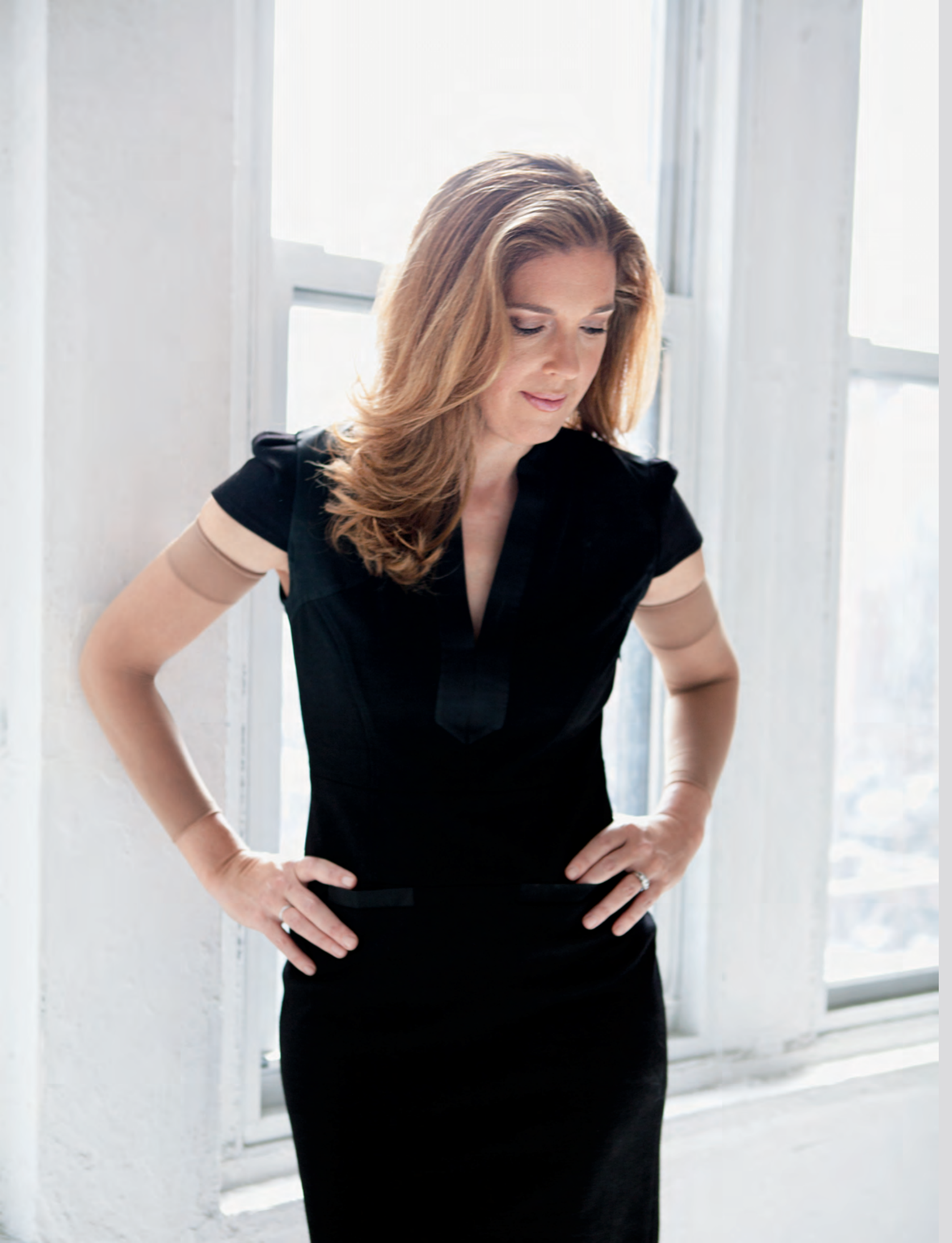


With an outsider's perspective, Leslie Vosshall has changed thinking about the meaning of olfaction—for humans and insects.

AVANT GARDE SCIENTIST

by Robin Marantz Henig
photography by Jon Moe

When Leslie Vosshall opens the door to her sprawling Manhattan apartment, I notice a child's drawing on the front door asking visitors to take off their shoes. Vosshall would never ask me outright, but this crayoned request from her 10-year-old daughter Ophelia is too charming to ignore. I do as directed, and we conduct the interview in our socks.

