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1. INTERVIEW WITH GEORGE EMIL PALADE

TI Oprea

Professor George Emil Palade, a Romanian native born in Jassy (Iasi), studied medicine at the University of Bucharest between 1930 and 1940, before moving to the Rockefeller Institute for Medical Research in New York in 1946. He is best known for his work in electron microscopy and for the discovery of ribosomes – for which he was awarded the Nobel Prize in Medicine and Physiology in 1974 (together with Albert Claude and Christian de Duve). He kindely afreed to have this conversation on February 11th 2002, in his office at the University of California San Diego School of Medicine, where he serves as Dean for Scientific Affairs.

Tudor I Oprea (TIO): Professor Palade, if you were to look back at the over six decades of scientific endeavor that are covered by your career, what lesson would you like to share with young scientists?
George E Palade (GEP): Select problems of broad science. Problems that should open new perspectives and new ways for the phenomena you are analyzing. You should have a long term perspective, rather than following dead-end developments.
TIO: How does one choose problems that are significant?
GEP: This is by far the most important decision a scientist can face. You should choose a problem on the basis that it offers solutions that lead to other problems, rather than to dead-ends.
TIO: How do you deal with such critical problems?
GEP: After finding something that is both exciting and not understood, one should try to figure out what technological developments are required and use whatever method is necessary. What counts is finding solutions to important problems rather than applying technology. Count on the opportunity to use converging technologies based on different starting principles in the analysis of the function of the different structures that are discovered and characterized. Of course, there are problems in which the application of single technologies is sufficient, since it provides all the information that is necessary to figure out what happens. X-ray crystallography is such an example. But in fact, what characterizes problems of significance (in biology) is the application of convergent technologies: morphology, microscopy at the highest possible resolution, structural studies based on x-ray diffraction, combined with biochemically relevant information and with a perspective of how these findings are relevant in biological problems of current interest.
TIO: Is there a real effort to integrate scientific discoveries?
GEP: The integrating efforts relate to important advances in recent decades, which illustrate the application of convergent technologies, as a result of teamwork, by combining the different technological approaches.
TIO: How does teamwork reconcile with the “people problem”? It is often the case that creating a real team needs to address the inter-personal chemistry problem.

GEP: People appreciate pragmatic approaches and concrete results. If they are interested, they will react enthusiastically to general theories that try to explain the phenomena, and will not show positive reactions to problems in which they are only peripherally interested.
TIO: Could you share some insight into your activity – in particular related to your student days?
GEP: as a young man in my twenties, before the 2nd world war, The (European) continent was thorn apart by all kinds of ideological movements. This was rather traumatic. This is a period that continues to be difficult to understand. Policies were based on nationalistic principles, as well as the idea that the only way to solve a conflict is to go to war. Economic cooperation was actually not considered the best solution. Economic dominance after a successful war was supposed to be the way to solve problems. This was really not only the policy of Nazi Germany (and of the Germany before becoming Nazi), but also the policy of relatively modest powers like Italy. This state of insecurity had significant impact during my studies. A lot of trouble and fighting was caused, e.g., by the *numerus clausus*.
TIO: Were you affected by the *numerus clausus?*
GEP: No, it did not affect me personally because there was nothing in my origin to justify it, but it affected the whole human environment around me.
TIO: Were you politically active at the time?
GEP: No, I did not participate in any political movement. I naturally had some sympathies for the old democratic parties, in particular for Iuliu Maniu.
TIO: What made you come back to research, after working in the clinic?
GEP: First, you have to understand how the system was organized: you had to study six years of hospital practice (externat/internat), period which overlapped with the theoretical studies at the medical school (also six years). Hospitals were a separate entity, outside of the control of the educational system. It was a good system, but elitist by nature: not every student succeeded in having a valid practical education in the externat/internat system. Then, you have to transport yourself back to the 1930-1940 decade, before the discovery of antibiotics. The ability of a young physician to solve practical problems with adequate, effective treatment was very limited. Your patients expected you to do all sorts of treatment, but the scientific basis not yet exist. In short, we did not know enough. But in the same time, most importantly, we had to start working on basic problems of human physiology – all the way from cells to human organisms.
TIO: You worked with both Francisc Rainer and Grigore Popa – who arose your interest for physiology?
GEP: It was Francisc Rainer.
TIO: What made you decide to leave Romania?
GEP: The general idea that I did not know enough, and if I want to do something valid I have to go somewhere else – in places where science activities appeared to be more interesting.
TIO: Was the political climate a contributing factor?
GEP: The communists and their politics affected me in two ways: the basic set of premises which was that Romania was not going to be forever communist, and that we should be better equipped in terms of research experience for the years that would follow communism. Furthermore, that our scientific standards of achievement needed serious upgrading.
TIO: This is still true today. Should you find yourself in the position to lead the effort for scientific reform in Romania today, what would you do?
GEP: I would open the doors to encourage as many cooperative interactions and studies as possible, with countries that have better science and better standards. I would insist in having good science as opposed to national science, and would then create conditions (infrastructure as well as support) that would allow young talented individuals to come to science, and to stay in science. Here is a dilemma: do you want Romanian science from the very beginning, or do you want good science. If you want Romanian science, you are handicapped because you cannot support Romanian science for practical reasons, but also because the future belongs to multination science. It is therefore much better not to use a nationalistic formula.
TIO: Are there any principles that should be communicated to governmental factors?
GEP: A reasonably efficient government should create conditions under which the genetic potential of gifted individuals has the best chance to be realized. This of course has to be made efficient by education.

