FROM RIBOSOMES TO CELLULAR AND MOLECULAR BIOLOGY, WITH GEORGE EMIL PLADE

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The year 1953 has proved to be a great one for world's science, as it is the issuing year of the studies announcing two of the greatest discoveries in life sciences, namely: elucidation of the spatial molecular structure of deoxyribonucleic acid (DNA) by J.D.Watson, F.H.Crick and M.H.F.Wilkins – and ribosome's putting into evidence – by George Emil Palade.

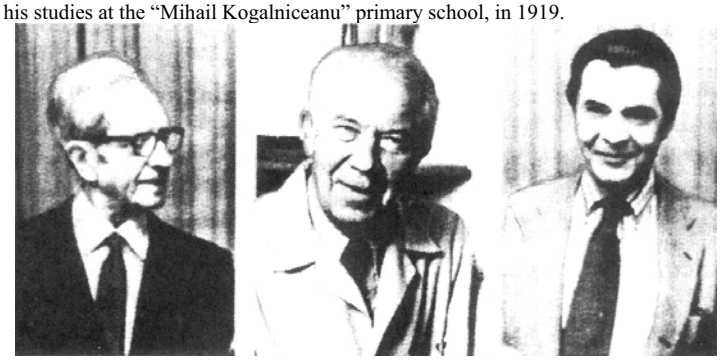
The memorable importance of these two great discoveries has been unanimously recognized within the international scientific community, by the awarding of the Nobel Prize, in 1962 – for the DNA structure and, respectively, in 1974 – for ribosome and cell ultrastructure's elucidation.

Thus, in the year 2003, the whole scientific world has marked the 50th anniversary of these two events which laid the basis of a new biological science, already proved as having a most promising future, namely cellular and molecular biology which, together with molecular genetics and quantic physics, has enlarged the horizons of life's and matter's deep knowledge.

At the same time, the year 2003 recorded a rare coincidence that between the celebration of one of the most representative men-of-science in the last half of the XXth century, and of its exceptional scientific work, materialized in the homage paid to Professor George Emil Palade for his 90 years of life and 60 years of uninterrupted scientific activity.

In such a special, indeed, occasion, besides the scientific manifestations dedicated to such fortunate anniversaries, it would be appropriate to evoke, too, the most noteworthy aspects of the life and impressive achievements of the contemporary scientist – happily, a fellow citizen of ours, as well – a prominent personality of world science, the explorer of major discoveries on living cells' ultrastructure and on the mechanism of some fundamental living processes, our Nobel Prize winner, George Emil Palade.

His biography is an illustrative one. Born on November 19, 1912, in the city of Jassy, Romania, in a family of intellectuals – his father, Emil Palade, taught philosophy and pedagogy at the "Alexandru Ioan Cuza" University of Jassy, his mother, Constantza Cantemir-Palade, was a secondary education teacher. George Emil Palade began his studies at the "Mihail Kogalniceanu" primary school, in 1919.



Albert Claude, Christian de Duve and George Emil Palade

After 3 years, in 1922, he moved with his family to Buzau, where he completed his secondary education at the "B.P.Hasdeu" Lyceum, graduating in 1929.

Between 1930-1936 he attended the courses of the Faculty of Medicine, in Bucharest, where the foundations of his solid biomedical training have been laid by excellent professors, such as the well-known anatomist Francisc Rainer and the reputed biochemist André Boivin.

Starting with his student years and, later on, as a graduate, G.E.Palade worked as a resident medical student for 6 years, between 1934-1939, in the main hospitals of Bucharest: Coltea, Pantelimon and Colentina. Then he was invited to become an assistant lecturer in the Department of Anatomy – Faculty of Medicine, chaired by professor Francisc Rainer, and soon promoted to the position of assistant professor in the same department, now led by another reputed professor, Grigore T. Popa – the discoverer, together with Unna Fielding from Cambridge University, of the porthypophysary system, in 1930.

