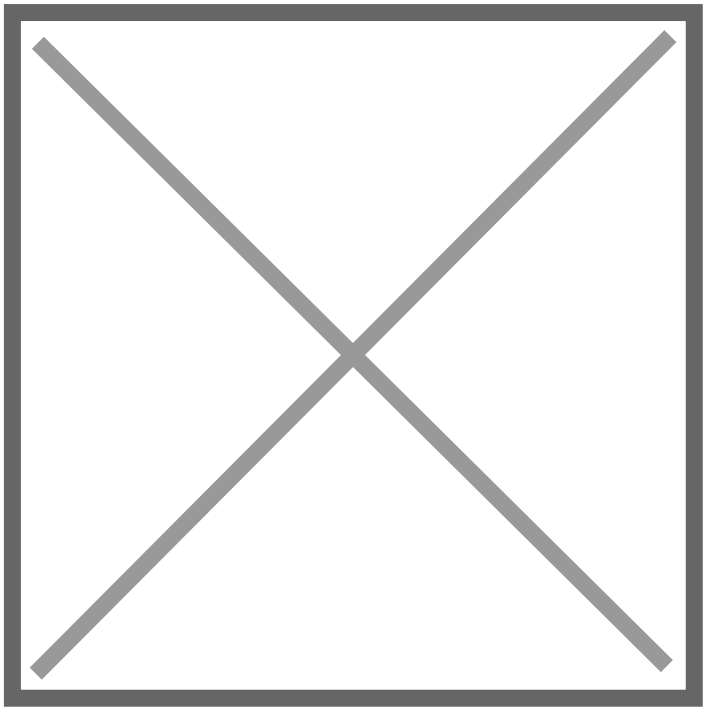
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04 November 2004 | News



p>The Nobel Laureates

The Nobel Prizes for the current year, which were announced recently, have stirred the scientific circles. Significantly, the prizes in Chemistry and Physiology/Medicine were awarded for work at the molecular/gene level having long-term implications for the human health. The Royal Swedish Academy of Sciences awarded the Nobel Prize in Chemistry for 2004 "for the discovery of ubiquitin-mediated protein degradation" jointly to Aaron Ciechanover and Avram Hershko from the Technion, Israel Institute of Technology, Haifa, and Irwin Rose from the University of California, Irvine, USA. Ciechanover and Hershko are the first Israelis to win a Nobel Prize for science.

The Nobel Assembly at Karolinska Institutet awarded the Nobel Prize in Physiology or Medicine for 2004 jointly to American research duo Richard Axel and Linda B Buck for their discoveries of "odorant receptors and the organization of the olfactory system".

BioSpectrum encapsulates a brief profile of these distinguished scientists who have contributed immensely to solve the jigsaw puzzle of life.

Nobel Prize for Chemistry

In the late 1980s, Ciechanover, Hershko and Rose conducted studies that described a cellular pathway by which proteins are marked for destruction. The proteins are labeled with a small molecule called ubiquitin and then rapidly broken down in cellular waste disposers called proteosomes.

The Citation for the Prize read, "In the past few decades, biochemistry has come a long way toward explaining how the cell produces all its various proteins. But as to the breaking down of proteins, not so many researchers were interested. Aaron Ciechanover, Avram Hershko and Irwin Rose went against the stream and at the beginning of the 1980s discovered one of the cell's most important cyclical processes, regulated protein degradation. For this, they are being rewarded with this year's Nobel Prize in Chemistry."

"They (the winners) brought us to realize that the cell functions are a highly efficient checking station where proteins are built up and broken down at a furious rate. The degradation is not indiscriminate but takes place through a process that is controlled in detail so that the proteins to be broken down at any given moment are given a molecular label, "a kiss of death," to be dramatic. ...Thanks to the work of the three Laureates, it is now possible to understand at molecular level how the cell controls a number of central processes by breaking down certain proteins and not others."

The prizes, which include a $1.3 million check, a gold medal and a diploma, will be presented on December 10, the anniversary of Nobel's death.

Nobel Prize for Medicine or Physiology

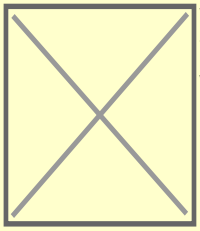
Richard Axel and Linda B Buck were selected by a committee at Stockholm's Karolinska Institutet for their work on the sense of smell. They clarified the intricate biological pathway from the nose to the brain that lets people sense smells.

