

Cell death pathways in response to antitumor therapy

José Portugal, Marc Bataller, and Sylvia Mansilla

Instituto de Biología Molecular de Barcelona, CSIC, Parc Científic de Barcelona, Barcelona, Spain

ABSTRACT

Failure to eliminate cancer cells that have been exposed to cytotoxic agents may contribute to the development of resistance to antitumor drugs. A widespread model in present day oncology is that antitumor therapy involves the triggering of tumor cells to undergo apoptosis, and cells that can avoid apoptosis will be resistant to such therapy. Apoptosis is a defined program of cell death that is markedly influenced by the fact that many routes leading to it are mutated or deregulated in human cancer. Mutations in the tumor suppressor protein p53, a common feature of many cancers, may decrease the sensitivity of cells to some antitumor agents. Moreover, it has been increasingly reported that antitumor therapy not only causes apoptosis, but other forms of cell death as well, such as mitotic catastrophe, necrosis and autophagy, or a permanent cell arrest with phenotype characteristics of senescence. Mitotic catastrophe is a form of cell death that results from abnormal mitosis, which does not seem to depend on wild-type p53. Sometimes mitotic catastrophe is used restrictively for faulty mitosis leading to cell death, which may occur via apoptosis or necrosis. We critically review herein how antitumor therapy may elicit the response of human cancers through different cell pathways leading to cell death.

Key words: antitumor agents, apoptosis, mitotic catastrophe, necrosis.

Acknowledgments: Original research in our laboratory was supported by a grant from the Spanish Ministry of Education and Science (BFU2007-60998) and the FEDER program of the European Community. MB was recipient of a fellowship from Parc Científic de Barcelona - CSIC.

Correspondence to: Dr José Portugal, Instituto de Biología Molecular de Barcelona, CSIC, Parc Científic de Barcelona, Baldiri Reixac, 10; E-08028 Barcelona, Spain.

Tel +3493-403-4959;
fax +3493-403-4979;
e-mail jpmbmc@ibmb.csic.es

Received April 16, 2009;
accepted April 24, 2009.