Interaction Between CD47 and EGF Receptors in Breast Cancer Stem Cells

Arora, Ashi

CD47 is a ubiquitously expressed cell surface receptor for thrombospondin-1 and the counter receptor for signal-regulatory protein alpha- (SIRPa). High expression of CD47 on several types of cancer cells projects a ‘don’t eat me signal’ that inhibits their killing by macrophages or NK cells. The CD47-blocking antibody B6H12 blocks SIRPa binding, enhancing macrophage-dependent clearance of tumors in several mouse models. To investigate the effects of a function-blocking-CD47 antibody (Ab) in breast cancer, estrogen receptor-positive MCF7 and T47D1 and estrogen-negative breast cancer cell lines were used. It was found that CD47 interacts with epidermal growth factor receptor (EGFR) by immunoprecipitation, and the B6H12 antibody disrupted this interaction. No co-localization was observed using immunofluorescence at the surface of MCF7 and T47D1 cells between CD47 and EGFR or the related receptor HER2. The decreased fluorescence of EGFR and CD47 in treated cells suggest that this interaction may have a role in exocytosis or endocytosis. It was found that B6H12 Ab inhibits proliferation of T47D1 cells but not MCF7 cells. As T47D1 and MCF7 cells have high expression of HER2, HER2 phosphorylation was measured; B6H12 does not alter HER2 tyrosine phosphorylation. This data suggests that expression of CD47 and EGFR and their interaction are important on cancer stem cells as it is reported that estrogen receptor negative cells and the T47D1 cells have cancer stem cells and high expression of EGFR and HER2. The association of CD47 with EGFR and/or HER2 could be a novel therapeutic target to treat breast cancer.

Awards Won: