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Linda Buck and the Science of Scent

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Linda Buck has pioneered research in olfactory neuroscience, opening up an entire field of study that has grown immensely over the past 20 years. Throughout her career, she has been fortunate to have support and opportunities in all the right places. Buck was born in 1947 in Seattle, Washington. As a young girl, she was full of curiosity and spent much of her free time on what she dubbed adventures. Her parents were very supportive and encouraged Buck to "think independently and to be critical of [her] own ideas;" they wanted her "to do something worthwhile with [her] life." Buck received a bachelor's degree in psychology from the University of Washington, but it wasn't until she took a class in immunology several years after graduation that she realized she wanted to be a biologist (1).

Throughout the beginning of her scientific career, Buck worked all over the country in laboratories at well-known universities and medical centers. Each stage of Buck's career has influenced her interests and guided her to where she is today. In graduate school at the UT Southwestern Medical Center in Dallas, Texas, Buck's research focused on molecular mechanisms at work in biological systems. She did extensive work with cell-surface immunoglobulin used as antigen receptors. In 1980, she moved to New York City to do her postdoctoral work at Columbia University. While carrying out her research in immunology, Buck realized that in order to participate in the molecular studies about which she was passionate, she needed to keep up with new technology and learn about modern molecular biology techniques. This prompted her to move the lab of Richard Axel at Columbia University. At the time, Axel was studying molecular aspects of the nervous system of Aplysia, a sea snail. However, Buck was interested in searching for genes encoding receptors on the surfaces of neurons. Because of this, she decided to develop a technique for cloning genes expressed in a single neuron using Aplysia (2). This technique would later become vital for her olfactory research.

Buck first became interested in the sense of smell and odor detection when she read the 1985 article from Sol Snyder's group discussing the subject. In 1988, she began a three-year research project to find the genes encoding for odorant receptors. Buck had been working on developing

a method to identify rearranged genes in mammalian nervous systems and believed that such past rearrangements may provide insight into the diversity of genes encoding olfactory receptors (2). In 1991, after three years of 12 to 15 hour work days in the lab, Buck and Axel published the article, which would eventually lead to their reception of the 2004 Nobel Prize in Medicine or Physiology (3).

Buck and Axel's 1991 article made huge advances in understanding the sense of smell. Together, they provided evidence that odorant receptors are G-protein coupled receptors, there is a multigene family that encodes for the varied but related odorant receptors, and olfactory receptors are selectively expressed in the olfactory epithelium (4). Buck's research also indicated that there are hundreds of receptors, making the multigene family that encodes for them possibly one of the largest in the human genome. Additionally, they suggest that each receptor accepts multiple odorants, which would account for the tens of thousands of odors detectable by humans (4). This research raised many more questions than it answered, prompting Buck to continue studying the nature of the olfactory system.

Buck's work and the research performed by other laboratories as a result of her discoveries have vast implications for the public. With a true understanding of olfactory receptors, scientists may be able to find a way to switch them on or off. This could be used in simple ways, for example employing a chemical in dirty subways and bathrooms to shut off olfactory receptors and block bad smells. Scientists could possibly clone olfactory receptors of dogs that can detect bombs and drugs to create "ultra sniffers." Implications also lie in the realm of health; blocking olfactory receptors is a technique that could be used to decrease food cravings in people with obesity and to help increase the appetites of cancer patients (3).

Buck continued her work in the underlying mechanisms of the olfactory system after her three-year project. Initially, she looked into how neurons are organized on the olfactory epithelium – where neurons with the same olfactory receptor are spread randomly within an olfactory receptor expression zone – and the olfactory bulb – where axons of similar neurons converge in glomeruli at specific sites (5). Her team ascertained that many odorant sensory neurons recognize not just one odorant, but also a subset of odorants sharing similar structures. Odorant sensory neurons may recognize a large number of odors because each odor code is made up of multiple molecules and activates multiple types of odorant sensory neurons. They also found that other odorant sensory neurons that only recognize a few odorants are animal specific (6).

Buck has continued her research in areas pertaining to nasal detection ability, as well as other areas of research. Her team has performed research pertaining to the detection of pheromones, which are detected by the vomeronasal organ. They suggest that pheromones may be detected by only a few receptors rather than a complex array of receptors as is with odors (5). More recently, Buck's work has turned toward aging. Her team has identified multiple drugs already approved for human use that extend the lifespan of Caenorhabditis elegans, a nematode. They believe that these compounds can now be used with aging mammals to test the effect of the drugs on non-nematode organisms (7).

Linda Buck has greatly influenced the field of neuroscience. She forged the foundation for olfactory research and understanding and is now working to defy time and reduce the effects of aging. As a woman in a predominantly male profession, Buck faced seemingly few obstacles. That said, she still had to work hard to prove herself, just as anyone does in a cutthroat profession. She was fortunate to have parents who shaped her childhood so that as an adult, she would work hard to reach higher goals and obtain many amazing opportunities to work with excellent scientists, which allowed her to establish herself as a prominent and influential neuroscientist.

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