BIOGRAPHICAL SKETCH

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NAME: Leslie B. Vosshall Ph.D.

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POSITION TITLE: Robin Chemers Neustein Professor

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)*	Completion Date MM/YYYY	FIELD OF STUDY
Columbia University	A.B.	06/1987	Biochemistry
The Rockefeller University	Ph.D.	06/1993	Molecular Genetics
Columbia University	Postdoc	09/1997	Molecular Neurobiology

A. Personal Statement

I am a molecular neurobiologist who studies how behaviors emerge from the integration of sensory input with internal physiological states. I am the Robin Chemers Neustein Professor, Head of the Laboratory of Neurogenetics and Behavior, and Director of the Kavli Neural Systems Institute at The Rockefeller University, and have been an investigator of the Howard Hughes Medical Institute since 2008. My group is known for our work on the genetic basis of chemosensory behavior in both insects and humans. My notable contributions to science include the discovery of the insect odorant receptors, and the elucidation of general principles of their function, expression, and the connectivity of the sensory neurons that express them to primary processing centers in the brain. Our research program in human olfactory perception has led to discoveries in the genetic basis of smell disorders, and how odor stimuli are converted to olfactory percepts. We are translating this work to produce a novel clinical test for smell dysfunction. Much of our current research is aimed at understanding the molecular neurobiology of host-seeking and blood-feeding in mosquitoes that spread dangerous infectious diseases. Since 2008, my group has established the Aedes aegypti mosquito as a genetic model organism. We were the first to use CRISPR-Cas9 genome-editing in this species and led the effort to resequence, assemble, and annotate the genome of this deadly vector mosquito. Our work has shed light on how these mosquitoes integrate sensory cues to hunt humans and we have developed small molecules that block mosquito biting behavior. I am a member of the board of bioRxiv, and a proponent of pre-prints and open science, as well as a strong supporter of initiatives to increase diversity in STEM. I received an A.B. in Biochemistry from Columbia University in 1987 and a Ph.D. from The Rockefeller University in 1993 working with Michael Young. Following postdoctoral work at Columbia University in the laboratory of Richard Axel, I joined the Rockefeller faculty in 2000 and have remained here since. I am the recipient of the 2008 Lawrence C. Katz Prize from Duke University, the 2010 DART/NYU Biotechnology Award, the 2011 Gill Young Investigator Award, and the 2020 National Academy of Sciences Pradel Research Award. I am an elected fellow of the American Association for the Advancement of Science and was elected to the National Academy of Sciences in 2015.

B. Positions and Honors

Positions and Employment

1994	Instructor, Neurobiology Course, Marine Biological Laboratory, Woods Hole, MA
1997-2000	Associate Research Scientist, Center for Neurobiology and Behavior, Howard Hughes Medical Institute, Columbia University, New York, NY. In the laboratory of Dr. Richard Axel
2000-2003	Annenberg Assistant Professor and Head of the Laboratory of Neurogenetics and Behavior, The Rockefeller University, New York, NY

2003-2006	Chemers Family Assistant Professor and Head of the Laboratory of Neurogenetics and Behavior, The Rockefeller University, New York, NY
2005-2007	Faculty, Neural Systems and Behavior Course, Marine Biological Laboratory, Woods Hole, MA
2006-2010	Chemers Family Associate Professor and Head of the Laboratory of Neurogenetics and Behavior, The Rockefeller University, New York, NY
2008-	Investigator, Howard Hughes Medical Institute
2010-	Robin Chemers Neustein Professor, and Head of the Laboratory of Neurogenetics and Behavior, The Rockefeller University, New York, NY

Other Experience and Memberships

2002-	NIH CSR review panels (NIDCD ZDC1 SRB-S, NIDCD ZDC1 SRY-Y, NIDCD CDRC, NIH/CSR SCS, NIH SCS CBSS)
2005-2016	The FASEB Journal Associate Editor
2005-	Current Biology Editorial Board
2007-	Chemical Senses Editorial Board
2007-2012	Journal of Neuroscience Associate Editor
2007-2014	Max Planck Institute of Chemical Ecology Scientific Advisory Board
2008-2009	NINDS Basic Module Advisory Panel
2008-2015	McKnight Scholar Award Selection Committee
2008-2015	Alfred P. Sloan Research Fellowships in Neuroscience Program Committee
2008-	Vilcek Prize for Creative Promise Jury
2010-2014	Board of Scientific Counselors, NIH, NIDCR
2010-2019	Member, BMC Biology Editorial Board
2011-2019	Institute of Molecular Pathology (IMP), Vienna, Austria, Scientific Advisory Board
2012-2019	PLoS Biology Editorial Board
2013-	bioRxiv Advisory Board
2013-2017	Simons Foundation Quanta Magazine Advisory Board
2015-	Science Advances, Associate Editor (2015-2018) Deputy Editor (2018-)
2017-	Pearl Meister Greengard Award Selection Committee
2018-	The McKnight Endowment Fund for Neuroscience Board of Directors
2018-	The Wenner-Gren Foundation for Anthropological Research Board of Trustees
2018-	National Academy of Sciences, Chair of Section 24 (Molecular and Cellular Neuroscience)
2019-	Instituto Gulbenkian de Ciência (IGC), Lisbon, Portugal, Scientific Advisory Board
2020-	Helen Hay Whitney Foundation Board of Directors
2020-	Lasker Prize Jury
2020-	Pew Foundation Biomedical Scholars National Advisory Committee

