

## HLA-G, a Neglected Immunosuppressive Checkpoint for Breast Cancer Immunotherapy

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**Abstract :** HLA-G binds to the inhibitory receptors of uterine NK cells and plays an important role in protection of fetal cells from maternal NK lysis. HLA-G also mediates tumor escape, but the immunosuppressive role is often neglected. These studies have focused on the examination of HLA-G expression in human breast carcinoma and HLA-G immunosuppressive role in NK cytotoxicity. We examined HLA-G expression in breast cell lines by real time PCR, ELISA and immunofluorescent staining. We treated the breast cancer cell lines with anti-human HLA-G antibody or progesterone. Then, NK cytotoxicity was measured by using MTT assay. We find that breast carcinoma cell lines increase the expression of HLA-G mRNA and protein, compared to normal cells. Blocking HLA-G of the breast cancer cells by the antibody increases NK cytotoxicity. Progesterone upregulates HLA-G mRNA and protein of human breast cancer cell lines. The increased HLA-G expression suppresses NK cytotoxicity. In summary, human breast carcinoma overexpress HLA-G immunosuppressive molecules. Blocking HLA-G protein by antibody improves NK cytotoxicity. In contrast, upregulation of HLA-G expression by progesterone impairs NK cytotoxic function. Thus, HLA-G is a new immunosuppressive checkpoint and potential cancer immunotherapeutic target.

**Keywords :** HLA-G, Breast carcinoma, NK cells, Immunosuppressive checkpoint

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