

## George Emil Palade - a Great Personality of the World Biology

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### Abstract

The paper presents the life and the scientific work of the Romanian - American George Emil Palade, one of the greatest world scientist of the twentieth century. Along with other researchers contributed to the foundation of Cell Biology as a research area. George Emil Palade, together with Albert Claude and Christian de Duve, received Nobel Prize in October 1974 "for their discoveries concerning the structural and functional organization of the cell". His legacy is huge, overwhelming, incredible. The paper is an homage of this scientific giant at an important moment - the Romanian Union Centenary.

**Key words:** George Emil Palade, life, discoveries, scientific work, worldwide validation, awards.

Each country takes pride in its great champions and their success in various sports. The performers in various fields of science are great champions, as well, without whom the achievements of current human civilization and the improvements of our life would not be possible. It's a pity that some of these great personalities are rarely mentioned. Such is the case of the Romanian - American George Emil Palade, perhaps the greatest scientist in our country.

### 1. The professional formation

He was born in Iași (Romania), in a family of scholars, on November the 19<sup>th</sup> 1912. His father, Emil Palade, was a professor of Philosophy, and his mother, Constanța Cantemir Palade, a teacher. This intelectual environment instilled a deep respect for books, school and education in the young George Emil, as he later confessed. He attended the first three school years (1919-1922) in the 'Mihail Kogălniceanu' school. Due to the fact that his family moved to Buzău, he continued his education in 'B. P. Hașdeu' highschool, he passed the maturity final exam there, as well. He was a straight 10 pupil all those years. Though his father wanted his son to attend Philosophy courses, he started to attend the classes of the Faculty of Medicine in the University of Bucharest in 1930, he was in top of the

list, passed the admittance exam with a maximum grade. Many of his colleagues, among which the brilliant surgeon-to-be Ion Juvara, thought he might be a blunt young man, with big glasses, a big geek. When the academic courses began, the students were surprised to see that George Emil Palade was a handsome man, very witty, playfull, a great mind. As a student, he was particularly interested in Anatomy and Biochemistry, due to the great professors who taught those courses - Francisc Rainer, and André Boivin, respectively. In 1936 he brilliantly ended his academic studies, and was offered a position in the Department of Anatomy, subsequently promoted as an assistant professor, then a lecturer. Apart from his teaching, he worked as a doctor, and prepared his PhD in the Anatomy lab, that he finished in 1940 – a microscopic anatomical research on the urinifer tubes in dolphins. It appeared that the scientist was more attracted by research than by medical practice [2, 3, 13].

Palade served in the Medical Corps with the Romanian Army during the second world war (1942 - 1945). In 1941 (not 1946, as many sources state) he married Irina Malaxa, the daughter of the prominent Romanian businessman Nicolae Malaxa. The couple had two children: Georgia Palade (married Van Dusen), and Philip Palade (professor of neurophysiology). When the war ended, George Emil Palade was encouraged to specialize abroad by professor Grigore Popa (Rainer's successor in the Anatomy Department), and offered to help him by writing some letters of recommendation. As times were troubled in Romania back then, at the end of 1945 he secretly (from the black market) obtained a passport and a visa for the USA, and one night he left Romania for New York, via Turkey (where he reunited with his wife and daughter), [2]. Professor Popa's letter of recommendation helped Palade to obtain a position of visiting investigator in Robert Chambers's laboratory in the University of New York, that he will attend for only a few months. By means of a workshop, he had the chance of meeting dr. Albert Claude, a Belgian scientist who worked in the Rockefeller National Medical Research Institute (later the Rockefeller University) of New York, who presented the new possibilities of studying the cell using the electron microscope. Palade was fascinated by the new perspectives offered by this new device, discussed with Claude, and the latter invited him to join the Rockefeller Institute (considered the first on top of the American biological research), as a researcher, [13]. This is a true example of having a chance in life! Let's remember that 'the chance smiles for the well prepared ones', and Palade was a professional. In 1946 he joined the Department of Cytology. In 1952, Palade became a naturalized citizen of the United States [2].

