BIOGRAPHICAL SKETCH

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NAME: ZWIEBEL, LAURENCE J

eRA COMMONS USER NAME (credential, e.g., agency login): LJZWIEBEL

POSITION TITLE: Cornelius Vanderbilt Professor of Biological Sciences

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
SUNY at Stony Brook, Stony Brook, NY	BS	01/1979	Biochemistry
University of Michigan, Ann Arbor, MI	MS	05/1982	Biology
Brandeis University	PHD	01/1991	Molecular Biology
European Molecular Biology Laboratory, Heidelberg	Other training	06/1992	Microinjection
Harvard University, Cambridge, MA	Postdoctoral Fellow	05/1994	N/A
European Molecular Biology Laboratory, Heidelberg	Postdoctoral Fellow	12/1997	N/A

A. Personal Statement

My academic research has been centered around a long-standing interest on gene expression, evolution and the genetic and molecular basis of behavior. I have been working on these areas initially as a graduate student examining the role of the period gene on circadian rhythms in the Drosophila model system and more recently as an independent investigator as I have taken my interest forward to address this issue in non-model biological systems of critical importance to global health and ones of unique biological significance. To this end, I have maintained a long-term focus on the molecular and neurological characterization of host (i.e. blood-meal source) selection and other critical behaviors in two mosquitoes: *Anopheles gambiae*, which is the principal vector for malaria in Sub-Saharan Africa and *Aedes aegypti*, the Dengue and Yellow Fever virus vector. My laboratory examines the molecular events of olfaction as this sensory modality predominates the overall host preference behaviors in mosquitoes and other insects and as such makes a significant contribution to the vectorial capacity of these mosquitoes. Within this context, we are specifically focused on the role of several diverse families of chemosensory receptors/transporters, most notably the odorant receptors (ORs) in these processes. In addition to ORs we also study the ionotropic (IR), gustatory receptor (GR) and ammonium transporter (AMT) gene families that also play important roles in these processes. Knowledge from these studies will be used to adapt new approaches for modifying mosquito behaviors-specifically the strong attraction to humans. In addition to several federally funded research projects, I was the lead investigator of an international network of laboratories that was selected for a highly competitive Grand Challenge in Global Health award from the Bill and Melinda Gates Foundation for the specific purpose of using state of the art molecular approaches to design a new generation of mosquito repellents and attractants and as part of a multi-lab collaboration we have begun to explore the molecular basis of a range of complex behaviors in two species of eusocial ants. Ants are extremely interesting because they exhibit the sophisticated ability to discriminate and respond to a wealth of socially relevant chemical cues that are highly related in structure. This inherent circuitry is likely to provide us with a rich reservoir of information regarding the evolution and caste and sex-specific modulation of chemosensory receptor space, as it applies specifically to social organization- a question that is not applicable to vector mosquitoes.

Over and above my research interests, I am committed to the mentoring and training of the undergraduate and graduate students, postdoctoral fellows and other research scientist that constitute my research group as well as the larger academic community as they become the next generation of research-active scientists, scholars and informed members of our society. In that context I continually review subjects such as strategic research planning, grant proposals, laboratory management and most importantly the responsible conduct of research (RCR) across a range of salient topics including authorship responsibilities, data management/reproducibility and scientific ethics. Much of this effort is aligned with similar training modules that are presented at Vanderbilt University as part of the CDIB and other training grants. In addition, because so much of our work has focused

on developing non-laboratory applications we also engage in substantial discussions centered around intellectual property (IP) and patents in the academic and real world-this effort with is conducted with the assistance of Vanderbilt's Center for Technology Transfer and Commercialization (CTTC). Taken together, I believe these elements represent a solid training environment that in my view is uniquely tailored to how to do cutting edge science in the modern world.

B. Positions and Honors

1988 - 1991	NIH Predoctoral Fellowship (F31MH09757-01), NIMH
1992 - 1994	Postdoctoral Fellow, Harvard University, Cambridge, MA
1992 – 1994	Visiting Fellow, Institute of Molecular Biology and Biotechnology, Heraklion, GREECE.
1992 - 1995	Postdoctoral Fellowships-NSF/NATO/USDA(RCD-9255297/92-3702-8343)
1993 - 1993	Co-Director, MacArthur Foundation Vector Biology Summer Course, Heraklion, GREECE
1994 - 1997	Postdoctoral Fellow, European Molecular Biology Laboratory, Heidelberg, GERMANY
1995 - 1997	Research Investigator, (V30/181/162), World Health Organization
1998 - 2003	Assistant Professor Biology/Biological Sciences, Vanderbilt University, Nashville, TN
2004 - 2005	Associate Professor, Department of Biological Sciences, Center for Molecular Neuroscience, Institute for Chemical Biology, Programs in Developmental Biology and Genetics, Vanderbilt University, Nashville, TN
2006 -	Professor, Departments of Biological Sciences and Pharmacology (since 2008), Vanderbilt Brain Institute, Institutes for Chemical Biology and Global Health, Programs in Developmental Biology and Genetics, Vanderbilt University, Nashville, TN
2012 -	Cornelius Vanderbilt Professor of Biological Sciences, Vanderbilt University, Nashville, TN