Honors

1987	John Jay Scholar, Columbia College of Columbia University
2001	Beckman Young Investigator
2001	National Science Foundation CAREER Award
2001	McKnight Scholar
2002	John Merck Fund Award
2002	Presidential Early Career Award for Scientists and Engineers (PECASE)
2005	Rockefeller University Teaching Award
2005	New York City Mayor's Young Investigator Award for Excellence in Science and Technology
2007	Blavatnik Award for Young Scientists from the New York Academy of Sciences
2008	The International Society of Chemical Ecology Silverstein-Simeone Lecture Award
2009	Lawrence C. Katz Prize, Duke University
2010	Dart/NYU Biotechnology Alumnae Achievement Award
2011	Gill Center Young Investigator Award
2014	AAAS Fellow Election
2015	Election to the National Academy of Sciences
2020	National Academy of Sciences Pradel Research Award

C. Contributions to Science

1. The chemosensory receptors that detect the vast number of odorants that animals can perceive were initially described in 1991 by Linda Buck and Richard Axel, but the corresponding genes in the insect were unknown when I started my postdoctoral training with Richard Axel in 1993. My early work led to the discovery of two large multi-gene families that encode insect chemosensory receptors for odorants, pheromones, and carbon dioxide. The insect odorant receptors (ORs) are atypical seven transmembrane domain proteins with no homology to odorant receptors in vertebrates. My group provided the first experimental evidence that ORs adopt an inverted topology relative to G protein-coupled receptors, that the active odorant receptor is a multimeric complex of a ligand-selective OR subunit and a co-receptor called Orco, and that they function as odor-gated non-selective cation channels. We showed that two members of the distantly related GR gene family cooperate to form a membrane receptor for carbon dioxide, an important sensory cue for insects. We identified a second gene family, the ionotropic receptors (IRs), that is related to ionotropic glutamate receptors. We showed that several of these receptors are tuned to volatile amines and acids, cues of particular relevance to vector mosquitoes. This work, begun by me as a postdoctoral fellow with Richard Axel, and continued in my own group from 2000-2008, has spawned a large field with many laboratories investigating olfactory function in a diverse group of insects. The work has practical and medical importance because it provides a means to control olfactory-guided behaviors that attract agricultural pests to food crops and disease vector insects to human hosts.

    a. Larsson MC, AI Domingos, WD Jones, ME Chiappe, H Amrein, and **LB Vosshall**. 2004. *Or83b* encodes a broadly expressed odorant receptor essential for *Drosophila* olfaction. Neuron 43:703-714 PMID: 15339651
    b. Benton R, S Sachse, SW Michnick, and **LB Vosshall**. 2006. Atypical membrane topology and heteromeric function of *Drosophila* odorant receptors *in vivo*. PLoS Biol 4:e20 PMID: 16402857
    c. Sato, K., M Pellegrino, T Nakagawa, T Nakagawa, **LB Vosshall**, and K Touhara. 2008. Insect olfactory receptors are heteromeric ligand-gated ion channels. Nature 452:1002-1006 PMID: 18408712
    d. Benton, R, KS Vannice, C Gomez-Diaz, and **LB Vosshall**. 2009. Variant ionotropic glutamate receptors as chemosensory receptors in *Drosophila*. Cell 136:149-162PMID: 19135896

