

Targeting Trends

Reporting the latest news in Molecular Surgery

Safety and Efficacy of Substance P-SAP

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Substance P-saporin (SP-SAP, Cat. #IT-07) is a targeted neurotoxin that selectively lesions cells containing the Neurokinin-1 (NK-1) receptor. Previous studies in rodents have shown that a single intrathecal injection can prevent formation of chemically induced thermal hyperalgesia and reverse mechanical allodynia caused by nerve injury without altering normal thermal or tactile function. While these results were very promising, it was unclear if SP-SAP would be effective in larger species given the distance the molecule would need to radially diffuse to its site of action, the spinal dorsal horn. With support provided by the National Institutes of Health a series of studies were performed in beagle dogs, a standard large animal model for intrathecal safety. The primary endpoint of this study was designed to determine intrathecal dosing levels in dogs. Secondary endpoints were to characterize the distribution of SP-SAP in the spinal space and to examine effects of an inadvertent intravenous delivery.

Purpose-bred laboratory beagles were surgically implanted with an intrathecal catheter that terminated in the upper lumbar space. All animal studies were conducted in the laboratory of Dr. Tony Yaksh, Dept of Anesthesiology, University of California, San Diego. Animals were allowed to recover for approximately 3 days at which time they received a single 0.3 ml intrathecal bolus of SP-SAP. Control animals received either phosphate-buffered saline (PBS) or non-targeted recombinant saporin (SAP). Dogs were dosed with 1.5, 15, 45 or 150 μg SP-SAP while dogs in the control groups received 0.3 ml of PBS or 150 μg SAP. Dogs were fully conscious during dosing and behavior was assessed for at least 8 hours immediately following dosing and twice daily thereafter. Catheters were removed about 3 days after dosing to prevent any effects induced by long-term presence of the catheter.

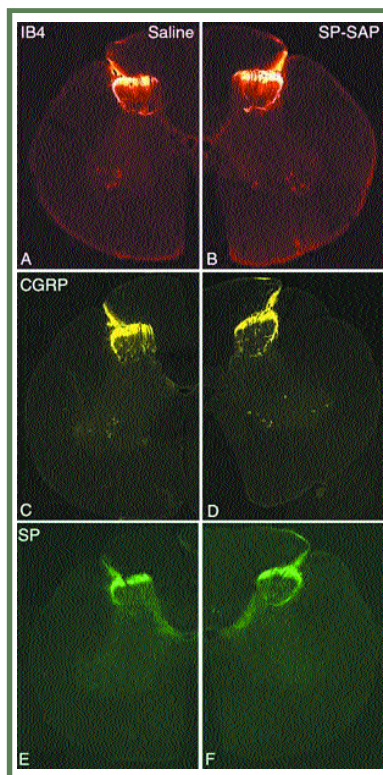


Figure 1.

Staining of coronal spinal cord sections for IB4 (top panel), CGRP (middle panel) and SP (bottom panel). Left panel dog was treated with PBS; right panel dog was treated with SP-SAP.

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Denise Higgins, Editor

ADVANCED TARGETING SYSTEMS

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