



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP170382

Project Title:  
Primary Cilia in Cell Cycle Control and Tumorigenesis

Award Mechanism:  
Individual Investigator

Principal Investigator:  
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Entity:  
The University of Texas Southwestern Medical Center

### Lay Summary:

Although several drugs have been developed to target breast cancers expressing estrogen receptor (ER), progesterone receptor (PR) or Her2/neu, but effective treatment for aggressive breast cancer is still lacking. Increasing evidence suggest that a broad spectrum of human cancers including breast, ovary, prostate, and pancreatic cancers have reduced primary ciliogenesis, suggesting that defect in ciliogenesis might associate with tumorigenesis. The primary cilium is an antenna-like structure that protrudes from the surface of virtually all cells in the mammalian body. Cilia transduce signals from extracellular stimuli to a cellular response that regulates proliferation, differentiation, transcription, migration, polarity and tissue morphology. Dysfunctional cilia underlie a broad spectrum of human diseases, namely ciliopathies. Our published and preliminary results demonstrate that inhibition of OFD1, a ciliary suppressor, promotes ciliogenesis in human cells. We hypothesize that primary cilia elicit a previously undescribed cell cycle "checkpoint" to stop cell cycle progression and activation of this checkpoint relies on the presence of primary cilia, and through this cell growth inhibition effect, primary cilia functions as a tumor suppression mechanism in breast cancer tumorigenesis. Restoration of primary cilia that are present in normal cells but lost in cancer cells might have minimum side effect to normal cells. Our study will provide the first Proof-of-Concept evidence for novel anti-cancer therapy by reverting primary ciliogenesis in breast cancer cells. Chemical compounds and peptides targeting this pathway may serve as potential drugs for breast cancer therapy. In a broad sense, we believe this ciliary cell cycle checkpoint and tumor suppression mechanism is not limited to breast cancers but also apply to a broad spectrum of human cancers, which will provide a brand new angle for cancer therapy and diagnosis.