ImmunoTools *special* Award 2014

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Cytokines and other pro-implantatory factors involved in the macrophage-trophoblast cell interaction

Gestational complications associated with placental insufficiency and vascular remodeling defects involving the immune system, as pre-eclampsia (PE) and intrauterine growth restriction (IUGR), are two of the main causes of maternal and neonatal morbimortality. 5 a 7 % of pregnancies are affected by PE being one of the most important causes of maternal morbimortality worldwide. PE is currently diagnosed after the 20th week of gestation by the appearance of hypertension and proteinuria in previously normotensive women. Thus, many laboratories are interested in finding specific biomarkers and tests to enable an earlier diagnosis and even that could offer the possibility of planning preventive treatments.

During normal early pregnancy circulating monocytes are recruited to the maternal–placental interface where they differentiate to macrophages expressing different functional phenotypes for the maintenance of tissue homeostasis. Accordingly, macrophage phagocytic dysfunction seems to partly underlie endometriosis as well as pathological pregnancies especially those complicated with PE. Macrophages represent 20-30% of decidual immune cells and in contrast to other immune cells they keep those levels in decidua throughout pregnancy. Several molecules modulate and influence the cells that are directly involved in the generation and maintenance of an active immunotolerance toward the fetus. In early pregnancy, macrophages are activate in an alternative profile an then participate in the tissue repair and “silent” phagocytosis of apoptotic bodies secreting suppressor mediators like IL-10, TGF-beta and Prostaglandin E2 which contribute to the immunological tolerance and vascular remodeling. In contrast, the macrophage activation in an inflammatory profile has been associated with pregnancy complications like PE. Previous results from our laboratory in the non obese diabetic strain of mice (NOD), indicated that implantation sites with resorption processes present lower TGF-beta and IL-10 expression levels and increased IL-17 expression than viable sites. Moreover, pregnancy switched the characteristic inflammatory profile of peritoneal macrophages of these mice to a predominant alternative activation profile reducing TNF-alpha and IL-12 production.

Supportive evidence indicates that trophoblast cells have a central role to modulate macrophage activation profile through autocrine/paracrine interactions with decidual

immune cells. We have recently shown that human trophoblast cells restrain macrophage migration and response upon different pathogenic stimuli. Among the cytokines secreted by epithelial, trophoblast and immune cells that can modulate the trophoblast function two members of the gp130 family, IL-6 and LIF have been described. IL-6-/- mouse showed implantation failures while LIF or LIFR deficient females suffer more severe complications including not only defective implantation but also placentation alterations.

Considering that defects in the differentiation and proliferation of trophoblast cells, as well as in vascular remodeling, are described as part of PE and intrauterine growth restriction (IUGR) etiopathogenesis, we are currently focused on elucidate whether defective trophoblast-macrophage interaction could have a role in these pregnancy complications. Through studying this issue in human cell co-cultures and mouse models of pregnancy complications we aim to get insight into cytokines and other factors to be used as a direct reflection of placental function and/or biomarker identification for an early diagnosis and management of these pathologies.

Our group is characterized by the enthusiasm and the strong vocation of its members as well as its human quality. Getting this award would be very useful for carrying out part of this project, so we will be really grateful in case Immunotools decides to give us this important benefit.

ImmunoTools *special* AWARD for **Daiana Marina Vota**

includes 25 reagents

FITC - conjugated anti-human IL-6, CD11b, CD16, CD62L, control-IgG2b,

PE - conjugated anti-human TNF-alpha, IFN gamma, CD14, CD40, control-IgG1, control-IgG2a,

APC - conjugated anti-human CD11c,

human IL-6 ELISA-set for 96 wells (each 3 reagents),

recombinant human cytokines: rh IL-6, rh TNF-alpha, rh LIF, rh M-CSF,

PE - conjugated anti-mouse Gr-1,

PerCP - conjugated anti-mouse CD4,

APC - conjugated anti-mouse CD4, CD11b,

recombinant mouse cytokines: rm LIF, rm TNF-alpha

DETAILS more AWARDS