Triptolide Promotes Cell Death in Cancer cells by Targeting Na+/K+ ATPase Pump

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Chemotherapeutic drugs have improved the prognosis and outcome of a variety of human cancers, however these types of therapies result in limited efficacy as well as cytotoxicity to the normal tissues and the organs still remain a major problem. There is also the problem that many of the chemotherapeutic drugs also lead to drug resistant and relapsed tumor growth. Therefore, identification of drugs that are able to target the cancer cells without having toxic effects to normal cells would be more beneficial in the long term to the patients. Thus, the challenge is to identify agents that have selective cell death effects in cancer cells that may be derived from natural phyto-extracts. In the healthcare sector, phyto-compounds are known to be beneficial by contributing to alleviating a variety of diseases including exhibiting anti-cancer abilities. However, the exact molecular mechanism on how these phyto-compounds exert anti-cancer properties is unclear. We have recently been interesting in several phyto-compounds and their effects in promoting cell death in cancer cells We have recently reported the phyto-compound *annonacin* has selective cell death effects in cancer cells that may be mediated via inhibiting Na+/K+-ATPase (NKA) and sarco-endoplasmic reticulum Ca2+ ATPases (SERCA). We now have preliminary data that suggest that another plant extract we are interested in *Tripterygium wilfordii Hook F* (TWHF) also has selective cell death promoting effects on various cancer cell lines but very little toxic effects on normal cells. In silico analysis suggest that one of the phyto-compounds present in TWHF, triptolide also targets NKA but not SERCA. Moreover, ouabain (1mM) a NKA specific inhibitor was shown to also induce selective cell death in several cancer cells lines. Finally, bio-profiling studies show a strong association between overexpression of both *NKA* gene expression and reduced survival rates. The present data indicates that TWFH/triptolite is able to promote cell death by targeting and inhibiting Na+/K+ ATPase pump and therefore may be potential therapies for the treatment and prevention of cancer.