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POSTER PRESENTATIONS

P-1173

Staphylococcal enterotoxin B (SEB) activates TCR- and CD28-mediated inflammatory signals in the absence of MHC class II molecules

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The inflammatory activity of staphylococcal enterotoxin B (SEB) relies on its capacity to trigger polyclonal T-cell activation by binding both T-cell receptor (TCR) and costimulatory receptor CD28 on T cells and MHC class II and B7 molecules on antigen presenting cells (APC). Previous studies highlighted that SEB may bind TCR and CD28 molecules independently of MHC class II, yet the relative contribution of these interactions to the pro-inflammatory function of SEB remained unclear. Here, we show that binding to MHC class II is dispensable for the inflammatory activity of SEB, whereas binding to TCR, CD28 and B7 molecules is pivotal, in both human primary T cells and Jurkat T cell lines. In particular, our finding is that binding of SEB to B7 molecules suffices to trigger both TCR- and CD28-mediated inflammatory signalling. We also provide evidence that, by strengthening the interaction between CD28 and B7, SEB favours the recruitment of the TCR into the immunological synapse, thus inducing lethal inflammatory signalling

Keywords: Adaptive immunity, biology of the immune system, cell signalling, molecular immunology

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The human placenta induces a pregnancy-specific maternal macrophage population during early pregnancy

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Decidual macrophages play a vital role in maternal tissue homeostasis during pregnancy. The question whether macrophages at the maternal-fetal interface (decidua basalis; DB) differ from those in areas not affected by placentation (decidua parietalis; DP) has not been comprehensively addressed. We aimed to investigate the differences between these populations and study possible effects of placental extravillous trophoblasts (EVTs) on macrophage polarization. Macrophages in human first trimester DB and DP were extensively characterized by flow cytometry, *in situ* immunofluorescence staining, and EdU-labeling for analysis of *ex vivo* proliferation. Macrophages were isolated from patient-matched decidual tissues and analyzed by RNAseq, Luminex, and cytological staining. Isolated macrophages were treated with EVT supernatants and gene expression was monitored using SLAMSeq, specifically detecting newly transcribed RNA. EVT supernatants were also used to treat DP tissue explants for further analyses. Macrophages in DB and DP showed major differences in frequency, appearance, and proliferation, with macrophages being significantly more abundant, more granulated, and more proliferative in DB. More than 700 genes were differentially expressed, and a selection of these was confirmed on protein level. SLAMSeq revealed upregulation of more than 400 genes involved in immune processes upon stimulation with EVT supernatants. The secretome of EVTs also induced proliferation of DP macrophages. We identified a pregnancy-associated maternal macrophage signature and defined a central role for invasive trophoblasts in the induction of this signature. Together these data provide evidence for a placenta-guided adaptation of the immune microenvironment at the early maternal-fetal interface.

Keywords: Immune communication, macrophage, microenvironment, reproductive immunology, RNAseq

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IL-10 receptor-expressing B cells in the draining lymph nodes of breast cancer

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IL-10 is a pleiotropic cytokine mostly known for its immune suppressing functions however, it plays an important role in plasma cell differentiation and antibody production. IL10 receptor (IL-10R) is expressed on many cell types such as mast cells, DC, T and B cells. Herein, we investigated the expression of IL10R on CD19+ B cells in breast tumor draining lymph nodes (TDLN). We prepared mononuclear cell suspension from 46 axillary LN samples and stained the cells with antibodies against CD19 and IL10R and examined by flow cytometery. B cells comprised 34.5±14.1% of lymphocytes in the breast TDLNs and of them 42.6±15.8% expressed IL-10R without significant differences in involved and uninvolved LNs. Most (70.4±18.7%) IL-10R+ B cells showed CD24hiCD27+, active/memory, phenotype. In patients without LN involvement, the percentage of B cells was significantly higher in those with tumor sizes>2 cm (P=0.011) and correlated directly with the tumor size (R=0.8, P<0.0001). The frequency of IL-10R+ B cells did not show significant association with breast cancer parameters, however it exhibited a nonsignificant increasing trend in stage III compared with stage I+II. Nearly half of the B cells in the involved or uninvolved breast cancer draining LNs express IL-10R without significant association with tumor size, LN involvement and cancer stage.

Keywords: B lymphocytes, cancer immunology, cytokines and mediators, lymphoid organs