Targeting Topics: Recent Scientific References

Reviewed by Matthew Kohls

Cortically projecting basal forebrain parvalbumin neurons regulate cortical gamma band oscillations.

Kim T, Thankachan S, McKenna JT, McNally JM, Yang C, Choi JH, Chen L, Kocsis B, Deisseroth K, Strecker RE, Basheer R, Brown RE, McCarley RW.

Proc Natl Acad Sci U S A Epub2015.

Measurements of cortical EEG capture gamma band oscillations (GBO). Abnormalities in these GBO have been found in some neuropsychiatric disorders such as Alzheimer's disease and schizophrenia. The authors analyzed GBO neuronal groups by administering 650-ng bilateral icv injections of mu p75-SAP (Cat. #IT-16) to mice to determine the role of basal forebrain cholinergic neurons in the generation of GBO. The results indicate GABAergic basal forebrain neurons containing parvalbumin were important for GBO integrity, but cholinergic neurons in the basal forebrain were not involved.

alphaCGRP is essential for algesic exocytotic mobilization of TRPV1 channels in peptidergic nociceptors.

Devesa I, Ferrandiz-Huertas C, Mathivanan S, Wolf C, Lujan R, Changeux JP, Ferrer-Montiel A.

Proc Natl Acad Sci U S A 111(51):18345-18350, 2014.

The sensitization of transient receptor potential vanilloid 1 (TRPV1) can lead to the development and maintenance of chronic pathological pain conditions. In this work the authors determined that TRPV1 receptors use membrane insertion mechanisms in order to potentiate neuronal excitability. In order to specifically link this activity to peptidergic neurons the authors treated rat primary dorsal root ganglion cultures with 10 mM rIB4-SAP (Cat. #IT-10) to deplete the non-peptidergic neurons.

Monoclonal Antibodies Targeting LecLex-Related Glycans with Potent Anti-Tumor Activity.

Jia CX, Vankemmelbeke M, McIntosh RS, Clarke PA, Moss R, Parsons T, Spendlove I, Zaitoun AM, Madhusudan S, Durrant LG.

Clin Cancer Res 2015.

In this work the authors characterized two monoclonal antibodies that target glycans containing Lewis carbohydrate antigens. One of the methods used was to combine varying concentrations of the antibodies with 50 ng mouse Fab-ZAP (Cat. #IT-48) and apply the conjugates to cells for 72 hours. The antibodies were demonstrated to have efficient internalization, supported by potent *in vivo* anti-tumor activity.

Light-controlled endosomal escape of the novel CD133-targeting immunotoxin AC133-saporin by photochemical internalization - A minimally invasive cancer stem cell-targeting strategy.

Bostad M, Olsen CE, Peng Q, Berg K, Hogset A, Selbo PK.

J Control Release 206(28):37–48, 2015.

Previously the authors demonstrated the use of photochemical internalization of a custom conjugate consisting of a CD133 antibody coupled to saporin (ATS Custom conjugation). Several cancer cell lines were plated, and incubated in the presence of a photosensitizer with either CD133-SAP at 8.6 pM or Saporin (Cat. #PR-01) at 24 pM. The different concentrations equalized the number of saporin molecules in each sample. A light source was used to initiate the internalization of the molecules. The results indicate that this is a viable strategy for the targeted treatment of cancer stem cells.

High-content analysis of antibody phage-display library selection outputs identifies tumor selective macropinocytosis-dependent rapidly internalizing antibodies.

Ha KD, Bidlingmaier SM, Zhang Y, Su Y, Liu B.

Mol Cell Proteomics 13(12):3320-3331, 2014.

Macropinocytosis, the internalization of large endocytic vesicles called macropinosomes, is upregulated in Ras-transformed cancers. To date, large-scale antibody generation strategies have not incorporated a selection method for antibodies. In this work the authors demonstrate screening and validation of the antibodies that utilize the macropinosome pathway. One method used was to biotinylate the antibodies and combine them with Streptavidin-ZAP (Cat. #IT-27) at a 1:1 ratio. The conjugate was applied to cells in a concentration curve starting at 200 nM in order to demonstrate internalization and cell killing.

T-box transcription regulator Tbr2 is essential for the formation and maintenance of Opn4/melanopsin-expressing intrinsically photosensitive retinal ganglion cells.

Mao CA, Li H, Zhang Z, Kiyama T, Panda S, Hattar S, Ribelayga CP, Mills SL, Wang SW.

J Neurosci 34(39):13083-13095, 2014.

Opsin 4/melanopsin-expressing intrinsically photosensitive retinal ganglion cells (ipRGCs) are responsible for controlling non-image-forming visual functions in the retina. The findings show that opsin 4 is only expressed in Tbr2-positive ipRGCs, no ipRGCs are found if Tbr2 is deleted before RGC specialization, and most ipRGCs are eliminated when Tbr2 is deleted from established ipRGCs. An antibody against melanopsin (Cat. #AB-N39) was used at a 1:1000 dilution for immunohistochemical analyses.

TrkA in vivo function is negatively regulated by ubiquitination.

Kiris E, Wang T, Yanpallewar S, Dorsey SG, Becker J, Bavari S, Palko ME, Coppola V, Tessarollo L.

J Neurosci 34(11):4090-4098, 2014.

The high affinity nerve growth factor receptor, trkA, plays an intrinsic role in the regulation of various aspects of the mammalian nervous system. The post-translational attachment of ubiquitin to trkA plays a role in the final disposition and function of many proteins; in this work the authors investigate the result of trkA ubiquitination. By removing a 3 amino acid sequence from the receptor the ubiquitination of TrkA was reduced which resulted in an increase in TrkA protein levels and activity. In mice containing this mutation, the rise in TrkA activity was accompanied by enhanced thermal sensitivity and inflammatory pain. Anti-trkA (Cat. #AB-N03) was used at a concentration of 1:500 in immunohistochemistry.

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