ImmunoTools IT-Box-Cy55M-Award 2013

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The role of Prokineticin system in inflammatory pain

Mammalian Bv8 (also called prokineticin-2, PK2) belongs to a new family of small proteins identified in several species from reptiles to mammals. Intensive research of the prokineticin system over the past decade has revealed a dazzling array of biological activities, including angiogenesis, hematopoiesis, immune processes, inflammation and nociceptive transmission. Bv8/PK2 is overexpressed in inflamed tissues and has a crucial role in neutrophil-dependent inflammatory hypernociception. It activate two closely related G-protein coupled receptors (GPCRs): prokineticin receptor 1 (PKR1) and 2 (PKR2) localized in the brain, dorsal root ganglia (DRG), neurons, granulocytes, macrophages and endothelial cells. In rodents, exogenous administration of Bv8/PK2 reduces the nociceptive threshold to thermal and mechanical stimuli acting on PKRs in primary sensitive nerves and in spinal cord and PK2 released from inflammatory granulocytes is the main mediator of inflammatory pain (*Giannini et al., 2009*). Many reports indicate the Bv8/PK2 as main inflammatory mediators also in humans. Literature data (Shojaei *et al.,* 2007) demonstrated that bone marrow mononuclear cells (BMMNCs) from naïve mice, incubated with a series of cytokines and chemokines, showed a different Bv8 expression profile. Although most of the cytokines had no significant effect, the presence of G-CSF resulted in a marked increase in Bv8 expression. Similarly, $CD11b^+$ $Gr1^+$ cells (consisting primarily of neutrophils, but also including cells of the macrophages lineage), incubated with IL-6 and SDF1, resulted in a up-regulation of Bv8.

Considering that prokineticins and their receptors are expressed in neurons of DRG, we are interested to observe if cytokines and chemokines of the ImmunoTools *IT-Box-Cy55M*, like IL-1α, IL-2, IL-4, IL-6,IL-10, IL-17, IL-33, MPC1/CCL2, M-CSF, MIP1α/CCL3, MIP1β/CCL4, MIP3α/CCL20, NGFβ, EGF, GM-CSF, RANTES/CCL5, SDF1α/CXCL12α, SDF-1β/CXCL12β, TNFα, VEGF, G-CSF induce the up-regulation of Bv8/PK2 and its receptors. For this purpose we will use primary DRG neuronal cultures.

ImmunoTools *IT-Box-Cy55M* for **Angela Cappiello**
includes 55 recombinant mouse cytokines

rm EGF, rm Eotaxin / CCL11, rm FGF-a / FGF-1, rm FGF-b / FGF-2, rm FGF-8, rm Flt3L / CD135, rm G-CSF, rm GM-CSF, rm GRO-a / CXCL1, rm GRO-b / CXCL2, rm IFNgamma, rm IL-1alpha, rm IL-1beta, rm IL-2, rmIL-3, rm IL-4, rm IL-5, rm IL-6, rm IL-7, rm IL-9, rm IL-10, rm IL-11, rm IL-13, rm IL-15, rm IL-16, rm IL-17A, rm IL-17C, rm IL-17F,

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rm IL-19, rm IL-20, rm IL-21, rm IL-22, rm IL-25 / IL-17E, rm IL-27, rm IL-31, rm IL-33, rm IP-10 / CXCL10, rm LIF, rm MCP1 / CCL2, rm M-CSF, rm MIP-1α/ CCL3, rm MIP-1β / CCL4, rm MIP3α / CCL20, rm MIP3β / CCL19, rm NGF-beta, rm PDGF-AA, rm PDGF-BB, rm RANTES / CCL5, rm sCD40L / CD154, rm SCF, rm SDF-1α / CXCL12a, rm SDF-1β / CXCL12b, rm TNFα, rm TPO, rm VEGF DETAILS