

## Chemistry in the News

## 1997 Nobel Prizes

## Chemistry

The Royal Swedish Academy of Sciences has awarded the 1997 Nobel Prize in Chemistry with one half to Paul D. Boyer (University of California, Los Angeles, USA) and John E. Walker (Medical Research Council Laboratory of Molecular Biology, Cambridge, UK) for elucidation of the mechanism of action of ATP synthase, which catalyzes the synthesis of adenosine triphosphate (ATP); and one half to Jens C. Skou (Aarhus University, Denmark) for the first discovery of an ion-transporting enzyme,  $\text{Na}^+/\text{K}^+$ -ATPase. The three laureates have performed pioneering work on enzymes that catalyze reactions of the "high-energy" compound adenosine triphosphate (ATP).

*ATP: The Universal Energy Carrier in the Living Cell*

The German chemist Karl Lohmann discovered ATP in 1929. Its structure was determined some years later; and in 1948, the English Nobel laureate of 1957, Alexander Todd, synthesized ATP chemically. During the years 1939–1941 the 1953 Nobel laureate in Medicine, Fritz Lipmann, showed that ATP is the universal carrier of chemical energy in cells in all living organisms, from bacteria and fungi to plants and animals (including humans). ATP has been termed the cell's energy currency.

Adenosine triphosphate (ATP) consists of adenosine linked to three phosphate groups. On removal of the outermost phosphate group, adenosine diphosphate (ADP) is formed. The energy released can cause other reactions to occur. Conversely, with the help of energy, an inorganic phosphate group can be bound to ADP to form ATP. In one day an adult human at rest converts a quantity of ATP corresponding to about one-half of the body's weight. During hard work the quantity can rise to almost a ton. Most of the ATP synthesis is carried out by the enzyme ATP synthase. At rest,  $\text{Na}^+/\text{K}^+$ -ATPase uses up one third of all ATP formed.

*ATP Synthase: An Exceptional Molecular Machine*

During the 1940s and 1950s it was determined that the bulk of ATP is formed during cell respiration in the mitochondria and photosynthesis in the chloroplasts of plants. In 1960 the American scientist Efraim Racker and his co-workers isolated from mitochondria the enzyme  $\text{F}_1\text{F}_0$  ATPase, which we now call ATP synthase. The enzyme can be divided into an  $\text{F}_1$  part containing the catalytic center and an  $\text{F}_0$  part, which couples the  $\text{F}_1$  part to the membrane (see Fig. 1). In 1961, Peter Mitchell, who received the Nobel prize in 1978, showed that cell respiration leads to a difference in pH inside and outside the mitochondrial membrane, and that a stream of hydrogen ions drives the formation of ATP. The coupling of ATP synthase to hydrogen ion transport takes place via the  $\text{F}_0$  part.

The information about the 1997 Nobel Prizes was adapted from the press releases of the Royal Swedish Academy of Sciences. Further information is available from the Academy of Sciences, Information Department, Box 50005, SE-104 05 Stockholm, Sweden. Phone: +46 8 673 95 25; fax: +46 8 15 56 70; email: info@kva.se; Web site: www.kva.se.



Paul D. Boyer began his studies of ATP formation in the early 1950s, seeking to learn by isotope techniques how ATP synthase functions and particularly how it uses energy to create new ATP. His work has been crowned with unusual success in the past few years. ATP synthase has a mode of function unusual for enzymes, and this required much time and extensive studies to establish. John E. Walker made his first studies of ATP synthase at the beginning of the 1980s. His starting thesis was that a detailed chemical and structural knowledge of an enzyme is required to understand in detail how it functions. He therefore determined the amino acid sequences in the constituent protein units. During the 1990s he has collaborated with crystallographers to elucidate the three-dimensional structure of ATP synthase. So far, the structure of the enzyme's  $\text{F}_1$  part has been established. Walker's work complements Boyer's in a remarkable manner and further studies based on this structure demonstrate the correctness of the mechanism proposed by Boyer.

ATP synthase (Fig. 1) consists of a membrane-bound part,  $\text{F}_0$ , which transports hydrogen ions, and a protruding part ( $\text{F}_1$ ), which carries out its catalytic function. Each  $\text{F}_1$  part consists of three types of protein subunits in differing numbers:  $\alpha$  (1),  $\beta$  (2), and  $\gamma$  (9–12). The  $\text{F}_1$  part consists of five subunits,  $\alpha$ ,  $\beta$ ,  $\gamma$ ,  $\delta$ , and  $\epsilon$ . There are three each of  $\alpha$  and  $\beta$  subunits, but only one unit of each of the others. It has been shown that the synthesis of ATP occurs on the  $\beta$  units. The analysis of amino acid sequences that Walker and co-workers did at the beginning of the 1980s showed that subunits  $\gamma$ ,  $\delta$ , and  $\epsilon$  are not symmetrical—a feature important for understanding how ATP synthase functions.

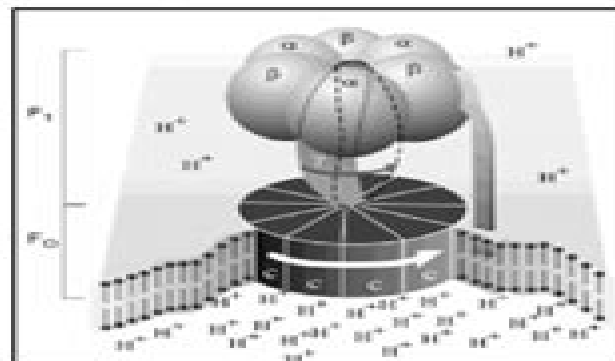


Figure 1. The 3-dimensional structure of ATP synthase, illustrating the membrane-bound, hydrogen-transporting part ( $\text{F}_0$ ) and the protruding catalytic part ( $\text{F}_1$ ).

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little evidence that they are doing so in large numbers or systematic ways This book reviews the literature on screening identification intervention and prevention of partner violence across healthcare specialties and disciplines to benefit the development of effective domestic violence prevention programs Primary care psychiatric and mental health care emergency department settings as well as subspecialties such as emergency rooms ophthalmology and infectious disease are considered

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