Targeting Talk: Product Q&A

Q: Hello, I have used your Anti-DBH-SAP (Cat. #IT-03) conjugate, and I'm having a hard time finding this citation: R.G. Wiley, D.A. Lappi. Suicide Transport and Immunolesioning. Molecular Biology Intelligence Unit, R.G. Landes Co, Austin, TX (1994). Do you know where I could find a copy?

A: This book is available in many university libraries and can also be purchased here: http://www.amazon.com/Suicide-Transport-Immunolesioning-Molecular-Intelligence/dp/1570590958

Q: I'm trying to find out if enough Anti-DBH-SAP will be retrogradely transported and taken up by non targeted sympathetic neurons by bulk fluid-phase endocytosis. Does saporin become degraded after it kills the neuron or does it enter the extracellular matrix?

A: It is very unlikely that a targeted toxin such as Anti-DBH-SAP is freed from the targeted neuron in a meaningful condition. There has never been a reported identification of a targeted toxin, functionally or not, after it has eliminated its targeted neuron. Current evidence indicates that effective suicide transport agents undergo endocytosis at nerve terminals followed by retrograde axonal transport of the endocytic vesicles containing the toxin. Experiments using vincristine have shown that the retrograde axonal transport of suicide transport toxins utilizes the fast transport system (microtubules). However, it is not known what determines whether or not a specific toxin-ligand undergoes axonal transport after internalization.

Empirically, it has been observed that immunotoxins (OX7-SAP [Cat. #IT-02], 192-IgG-SAP [Cat. #IT-01], Anti-DBH-SAP) and lectin-toxins (ricin, volkensin, IB4-SAP) all undergo retrograde axonal transport and are therefore effective suicide transport agents. This is not true, however, for neuropeptide-toxin conjugates, such as dermorphin-SAP. For example, in an unpublished study, we injected large doses (1-2 µg) of Dermorphin-SAP (Cat. #IT-12) into the lumbar intrathecal space of rats. After 2-3 days, rats were sacrificed and lumbar dorsal root ganglia examined for evidence of toxin effect (striking chromatolysis). None was found after examining numerous ganglia and >15,000 primary afferent neurons. Apparently, dermorphin-SAP is not retrogradely transported even if it is taken into the primary afferent terminals that express the mu opioid receptor (MOR).

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animals displayed more frequent face-rubbing responses on the administration of formalin, indicating that IB4-binding neurons in the trigeminal nerve play an anti-nociceptive role in response to this type of pain.

Hippocampal acetylcholine depletion has no effect on anxiety, spatial novelty preference, or differential reward for low rates of responding (DRL) performance in rats.

McHugh SB, Francis A, McAuley JD, Stewart AL, Baxter MG, Bannerman DM.
Behav Neurosci 129(4):491-501, 2015.

It is unclear whether cholinergic lesions in the hippocampus affect both learning and behavior, or learning only. In this study the authors lesioned cholinergic neurons in the medial septum/vertical limb of the diagonal band of Broca of rats with bilateral 30-ng injections of 192-IgG-SAP (Cat. #IT-01). Although hippocampal cholinergic innervations were significantly reduced, with a concomitant reduction in choline acetyltransferase activity, the lesioned animals did not perform differently in several behavioral tests. The data do not provide evidence that the septo-hippocampal cholingeric projections play a role in anxiety, spatial novelty preference, or differential reward for low rates of responding tests.

Selective C1 Lesioning Slightly Decreases Angiotensin II Type I Receptor Expression in the Rat Rostral Ventrolateral Medulla (RVLM).

Bourassa EA, Stedenfeld KA, Sved AF, Speth RC.
Neurochem Res Epub2015.

Exogenous angiotensin II administered to the RVLM produces a significant pressor response that can be countered by angiotensin II type I receptor antagonists. In this work the authors examined the relative contribution of C1 and non-C1 neurons in the RVLM to this angiotensin II response. Rats received 10 or 15 ng of Anti-DBH-SAP (Cat. #IT-03) as unilateral injections into the RVLM. Mouse IgG-SAP (Cat. #IT-18) was used as control. The data indicate that the majority of angiotensin II type 1 receptors are expressed on non-C1 neurons or glia.

Pain from intra-articular NGF or joint injury in the rat requires contributions from peptidergic joint afferents.

Kras JV, Weisshaar CL, Pall PS, Winkelstein BA.
Neurosci Lett 604:193-198, 2015.

Both peptidergic and non-peptidergic neurons innervate the facet joint, which is the source of pain in a majority of neck trauma. In this work the authors examined these subpopulations of neurons to determine the contribution of each in facet joint pain. 100 ng of SSP-SAP (Cat. #IT-11) was injected into bilateral C6/C7 facet joints of rats. Alternatively, rats received 5 µg of rIB4-SAP (Cat. #IT-10) via the same method. Saporin (Cat. #PR-01) was used as control. SSP-SAP, but not rIB4-SAP was able to prevent NGF-induced mechanical and thermal hypersensitivity. SSP-SAP administration also prevented behavioral hypersensitivity and NGF upregulation in the dorsal root ganglion after facet joint distraction. The data indicate that interference with peptidergic signaling within the facet joint may be a treatment for pain originating in that location.