ImmunoTools IT-Box-Cy55M-Award 2013

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Tristetraprolin-mediated mRNA-decay in Acute Subcutaneous Infections

Tristetraprolin (TTP) is an mRNA-binding protein which interacts with adenine-uridine rich elements (AREs) in the 3' untranslated region of target mRNAs. When TTP binds mRNAs rapid decapping and deadenylation are initiated leading to degradation of the bound mRNA. I participated already in a work in our laboratory where we could show that one-third of lipopolysaccharide-induced unstable mRNAs is targeted by TTP for degradation in bone-marrow derived macrophages. Among this pool of mRNAs one can find mostly cytokines and chemokines, like TNF-α, CCL-2, CCL-3, CXCL-1, CXCL-2, IL-1β, IL-6, , etc (Kratochvill *et al*, Mol Sys Biol, 2011). My PhD project is focused on TTP's function *in vivo*. Therefore we are employing a model of an acute subcutaneous *Streptococcus pyogenes* infection using conditional knockout mice ablating TTP in the myeloid lineage.As a matter of fact, we are not able to decipher whether the *in vivo* effects we see are due to elevated cytokine or chemokine levels because macrophages ablating TTP produce e. g. more TNF-α, or cells ablating TTP react differently to certain cytokines or chemokines. The cytokines and growth factors provided in the IT-Box Cy55M, would be of great benefit answering questions whether cells ablating TTP show differences in their functions *in vitro*, e. g. phagocytosis, expression of barricidal proteins, migration towards a chemokine gradient or proliferation.

The overlap of TTP's targets with the cytokines and growth factors provided in your box is tremendous and having the box would help explaining molecular mechanisms regulated by TTP in more detail. Furthermore, having the opportunity to do more experiments *in vitro* could probably help to reduce the amount of animal experiments and would be in line with the 3R principle.

ImmunoTools IT-Box-Cy55M for Florian Ebner includes 55 recombinant 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, 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