Targeting Topics: Recent Scientific References

Reviewed by Matthew Kohls

Alterations in the rostral ventromedial medulla after the selective ablation of mu-opioid receptor expressing neurons.

Harasawa I, Johansen JP, Fields HL, Porreca F, Meng ID.

Pain Epub2015.

The rostral ventromedial medulla (RVM) has both excitatory and inhibitory control over nociceptive neurons in the medullary dorsal horn and spinal cord. Previous work has demonstrated that elimination of mu-opioid receptor-expressing neurons in the RVM reduces stress and injury-induced behavioral hypersensitivity, but the effect of losing these cells on the descending inhibitory system has not been examined. The authors administered 1.2 pmol of Dermorphin-SAP (Cat. #IT-12) to each side of the RVM of rats. Saporin (Cat. #PR-01) was used as a control. Characterization of RVM neurons in lesioned animals showed a reduction in on- and off-cells, but no change in the number of neutral cells. These data indicate that mu-opioid receptor-expressing cells in the RVM are not needed for analgesia produced by activation of RVM neurons.

CD103+ Dendritic Cells Elicit CD8+ T Cell Responses to Accelerate Kidney Injury in Adriamycin Nephropathy.

Cao Q, Lu J, Li Q, Wang C, Wang XM, Lee VW, Wang C, Nguyen H, Zheng G, Zhao Y, Alexander SI, Wang Y, Harris DC.

J Am Soc Nephrol Epub2015.

Although it is known that dendritic cells (DCs) are involved in chronic kidney disease, it is not well understood how they either resolve or aggravate the condition. CD103+ dendritic cells in particular, are known to maintain tolerance through interaction with regulatory T cells, as well as protect against infection through interactions with CD8+ T cells. In this work the authors depleted CD103+ DCs by administering 1 mg/kg of anti-CD103-SAP (Cat. #IT-50) to the intraperitoneal space of mice subject to adriamycin nephropathy. Rat IgG-SAP (Cat. #IT-17) was used as a control. Elimination of the CD103+ DCs attenuated the kidney injury, indicating that in murine chronic kidney disease CD103+ DCs are pathogenic rather than therapeutic.

Anti-EFNA4 Calicheamicin Conjugates Effectively Target Triple-Negative Breast and Ovarian Tumor-Initiating Cells to Result in Sustained Tumor Regressions.

Damelin M, Bankovich A, Park A, Aguilar J, Anderson W, Santaguida M, Aujay M, Fong S, Khandke K, Pulito V, Ernstoff E, Escarpe P, Bernstein J, Pysz M, Zhong W, Upeslacis E, Lucas J, Lucas J, Nichols T, Loving K, Foord O, Hampl J, Stull R, Barletta F, Falahatpisheh H, Sapra P, Gerber HP, Dylla SJ.

Clin Cancer Res 21(18):4165-4173, 2015.

Triple-negative breast cancer (TNBC) is characterized by tumors lacking HER2, estrogen receptor, and progesterone receptor. TNBC has proved to be very difficult to treat, in large part because of the absence of consensus targets on the surface of the tumor cells. In this work the authors empirically established a set of surface markers associated with TNBC tumor initiating cells, as produced by patient-derived xenografts. Ephrin-A4 was selected as a therapeutic target, and a cell line transfected with the ephrin-A4 gene was challenged with two versions of biotinylated anti-ephrin-A4 coupled to Streptavidin-ZAP (Cat. #IT-27). Both the mouse monoclonal and the humanized antibodies reach an EC_{50} of 10 ng/ml, indicating that ephrin-A4 has promise as a therapeutic target for TNBC.

KNDy neurons modulate the magnitude of the steroid-induced luteinizing hormone surges in ovariectomized rats.

Helena CV, Toporikova N, Kalil B, Stathopoulos AM, Pogrebna VV, Carolino RO, Anselmo-Franci JA, Bertram R.

Endocrinology Epub2015.

Maturation and reproductive function in mammals is controlled by the kisspeptin neuropeptide. Kisspeptin modulates numerous systems within this framework including the mediation of positive and negative feedback effects of estradiol on luteinizing hormone (LH). In the rat, two kisspeptin neuronal populations exist; one in the anteroventral periventricular nucleus (AVPV), and the KNDy (kisspeptin/neurokinin B/dynorphin) neurons in the arcuate nucleus. In this work the authors examine the role of KNDy neurons in estradiol positive feedback effects by administering 10-ng bilateral injections of NK3-SAP (Cat. #IT-63) into the arcuate nucleus of rats. The results indicate that KNDy neurons use dynorphin to inhibit AVPV neurons, establishing a regulatory mechanism for the amplitude of steroid-induced LH surges.

Membrane associated cancer-oocyte neoantigen SAS1B/ovastacin is a candidate immunotherapeutic target for uterine tumors.

Pires ES, D'Souza RS, Needham MA, Herr AK, Jazaeri AA, Li H, Stoler MH, Anderson-Knapp KL, Thomas T, Mandal A, Gougeon A, Flickinger CJ, Bruns DE, Pollok BA, Herr JC.

Oncotarget Epub2015.

Ovastatin is a zinc matrix metallo-proteinase thought to play roles in sperm-egg interaction and the prevention of polyspermy in eutherians. This protein is not found in normal adult tissues, but is expressed by uterine carcinosarcomas. The authors investigated the possibility of targeting ovastatin as a tumor surface neoantigen for therapeutic purposes. SNU539 cells, a uterine malignant mixed Müllerian tumor-derived cell line, were challenged with 1 µM, 0.1 µM, and 0.01 µM rabbit polyclonal anti-ovastatin coupled to 5.42 nM Fab-ZAP rabbit (Cat. #IT-57). Rabbit IgG-SAP (Cat. #IT-35) was used as a control. The results indicate that for this form of uterine cancer, ovastatin is a viable therapeutic target.

Neuropsin (OPN5)-mediated photoentrainment of local circadian oscillators in mammalian retina and cornea.

Buhr ED, Yue WW, Ren X, Jiang Z, Liao HR, Mei X, Vemaraju S, Nguyen MT, Reed RR, Lang RA, Yau KW, Van Gelder RN.

Proc Natl Acad Sci U S A Epub2015.

Circadian clocks are found in most mammalian tissues. These clocks are

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