Attracted by the study of living structures, G. E. Palade devoted his Ph. D. thesis to a subject of general biology, the title of his dissertation, supervised by prof. Fr.Rainer and publicly defended in 1940 being : "Dolphin's uriniferous tube – a study of comparative morphology and physiology".

During the elaboration of his thesis, G. E. Palade worked at the Station of Marine Biological Researches of Agigea (Constantza) of the "Al.I.Cuza" University of Jassy, founded in 1926 by the reputed biologist of Jassy, prof. Ioan Borcea, who had attended his studies of biology in France,at Sorbona University.

In the years of his becoming a genuine researcher, when the bases of his serious scientific training and his large intellectual horizons have been established G. E. Palade has been deeply influenced by his great professors from the University of Bucharest. Thus, under the careful guidance of prof. Fr. Rainer and Gr.T.Popa, he directed his scientific concerns towards the study of morphology, physiology, cytology, chemistry, general biology and genetics, while prof. A.Boivin aroused his interest in nucleic acids and in the role they play in intimate cell processes. During the Second World War, G. E. Palade joined the medical stuff of the Romanian Army, and, in 1946 - advised by his professors, Gr.T.Popa, A. Boivin and D. Bagdasar, with the direct assistance of G.Tatarascu – Minister of Foreign Affairs by that time – and of George Lesnea, one of Jassy's well-known poets – he left for the United States of America to complete his studies.

From that moment on, his stupendous, assiduous research of the universe represented by cellular biostructures began, to be brilliantly crowned by the awarding of the Nobel Prize for Medicine and Physiology, together with Albert Claude and Christian de Duve, in 1974.

In the States, G. E. Palade worked first at the New York University, Department of Biology, chaired by professor Robert Chambers. Here, during a seminar of electronic microscopy, he met professor. Albert Claude, who invited him to join the research team of the Rockefeller Institute for Medical Research – a true citadel of science – funded in 1902 by J. D. Rockefeller senior.

In the Rockefeller Institute of New York, G. E. Palade developed a rich, highly scientific activity, first in the Department of Pathology, together with George Hogeboom and Walter Schneider, where he also met Keith Porter, who developed studies of electronic microscopy on cultures of animal cells. Soon, G. E. Palade come to be recognized as one of the most reputed investigators of the institute, publishing in 1948, together with G. Hogeboom and W. Schneider, his first contributions on the methods of homogenization and cellular fractionation in sucrose-containing media; an year later, in 1949, together with his co-worker Albert Claude, he elaborated an electronic microscopy-based study on the ultrastructure of the Golgi apparatus.

After A.Claude's leaving for Belgium (1949), G. E. Palade continued his investigation with Keith Porter, the two scientists creating and developing an authentic school of electronic microscopy,where the future specialists all over the world came to be formed.

In 1961, Keith Porter moved to Harvard University, G. E. Palade thus remaining the only head of the "Rockefeller Institute group".

After 28 year of a prestigious and fruitful scientific activity at the Rockefeller Institute, G. E. Palade moved in 1973 to the Yale University – New Haven, where he became professor emeritus and Head of the Cellular Biology Section. In 1990, he moved again, this time to California, at the San Diego University (La Jolla) as professor emeritus and Dean for Problems of Science, where he is stile happily active.

The personal life of G. E. Palade has been, also, extremely rich in achievements. In Romania, he had married Irina Malaxa, daughter of Bucharest's most famous manufacturer, Malaxa. They had two children: Georgia Palade van Duzen and Phillip Palade. In 1970, he contracted another marriage, this time to his coworker from Rockefeller Institute, Marilyn Gist Farquha. G. E. Palade was a great admirer of nature and of the high values of the universal spiritual creation, being especially fond of music - he was a friend of the Romanian conductor Ionel Perlea, he met composer George Enescu, too.

A real citizen of the planet, if considering his world-wide scientific reputation, G. E. Palade has never forgotten his native country, Romania, where he returned several times, visiting his city, Jassy, each time he came.