## 2. A brilliant mind in a fertile environment

At Rockefeller Institute for Medicine Research, he was appointed an assistant professor in 1948, subsequently a full professor and Head of the Laboratory of Cell Biology. In his early researches with his new team, Palade, together with George Hageboom and Walter Schneider (Albert Claude's co-workers in the Department of Pathology) were focussed on cell fractioning procedures, and discovered the sucrose method ("ultracentrifugation in sucrose density gradient") in order to homogenize and fraction the liver tissue and isolate the mitochondria. The value of this discovery was underlined by Kresge et al. (2005): "*The sucrose method was a great improvement over previous methods, which used either water or saline for homogenation ..... By fractionating their cells in 0.88 M sucrose, Palade, Hageboom, and Schneider were able to isolate and characterize intact mitochondria for the first time*" [6]. Therefore, this method was expanded by means of isolating other cell organelles, as well: lysosomes, Golgi complex, microsomes, secretory granules. Keith Porter worked in the same department, that used the electron microscope to study the animal cell cultures. Palade and Porter improved the techniques in microtomy and tissue fixation (they invented Palade's fixation agent - the use of buffered osmium tetroxide for a better contrast), that facilitated the making of more adequate specimens, proper to be thoroughly analyzed using the electron microscope [11]. Marilyn Farquhar (2012) thought that the technical progress '*marked the beginning of the golden era in electron microscopy*' [2].

Either by himself or together with his co-workers, Palade defined the intimate structure of mitochondria and described the organization of their internal cristae, discovered small cytoplasmatic corpuscles (floating in the cytoplasm or attached to the endoplasmic reticulum) - the Palade granules, that were subsequently named ribosomes. Palade and Porter researched the local differences in the endoplasmic reticulum (RE), and with Sanford Palay - the fine structure of the Nissl bodies in neurons, that allowed the further description of interneuronal, and neuro-muscular synapses. Their laboratory became a training centre for the use of the electron microscope in Biology [13].

In the mid 1950s, Palade resumed the cell fractioning and fraction monitoring by means of the electron microscope, aiming to define the chemical composition and the role of the discovered cellular components. Together with Philip Siekevitz he observed that the microsomes found by Albert Claude were fragments of the RE, and the ribosomes were ribonucleoprotein particles. They subsequently effected morphological and biochemical tests on the RE role and that of the attached ribosomes in the lab mice pancreas, and proved that the ribosomes are the sites for the protein synthesis. This research group led by Keith Porter since 1953 (as in 1949 Albert Claude returned to Belgium as a

manager of the 'Jules Bordet' Institute), contributed to the foundation of Cell Biology as a research area, of the '*Journal of Cell Biology*' (1955), of the American Society for Cell Biology (1960), and later on (1985) – of the '*Annual Reviews of Cell Biology*' [2, 9, 13, 14].

After the 1960's the Palade-Siekevitz group approached several studies on the membrane biogenesis, protein secretion, and capillary permeability. In the mid 1960s, the research emphasized on the eukariotic cells' membrane biogenesis, that displayed that the new membrane is not produced *de novo*, it is an expansion of the existent membrane. The collaboration with Ewald Weibel led to the discovery of some organelles in the endothelial cells, subsequently named the Weibel-Palade bodies, that over the years will be proved to be some secretory granules produced by injury or by inflammation [1, 2]. By means of autoradiography and electron microscopy, the research group obtained information on the protein synthesis and the intracellular processing, the protein movement from the synthesis site to the extracellular release site. Therefore, together with Lucian Caro, Palade described the involvement of the Golgi complex in the intracellular transport, and in collaboration with James Jamieson - the dynamics of intracellular transport of secretory proteins, from the ribosomes of the rough ER to the Golgi complex and then to zymogen granules before reaching the plasma membrane [11]. Teaming with Marilyn Gist Farquhar – a pathologist and cell biologist (his wife since 1970, as Irina Malaxa died in 1969), Palade researched the glomerulus capillaries, and noticed that the basal membrane is a barrier against the filtration of molecules wider than 100Å.

