ImmunoTools IT-Box-Cy55M-Award 2013

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Lymphangiogenesis and its role in periapical disease development

This project aims at investigating the potential role of lymphangiogenesis, especially of vascular endothelial growth factors (VEGFs) family, in development of chronic inflammation and in inflammatory bone resorption in dental tissues – hallmarks of the periapical disease. The information can give new insight to the pathogenesis of apical periodontitis, a condition that requires costly and time consuming root canal or surgical treatment. The VEGFs are involved in the development of various diseases and have also been described in chronic inflammation, such as rheumatoid arthritis (Weber et al., 2000), where they exert increased vasculogenic activity via their receptors (VEGFRs). Their involvement in periapical disease development is still unclear. It is known that bone resorption occurs due to the osteoclastic activity, which is stimulated by increased levels of pro-inflammatory cytokines (IL-1, IL-6, TNF-α). These regulate VEGF-C expression and VEGF-C is also shown to be produced by the cytokine-activated bone resorbing osteoclasts (Zhang Q et al., 2008). Recently published work from our group (Bletsa et al., 2012 and Virtej et al., 2013) has shown the presence of VEGFs and VEGFRs in periapical lesions of both animal and human origin. Vessels as well as macrophages, neutrophils, lymphocytes were identified as carriers of VEGFs (-A, -C and -D) and VEGFRs in these bone resorptive lesions, whereas osteoclasts were the source of their receptors (VEGFRs-2 and – 3).

In human periapical lesions collected from patients we will isolate mononuclear cells as described by Colic et al., 2006, and measure the production of VEGF-A,- C and -D after stimulation with pro-inflammatory cytokines known to be increased in apical lesions – IL-1beta, IL-4, IL-6, TNF-alpha, RANTES, IL-17A or IFNgamma.

Weber AJ, De Bandt M. Angiogenesis: general mechanisms and implications for rheumatoid arthritis. Joint Bone Spine 2000;67:366–83.
Zhang Q, Guo R, Lu Y, et al. VEGF-C, a lymphatic growth factor, is a RANKL target gene in osteoclasts that enhances osteoclastic bone resorption through an autocrine mechanism. J Biol Chem 2008;283:13491–9.
Vascular endothelial growth factors and receptors are up-regulated during development of apical periodontitis.Bletsa A, Virtej A, Berggreen E. J Endod. 2012 May;38(5):628-35. doi: 10.1016/j.joen.2012.01.005. Epub 2012 Feb 1.
Localization and signaling patterns of vascular endothelial growth factors and receptors in human periapical lesions. Virtej A, S. Løes, E. Berggreen, A. Bletsa. J. Endod. 2013. Article in press.
Correlation between phenotypic characteristics of mononuclear cells isolated from human periapical lesions and their in vitro production of Th1 and Th2 cytokines. M. Colic, A. Lukic, D. Vucevic, P. Milosavljevic, I. Majstorovic, M. Marjanovic, J. Dimitrijevic. Arch. Oral. Biol., 51 (2006), pp. 1120–1130.

ImmunoTools *IT-Box-Cy55M* for **Anca Virtej** 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