As it happens, Vosshall is wearing socks all over her body—thin nylon socks, one pair under her regular socks, and another pair with the feet cut off on her arms. The extra layer of clothing is all in the interest of science, specifically Vosshall's decades-long fascination with the mechanics of the olfactory system. To generate enough samples of human scent for their insect experiments, the people in Vosshall's lab occasionally wear socks on their arms and legs, while working up a sweat and foregoing deodorant or showers. After 24 hours the socks are removed, rolled up, and thrown into a freezer until needed. Her team uses the aromatic power balls to investigate how human scent attracts female mosquitoes.

Other scientists might have left such vaguely unpleasant tasks to their assistants. But Vosshall, an HHMI investigator at Rockefeller University, engages in the stinky socks enterprise the way she engages in so many things—with a spirited and contagious enthusiasm. After our chat in her apartment, which includes a tour of the artwork she collects from contemporary painters and photographers (as well as a quick hello to Ophelia's pet tarantula), we head crosstown to her lab. There she opens the freezer to show me where the socks are stored, and laughs at how many of the labeled specimens are hers.

The science of smell has intrigued Vosshall for years, and wearing odiferous nylons is just a small piece of it. In her office at Rockefeller, where she is head of the Laboratory of Neurogenetics and Behavior, several small refrigerators house rows of another kind of art she collects, high-end perfume (her personal favorites are two scents from the Parisian house of Frédéric Malle: Lys Méditerranée for summer, Dans tes Bras for winter). She says refrigeration keeps the scents fresher. Another fridge contains a strictly scientific collection of small vials of smell samples, part of Vosshall's attempt to categorize scents according to their chemical structure, a kind of periodic table of smell. Eventually, she hopes—but this is a long way off—scientists will be able to do for smell what is possible for vision and sound: provide an objective measurement (like a wavelength for a particular color or musical note) from which to infer a particular smell.

Her work on the mechanics of mosquito olfaction carries implications for global public health. Because mosquitoes detect their human targets by smelling them, her research might one day reduce the incidence of common and deadly mosquito-borne infections, such as malaria and yellow fever.

AN INSECTS-ONLY SMELL SYSTEM

Vosshall has been working in olfactory science since 1993, when she became a postdoc in the laboratory of neuroscientist and HHMI investigator Richard Axel of Columbia University. Her first discovery was controversial, since it described an olfactory receptor system that was unique to insects. This went against the conventional wisdom that most receptor systems are conserved from worms to humans. Her work on the insect olfactory receptor, called Orco, was originally done in the fruit fly *Drosophila melanogaster*. Later, Vosshall and her colleagues decoded an olfactory sensory map in the fruit fly brain, through which the activation of a particular fly odorant receptor leads to a particular behavior.

In 2008, Vosshall's lab group, which consists of six to nine postdocs and about five graduate students, began to shift its attention to mosquitoes—which explains the socks in the freezer. In 2008 and in subsequent studies in 2011, her group elucidated the first modern scientific explanation for how the popular anti-mosquito compound DEET works—it confuses the insects by jamming their odor receptors. Ultimately, Vosshall says, she hopes to help develop more targeted, more efficient insect repellants, a crucial weapon against mosquito-borne diseases like malaria.

ENTICING AROMAS

Reaching into her office fridge, Vosshall opens a vial and smells it, then passes it to me. "This is violet," she says, and I sniff. The smell is luscious and a little heady, almost more food than flower. Reluctantly, I give it back to her. (I probably couldn't have continued smelling with such pleasure even if I had held on to it; even a strong scent will pretty much disappear when you try to inhale it a second time.)

She opens another vial, sniffs, and visibly shudders. "Gaaaah," she says. "I didn't realize what this was. Here, smell." Foolishly, I sniff the vial that had thoroughly disgusted her. But I can't smell anything at all. Vosshall seems delighted.

