

Annonaceous Acetogenins Promote Cell Death in Cancer cells by Targeting both Na⁺/K⁺ ATPase and SERCA ATPase Pumps

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The leaves of *Annona muricata*, commonly known as Graviola, are known to be rich in flavonoids as well as annonaceous acetogenins. Graviola extracts have previously been shown to have anti-cancer activity. The precise target of action for these plant-base anti-cancer agents is unclear. Recently, using an *in silico* approach, we showed that the active agent acetogenins of Graviola is a novel target for inhibiting Na⁺/K⁺ ATPase and SERCA ATPase Pumps. In the present study we demonstrate that that acetogenins are able to promote cell death in a variety of cancer cell lines but not in non-transformed cells. Moreover, specific inhibitors to Na⁺/K⁺ ATPase and SERCA ATPase Pumps were shown to induce cell death in cancer cells but had little toxic effect on normal cells. Finally, using an *in vivo* xenograft model, Graviola acetogenins was able to reduce the tumour size/volume. The present data indicates that acetogenins are able to promote cell death by targeting and inhibiting Na⁺/K⁺ ATPase and SERCA ATPase Pumps and therefore may be potential therapies for the treatment and prevention of cancers.