ImmunoTools *special* Award 2014

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Effect of cardiac glycosides on macrophage polarization and angiogenesis and its significance for anticancer therapy

Cardiac glycosides (CGs) are inhibitors of Na/K-ATPase (sodium pump) and traditionally used for the treatment of congestive heart failure and cardiac arrhythmias. In the last years, many studies have demonstrated that binding of cardiac glycosides to Na/K-ATPase, at concentrations not affecting the pumping function, may cause the activation of multiple signaling cascades that regulate cell proliferation, differentiation and survival [1]. In normal cells CGs induce proliferation or protect from apoptosis, while in cancer cells these drugs inhibit proliferation and/or induce cell death [1;2;3]. It should be noted that in vitro studies performed on cancer cells are consistent with epidemiological data reporting a protection from some types of cancer (i.e. breast, lymphoma/leukaemia, prostate/urinary) in patients who are on cardiac glycoside treatment [4]. Considering the opposite effect CGs on endothelial and cancer cells, further research on the effect of these drugs on tumor angiogenesis is advisable. Angiogenesis is essential for tumor growth and for the spreading of metastases, thus constituting an important target for anticancer therapy. Nevertheless, studies on the effect of CGs on tumor angiogenesis are scarce. Tumor angiogenesis is profoundly influenced by the inflammatory microenvironment that is present in the growing tumor and increasing evidence suggest that macrophages contribute to tumor progression, with increasing number of tumor-associated macrophages (TAM) correlating with poor outcomes [5]. Macrophages are highly plastic and heterogeneous cells that can rapidly change their function in response to local signals. It's well established that macrophages exist in at least two distinct phenotypes of differentiation/activation: classical/proinflammatory (M1) and alternative/anti-inflammatory (M2). However, in contrast to this binary M1/M2 definition, TAM are composed of several distinct populations that often share features of both types [6]. Little is known about the activity of CGs on inflammation and, to our knowledge, there are no studies reporting the effect of CGs on inflammation associated to tumor microenvironment. In this context, it would be of interest to explore if part of the anticancer activity of CGs could be related to an effect on TAM, in particular on their ability to promote angiogenesis.

The objectives of the research program will be achieved through the study of the effect of conditioned media from M1-, M2-or TAM polarized human monocyte-derived macrophages on human endothelial cell migration and tube-like formation in order to determine the angiogenic potential of human M1-, M2- and TAM polarized macrophages and whether CGs can modulate it. We will also investigate the effect of CGs on growth factor-and chemokine-induced endothelial migration and tube formation. So, the ImmunoTools selected products would be of great benefit to this project as they would be used to assess expression of surface antigens for macrophage M1-, M2- and TAM phenotype, to determine cytokines production and to test the capacity of endothelial cells to migrate and form tube-like structures.

1) Schoner W, Scheiner-Bobis G. Am J Physiol Cell Physiol 2007; 293:C509-36
2) Trevisi L et al. Biochem Biophys Res Commun 2004;321:716-21
3) Trenti A et al. Biochem Pharmacol 2014, http://dx.doi.org/10.1016/j.bcp.2014.02.021
4) Newman RA et al. Mol Interv 2008; 8:36-49
5) Steidl C. New Engl J Med 2010; 362:875-85
6) Qian B and Pollard J. Cell 2010; 141: 39-51

ImmunoTools *special* AWARD for **Annalisa Trenti** includes 25 reagents

FITC - conjugated anti-human CD16, CD86, Annexin-V,

PE - conjugated anti-human CD80,

human IL-8 ELISA-set for 96 wells, human IL-8 ELISA-set for 96 wells, human TNFa ELISA-set for 96 wells (each 3 reagents),

recombinant human cytokines: rh EGF, rh FGF-b / FGF-2, rh GM-CSF, rh IFNgamma, rh IL-1beta /IL-1F2, rh IL-3, rh IL-4, rh IL-6, rh IL-8, rh IL-10, rh IL-13, rh M-CSF, rh MCP1 / CCL2, rh MIF, rh PDGF-AA, rh PDGF-BB, rh TNFα, rh VEGF-A/VEGF-165 DETAILS more AWARDS