Targeting Topics: Recent Scientific References

Reviewed by Matthew Kohls

The rate of fall of blood glucose determines the necessity of forebrain-projecting catecholaminergic neurons for male rat sympathoadrenal responses.

Jokiaho AJ, Donovan CM, Watts AG.
Diabetes 63(8):2854-2865, 2014.

Different sets of glucosensors detect insulin-induced hypoglycemia depending on the onset rate. This detection controls the activation of sympathoadrenal counterregulatory responses (CRRs). Slow onset hypoglycemia, common with insulin therapy, is detected by glucosensors in the portal-mesenteric veins. Fast onset is detected by brain elements. The authors lesioned hindbrain catecholaminergic neurons to determine which set of responses-they interact with. Rats received 42 ng bilateral injections of Anti-DBH-SAP (Cat. #IT-03) into the paraventricular nucleus of the hypothalamus. Mouse IgG-SAP (Cat. #IT-18) was used as a control. The data indicate that these neurons are critical for detection of slow-onset insulin-induced hypoglycemia.

Intratumoral anti-HuD immunotoxin therapy for small cell lung cancer and neuroblastoma.

Ehrlich D, Wang B, Lu W, Dowling P, Yuan R.
J Hematol Oncol 7(1):91, 2014.

HuD protein is a 40-kDa neuronal RNA-binding protein that is expressed in 100% of small cell lung cancer (SCLC) tumor cells. An anti-HuD monoclonal was biotinylated and combined with Streptavidin-ZAP (Cat. #IT-27); this conjugate was tested both *in vitro* and *in vivo*. Anti-HuD-SAP eliminated NCI-H69 and Neuro-2a cells at an EC_{50} of <0.5 µg/ml. 1 mg/kg of the conjugate injected directly into subcutaneous tumors generated in mice resulted in a temporary lack of tumor growth or regression of the tumor.

Respiratory function after selective respiratory motor neuron death from intrapleural CTB-saporin injections.

Nichols NL, Vinit S, Bauernschmidt L, Mitchell GS.
Exp Neurol Epub2014.

Amyotrophic lateral sclerosis (ALS) ultimately causes death from ventilator failure. Genetic models of ALS suffer from high variability of the rate, timing, and extent of respiratory motor neuron death. The authors created a novel model of induced respiratory motor neuron death using CTB-SAP (Cat. #IT-14). Rats received 25 µg or 50 µg intrapleural injections of CTB-SAP; Saporin (Cat. #PR-01) was used as a control. After 7 days, motor neuron survival approximated what is seen in end-stage ALS rats, while there was minimal cell death in other brainstem or spinal cord regions. CTB-SAP also caused microglial activation, decreased breathing during chemoreceptor stimulation, and diminished phrenic motor output in anesthetized rats – all hallmarks of ALS.

Hypocretin/orexin antagonism enhances sleep-related adenosine and GABA neurotransmission in rat basal forebrain.

Vazquez-DeRose J, Schwartz MD, Nguyen AT, Warrier DR, Gulati S, Mathew TK, Neylan TC, Kilduff TS.
Brain Struct Funct Epub2014.

The basal forebrain (BF) is one of the regions receiving excitatory input from orexin neurons. The authors investigated the hypothesis that orexin antagonists induce sleep at least in part by interfering with the facilitation of BF neurons. Rats received bilateral 500-ng injections of 192-IgG-SAP (Cat. #IT-01) into the BF. Lesioned animals displayed no abnormal responses to a benzodiazepine agonist or vehicle. An orexin antagonist, however, was less effective than the control at inducing sleep in lesioned rats.

Increasing inflationary T-cell responses following transient depletion of MCMV-specific memory T cells.

Sims S, Klenerman P.
Eur J Immunol Epub2014.

The standard CD8+ T-cell response to infection is a rapid proliferation followed by a reduction in number after the infection is cleared. Murine cytomegalovirus is an exception in that an infection generates a life-long latency with low-level sporadic replication. Immunodominant cells accumulate over time and stabilize at a high frequency. The authors examined a paradoxical boost following depletion of these cells with an M38 antibody attached to Streptavidin-ZAP (Cat. #IT-27). Mice were treated with 44 pM intraperitoneal injections. M38 is an epitope present on the effector CD8+ T cells. Following a significant depletion of cells, the population rebounded and reached a higher percentage of total CD8+ T-cells than before the depletion.

A combination of targeted toxin technology and the piggyBac-mediated gene transfer system enables efficient isolation of stable transfectants in nonhuman mammalian cells.

Sato M, Inada E, Saitoh I, Matsumoto Y, Ohtsuka M, Miura H, Nakamura S, Sakurai T, Watanabe S.
Biotechnol J Epub2014.

In this work the authors developed a new transfection strategy that takes advantage of the fact that many cell lines endogenously express α-1,3-galactosyltransferase (α-Gal), the target of rIB4-SAP (Cat. #IT-10). After transfection low expressing or non-transfected cells are killed by an application of rIB4-SAP at 80 µg/ml for 2 hours. The surviving cells eventually express α-Gal again, and require no selective agent to maintain expression of the gene of interest. These transfected cells can be transfected again using the same method.

Cholinergic neurons of the basal forebrain mediate biochemical and electrophysiological mechanisms underlying sleep homeostasis.

Kalinchuk AV, Porkka-Heiskanen T, McCarley RW, Basheer R.
Eur J Neurosci Epub2014.

Previous work has indicated that non-rapid eye movement during recovery sleep after sleep deprivation requires cholinergic neurons in the BF. The authors examined how BF cholinergic neurons affect the levels of HSP markers during sleep deprivation. Rats received 230-ng injections of 192-IgG-SAP (Cat. #IT-01) into the horizontal limb of the diagonal band/substantia innominata/

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