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FOREWORD TO THE SPECIAL ISSUE ON APOPTOSIS

Dear Reader!

The 2012 Special Issue of *Experimental Oncology* is devoted to the 40th anniversary of one of the crucial milestones in biology and medicine, recognized today as the «birthday» of apoptosis research. The term apoptosis was coined by John Kerr, Andrew Wyllie and Alastair Currie in the article published in British Journal of Cancer in 1972. Besides the important statement that apoptosis «is an active, inherently programmed phenomenon», the authors speculated that «hyperplasia might sometimes result from decreased apoptosis rather than increased mitosis» and also proposed that «histological assessment of the «apoptotic index» of a tumour several days after the commencement of therapy might, in some cases, provide a useful measure of its response» [1]. Initially met without enthusiasm, the concept of apoptosis has been confirmed in numerous studies and as of the autumn of 2012, this landmark paper had received 11657 (!) citations.

The reviews presented in the issue prove the tremendous progress made in recent years in the study of apoptosis and related phenomena applied to cancer research. The contributing authors from Canada, Iran, Ireland, Italy, Japan, New Zealand, Switzerland, The Netherlands, Ukraine and USA (chiefly) are the authoritative experts in their fields. Two opening reviews deal with historical aspects of cell death research [2, 3]. The following four papers are devoted to the analysis of extrinsic, death receptor-dependent apoptotic pathway, providing an outlook on caspase-8-mediated cell-suicide signaling [4–7]. The role of c-FLIP isoforms as critical anti-apoptotic/drug resistance factors and novel c-FLIP targeted agents for cancer therapy are also discussed [7]. Subsequent two papers provide in-depth information on the intrinsic (mitochondrial) death pathway with particular reference to the role of the Bcl-2 family members [8, 9]. The next paper describes the inhibitors of apoptosis (IAP) proteins and their role in cell death and signaling pathways [10]. A great deal of attention has been paid to the development and testing of the IAP antagonists. Next, our current knowledge of alternative splicing of apoptosis-associated genes as well as mechanisms of translation control in apoptosis is summarized [11, 12]. The authors of the review [13] dwell on the sphingolipid-mediated regulation of apoptosis. A detailed discussion of the cell-cycle checkpoint signaling, DNA repair system and apoptotic pathways activated in response to DNA damage is also presented [14].

The following part of the issue moves from cell death signaling to modern approaches used for detection and quantification of apoptotic cells (see [15–17]). The application of *in vivo* apoptosis imaging by means of ^{99m}Tc-annexin V scintigraphy to monitor early response to therapy is analyzed more thoroughly due to the large clinical experience of authors [17]. Recent progress in studying cell death and cell proliferation during and after radiation treatment is in the focus of the following paper [18]. Of special importance are the new data on the involvement of tumor microenvironment in response to irradiation.

Over the decades of the intense research, it is becoming clear that several cell death modalities exist which are distinct from apoptosis. Some of these cell death subroutines including autophagy [19], necroptosis [10], cellular senescence [20] and «cannibalism» [21] are mainly discussed in the final part of this issue. Since nonapoptotic modes of the cell demise appear to be responsible for the elimination of cancer cells, both spontaneous and therapy-induced, this information will be useful from the viewpoint of the search for alternative approaches in cancer therapy.

Finally, I am grateful to all the authors for their generous contributions to this issue. My special thanks to Dr. Alex Philchenkov for the original idea and its successful realization.

Prof. V.F. Chekhun, Editor-in-Chief

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