DEXAMETHASONE MODULATES TRYPTOPHAN 2,3-DIOXYGENASE EXPRESSION AND ACTIVITY IN SK-MEL-28HUMAN MELANOMA CELL LINE

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Introduction: Tryptophan 2,3-dioxygenase (TDO) and indoleamine 2,3-dioxygenase (IDO) catalyze tryptophan (trp) degradation. IDO expression is upregulated in melanoma contributing to immunologic evasion. Some IDO inhibitors have been/are currently being tested in humans in phase 1and 2trials, and their benefit have not completely demonstrated, suggesting a role for TDO. Recent studies have revealed that TDO is constitutively expressed in a wide variety of cancer cells including malignant melanoma. Glucocorticoids, such as dexamethasone (dex), are broadly used in cancer therapy and have cell type-specific pro- or antiapoptotic effects. We aim to characterize TDO expression and its modulation by dex in human malignant melanoma cells SK-Mel-28.

Methods: TDO expression was studied by means of real time RT-PCR and western blot. Cell proliferation was assessed as cell duplication. Cell cycle was assessed by flow cytometry.

Results: SK-Mel 28express TDO2mRNA which was time-dependent increased by dex. The addition of selective IDO1inhibitor,1-methyl-dl-tryptophan, increased TDO2mRNA expression. Dex stimulated cell proliferation, which was further increased by the IDO1inhibitor and was prevented by a TDO selective inhibitor, 680C91. Moreover, 680C91did not show pro-apoptotic effects on SK-Mel-28, while blocked their cell cycle in G2phase.

Conclusion: These data demonstrate that TDO is expressed in Sk-Mel-28cells which is modulated by dex and ido1inhibitor, highlighting TDO involvement in melanoma cell growth.