

ASSOCIATION OF HSD3B1 (1245C) GENOTYPE WITH RECURRENCE AMONG POST-MENOPAUSAL WOMEN WITH ESTROGEN RECEPTOR-POSITIVE, HER2-NEGATIVE BREAST CANCER



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Dr. Meghan Flanagan, Assistant Professor, Division of General Surgery, is a breast surgical oncologist who joined the UW Department of Surgery faculty in 2018. Furthering relationships she had established during her surgical residency at UW, she formed a cross-institutional, multidisciplinary team of researchers and physicians with basic science, clinical, translational and population health experience to investigate whether breast cancer outcomes are worse for the 25% – 30% women with postmenopausal estrogen receptor positive (ER+) breast cancer who harbor a genetic variation that changes the way they metabolize hormones. Inheritance of a single nucleotide polymorphism (1245A>C) in the gene hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1 (*HSD3B1*) results in gain-of-function in a key enzyme (3 β HSD1) involved in the conversion of adrenal androgens to estrogen. Her research team hypothesized that inheritance of the *HSD3B1* (1245C) allele would negatively impact breast cancer outcomes.

For this project, the gene was sequenced in 635 post-menopausal women with stage I-III, ER+, HER2/neu negative (HER2-) breast cancer who had been enrolled in a population-based study in Western Washington. Using extensively collected clinical and pathologic data about patient demographics, tumor and treatment data and recurrence rates, the team was able to show that women with two mutations in the *HSD3B1* gene had higher rates of distant metastatic recurrence compared to those women who did not have this mutation. Future studies will be forthcoming to determine how this

mutation may decrease the effectiveness of anti-estrogen medications that are used universally in post-menopausal ER+ breast cancer. This mutation is found in up to 15% of ER+ post-menopausal breast cancer patients, and if shown to decrease the effectiveness of anti-estrogen medications, there would be potential indications for alternative treatment strategies in these patients.

