

Apoptosis: Basic Biology and Relationship to Cancer

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Apoptosis is recognized as a common mode of cell death characterized by distinctive biochemical and morphological features. These include endonuclease activation, condensation of chromatin and its degradation in oligonucleosome fragments, cellular shrinkage, plasma membrane blebbing, and cell disruption into apoptotic bodies. The bodies are readily removed by macrophages or neighboring cells. Apoptosis is a physiological, genetically encoded program of cell death frequently termed programmed cell death, and depends on a variety of local and systemic influences such as tissue specific hormones and growth factors. A number of apoptosis-regulating genes have recently been discovered, including bcl-2, p53, and c-myc. Apoptosis is an essential physiological process in tissue homeostasis. By removing unnecessary and redundant cells, it ensures normal development, and maintains tissue balance throughout life.

Disregulation of apoptosis is an underlying mechanism of many pathological syndromes and diseases, including cancer. Apoptosis plays an important role in regulation of oncogenesis, tumor growth, and tumor response to various forms of cancer therapy, including radiotherapy and chemotherapy. Apoptosis develops rapidly, within hours, after cytotoxic treatments, and is dose-dependent. The apoptotic response correlates well with the antitumor efficacy of radiation and chemotherapy, and might serve as a predictor of tumor treatment response. There exists a significant heterogeneity among tumors in their susceptibility to apoptosis induction, and resistance to apoptosis has emerged as a major mechanism responsible for failure of tumor response to cytotoxic treatments. Hence, regulating apoptosis might be an effective way to improve tumor therapy; therapeutic gain would be achieved by increasing apoptotic response of tumors or by inhibiting apoptotic response of normal tissues. Diverse approaches to apoptosis are being investigated, with emphasis on gene therapy.

Key words: apoptosis; biochemistry; oncogenes; tumor cells