Discovery Of The Odorant Receptor

2004 Nobel Prize Medicine

Richard Axel and Linda Buck were the recipients of the 2004 Nobel Prize in Medicine or Physiology for their study which shed light on odorant receptors and its role on how our olfactory system works.

The Organization of the Olfactory System

Axel and Buck discovered a large family of genes responsible for the different olfactory receptors. They also discovered that there is high specificity when it comes to signal transduction since all receptors from a single family send impulses to a single glomerulus in the olfactory bulb. Information from the olfactory bulb is then sent to the different parts of the brain.

The Importance of the Olfactory System

Olfaction is the process by which we identify chemical substances in the environment via the olfactory receptors in our olfactory epithelium. This process is one of our vital survival mechanisms since it helps us differentiate harmful and poisonous foods from healthy foods. It has been shown that our degree of dependence to our sense of smell is also directly

proportional to the number of odorant receptors in a given species. Fishes, which are not highly dependent to their olfactory system, only have 100 olfactory receptors while mice, which are highly dependent to their olfactory system, were found to have 1000 olfactory receptors and humans have less than 1000 receptors, some of which were lost during evolution.

The Minds Behind the Discovery

Richard Axel was born in Brooklyn, the first child in the family of immigrant parents. During his early years, he immediately fell in love with biology. During the early 60s, he worked as a glassware washer in a laboratory to support his college education. He was then fascinated by Molecular Biology and worked as a research assistant in the same laboratory. After college, he then decided to attend graduate school in genetics. Before he could finish his graduate studies, a war started and he decided to go to medical school at John Hopkins University School of Medicine.

Linda Buck was born in 1947 in Seattle, Washington. She initially wanted to be a psychotherapist so she took psychology in her undergraduate years. Her interest then shifted when she encountered immunology and decided that she wanted to become a biologist. Buck is only the seventh woman ever to receive the Nobel Prize in Medicine or Physiology.

The Path Towards the Discovery

During the 1980s, Richard Axel developed a fascination in the problem of perception, especially towards olfaction. He thought that if genes are the links to what we perceive in the outside world, then the understanding of these genes can provide important insight to the manner by which we experience perception. During the same time, Linda Buck was also fascinated by the unknown mechanism underlying odor detection. She first thought that to solve her problem, she need to know how the odorants are detected by the nose.

In 1988, Axel and Buck together embarked on a research on odorant receptors [1], the answer to both of their questions. During that time, the only things that they know about olfactory receptors were the following: that odorants depolarize and activate olfactory sensory neurons in the nose and that olfactory transduction involves G-protein linked receptors which causes increase in cAMP. Their initial step in the research was to establish three assumptions. First, since the odorants are known to vary in structure, there would also be a variety of related odorant receptors which can be encoded by a multigene family. Second, the odorant receptors are also related to the relatively small set of G-protein receptors which were known during those times. Third, the odorant receptors are expressed in the olfactory epithelium where the sensory neurons can be found.

Buck’s method employed a micropipette to empty the contents of an olfactory receptor cell and then shows exactly which odorant receptor gene was expressed in the given cell. After multiple trials, Linda Buck was able to come up with experimental data showing that there were 1000 odorant receptor genes in the rat genome, the largest family of genes in the chromosome and this gave them the solution to the problem of diversity of odor recognition. They also noted that the 1000 different genes give rise to an equivalent number of olfactory receptor types. Furthermore, they also discovered that each olfactory receptor cell only has one odorant receptor type. Each of these receptors can only detect a limited number of

odorant substances. Receptor cells then send information to glomeruli found in the olfactory bulb. All similar receptor cells send information to a single, complementary glomerulus. The glomeruli then relay the information to the other parts of the brain.

Current Information about the Olfactory System.

Processes Involved in Olfaction

The very first thing that happens prior to scent perception is the binding of the odorants to the olfactory receptors. Olfactory receptors [2] are responsible for the detection of odor molecules. The noteworthy characteristic of the receptor-odorant relationship is that the receptors display affinity for a range of odorants and not just a single odorant. This means that an odorant can bind to a number of different receptors but with different affinities. The binding of the odorant causes structural change to the receptor which activates the G-protein linked receptor in the receptor neuron. The G-protein then activates adenylate cyclase which will then convert ATP to cAMP. cAMP will then open calcium and sodium channels that will allow extracellular sodium and calcium to enter the cells. The depolarization of the cell will begin an action potential which will transmit the information to the different parts of the brain. From the olfactory bulb, olfactory information will then be relayed to both the cerebral cortex which will handle conscious thought processing, and to the limbic system which will generate emotional feelings. This is also the reason why certain feelings and memories are elicited by the scent of a certain odorants.

The story of the discovery of Buck and Axel is a great example of how molecular biology can bring light to mysteries concerning the human brain and its sensory processes. We must remember that both of the authors are not physiologists, but still, they were able to unravel the basics of the olfactory system by the use of molecular biology.

Links
[1] http://en.wikipedia.org/wiki/Olfactory_receptor
[2] http://genomebiology.com/2001/2/6/research/0018/