



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP150346

Project Title:
Targeting Twist1 for Prevention and Treatment of Non-Melanoma Skin
Cancer

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas at Austin

Lay Summary:

Nonmelanoma skin cancer (NMSC) with more than 3.5 million cases diagnosed in the U.S each year is the most common cancer and consists of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). Solar ultraviolet radiation (UVA + UVB) is the primary etiologic factor for NMSC. Actinic keratosis (AKs) or solar keratoses are premalignant skin lesions with the potential to develop into SCC. The currently approved treatments for AKs include, cryosurgery and other surgical methods, topical treatment with 5-fluorouracil, diclofenac sodium, imiquimod and ingenol mebutate as well as photodynamic treatment. The current topical agents used to treat AKs have significant negative features, including irritation, decreased quality of life, and limited efficacy. Given the prevalence, as well as the social and economic burden of this disease, there remains a pressing need for development of novel prevention and treatment strategies for NMSC. Preliminary findings suggest that the transcription factor Twist1 plays a role in skin carcinogenesis by regulating keratinocyte proliferation during tumor promotion via modulation of cell cycle proteins and cell cycle progression. In this proposal, we will test the hypothesis that Twist1 plays a critical role in proliferation and survival of keratinocytes, including keratinocyte stem cells (KSCs), during tumor promotion and skin tumor development by regulating levels of key G1/S phase cell cycle proteins. In addition, as part of this proposal we will develop novel, nuclei acid based Twist1 targeting agents (i.e., decoy oligonucleotides or dODNs) to test the hypothesis that targeting Twist1 alone or in combination with targeting Stat3 can prevent the progression of premalignant skin lesions to SCCs. Completion of the proposed studies will elucidate the role of Twist1 in the development of skin tumors and could lead to novel approaches for the prevention and treatment of NMSC in humans through targeting this transcription factor.