The In Vitro Effects of Actinomycin D and DMAPT on Panc-1 Pancreatic Cancer Cells
G. J. Lamture, P. A. Crooks, M. J. Borrelli
University of Arkansas for Medical Sciences

**Purpose**
Pancreatic cancer’s late diagnosis and the stromal barrier which develops around the tumor are reasons for the difficulty in treatment. The tumor associated stroma is one of the biggest hurdles in treating pancreatic cancer. This stroma is supports tumor growth, metastasis and resistance to therapy. New methods of drug delivery or new drug molecules, used alone or in combination are needed. A novel anti-cancer drug, Dimethylaminoparthenolide (DMAPT), is the water soluble analogue of Parthenolide, and acts by inhibiting the NFkB pathway and by depleting glutathione. Actinomycin D is a polypeptide antibiotic binds to DNA and inhibits RNA and protein synthesis, by inhibiting RNA polymerase II. The JNK pathway is involved in apoptotic cell death and is involved in increasing the expression of pro-apoptotic genes, like TNF. TNF requires Act D for apoptosis and activation of the JNK pathway. Actinomycin D is a very potent drug against pancreatic cancer; however, it failed in the clinical trials due to toxicity issues.

**Methods**
The Panc-1 pancreatic cancer cells were treated with DMAPT and Actinomycin D individually and in combination. The initial assessment was done by the Caspase assay and the FDA/PI Live dead assay. The GI50 for each drug was calculated by the MTT cell viability assay.

**Results**
Cells treated with the drugs individually and in combination were analyzed microscopically with Caspase assay. The cells treated with the drug combination showed brighter fluorescence, under the microscope, than individually treated cells. The Live Dead assay analyzed on the flow-cytometer, showed similar results with almost a 2 fold increase in cell death, with combination treated cells. The MTT assay provided the GI50 of DMAPT and Actinomycin D on Panc-1 cells as 15 µM and 17 ng/mL (0.012 µM) respectively.

**Conclusion**
Actinomycin D and DMAPT are both effective anti cancer agents, against Panc-1 cell growth. The combination shows a higher percentage of cell death than the individual agents. Suggesting the synergistic action by inhibiting the NFkB pathway and avoiding the inactivation of the JNK pathway and TNF induced apoptosis.