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2004 NOBEL PRIZE IN CHEMISTRY

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Drug Development in the 21st century. Are we going to cure all diseases?

Many important drugs such as penicillin, aspirin, or digitalis, were discovered by serendipity — some by curious researchers who noted an accidental phenomenon, some by isolation of active ingredients form plants known for centuries to have a specific therapeutic effect. Other major drugs like statins were discovered using more advanced technologies, such as targeted screening, yet, the discoverers were looking for a different effect. In all these cases, the mechanisms of action were largely unknown at the time of their discovery, and were discovered only later. With the realization that not all patients with diseases that physically and histopathologically appear to be the same —different malignancies for example— respond similarly to treatment, and their clinical behavior is different, we have begun to understand that their molecular basis is distinct. Accordingly, we are exiting the era where our approach to treatment is "one size fits all", and enter a new one of "personalized medicine" where we shall tailor the treatment according to the patient's molecular/mutational profile. Here, unlike the previous era, the understanding of the mechanism will drive the development of the new drugs. This era will be characterized the development of technologies where sequencing and processing of individual genomes will be cheap (US$ <1,000) and fast (a few min), by identification and characterization of new disease-specific molecular markers and drug targets, and by design of novel, mechanism-based, drugs to modulate the activities of these targets. It will require a change in our approach to scientific research and development and to education, where interdisciplinarity will domineer and replace in many ways the traditional, discipline-oriented approach.

BIO

Aaron Ciechanover was born in Haifa (Israel). He received his MSc (1971) and MD (1975) from the Hebrew University in Jerusalem, and his DSc (1982) from Technion of which he is a Distinguished Research Professor. There, as a graduate student with Prof. Avram Hershko and in collaboration with Prof. Irwin A. Rose from the Fox Chase Cancer Center in Philadelphia, Pennsylvania (USA), they discovered that covalent attachment of ubiquitin to a target protein signals it for degradation. They deciphered the mechanism of conjugation, described the general proteolytic functions of the system, and proposed a model according to which this modification serves as a recognition signal for a specific downstream protease. As a post doctoral fellow with Prof. Harvey Lodish at the Massachusetts Institute of Technology (MIT) in Cambridge, Massachusetts, Prof. Ciechanover continued his studies on the ubiquitin system. Through further research it became clear that ubiquitin-mediated proteolysis plays major roles in numerous cellular processes, and aberrations in the system underlie the pathogenetic mechanisms of many diseases, among them certain malignancies and neurodegenerative disorders. Consequently, the system has become an important platform for drug development. Among the numerous prizes Prof. Ciechanover has received are: the 2000 Albert Lasker Award, the 2003 Israel Prize, and the 2004 Nobel Prize in Chemistry which was shared with Prof. Hershko and Prof. Rose. Ciechanover is member of the Israeli National Academy of Sciences and Humanities, the Pontifical Academy of Sciences of the Vatican, the American Academy of Arts and Sciences, the National Academy of Sciences (USA), and the Institute of Medicine of the National Academy of Sciences.