. Orio (2021). Extracting temporal relationships between weakly coupled peptidergic and motoneuronal signaling: Application to *Drosophila* ecdysis behavior. PLoS Comput Biol 17(12): e1008933. doi:10.1371/journal.pcbi.1008933

Silva, V., A. Palacios-Muñoz, M. Volonté, L. Frenkel, J. Ewer and S. Ons (2021). Orcokinin neuropeptides regulate reproduction in the fruit fly, *Drosophila melanogaster*. Insect Biochem Mol Biol 139: 103676. doi:10.1016/j.ibmb.2021.103676

Mark, B., L. Bustos-Gonzalez, G. Cascallares, F. Conejera and J. Ewer (2021). The circadian clock gates *Drosophila* adult emergence by controlling the timecourse of metamorphosis. Proc Natl Acad Sci U S A 118(27): e2023249118. doi: 10.1073/pnas.2023249118

Anreiter, I., A. M. Allen, O. E. Vasquez, L. To, S. J. Douglas, J. V. Alvarez, J. Ewer and M. B. Sokolowski (2021). The *Drosophila foraging* gene plays a vital role at the start of metamorphosis for subsequent adult emergence. J Neurogenet: 1-13. doi: 10.1080/01677063.2021.1914608

Silva, V., A. Palacios-Muñoz, Z. Okray, K. L. Adair, S. Waddell, A. E. Douglas and J. Ewer (2021). The impact of the gut microbiome on memory and sleep in *Drosophila*. J Exp Biol 224(Pt 3), p.1-11. doi: 10.1242/jeb.233619

Aspé-Sánchez, M., Mengotti, P.,Rumiati, R.I., Rodriguez-Sickert, C., Ewer, J., and Billeke, P. (2020) Late frontal negativity discriminates outcomes and intentions in

trust-repayment behavior. Front. Psychol. **11**: 532295. doi: 10.3389/fpsyg.2020.532295.

Scott, R. L., F. Diao, V. Silva, S. Park, H. Luan, J. Ewer and B. H. White (2020). Non-canonical Eclosion Hormone-Expressing Cells Regulate *Drosophila* Ecdysis. iScience **23**(5): 101108. doi: 10.1016/j.isci.2020.101108.

Flaven-Pouchon, J., J. V. Alvarez, C. Rojas and J. Ewer (2020). The tanning hormone, bursicon, does not act directly on the epidermis to tan the *Drosophila* exoskeleton. BMC Biol **18**(1): 17. doi: 10.1186/s12915-020-0742-5.

Whitlock, K. E., J. Postlethwait and J. Ewer (2019). Neuroendocrinology of reproduction: Is gonadotropin-releasing hormone (GnRH) dispensable? Front Neuroendocrinol. doi: 10.1016/j.yfrne.2019.02.002.

Palacios-Munoz, A. and J. Ewer (2018). Calcium and cAMP directly modulate the speed of the *Drosophila* circadian clock. PLoS Genet 14(6): e1007433. doi: 10.1371/journal.pgen.1007433.

Selcho†, M., Millán†, C., Palacios-Muñoz†, A., Ruf, F., Ubillo, L., Chen, J., Bergmann, G., Ito, C., Silva, V., Wegener*, C., and Ewer*, J. (2017). Central and peripheral clocks are coupled by a neuropeptide pathway in *Drosophila*. Nature Comm **8**:15563; doi: 10.1038/ncomms15563

† Equal contribution; * co-corresponding authors

Mena, W., S. Diegelmann, C. Wegener and J. Ewer (2016). Stereotyped responses of *Drosophila* peptidergic neuronal ensemble depend on downstream neuromodulators. eLife **5**:e19686 doi: 10.7554/eLife.19686

Flaven-Pouchon, J., Farine, J.P., Ewer, J., and Ferveur, J.F. (2016). Regulation of cuticular hydrocarbon profile maturation by *Drosophila* tanning hormone, bursicon, and its interaction with desaturase activity. Insect Biochem Mol Biol **79**:87-96. doi: 10.1016/j.ibmb.2016.10.007.

Diao, F., W. Mena, J. Shi, D. Park, F. Diao, P. Taghert, J. Ewer and B. H. White (2016). The Splice Isoforms of the *Drosophila* Ecdysis Triggering Hormone Receptor have developmentally distinct roles. Genetics. **202**(1): 175-189. doi: 10.1534/genetics.115.182121.

