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Targeting Trends

Reporting the latest news in Molecular Surgery

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Denise Higgins, Editor

ADVANCED TARGETING SYSTEMS

HCRT-SAP Lesion Produces Sleepiness While anti-DBH-SAP Lesion Does Not

Carlos Blanco-Centurion contributes this report resulting from work done for an abstract at the 2001 Society for Neuroscience meeting: ***Hypocretin B-Saporin Lesions of the Brainstem Increase REM Sleep at Night*** *CA Blanco-Centurion, RJ Salin-Pascual, D Gerashchenko, MA Greco, PJ Shiromani. Harvard Medical School & UNAM, Mexico City.* This abstract won the ATS Abstract Award. Note: HCRT-SAP is also known as orexin-SAP.

Loss of hypocretin (HCRT, orexin) neurons has been linked to narcolepsy.[1] These neurons project widely throughout the brain,[2] but it is not known which projection to which target site produces what symptom of narcolepsy. Recently we showed that HCRT receptors are present in brainstem areas implicated in REM sleep.[3] Since abnormal triggering of REM sleep characterizes narcolepsy, we have used HCRT-SAP, a targeted toxin that selectively lesions HCRT-2 receptor-bearing cells, to assess the effect on sleep. We also used anti-DBH-SAP to destroy specifically noradrenergic neurons of the locus coeruleus (NA-LC), which are the major brainstem output of HCRT neurons. We knew that hypocretin neurons project to the pons but the goal of this study was to determine which pontine neurons regulate sleep.

Methodology. Rats were implanted with electrodes for polysomnographic recordings. At the same time rats received either a bilateral single microinjection of pyrogen-free

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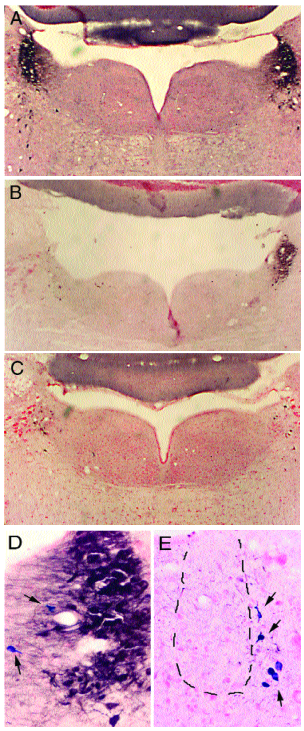

Figure 1. Panel A=saline, B=unilateral lesion with HCRT-SAP, C=bilateral lesions with HCRT-SAP. D and E are magnifications showing the effect of saline and anti-DBH-SAPmicroinjections respectively. Arrows indicate NADPH+ cells (cholinergic).

SP-SAP licensed to Cell Targeting Technologies

Advanced Targeting Systems has exclusively licensed the Substance P-Saporin (SP-SAP) compound to Cell Targeting Technologies for development as a pharmaceutical agent. ATS and collaborators at University of Minnesota and University of California, San Diego have completed several preclinical studies using SP-SAP and have thus far found it safe and effective in two animal models. The journal *Science* reported the results of studies in a rat chronic pain model showing that SP-SAP appears to eliminate chronic pain permanently while not interfering with the perception of normal, acute pain sensations. Cell Targeting Technologies will raise capital to fund in-depth toxicology studies and plans to bring SP-SAP to clinical trial within the next two years.