An integrated approach for comprehensive molecular and tumor microenvironment characterization of invasive lobular carcinoma

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Introduction
Although recent studies have shown that invasive lobular carcinoma (ILC) is associated with worse long-term outcomes compared to invasive breast cancer (BC) originating from other subtypes, they are clinically treated in a similar manner. Therefore, classification approaches to better understand the histological characteristics associated with the different BC subtypes are needed. Here, we describe an integrative analytical approach to comprehensively characterize ILC samples.

Methods
We collected genomic and transcriptomic data for ILC/LS samples from datasets forming a BC metadataset, which were externally annotated as ILC or not as an uncurated CGP gene set. Integration of expression analysis was used to classify the samples into the PAM500 (BC) molecular subtypes (Bazil, Luminal A, Luminal B, HER2, and Basal-like) and performed molecular grading using methods described by Antipova et al. [2]. For gene expression analysis, the Pearson’s chi-square test was used. To evaluate the expression of Biomarker, transcriptomic data was median-scaled using the Mann-Whitney U test was used for statistical analysis (Fig. 3). Using methods described by Huang et al. [3], functional gene expression signatures were selected, and unprocessed cancer causation was performed to identify cancer microenvironment (immune) subtypes. The tertiary lymphoid structure (TLS) gene signature was evaluated using methods described by Stanta-Franklin et al. [4].

Results
Histomolecular characterization of the BC metagroup showed that 12% were LC, and 36% were NST (Fig. 1). Classification into the PAM500 subtypes showed that a greater amount of Luminal A samples were found in the LC subtype (40%) compared to the NST subtype (24%) (Fig. 1). While HER2 (HER2) high and HER2 and Basal-like samples were present in the LS subtype samples, there was a larger percentage found in the NST subtype (P = 0.01), (Fig. 3A). A lower molecular grade was more typical of the LC samples compared to LS in Luminal (P = 0.01), (Fig. 3B) and Basal-like (P = 0.01), (Fig. 3C) subtypes.

Figure 1. Histogramological classification of the BC metagroup

Figure 2. Distribution of PAM500 (BC) subtypes across histological subtypes

Conclusions
These results provide in-depth molecular and tumor microenvironment characterization of ILC. Further optimization of this analytical approach could lead to development of more effective therapeutic strategies.

Reference

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