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FACULTY OF SCIENCE  
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A Nobel Laureate Lecture

Life and death – Why our proteins have  
to die so we shall live

by

Prof. Aaron Ciechanover, M.D., D.Sc.,  
2004 Nobel Laureate for Chemistry

2.00 – 3.00 pm. 10 April 2008  
L-01 Room, Lecture Building  
Faculty of Science, Mahidol University

Rama VI Rd., Bangkok 10400

# **“Life and death – Why our proteins have to die so we shall live”**

by

**Prof. Aaron Ciechanover**

2004 Nobel Laureate for Chemistry

## **Abstract**

Proteins are the machines that drive our body. They are responsible for all our activities such as walking, seeing, hearing, heart beeping, digestion, respiration, secretion of waste materials. Unlike the items that surround us and that we use daily, like furniture and our clothes, the body proteins are in a dynamic state, they are being destroyed and renewed all the time and in an extensive manner. We are destroying daily up to 10% of our proteins and generating new ones instead. The obvious questions are (i) why this occurs, (ii) what is the mechanism that carries out this function, (iii) what are the diseases that result if the mechanism does not work properly, and (iv) how can we cure these diseases. In the lecture Prof. Ciechanover shall try to shed light on these problems and help us to understand the value of basic research for the development of drugs to target cancer and neurodegenerative disorders like Alzheimer's.

# Biography

## Prof. Aaron Ciechanover

Prof. Aaron J. Ciechanover is a 2004 Nobel Laureate for Chemistry and a Distinguished Research Professor in the Faculty of Medicine of the Technion Israel Institute of Technology in Haifa.

Born in Haifa, Aaron Ciechanover received his Master of Science in 1970 and his M.D. in 1975 from the Hadassah Medical School of the Hebrew University in Jerusalem. He received his doctorate in medicine in 1981 from the Technion and has been a Distinguished Research Professor at the Center for Cancer and Vascular Biology and the Director of the Rappaport Family Institute for Research in Medical Sciences at the Technion. In 2004 he shared the Nobel Prize for Chemistry with Professor Avram Hershko and Professor Irwin Rose for the discovery of ubiquitin-mediated protein degradation, a mechanism by which the cells of most living organisms cull unwanted proteins.

Proteins build up all living things: plants, animals and therefore us humans. In the past few decades biochemistry has come a long way towards 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 were rewarded with the Nobel Prize for Chemistry.

Aaron Ciechanover, Avram Hershko and Irwin Rose have brought us to realize that the cell functions as 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 moment are given a molecular label, a 'kiss of death', to be dramatic. The labeled proteins are then fed into the cells' "waste disposers", the so called proteasomes, where they are chopped into small pieces and destroyed.

The label consists of a molecule called *ubiquitin*. This fastens to the protein to be destroyed, accompanies it to the proteasome where it is recognized as the key in a lock and signals that a protein is on the way for disassembly. Shortly before the protein is squeezed into the proteasome, its ubiquitin label is disconnected for re-use.

Thanks to the work of the three Laureates it is now possible to understand at a molecular level how the cell controls a number of central processes by breaking down certain proteins and not others. It has become clear that ubiquitin-mediated degradation of proteins is central to the regulation of basic cellular processes including cell cycle, transcriptional regulation, growth and development, differentiation, apoptosis, receptor modulation, DNA repair and the maintenance of the cell's quality control. With the multiple substrates targeted and processes involved, it is not surprising that the system has been implicated in the pathogenesis of many diseases, a broad array of malignancies and neurodegenerative disorders among them. This led pharma companies to initiate efforts to develop mechanism-based medications, and one successful drug to combat cancer is already on the market, with many more in the pipeline.

Besides being awarded the Nobel Prize Professor Ciechanover shared the prestigious Albert Lasker Award for Basic Medical Research, the second most prestigious prize in life sciences and medicine, and the Israel Prize, the highest recognition bestowed by the State of Israel. Among many esteemed bodies, he is a member of the Israeli National Academy of Sciences and Humanities, the Pontifical Academy of Sciences of the Vatican and the American Philosophical Society.



## **Introduction to the Faculty of Science, Mahidol University**

The Faculty of Science was founded as a Premedical School in 1958 by **Prof. Dr. Stang Mongkolsuk**, and took the name of Faculty of Science, Mahidol University in 1969 with the main objectives;

- To continuously develop graduates, scientific and technological personnel who have the highest expertise and ethical standards to serve the societies and the country,
- To generate research of international standard and offer services of international quality and standard to every level of educational institution, as well as to transfer knowledge and appropriate technology to the public for the benefit of sustainable development of every community and all mankind,
- To instigate in students as well as faculty staff discipline, ethics, professional codes of conduct, and maintenance of the country's cultural heritage.

