



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP101120

Project Title:  
Creation of Animal Models and Characterization of Nicotinic Receptor  
Cancer Risk Factors

Award Mechanism:  
Individual Investigator

Principal Investigator:  
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Entity:  
Baylor College of Medicine

### Lay Summary:

Tobacco use is directly responsible for approximately 1/3 of all cancer deaths annually in the United States. Therefore, the genetic predispositions and causes for tobacco use are in fact predispositions and causes of cancer. Nicotine is the addictive component of tobacco that motivates and drives cigarette smoking despite the harmful effects. A genetic factor that is associated with cancer was found within a receptor of the human brain, and that receptor binds the addictive drug, nicotine. Results showed that this nicotine receptor is a vital link between normal human genetic differences and cancer, but the mechanism that underlies this cancer risk has never been analyzed. In this study, we will create 2 different rodent animal models to analyze how normal genetic differences within a nicotine receptor in the brain can underlie risk for cancer. We hypothesize that genetic differences within this nicotine receptor produce differences in the likelihood and intensity of cigarette smoking. This difference in tobacco use arises because the "reward center" of the brain responds differently to nicotine from tobacco depending on the genetic makeup of this nicotine receptor. Work from our lab and others has previously shown that nicotine induces neural signals from the "reward center" that underlie the drive for cigarettes. Using a wide arsenal of techniques, we will examine the rodent animal models to understand how genetic risk factors for cancer may arise from changes in the activity of the neural "reward center". The resulting knowledge will guide future research aimed at methods to prevent tobacco use that underlies more than 80% of lung cancer deaths.