

James & Esther King Biomedical Research Program

Papke, Roger

*Pharmacology and Therapeutic Research
University of Florida*

*2010 Program
Research Project Grant
(5-year project)*

Project Title: Therapies to Improve Smoking Cessation in Neuropsychiatric and Depressed Patients

Project Summary: Smoking is more common in people with depression and other neuropsychiatric conditions than in the general population. It is believed that for these individuals, smoking is driven by a desire to self-medicate by stimulation of alpha7 type of nicotine receptor, which is decreased under stressful conditions and in neuropsychiatric populations. Varenicline, a drug developed to help people quit smoking, is a weak stimulator of the alpha7 beta2* receptors associated with addiction. It is believed to partially replace and suppress the rewarding effects of nicotine. However, our data show that varenicline also further decreases the function of alpha7 receptors. Reports of suicide and worsened depression in patients taking varenicline have led the FDA to issue a black box warning on the drug. We have shown that GTS-21, an approved drug for human studies, currently in clinical trials for schizophrenia, is a selective partial activator of alpha7 receptors. Our data indicates that GTS-21 should reverse the negative effects of varenicline on the alpha7 receptors of the brain, and propose that if GTS-21 were given as an adjunct therapy to varenicline, it would lessen depression and improve successful smoking cessation in a patient population at high risk for depression or other neuropsychiatric disorders. We will test this idea with humans at high risk for mental illness and conduct pre-clinical studies to validate and advance this approach.