The scientific activity of G. E. Palade at the Rockefeller Institute, developed mainly in the Laboratory of electronic microscopy, involved both the improvement of the existing laboratory techniques and the study of cell submicroscopic universe, as based on techniques of electronic microscopy. Consequently, he first developed techniques of homogenization, ultracentrifugation and cellular fractionation, alongwith the techniques of preparation, microtomy and fixation tissue sections for electronic microscopy. To this end, he prepared, in 1952, the well-known "Palade fixing agent", based on osmium tetraoxide buffered at a pH of 7.4, similar to that of the living cell, which eliminated images' deformation and increased the resolution of the electronic microscope, the double membrane of the mitochondria and also the structure of the mitochondrial inner membrane's cristae thus becoming visible.

The ultimate moment in the conclusive settlement of G. E. Palade's scientific prestige has been represented by the discovery of ribosomes on the surface of the endoplasmic reticulum membrane, which he described in 1953 in a study published in "The Journal of Applied Physics" as "small granulated particles", later on denominated – in his honour – as "Palade's granules", or ribonucleoproteic granules.

The study of the endoplasmic reticulum from different cell types, developed together with K. Porter, stated the existence of two categories of reticulum, namely: the granular one, with ribosomes on its surface and, respectively, the agranular or the smooth one – without ribosomes .

Also, the different types of agranular endoplasmic reticulum, such as the sarcoplasmic reticulum from the striated muscle fibers and the nervous cells' subplasmalema cistern, have been described. In parallels, they elucidated ribosomes' intimate ultrastructure and their functional role.

Thus, G. E. Palade's studies on the endoplasmic reticulum and on the Golgi apparatus, simultaneously with the researches of Christian de Duve, established that ribosomes represent the center of proteins' synthesis processes, which involves an indispensable correlation between ribosomes and the nucleic acids (DNA, mRNA tRNA).

Thus, the destiny of the two great discoveries – on the molecular and ultrastructural compounds of the living cell, namely the DNA structure and the ribosomes – was to bee fulfilled simultaneously in 1953.

At the same time, on the basis thus stated, the essence of molecular biology's main concept, namely:

DNA (transcription) →RNA (translation) →Proteins,

was asserted in a definite manner.

Also, G. E. Palade's investigations developed on the exocrine pancreas' cells established the stages of the secretory cycle covered by the proteins synthesized on the ribosomes attached to the granular endoplasmic reticulum, on specifying their successive phases, their duration and localization, as well as the molecular transformations of the secretory proteins along the path covered in the lumen of the granular and agranular reticulum, and further on in the microvesicles, dictyosomes (cisternae) and macrovesicles of the Golgi complex, where processes of glycosylation, segregation, condensation and molecular complexation – followed by their elimination through exocytosis, as "export proteins" – occur

In the laboratories of the Rockefeller Institute, G. E.Palade initiated, too, some investigations of cellular biochemistry and biophysics, as early as 1955, when the biochemist Philip Siekevitz from the in Wisconsin University and the biophysicist Lucian Caro from the Yale University (New Haven) joined his researcher team. In time, the biochemists Lewis Green, David Sabatini and Yukata Tashiro came to complete the group. Lucian Caro and James Jamieson developed the technique of self- radiography applied to electronic microscopy. The result of G. E. Palade's collaboration with these specialists, i. e. investigations on pancreas' exocrine cells, was materialized in the elucidation of the mechanism of cellular secretion.

Thus, at the Rockefeller Institute, an authoritative interdisciplinary research team - including, besides the two recognized masters: Keith Porter and G. E. Palade, a series of reputed physicians, biologists, biochemists and biophysicists – was working as an international school of cellular biology, to which, along the years, young researchers from all over the world came to improve their knowledge . Thus, mention should be made, in this respect, of Iacobo Meldolesi , Francesco Clementi, Bruno Cecareli from Italy, Yukada Tashiro, Tzuneo Omura, I.Ito – Japan, Günther Blobel, Fritz Miller, Volker Herzog – Germany, and many others well-known scientists.