In 1973, after 28 years of sustained work and astonishing results, George Emil Palade decided to leave the Rockefeller Institute, to which he had been so devoted (and that comprised five Cell Biology laboratories), for the Medical School of the Yale University. He considered that it was time to use his entire experience as a cell biologist in Pathology and in Clinical Medicine: '*... my belief that the time had come for fruitful interaction between the new discipline of Cell Biology and the traditional fields of interest of medical schools, namely Pathology and Clinical Medicine*' [13]. He took that step together with Marylin Farquhar, James Jamieson and their collaborators. They laid the foundation of the Cell Biology Department and focussed on the membrane biology, the membrane biogenesis and the membrane trafficking. They came up with innovative techniques of fractioning and characterization of the secretory metabolism subunits, and they developed imune isolation protocols. Together with the Romanian scientists Nicolae and Maya Simionescu, Palade researched the fenestrated visceral capillaries and also the muscle capillaries, research that lead to the identification of the passage ways for large molecules soluble in water, in both types of capillaries, and of small molecules in the visceral capillaries. He granted a special focuss on the disclosure of the fine structure and the function of

microvasculature (arteries, veins, capillaries, venules) under normal and pathological conditions. In a series of conferences held after 1980 in various scientific meetings, Palade displayed the difficulties in this domain, insisting '*especially with how membrane and secretory proteins are processed and transported and how vesicular trafficking is controlled*'. Palade's research group put a special emphasis on teaching new young specialists in Cell Biology, introducing new courses and lectures for students, PhD students, post-doctoral studies, workshops, etc., at the Yale University, [2].

In 1990, George Palade and his wife Marilyn Farquhar, left the University of Yale, accepting the invitation of Gerard Burrow - Vice Chancellor and Dean of the School of Medicine, in order to found the New Division of Cellular and Molecular Medicine at the new University of California - San Diego (UCSD), in which the great scholar was appointed Dean of Science and where he worked for his last ten years of his brilliant career [5]. The university's managers offered them the financial and human resources that would allow the continuity for their research, and the approach of new promising fields in Cell Biology: cell motility, glycobiology, gene transcription and RNA processing etc. Palade was particularly interested in vesicular trafficking in hepatocytes, considering that the plasmalemmal vesicles and transendothelial channels play a major role in the capillary permeability. The research grant in UCSD gathered many scientists from various countries, among which the Romanians Dan Predescu, Sanda Predescu, Radu Stan, and Lucian Săucan. In his 50 years career, George Emil Palade published more than 200 scientific papers, together with his about 80 collaborators [2]. Our brilliant countryman was an open mind person, considering that: '*... the human mind belongs to mankind, above nations and above any frontier*' and '*the science has an international character and do not develop in isolation*' [1].

At the end of the year 2000 Palade gave up his position of Dean of Science, but he continued to attend the university every day, as an advisor to the UC San Diego School of Medicine, and collaborate with his research group until 2002, when his health weakened. To honour him, the Cellular and Molecular Medicine West Building was re-named as the George Palade Laboratories in 2004 [4].

He passed away on October the 7<sup>th</sup> 2008, after a long, deep sufferance. His last wish was that he would be incinerated and his ashes would be spread both over the Rocky Mountains and over the Carpathians, [3].

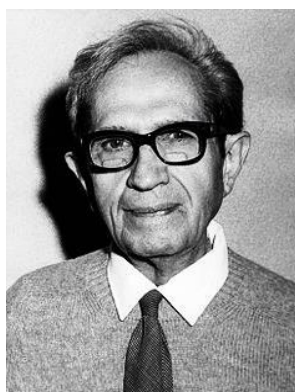
As one acknowledges his relentless work in science and in education for more than five decades, his prolific research and huge contribution to the funding and development of Cell Biology, one may wonder if George E. Palade took any spare time for himself. A review published in 2012 by his wife, Marilyn Farquhar, revealed that the great scientist was keen on history and museums (he often challenged the curators with his knowledges), was a refined art, music and poetry

lover, enjoyed opera and theater, adored both the mountains and the sea, loved to travel [2].

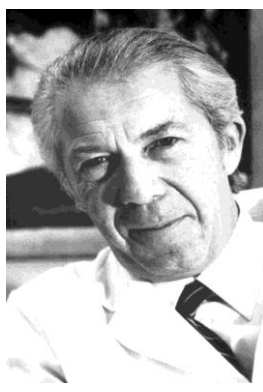
### 3. Worldwide validation

George Emil Palade was the professor and the mentor of many famous cell biologists worldwide. He was certain that the scientific research is '*an enterprise that continues generation after generation*' [12]. His early work in electron microscopy and cell fractioning that made possible to decipher the cell inner structures and mechanisms, synthesis paths, protein transport within the secretory metabolism, were nationally and internationally acknowledged. His scientific work had been praised long before he received the Nobel Prize and he joined the National Academy of Science (USA) in 1961, received many honours and awards, among which: the Passano Award (1964), the Albert Lasker Award (1966), the Gairdner Special Award (1967), and the Hurwitz Prize - shared with Albert Claude and Keith Porter (1970), [3, 7, 13, 14, 16].

