



**CALIFORNIA STATE SCIENCE FAIR
2009 PROJECT SUMMARY**

Name(s) Paul Tran	Project Number S0428
Project Title Further Investigation of the Inhibitory Effect of HKa on Metastasis of Prostate Cancer Cell Line DU145	
<p style="text-align: center;">Abstract</p> <p>Objectives/Goals Prostate Cancer metastasis caused by the activation of cell surface receptors, such as EGFR, ERK, and AKT1. Cleaved high molecular-weight kininogen (HKa) is an anti-adhesive protein which, in zinc (Zn²⁺)-dependent manner, induces apoptosis and inhibits angiogenesis in vivo by binding to/preventing activation of cell surface receptors. The purpose of this research was to identify the role HKa and Zn²⁺ play in inhibiting Prostate Cancer metastasis by preventing phosphorylation of EGFR, ERK, and AKT1.</p> <p>Methods/Materials (1) Immunofluorescence Microscopy was used to observe cellular proliferation and changes in cellular morphology. In the first study, DU145 cells were treated with a high dose of Zn²⁺ (13.3µL). In the second study, DU145 cells were treated with HKa (4.5µL) and Zn²⁺ (2µL). (2) To detect phosphorylation of EGFR, ERK, and AKT1, DU145 cells were harvested from both Zn²⁺ Treated and HKa+Zn²⁺ Treated samples. Western Blot was performed using infrared LI-COR Odyssey Machine. (3) After plating DU145 cells in a dose on a 96-well plate, BrdU Immunohistochemistry System (Oncogene) was used to quantify the proliferation of DU145 cells in both Zn²⁺ Treated and HKa+Zn²⁺ Treated samples.</p> <p>Results (1) In the first study, Immunofluorescence Microscopy showed significant proliferation and changes in cellular morphology in Zn²⁺ Treated samples as the cells grew in clumps and took on a sickle shape. However, in the second study, Immunofluorescence Microscopy showed no proliferation and changes in cellular morphology in the HKa+Zn²⁺ Treated samples. (2) In the first study, Western Blot showed consistent phosphorylation of EGFR (170 kDa), ERK (42/44 kDa), and AKT1 (56 kDa) in Zn²⁺ Treated samples. In the second study, Western Blot showed consistent deregulation of EGFR, ERK, and AKT1 in the HKa+Zn²⁺ Treated samples. (3) In the HKa+Zn²⁺ Treated samples, Proliferation Assay showed that DU145 cells proliferated in the Control (83 per 100 cells) more so than the HKa+Zn²⁺ Treated (47 per 100 cells) samples. A p-value of 0.0107 suggested significant difference.</p> <p>Conclusions/Discussion HKa+Zn²⁺ have a higher potency of preventing phosphorylation of EGFR, ERK, and AKT1 than Zn²⁺ alone. This suggests that HKa can potentially inhibit Prostate Cancer metastasis by competitively binding to/preventing the activation of cell surface receptors responsible for cellular proliferation and migration.</p>	
Summary Statement HKa, a plasma protein that induces apoptosis and inhibit angiogenesis, is used to inhibit Prostate Cancer metastasis by preventing the activation of cell surface receptors responsible for tumor proliferation, namely EGFR, ERK, and AKT1.	
Help Received Utilized facilities and equipment at Sol Sherry Thrombosis Research Center (Temple University School of Medicine, Philadelphia, PA) under supervision of Yuchuan Liu, PhD.	