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Triple Negative Breast Cancer: It's Time to Kick the Can down the Road

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Introduction

Breast cancer as an entity represents classic disease diversity. Yet we continue to define a subset of patients as triple negative breast cancer (TNBC) based on solely the absence of expression profiling of ER, PR and Her2 neu. These biomarkers are obtained since therapies exist to target breast cancer treatment. By definition TNBC does not have measurable detection of these biomarkers and therefore does not have an associated targeted therapy.

Approximately 15% of breast cancer patients will be diagnosed with TNBC [1]. TNBC appear to be more common in young women and those that are BRCA mutation carriers. In fact, about 70% of the cancers identified in BRCA1 mutation carriers will be triple-negative [2-4]. It is also found more commonly in black women compared to white women [2].

TNBC are actually a heterogeneous population. While the clinical phenotype includes the basal-like molecular subtype, the two are not synonymous [5]. The basal TNBC is characterized by genomic expression of the basal cluster. The basal cluster includes the epidermal growth factor receptor, EGFR that is also called Her1. The cluster of genes also contains the basal cytokeratins of 5 and 6. In addition the cluster encompasses the proto-oncogene c-Kit, the proliferation cluster, the hormone receptors and Her 2 genes [6,7]. Historically, tissue microarray IHC studies have identified 2 groups of TNBCs with differing cytogenetic alterations and protein expression patterns [8,9]. Lehmann and colleagues identified 6 TNBC subtypes using cluster analysis. These subtypes displayed unique gene expression profiles and properties. The subtypes were defined by 2 basal-like (BL1, BL2), a mesenchymal stem-like (MSL), a mesenchymal (ML), an immunomodulatory (IM) and a luminal androgen receptor (LAR) [10]. This classification has been demonstrated to correlate to response to inductive chemotherapy and therefore can serve to guide treatment [11]. The possible identification of these cell subtypes may prove predictive for outcomes to treatment response and drivers for targeted therapy. There is also an evolving body of research exploring the role of CDK4 and CDK6 that contributes to the understanding of the molecular biology of TNBC and clinical behavior. While the standard of care in TNBC is chemotherapy, the use of platinum based chemotherapy, PARP inhibitors and VEGF-directed monoclonal antibodies may be influenced by these sub-classifications.

It is important that we apply the lessons learned to date regarding the influence of biological, molecular and behavioral differences in the management of our breast cancer patients. We have entered an era where guidelines should embrace the histology and move beyond ER, PR and Her 2 neu status. With the clinicians' recognition, targeted therapies will evolve into the true concept of precision medicine.

References

1. Burell RA, McGranahan N, Bartek J (2013) The causes and consequences of genetic heterogeneity in cancer evolution. Nature 501: 338-345.
2. Trivers KF, Lund MJ, Porter PL (2009) The epidemiology of triple-negative breast cancer, including race. Cancer Causes Control 20: 1071-1082.
3. Gonzalez-Angulo AM, Tims KM, Liu S (2011) Incidence and outcome of BRCA mutations in unselected patients with triple receptor-negative breast cancer. Clin Cancer Res 17:1082-1089.
4. Foulkes WD, Metcalfe K, Sun P (2004) Estrogen receptor status in BRCA1- and BRCA2-related breast cancer: The influence of age, grade, and histological type. Clin Cancer Res 10: 2029-2034.
5. Bertucci F, Finetti P, Cervera N (2008) How basal are triple-negative breast cancers? Int J Cancer 123: 236-240.
6. Livasy CA, Karaca G, Nanda R (2006) Phenotypic evaluation of the basal-like subtype of invasive breast carcinoma. Mod Pathol 19: 264-271.
7. Korcsching E, Packeisen J, Agelopoulos K (2002) Cytogenetic alterations and cytokeratin expression patterns in breast cancer: Integrating a new model of breast differentiation into cytogenetic pathways of breast carcinogenesis. Lab Invest 82: 1525-1533.
8. Perou CM, Sorlie T, Eisen MB (2000) Molecular portraits of human breast tumours. Nature 406: 747-752.
9. Sorlie T, Perou CM, Tibshirani R (2001) Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci USA 98: 10869-10874.
10. Lehmann, BD, Bauer JA, Chen X (2011) Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies. J Clin Invest 121: 2750-2767.
11. Masuda H, Baggerly KA, Wang Y (2013) Differential response to neoadjuvant chemotherapy among 7 triple-negative breast cancer molecular subtypes. Clin Cancer Res 19: 5533-5540.

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