Cure of Breast Cancer, Year 4: First Discovery of Target Therapy for Aggressive Hormonal Breast Cancer using Clinical Database and 3D Model

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The anti-estrogen tamoxifen is a highly effective hormonal therapy for hormonal (HR+) breast cancer patients. However, the estrogen receptor-negative, progesterone receptor–positive (ER-/PR+) subtype does not get the benefits of tamoxifen. Therefore ER-/PR+ breast cancer have a poor clinical outcome, but drug development for ER-/PR+ breast cancer are not well studied. Here, we found that gene expression in ER-/PR+ HR+ breast cancer is positively related to triple negative breast cancer (TNBC) not HR+ breast cancer using 4,319 breast cancer patients database. Especially, inflammation-related genes, USP1, CDC20 and CASP1, which are highly expressed in TNBC, are also upregulated in ER-/PR+ HR+ breast cancer. Suppression of USP1, CDC20 and CASP1 inhibit cancer cell growth and metastasis in ERα KO (ER-/PR+) cell lines. Interestingly, loss of ERα in HR+ cell lines is not responsive to tamoxifen, but highly sensitive to inflammation inhibitor, Ac-YVAD-CHO. In in vitro and ex vivo models, inflammation inhibitor specific blocks ER-/PR+ tumor proliferation and migration. These findings suggest that the inflammation inhibitor might be a first potential target therapy for ER-/PR+ HR breast cancer patients.

Awards Won:

Second Award of $2,000

National Anti-Vivisection Society: First Award of $10,000