CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180863

Project Title:
Chemoprevention of Colon Cancer Progression in FAP Children

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
University of Houston

Lay Summary:

Familial Adenomatous Polyposis (FAP) is a rare form of hereditary colon cancer predisposition that affects children as young as age 7. There is no drug treatment for FAP. The current standard of care is periodic colonoscopy to remove polyps and the removal of the whole colon to prevent the colon cancer development in adolescence, severely affecting their quality of life. Previously celecoxib was approved to treat FAP, but was withdrawn due to increased incidences of heart attack and death. The toxicities of celecoxib were due to its actions on the organs other than the target (colon). The goal of this research project is to develop a new class of COX-2 inhibitors that will only be active in colon and not cause toxicity to other organs. The approach used here is to use our body's own physiological process to limit the drug exposure to colon only, by inactivating (metabolism by enzymes) the drugs before entering blood. These metabolites are then recycled back to intestine via bile secretion. In addition, the drugs are designed so these metabolites can become active again (convert back to drug) in the colon with the help of gut bacteria. Therefore, we called this new class of drugs recycled locally bioavailable COX-2 inhibitors (ReCOX). Using this innovative design, we have derived a lead drug 7a1 that is highly active in colon but unavailable to other organs. The goals of this study is to determine the efficacy and safety of 7a1. We will use an animal model called (polyps in rat colon) Pirc rat model for our study because these rats mimic human FAP (i.e., possess similar genetic mutation and develop polyps at a young age). Our research will provide the necessary proof-of-principle results to determine the effectiveness and safety of our lead ReCOX drug 7a1 in treating polyps to prevent colon cancer in the Pirc model. If successful, 7a1 will likely become the first drug for children with FAP and also be useful for colon cancer prevention in other high-risk population.