"That's androstenone," she tells me. "It's a component of male sweat, and a small percentage of people are unable to smell it." Most people are totally grossed out by the scent, she says. Another 15 percent or so find it less disgusting—some even like it, describing it as smelling sort of like vanilla. And within that group is an unknown minority of people who, like me, can't smell androstenone at all. The key is the gene for the olfactory receptor OR7D4. Vosshall probably has two good copies. I probably have two faulty

copies. She's doing some studies now to test the sensitivity of young women to these odors at the most fertile point in the menstrual cycle. The women sniff from two vials of androstenone in different concentrations, as well as two control vials, while their sweat response and cortisol response are measured. Her "long-term dream," she says, is to study the effect of OR7D4 and other receptors on general sociability or sexual responsiveness, but these studies are especially difficult to conduct.

"The only available experiments are very indirect," she says. Asking a person to sit in a laboratory and smell a sex-related odor and give a rating of how pleasant or unpleasant the scent is, she says, "is very far abstracted from human sexuality and does not really capture the biology well."

Vosshall discovered OR7D4 with her Rockefeller collaborator Andreas Keller and a team led by Hiroaki Matsunami at Duke University. When they announced their finding of the androstenone-sensing receptor in 2007, there was a little ripple of amazement in the olfactory science world. A *Newsweek* report referred to some good-natured jealousy among other smell investigators.

WORKING AT THE FRINGES

"There are some people you meet and you know that they will do something very meaningful in science," Vosshall's postdoc advisor Axel told me in a phone conversation laden with superlatives. "She's really strikingly dynamic, and that's coupled with experimental fearlessness and thoughtfulness."

Axel said he is particularly impressed by Vosshall's perseverance, no matter how many wrong turns she takes along the way. "Leslie is able to enter into new and difficult experimental arenas with the knowledge that it's going to take a depth of understanding and time to make a meaningful contribution."

Vosshall's discovery of a unique olfactory system for insects was a bonanza, she says. "The fact that the target proteins are only present in insects is a huge convenience." It means scientists will be able to prevent and reduce mosquito biting in a way that should have no effect on humans. To move in that direction, she is collaborating with Bayer CropScience in Germany to devise an insect repellant that blocks the insect's ability to smell. The goal is to find a product as effective as DEET that is longer lasting, less oily, less toxic, and safe enough to use on infants.

Vosshall says she has always preferred working at the fringes of science, where the questions are most interesting and least explored. Her rule of thumb for whether to pursue a specific scientific inquiry: unless precisely three laboratories are already working on it, forget it. More than three and the topic is already too popular for her. Fewer and there aren't enough colleagues who are knowledgeable about the subject with whom she can exchange ideas.

When she studied the function of insect odorant receptors, for instance, the only other people she says were working on the problem were Kazushige Touhara in Tokyo and Bill Hansson in

With an eye for the uncommon, Leslie Vosshall's life is imbued with art, enterprising research, and community engagement—which feeds back into her science.

Germany, both of whom she eventually collaborated with. "When the field gets very large," she says, "collaborations become harder to arrange, and secrecy is more of a barrier."