2. Following my discovery of the insect ORs, I initiated a research program to discover how olfactory information is represented in the fly brain. Together with my trainees, I generated a complete set of genetic reagents that permitted us to map the projections of each class of OR-expressing sensory neurons to their targets in the early olfactory area of the brain. We discovered that each class of neurons innervates a specific glomerulus in either the larval or adult antennal lobe. This hard-wired circuit can be modulated by odor exposure, and this plasticity causes long-term changes in both the anatomy and function of olfactory circuits. By carrying out behavioral genetic experiments in the anatomically simple *Drosophila* larva, we identified populations of sensory neurons that respond to different concentrations of the same odor ligand. These neurons function in combinations to encode the perception of changing concentrations of odorants in the environment. The genetic strains produced in this phase of my career have been extremely influential and are used in dozens of laboratories worldwide to study the development, function, and plasticity of neural circuits. Because the anatomical organization of the fly olfactory system strongly resembles that of vertebrates, our work enabled new discoveries in circuit function in all animals.

    a. **Vosshall LB**, AM Wong, and R Axel. 2000. An olfactory sensory map in the fly brain. Cell 96:725-736 PMID: 10943836
    b. Fishilevich E, and **LB Vosshall**. 2005. Genetic and functional subdivision of the *Drosophila* antennal lobe. Curr Biol 15:1548-1553 PMID: 16139209
    c. Sachse, S, Rueckert, E, Keller, A, Okada, R, Tanaka, NK, Ito, K and **LB Vosshall**. 2007. Activity-dependent plasticity in an olfactory circuit. Neuron 56:838-850 PMID: 18054860
    d. Asahina, K, M Louis, S Piccinotti, and **LB Vosshall**. 2009. A circuit supporting concentration-invariant odor perception in *Drosophila*. J Biol 8:9 PMID: 19171076

3. Parallel to my insect olfaction program, I have been studying the basic rules of the human sense of smell since 2002. Together with my collaborator Andreas Keller, I carried out psychophysical experiments to debunk a controversial theory of olfaction that posited that molecular vibrations of odor molecules are sense by human ORs. We established the Rockefeller University Smell Study, which has screened the sense of smell more than 1700 human subjects. We have used this dataset to investigate some of the most central questions in olfaction: what are the interindividual differences in the human sense of smell? How many olfactory stimuli can humans discriminate? How does the chemical structure of an odorant relate to its perceived odor? Working with Hiro Matsunami's group, we discovered the first genetic basis of a specific anosmia. Humans carrying loss-of-function polymorphisms in a single OR that detects sex steroid-derived odorants show dramatically reduced sensitivity and altered perception of these smells. To test the capacity of humans to discriminate olfactory stimuli, we carried out psychophysical testing that asked subjects to distinguish complex odor mixtures with increasing component overlap. From the results, we estimated that humans can discriminate a very large number of olfactory stimuli. This work is important because the sense of smell is poorly understood relative to vision and hearing. Our work has the potential to aid in detection of smell disorders in humans.

    a. Keller A*, H Zhuang*, Q Chi, **LB Vosshall**, and H Matsunami. *equal contribution. 2007. Genetic variation in a human odorant receptor alters odour perception. Nature 449:468-472 PMID: 17873857
    b. Bushdid, C, MO Magnasco, **LB Vosshall**, and A Keller. 2014. Humans can discriminate more than 1 trillion olfactory stimuli. Science 343:1370-1372 PMID: 24653035
    c. Keller A, Gerkin RC, Guan Y, Dhurandhar A, Turu G, Szalai B, Mainland JD, Ihara Y, Yu CW, Wolfinger R, Vens C, Schietgat L, De Grave K, Norel R; DREAM Olfaction Prediction Consortium., Stolovitzky G, Cecchi GA, **Vosshall LB**, Meyer P. 2017. Predicting human olfactory perception from chemical features of odor molecules. Science 355:820-826 PMID: 28219971
    d. Hsieh JW, Keller A, Wong M, Jiang R-S, **Vosshall LB**. 2017. SMELL-S and SMELL-R: Olfactory tests not influenced by odor-specific insensitivity or prior olfactory experience. Proc. Natl. Acad. Sci. U.S.A. 114:11275-11284. PMID: 29073044

4. Innate behaviors such as courtship and feeding are encoded in hard-wired circuits that are subject to modulation. We have been studying these behaviors in the fly, *Drosophila melanogaster*. We developed high-throughput screening techniques in live animals to screen FDA-approved drugs for their ability to modulate feeding behavior in *Drosophila* larvae. At this life stage, these animals eat continuously, making them a possible experimental model for binge-eating disorder. This work identified potent antagonists of serotonin receptors as anti-feedants, and showed that the 5HT2 serotonin receptor is the sole target of this drug. We went on to discover a new taste circuit in adult flies that permits direct detection of ingested food in the pharynx and relays information on the quantity and quality of the meal to the brain, where this is integrated with information on hunger state to regulate ingestion. In the area of courtship behavior, we identified circuits that govern copulation behavior and female receptivity. These behaviors are critical for animals to time their courtship and sexual behavior according to external conditions and their internal physiological state. We discovered a compact circuit that monitors external dangers and weighs them against the temporal progress of effective fertilization to time copulation behavior. This work points to the existence of an internal timing mechanism that operates on a scale of minutes, an important phenomenon that has been little-studied in biology.

