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Hutch scientist unlocked secret to sense of smell

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- Author/Byline: Carol M. Ostrom, Seattle Times staff reporter
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- Correction: Correction Publication Date: 10/06/2004 - Dr. E. Donnall Thomas of the Fred Hutchinson Cancer Research Center received the Nobel Prize in physiology or medicine in 1990. His name was misspelled.
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Her mother used to grumble about her stubborn persistence and "one-track mind" when faced with a problem. In later years, she focused on her lab work with laser-beam intensity, reducing time away to the "one-minute dinner."

Curiosity and a propensity for becoming intrigued with thorny questions paid off for Dr. Linda Buck, informed yesterday at 2:30 in the morning that she had won the Nobel Prize in physiology or medicine for her research on the sense of smell.

Buck, a member of the Basic Sciences Division at Fred Hutchinson Cancer Research Center in Seattle, fumbled the phone and accidentally hung up on Stockholm, Sweden. But Stockholm called back, and yesterday, with one hour of sleep, she faced a roomful of reporters and admirers, eager to learn exactly what it was she'd done in the lab.

Dr. Lee Hartwell, president and director of "The Hutch," took the first crack: "Today's Nobel laureate, Dr. Linda Buck, has discovered the molecules that detect odors and relay that information to our nervous system."

With Dr. Richard Axel of Columbia University, Buck has gone on to "illuminate fundamental aspects of our sense of smell and how our nervous system detects those smells," said Hartwell, himself a Nobel Prize winner in 2001.

Axel and Buck will share the $1.35 million prize, which they'll receive Dec. 10 in Stockholm.

Smell is an important sense, connecting the brain directly to the outside world through a pathway that was little understood before Buck and Axel co-published their groundbreaking work in 1991, defining the genes and proteins involved in transmission of "smell" information. Buck worked in Axel's lab at Columbia as a postdoctoral fellow.

A graduate of Seattle's Roosevelt High School and the University of Washington, Buck earned a doctorate in immunology at the University of Texas Southwestern Medical Center at Dallas. She spent 11 years at Harvard Medical School before she came to The Hutch in 2002.

Buck, 57, said her discoveries may not have immediate practical or commercial applications.

Eventually, she's sure they will play a part in treating disease, by helping reveal the mechanisms the nervous system uses to organize and encode information. Smells link to memories and perceptions, as well as to emotions and physiological changes such as fear, stress and appetite.

"You do basic science research to understand mechanisms," Buck said. "You know — it's absolutely certain — that from those basic mechanisms will come information that's critical to treating disease. There's just no doubt about that."

Mentors

Buck is the 11th woman to win a Nobel in sciences.

Her mother was a homemaker who was obsessed with puzzles. Her father was an electrical engineer who pushed his three daughters to join him in tinkering on various projects at home.

Buck said she was fortunate to have excellent mentors in research, including Dr. Ellen Vitetta, now director of the Cancer Immunobiology Center at University of Texas Southwestern.

As a graduate student, Buck worked with Vitetta to describe a class of cells that helps fight infection.

"If there is somebody who demands excellence and perfection, then that's instilled in you, from your earliest experiences, and you maintain that demand on getting it right, and being a careful scientist," Buck said. "Ellen Vitetta was an excellent mentor. She taught everyone in her lab how to do excellent science."

Vitetta, in a statement from UT Southwestern, called Buck a "highly creative and unusual individual" whose interest in the diversity of the

olfactory system began with her interest in the diversity of the immune system.

Her former mentor attributed Buck's achievement to "hard work, good luck and a good nose."

Lisa Horowitz, a medical doctor who worked in Buck's lab in the mid-'90s at Harvard as she received her doctorate , described Buck as "a very intense, driven — but passionate and excited — scientist."

"She wants to explore what she feels are important and exciting areas of science," said Horowitz, who is working in Buck's lab again. "She's willing to take risks, as well."

Buck, asked if she'd ever felt discriminated against as a woman in a mostly male field, said there may have been barriers, but she didn't notice.

"She's the kind of person who wouldn't notice those things," Horowitz agreed. "She focuses on the things she thinks are important."

