Studies show increasing evidence that androgen drives breast cancer

Estrogen and progesterone receptors, and the gene HER2 â€“ these are the big three markers and/or targets in breast cancer. Evidence presented at the AACR Annual Meeting 2013 adds a fourth: androgen receptors.

"This is a continuing line of work with all evidence pointing toward the addition of the androgen receptor as potential target and useful marker in all of the major subtypes of breast cancer," says Jennifer Richer, PhD, investigator at the University of Colorado Cancer Center and co-director of the CU Cancer Center Tissue Processing and Procurement Core.

The finding of androgen receptors (AR) as a potential target in breast cancer is especially important in light of its prevalence in breast cancers that don't express other hormone receptor targets or have developed resistance to treatments that target estrogen dependence. Overall, approximately 77 percent of breast cancers are positive for AR, including 88 percent of cancers that are estrogen receptor positive, 59 percent of those that are HER2 positive, and 20-32 percent of triple negative breast cancers.

The study presented this week explores the ability of estrogen-positive (ER+) breast cancers to develop resistance to anti-estrogen drugs by potentially developing an alternative addiction to AR â€“ and hypothesizes that anti-androgen therapy, such as the drug enzalutamide (formerly MDV3100) as successful counters to breast cancers' evolution. First, Richer and colleagues used breast cancer tumor registries to discover that cancers with higher ratios of AR to ER protein had shorter time to relapse after anti-estrogen therapies. Cut off from their estrogen addition, these cancers may have turned to growth and survival via androgens instead.

The group then returned to the lab to explore the effects of anti-androgen therapies in cell lines and preclinical models.

"Remarkably, the anti-androgen drug enzalutamide had effects comparable to the anti-estrogen drug tamoxifen in breast cancer cells that expressed both ER and AR," Richer says. HER2 cell lines that were also AR+ showed promising responses as well.

"We are excited to move toward clinical trials of anti-androgen therapies in breast cancer," Richer says. "And this study shows that patients with a high AR/ER ratio who relapse while on estrogen targeting therapies might be good candidates for this kind of therapy."

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