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BOOK REVIEW

Review of the book "RNA/DNA and Cancer" written by Joseph G. Sinkovics (*Springer International Publishing, Switzerland*, *2016*, ISBN 978-3-319-22278-3, DOI 10.1007/978-3-319-22279-0)

The author of this book, *Joseph G. (József Géza) Sinkovics*, was born in Budapest, Hungary. He graduated from the Medical Faculty of Péter Pázmány University with *summa cum laude* medical doctorate degree in 1948. He started working as an adjunct professor at the University Institute of Microbiology and as a senior virologist and board-certified clinical pathologist at the State Institute of Hygiene in Budapest. After the Hungarian Uprising of 1956, Sinkovics had to leave the country; he went to the United States, where he was sponsored by Albert Sabin for a Rockefeller Fellowship. From 1962, he continued working at the M.D. Anderson Hospital, where he later was elevated to the rank of professor of medicine. He became the clinical chief of the united Sarcoma-Melanoma Clinics and In-patient Services at the M.D. Anderson Hospital; and worked as the Chief of the research laboratories, Section of Clinical Tumor Virology & Immunology, within the Department of Medicine. In the Section, during the mid-1960s, Sinkovics recognized a naturally formed murine hybridoma, in which leukemia virus-producer lymphoma cells fused with specific antiviral antibody-producer normal plasma cells. He published this first described phenomenon in January 1970 in the journal *The Lancet*. In the late 1960s, Sinkovics recognized that cancer cells of patients of both genders could be killed by large granular lymphocytes derived from his own blood. Those patients with cancer, who received an autologous viral oncolysate vaccine (produced at the Section in an institutionally approved protocol), increased producing this type of cells in their blood. In the early 1980s, Sinkovics was offered the directorship of the outstanding St. Joseph's Hospital of Tampa, FL, to its newly constructed free-standing 30 beds cancer hospital with research facilities. He was also invited to the University of South Florida College of Medicine external professorial teaching staff position. He published the textbook *Sinkovics J.G.: Medical Oncology – An Advanced Course*, Marcel Dekker, New York (second edition in 1986) and in 2008 his superbly illustrated monograph on "Cytolytic Immune Lymphocytes" by Schenk Buch-verlag, Passau/Budapest.

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The retired professor Sinkovics, investigator and clinician, introduces his readers to his unique and inmost views on cancer biology. The work is excellent, citing plenty of convincing references and illustrations. The tables and the figures cross-refer to one another and cite the most important literature.

The first eukaryotes of the ancient Earth acquired a special way to outlast and expand, using their unique life survival pathways, an independent immortalized manner, as Sinkovics points out in the summary of the book:

> *The ancestors of the oncogenes were the "cell survival pathway" genes of the first unicellular life forms; these genes remain conserved in their extant descendants. The beta-catenin-dependent Wnt pathway encodes the body axes in unicellular and early multicellular eukaryotes (choanoflagellates; Ciona; Nematostella, Spongiae). In the human genome, the Wnt pathway is a proto-oncogene.*
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> *The derivatives of these primordial genes, for example the achaete-scute genes of the amphioxus (Branchiostoma floridae) encode now neuroblastomas (the esthesioneuroblastoma) and transform adenocarcinoma cells into highly resistant neuroectodermal/neuroendocrine malignant cellular entities. Proteins essential for life in the archaea, prokaryota and unicellular eukaryota rise in selected single cells of the multicellular host to induce, promote, or chaperone their "malignant transformation".*

The ancient cell survival pathways evolved in time in order to fit into complex multicellular hosts. The human cerebral cortex recognizes the oncogenic pathways for rejection with congenial means of chemoimmunotherapy as enemies of the organized cell communities. Or, the complex hosts may support the transformed cells, as if they were immortalized life forms for the eventual population of the Universe.

There is a significant difference between the oncogenesis indicated by exogenous pathogens and the endogenously generated process. The conserved ancient cell survival pathways triggered by exogenous viruses, bacteria or parasites, activate resistance, and defensive reactions of the host. On the contrary, endogenously activated by ancient proviruses preserved in the host genome, like the LINE elements, in some selected cells, the cell survivor pathways are reactivated endogenously by the RNA/DNA complex. These cells use mimicry to protect and maintain themselves, as the host organ is evolutionarily trained to act with immunological tolerance toward them. This way, the human host not only tolerates, but also actively supports this mechanism of oncogenesis. This novelty is described and explained in great detail in this book, like never before in the literature.

It is known that malignantly transformed human cells are maintained under laboratory circumstances as immortalized cultures even after storage in liquid nitrogen. It indicates that these cells may be even capable of reorganizing to multicellular colonies if the environmental conditions are appropriate.

Although originally the process of oncogenesis served for the rescue of cellular life, it leads to uncontrolled transformation in the human host. To cure this error and its consequences, all kinds of therapeutic methods, the human cerebral cortex has ever invented, must be applied. The diversity of these techniques is well assumed in this volume:

> *Avoid mutagenic toxic exposures and utilize the consumption of natural substances (phytochemicals) that prevent random and even inherent genomic mutations. Manipulate the epigenome in favour of the tumour suppressor genes. Laboratory-made miRs will neutralize the mRNAs of the oncoproteins; circulating oncoprotein kinases will be marked for ubiquitination by small molecular inhibitors fitted into their specific domains (their "side pockets"); monoclonal antibody-complexed oncoproteins will be naturally eliminated (by ubiquitination); tumour suppressor genes will be vectored by lentiviruses; and tumour masses will be dissolved by targeted small molecular inhibitors or oncolytic viruses. Avoid indiscriminate attacks on the genomes; target the oncogene by highly specialized gene therapy; target the oncoprotein by specific immunotherapy; and combine these modalities of treatment. Use inhibitory monoclonal antibodies to release NK and immune T cells from the evolutionarily installed checkpoints (CTLA4; PD1) for the attack on malignantly transformed cells masquerading as 'self'. Intensify CAR therapy for solid tumours. The multicellular host is to be rescued intact, not just as a disorganized cell community preserved in a tissue culture flask.*

Working for many years as medical oncologist, Sinkovics not only conquered the malignant disease when accomplishing complete remissions, but also experienced devastating failures when relapses occurred. The increasing numbers of successful treatments helped him to overcome the difficult times and gave force to work tirelessly on therapeutics with fewer side effects.

In this huge and complex work, only a few editorial errors remain. The legends of some figures are explained in full detail not customarily in the text, but separately in the two (most useful) appendices. The index is missing a few important passages. Some pre-digital era illustrations are not of first-class quality.

The work is unique, unparalleled in the literature, it is an excellent teaching material to advanced students and provides a view of life and cancer never described before.

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