Solving the puzzle

Like many scientists, Buck focused on a question "she found exciting and worth sacrifice," Horowitz said, and gave "much of her energy and her life to her career."

That's one of the reasons she stayed longer than the typical post-doc fellow at Axel's lab: She became obsessed with solving the puzzle of smell.

"The question we were interested in really has two parts," Buck said. " One question is: How can we detect so many different chemicals as having smell? It's been estimated that humans can detect anywhere from 10,000 to 100,000 different chemicals as having an odor."

Even a small chemical change is detectable by us, perhaps changing a "rose and orange" smell to "sweaty and sour," she said.

The second question: "How does the brain translate information into perceptions?"

She and Axel strategized there must be many kinds of receptors. Humans, they found, have about 350 different odor receptors, whereas mice have about 1,000. And the receptors work together, in different patterns.

They found that a single odor — typically made up of multiple odorant molecules — is recognized by multiple receptors. One receptor can recognize different odorants, but different odorants are recognized by different combinations of receptors.

"One analogy I've used ... is the use of letters of the alphabet to form different words," Buck explained yesterday. "You put letters of the alphabet together in different combinations and you have different words. Similarly, you can put these different receptors together and get different smells."

But how does the brain organize that information? And what does the brain do with the information to generate perceptions?

Buck said her lab and Axel's lab, working independently, made a discovery: When information about a smell goes from receptors in the nose to the olfactory bulb in the brain, and then to the olfactory cortex in the brain, there is a different organization or "map" at each level.

So the information from that first whiff of a rose, say, is "deconstructed" into tiny parts, going to receptors contained in perhaps 5,000 different neurons in the nose. Eventually, the information comes together in single neurons in the olfactory cortex, a part of the brain. From there, the information goes to higher levels of the cortex, "and we know nothing about those," Buck said.

She's still researching smell, but Buck has added a new scientific interest: aging. Using nematodes, a type of worm, she's studying how chemicals extend life span. She thinks it's possible a small group of cells programs aging throughout the body.

She receives funding from the National Institutes of Health and the Howard Hughes Medical Institute, she said.

Buck, who recalled a period "filled with angst" in her 20s as she tried to figure out what to do with her life, said she feels extremely lucky to be a scientist.

For her, there are many questions yet to be answered. For example: Why do mice hate skunk smell as much as we do? And why are they crazy about the smell of vanilla?

"The important thing is that persistence," Buck said. "There's a lot left to discover. Even though we've been working on this puzzle for about 16 years, we're just scratching the surface of it."

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Seattle's Nobel connection Linda Buck is the sixth Nobel laureate from Seattle since 1989. The others are:

Hans Dehmelt, University of Washington, 1989: Dehmelt became the first sitting UW faculty member to win a Nobel when he and Wolfgang Paul of Bonn University won the physics prize for isolating individual electrons and ions and measuring them. The discoveries led physicists to revise their estimate of the size of an electron by a factor of 10,000.

E. Connall Thomas, Fred Hutchinson Cancer Research Center, 1990: Thomas won the 1990 Nobel Prize in physiology or medicine for his research on bone-marrow transplantation. Thomas shared the award with Joseph Murray of Boston, who developed related therapies to retard tissue rejection in organ transplants.

Edmond Fischer and Edwin Krebs, UW School of Medicine, 1992: Fischer and Krebs received the Nobel Prize for physiology or medicine for their discoveries in the 1950s of proteins that are important in cell-to-cell communication.

Lee Hartwell, Fred Hutchinson Cancer Research Center, 2001: An expert in yeast genetics, Hartwell won the Nobel Prize for physiology or medicine for work that showed how normal cells divide and the mechanisms behind the uncontrolled growth of cancer cells. He conducted much of his research at the University of Washington.

- Caption: photo,illustrationSteve Ringman / The Seattle Times : Dr. Linda Buck answers questions yesterday at the Fred Hutchinson Cancer Research Center in Seattle. (0394828362)Knight Ridder Newspapers: How the sense of smell works (GFNOF551)Steve Ringman / The Seattle Times : Dr. Linda Buck answers questions yesterday at the Fred Hutchinson Cancer Research Center in Seattle. (0394828362)Knight Ridder Newspapers: How the sense of smell works (GFNOF551)

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