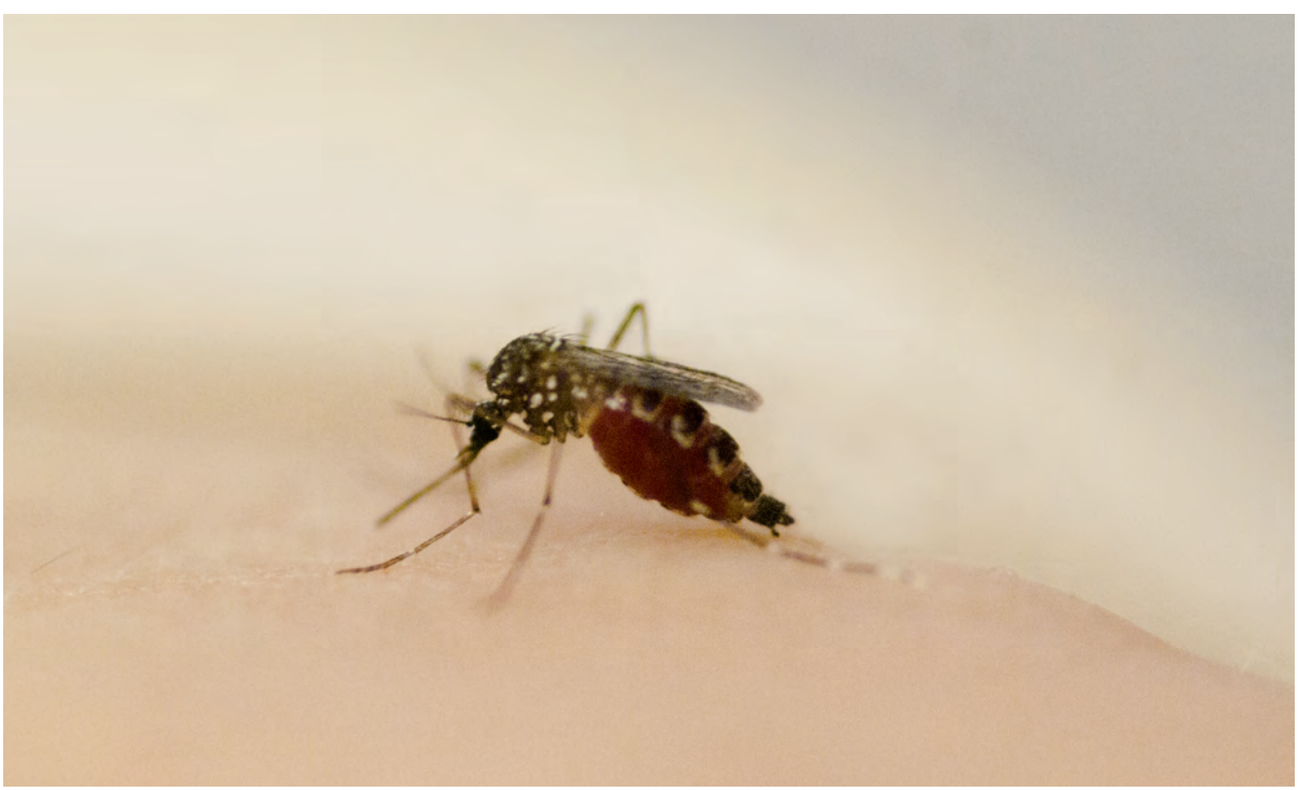
Vosshall's outsider status goes back to childhood. She was born in Lausanne, Switzerland, the eldest of three children of nomadic, adventurous parents. Before she was eight years old, she had moved six times to four countries, going back to Switzerland every summer for family vacations crammed into a bare-bones shack high in the Swiss Alps. On the first day of third grade in suburban New Jersey, where the Vosshalls finally settled, young Leslie didn't speak a word of English. She picked it up quickly—she's pure New Yorker now—but she always held on to that feeling of being just outside the normal flow of things.

"Even in high school she was fairly counterculture," says her sister, Nicki Dugan, a public relations executive in San Francisco. "We spent a lot of time poring through the Salvation Army men's department looking for ties and David Byrne–style big jackets. She tended to want to stand out."

Stylistically, Dugan says, Vosshall was into angular haircuts, multiple ear piercings, and hair dyed colors that nature never intended. As a young teenager she spent weekend afternoons exploring Manhattan on her own, and took solo summer trips, first to Greece and then to Cape Cod. It was during two summers at the Marine Biological Laboratory in Woods Hole, Massachusetts, where she worked for her uncle, Philip Dunham of Syracuse University, that she fell in love with science.

"Mainstream was just taboo for Leslie," says her sister. But even though Vosshall favored the punk scene and avant-garde music, she was an attentive student who graduated in 1983 as valedictorian at Kinnelon High School. She chose Columbia over the other Ivy League schools she could have attended, partly because she liked being in its pioneering first coed class, and partly because it was in New York, a city she always wanted to live in and now can't imagine leaving.

From Columbia, where she majored in biochemistry, Vosshall went to Rockefeller University for her doctorate, where she studied circadian rhythms in the fruit fly. "Even back then she was fearless," says Marina Picciotto, a close friend from graduate school who is now a professor of psychiatry, neurobiology, and pharmacology at Yale School of Medicine. "In every interaction you ever have with Leslie, she's always herself, always speaks her mind." Picciotto and Vosshall have remained close friends, both married to neuroscientists and with children about the same age. Sometimes the families attend scientific conferences together, so one of the parents can take the kids to the zoo while the other three attend the scientific sessions.



