LifeSciences SOUTH FLORIDA

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Tuesday
March 17, 2015
12:30 to 1:30 p.m.

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Discovery of Novel Nicotinic Acetylcholine Receptor Antagonists as Smoking Cessation Medications

featuring

Dr. Lawrence Toll
Director of Neuropharmacology,
Torrey Pines Institute for Molecular Studies

Meeting Room Link
https://connect.fiu.edu/lssfmarch2015/

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Smoking remains the number one avoidable cause of death in the United States and costs the economy tens of billions of dollars every year. Nicotine, the active ingredient in tobacco smoke responsible for the addiction, acts by binding to nicotinic acetylcholine receptors (nAChRs) in the brain, of which there are several subtypes. The nAChR most closely associated with the addictive nature of cigarettes is the alpha4beta2 nAChR. Activation of this receptor is considered to be the primary mediator of nicotine reward and the selective alpha4beta2 nAChR partial agonist varenicline (Chantix) is clinically used to treat addiction to cigarettes. Varenicline has been demonstrated to block nicotine self-administration in rodent models and in people. However, varenicline is only effective in less that one third of smokers who want to quit and it has been implicated in inducing suicidal tendencies in smokers trying to quit. In order to discover novel compounds as potential superior smoking cessation medications with fewer side effects, we screened the Torrey Pines Combinatorial Library collection and used standard medicinal chemistry to identify selective high affinity alpha4beta2 nAChR antagonists. Our newly discovered compounds, such as TPI-202, block both acquisition of nicotine self-administration in rats, as well as stress-induced relapse. Studies are now underway to improve the drug-like characteristics and further develop this class of compounds.