C. Contribution to Science

1. My PhD studies (w/ 2017 Nobel Prize Laureates M. Rosbash & JC Hall at Brandeis University) began my long-term interest in understanding the role of genetics in determining animal behavior. To address that question, I focused on the molecular genetics of circadian rhythms in the fruit fly Drosophila melanogaster where biological clocks drive many important behavioral programs. My contribution was in helping to examine the biochemistry of the system and in particular, the regulatory role of the period protein in driving locomotor and other rhythms in the fruitfly as a model system.

    a. Edery I, Zwiebel LJ, Dembinska ME, Rosbash M. Temporal phosphorylation of the Drosophila period protein. Proc Natl Acad Sci U S A. 1994 Mar 15;91(6):2260-4. PubMed PMID: 8134384; PubMed Central PMCID: PMC43350.

    b. Liu X, Zwiebel LJ, Hinton D, Benzer S, Hall JC, Rosbash M. The period gene encodes a predominantly nuclear protein in adult Drosophila. J Neurosci. 1992 Jul;12(7):2735-44. PubMed PMID: 1613555.

    c. Zwiebel LJ, Hardin PE, Liu X, Hall JC, Rosbash M. A post-transcriptional mechanism contributes to circadian cycling of a per-beta-galactosidase fusion protein. Proc Natl Acad Sci U S A. 1991 May 1;88(9):3882-6. PubMed PMID: 1902573; PubMed Central PMCID: PMC51557.

    d. Liu X, Yu QA, Huang ZS, Zwiebel LJ, Hall JC, Rosbash M. The strength and periodicity of D. melanogaster circadian rhythms are differentially affected by alterations in period gene expression. Neuron. 1991 May;6(5):753-66. PubMed PMID: 1902699.

2. Shifting away from model insect systems, my postdoctoral work (w/FC. Kafatos at Harvard/EMBL) was aimed at helping to establish transgenic approaches and molecular genetics in the medfly *Ceratitis capitata*. In this light, I was able to clone and characterize a series of phenotypic markers for germline transformation

    a. Gomulski LM, Pitts RJ, Costa S, Saccone G, Torti C, Polito LC, Gasperi G, Malacrida AR, Kafatos FC, Zwiebel LJ. Genomic organization and characterization of the white locus of the Mediterranean fruitfly, *Ceratitis capitata*. Genetics. 2001 Mar;157(3):1245-55. PubMed PMID: 11238408; PubMed Central PMCID: PMC1461546.

b. Zwiebel LJ, Saccone G, Zacharopoulou A, Besansky NJ, Favia G, Collins FH, Louis C, Kafatos FC. The white gene of *Ceratitis capitata*: a phenotypic marker for germline transformation. Science. 1995 Dec 22;270(5244):2005-8. PubMed PMID: 8533095.

3. Starting my own lab at Vanderbilt as independent investigator in 1998 allowed me to further refine my interest on the role of genetics on insect behavior by focusing on the role of the olfactory system in general and odorant receptors (ORs) in particular in determining host preference and selection and other in the malaria vector mosquito *Anopheles gambiae*. Since establishing this work, the lab has been at the forefront of studies to identify and characterize olfaction and the OR superfamily in vector mosquitoes and, more recently, the ionotropic receptors IRs. In the course of that work we have defined the odor coding around the olfactory appendages of *An. gambiae*, analyzed the structure function and evolutionary relationships of mosquito ORs and have carried out a series of RNAseq studies to examine the implications of dynamic alterations in the transcriptome profiles of OR and other chemosensory receptors in Anophelines. We have also been the first to establish that ORs are expressed in insect spermatozoa where they act in a novel non-neuronal role in reproduction.

   a. Rinker DC, Pitts RJ, Zhou X, Suh E, Rokas A, Zwiebel LJ. Blood meal-induced changes to antennal transcriptome profiles reveal shifts in odor sensitivities in *Anopheles gambiae*. Proc Natl Acad Sci U S A. 2013 May 14;110(20):8260-5. PubMed PMID: 23630291; PubMed Central PMCID: PMC3657813.
   b. Wang G, Carey AF, Carlson JR, Zwiebel LJ. Molecular basis of odor coding in the malaria vector mosquito *Anopheles gambiae*. Proc Natl Acad Sci U S A. 2010 Mar 2;107(9):4418-23. PubMed PMID: 20160092; PubMed Central PMCID: PMC2840125.
   c. Hallem EA, Nicole Fox A, Zwiebel LJ, Carlson JR. Olfaction: mosquito receptor for human-sweat odorant. Nature. 2004 Jan 15;427(6971):212-3. PubMed PMID: 14724626.
   d. Hill CA, Fox AN, Pitts RJ, Kent LB, Tan PL, Chrystal MA, Cravchik A, Collins FH, Robertson HM, Zwiebel LJ. G protein-coupled receptors in *Anopheles gambiae*. Science. 2002 Oct 4;298(5591):176-8. PubMed PMID: 12364795.