Vosshall's arm offers a pleasing scent to this mosquito, which detects its prey through smell. She aims to block that olfactory system to stop diseases like malaria, which kills up to 1 million people each year.

Leslie Vosshall lab

In grad school, Vosshall held on to a separate, bohemian life in addition to her workaday scientific world. She tried her hand at experimental filmmaking. "I made lots of really bad Super 8 nonnarrative films," she says. "I lived downtown at the time—I was married to a musician and I had a lot of friends who were filmmakers. I wanted to get into the action, too."

Picciotto remembers being cast in one of Vosshall's films as Julia Child in the laboratory, whipping up a preparation of brain specimen in a Sunbeam blender. That artsy phase was short-lived, Vosshall says. "You have to know your limits. Now I just buy a lot of art."

THE WOMAN'S ROLE

Vosshall takes her role as a woman in science seriously, but she doesn't put it at the forefront of her activities as some woman scientists do. "She's not afraid of taking risks or of being perceived as exactly who she is," Picciotto says, "which is an incredibly brilliant scientist with an extremely strong aesthetic sense—and also a woman in a world dominated by men."

At age 47, Vosshall says she is lucky to be part of the bridge generation, when it became much easier to be a woman in science. "I felt like, with a few exceptions, people expected me to be a scientist and encouraged me." She always had lots of female peers and colleagues, she says—that is, until recently. After their postdoctoral work, a "disappointing" number of women drop out of the tenure-track academic career path that she was on—meaning that now, as a full professor, she says she is "constantly the only woman in the room."

It's often the career-versus-family quandary that forces women to leave science, but Vosshall says she managed to have a child without breaking stride largely because Rockefeller made it easy. "There is terrific day care right here on campus," she says. And her husband, Kevin Lee, executive director of the Ellison Medical Foundation, is a hands-on father, taking Ophelia to fencing, art, and rock guitar lessons so Vosshall can spend time in the lab, or at home at her desk in a corner of the expansive living room.

PUBLIC TALKS AND SCHNOZMOPOLITANS

Vosshall takes her public role seriously and is committed to explaining her work to the public. She was featured last year at the World Science Festival, a three-day annual event in New York that brings together smart lay people and marquee-name scientists. At the session called "The Science of Smell," Vosshall entertained her audience with tales of "strip club science" (studies showing that female strippers get more tips when they're ovulating, possibly because they're sending off unconscious scent signals) and, as she put it, the "empirical" and "artistic" nature of perfumery.

She was also an early participant in the popular Secret Science Club, which meets monthly at a Brooklyn bar where people go to talk science, ask questions, and drink thematic cocktails. The one cooked up for Vosshall's lecture about smell was called the "Schnozmopolitan."

> MAINSTREAM WAS JUST TABOO FOR LESLIE.
>
> —NICKI DUGAN

Through these public appearances, Vosshall is not only disseminating scientific information to the public, she's also indirectly finding hundreds of volunteers for her smell studies. Her work on mosquitoes was detailed in *The New Yorker*, which brought forth hundreds of people willing to tell their mosquito-biting stories. Some people seem never to get bitten, others are mosquito magnets, and everyone has a pet theory about what distinguishes the two in terms of what they eat, what color clothing they wear, what their blood type is, or what cologne they use.

Vosshall is aiming at a more scientific analysis, bringing those volunteers to Rockefeller for a formal study involving blood analysis, detailed medical histories, and follow-up to see if she can find any genetic or other traits that make some people absolutely irresistible to mosquitoes.

She is also conducting a study of more than 1,000 volunteers who are brought in to give blood samples (for genetic analysis) and to describe a battery of smells according to 146 standard descriptors (such as smoke, soil, excrement, urine, gasoline, or rose). Her goal, she says, is to "try to correlate their olfactory idiosyncrasies to their DNA."

With so many different projects grabbing her interest at once, Vosshall is demonstrating the style and pacing that she's maintained her whole career. As her friend Picciotto says, "Leslie is always thinking of next steps rather than last steps." ■

FOR MORE INFORMATION: To see Vosshall speak at the 2011World Science Festival, visit www.worldsciencefestival.com/videos/how_do_we_smell.