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## JĀNIS OĻĢERDS ĒRENPREISS AND HIS THEORY OF CARCINOGENESIS

Jānis Oļģerds Ērenpreiss (1929–1996) was the only oncologist in Latvia who studied the very fundament of oncology – carcinogenesis. Second, Ērenpreiss was a morphologist. The chosen field and method of research can be understood from his personality. This is courage to challenge the most difficult questions, which is gifted to those whose mind is regular and strong to inquire them. This is also an ability to comprehend the world through a microscope as a whole. Because only through the whole one can see the essence of things.

This unique composition of features displayed itself very early and certainly, when as a student of the second year he made, under patronage of the histologist professor Bogoyavlensky, the first steps in science and at once he began to study the mechanisms of carcinogenesis. In the first work in 1953–1954, treating the rat skin with the carcinogen dimethylbenzanthracene he investigated by means of histochemical reactions for nucleoproteins the route of carcinogenesis. He noticed something new – cell nucleus achromasia, which appeared as a response to the initial stage of carcinogenesis. Later, the detailed study around this phenomenon shaped his doctor dissertation and the research of his pupils. His investigations in the nucleoprotein cytochemistry introduced in Latvia by his teacher professor Bogoyavlensky advanced him as a leading researcher in this field in the Soviet Union. The second field of research, which he also initiated as a student, was devoted to attempts to normalise malignant tumours in the regeneration field. From professor Zilber in Moscow rat sarcoma cell line 465 was obtained, its piece was introduced into the defect of the respec-ted tibia (thus modelling bone fracture) and the behaviour of sarcoma was followed in the time course. It was revealed that during the second phase of bone regeneration (cartilage callus formation) the malignancy of sarcoma displayed as an ability to grow, invade, and destruct host tissues, was depressed. Even more, sarcoma cells or carcinoma's stroma (when the experiments were carried out with the Geren's tumour) was found to participate in the regeneration callous formation. This work which was continued after graduation from High School and which embraced a very large number of experiments, was laid

in the basis of Jānis Ērenpreiss candidate (*PhD*) dissertation and several following publications. He reported it in 1960 at the Second International Congress of Oncologists and was distinguished there.

The chosen experimental model was not even. It corresponded the to understanding of the essence of malignancy, which Jānis Ērenpreiss began theoretically to create about 1958–1959. He was convinced that nothing was “broken” in a tumour cell, which represented in fact, just a norm with unusual behaviour, corresponding to an analogy of some evolutionary process. In his notes of this time, where he is reasoning on the inability of tumours to completely differentiate, on the one side, and to differentiate only within their histogenetic potency, on the other, he turns to the question “what is differentiation?”

He is searching for an answer in literature and finds that the issue is highly unclear, not resolved. He understands that an answer to this question is a key for understanding the nature of cancer and begins investigations of a differentiation in normal tissues and tumours (later applying also electron microscopy). These became one of the main directions of his laboratory.

Thus, in the very beginning of his research he is going into the very depth of the cancer biology, not avoiding the most challenging questions, however never missing the essence and his view on the problem. This is a characteristic feature of fundamental science and his school. This is the feature of true science as such.

Unfortunately, often we see the contrary – a tendency to pollute scientific journals with non-digested facts obtained with the most modern and expensive methods and, most important, on the foam of the modern scientific stream, without any effort of serious conceptual analysis of the problem. Jānis Ērenpreiss was one of a few courageous who dared to swim against stream.

However, he made a rich contribution to his time, too. At the beginning this was molecular biology, where in 1963 he wrote his first and the outstanding monograph, in which he tried to connect the molecular biological concepts of that time with a theory of carcinogenesis. The book had a big informative potential. Therefore, it was translated into English and republished abroad; foreign Universities recommended it as an obligate reading to their doctorants. When in 70<sup>th</sup> the oncogene era began, he began an arduous study of the growing hill of its facts.

His monograph of the year 1987 “*Current concepts of malignant growth*” in Russian as well as his last new book, with the same supertitle in English, which appeared in 1993, represent a result of fantastic work gathering and analysing the data on oncogenes. However, Jānis Ērenpreiss never missed the horizon of this own viewing carcinogenesis. When the number of discovered oncogenes appeared to be too abusive and when it turned out that these are taking part in the main development processes, when it seemed that this oncogene “bubble” was about to burst and when many theoreticians were again ready to retreat



from the hope to create a united carcinogenesis theory, he connected this seemingly shapeless mountain of facts with a path to the biologically significant process and this key process was the development of a sex cell – gametogenesis. This theory, to which Jānis Ērenpreiss was factually approaching all his life, represents a variant of the eldest carcinogenesis concept – an embryological theory of Conheim (1977–1980).

The regularity formulated by Ērenpreiss in his book of 1993 sounds as follows: *“All of the basic traits inherent in cancer cells are displayed in gametes and vice versa. Nothing but cell fetalization occurs during carcinogenesis and a cancer cell possesses no other properties but fetal”*.

This challenging formula is a summit of his huge fanatic work; it is followed by a three-page table, summarising the known facts and yet blank places on the features of oncogenes and developmental genes common in cancer and germ cells. The main biological key of this idea is immortality of both cell types.

The subtitle of the book is *“Part A: From normal cell to cancer”*. He was preparing to publish also the *“Part B: From cancer to normal cell”*, which would lay a theoretical basis for causal anticancer therapy, unfortunately sudden death interrupted this work.

In Latvia Jānis Ērenpreiss received the Paul Stradiņš Award for this book. However, his theory did not get enough support abroad. It was already after his death when his pupils in collaboration with English oncologists revealed that human lymphoma cells are capable to behave after gamma-irradiation like germ cells displaying the features of its basis process, meiosis (Erenpreisa et al., 2000). Therefore, it seems that an hour of the true Jānis Ērenpreiss's glory has not hit yet.

Short information: Jānis Oļģerds Ērenpreiss wrote five monographs, published (141) scientific articles and conference abstracts. From 1958 to 1963 he worked as an assistant at the Histology and Embryology Department of the Riga Medical Institute, in 60–70 ths he delivered lectures on molecular biology and cytology in Latvian University, working at the same time as a researcher in Latvian Institute of Experimental and Clinical Medicine, from 1971 he organised his own laboratory of the Chemistry of Tumour Cell (in 1993 it moved under the title of the Laboratory of the Tumour Cell Biology into A. Kirchenstein Institute of Microbiology and Virology) which he directed up to his death in 1996. In 1993 he was elected a Member of the Latvian Academy of Sciences.

Under his guidance five dissertations were defended by his pupils: Rasma Krampe, Ruta Zirne, Zinaīda Frolenko, Jekaterina Ērenpreisa (Chernyak), Olga Demidenko. Besides theoretical and experimental oncology, he directed the research on cell nucleus structure.

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