Ivermectin Induces Apoptosis, Cell Cycle Arrest and Senescence in C4-2 Prostate Cancer Cells

Moniz, Taylor (School: Kamehameha Schools Kapalama Campus)

Ivermectin, awarded the Nobel Peace Prize for Physiology or Medicine in 2015, was originally used as an anthelmintic. Ivermectin was invented by William Campbell and Satoshi Omura to treat parasites, mainly onchocerciasis. Ivermectin has been FDA approved for use in humans and has no side effects on human safety. Due to this, Ivermectin has been researched in multiple cancer cell lines and was found to have anticancer activity in various types of cancer. This project focuses on the effect of Ivermectin on the C4-2 prostate cancer cell line, which has not been researched with Ivermectin. The C4-2 prostate cancer cell line is a human castration resistant cell line derived of the LNCaP cell line. Multiple experimental procedures were used to test the effect of Ivermectin on the C4-2 cell line. For all experiments C4-2 cells were treated with a DMSO control and various concentrations of Ivermectin. It was found that Ivermectin induces apoptosis, cell cycle arrest in the G1/G0, and cell senescence. Lastly, ivermectin was found to decrease the FOXA1 protein which is necessary for AR binding to DNA, thus causing decreased AR expression and AR activity which is important in DNA damage repair. Therefore, increased DNA damage was detected in Ivermectin treated cells. The effect of Ivermectin on RPMI myeloma cells and HCT colorectal cancer cell lines was also tested. It was found that Ivermectin can decrease the cell density of RPMI myeloma cells without causing cell death, but no clinically relevant effect was found in HCT colorectal cancer cells.