The press release announcing the Nobel Prize's contenders in Physiology or Medicine for that current year was issued in October 1974, nominating Albert Claude (manager of Jules Bordet Institute - Belgium), Christian de Duve (professor of Biochemistry in Catholic University of Louvain, Belgium), and George Emil Palade (professor in Yale University, New Haven, USA), "*for their discoveries concerning the structural and functional organization of the cell*".



**Albert Claude**  
(1899-1983)  
discovered the ER  
and the mitochondrial  
functions in the cell



**Christian de Duve**  
(1917-2013)  
discovered the lysosomes  
and their cell functions



**George Emil Palade**  
(1912 – 2008)  
discovered the ribosomes  
and their cell functions

Regarding G. E. Palade's scientific contribution, the Nobel Committee stated: "*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 ... in order to obtain biologically basic information*". In his acceptance speech delivered during the Nobel Prize banquet (December 10th, 1974), Palade declared, among other things: '*We finally understand in general terms how a cell is organized, how its specialized organs function in a well integrated manner to insure its survival and replication. This new knowledge has already begun to be put to good use in understanding abnormal cell function. Many of the major medical problems of our day are degenerative diseases which can be traced to malfunctions in the regulatory mechanisms of cellular activities. Cell Biology finally makes possible a century old dream: that of analysis of diseases, at the cellular level – the first step towards their final control*' [12].

George Palade was the recipient of the National Medal of Science (1986), a member of the the American Academy of Arts and Sciences (1988), the Royal Belgian Academy of Medicine, and the Royal Society of London. To honour him, the University of San Diego held a scientific symposium in 1999. Many scientists from all over the world attended it, and it was the occasion to found '*The George E. Palade Fellowship Fund*'. In April 2010, Marilyn Farquhar inaugurated the '*George E. Palade Memorial Lecture in Cell Biology*' at the Yale School of Medicine, as a platform for renowned scientists to share their expertise in Cell Biology [2, 11].

His native country, Romania, praised and honoured the illustrious scientist in many ways. In March 1975 Palade was elected an honorary member (from abroad) of the Romanian Academy. In 1994 he was appointed counselor of the Romanian Academy's president. By means of the Government Resolution no. 764/1994, Palade's birthday (November 19th) was established the Researcher's and Designer's Day in Romania. In 1993, Professor Radu Iftimovici dedicated him a volume, written in Romanian, entitled '*George Emil Palade, the first Romanian laureate of Nobel Prize*', and in 2006 the volume '*Confession of a winner*' [1]. In 1988 he was elected an Honorary Member of the American-Romanian Academy of Arts and Sciences [5]. He was an Honorary Member of the Romanian Academy of Scientists. For his entire scientific activity, the Romanian Presidency offered him the Star of Romania Order (The Grand Cross) in 2000, and the Star of Romania Order (The Collar) in 2007. In 2012, on the occasion of the Palade Centenary, the Nobel ceremony film was displayed in Romania for the first time, and the Romanian National Bank released a silver coin (with a numismatic value) to honour 100 years since the scientist's birth [16].

#### 4. Palade and his family's connection with Romania

In an interview from 2002, Tudor Oprea (a researcher at the New Mexico University in the US) asked Palade if he dealt with Elena și Nicolae Ceaușescu, and he answered he had to meet them at their request, to talk about a model institute to be shown to foreign visitors. According to what Palade believed, the presidential couple was 'interested in the propagandistic benefit of relating to me' [8]. His opinion was of great importance, and that institute came into being. It is the Biology and Cell Pathology Institute in Bucharest, inaugurated in 1979, event to which great scientists took part, among which three Nobel laureats: Christian de Duve, Gunter Blobel and George Emil Palade (see photo). The institute was to be later managed by two of his former collaborators: the academy member Nicolae Simionescu until 1995, and since 1995 by the academy member Maya Simionescu.



