How many cell death pathways that Doxorubicin can affect HepG2 cells?

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Doxorubicin (DOX) is a potent antibiotic anti-cancer drug that is used either in isolation or in combination, for treating ovary, haematological, breast, stomach, liver, and prostate cancers. This drug has the ability to damage DNA and inhibit macromolecules (DNA and RNA) by producing free-radicals. Several studies have shown that Dox induces P53 activation leading to apoptosis in both normal and tumour cells, by causing cytochrome c release from the mitochondria which ultimately leads to apoptosis via caspase 3. We have investigated the molecular mechanisms of DOX induced hepatic cell death. This study shows that DOX can induce cell death in HepG2 cells through two different mechanisms. The use of caspase substrates and caspase inhibitors confirm that apoptosis through caspase 9 and caspase 3 are involved. Using HepG2 cells transfected with LC3-GFP, it was also noted that a high percentage of LC3-GFP puncta were seen using fluorescence microscopy, following DOX treatment, which suggests that autophagy is also involved. However, lactate dehydrogenase release assays and the use of necrostatin, on DOX treated cells indicate that necrosis is unlikely to be involved.

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