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review

Balance between life and death

Balance between cell proliferation and cell death is crucial to a metazoan's well being. Linking these two opposite processes is one means towards this end. In this review we focus on the current data examining the role of cyclin-dependent kinases and pRb in apoptosis. While a large portion of the evidence implicating the cell cycle machinery in apoptosis is circumstantial, there are intriguing and substantial connections between these pathways that may lead to greater insight in cancer biology.
corresponding author: MM Kasten

Divide or die? p53 helps to decide

One of the many interesting paradoxes in cancer biology is the observation that deregulation of the c-myc oncogene can either increase the proliferative capacity of a cell or increase cellular sensitivity to apoptosis depending on the cellular environment. Hypoxia, which occurs in solid tumors, can induce apoptosis in cells with deregulated c-*myc*. Futhermore, c-*myc* activation sensitizes cells to ionizing radiation. Execution of the c-*Myc*-mediated apoptotic program in hypoxic conditions or following irradiation requires accumulation of the tumor suppresser p53. Therefore, the activities of c-*myc* and p53, two of the most commonly mutated genes in human cancers, appear to function together to regulate apoptosis under conditions which can affect both tumor evolution and responses to cytotoxic therapies
corresponding author: B Rupnow

p53- how much is enough?

To clarify whether the biological effect of p53 depends on the level of its expression in small cell lung carcinoma (SCLC) cells, we assessed the effect of various p53 levels on a p53-null SCLC cell line. High and low p53 expression induced apoptosis and transient G1 arrest respectively. High p53 expression down-regulated Bcl-2 expression, while Bax was consistently expressed irrespective to p53 expression levels. These results suggest that p53-mediated apoptosis and G1 arrest depend on p53 expression levels in SCLC cells and that the relative dominancy of Bax to Bcl-2 is involved in apoptosis by high p53 expression.
corresponding author: J Yokota

PAI in cell death

Plasminogen activator inhibitor type-2 (PAI-2) is a member of the serine proteinase inhibitor or serpin superfamily. PAI-2 is unusual in that the glycosylated extracellular form of PAI-2 is an inhibitor of urokinase, whereas intracellular PAI-2 protects from tumour necrosis alpha (TNFα) induced apoptosis by a urokinase independent mechanism. Dickinson *et al*, show that a unique peptide loop domain of the PAI-2 molecule plays a critical role in protection from TNFα induced apoptosis. This domain does not appear to be involved in intramolecular cross-linking of PAI-2, but evidence suggests an alternate mechanism of action.
corresponding author: TM Antalis

Proteolysis in apoptosis and necrosis

The activation of a proteolytic cascade is a central event in apoptosis. Intracellular proteolysis also occurs during necrosis, but the identity of the proteases involved and their subtrates remain unclear. Casiano *et al* show, using autoantibodies to cellular proteins as detecting probes in immunoblotting, that a similar set of nuclear proteins is selectively cleaved, albeit differently, during both apoptosis and necrosis. The data suggest that different proteases act in apoptosis and necrosis, and that although both cell death processes result in selective cleavage of almost identical cellular proteins, they can be distinguished immunochemically on the basis of their cleavage products.
corresponding author: CA Casiano

Ceramide shakes-up dogma

Traditional antitumor research dictates that cytotoxicity is essentially determined by the level and/or perpetuity of cellular lesions. Recently, it has been proposed that since apoptosis is a general response of cells to clinically relevant doses of ionizing radiation, the effective activation of an apoptotic response in tumor cells will determine the success of ionizing radiation therapy. The observation that sensitivity to ionizing radiation-triggered apoptosis is more directly related to ceramide generation rather than to DNA double-strand break repair, which should provoke a conceptual challenge in defining anticancer therapeutic strategies.
corresponding author: J.P. Jaffrézou