Immune disbalance in peripheral blood mononuclear cells of pancreatic cancer patients is related to low expression of AhR

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Introduction: Post-transcriptional regulation may allow tumor cells to avoid immunosurveillance. We hypothesized that aryl hydrocarbon receptor (AhR) expression in pancreatic cancer patients could affect and/or reflect anticancer immunity functions. The aim of study was to identify the relation of AhR expression and immune response in peripheral blood mononuclear cells (PBMC) of PDAC patients.

Method: PBMCs from 20 patients with histologically confirmed diagnosis of PDAC and 20 healthy controls (HC) were obtained from venous blood and isolated by Ficoll-Paque gradient centrifugation. Expression of AhR, PD1, IL1b, IL4, IL6, IL10 genes mRNA was evaluated by qRT-PCR. Phagocytosis was measured after induced activation. Monocytes differentiation was evaluated by FACS analysis. Patients were divided into 3 groups according by AhR expression. Expression of AhR in High and Medium AhR groups did not differ significantly from HC. However, Low AhR group was significantly different.

Result: The expression of AhR strongly correlated with the expression of measured cytokines and PD1 receptor in PBMCs’ from PDAC patients. AhR expression in PBMC’s of PDAC patients was lower than in healthy controls. As well as expression of evaluated cytokines and PD1. The subgroup of PDAC patients with significantly lower AhR expression in PBMC’s was identified. This Low AhR group of patients was further characterized by significantly lower expression of cytokines (IL1b, IL4, IL6, IL10) in PBMC’s as well as low levels of PD1 expression. Moreover, Low AhR group demonstrated lower levels of relative monocyte count. In addition, the phagocytosis function of monocytes was significantly diminished in this particular subgroup of patients.

Conclusion: The immune response disbalance with regards of cytokine production, monocyte count and function as well as PD1 expression in PBMCs is related to low AhR gene expression. This might explain the checkpoint inhibitor treatment failure in particular subset of patients (low AhR expression group).