**Photo:** At the opening of the Institute of Cellular Biology and Pathology, Bucharest, 1979. Front row (left to right): Werner Franke, Maya Simionescu, Gunter Blobel, Marilyn Farquhar, George Palade, Christian de Duve, Nicolae Simionescu, David D. Sabatini, (M. Farquhar, 2012)

Interviewed on how he would make a scientific reform in Romania, Palade replied: *'I'd widely open the gate for international collaboration, to begin with, mainly with those countries that are highly equipped both scientifically and ethically. I'd insist on having a quality science rather than a national science by providing the favourable conditions (infrastructure and support) to draw the prodigy youngsters to science and make them stay into science. This is the dilemma: should it be a Romanian science, or a quality science? If one wants a Romanian science, it would be a prejudice, because a purely Romanian science won't be sustainable, as the future belongs to international science'*. Asked what



is unique about Romania, he replied *'the left and right politicians' tendency of living in an imaginary world'* [8].

In September 2010, Georgia and Philip (Palade's children) came to Romania for the first time, to fulfill the dying wish of their father. Asked what he learned from his parent, Philip Palade – professor of Pharmacology and Toxicology at the Medical Sciences University of Arkansas (USA), answered: *'it is not enough to do everything very well, you have to be the absolute best in everything you do'*. Asked if his father would have become famous working in Romania, he declared: *'it's very unlikely that he would have had the same opportunity in the post-war Romania. I'm certain he would have been a great scientist, but not with the same major discoveries in Romania. Most probably, Romania does not have the scientific infrastructure for brilliant scientific breakthrough, not even at present. Nevertheless, it is most likely that Romania can bring up people that would become remarkable scientists in other countries, with many facilities'* [15].

Another significant moment, proving George Emil Palade's love and respect for his native country and people, took place recently. The Nobel Prize laureate diploma and medal were donated to the Romanian National History Museum by his son, Philip, who fulfilled another wish of his father's. These honours are exhibited for public since May 2018. In addition to that, all the distinctions received by our illustrious compatriot were donated to the 'Carol Davila' University of Medicine and Pharmacy in Bucharest [15].

## **5. The perception on George E. Palade as a person and as a scientist**

In 2004, David Sabatini, one of his early graduate students at the Rockefeller Institute, described his mentor as it follows: *'Palade's personal attributes make him one of the most admired and beloved figures in thoday's scientific scene. Palade not only has a powerful intellect that allows him quickly to cut to the essence of a scientific problem and propose for it a feasible solution, but is also a man of great human qualities - warm and sensitive, polite and gracious'* [5]. Peter Novick, PhD, said: *'During my graduate training and formative years as a junior faculty member at Yale, George was always my hero and keenly insightful advisor. He started our field of membrane traffic and challenged us all to bring the field to the advanced level of mechanistic detail that it has since attained.'* [4].

The opinion of three of his fellow Nobel Prize laureates on his great personality are most eloquent. Professor Günter Blobel (recipient of the Nobel Prize in 1999) stated that: *'George Palade is among the greatest biologists of the 20th century'.... 'He is one of the founding fathers of Cell Biology. His discoveries are followed up by thousands of scientists all over the world. He has been a*

mentor, an inspiration and a role model for several generations of cell biologists. It has been my greatest privilege to get to know him and to work with him.' [4]. These are the words of Christian de Duve (aged 95): '*Multidisciplinary, as opposed to many of his contemporary people, Palade did not stick to just one field, either Morphology, Biochemistry, or others. He persevered in combining them all, proving an overview approach on the structural and functional cell organization. A perfectionist - this is Palade's second feature. He was keen on being thorough and on quality work, concerning both himself and his collaborators. Science was art, as well, for him. Last, but not least, Palade was charming. He was an old school gentleman, with outstanding class and charisma. He perspired authority without any trace of arrogance*' [3]. Interviewed on the acceptance of the Nobel Prize in 2013, Randy Schekman said: "*So well, to begin with I want to credit George Palade who really pioneered the field of cell biology by developing the techniques of electron microscopy to visualise membranes within human cells, and it was his genius to realise, to appreciate how proteins that are going to be exported from cells are assembled, in a kind of assembly line process inside the cell*" [10].

