CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120028

Project Title:
Targeting prostaglandin substrate availability in colon cancer: Characterization of a novel arachidonic acid-deficient mouse model

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
Texas Agrilife Research

Lay Summary:

It is now apparent that products of fat metabolism, i.e., prostaglandins, promote colon cancer development by enhancing intestinal cell growth, migration and invasion, while inhibiting cell death. Not surprisingly, most studies to date have targeted prostaglandin biosynthetic and degradation enzymes in an attempt to suppress the tumor promoting action of prostaglandins. However, due to safety concerns surrounding the use of pharmaceutical drugs designed to target the cell machinery that synthesizes these metabolites, it is important to identify new targets of this critical dysregulated pathway. In this proposal, we will determine the utility of antagonizing the precursor molecules that can generate prostaglandins as a novel approach to suppressing colon cancer. To address this goal, we generated a unique genetic model, i.e., the FADS1 (delta-5 desaturase) “deleted” mouse, for the purpose of establishing a new molecular framework for the evaluation of strategies for colon cancer prevention. Aim 1 will assess the impact of a cancer-causing carcinogen on intestinal tumor (cancer) formation in mice lacking the FADS1 gene. Aim 2 will assess the effect of FADS1 deletion on fat-derived prostaglandin levels. We anticipate that mice lacking FADS1 will be resistant to the development of colon cancer, identifying the FADS1 gene as a novel drug/dietary target.