

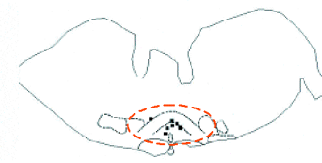
[Tyr²-SO₃]CCK-8, Retains High Affinity for CCK₂ Receptors

(continued from page 1)

injections, rats were evaluated again for their sensory thresholds to both innocuous and noxious stimuli in the hind paw. Coronal sections of the brain stem containing the RVM were processed for the detection of CCK₂ receptor-expressing cells by *in situ* hybridization using a digoxigenin labeled riboprobe for CCK₂. CCK-8(SO₃)-SAP pretreatment did not alter the tactile or thermal sensory thresholds in rats when compared to naïve, CCK-8(SO₃) or saporin pretreated rats. However, CCK-8(SO₃)-SAP pretreatment, but not CCK-8(SO₃) or saporin pretreatment, resulted in a significant reduction in the number of cells expressing CCK₂ transcripts in the RVM (Figure 2). This reduction in the number of CCK₂ immunoreactive cells was seen in serial sections taken throughout the ~1 mm rostral-caudal extent of the RVM, representing a >80% reduction in the total number of labeled cells (*p*<0.05). There was no evidence of necrosis or significant cell loss in the RVM and surrounding regions of the brain stem. These data suggest that the targeted microinjection of a low dose of CCK-8(SO₃)-SAP can significantly reduce the population of RVM cells that express CCK₂ receptors.



SAP Pretreated



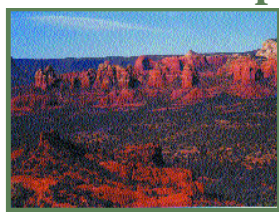
CCK-SAP Pretreated

Figure 2. Map of cells that are immunoreactive for CCK₂ receptor mRNA on representative coronal sections (20 μ m) of the RVM and its adjacent regions of the medulla from rats that have been pretreated with saporin (control, left) or CCK-8(SO₃)-SAP (right). CCK₂ receptor mRNA were detected by *in situ* hybridization using a digoxigenin labeled riboprobe for CCK₂. The riboprobe was detected by an anti-digoxigenin Fab (Roche Diagnostics, Indianapolis, IN) conjugated with alkaline phosphatase. The immunoreactivity was detected chromogenically using fast red as substrate. Computer-assisted mapping was carried out using Neurolucida software (Microbrightfield Inc., Baltimore, MD). Each black dot marks the location of a single cell that was labeled for CCK₂. In the left panel, CCK₂ immunoreactive cells are localized to the RVM (approximately denoted with dashed red line) and the nucleus gigantocellularis dorsal to the RVM. In the right panel, 28 days after CCK-8(SO₃)-SAP treatment, few CCK₂ immunoreactive cells are detected.

Acknowledgments

The authors thank Dr. Alan Kopin for the generous gift of the cDNAs for hCCK₁ and hCCK₂ and Dr. Richard Agnes for the synthesis of CCK-8(SO₃).

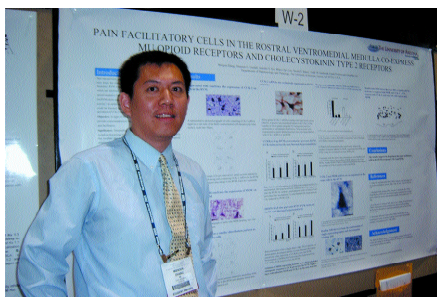
17th Annual Spring Brain Conference: March 15-18, 2006 - Sedona, Arizona



The Spring Brain Conference (SBC) brings together top neuroscientists with varied backgrounds, interests and approaches to promote the development of new strategies to investigate and stimulate the development of new therapeutic approaches to disorders of the CNS. The conference will consist of a general poster session along with 8-10 plenary sessions each organized around a central theme or topic. For additional information contact Dr. Bob Yezierski (ryezierski@dental.ufl.edu) or visit the SBC website: www.springbrain.org.

2005 Society for Neuroscience Poster Award Winner:

"PAIN FACILITATORY CELLS IN THE ROSTRAL VENTROMEDIAL MEDULLA COEXPRESS OPIOID- μ RECEPTORS AND CHOLECYSTOKININ TYPE 2 RECEPTORS" W. Zhang; S.E. Gardell; Y. Xie; M. Luo; N.E. Rance; T.W. Vanderah; F. Porreca; J. Lai, Univ. Arizona.



Wenjun Zhang at his winning poster at the SfN meeting in Washington DC.

Each year, ATS is pleased to see the interesting ways in which scientists use our products and present their data in abstracts, posters, and presentations. This year we were excited to see the excellent work by Wenjun Zhang and his colleagues at the University of Arizona that was presented in this year's Poster of the Year at the Society for Neuroscience meeting in Washington, Nov 12-16, 2005. Of course we were doubly pleased by the use of both dermorphin-SAP and CCK-SAP (the latter the subject of the cover article in this newsletter), but that was a small part of the nice science that was

presented. The use of these reagents to demonstrate the characteristics of "ON cells" was quite original and clever. Congratulations to them!



Doug Lappi presents the awards for best poster -- a copy of the book, "Molecular Neurosurgery With Targeted Toxins," an ATS mug, an ATS ball cap, \$500 in product credit, and the opportunity to publish a cover article in *Targeting Trends*. Dr. Josephine Lai accepted the prizes on behalf of Dr. Zhang.