題名:Placental growth factor down-regulates type 1 T helper immune response by modulating the function of dendritic cells.

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摘要:Placental growth factor (PlGF) belongs to the vascular endothelial growth factor (VEGF) family and represents a key regulator of angiogenic events in development and pathologic conditions. In this study, PlGF-modulated differentiation and maturation of human dendritic cells (DCs) from CD14+ monocytes were investigated. The DC, differentiated from CD14+ monocytes in the presence of PlGF during 5 days, was referred to as "PlGF-DC", in contrast to the "classical-DC", obtained in the absence of PlGF. Treatment of PlGF-DC or classical-DC with PlGF resulted in the down-regulation of CD80, CD86, CD83, CD40, and HLA-DR expression, and CD1a was increased, as well as the inhibition of IL-12 p70, p40, IL-8, and TNF-alpha production in response to LPS stimulation. This PlGF-induced DC dysfunction was recovered by anti-human VEGF receptor 1 mAb. In addition, treatment of PlGF-DC or classical-DC with PlGF resulted in the suppression of naïve CD4+ T cell proliferation in an allogenic MLR but up-regulated the IL-5 and IL-13 secretion of the CD4+ T cell. PlGF was also able to inhibit LPS-induced IkappaBalpha phosphorylation and NF-kappaB activity. Taken together, our data demonstrate that the immunosuppressive properties of PlGF are through the NF-kappaB signaling pathway. PlGF might play a major role in the pathogenesis of tumors and act as an effector molecule to skew T cell response to the Th2 phenotype, which might be more beneficial for pregnancy.