Starting with 1961, after Keith Porter's leaving, the chief of this prestigious school remained G.E. Palade.

Out of the Romanian researchers who had the chance of working in this team, one of the first was Petre G. Ploaie (in 1968), specialized in electronic microscopy, who, after his return home, where he initiated investigations on virusi, discovered a group of parasite mycoplasmas and wrote a book on the techniques of electron microscopy. An year later, in 1969, there came Maya and Nicolae Simionescu, reputed specialists in cellular physiology and pathology, then L. Saucan, S.A. Predescu and D.N. Predescu who, under the guidance

of G. E. Palade, investigated the transmembranary transport of proteins, the transcytosis and the biogenesis of cellular membranes.

The experience accumulated and the scientific prestige gained by Maya and Nicolae Simionescu during their studies with G. E. Palade contributed decisively to their being elected - once returned to Romania – members of the Romanian Academy, a quality which helped them to create – once more with the direct support of their master – the Institute of Cellular Biology and Pathology, inaugurated in Bucharest on September 3,1979. Nowadays, this institute has become itself a prestigious school of cellular and molecular biology; thus, since 1990, it is a member of the "UNESCO global network for molecular and cell biology", in the year 2000 being recognized as a Center of Eminence of the European Community. Also, the institute is the residence of the Romanian Society of Cellular Biology, affiliated to the European Organization of Cellular Biology (ECBO).

The stupendous scientific activity developed by G. E. Palade's team within the Rockefeller Institute established cell biology as a new branch of the biological sciences, different from classical cytology; in parallels, the American Society of Cell Biology has been founded, and G. E. Palade created, in 1955, the publication "The Journal of Biophysical and Biochemical Cytology" later on called "The Journal of Cell Biology".

The scientific honour list of G. E. Palade, impressive indeed, gathers data referring to the whole cellular universe, representing the results of the fruitful cooperation with the most outstanding personalities of the XXth century biology science, as mentioned in an eulogistic study, published in "The Journal of Cell Biology" in 1983, on the occasion of G. E. Palade's 70th anniversary.

Equally, among other scientific concerns of G.E. Padlade special mention should be made of: study, as early as 1960, on the structure and biogenesis of eucaryote cell membranes, more precisely, investigation, in collaboration with P.Siekevitz, D. Dalnerr and A.Leskes, of the membrane of the endoplasmic reticulum from hepatocytes; the structure of chloroplasts and of their thylacoid membranes in the green alga Chlamydomonas reinhardtii, a research developed together with P.Siekevitz, K.Hoaber, I. Ohad and R.Sager (1957), which laid the bases of new branch of cell biology, namely Biomembranology.

By enriching and improving previous concepts, such as those of Robertson and Frey-Wyssling, G. E. Palade stated that the cell membranary system is not born de novo, instead it derives from old, pre-existing membranes.

Thus, prior to its division, one cell assures a membrane dowry to its daughter-cells, through the addition of new molecules in its own membrane, which are inserted asynchronously and distributed randomly, but still obeying the specific membranary structure.

At the same time, Christian de Duve's researches on the endoplasmic reticulum, Golgy complex and lysosomes described the intracell traphic of membranary structures, which led to the elaboration of the "GERL theory"

In parallels with such scientific concerns, G. E. Palade observed , as early as 1950, several plasmalemal vesicles in the cells of the sanguine cappillaries' epithelium, which urged him to study, together with Marylin Farquhar, the structure and functions of capillaries from renal glomerules, thus stating the role of filtering barrier played by the basal membrane and the ultrastructure of the complex intercell junctions from various epithelia.

The investigations, extended to visceral capillaries, have been performed together with F. R. Clementi, as well as to to muscular capillaries, together with R. Burns, and Nicolae and Maya Simionescu, the latter ones continuing and studying thoroughly such aspects in Bucharest, at the Institute of Cell Biology and Pathology.

