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Determining the Role of Ferroptosis in Parthenolide and Its Analog Mediated Cell death in AML

Parthenolide (PTL) is a drug that is shown to selectively target cancer stem cells, unlike most current cancer treatment options. PTL's intermediate, MMB, is miscible in water, unlike PTL, and produces highly selectively cytotoxic dimers (JVM), which may be useful to study. The goal of my research is to determine whether PTL and its analogs use ferroptosis as a mechanism of cell death, which may explain why these drugs can selectively target cancer stem cells. Current literature indicates that PTL uses apoptosis as its mechanism of cell death. However, the pathways targeted in experiments conducted to determine whether PTL uses apoptosis are also affected in ferroptosis, another mechanism of cell death. To determine whether these drugs use ferroptosis, I investigated cytotoxicity with ferroptosis inducers and inhibitors, protein levels, and glutathione levels. I found that PTL uses ferroptosis but MMB does not use ferroptosis, which was unexpected, considering that it is PTL with the addition of a hydroxyl group. I discovered that PTL's dimers, JVM, partially use ferroptosis and partially use another mechanism of cell death to selectively induce cancer cell death. This study offers new insight into the mechanisms of PTL and its analogs in selectively inducing cancer cell death and may enable the discovery of a novel mechanism of cell death that is used by JVM in addition to ferroptosis. These findings may also lead to the determination of the specific pathway used by ferroptosis to selectively target cancer cells, which can be further targeted to create a new drug.