The Citation for the Prize said, "The sense of smell long remained the most enigmatic of our senses. The basic principles for recognizing and remembering about 10,000 different odors were not understood. This year's Nobel Laureates in Physiology or Medicine have solved this problem and in a series of pioneering studies clarified how our olfactory system works. "

Richard Axel, New York, USA, and Linda Buck, Seattle, USA, published the fundamental paper jointly in 1991, in which they described the very large family of about one thousand genes for odorant receptors. Axel and Buck have since worked independent of each other, and they have in several elegant, often parallel, studies clarified the olfactory system, from the molecular level to the organization of the cells.

Aaron Ciechanover

Currently a professor in the unit of biochemistry, Aaron Ciechanover is also the director of the Rappaport Family Institute for Research in Medical Sciences at the Technion (Israel Institute of Technology) in Haifa, Israel. Born in 1947 in Haifa, Israel, Ciechanover shared the 2004 Nobel Prize for Chemistry with Avram Hershko, 67, also from Technion-Israel Institute of Technology and Irwin Rose, 78, from the University of California, Irvine. The trio discovered the process by which a protein called ubiquitin attaches itself to unwanted proteins, giving them the so-called "kiss of death" that marks them for destruction.



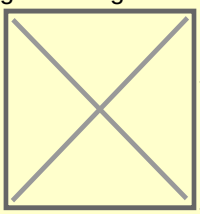
When Ciechanover got the call informing him about the award, he was preparing to go out with his family. This sudden honor took him completely by surprise. "Exhausting", "overwhelming" and "hard to digest" were the words that the 57-year-old scientist used to describe his feelings. "Certainly not in chemistry. I had some thought of medicine. I'm a physician by education and biochemistry. If I thought of it ever, it was in the direction of medicine and physiology, if at all," he said in a telephonic interview to the Nobelprize.org, which is the official website of the Nobel Foundation. "It's wonderful. That's the climax that every scientist can ever dream of. I will not deny that I am proud for me, for this science, for the state of Israel, for my family, for everybody. It's wonderful." he exclaimed.

Ciechanover became a professor at the Technion in 1992 and was an associate professor there from 1987 to 1992. He has also been a visiting professor of pediatrics at Washington University School of Medicine in St Louis since 1987, spending a portion of each year in the School of Medicine's department of pediatrics. He studied medicine at the Hebrew University Medical School in Jerusalem, receiving an MD degree in 1974. Subsequently, he took a break from active academics and served in the Israel Defense Forces during 1974-77. Ciechanover received a PhD degree in 1981. In 1982-84, he was a postdoctoral fellow at the department of biology, MIT, where he worked in the laboratory of Harvey Lodish. Following four years at the Massachusetts Institute of Technology, Ciechanover returned to Haifa as a senior professor. In 2000, Ciechanover and Hershko received the Lasker Prize for their work on the ubiquitin-mediated protein degradation system.

Interestingly he was a graduate student in biochemistry with Hershko at the Technion. Their studies, many of which were in collaboration with Rose, elucidated the protein degradation system. Presently in the same faculty with Hershko at Technion, Ciechanover no longer works with him but heads an independent group, though sometimes they do sit together to write reviews. Still an active scientist, who loves his lab and students, his independent work began in 1986, at the unit of biochemistry, Technion.

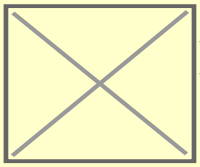
Avram Hershko

Nobel Laureate Avram Hershko is a distinguished professor in the faculty of medicine, Technion-Israel Institute of Technology, Haifa, Israel. He was born in 1937, in Karcag, Hungary and in 1950, Hershko and his family emigrated from Hungary to Israel. The day when the awards were announced, it was a holiday in Israel and he was out on a picnic with his granddaughters. He thus never received the customary call informing him about the Prize and later came to know from a cousin who heard it on the radio. Extremely delighted and excited, about the news, he always had an intuition about the enormous importance of the molecule. Sharing his thoughts with the representative of the Nobel foundation on the phone he advised youngsters to, "Try to find something novel, and open up new problems which is not yet reached a big level at this time, not yet interested, but you think is important. I think that's what I did about 35 years ago. And then, continue with it. Try to find a unique problem which is important, but which is not yet in the center of the attention of biology or of chemistry. I think that is true for discoveries, that's how it should be done".