Another important domain of G. E. Palade's researches is represented by the ultrastructure, molecular organization and functions of mitochondria; in 1952, in the journal "The Anatomical Record", he published his first observations on mitochondria of various types of animal cells (glandular, muscular, fibroblasts, neurons). Concomitantly with the studies developed by F. Sjöstrand (Sweden) and H.Fernandez-Moran (Venezuela), and by biochemists such A. Lehninger on mitochondria, G. E. Palade contributed to dehydrogenases' evidencing and to the elucidation of mitochondrial membranes' ultrastructure – especially of the cristae of the internal membrane with their tripartite functional units. It is known that such units contain the enzymatic systems of the electron-carrier breathing chain which assures the production of cellular energy through the biosynthesis of ATP molecules, within the process of oxidative phosphorylation – the mechanism of which had been elucidated by P. Mitchell in 1961 (the chemiosmotic theory). To all these, one should add the establishment of the succession of the bioenergetic processes from the tricarboxylic acid cycle (Krebs cycle), which justifies the denomination of "cellular energetic plants" attributed to mitochondria.

Worth mentioning, too, are the studies of G. E. Palade on the ultrastructure of chloroplasts, which are similar to mitochondria (the first results being published in 1957), thus elucidating the membrane structure of the thylacoids from chloroplasts, and permitting deciphering of photosynthesis' mechanism, the magnificent process of the primary production of organic matter in chlorophyl-containing plants, on the basis of solar energy.

Equally important, other investigations – initiated together with S.Palay in 1955 – have elucidated several aspects of neurons' fine structure, of chemical synapses and of neurosecretion's mechanism.

The quite numerous research works developed in the last half of the XXth century have elucidated some of the most intimate structural-functional aspects of the "cellular universe", leading to the substantiation of one of the most modern and dynamic of today's sciences – cellular and molecular biology, among its most noteworthy creators along with Albert Claude, Christian de Duve and Keith Porter being the Romanian George Emil Palade.

For the essential contributions brought to the domain, G. E. Palade received, together with A. Claude and Ch. de Duve, the Nobel Prize in 1974, being considered as "the main cartographer of the living cell" and "the greatest biologist of the XXth century" (G.Blobel, 1980). Also, in recognition of his international prestige, several scientific titles, honours and awards have been conferred to him, among which mention should be made only of the following: member of the National Academy of Sciences of USA (1961) and member of its Scientific Council, member of the American Academy of Arts and Sciences, honorary member of the Romanian Academy (1975) and Counselor of its President, "Doctor Honoris Causa"of numerous universities all over the world, such as: Yale, Philadelphia, Chicago, Michigan, Ohio, Columbia, Bristol, New York, Bern, Siena, Upsala, and the "Al.I.Cuza" University of Jassy and the "Gr.T.Popa" University of Medicine and Pharmacy of Jassy (1994); the A.Lasker Prize, the special Gairdner Prize (1967) the L.G.Horovitz Prize – together with A. Claude and K.Porter (1970), the Brown-Hazen Prize (1983) the Sehleiden Medal of the Leopoldine Academy (1985), the National Medal for Science of USA (1986),also, he is member of the Editorial Boards of prestigious journals of cell and molecular biology, such as Journal of Cell Biology (whose founder he actually is), Journal of Molecular Biology, Journal of Membrane Biology, Annual Review of Cell Biology Hepatology etc.

The researches devoted to cell and molecular biology, the foundations of which had been laid 50 years ago, by the elucidations of DNA's spatial structure and discovery of ribosomes and of their correlations with nucleic acids for transmitting the information necessary in the biosynthesis of proteins, have reached nowadays uncommon performances, opening new horizons for the science of the XXIst century, if considering only the cloning processes, genic therapy, molecular biotechnologies, transgenic organisms, production of useful substances through controlled cellular processes, along with other spectacular discoveries at infracell level, with macrobiological implications.

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