During Palade's funeral ceremony, Chancellor Marye Anne Fox stated: '*Dr. Palade had a tremendous impact on the course of science, as well as a personal impact on countless colleagues and students who were inspired by his teaching and his example. His legacy will certainly live on in the work of so many brilliant scholars who benefited from Dr. Palade's guidance and wisdom.*' [4]. James Jamieson, another collaborator, stated after the loss of this '*Cell Biology giant*': '*He inspired so many students, postdocs, and faculty to ask important questions and to teach according to the wonderful example set by both him and his wife, cell biologist Marilyn Farquhar*', [5].

David A. Brenner, M.D., Vice Chancellor, Health Sciences at UC San Diego said: '*George Palade was not only one of the leading scientists of his era, but was a pioneer in modern Cell Biology.... I personally learned about cell biology from him and his wife, Marilyn Farquhar, at Yale University. UC San Diego will always be indebted to him for his leadership in building the basic sciences at the School of Medicine. With his exquisite taste in recruitment he brought many talented individuals here who continue his legacy, and he was instrumental in bringing such important programs as the Howard Hughes Medical Institute and the Ludwig Institute for Cancer Research to UCSD.*' [4]. Marilyn Farquhar (in 2012) said that '*George Palade was truly A man for All Seasons*', that her husband '*believed that the most important thing in life is to leave something behind for future generations*' and that '*he is considered by many to be the father of modern Cell Biology and leaves behind an unparalleled legacy of discoveries*' [2].

Finally, the Romanian Academy member Maya Simionescu, one of Palade's closest collaborators, characterized him as it follows: *'He was a virtuoso of science, a chance for the human kind, and a chance for us, the Romanians. Above his greatness, George Emil Palade was a charming man, handsome and elegant. He was drawn to History, and he knew well the Romanian history. He loved classical music, recited the lines of our great poets, and we sometimes sing some of Maria Tănase's songs'*.

## 6. Instead of conclusions

The scientific discoveries in Cell Biology of the last century's 50's and 60's to which our compatriot and his school had a major contribution, opened the path for Molecular Genetics and its amazing discoveries, awarded many Nobel Prizes: the discovery of the hereditary substrate, the deciphering of the DNA structure, of the genetic code, of the protein synthesis mechanism, etc. There was only one small step to the artificial gene and protein synthesis and to the transgenesis. Biology held all the headlines with its remarkable breakthrough all along the second half 20's century. I remember how proud and moved I was, as a student, when I first heard that the name of subcellular fractions newly discovered were named in honour of one our Romanians, who turned into a great scientist in the US - George Emil Palade, and few years after that, to find out his research was awarded a Nobel Prize. His legacy is huge, overwhelming, incredible.

Deeply impressed by this prolific valuable scientific work, I felt I have the duty of honour to remember this scientific giant, to bring him an homage on such an important moment – the Romanian Union Centenary, as Palade's almost entire life spanned in this time period. Moldavia took pride with its remarkable people - great artists and scientists. Among all those, two are exquisite: Mihai Eminescu - the star of the Romanian poetry and culture, and George Emil Palade - a genius for the international science. My opinion is that our school has a deficit in promoting these great personalities amongst the youth, to make them aware that the true heroes are not only those who die in battles, but also those who sacrifice to render us a better life, making us proud to be Romanians.

In the end of this article, I have to make a confession. Impressed and convinced by professor Palade's great personality, in 2007 (while he was still alive), I intended to put his name on the frontispiece of an university of his native Moldavia, institution that I managed as its rector. Its former name (the University of Bacău) appeared to me as inappropriate, deprived of identity. My proposal to the Senate colleagues was to name our institution after the greatest Romanian scientist - George Emil Palade. I thought this would fulfill many purposes: an eternal well deserved homage would be rendered to the most illustrious Romanian researcher, a greater respect for our university, more responsibility and

professional dedication within the professors of our institution. The university's Senate agreed to my proposal unanimously. Palade's approval was requested, or his family's one, therefore I asked academy member Mrs. Maya Simionescu, his former collaborator, to help me with this matter. Unfortunately, Palade's health state was extremely poor, and his wife was more likely overwhelmed with too many problems, and did not respond to our request. Had I succeeded, my satisfaction would have been huge, both as a Romanian and as a scientist. It wasn't meant to be, and that fact deeply upset me. A great personality as George Emil Palade is worth of such honour on our behalf!

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