TIO: Do you favor a culture of elites?
GEP: It's not what I favor; it's a matter of probability. What is the probability that, in the general population, people with different IQ's and different education will accomplish something of significance? As for the conditions, the government should organize an education system that facilitates the full expression of the genetic potential – and to provide the infrastructure that makes these people productive.
TIO: They will object: "We don't have the money".
GEP: This points to the basic problem, which is the economy of this country. The government should favor the integration of Romania into the framework of systems that will improve the economy to begin with, and scientific activities to end with.
TIO: Such as European Union?
GEP: The European Union is the formula for the moment. But this can change. Politicians need to recognize which particular system will end creating a reasonably high standard of living, and the conditions of realizing the genetic potential of the population.
TIO: Would you choose a career in science in Romania, as opposed to abroad? Could you give any advice to young Romanians facing this dilemma?
GEP: They should start by being scientists in Romania. Then the best of them should gain reasonably extensive scientific experience abroad. They could come back better equipped to do science in Romania, or they could do the rest of their work abroad.
TIO: Did you ever want to go back to Romania to work as a scientist?
GEP: For many, many years, this was a mute question: I did not want to go back there and end in jail. But I believe it is possible to go to Romania. For example to go back to teach as you are doing – a very noble type of activity – but also to do science. This is a practically intelligent formula, to work on both fronts – both in the country and outside.
TIO: Eliade used to say that exile is a wound that never heals – have you ever felt the need to go back?
GEP: I did not look at exile as a wound; I looked at it as a challenge to show what you can do.
TIO: Did you miss the "mititei" and "sarmale"?
GEP: I went from time to time to Romania, and yes, I did have "mititei" and "sarmale". But Romania is much more than "mititei" and "sarmale".
TIO: Is there anything in Romania that you could not find elsewhere?
GEP: Yes, the tendancy of both leftwing and rightwing politicians to live in a world of fantasy.
TIO: Do you realistically see any role for the "Ad Astra" journal, in rallying Romanian scientists, and helping create a dialogue between established scientists working abroad and young students from Romania?
GEP: Diaspora is by definition something difficult to organize and coordinate. Such initiatives should therefore be encouraged. Above all, you need to provide something concrete, practical, with hands-on experience, in which the practical nature of problems is combined with sophisticated instrumentation. Not for the sake of sophistication, but for its efficiency. Besides your example, going to Romania to teach, there is also the reverse example: somebody invites young Romanian scientists abroad, then they go back and organize something significant there. I did this with Maya and Nicolae Simionescu.
TIO: Did you have to deal with the Ceausescus in doing so?
GEP: Yes, I had to deal with both Nicolae and Elena.
TIO: Did you approach them?
GEP: They approached me. They were clearly interested in the propaganda value, not in the idea of training young Romanians to do science. What they really wanted was to have an institute that they could show to foreign visitors.
TIO: Did you have any contacts with today's government?
GEP: I briefly met President Iliescu, but I was not approached in any way to contribute to the scientific reform in Romania.
TIO: So at least Ceausescu had a positive initiative.
GEP: Again, this was done for propaganda mostly, not for its scientific value.
TIO: Any additional thoughts?