The Faculty is located on Rama VI Road, Ratchathewi District. The Faculty is responsible for teaching science to all first year undergraduate students of the university, presently numbering 3,500 students per year, using its facilities at the Salaya Campus, and also assists in teaching second year students in the allied health sciences and medicine. The Faculty of Science offers B.Sc. programs in seven disciplines, namely Chemistry, Computer Science, Biology, Biotechnology, Mathematics, Plant Science, and Physics, to a total of some 300 students per year. The Faculty also has very strong, well-established international graduate programs, 22 programs at Master's level and 21 programs at Ph.D. level, in various scientific disciplines. There are about 600 students at Master's level and 400 at the Ph.D. level. The Faculty is one of the most prestigious institutes for research and post-graduate training in Thailand and ASEAN.

The Faculty of Science places a strong emphasis on research, not only as part of the thesis work for graduate programs, but also as an ongoing commitment to international scientific advancement and national

development. This serious and sustained emphasis on research has created an excellent academic atmosphere within the Faculty, which has allowed staff to compete successfully for grants, both nationally and internationally, and to perform work of excellent quality. Moreover, staffs from the Faculty have won numerous awards for their outstanding research work at the national, regional and international levels. Staffs at the Faculty have also performed many administrative and advisory functions in various academic organizations at the national, regional and international levels. Currently, the Faculty of Science consists of 13 departments: Anatomy, Biochemistry, Biology, Biotechnology, Chemistry, Computer Science, Mathematics, Microbiology, Pathobiology, Pharmacology, Physics, Physiology, and Plant Science. The Faculty of Science currently has a total of 813 staff, with 314 being academic staff, 155 teaching assistants, 232 support staff and 112 employees. The main goals of **Professor Dr. Skorn Mongkolsuk**, the present Dean, are for the Faculty to achieve sustainable development, academic excellence, effective teaching and learning, and high quality research with the harmonious environments of internationalization.

### **The Teaching and Learning**

The Faculty of Science is responsible for teaching about 1,669 undergraduate students majoring in Faculty, 666 Master's students and 468 Doctoral students. In addition, the Faculty offers courses in Basic Sciences and English to all first year undergraduate students of the university, as well as to second year undergraduate students of some faculties, amounting to another 4,003 students. The Faculty also teaches preclinical science subjects to medical students from Ramathibodi Hospital and Bangkok Metropolitan Administration Hospital.

### **Research Areas**

Research is one of the most important responsibilities of the Faculty of Science. The emphasis of research is generally on problems of local relevance, so researchers have the advantage of greater accessibility to samples, local expertise and potential benefits to the community. Presently, the Faculty is now an internationally known research center for science, technology and medical science. Academic staffs publish some 130-160 articles per year in reputable international journals, more than any other institutions in Thailand for the past 10 years. The Faculty's academic staffs have excelled in many areas of research, particularly those that are relevant to the national and regional needs. Major research projects undertaken by biomedical science groups involve the application of innovative biotechnology and genetic engineering techniques for the diagnosis,

prevention and treatment of tropical diseases in humans and animals, i.e. malaria, melioidosis, schistosomiasis, filariasis, liver flukes, babesiosis, dengue and thalassemia; the reproduction of cattle and important food and medical substances for man and animals from indigenous natural materials; the control and improvement of the environment. The physical science groups have engaged in many important research projects, such as the studies of physico-chemical properties and utilization of liquid crystals, natural and synthetic polymers, the development of ferrite-polymer composites for industrial applications, chemistry and applications of natural products, organic syntheses of drugs for tropical diseases and other useful compounds, and the use of computers in chemistry, chemical physics and mathematical modeling.

### **Leading researchers**

Apart from teaching, all faculty members also concentrate on research work. So the Faculty of Science has many leading researchers, who have been awarded numerous research grants from various agencies, such as the Thailand Research Fund (TRF), National Science and Technology Development Agency (NSTDA), National Research Council of Thailand (NRCT), as well as overseas funding agencies. Several staff at the Faculty has been awarded the Outstanding Scientist of Thailand Award, as well as the Outstanding Researcher Award of National Research Council of Thailand. In addition, staffs in the Faculty have received international honors, such as the Borden Award, the IRRI Award, the Taguchi Award and ASEAN Award.

### **Outstanding Achievements of the Faculty**

1. The Faculty of Science has produced the most number of Master's and Doctoral graduates in science and medical science disciplines in Thailand up to now.
2. The Faculty of Science has produced research work of the highest quality in the fields of Basic Sciences, Applied Science and Bioscience, and has the most research publications in international scientific journals in country.
3. The Faculty of Science has produced medical teachers and researchers for all medical universities nationwide, under the first MD - Ph.D. program of the country.

### **Challenges and chances**

This decade is an important decade for the Faculty of Science, since it faces the important challenges of university autonomy. It is also a period in which

Thailand must compete on the world's stage, and to be successful, this will require science and technology, both in creating a new body of knowledge and for inventing new products. In order to reach our mission to be the leader in science and research, assisting in the development of the country's science, technology, economy and human resources, the Faculty of Science has taken this opportunity into challenge, by preparing its infrastructure and improving staff quality to achieve academic excellences for the benefit of the country and of mankind.