## The programmed cell death protein 1 (PD1) and the programmed cell death ligand 1 (PD-L1) are significantly downregulated on macrophages and Hofbauer cells in the placenta of preeclampsia patients

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Preeclampsia is a pregnancy-specific disease characterized by abnormal placentation, endothelial dysfunction, systemic inflammation and a disruption of the immune system. The goal of this study was to characterize the PD-1/PD-L1 system, an important immune checkpoint system, on macrophages and Hofbauer cells (HBC) in the placenta of preeclamptic patients. The expression of the macrophage markers CD68 and CD163 and the proteins PD1 and PD-L1 in the placenta of preeclamptic patients and healthy controls was examined by immunohistochemistry and immunofluorescence. The numbers of CD68-positive and CD163-positive macrophages were significantly downregulated in the decidua ($p = 0.021$ and $p = 0.043$) and the chorionic villi ($p < 0.001$ and $p < 0.001$) of preeclamptic patients. The majority of macrophages in the decidua and the chorionic villi were identified to be CD163-positive, indicating a predominantly M2-polarisation. The expression of PD1 on maternal macrophages of the decidua ($p < 0.001$) and on Hofbauer cells ($p < 0.001$) was shown to be significantly lower in preeclampsia. The expression of PD-L1 was proven to be downregulated on maternal macrophages in the decidua of preeclamptic patients ($p = 0.043$). This difference was only caused by a downregulation of PD-L1 expression in male offspring ($p = 0.004$) while there was no difference in female offspring ($p = 0.841$). The variation of the immune checkpoint molecules PD1 and PD-L1 in preeclampsia might play an important role in the development of inflammation seen in preeclamptic patients. It might thereby be an important target in the therapy of preeclampsia.

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