GEP: Today, the people involved in scientific education in Romania are not perfect, and the conditions for living and working are rather miserable – which makes them corruptible. This can only be avoided by making their standard of living above corruption (e.g. good salaries). Since this is a long-term process, it may take a while for things to improve.

2. BRIEF REVIEW: HEPATITIS C AND ACUTE REJECTION IN LIVER ALLOGRAFTS

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ABSTRACT
Post orthotopic liver transplantation (OLT) recurrence of hepatitis C is nearly universal, as defined by the presence of HCV_RNA in serum or liver allograft biopsy. Clinical findings are often absent or mild; the liver laboratory tests are not specifically elevated. But, unfortunately, the same unspecific picture is found in an acute rejection episode during the first 1-2 months post-OLT, too. In order to establish the diagnosis, examination of the sore needle biopsy of the liver allograft is the gold standard method. Acute rejection and hepatitis C share some histological features, which may make the histopathological distinction between the two difficult. Careful assessment and correlation with clinical and laboratory findings should allow the appropriate distinction between acute rejection and hepatitis C in most cases.

Key words: liver allograft, hepatitis C, acute rejection.

3. THE INFLUENCE OF SEROTONIN ON SOME EXCITABILITY PARAMETERS AND ON FIBRILLATION THRESHOLD IN ISOLATED PERFUSED GUINEA PIG HEARTS

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ABSTRACT
Serotonin perfusion in spontaneously beating isolated perfused guinea pig hearts induced a very significant bradycardia and the decrease of the cardiac excitability. In overpaced heart, contrary effects were seen. The changes of the heart rate and the cardiac excitability were due, partly, to the involvement of the vagal and adrenergic mechanisms. The serotonin receptors, which were involved in these phenomena, were probably of 5HT2 subtype.

Key words: serotonin, excitability, fibrillation threshold, isolated perfused hearts.

4. INTERACTIONS BETWEEN CA^{2+} CHANNELS AND CYTOSKELETON IN RAT TRACHEAL SMOOTH MUSCLE (CA^{2+} CHANNELS AND CYTOSKELETON)

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ABSTRACT
The alkaloid colchicines is known to act by binding to tubulin, the heterodimeric subunit of microtubules. The aim of our study was to observe the effects of colchicines upon both electro-mechanical contraction (induced by depolarization with 40 mM K^+) and pharmaco-mechanical contraction (induced by carbachol 10^{-5}M) in tracheal smooth muscle preparations. Colchicines (10^{-3} M) decreased the maximal amplitude of responses, when was added to the organ bath either as pre-treatment (15 minutes) or during the plateau (10 minutes) of carbachol-and depolarization-induced contractions. A slightly higher degree of inhibition was obtained when colchicines was added in the plateau of the contractions. It is also to be mentioned the fact that colchicines induced a higher effect on contractile effects induced by depolarization, as compared to agonist. Furthermore, 10^{-4} M colchicines exhibited high inhibitory actions on contractile effects when was administered as a pre-treatment of depolarization in Ca^{2+}-free buffer. Thus, the associations of cytoskeleton (microtubules) with plasma membrane L-type Ca^{2+}-channels during the contractile activity in rat tracheal smooth muscle are obvious. Finally, our date show that the reduction of the effects of agonist (carbachol)- and depolarization-induced contractions of the rat tracheal smooth muscle through the cytoskeleton disruption by colchicines mainly involves the plasmalemmal L-type Ca^{2+} channels inhibition. Thus, cytoskeleton microtubules might be important components of the signaling pathways of such contractions.

Key words: colchicines, cytoskeleton, tracheal smooth muscle, L-type Ca^{2+} channels.

5. COAGULATION MONITORING IN PATIENTS WITH HIP FRACTURES, UNDER ANTICOAGULANT TREATMENT

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ABSTRACT
Our study was performed in the Department of Orthopedy from the County Hospital of Constanta on a group of 20 hospitalized and operated patients between 16 of November and 7 of December 2001. All of them presented complete fractures of the hips and required surgical interventions. From the very beginning, in order to prevent vessels thrombosis, treatment with anticoagulant substances was administered.
We made tests in order to appreciate the blood coagulation before surgery, immediately after it and after seven more days. We noticed variations of these parameters induced by the fractures themselves and by the anticoagulant treatment as well.

Key words: fracture, hemostasis, anticoagulants.