NIDA funds ATS research on Galanin

Advanced Targeting Systems (ATS) has just been awarded a $100,000 research grant from the National Institute on Drug Abuse (NIDA). This Phase I SBIR (Small Business Innovation Research) grant proposes to develop a research reagent to study the function of the neuropeptide, galanin. This will be an important tool for scientists to use in the study of galanin's influence in many biological systems: pain, depression, anxiety, memory and feeding.

Galanin is a 29/30 amino acid peptide and asserts its biological effect through G-protein-coupled receptors that are widely distributed. In the brain, I^{125}-galanin or galanin-analog binding studies show high levels of binding in the cerebral cortex, thalamus, pons, and cerebellum. Outside the brain, the anterior pituitary, pituitary tumors, astrocytes, spinal cord, and gastric and jejunal smooth muscle show ligand binding (1).

At the molecular level, multiple second messenger pathways are activated: inhibition of cyclic AMP, activation of channels including ATP-sensitive K+ channels, inhibition of L-type and N-type calcium channels, stimulation of inositol phospholipid turnover, stimulation and inhibition of calcium mobilization, stimulation of phospholipase A2, activation of MAP kinase, mitogenesis and stimulation of cyclic AMP accumulation (1).

This diversity of biochemical activities leads to a wide array of effects in biological systems. Galanin is reported to modulate feeding and sexual behavior, play a role in pain transmission, affect depression, and may be involved in the pathogenesis of Alzheimer's disease (2).

For the next six months, ATS will develop and test a galanin-saporin fusion protein to be offered commercially to research scientists worldwide. This targeted toxin will be a valuable research tool to study biological systems and for the study of drug abuse. The presence of galanin receptor-expressing cells in systems that control depression, pain and eating disorders, along with the connection between the opiate receptors, may indicate that galanin plays a role in drug abuse. The removal of these neurons, and their effects on neurons that express opiate receptors, will be a powerful tool to examine the role of galanin in drug use and abuse.

1. Williams RL; Hilton DJ; Pease S; Willson TA; Stewart CL; Gearing DP; Wagner EF; Metcalf D; Nicola NA; Gough NM. *Nature* 1988, 336, 684-687.
2. Kask K; Berthold M; Bartfai T. *Life Sci.* 1997, 60 (18), 1523-1533.

Dr. Douglas Lappi is Principal Investigator on the recently-funded SBIR Phase I grant from NIDA.

Upcoming Events

Society for Neuroscience
New Orleans, LA • November 4-9, 2000
Booth #438

Chronic Pain Therapeutic

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imaging of tissue samples from the study. Dr. Douglas Lappi (President and Senior Scientist at ATS) is Principal Investigator for this project and plans to begin synthesis of SP-SAP for use in these studies early in October.

The toxicology/safety studies will provide important information about the way SP-SAP may be used to treat intractable pain in humans. First, these experiments should tell us whether SP-SAP has toxic side effects. Second, they should give indications of how safe the drug will be at various doses. Finally, this will be the first time we will study the way the body reacts to the drug: how quickly it is absorbed, how it is broken down in the body, whether any of these breakdown products are toxic, and how quickly the drug and its breakdown products are eliminated from the body. If, after this intensive series of experiments, SP-SAP is determined to be safe to use in humans, ATS will initiate the first clinical trials.

The FDA has advised us that SP-SAP may best be developed as an orphan drug for treatment of pain in patients with terminal cancer. ATS will interact closely with the FDA during the drug development process and will publish updates in our quarterly newsletter and on our website at ATSbio.com.