Are Triple-Negative and Basal-Like Breast Cancer Synonymous?

To the Editor: In a recent issue of Clinical Cancer Research, Dent and colleagues (1) have reported on the prognostic significance of estrogen negative, progesterone negative, and HER2 negative (triple-negative) class in a large cohort of breast cancer patients. Triple-negative tumors are undeniably one of the most relevant subgroups of breast cancer from a medical oncologist’s perspective, given the lack of targeted therapies for this group and their aggressive clinical behavior. We believe, however, that equating basal-like cancers to triple-negative tumors may be misleading because the basal-like category of tumors is composed almost entirely of triple-negative breast cancers (1). If expression profiling analysis using the intrinsic gene list is considered the “gold standard” for the identification of basal-like cancers, intuitively, one would claim that the majority of basal-like cancers would lack hormone receptors and HER2 expression. In two studies in which the expression of hormone receptors were analyzed in tumors classified according to the intrinsic gene list, however, ER expression was seen in 5% to 45% of basal-like cancers. In addition, Rouzier and coworkers (2) have shown that 14% of basal-like cancers also express HER2.

On the other hand, triple-negative tumors are not necessarily basal-like cancers. In fact, a significant proportion of normal breast–like cancers as defined by expression arrays would also lack hormone receptors and HER2. Although the latter group is still poorly characterized, they are reported to have a prognosis that seems to be better than that of basal-like cancers (3, 4) and do not seem to respond to neoadjuvant chemotherapy (2, 5). In fact, in one study, 45% of patients with basal-like cancer showed pathologic complete response after anthracycline + taxanes neoadjuvant chemotherapy, whereas none of the normal breast–like cancers did so (2).

We (6) and others (7) have shown that the expression of basal markers (i.e., basal cytokeratins and epidermal growth factor receptor) identifies a clinically significant subgroup within the triple-negative group. On the other hand, expression of basal cytokeratins and/or epidermal growth factor receptor (6–8), regardless of the expression of estrogen or progesterone status, identifies a subgroup of cancers that consistently display a poor prognosis, even at 10 years.

Caution should be exercised when using definitions based on the lack of expression markers. As stressed by Nielsen and colleagues (9), “lack of staining for estrogen and HER2 alone to identify basal-like breast cancers risks misassignment based on technical failures.” In fact, estrogen has a documented technical false-negative rate (10) and problems with HER2 interpretation, in particular, when data are retrieved from pathology reports without a central review, may lead to biased results (11).

Clinical studies addressing triple-negative cancers are undoubtedly required; however, large-scale studies comparing the expression of estrogen, progesterone, and HER2 in cases classified as basal-like by expression arrays are required before we can safely say that a triple-negative phenotype can be used as an accurate surrogate for basal-like cancers.

References
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