



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160577

Project Title:
A novel function of Itch in controlling IL-17-induced inflammation in colon cancer

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
Baylor Research Institute

Lay Summary:

Approximately 124,000 new cases and 49,700 deaths are expected from colorectal cancer (CRC) this year alone in the US. Many factors cause CRC including genetic mutations (changes in the DNA), high-fat diet, and inflammation. Recent studies suggest that the microorganisms in the intestine trigger interleukin-17 (IL-17), a type of protein that helps the immune system keep gut bacteria under control. However, when overproduced it can enhance cancer-promoting inflammation. IL-17 expression is very high in CRC patients. Understanding the detailed molecular mechanisms that naturally inhibit IL-17 production and inflammation in the colon is essential to develop more effective preventive and therapeutic strategies. Our studies suggest that mice that lack an enzyme (named Itch) that is involved in protein degradation in immune cells develop severe inflammation, rectal bleeding and growth of colon cancer. The immune cells of these mice secrete higher levels of IL-17. Additionally, we have found that a pathogenic bacteria (*Helicobacter typhlonius*) was found in the intestine of these mice, suggesting that itch is important for controlling the growth of this bacteria. We propose to investigate how this enzyme blocks the inflammation that promotes colon cancer. We will test whether this enzyme degrades ROR-gt, a protein that is necessary for IL-17 production. If successful, our results might lead to new types of treatment for patients with colon cancer and help us to develop cancer-preventing vaccines.