CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP140563

Project Title:
PAF, a Novel Wnt Signaling Regulator, in Colorectal Cancer

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Background Cellular signalings play crucial roles in tissue maintenance and regeneration. Conversely, deregulated cellular signalings leads to human cancer. Among those cellular signalings, we have consistently studied Wnt signaling, which controls cell proliferation. Genetic mutation in Wnt signaling lead to abnormal hyperactivation of Wnt signaling, results in accelerated cell proliferation and subsequent colorectal cancer. Thus, elucidating the regulatory mechanisms of Wnt signaling to allow for its targeted manipulation will thus provide a milestone in colorectal cancer research and treatment. Previous Studies Recently, we revealed unexpected roles of PAF, a protein required for DNA repair. We found that PAF is specifically expressed in colorectal cancer cells and increases Wnt signaling activity in various animal models. Our studies highlight that PAF hyperactivates Wnt signaling, possibly in colorectal cancer. Significance Our proposed research will address how PAF contributes to colorectal cancer development. With efforts by biotechnology companies producing only limited success to date, there is a critical need to develop novel approaches to regulate Wnt signaling. A complication is that Wnt signaling is needed for normal intestinal tissue maintenance. Thus, the targeting of components whose expression is very largely restricted to colorectal cancer cells provides an opportunity to minimize side effects. Importantly, PAF is highly elevated in colorectal cancer cells compared to normal intestine. These facts suggest potential therapeutic advantages in future studies. Goal Our long-term goal is to reveal molecular mechanisms that promote intestinal tumorigenesis and to develop therapeutic methods to counter colorectal cancer cell proliferation and metastasis. Hypothesis We hypothesize that pathologically high PAF expression plays a key role in colorectal cancer, which will be addressed by employing mouse models and biochemical approaches.