Indoleamine 2,3-Dioxygenase (IDO) Gene Expression as a Signature for Malignant Transformation in Prostate Cancer

Summary / Zusammenfassung

A number of immunosuppressive factors have been suggested to play a role in functional impairment of the immune system in prostate cancer (PCa) patients. Among all, indoleamine 2,3-dioxygenase (IDO) has been considered to favour tumoral immune escape based on tryptophan degradation. We evaluated and compared the expression of genes encoding potential immunosuppressive factors such as IDO, ARG II and IL23 in human benign prostatic hyperplasia (BPH) and PCa also according to alpha-methylacyl-CoA racemase (AMACR) gene expression and kynurenine/tryptophan ratios. Furthermore, impairments of CD4+ and CD8+ T cells proliferation upon homeostatic cytokines (IL-2, IL-7, IL-15) stimulation was also quantified. 40 BPH and 36 PCa patients were enrolled upon informed consent. Quantitative RT-PCR was used to determine gene fold increases of immunosuppressive factors suggested to play a role for immune functional impairment in PCa. Peripheral blood mononuclear cells from same BPH and PCa patients or healthy donors were used for proliferative assays upon homeostatic cytokines stimulation. IDO protein expression was evaluated by immunohistochemistry. Tryptophan and its catabolites concentrations were evaluated in serum patients by HPLC. Statistic was performed using SPSS software package. IDO gene expression significantly correlated with both histological malignancy (p=0.004) and AMACR (p=0.001) accounting for almost 57% of PCa patients. Interestingly, IDOhigh gene expression (39% of IDO positive patients) was also correlating to serum kynurenine/tryptophan ratio (p=0.021).

In contrast, ARG II, IL23, iNOS, eNOS genes were not significantly more expressed in PCa, as compared to BPH, while IL-17 expression was not modified. IL-6 gene expression was significantly (p=0.002) enhanced while TGFb gene expression was significantly (p=0.035) decreased in PCa. Unfortunately, we could not find a significant reduction of T cells proliferation under homeostatic cytokine stimuli. IDO gene expression, frequently detectable in PCa and correlating with AMACR expression, appears to qualify as a marker of malignant transformation in prostate cancers. Further research is warranted to clarify its consequences on immune responsiveness in PCa patients.

Weitere Informationen unter http://www.urologie.usz.ch/LehreUndForschung/Grundlagenforschung/Projekte/Seiten/UroOnkoProjekt3.aspx

Publications / Publikationen


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