

Nobel Prize in Medicines 1974



Albert Claude



Christian de Duve



George E. Palade

The Nobel Prize in Physiology or Medicine 1974 was awarded jointly to Albert Claude, Christian de Duve and George E. Palade "for their discoveries concerning the structural and functional organization of the cell"

The last 30 years have seen a new discipline, cell biology, appear and develop into one of the more important biological areas. It is true that the cell could be studied with the aid of the light microscope earlier since the middle of the 19th century, but its power in resolving structure and composition of the components in the cell responsible for its activities is very limited.

A decisive improvement in the possibilities of studying the role of the cellular components was brought about by two different procedures, both introduced at The Rockefeller Institute in New York during the mid-forties. One was the application of procedures for using the electron microscope, already available since several years, for the study of cellular structures with a resolution far above that of the light microscope. The other was the development of procedures for the chemical study of the components that could be seen under the electron microscope. For this purpose tissues or cells were

carefully homogenized after which cell components of different kinds were separated from each other. In principle one achieved this by taking advantage of the fact that different components differ in size and weight and are therefore influenced differently by gravity. Their natural sedimentation towards the bottom of a test tube was speeded up by centrifugation and the different components were allowed to sediment in steps, the heaviest, the cell nuclei first and then the others in turn and order after their weight. After each step the sedimented fraction was collected for analysis. This procedure is called differential centrifugation and is an excellent supplement to the structural studies with the electron microscope.

Albert Claude, working during the 1930's and 40's at the Rockefeller Institute had a dominating role both for the application of the electron microscope for the study of animal cells and for the development of the differential centrifugation. The first electron microscopic pictures of cells and cell components which offered new and relevant biological information were published around 1945. Somewhat later he published the method for differential centrifugation, a technique which with some improvements is still one of the more important ones in cell biology. The advent of these two procedures meant a breakthrough for the field and an initiation of modern cell biology.

The line of research introduced by Claude was taken up by younger coworkers, notably George Palade who became associated to the Rockefeller Institute in 1947. He added important methodological improvements both to the differential centrifugation and to the electron microscopy. In particular he became instrumental in combining the two techniques, often in combination, in order to obtain biologically basic information. His early work, largely in collaboration with K. Porter was mainly descriptive, morphological, and was devoted to components in the area of the cell outside its nucleus, the cytoplasm. In particular they studied a network of submicroscopic membranes, called the endoplasmic reticulum, originally discovered by Claude and Porter. They showed that the reticulum can be described as a multiply folded, more or less deflated sack occupying most of the cytoplasm. Palade discovered and described small granular components now known under

the name of ribosomes covering the outside of the membranes and he showed, with other groups, that the ribosomes carry out the protein synthesis in the cell. In a series of extremely elegant papers he and his coworkers showed how in secretory cells the secretory proteins, produced by the ribosomes on the outside of the reticulum enter the space between its membranes, migrate to a special organelle, the Golgi complex, where they are changed to a form suitable for secretion. Many fascinating details of the secretory process were demonstrated. The work of Palade includes many other important structural-functional analyses of different cellular components.

Whereas Palade is in the first hand the morphologist searching the chemical correlate of the structures he has observed Christian de Duve is the biochemist who through his work can make predictions about new structural entities. Also the work of de Duve was a direct consequence of Claude's contributions in the area of chemical fractionation of cell components. de Duve started his work using differential centrifugation and he looked for the distribution of different enzymes among the four fractions resulting from Claude's procedure. These were nuclei, mitochondria (energy producers of the cell), microsomes (fragmented endoplasmic reticulum) and cell sap. He then found that certain enzymes sedimented such that they could not belong to any of the known morphological components. He discovered that they would sediment with a special class of particles, a fifth fraction. Interestingly all the enzymes were of a kind attacking protoplasmic components and de Duve therefore postulated that they had to be confined to membrane limited particles in order not to damage the cell. In accordance with this he found that agents dissolving membranes liberated the enzymes. It was soon possible for de Duve in collaboration with electron microscopists to make a morphological identification of the isolated components which were named lysosomes.

Lysosomes have now been shown, by de Duve and others, to be engaged in a series of cellular activities during which biological material must be degraded. The lysosomes are used in defense mechanisms, against bacteria, during resorption and secretion. They can also be used for a controlled degradation of the cell in which they are contained, e.g. to

remove worn out components. Normally the cell is protected from the aggressive enzymes by protecting membranes but during certain conditions the lysosomal membranes may break down and the lysosomes are then real suicide pills for the cell. In medicine the lysosomes are of interest in many areas. There are a number of hereditary diseases with lysosomal enzyme deficiencies. This leads to accumulation of undigestible material in the lysosomes which swell and engorge the cell so as to prevent its proper functioning.

de Duve has not only a highly dominating role in lysosome research, he is also the discoverer of another cell component, the peroxisome, the function of which is still enigmatic but which may very well offer a story as fascinating as that of the lysosomes in the future.

To conclude it can be stated that the 1974 Prize Winners in Physiology or Medicine by their accomplishments have been largely responsible for the creation of modern Cell Biology. What used to be a cell with components, the reality of which was often a matter of dispute and functions as a rule unknown is now a system of great organizational sophistication with units for the production of components essential to life and units for disposal of worn out parts and for defense against foreign organisms and substances.

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http://www.nobelprize.org/nobel_prizes/medicine/laureates/1974/press.html