Dicloroacetato de sódio – DCA - e câncer endometrial

Dicloroacetate induces apoptosis in endometrial cancer cells.


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PURPOSE: A recent landmark study demonstrated that Dichloroacetate (DCA) treatment promoted apoptosis in lung, breast, and glioblastoma cancer cell lines by shifting metabolism from aerobic glycolysis to glucose oxidation coupled with NFAT-Kv1.5 axis remodeling. The objective of this study was to determine whether DCA induces apoptosis in endometrial cancer cells and to assess apoptotic mechanism. METHODS: A panel of endometrial cancer cell lines with varying degrees of differentiation was treated with DCA and analyzed for apoptosis via flow cytometry. Biological correlates such as gene expression, intracellular Ca(2+), and mitochondrial membrane potential were examined to assess apoptotic mechanism. RESULTS: Initiation of apoptosis was observed in five low to moderately invasive cancer cell lines including Ishikawa, RL95-2, KLE, AN3CA, and SKUT1B while treatment had no effect on non-cancerous 293T cells. Two highly invasive endometrial adenocarcinoma cell lines, HEC1A and HEC1B, were found to be resistant to DCA-induced apoptosis. Apoptotic responding cell lines had a significant increase in early and late apoptosis, a decrease in mitochondrial membrane potential, and decreased Survivin transcript abundance, which are consistent with a mitochondrial-regulated mechanism. DCA treatment decreased intracellular calcium levels in most apoptotic responding cell lines which suggests a contribution from the NFAT-Kv1.5-mediated pathway. DCA treatment increased p53 upregulated modulator of apoptosis (PUMA) transcripts in cell lines with an apoptotic response, suggesting involvement of a p53-PUMA-mediated mechanism. CONCLUSIONS: Dichloroacetate effectively sensitizes most endometrial cancer cell lines to apoptosis via mitochondrial, NFAT-Kv1.5, and PUMA-mediated mechanisms. Further investigation of the cancer therapeutic potential of DCA is warranted.