Krüger, E., W. Mena, E. C. Lahr, E. C. Johnson and J. Ewer (2015). Genetic analysis of Eclosion hormone action during *Drosophila* larval ecdysis. Development. **142**(24): 4279-4287. doi: 10.1242/dev.126995.

Diao, F., H. Ironfield, H. Luan, F. Diao, W. C. Shropshire, J. Ewer, E. Marr, C. J. Potter, M. Landgraf and B. H. White (2015). Plug-and-Play Genetic Access to *Drosophila* Cell Types using Exchangeable Exon Cassettes. Cell Rep. **10**(8): 1410-1421. doi: 10.1016/j.celrep.2015.01.059. Epub 2015 Feb 1426.

Ardiles A, Ewer J, Acosta ML, Kirkwood A, Martinez A, Ebensperger LA, Bozinovic F, Lee TM, Palacios AG. (2013). *Octodon degus* (Molina 1782): A model in comparative biology and biomedicine. Cold Spring Harbor Protocols. pp. 312-18; doi:10.1101/pdb.emo071357

Sundram V., Fanny S. Ng, F.S., Roberts, M.A. Millán, C, Ewer, J. and Jackson, F.R. Jackson. (2012). Requirements for LARK in the *Drosophila* Circadian System. J. Biological Rhythms, **27**(3):183-95. doi: 10.1177/0748730412440667.

Lahr, E.C., Dean, D., and Ewer, J. (2012). Genetic analysis of ecdysis behavior in *Drosophila* reveals partially overlapping functions of two unrelated neuropeptides. J. Neurosci. **32**(20): 6819 – 6829. doi: 10.1523/JNEUROSCI.5301-11.2012.

Grbić, M., Van Leeuwen, Clark, R.M., Rombauts, S., Rouzé, P., *et al.* (2011). The genome of *Tetranychus urticae* reveals herbivorous pest adaptations. Nature 479: 487-492. doi: 10.1038/nature10640.

Paré, A. C., D. M. Dean and J. Ewer (2009). "Construction and characterization of Deletions with defined endpoints in *Drosophila* using P-elements *in trans*." Genetics. **181**(1):53-63.

Lin, D. M., B. Loveall, J. Ewer, D. L. Deitcher and N. J. Sucher (2007). "Characterization of mRNA expression in single neurons." Methods Mol Biol. **399**: 133-52.

Zilberstein, Y, Ewer, J, and Ayali, A. (2006) Molt-related neuromodulation of the locust frontal ganglion - A novel target for insect ecdysis peptides. J. Exp. Biol. 209: 2911-9.

Hardstone, M.C., Baker, S.A., Gao J., Ewer, J., Scott, J.G. (2006) Deletion of *Cyp6d4* does not alter toxicity of insecticides to *Drosophila melanogaster* Pestic. Biochem. Physiol. 84:236-242.

Dulcis D, Levine R, Ewer J. 2005. Role of the neuropeptide CCAP in *Drosophila* cardiac function. J. Neurobiol. 64:259-274.

Luo C-W, Dewey EM, Sudo S, Ewer J, Hsu SY, Honegger H-W, Hsueh AJW. (2005). Bursicon, the insect cuticle hardening hormone, is a heterodimeric cystine knot protein that activates G protein-coupled receptor LGR2. Proc. Natl. Acad. Sci. USA 102:2820-2825.

Dewey, E.M*, S.L. McNabb*, J. Ewer, G.R. Kuo, C.L. Takanishi, J.W. Truman and H.-W. Honegger. (2004). Identification of the gene encoding bursicon, an insect neuropeptide responsible for cuticle sclerotization and wing spreading. Curr. Biol. **14**:1208-1213. (*) Co-first authors. Commentary: Chong, L.D. (2004). Acquiring a tan. Science **305**:575..

Clark AC*, M.L. Del Campo*, and J. Ewer. (2004). Neuroendocrine control of larval ecdysis behavior in *Drosophila*: complex regulation by partially redundant neuropeptides. J. Neuroscience **24**:4283-4292. (*) Co-first authors. Commentary: Casci, T. (2004). Shedding degeneracies. Nat. Rev. Genet. **5**:488.

Husain Q.M. and J. Ewer. (2004). Use of targetable gfp-tagged neuropeptide for visualizing neuropeptide release following execution of a behavior in *Drosophila*. J. Neurobiol. 59:181-191.

