In cancer and aging, interconnected roles for apoptosis and cellular senescence

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A common feature of cancer and aging is cells' reduced ability to respond to stress-induced damage to DNA or cellular structures. Specifically, changes occur in the protective processes of apoptosis and cellular senescence, whose roles in cancer and aging are thoroughly reviewed by Cerella et al. in *Current Drug Targets* (Bentham Science Publishers). The authors outline the evidence that these processes are regulated by separate but intertwined pathways. Understanding the precise mechanisms, they conclude, could lead to combination therapies for cancer and aging able to harness the benefits of both apoptosis and senescence, while limiting the drawbacks of either.

The review highlights anti-apoptotic mechanisms relevant for cancer therapy (eg. inhibition of Bcl-2 family members blocking cell death, or of COX-2, whose aberrant expression is correlated with chronic inflammation and the most aggressive forms of colorectal cancer). The authors also discuss the dual nature of apoptosis in aging, contrasting its protective removal of cells 'damaged' by telomere attrition—a hallmark of aging—versus the lifespan reduction recently observed in Drosophila exhibiting hyperactive apoptosis.

Similarly, while cellular senescence is shown to be an alternative to apoptosis, blocking damaged cells from proliferating, it is also capable of promoting tumorigenesis and aging. The review outlines the current knowledge on cellular avoidance of senescence, as well as clues to its reversibility.

Cerella et al. find no consensus on the complex interactions between programs for apoptosis and senescence: one may back up the other, or they may play equally essential, complementary roles. Importantly, the authors note that certain cancer treatments triggering apoptosis actually activate senescence, too. The latter's sensitivity to epigenetic mechanisms could provide avenues for reactivating senescence in cancer cells, thus improving current therapies. However, for combined treatments, researchers need to uncouple the beneficial effects (anti-cancer, anti-aging) from the undesirable ones (tumor growth and aging).

More information: Claudia Cerella et al, Roles of Apoptosis and Cellular Senescence in Cancer and Aging, *Current Drug Targets* (2016). DOI: 10.2174/1389450116666150202155915

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