4. An important element of our efforts has been to target the olfactory system of *An. gambiae* to identify small molecule OR modulators that act as novel attractant and repellents for mosquitoes and other insects. To this end we have discovered a novel class of VUAA-class molecules that agonize and antagonize the highly conserved Orco OR co-receptor. We have expanded the chemical space around VUAA-class actives to examine their structure-activity relationships and have begun to develop their activity as broadly active insect excito-repellents.

   a. Taylor RW, Romaine IM, Liu C, Murthi P, Jones PL, Waterson AG, Sulikowski GA, Zwiebel LJ. Structure-activity relationship of a broad-spectrum insect odorant receptor agonist. ACS Chem Biol. 2012 Oct 19;7(10):1647-52. PubMed PMID: 22924767.
   b. Jones PL, Pask GM, Romaine IM, Taylor RW, Reid PR, Waterson AG, Sulikowski GA, Zwiebel LJ. Allosteric antagonism of insect odorant receptor ion channels. PLoS One. 2012;7(1):e30304. PubMed PMID: 22272331; PubMed Central PMCID: PMC3260273.
   c. Rinker DC, Jones PL, Pitts RJ, Rutzler M, Camp G, Sun L, Xu P, Dorset DC, Weaver D, Zwiebel LJ. Novel high-throughput screens of *Anopheles gambiae* odorant receptors reveal candidate behaviour-modifying chemicals for mosquitoes. Physiological entomology. 2012; 37:33-41.
   d. Jones PL, Pask GM, Rinker DC, Zwiebel LJ. Functional agonism of insect odorant receptor ion channels. Proc Natl Acad Sci U S A. 2011 May 24;108(21):8821-5. PubMed PMID: 21555561; PubMed Central PMCID: PMC3102409.

5. We have extended our studies on chemosensory-driven behaviors to ants to take advantage of the large body of work that suggests that behavior and social organization in ants are largely modulated by chemosensory communication, often encoded by complex mixtures of volatile cuticular hydrocarbons (CHCs). We have molecularly characterized the extraordinary expansion of OR gene families in ants which directly links them to a role in eusociality and have carried out functional studies on these chemoreceptors. We have recently completed studies establishing the odor coding paradigms that underlie chemical communication in these systems.

a. Odor Coding of Nestmate Recognition in the Eusocial Ant *Camponotus floridanus*. Stephen T. Ferguson, Alexandra R. Ruff, Kyu Y. Park, Isaac Bakis and **Laurence J. Zwiebel**, *Journal of Experimental Biology* (2020) doi:10.1242/jeb.215400. PubMed PMID:31900348; PubMed Central PMCID: PMC7033718
b. Yan H, Opachaloemphan C, Mancini G, Yang H, Gallitto M, Mlejnek J, Leibholz A, Haight K, Ghaninia M, Huo L, Perry M, Slone J, Zhou X, Traficante M, Penick CA, Dolezal K, Gokhale K, Stevens K, Fetter-Pruneda I, Bonasio R, Zwiebel LJ, Berger SL, Liebig J, Reinberg D, Desplan C. An Engineered orco Mutation Produces Aberrant Social Behavior and Defective Neural Development in Ants. Cell. 2017 Aug 10;170(4):736-747.e9. PubMed PMID: 28802043; PubMed Central PMCID: PMC5587193.
c. Slone JD, Pask GM, Ferguson ST, Millar JG, Berger SL, Reinberg D, Liebig J, Ray A, Zwiebel LJ. Functional characterization of odorant receptors in the ponerine ant, *Harpegnathos saltator*. Proc Natl Acad Sci U S A. 2017 Aug 8;114(32):8586-8591. PubMed PMID: 28696298; PubMed Central PMCID: PMC5559025.
d. Zhou X, Rokas A, Berger SL, Liebig J, Ray A, Zwiebel LJ. Chemoreceptor Evolution in Hymenoptera and Its Implications for the Evolution of Eusociality. Genome Biol Evol. 2015 Aug 12;7(8):2407-16. PubMed PMID: 26272716; PubMed Central PMCID: PMC4558866.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/laurence.zwiebel.1/bibliography/41167651/public/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

-RO1 GM128336-01 (NIGMS) ZWIEBEL, LAURENCE J (PI) 07/01/18-06/31/23
Molecular Neurogenetics of Olfactory Driven Aggression and Social Hierarchy in a Model Insect System.
The major goals of this continuing project are to characterize the biological role and functional mechanisms of olfaction in maintain eusocial characteristics in two ant species. The PI is responsible for the overall guidance of the research program and there is no scientific or other overlap with other proposals.

-R21 AI1138157-01 (NIAID) ZWIEBEL, LAURENCE J (PI) 06/01/18-05/01/21
Identification of Carbon Dioxide Mimics for Effective Trapping of Malaria Vector Mosquitoes
The major goals of this project to investigate the structure function of CO_2 receptors and identifying small molecules that can act as CO_2 mimics in the olfactory system of the malaria vector mosquito *An. gambiae*. The PI is responsible for the overall guidance of the research program and there is no scientific or other overlap with other proposals.