ImmunoTools IT-Box-Cy55M-Award 2013

Sandra Leisz

PhD Supervisor: Prof. Dr. Barbara Seliger

Martin Luther University Halle-Wittenberg
Institute of Medical Immunolgy
Magdeburgerstr. 2
06112 Halle (Saale)

Characterization of HER-2/neu-mediated biglycan downregulation and its molecular mechanisms

The extra cellular matrix protein biglycan (Bgn) is a leucine-rich proteoglycan, which is involved in the matrix assembly, cellular migration and adhesion, cell growth and apoptosis. Although a distinct expression of Bgn was found in a number of human tumors the role of this protein in the initiation and maintenance of neoplastic transformation has not yet been studied in detail. Using an *in vitro* model of oncogenic transformation we could show a downregulation of Bgn expression both in murine and human HER-2/neu-transfected cells. HER-2/neu, a member of epidermal growth factor receptor family, is overexpressed in breast, ovarian as well as stomach cancer. The reconstitution of Bgn expression in HER-2/neu$^+$ cells was associated with a reduced growth, wound healing, migration capacity and tumor growth *in vivo*. On the other hand silencing of Bgn in HER-2/neu$^-$ murine fibroblasts increased the growth rate and migration capacity of these cells (Recktenwald *et al*. 2012). Thus, Bgn acts as a tumor suppressor gene in the respective mouse models, but the molecular mechanisms of the deregulated expression are unknown so far. Previous studies showed a transforming growth factor-β_1 (TGF-β)-inducible Bgn expression, while TGF-β did not affect the Bgn expression in HER-2/neu$^+$ cells (Recktenwald *et al*. 2012). Furthermore the modulation of Bgn through treatment with FGF2, PDGF-BB, EGF, IL-6 and TNFα was described in different tumor cell models. Based on these studies we would like to determine the mechanism of Bgn regulation upon HER-2/neu oncogene transformation and the relevant signal transduction pathways.

Recktenwald CV*, Leisz S*, Steven A, Mimura K, Müller A, Wulfänger J, Kiessling R, Seliger B. HER-2/neu-mediated downregulation of biglycan associated with altered growth properties. *J Biol Chem. 2012 Jul 13;**287**(29):24320-9, **both authors contributed equally to this manuscript*

ImmunoTools IT-Box-Cy55M for Sandra Leisz

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, 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