macrophages. Stromal accumulation of intrinsic immunoglobulins stimulated by humoral immunity has been shown to activate FcγRs and promote neoplastic progression through interaction with myeloid cells in a model of squamous cell carcinoma.1 Macrophages express high levels of activating FcγRs, are abundant in tumor cells, and are known to be a bad prognostic factor in breast cancer.4 Tumor-associated macrophages can promote invasion, angiogenesis, and metastasis of tumor cells and furthermore inhibit antitumor immune responses mediated by T cells.5,6 Moreover, studies have shown that tumor-associated macrophages play a critical role in the regulation of epithelial-mesenchymal transition in cancer and resultant resistance to chemotherapy and immunotherapy.6 Our finding that antibodies with low-binding FCγRIIIa alleles were associated with better prognosis in the chemotherapy arm may indicate that the attenuated interaction of natural immunoglobulins with certain tumor cells may limit an immunosuppressive or immune-tumor promoting cascade. However, additional studies will be required before conclusions can be drawn regarding a mechanism for these observations. Despite the fact that the association of FCGR3A polymorphisms with prognosis was a result of an exploratory analysis in our study, we believe that there is sufficient evidence to warrant future studies to examine this association in other randomized trials and highlight the importance of therapeutic interventions targeting the tumor microenvironment for future studies.

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