Hershko obtained his MD degree from the Hebrew University-Hadsassah Medical School in 1965 and his PhD degree in 1969 from Hebrew University in Jerusalem. During 1965-67, he worked as a physician in the Israel defense forces. He carried out post-doctorial research with the late Dr Gordon Tomkins at the University of California Medical Centre, San Francisco from 1969 to 1971. Hershko has pursued his research on intracellular proteolysis at the Technion, where he was appointed associate professor in 1972, professor in 1980 and distinguished professor in 1998. Through rigorous biochemical experimentation, he discovered the role of ubiquitin modification in energy dependent proteolysis and defined the enzymatic machinery that catalyzes ubiquitin conjugation. A passionate scientist, even now, at the age of 67, he enjoys bench work and tries to do an experiment every day. "I think I can still contribute. Not in the same big way as 25 years ago, but still contributing and then still having a lot of fun at the bench," Hershko shared with the Nobel Foundation representative. Since 1987, he has been a member of the Rappaport Institute for Research in the medical sciences, and member of the European Molecular Biology Organization (EMBO) since 1993. A recipient of many awards and honors, Hershko was awarded the Weizmann Prize for sciences in 1987; Israel Prize for biochemistry and medicine in 1994; Wachter Prize by the University of Innsbruck, Austria, in 1999; and Gairdner International Award by the Gairdner Foundation, Canada, also in 1999. Ironically, Hershko has never visited the Nobel website and now he will be immortalized there as part of the galaxy of scientists whose contributions have made a significant difference in human lives.

Irwin Rose

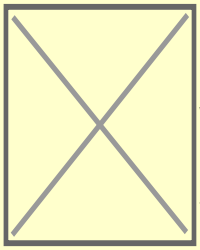


Born in Brooklyn, New York, in 1926, Irwin A Rose grew up in Spokane, Washington. He studied at Washington State College and then served in the US Navy as a radio technician near the end of World War II. He completed his undergraduate degree under the GI Bill of Rights in 1949 at the University of Chicago and went on to earn his PhD in biochemistry at the same university in 1952. At Chicago, Rose, known at the time as "Ernie," worked in professor Birgit Vennesland's laboratory, where he wrote his dissertation on the biochemical synthesis of nucleic acids. He served on the faculty of Yale Medical School's biochemistry department from 1954 to 1963. Prior to his appointment at Yale, he held one-year postdoctoral fellowships in the department of medicine at what is now Case-Western Reserve University in Cleveland and in the department of pharmacology at New York University. In 1963, he became a senior member of the Fox Chase Cancer Center's division of basic science in Philadelphia where he stayed until retiring in 1995. In the late 1970s, Rose and Hershko met at a scientific conference and realized they were working on the same problem. They began collaborating and later Hershko visited Fox Chase Cancer Center in Philadelphia, where Rose was then working. Many of the studies that led to the Prize were done when Hershko and Ciechanover took sabbatical leave and worked with Rose in Fox Chase, Philadelphia. While at Fox Chase, Rose was elected to the National Academy of Sciences in 1979. In 1997, he accepted a special appointment as emeritus researcher at the department of physiology and biophysics, College of Medicine, University of California at Irvine (UCI), where he continues to have research responsibilities.

A fantastic human being and a fantastic scientist, Rose, said that he enjoyed working with the faculty and students of University of California at a reception hosted in his honor on October 8 at the UCI. Chancellor Ralph J Cicerone who was also present at the reception said that Rose has been a big contributor to the department and he believed that even though Rose is 78 years old, he would not hang his boots and continue his research work. Praising Rose for his contributions, UC President Robert C Dynes said in a UCI press release that, "The breakthrough work of Professor Rose will help us create medicines and therapies enabling people to live longer and live better."

Richard Axel

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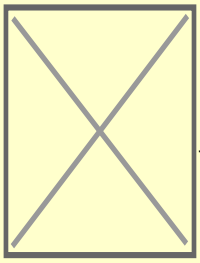


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Linda Buck

Linda B Buck was born in 1947, in Seattle, Washington. She earned her PhD in immunology in 1980 from University of Texas, Southwestern, in the lab of Dr Ellen Vitella. She then spent two years (1980-82) doing postdoctoral research in immunology at Columbia University College of Physicians and Surgeons (laboratory of Dr Benvenuto Pernis), at which time she made a major career change and moved to the molecular neuroscience laboratory of Richard Axel. From 1982-1991, she conducted postdoctoral research in the Axel lab, and it was there that she made her groundbreaking discovery of the olfactory receptor gene family, which consists of a large gene family of G-protein coupled receptors that are selectively expressed in olfactory epithelial neurons. This work is the first to define one of our sensory systems in the most detailed manner possible by defining the genes and proteins that control this remarkably complex response. This is a landmark achievement in the study of the nervous system.