    a. Gasque G, Conway W, Huang J, Rao Y, and **LB Vosshall**. 2013. Small molecule drug screening in *Drosophila* identifies the 5HT2A receptor as a feeding modulation target. Sci Rep 3:srep02120 PMID: 23817146
    b. Crickmore MJ and **LB Vosshall**. 2013. Opposing dopaminergic and GABAergic neurons control the duration and persistence of copulation in *Drosophila*. Cell 155:881-893 PMID: 24209625
    c. Bussell JJ, N Yapici, SX Zhang, BJ Dickson, and **LB Vosshall**. 2014. Abdominal-B neurons control *Drosophila* virgin female receptivity. Curr Biol 24:1584-1595 PMID: 24998527
    d. Yapici, N, R Cohn, C Schusterreiter, V Ruta, **LB Vosshall**. 2016. A taste circuit from pharynx to brain that regulates ingestion by integrating food and hunger signals. Cell 165:715-729 PMID: 27040496

5. In 2008, I initiated a mosquito genetics research program that aims to dissect the genes and circuits that drive female mosquitoes to seek out human hosts. We were among the first groups to apply genome-engineering techniques to generate mutant mosquitoes. Using zinc-finger nucleases, we generated mutant mosquitoes that lack the olfactory co-receptor *Orco*, and found that these mosquitoes lose the ability to discriminate human from non-human hosts. Moreover, they no longer avoid the insect repellent DEET. We went on to generate mosquitoes genetically unable to detect the important chemosensory cue carbon dioxide. These animals show defects in detecting unrelated sensory cues, indicating the multiple sensory cues synergize to drive mosquito behavior. Field collections of sub-species of *Aedes aegypti* with different host preferences led to the discovery that evolutionary changes in an odorant receptor are correlated with human preference. We have developed powerful techniques to edit the genome of this vector insect using CRISPR-Cas9. This work opens up the possibility to study a wide variety of sensory pathways in this insect, as well as probing the central brain circuits that govern attraction to humans. The health relevance of this work is that mosquitoes transmit deadly infectious diseases to humans both domestically in the US and internationally. Understanding the rules by which these animals target human hosts will enable us to devise tools to reduce their capacity to spread disease.

    a. DeGennaro M, CS McBride, L Seeholzer, T Nakagawa, EJ Dennis, C Goldman, N Jasinskiene, AA James, and **LB Vosshall**. 2013. *orco* mutant mosquitoes lose strong preference for humans and are not repelled by volatile DEET. Nature 498:487-491 PMID: 23719379
    b. McMeniman CJ, RA Corfas, BJ Matthews, Ritchie SA, and **LB Vosshall**. 2014. Multimodal integration of carbon dioxide and other sensory cues drives mosquito attraction to humans. Cell 156: 1060-1071 PMID: 24581501
    c. McBride CS, F Baier, AB Omondi, SA Spitzer, J Lutomiah, R Sang, R Ignell, and **LB Vosshall**. 2014. Evolution of mosquito preference for humans linked to an odorant receptor. Nature 515:222-227 PMID: 25391959
    d. Duvall LB, L Ramos-Espiritu, KE Barsoum, JF Glickman and **LB Vosshall**. 2019. Novel small molecule agonists of an *Aedes aegypti* neuropeptide Y receptor block mosquito biting behavior. Cell 176:687-701. PMID: 30735632

Complete List of Published Work in NCBI My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/leslie.vosshall.2/bibliography/40448629/public/?sort=date&direction=ascending

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

Ongoing

HHMI Investigator Award — Vosshall (PI) — 07/01/2008 – 08/31/2025
Modulation of Behavior by Internal Physiological State
Goal: understand how internal physiological states alter behavior.

RTDF Advanced Award — Vosshall (PI) — 10/1/2019 – 09/30/2021
Small Molecule GPCR Agonists to Block Mosquito Biting Agency: Robertson Therapeutic Development Fund
Project period: 10/1/2019 – 9/30/2021
Goal: To develop new chemical entities that are potent agonists of NPYLR7, for use in controlling mosquito biting behavior

RTDF Pre-Clinical Lead Optimization Award — Vosshall (PI) — 12/1/2019 – 11/30/2020
Development of a Digital Olfactory Test Device
Goal: To develop a new clinical smell test for diagnosis of olfactory dysfunction