

# Targeting Trends

Reporting the latest news in Molecular Surgery

## Inducing Central Sensitization with a Substance P/ Cholera Toxin Conjugate

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A substantial amount of work with Advanced Targeting Systems' substance P/saporin conjugate (SP-SAP) has demonstrated that neurokinin-1 (NK1) receptor-expressing neurons in the spinal cord and brain stem are necessary for the full expression of central sensitization following a peripheral injury [1-7]. Eliminating these neurons with SP-SAP suppresses the hyperalgesia (an enhanced sensation of pain) and allodynia (pain to normally non-painful stimuli) associated with the injury, yet, amazingly, leaves normal pain sensation intact. These findings indicate that the NK1 receptor marks an important set of pain processing neurons in the central nervous system and that

alterations in their function lead to an enhancement of the pain sensations experienced by an individual.

Studies on the molecular properties of central neurons during chronic pain conditions suggest that activation of several kinases through either enhanced calcium entry into the cells, enhanced internal calcium release or through the stimulation of cAMP production leads to the sensitization of these neurons [8-22]. These studies provide valuable information on the function of the NK1 receptor-expressing neurons, but they require an injury to produce the sensitization, which involves the activation of a large number of

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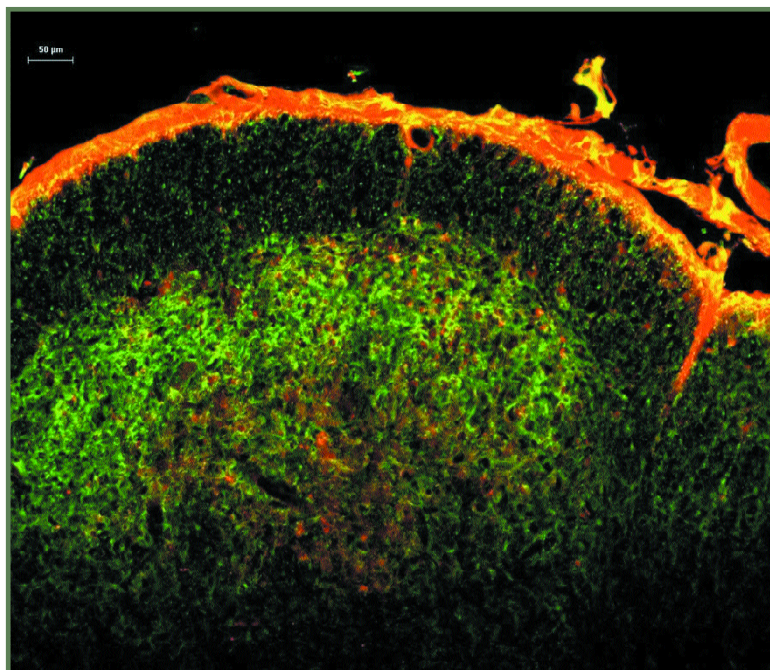
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Denise Higgins, Editor



**Figure 1.** Immunohistochemical localization of SP-CTA uptake in the dorsal horn of the cervical spinal cord. SP-CTA (10  $\mu$ g) was injected intracisternally into rats via a percutaneous puncture under isoflurane anesthesia. One hour later the animals were euthanized and sections (20  $\mu$ ) of the brain stem and cervical spinal cord were prepared for immunohistochemistry. Immunofluorescence co-labeling for the NK1 receptor (Green) and for the A subunit of cholera toxin (Red) was performed. The cholera toxin subunit was found only in neurons co-labeled with NK1 receptor. Note that at this time point a significant amount of the cholera toxin subunit is still on the surface of the cord.