Targeting Topics: Recent Scientific References

Summarized by Matthew Kohls

Selective Destruction of Medial Septal Cholinergic Neurons Attenuates Pyramidal Cell Suppression, but not Excitation in Dorsal Hippocampus Field CA1 Induced by Subcutaneous Injection of Formalin

Zheng F and Khanna S
Neurosci 103(4):985-998, 2001.

Previously, the authors have shown that an injection of formalin in the hindpaw of rats will excite a select population of CA1 pyramidal cells within a larger suppressed population. This response is accompanied by increased theta activation. The authors selectively eliminated medial septal cholinergic neurons using 192-Saporin (0.4 µl; Cat. # IT-01) to investigate the role of these neurons in response to a persistent noxious stimulus such as a formalin injection. The data indicate a CA1 network modulated by cholinergic neurons in the medial septal region may influence pyramidal cell theta and pyramidal cell suppression.

Sequential Upregulation of Cell Adhesion Molecules in Degenerating Rat Basal Forebrain Cholinergic Neurons and in Phagocytotic Microglial Cells

Hartlage-Rübsamen M, Schliebs R
Brain Res 897(1-2):20-26, 2001.

Neurodegeneration, found in brain disorders such as Alzheimer's, Parkinson's, and Huntington's diseases, is marked by a significant microglial response. This microglial activation is characterized by increased migratory activity and potential cytotoxic action on injured neurons. The interaction of microglial cells with degenerating axons and neural somata is known to be mediated by expression of cell adhesion molecules. The authors use a single intracerebroventricular injection of 192-Saporin (4 µg; Cat. # IT-01) to initiate neurodegeneration of choline acetyltransferase-immunoreactive neurons and follow the expression of two cell adhesion molecules, ICAM-1 and LFA-1, using immunohisto-chemistry. The results indicate that these adhesion molecules may function as intercellular recognition signals through which degenerating cholinergic neurons actively participate in their own targeting and removal by microglia.

Immunotoxic Destruction of Distinct Catecholamine Subgroups Produces Selective Impairment of Glucoregulatory Responses and Neuronal Activation

Ritter S, Bugarith K, Dinh TT
J Comp Neurol 432(2):197-216, 2001.

Control of regulatory responses to low glucose levels in the brain have been linked to catecholaminergic neurons. Studies of these neurons have been hindered by the lack of a selective and precise lesioning agent. Ritter *et al.* use anti-DBH-SAP (Cat. # IT-03) to create very precise lesions of catecholamine neurons in the paraventricular nucleus of the hypothalamus and spinal cord. Injection of anti-DBH-SAP into the spinal cord eliminates cells with caudal projections while injection into the paraventricular nucleus of the hypothalamus eliminated cells with rostral projections. This ability to selectively eliminate very specific subpopulations of cells is a valuable characteristic in dissecting neuronal function.

p75-Expressing Elements are Necessary for Anti-Allodynic Effects of Spinal Clonidine and Neostigmine

Paqueron X, Li X, Eisenach JC
Neurosci 102(3):681-686, 2001.

It has been suggested that α2-adrenergic agonists produce analgesia by activating spinal cholinergic neurons. The authors reason that since spinal cholinergic neurons in the ventral horn express p75 following peripheral nerve trauma, cholinergic dorsal horn neurons might also. Instead, they find that dorsal horn neurons express little or no p75 under normal conditions or following spinal nerve ligation. Since dorsal horn neurons do not express p75 they are not eliminated by 192-Saporin (0.1-0.6 µg; Cat. # IT-01), but the data indicate that p75-expressing elements do play a role in pain transmission in the dorsal horn. The authors note that when afferents that express p75 are eliminated, mechanical hypersensitivity is unaffected, but the reduction of hypersensitivity by α2-adrenergic agonists or cholinergic agents is blocked.

Neuropeptide-Toxin Conjugates in Pain Research and Treatment (Review)

Wiley RG
Reg Anesth Pain Med 25(5):546-548, 2000.

Several lines of evidence indicate dorsal horn neurons that respond to substance P (SP) play a role in nociception. Wiley discusses the attributes of SP-SAP (Cat. # IT-07), a targeted toxin that eliminates cells expressing the neurokinin-1 receptor. Animals treated with this material using a lumbar intrathecal injection show a decrease in both hyperalgesia and allodynia in several pain models. The success of SP-SAP indicates that other neuropeptides, hormones, and growth factors would be useful as targeted toxins.

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