ImmunoTools *special* Award 2013

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Role of TGFβ pathway on the immune system in acute heart disease

Our lab investigates the effects of inflammation on the recovery of acute heart disease. Acute heart disease develops after an infarction or an obstruction in its blood vessels. This leads to enormous damage of the heart cells. The recovery is in large part dependent on the ability of inflammatory cells as neutrophills and macrophages to clear death and damaged heart cells. However, an exorbitantly immune response will increase the damage, which can result in rupture of the heart. A precise balance of the immune system is thus crucial in the recovery.

In previous studies we found that the Transforming Growth Factor beta (TGFβ) pathway is involved in the differentiation of cardiac cells and the formation of new blood vessels. Mutations in the TGFβ pathway leads to impaired recovery of myocardial infarction in both mouse and human. In fact, TGFβ is a pleiotropic growth factor regulating many cellular responses during development and disease.

Not surprisingly, TGFβ also regulates the innate as well as the antigen specific immunity by modulating the proliferation, differentiation, and function of lymphocytes, macrophages, and dendritic cells.

In this project, we will investigate the regulatory role of TGFβ on the immune system after an acute myocardial infarction or tissue damage in both genetic mouse models as well as patients with mutations in the TGFβ pathway. We investigate whether this mutation changes the inflammatory status within the damaged tissue and in the blood.

Blood and tissue samples of 10 patients and healthy controls with and without tissue damage will be characterised by the screening of changes in subpopulations of macrophages; T-cells; B-cells; Neutrophills; NK-cells. Our patients are under control in a specialized center, which allows us to know the mutations and to obtain both blood and tissue samples.

To investigate the regulatory role of TGFβ more mechanistically we obtained several genetic mouse models, which show similar mutations and phenotypes as our patients. We will subject our mice to a myocardial infarction and isolate immune cells a few days later from the heart and check for circulating immune cells in the blood. The immune cells will be identified for their different subpopulation with the use of

antibodies of ImmunoTools. Other biochemical analyses will add to explore the mechanism of the effects of mutations in the TGFβ pathway.

Next to in-vivo, our laboratory also is specialized in culturing cardiomyocytes. To study the effects of inflammation directly on cardiomyocyte differentiation we will co-stimulate cultured cells with pro- (TNFalpha, MCP-1) and anti-inflammatory stimuli (IL-6; IL10).

Products of ImmunoTools will be used for the general characterisation by Flow cytometry of human monocytes (CD14, CD16) neutrophills (CD177, CD14); NK-cells, T-cells (CD3; CD4; CD8; CD25; CD69); B-cells (CD19; CD45R CD20, CD5) and additional mouse anitbodies (CD45, CD11b, CD3; CD4; CD8; CD69, CD25, CD5, CD19, CD20, CD45RB) will helps us identify the pattern of type of inflammation and recovery after tissue damage. Furthermore, changes in inflammatory response help us to adapt treatment strategies in short term and find patient specific treatment in long term.

ImmunoTools *special* AWARD for **Wineke Bakker** includes 25 reagents

FITC - conjugated anti-human CD5, CD25, CD69, CD45RA, CD14,

PE - conjugated anti-human CD4, CD20, CD177,

PerCP - conjugated anti-human CD8,

APC - conjugated anti-human CD16, CD19,

recombinant human cytokines rh IL-6, rh IL-10, rh TNFa, rh MCP1/CCL2, rh GM-CSF

human IL-6 ELISA-set, human IL-12p40 ELISA-set, human TNFa ELISA-set,

FITC - conjugated anti-mouse CD5, CD25,

PE - conjugated anti-mouse CD45RB,

PerCP - conjugated anti-mouse CD20,

APC - conjugated anti-mouse CD19,

DETAILS