From 1991 to 2002, Buck worked at the Department of Neurobiology at the Harvard Medical Institute. She joined the Harvard faculty in 1991 as an assistant professor of neurobiology located in the Department of Neurobiology at the Quad and was advanced to associate professor in 1996, and to professor in 2000. Dr Buck joined the Fred Hutchinson Cancer Research Center in 2002 after 11 years as a faculty member at Harvard and has been with the Center since then.

On being quizzed by the Nobel Foundation representative about her discovery having any clinical applications, Buch remarked, "I think, ultimately (it will). It hasn't yet, but in terms of olfactory disorders there's a possibility. But I think that, like in many other biological areas, the information that you gain doesn't have a direct or immediate clinical use, and rather it gives you insight into biological mechanisms, which then can be transferred into other areas. It provides insight into other areas, and also I think that using the odour receptors as molecular tools to investigate the brain, we may discover things about how the brain works that we don't necessarily know anything about yet. But of course we won't know that until we find out how it works."

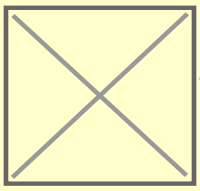
Buck, also a Howard Hughes Medical Institute investigator and an affiliate professor in the Department of Physiology and Biophysics at the University of Washington, is the recipient of many national and international scientific awards. In 2003, she received the Gairdner Award, the Perl-UNC Neurosceince Prize and was elected a member of the National Academy of Sciences. She's also the recipient of the Unilever Science Award, the Louis Vuitton-Moet Hennessy Science for Art Prize, the RH Wright Award in olfactory research and the Lewis S Rosenstiel Award for work in basic medical research.

Prof. K Kannan

The Indian who discovered the function of ubiquitin

Though many may not be aware but amongst all the excitement generated by the Nobel Prizes, an Indian scientist, Prof. Krishnamoorthy Kannan, a biochemist at the Guru Gobind Singh Indraprastha University in Delhi, might have just missed a share of this year's Nobel Prize in Chemistry. Reason: The Indian Government did not recognize his path breaking work on the ubiquitin molecule about 12 years ago.

Significantly, discovery of the intracellular function of ubiquitin molecule won the Nobel Prize in Chemistry this year, which was shared by two Israelis and an American.



Kannan was the first to identify an equally important function of ubiquitin outside the cells in the late Eighties. He discovered that ubiquitin homes in and binds to the haemopoetic stem cells. By staining it with a dye, he showed that ubiquitin could be used as a probe to seek out stem cells and separate them outside the body. This potentially opened novel avenues for treatment of leukemia and even AIDS. These difficult experiments were done with limited resources in not very sophisticated labs. He was then working at Span Diagnostic Research Centre, at Udhna, in Surat.

Kannan's work was published in the British Journal of Haematology in 1993. Incidentally, this was the first evidence of the extra cellular role of ubiquitin in the world. It has been cited in many international reviews but did not get due recognition in the country.

Speaking to BioSpectrum, Prof. Kannan said, "I am glad that the molecule has finally been recognized. We have worked on the extracellular role of ubiquitin. I started work on ubiquitin in 1986, in fact from 1982, with very limited resources. Ever since, I have been associated with Indraprastha University, I have been teaching my students about ubiquitin, in fact after the Prize was announced, one of my students sent me an e- mail saying that Congratulations Sir, your molecule has won the Nobel Prize!" "I was very convinced that this is a hot spot problem to work on. But the country did not have the vision to appreciate what I was saying then. They still suffer from the white man syndrome. Similarly, I was the first to show the importance of stem cells and the first to introduce this term to India about 15 years ago," he added.

In spite of not getting accolades, Kannan has been continuously working on the ubiquitin molecule. Next month, he along with his student will be presenting their work on ubiquitin as a novel tool to study early stages of brain development at Goettingen University in Germany. "We are also working on cancerous cell lines, tissue engineering where right now we are working on the blood cell formation but will ultimately work on organ and tissue development," he said. "Stem cells have a huge potential and I must create enough critical mass (trained researchers) for this field. For this, I am writing a book on education, as we have to excite the young brains and catch them young. I want India to be in the forefront in this area," he added.

Prof. Kannan did his bachelors and masters in Chemistry from the Delhi University and IIT Bombay respectively. He obtained his PhD in biochemistry from Mysore University. He has been closely associated with both the academia and industry and has had long stints with CCMB, Hyderabad and Ranbaxy Research labs, New Delhi. Presently he is a professor at the school of biotechnology in the Indraprastha University at Delhi.