

## Letter to the Editor

### **Aromatase Explains Why Testosterone Increases Breast Cancer Rate**

**To the Editor:** Sieri et al. (1) pointed out that there is an association between high serum levels of estradiol and increased risk of HER2<sup>-</sup> breast cancer. They used this association to conclude that the fact that higher serum levels of testosterone were associated with both HER2<sup>+</sup> and HER2<sup>-</sup> cancers suggested that testosterone increased the risk of breast cancer in postmenopausal women by some mechanism other than by aromatase converting testosterone to estradiol. However, this suggestion seems to assume that elevated levels of estradiol are not just associated with but actually cause breast cancers to have the HER2<sup>-</sup> phenotype, an assumption that seems to be inconsistent with existing evidence.

The level of aromatase activity in breast adipose tissue containing a tumor is strikingly increased when compared with breast tissue from disease-free women (2). There does not seem to be any correlation between the level of estradiol in the serum and the level of estradiol in the tissue of breast cancers, with the tissue levels being approximately the same for both premenopausal and postmenopausal women (3). The level of estradiol in the breast cancer tissue of postmenopausal women is reported to be 10 times higher than the level in their serum (4). For postmenopausal women without breast cancer, the level of estradiol in their breast tissue is approximately four times higher than their serum level (3). If in fact elevated levels of estradiol caused the HER2<sup>-</sup> phenotype in breast cancers, then almost all breast cancers in postmenopausal women would be expected to be HER2<sup>-</sup> because of the high local levels of estradiol present. Also, the intracellular androgen receptor and the membrane

androgen receptor both down-regulate the strongly anti-apoptotic protein Bcl-2, whereas estrogen receptor- $\alpha$  and membrane estrogen receptor both up-regulate Bcl-2 (5). All of this is consistent with the increase in breast cancer observed in postmenopausal women who had higher serum testosterone levels being due to the resulting increase in the local level of estradiol in the breast tissue.

### **Disclosure of Potential Conflicts of Interest**

No potential conflicts of interest were disclosed.

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### **References**

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