The Effect of Immune Checkpoint Inhibitor Ipilimumab on the Development and Proliferation of Breast Cancer Stem Cells

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Immune Checkpoint (ICP) system is recognized as a pathway to preventing the immune system from attacking cancer cells and thus allowing cancer cell survival. Several transcription factors are known to interfere with the activity and function of the ICP pathway. The aryl hydrocarbon receptor AhR is a transcription factor that plays a role in cancer development and initiation. Rationale: Although several studies have been conducted to examine the role of each pathway in cancer treatment, no single study has been conducted to explore the crosstalk between ICP and AhR. Objective: Thus, the main aim of this study was to examine the effect of inhibition of ICP using a clinically used medication Ipilimumab on the mRNA and protein expression of AhR and CYP1A1 in human triple-negative breast cancer cells MDA-MB-231. Methods: MDA-MB-231 cells were treated with increasing concentrations of ipilimumab 0, 5, 10, and 25 uM for 24, thereafter cell viability was determined using MTT assay. Then, the changes in target genes' mRNA and protein expression levels were quantified using RT-PCR and Western blot analyses, respectively. Results: Ipilimumab treatment significantly decreases the mRNA and protein expression of AhR and CYP1A1 at higher concentrations, 10 and 25 uM. Importantly, this was associated with a significant increase in the chemosensitivity of the triple-negative breast cancer cells as demonstrated by an increase in the expression of pro-apoptotic caspase3 and a decrease in the expression of anti-apoptotic BCL-2. Conclusion: This study demonstrated the first evidence of crosstalk between ICP and AhR/CYP1A1 in triple-negative breast cancer cells. It also opens the gates for developing a novel anti-cancer agent.

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