Title: Metabolism of long chain saturated fatty acids and prostate cancer progression

Dr. Cai is an assistant professor in the Department of Pharmacological and Biomedical Sciences at the University of Georgia. His laboratory is interested in understanding molecular mechanisms that facilitate the initiation and progression of advanced prostate cancer, and translate basic knowledge to drug discovery. One of his studies focuses on how metabolism of long chain fatty acids will promote prostate cancer progression.

Summary

Prostate cancer is the second leading cause of cancer-related death and the most common cancer in men in developed countries. Among numerous identified oncogenic events, over-expression and/or activation of Src kinase, a non-receptor tyrosine kinase, are commonly occurred in advanced stages of prostate cancer. We show that metabolism of dietary saturated fatty acids significantly accelerated Src-mediated tumor progression. Two long-chain saturated fatty acids, palmitate and myristate, exhibit two complementary mechanisms including alteration of ceramide compositions and elevation of Src kinase myristoylation, respectively to regulate oncogenic activity of Src kinase. The combination of these dual effects increased Src kinase levels in the cell membrane and its mediated oncogenic signaling. Bioconversion of these long-chain fatty acids to their corresponding fatty acyl-CoAs is required for the fatty acids to participate in metabolic processes. The process is catalyzed by long chain fatty acyl-CoA synthetases (ACSLs). We further demonstrate that expression levels of ACSL1 were significantly associated with the levels of a variety of acyl-CoAs, and were elevated in human prostate tumors. Knockdown of ACSL1 significantly inhibited prostate tumor progression. Our findings illustrate how oncogenic events could interact with environmental factor through metabolism of fatty acids to accelerate prostate tumor progression. Our results provide a therapeutic strategy for the treatment of prostate cancer by targeting fatty acid metabolism.