

## Q & A

### Leslie B. Vosshall

*Born in Lausanne, Switzerland, Leslie Vosshall spent her early childhood in Switzerland, Austria and Germany before moving to New Jersey at the age of 8. Vosshall has lived in New York City since 1983, when she matriculated in the first co-educational class of Columbia College at Columbia University. She trained at the Marine Biological Laboratory, New York University, Columbia University and The Rockefeller University where she is now Robin Chemers Neustein Professor and an Investigator of the Howard Hughes Medical Institute. Her laboratory studies olfactory and feeding behavior in flies, mosquitoes and humans by merging molecular biology, genetics and behavior.*

**How did you get into biology?** My uncle, Philip Dunham, was a biologist at Syracuse University and arranged a coveted position for me as dishwasher in his summer lab with Gerald Weissmann at the Marine Biological Laboratory (MBL) in Woods Hole. I spent three summers in his lab, from 17 to 19, and it was an incredible introduction to the practice of science.

**From dishwasher to scientist?** Phil and Gerry initially had me just wash the glassware, but there wasn't much of that to do and I am easily bored, so they sent me on errands to place orders or pick up sea urchins and sponges from the Marine Services building. Later they allowed me to do experiments. The first summer, we worked on sea urchin fertilization and what conditions could cause an egg to be fertilized by multiple sperm — polyspermy. This required me to hook up the boy sea urchins to electrodes and jolt them to get them to ejaculate and inject the girl sea urchins with KCl to get them to drop their eggs. I thought this was the coolest thing ever! We mixed egg and sperm under different conditions to study the protective membrane on the egg and what could defeat it. Phil and Gerry even let me present the work in a 5 minute talk at the MBL annual meeting in August 1982. The second summer, we started using marine sponges as a model for cell-cell recognition and

adhesion. We used urushiol, the active ingredient in poison ivy, as an agonist for aggregation. Of course, I never wore anything practical like pants or a lab coat and got a raging urushiol rash all over my legs. When I wasn't tampering with sea urchin reproduction or dripping urushiol on my thighs, I hung out with students and faculty in the legendary MBL summer courses and went to a lot of great talks and even greater parties. The whole experience gave me a taste of the countercultural spirit and intellectual freedom that academic scientists enjoy.

**Do you have a 'scientific hero'?** Yes, two heroes: Seymour Benzer, the father of neurogenetics in *Drosophila* and my postdoc mentor, Richard Axel. Reading the 1971 Konopka and Benzer paper describing fly mutants that lived short or long days or were arrhythmic directly influenced my choice to carry out PhD work on the *period* gene in Michael Young's lab at Rockefeller. Seymour laid out the groundwork for studying learning and memory, circadian rhythms, olfaction and trained a generation of leaders in our field. What was impressive is that he was constantly moving into new areas. Later in life he took on neuronal degeneration, longevity and feeding and made huge contributions in those areas as well. About six months before his death, I had the privilege of interacting with Seymour one final time while writing a piece for *Nature* that ended up being an elegy of Seymour and his contribution to neurogenetics. He shared some special historical photos of his crazy group that I included in the piece. It is a terrible injustice that Seymour was never awarded the Nobel Prize, but I am gratified to see that those who followed in his footsteps studying the *period* gene and who provided great insights into the mechanisms of the biological clock — Jeffrey Hall, Michael Rosbash and Michael Young — have recently been winning a lot of big prizes as a trio. Who knows, maybe they will accept the big prize in Sweden someday along with the ghost of Seymour, wearing a cardigan and his glasses low on the bridge of his nose!

**What about hero number two?** Richard Axel was incredibly patient with me while I fumbled in his lab for seven years as a postdoc trying to clone the insect odorant receptors



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with Hubi Amrein. Richard has a great sense of what makes a good problem, has excellent intuition in picking postdocs, and he is extremely smart and entertaining. Someone should be writing a book about Axel that compiles all the ridiculously vile jokes and outrageous stories he tells. Richard has an unparalleled record in mentoring — he has an impressively large number of successful scientific 'children', including many women. Like Seymour, he maintains a brisk pace of change in his research program, identifying new impossible problems to solve every few years, thereby avoiding direct competition with his departing offspring who solved the old problems.

**Now that you have your own lab, what would you say is the hardest thing about running a lab?** Picking the right people and picking the right problems! Two things I studied carefully in the Axel Lab and have been trying hard to emulate. I strive to have a diverse group, with each person bringing some unique perspective or skill to the lab. Having no experience whatsoever in what we do is a huge plus for me. Matthieu Louis, for instance, was a physicist with little bench biology skill when he joined, but he went on to do some of the most creative and sophisticated experiments on larval olfaction ever. His quantitative skills were crucial—the work would have not happened without him. Another example is Richard Benton,

who came to the lab with training in *Drosophila* developmental cell biology and left having done three very important pieces of work in olfactory neurobiology.

