Targeting Topics: Recent Scientific References

(continued from page 3)

Basal forebrain neurons suppress amygdala kindling via cortical but not hippocampal cholinergic projections in rat.

Ferencz I, Leanza G, Nasnobashvili A, Kokaia M, Lindvall O.
Eur J Neurosci 12(6):2107-2116, 2000.

Cholinergic mechanisms have been implicated in human epilepsy, possibly in the role of seizure suppression. Ferencz *et al.* used 2.5 µg 192-Saporin (Catalog #IT-01) by i.c.v. injection to investigate the effect of eliminating cholinergic projections to the hippocampal formation and cerebral cortex on the induction of epilepsy through electrical stimulation of the rat brain. The researchers used the specificity of 192-Saporin to determine that the loss of specific projections to the amygdala accelerates development of seizures. The hippocampus does not influence this process.

Repeated immunolesions display diminished stress response signal.

Gu Z, Yu J, Werrbach-Perez K, Perez-Polo JR.
Int J Dev Neurosci 18(2-3):177-183, 2000.

Cholinergic neurons in the basal forebrain are involved in neurotrophin release in general injury response although this response is impaired in the aged individual. Addition of pharmacological doses of NGF can repair this mechanism. Gu *et al.* used 192-Saporin (Catalog #IT-01) to model the endogenous stimulation of NGF in response to injury. They found that a one-time administration of 192-Saporin was more effective than chronic repeated administrations for inducing an increase in NGF levels. These results indicate that chronic lesions may cause a desensitization that differs from the acute toxic model.

Cholinergic excitation of septohippocampal GABA but not cholinergic neurons: implications for learning and memory.

Wu M, Shanabrough M, Leranth C, Alreja M.
J Neurosci 20(10):3900-3908, 2000.

It has long been assumed that the drug-induced enhancement of learning and memory in both young and aged rats was accomplished through a cholinergic pathway in the hippocampus. Wu *et al.* used a fluorescent labeling molecule, 192-IgG conjugated to Cy3 (Custom Service from ATS) to visualize these neurons. They found that the effects of cognition-enhancing drugs are not facilitated through action on cholinergic neurons. Instead, activation of GABA neurons is implicated in this model.

Attenuation of the bidirectional effects of chlordiazepoxide and FG 7142 on conditioned response suppression and associated cardiovascular reactivity by loss of cortical cholinergic inputs.

Stowell JR, Berntson GG, Sarter M.
Psychopharmacol 150(2):141-149, 2000.

The benzodiazepine receptor (BR) is involved in anxiety. It has been hypothesized that cholinergic projections from the CBF are necessary for modulation of the BR by agonists and inverse agonists. Stowell *et al.* directly injected 0.18 µg 192-Saporin (Cat #IT-01) into each hemisphere of the CBF in adult rats. The treated rats had altered responses to external stimuli during an operant conditioned task. These results indicate that the CBF plays an important role in response to fear and anxiety-related stimuli. This system may also mediate the actions of BR ligands.

Intracerebroventricular infusion of CHO5, a rat monoclonal antibody directed against mouse low-affinity nerve growth factor receptor (p75NTR), specifically labels basal forebrain cholinergic neurons in mouse brain.

Rossner, S, Schliebs, R, Bigl, V.
Metab Brain Dis 15(1):17-27, 2000.

192-Saporin (Catalog #IT-01) has long been a useful tool for neurobiological research in the rat. For various reasons, many researchers want to perform the same studies in the mouse but have been prevented from doing so by the lack of a suitable antibody against the mouse p75NTR. Rossner *et al.* describe a rat monoclonal antibody against the mouse p75NTR (Catalog #AB-N02) that demonstrates co-localization of p75NTR and ChAT, and also co-localization of p75NTR and TrkA in the mouse basal forebrain. Internalization and retrograde transport of this antibody in cholinergic basal forebrain neurons is also shown. This evidence indicates that the anti-mouse p75NTR will be effective for use as an immunotoxin.

(NOTE: ATS plans release of the mouse-specific p75 immunotoxin in early November -- see new product release notes on page 7 of this newsletter.)

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