Park, J., A. J. Schroeder, C. Helfrich-Förster, F. R. Jackson and J. Ewer (2003). Targeted ablation of CCAP neuropeptide-containing neurons of *Drosophila* causes specific defects in execution and circadian timing of behavior. Development **130**: 2645-2656.

Draizen, T., J. Ewer, and S. Robinow. (1999) Genetic and hormonal regulation of the death of peptidergic neurons in the *Drosophila* central nervous system. J. Neurobiol. **38**: 455-465.

Ewer, J., C.-W. Wang, K.A. Klukas., K.A. Mesce, J.W. Truman, and S.E. Fahrbach. (1998) Programmed cell death of identified peptidergic neurons involved in ecdysis behavior in the moth, *Manduca sexta*, J. Neurobiol., **37**: 265-280.

Ewer, J. and J.W. Truman. (1997) Invariant association of ecdysis with increases in cyclic 3',5'-guanosine monophosphate (cGMP) immunoreactivity in a small network of peptidergic neurons in the hornworm, *Manduca sexta*. J. Comp. Physiology A, **181**: 319-330.

Ewer, J., S.C. Gammie, and J.W. Truman. (1997) Control of insect ecdysis by a positive feedback endocrine system: roles of eclosion hormone and eclosion triggering hormone. J. Exp. Biol., **200**: 869-881.

Ewer, J. and J.W. Truman. (1996) Increases in cyclic GMP occur at ecdysis in an evolutionarily conserved insect neuronal network. J. Comp. Neurol., **370**: 330-341.

Truman, J.W., J. Ewer, and E.E. Ball. (1996) Dynamics of cyclic GMP changes in identified neurones during ecdysis behavior in the locust, *Locusta migratoria*. J. Exp. Biol., **199**: 749-758.

Ewer, J., J. De Vente, and J.W. Truman. (1994) Neuropeptide induction of cyclic GMP increases in the insect CNS: resolution at the level of single identifiable neurons. J. Neurosci., **12**: 7704-7712.

Horodysky, F.M., J. Ewer, L.M. Riddiford, and J.W. Truman. (1993) Isolation, characterization, and expression of the eclosion hormone gene of *Drosophila melanogaster*. Eur. J. Biochem. **215**: 221-228.

Ewer, J., B. Frisch, M.J. Hamblen-Coyle, M. Rosbash, and J.C. Hall. (1992) Expression of the *period* clock gene within different cell types in the brain of *Drosophila* adults and mosaic analysis of these cells' influence on circadian behavioral rhythms. J. Neurosci. **12**: 3321-3349.

Ewer, J., M.J. Hamblen-Coyle, M. Rosbash, and J.C. Hall, J.C. (1990) Requirement for *period* gene expression in the adult and not during development for locomotor activity rhythms of imaginal *Drosophila melanogaster*. J. Neurogenetics, **7**: 31-73.

Ewer, J., M. Rosbash and J.C. Hall. (1988). An inducible promoter fused to the *period* gene in *Drosophila* conditionally rescues adult *per*-mutant arrhythmicity. Nature **333**: 82-84.

James, A.A., J. Ewer, P. Reddy, J.C. Hall, and M. Rosbash. (1986). Embryonic expression of the *period* gene in the central nervous system of *Drosophila melanogaster*. EMBO J. **5**: 2313-2320.

Hooper, S.L., M.B O'Neil, R. Wagner, J. Ewer, J. Golowash, and E. Marder. (1986). The innervation of the pyloric region of the crab, *Cancer borealis*: homologous muscles in decapod species are differently innervated. J. Comp. Physiol A **159**: 227-240.

Reviews

Cavieres-Lepe, J. and J. Ewer (2021). Reciprocal Relationship Between Calcium Signaling and Circadian Clocks: Implications for Calcium Homeostasis, Clock Function, and Therapeutics. Front Mol Neurosci 14: 666673. doi: 10.3389/fnmol.2021.666673

Salazar, C., Valdivia, G., Ardiles, A.O., Ewer, J., Palacios, A,G (2016) Genetic variants associated with neurodegenerative Alzheimer disease in natural models. *Biol. Res.,* **49:** 14-22. doi: 10.1186/s40659-016-0072-9

Aspé-Sanchez, M., M. Moreno, M. I. Rivera, A. Rossi and J. Ewer (2016). Oxytocin and Vasopressin Receptor Gene Polymorphisms: Role in Social and Psychiatric Traits. Front Neurosci. **9**:510. doi: 10.3389/fnins.2015.00510.

