

CALIFORNIA STATE SCIENCE FAIR 2007 PROJECT SUMMARY

Name(s)

Aryeh B. Hillman

Project Number

S0407

Project Title

Activity Based Proteomic Profiling of Lysophosphatidic Acid Treated Cancer Cells

Abstract

Conclusions/Discussion

Ovarian cancer is a debilitating disease lacking effective treatments. A key feature of the disease is elevated levels of the mitogenic lipid lysophosphatidic acid (LPA) found in the ascities fluid surrounding tumors. LPA evokes a wide array of pro-tumorgenic effects in cells and was recently shown to stimulate the expression of a cancer-associated protease, urokinase type plasminogen activator (uPA). To discern whether LPA treatment resulted in active uPA, I applied a novel proteomic technique, activity-based protein profiling (ABPP), that specifically monitors the amount of protein activity rather than abundance. I utilized ABPP to examine the effect of the bioactive lipid LPA on uPA in a human ovarian cancer cell line SKOV-3. To achieve this I first developed a new strategy for analysis of secreted proteins and then determined that treatment of SKOV-3 cells with LPA does indeed result in increases of active uPA. In addition to this finding, I also detected elevated uPA activity upon treatment of structurally distinct forms of LPA that vary in acyl chain length. This finding has not previously been reported and demonstrates the power of ABPP to identify changes in the functional state of low abundance enzyme activities.

Summary Statement

I sought to characterize the effects of certain lipids on the expression and activity of enzymes implicated in cancer metastasis.

Help Received

Used laboratory equipment at The Scripps Research Institute in La Jolla, California under the supervision of Dr. Benjamin Cravatt