



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160512

Project Title:
Integrin-mediated IL-18 signaling in the prevention and treatment of
inflammation-associated colorectal cancer

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas Health Science Center at San Antonio

Lay Summary:

Worldwide colorectal cancer is the third and fourth most common cancer-related cause of death for women and men respectively. There are many factors that contribute colorectal cancer but uncontrolled inflammation is a major risk factor. This partially explains why people with inflammatory bowel disease, IBD, are at a significantly higher risk of developing colorectal cancer. A significant advance in our understanding of the link between IBD and colorectal cancer was made a few years ago when it was discovered that a set of genes that regulate inflammation through a cellular machine called the inflammasome, could protect against both IBD and colorectal cancer. The inflammasome leads to the production of a signaling protein called IL-18 in the intestine that is important for repairing the gut after inflammatory insult and has an overall anti-inflammatory effect on the gut. We recently defined the signaling pathways leading to inflammasome activation and IL-18 production in the cells that line the intestine called intestinal epithelial cells. In a major step towards harnessing IL-18 for treating IBD and colorectal cancer, we engineered bacteria that can induce IL-18 from intestinal epithelial cells. In the current application we propose to refine our understanding of IL-18 mediated responses in intestinal epithelial cells. Further, we will test if our engineered bacterial strains can be used to modify the microbial composition of the gut as a treatment for IBD and a preventative for colorectal cancer. If successful, this application represents a new approach for developing simple and cost effective methods for treating IBD and preventing colorectal cancer.