**And how do you pick your problems?**

My usual rule is that the question has to be extremely difficult but somehow tractable, and that if the problem is solved, the answer will be broadly interesting and important. It is very easy to fall into the trap of doing something just because it is possible to do it, without paying enough attention to the eventual impact the answer will have. I also am averse to publishing little incremental papers — in my ideal world a student or postdoc will do a huge comprehensive project that will yield one paper after 5 years. This drives some people in my lab crazy, and certainly makes it difficult for me to get NIH funding, but I like to hold out for the really big and complete stories. In the end, the big and complete stories are more widely read (and cited) than the little interim, incremental papers. We don't expect great novelists to churn out one book a year like romance or pulp mystery writers; I am mystified by the funding culture that pushes people to publish so much.

**Can you share some useful advice you've been given?**

Yes. The late and great Larry Katz told me that before he accepted any invitation to give a talk or attend a conference, he asked himself if he would go if the trip were tomorrow instead of 16 months into the hazy future. Only if the invitation still appealed, he would say yes. This is fantastic advice because one's life can be overtaken with too much travel unless carefully managed. You say yes, yes and yes, and suddenly you find yourself on six weeks of extended travel to all corners of the earth in what seemed like a great plan at the time. We scientists have the privilege of traveling to great places to disseminate our work, but if invitations are accepted without thought, mental and physical exhaustion and neglect of the home front can be a negative consequence.

**You've recently become a Howard Hughes investigator, how did that feel?**

Both incredibly great and incredibly terrifying. When Tom Cech, or now Bob Tjian, waves the magic

wand, your life changes in an instant: your salary is suddenly 100% covered, you have the funds to support a lab manager, hire that new postdoc, take risks by moving into new areas and buy fancy equipment or even do a major lab renovation. But the magic comes with the big catch that every five years you have to demonstrate to a group of very smart reviewers that you are still at the very top of your game. Any slippage unto mundane experiments that are merely very good or loss of innovative edge means you are phased out in two years and the magic is over. I was struck that at the initiation meeting of my HHMI class of 2008, most of us were already fretting about what would happen in 2013, the year we are all reviewed for the first time. I think on balance this terror is a good thing — it prevents complacency. It means that HHMI maintains incredibly high scientific standards in return for the considerable investment they make. The HHMI investigator meetings are an amazing thing — everyone is doing the best possible science in their area.

**What is your favorite conference?**

Bill Hansson organizes a small meeting on insect taste and smell called ESITO, which meets every two years at various locations in Europe, but returns to a little beach resort in Sardinia every four years. With fewer than 100 attendees and a diversity of topics — from chemical ecology to molecular biology and behavior — it has an intimate and relaxed atmosphere that has helped me strike up a lot of collaborations and taught me things I would not have learned elsewhere. The excellent Sardinian food and wine and the convivial atmosphere that Bill fosters don't hurt either.

**What would you say is the future of your field?**

I think we are at the very edge of the time when mechanistic and reductionist molecular biologists working in the traditional model organisms — *Drosophila*, mouse, *C. elegans*, yeast, zebrafish — will invade the fields of ecology and evolutionary biology. By that I mean that we will explore the functional consequences of genetic variation in an organism or work in new related organisms that inhabit unusual ecological niches or have interesting evolutionary adaptations. Some

examples would be Diana Bautista hunting for new mechanosensory genes in the star organ of the star-nosed mole, Elena Gracheva and David Julius working on infrared detection in snakes and vampire bats, Hopi Hoekstra discovering the genetic basis of coat color variation in wild mice, and Cori Bargmann studying natural variation in *C. elegans* strains from around the world. With the cost of genome sequencing dropping to almost nothing and the availability of new genomic modification tools (zinc finger nucleases and TALENs) to do genetics in virtually any creature on earth, there is no reason to stay with the usual model organisms. People will be able to more freely follow the biology, which may be more usefully studied in a Tasmanian devil or hawk moth than a typical laboratory animal. My own lab has certainly taken the plunge in recent years, switching from the *Drosophila melanogaster* fly to the *Aedes aegypti* mosquito. I look forward to this new and more diverse biological landscape.

**Finally, what are you wearing in the photo?**

Ah — a fashion question! I know, scientists are not supposed to care about fashion. My favorite science vs. fashion anecdote is from my friend Marina Picciotto, a neurobiologist at Yale. She was at a Society for Neuroscience annual meeting held in a convention center at the same time as a fashion convention. On the escalators, where scientists and fashionistas were commingled, Marina heard one fashionista ask another: "Who are all these badly dressed people!???" Anyway, I never wear pants or a labcoat. This here is a CK Bradley silk dress and a Kate Spade 'bamboozled' gold bamboo necklace. For as long as I can remember, scientists have given me a hard time about my love of shoes and fashion. Somehow being serious requires wearing either a suit and tie or a vendor t-shirt and cargo shorts. Neither 'uniform' works terribly well on a woman scientist, so I am taking my own path of being very interested in fashion and very interested in science. I do not think these things are incompatible.

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