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CHRONICLES

The Nobel Prize in Physiology and Medicine for 2009

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The Nobel Prize for 2009 has been awarded for discovery of telomeres and telomerase. Telomeres are special DNA sequences on the ends of chromosomes that prevent their degradation during replication and thus ensure the genome stability. This problem has direct implications for tumors, aging, and cloning of organisms.

The winners for the first time include two women, and both are Americans (although Elisabeth Blackburn was born on the island of Tasmania). The contribution of Blackburn to this discovery is doubtless. Even 15-20 years ago one might conclude that her experimental discoveries of telomeres in an unicellular organism *Tetrahymena* and then of a very unusual enzyme, telomerase, containing its own intrinsic RNA primer for elongating telomeres would be awarded with the Nobel Prize, especially because both these crucial works were performed in Blackburn's laboratory. Still as a very young researcher of this laboratory, Carol Greider, detected in 1988 an enzymatic activity elongating the telomeres. The Nobel Committee might "include" her as a nominee for the Nobel Prize but also might "not include" on consideration that she "simply had been working" under Blackburn's guidance. History of the Nobel Prize awarding knows both types of examples of behavior towards similar assistants to a discovery. Favorably for Greider, she was "included". This resulted in the youngest winner in Physiology and Medicine, and, moreover, the second woman this year. Hurrah!

In the lectures and contacts Elisabeth Blackburn, a University of California San Francisco professor, reminds one of a kind well-balanced mother. Her Australian breeding made her the very "model" and she "keeps distance" excellently but is not at all stiff. Carol Greider, a professor of Johns Hopkins University (Baltimore), seems much more artless as a typical American.

The contribution of J. Szostak, American of British origin and Harvard University professor, is also doubtless. In 1982 he conducted a crucial experiment (also together with Blackburn) that confirmed the telomere functioning in a heterologous system.

Thus, the abovementioned situation suggests that it would be more correct to give Blackburn half of the Prize and to divide the other half between Greider and Szostak.

Note that the most important components of the telomerase-associated part of the work, which included purification, cloning, and establishment of the telomerase structure and action mechanism remained without reward. This work was performed by other researchers, and this extremely difficult work is not yet considered as a discovery.

However, similarly to the previous year, the Prize awarding excited not only the joy for Science and its creators but also a not very pleasant feeling. It is well known that the biological problem of the chromosomal end shortening during replication was first formulated in 1971 and 1973 in theoretical articles by the Russian biologist Aleksei Matveevich Olovnikov who is now living among us. In fact, he predicted the phenomena, which were discovered by Blackburn and her colleagues 15 years later, although at that time he did not and could not know anything about the telomere structure or about the end-elongating enzyme telomerase. In all fairness it must be said that Aleksei Matveevich is not the only one who has not been given deserved attention. Thus, the works establishing the action mechanism of telomerase, which is a very interesting and unusual bicomponent enzyme containing internal RNA primer for synthesis, have been mentioned above. An extremely important discovery related to telomeres also belongs to L. Hayflick, who established limits of cell replication number in culture, which are directly related with the telomere shortening to the least allowed length.

A possible trivial explanation for the unpleasant situation with A. M. Olovnikov is that his theoretical works (initially published in the "great and mighty Russian" and with the author's own vocabulary) were simply unknown to the Nobel Committee members (what is "marginotomy" for them and what are they for "marginotomy" – Olovnikov's terminology). Possibly, these works could be unknown in foreign countries. And really, in the 1970s only a few Russian researchers were permitted to visit conferences (and, unfortunately, A. M. Olovnikov was not one of these). And he was a modest man not prone to self advertising.

But were these works really unknown? First, two prominent modern scientists (their works directly concerned telomerase) who were reading lectures in the educational immunology program in Moscow (www.oncoimmunology.ru) knew very well about Olovnikov's works

and were glad to make acquaintance with him personally. These are the Nobel Prize winner Prof. T. Czekh and the first discoverer of oncogenes and tumor suppressors Prof. R. Weinberg who himself is being nominated for the Nobel Prize for 20 years. In T. Czekh's laboratory telomerase was characterized, and the carcinogenesis theory of Weinberg comprises both telomerase and telomeres. Thus, the intellectuals knew the work of Olovnikov and referred it as prophetic.

Second, the work by Olovnikov published in 1973 in *Journal of Theoretical Biology* was cited more than 700 times and mainly by foreign authors. And these are very serious citations, which eliminate the hypothesis about "ignorance".

Third, A. M. Olovnikov has published in the 1990s in significant English-language journals some reviews connecting his theory with telomeres (using the universally adopted terminology).

Thus, either it was a lack of PR campaign without which modern science rarely exists (by the way, the campaign is not certainly driven by a contestant), or the Nobel Committee in Physiology and Medicine does not care for theoreticians. By the way, it should be noted that Olovnikov had been working in experimental biology but not in the field of telomeres. I suppose that if in the 1980-1990s he had obtained any experimental result in favor of his own theory, the situation could be quite different.

What conclusion can be extracted from this story for the future? It is necessary to promote outstanding Russian works and to start from their wide acknowledgement in their native country. The striking hypothesis of Olovnikov was known for a long time to broad circles of Russian biologists, and confirmation and enrichment of the hypothesis by the discovery of telomeres and telomerase is also known at least for 15 years. And why he, a worker of the Russian Academy of Sciences, has not been awarded any of various academy prizes up to now?[1] Why was he not nominated for any state or governmental prize or award? And finally, why was not he given the doctoral degree without the defense of the thesis? And why such remarkable scientists as Olovnikov have virtually no chance for being selected into the Russian Academy of Sciences. So, we shall not blame the Nobel Committee for everything.

But we can be glad that Aleksei Matveevich has many biological theories, and some of them have been proposed after the hypothesis about telomeres. Telomeres are ends of chromosomes but not of life. Let us wish him good luck.

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[1] The situation has been partially corrected by a decision of Demidov's Prize Committee: Aleksei Matveevich Olovnikov has been awarded this prize for 2009 among four outstanding Russian scientists.