Death-associated kinase (DAPK): a cancer “gene chameleon”

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There is a growing interest in understanding the signaling pathways and functions of DAPK in diseases and cancer. This issue in “Apoptosis” is especially dedicated to this interesting molecule and summarizes the major aspects of DAPK regulation, function and network, therefore earning the title “The Universe of DAPK”.

DAPK, an evolutionary highly conserved serine threonine kinase, has been originally characterized as a classical tumor suppressor due to its loss of expression during tumor development, progression or metastazation. Meanwhile there are many reports showing that DAPK behaves also in an opposite way under different experimental settings and shows antagonistic duality, a concept that has been originally described for the cell cycle inhibitor p21^{WAF1}. According to conventional textbook knowledge the functional loss of a classical tumor suppressor leads to unrestricted cell proliferation and the inability to promote repair mechanisms or cell cycle checkpoint activation. With antagonistic duality instead the tumor suppressor might stimulate cell survival. In this special issue several examples have been summarized demonstrating the ability of DAPK itself to act as an oncogene. The authors represent convincing data that DAPK shows a remarkable cell type specific response to different stimuli. This context-

dependent action of DAPK might be caused by the following facts: (i) the multi-domain structure of this molecule, (ii) the various possibilities for activating/inactivating DAPK and regulating its stabilization, (iii) the large number of known and yet unknown targets linking DAPK to a variety of signaling pathways, and finally (iv) the different levels of DAPK regulation, transcriptionally as well as post-transcriptionally. In addition, DAPK signaling is not only restricted to the kinase activity of the molecule. Instead there is an increasing number of reports emphasizing the importance of the scaffold function of DAPK to trigger and stabilize multi-protein complexes.

The considerable spectrum of cellular functions involving DAPK opens the great possibility to use it as a therapeutic target in treatment of human diseases and especially cancer. The antagonistic duality, however, also emanates the big challenge of developing the appropriate therapeutic strategy.

This review issue should not only give an overview of the current knowledge about this promising molecule it should also encourage researchers and scientists of many disciplines to enter into “The Universe of DAPK” and to develop a new translational era of DAPK.

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