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Expression of novel immunotherapeutic targets in triple negative breast cancer patients

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Background: Triple negative breast cancer (TNBC) is an aggressive form of breast cancer that lacks expression of ER, PR and HER2. Targeted treatment options for TNBC are limited, and novel potential molecular targets need to be evaluated. This study examined biomarkers involved in immune evasion including PD-L1 and its association with other biological pathways as potential treatment options for TNBC patients.

Methods: It was analyzed 511 TNBC samples using a multi-platform approach including whole genome mRNA expression (HumanHT-12 v4 BeadChip Illumina Inc., San Diego, CA), protein expression (immunohistochemistry), gene copy number changes (*in situ* hybridization) and gene sequencing. PD-L1 IHC was performed on 22 samples.

Results: Within the TNBC patient cohort, there were subsets with elevated mRNA expression of immune markers including PD-L1, CTLA4, IDO1 and B7-H3. Cancer cell-specific over-expression of PD-L1 protein was present in 50% of TNBC tumors. Androgen receptor (AR) was over-expressed in 17% of the TNBC cohort and AR-negative TNBC patients were more likely to express PD-L1 (p=0.05), CTLA-4 (p=0.001), and IDO1 (p=2.8e-05). Spearman correlation test showed a positive correlation of PD-L1 with CTLA-4 (0.52), IDO1 (0.48), PIK3CA (0.39), and PTEN (0.11). Differential expression analysis between high and low PD-L1 expressing tumors identified 144 genes. Pathway analysis of the 144 genes indicated significant enrichment of DNA repair genes. Consistent with these findings, PD-L1 expression was negatively associated with BRCA1 expression (p=0.001) and positively correlated with HUS1 and FANCA expression (p=8e-13).

Conclusions: The expression of immune regulatory targets in the TNBC population suggests that immune- targeted therapies may be effective in subsets of TNBC. This is particularly true for patients with AR-negative TNBCs who may benefit from PD-L1 and CTLA-4 targeted therapies. The positive correlation of PIK3CA and PD-L1 may indicate that combination therapy targeting both pathways may be beneficial. In addition, the inverse correlation of BRCA1 with PD-L1 suggests a potential role for platinum-based therapy in combination with anti-PD-L1. Further prospective validation of these findings is ongoing.

Biography

Gargi D Basu had completed her Ph D from All India Institute of Medical Sciences in 1999 and then joined Mayo Clinic for postdoctoral studies. She is currently working at Caris Life Sciences as a Senior Scientist and Director, Quality, Evidence and Reporting. She has published over 25 papers in reputed journals and her work has appeared in Dr. Robert Weinberg's book on "The Biology of Cancer" and also on the cover of AACR journal. Her work on breast cancer has been featured on Breast Cancer Net News Release and on AACR Press Release.

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