Understanding the DNA repair mechanisms of Andrographolide in prostate cancer

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Prostate cancer (PCa) is the most common diagnosed cancer and is the second cause of cancer mortality in men in the United States. Although in Puerto Rico, PCa is also the most frequently diagnosed, it is the first cause of cancer-related death in men. Andrographolide has been found to inhibit prostate cancer progression but nevertheless the mechanism of action remains unknown. Our lab studied the mechanism of action of Andrographolide using in vitro and in vivo models, and gene expression analysis. In vitro studies showed that Andrographolide decreased PCa cell migration and invasion while increased cell apoptosis. In vivo studies showed that Andrographolide decreased tumor volume, MMP11 expression and blood vessels formation. Gene expression analysis identified cellular compromise, cell cycle, and “DNA recombination, replication and repair” as the major molecular and cellular functions altered in tumors treated with Andrographolide. These data suggest that Andrographolide inhibits PCa by promoting DNA damage. Our approach for the next experiment is to study more in depth the mechanism of DNA repair. Particularly analyzing the expression of the phosphorylated H2AX histone, a protein phosphorylated by the formation of double-strand breaks. We will also focus in the analysis of Checkpoint kinase 2 (CHK2), p53 and ATM, which is considered a major physiological mediator of H2AX phosphorylation.