Targeting Topics: Recent Scientific References

Reviewed by Matthew Kohls

Activated Macrophages Create Lineage-specific Microenvironments for Pancreatic Acinar- and beta-cell Regeneration in Mice.

Criscimanna A, Coudriet GM, Gittes GK, Piganelli JD, Esni F.

Gastroenterology Epub2014.

In response to tissue damage or infection, monocytes are recruited to the injured area and differentiate into macrophages. These macrophages can perform different functions depending on the tissue type. The specific differentiation macrophages undergo in response to their environment is called polarization. The authors used a mouse pancreatic lesion model to examine the polarization of macrophages into the two distinct states known, M1 and M2. Mice received 20 µg of Mac-1-SAP mouse (Cat. #IT-06) in a tail vein injection following a pancreatic lesion, and were sacrificed on various days post-injection in order to evaluate macrophage presence at different response stages. The results demonstrate that various aspects of macrophage polarization are required for pancreatic regeneration.

Prolyl hydroxylation by EglN2 destabilizes FOXO3a by blocking its interaction with the USP9x deubiquitinase.

Zheng X, Zhai B, Koivunen P, Shin SJ, Lu G, Liu J, Geisen C, Chakraborty AA, Moslehi JJ, Smalley DM, Wei X, Chen X, Chen Z, Beres JM, Zhang J, Tsao JL, Brenner MC, Zhang Y, Fan C, DePinho RA, Paik J, Gygi SP, Kaelin WGJ, Zhang Q.

Genes Dev 28(13):1429-1444, 2014.

Members of the FOXO family are thought to act as tumor suppressor genes. In this work the authors investigated the hydroxylation of FOXO3a by EglN2. This hydroxylation pushes FOXO3a toward a protosomal degradation pathway. Loss of FOXO3a in turn allows the accumulation of Cyclin D1, which has been found to be overexpressed in some breast cancers. Some of the data were generated using immunoblots with anti-transhydroxylated proline (Cat. #AB-T044).

Cross-Inhibition of NMBR and GRPR Signaling Maintains Normal Histaminergic Itch Transmission.

Zhao ZQ, Wan L, Liu XY, Huo FQ, Li H, Barry DM, Krieger S, Kim S, Liu ZC, Xu J, Rogers BE, Li YQ, Chen ZF.

J Neurosci 34(37):12402-12414, 2014.

After itch detection, the itch pathway moves through an array of G-protein coupled receptors and transient receptor potential channels in dorsal root ganglion neurons into dorsal horn neurons which integrate and transduce these signals, sending them to the somatosensory cortex. The purpose of this work is to clarify whether gastrin-releasing peptide (GRP) or B-type natriuretic peptide regulates histaminergic itch. Several strains of knockout mice received 200, 300, or 400 ng intrathecal injections of bombesin-SAP (Cat. #IT-40). Blank-SAP (Cat. #IT-21) was used as a control. The data further define the respective functions of the neuromedin B receptor and GRP receptor in itch, and reveals a working relationship between the different interneuron populations.

Microglial VPAC1R mediates a novel mechanism of neuroimmune-modulation of hippocampal precursor cells via IL-4 release.

Nunan R, Sivasathiaseelan H, Khan D, Zaben M, Gray W.

Glia 62(8):1313-1327, 2014.

Postnatal and adult learning and memory require hippocampal neurogenesis. Cognitive dysfunction is frequently accompanied by neuroinflammatory pathogenesis, but the pathways by which the immune system affects neurogenesis are unclear. In this work the authors depleted microglia from primary hippocampal cultures by incubating the cells with 100 µg/ml Mac-1-SAP rat (Cat. #IT-33) for 24 hours. The hippocampal cells were then washed and cultured for further experiments. It was found that neural stem/progenitor cells had reduced survival and proliferation in cultures treated with Mac-1-SAP. These data sketch out the framework of an immune-neuronal pathway important in the regulation of hippocampal neurogenesis.

Light-Triggered, Efficient Cytosolic Release of IM7-Saporin Targeting the Putative Cancer Stem Cell Marker CD44 by Photochemical Internalization.

Bostad M, Kausberg M, Weyergang A, Olsen CE, Berg K, Hogset A, Selbo PK.

Mol Pharm 11(8):2764-2776, 2014.

CD44 is known as a common cancer stem cell (CSC) marker. Given that CSC's seem to have the ability to resist many therapeutic agents, the authors investigated the use of photochemical internalization (PCI) while targeting CD44-expressing CSC's. An immunotoxin was constructed by biotinylating a pan CD44 antibody and combining it with Streptavidin-ZAP (Cat. #IT-27*) at a 4:1 biotinylated antibody to Streptavidin-ZAP molar ratio. Various cancer cell lines were incubated with the toxin at a concentration of 0.825 nM. The toxin showed specific cytotoxicity to CD44-expressing cell lines, demonstrating the efficacy of PCI in conjunction with targeted toxins to treat some cancers.

See new Biotin-Z Kits on Page 7

Role of the cerebrospinal fluid-contacting nucleus in the descending inhibition of spinal pain transmission.

Liu H, Yan WW, Lu XX, Zhang XL, Wei JQ, Wang XY, Wang T, Wu T, Cao J, Shao CJ, Zhou F, Zhang HX, Zhang P, Zang T, Lu XF, Cao JL, Ding HL, Zhang LC.

Exp Neurol 261C:475-485, 2014.

The first synapse in the pain pathway is in the spinal dorsal horn, and several sites are involved in the descending control of pain. Previous studies have suggested that cerebrospinal fluid-contacting neurons may facilitate signal transmission and substance transport between the brain parenchyma and the CSF, including processes that modulate pain transmission. The authors administered CTB-SAP (Cat. #IT-14) into the right lateral ventricle of rats. Saporin (Cat. #PR-01) was

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New versions of Orexin-SAP are now in development and production. If you are interested in testing Orexin-SAP and/or orexin receptor antibodies, please contact us.