Langenhan, T., Barr, M. M., Bruchas, M. R., Ewer, J., Griffith, L. C., Maiellaro, I., Taghert, P. H., White, B. H. and Monk, K. R. (2015). Model Organisms in GPCR Research. Mol Pharmacol **15**(115): 098764. doi: 10.1124/mol.115.098764

Ewer, J., Jindra, M. (2014). Editorial overview: Development and regulation: Departing from paradigms. Curr. Op. Insect Sci. **1**: vii-ix. doi: 10.1016/j.cois.2014.05.006

White, B.H., and Ewer, J. (2014) Neural and Hormonal Control of Postecdysial Behaviors in Insects. Ann. Rev. Entomol. **59**:363-81. doi: 10.1146/annurev-ento-011613-162028

Honegger, H. W., E. M. Dewey and J. Ewer (2008). "Bursicon, the tanning hormone of insects: recent advances following the discovery of its molecular identity." J Comp Physiol A. **194:** 989-1005

Ewer, J. (2007) The Neuroendocrinology of eclosion. In: Invertebrate Neurobiology, Greenspan, R., and North, G., Eds. Cold Spring Harbor Press. P 555-579.

Ewer, J. (2006) Behavioral Endocrinology: Lighting Up Peptidergic Neurons that Mediate a Complex Behaviour. Curr Biol. 16:R682-4.

Ewer, J. (2005) Behavioral actions of neuropeptides in invertebrates: insights from *Drosophila*. Horm Behav. 48:418-429.

Ewer, J. (2005) Primer: How the ecdysozoan changed its coat. PLoS Biol 3: :e349. p. 1696-1699.

Ewer, J. and S. Reynolds. (2002) Neuropeptide control of molting in insects. In: Hormones, Brain and Behavior. Vol. 3, Ch. 35, D. Pfaff, Editor-in-Chief. Vol. 3, Ch. 35, pp. 1-92.

Ewer, J. and M.B. Sokolowski. (1998). *Drosophila*. In: Encyclopedia of reproduction. E. Knobil and J.D. Neill, Eds. Academic Press. Vol. 1.

Truman, J.W., R. Hewes, and J. Ewer. (1993) Action and interaction of peptides in regulating ecdysis behavior in insects. In: Insect Neurochemistry and Neurophysiology. A. B. Borkovec and M.J. Loeb, Eds. pp. 39-51. CRC Press.

Research Support (last 5 years)

Current

- John Ewer, PI; Dates: 11/2024-10/2027

Agency: Agencia Nacional de Investigación y Desarrollo: Proyecto de Exploración 2024, No: 13240159; Total direct costs: 320M$

- John Ewer, PI; Dates: 8/2022-7/2024

Agency: Agencia Nacional de Investigación y Desarrollo: FONDEF IDeA I+D, No ID22I10053; Total direct costs: 200M$

Title: “Validación de un protocolo de manejo de luz y oscuridad para modificar el reloj biológico de conductores durante los turnos nocturnos con el fin de mejorar su desempeño y salud”. (“Validation of a light management protocol to modify the biological clock of drivers during night shifts in order to improve their performance and health")

- John Ewer, PI; Dates: 3/2022-3/2025

Agency: FONDECYT; project No 1221270. Total direct costs; CLP262M.

Title: “Circadian control of *Drosophila* behavior”

Goals: This grant seeks to understand how the circadian clock imposes a daily rhythm to the pattern of adult *Drosophila* emergence".

Completed

- John Ewer, Co-PI (Ramon Latorre, Ph.D., Director); 3/2016-3/2021

Agency: MIDEPLAN/World Bank; Total direct costs; CLP700M/year (ca. US$1.4M/yr)
Title: "Centro Interdisciplinario de Neurociencia de Valparaíso (CINV)"
Goals: This "Center grant" award funds research that seeks to understand how the CNS produces behavior, from biophysics to behavior genetics.

- John Ewer (PI); 9/2016-9/2018

Agency: ONR (USA); Total direct costs: US$109,920
Title: "Impact of microbiome on the biological clock".
Goals: This grant seeks to understand how a organism's microbiota affects the functioning of the circadian clock.

- John Ewer, PI; Dates: 3/2018-3/2021

Agency: FONDECYT; Total direct costs; CLP237M (ca. US$360,000).
Title: "Neurogenetic analysis of neuropeptide function in *Drosophila*"
Goals: This grant seeks to understand how neuropeptides control ecdysis behavior in *Drosophila*.