New method to measure functional HER2-driven signaling activity in primary tumor cells identifies HER2-negative breast cancers with abnormal HER2 signaling activity: new group of patients may benefit from anti-HER2 therapy

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HER2 gene (ERBB2) amplification and/or HER2 protein overexpression is detected in approximately 15-20% of breast cancers and is associated with more aggressive disease. It is important to measure, in addition to expression and amplification of HER2, HER2-driven signaling as a means of identifying patients eligible for HER2 therapies.

Methods

HER2 IHC score/FACS

<table>
<thead>
<tr>
<th>Lymph Status</th>
<th>Histology</th>
<th>HER1</th>
<th>HER2</th>
<th>HER3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic</td>
<td>12</td>
<td>35</td>
<td></td>
<td></td>
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<tr>
<td>Invasive only</td>
<td>13</td>
<td>38</td>
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</tbody>
</table>

Reference Breast Cancer Cell Lines (HER2+ - T47D, SKBR3, HCC1954, and HER2- - MDA231, MCF7) were also analyzed with CELx HSF Tests. NRG1b-induced and EGF-induced CELx signals for tumor and cell line samples were dose-dependent on HER2 status and receptor expression.

Results

Figure 1. Characterization of Primary Tumoral Cells

Table 1. Summary of Patient Characteristics

Table 2. Antibodies Used in Flow Cytometry

Table 3. HER1-3 Expression in Primary Tumor Cells

Table 4. HER1-3 Expression in Breast Cancer Cell Lines

Figure 2. Platform Sensitivity Enables Quantification of HER2 Signaling

Table 5. HER1-3 Expression in Breast Cancer Cell Lines

Figure 3. Defining Test Conditions and Specificity of the CELx HSF Test Measured

Table 6. HER1-3 Expression in Breast Cancer Cell Lines

Figure 4. HER2-驱动 Signaling by CELx HSF Test

Table 7. HER1-3 Expression in Breast Cancer Cell Lines

Figure 5. HER2-Driven Signaling Activity Examples (HER2+/HER2 S+)

Conclusions

- HER2 IHC score and/or FACS analysis is not always sufficient to identify HER2 status
- HER2-driven signaling activity is a high priority target for HER2-negative breast cancer patients
- The CELx HSF Test may have more clinical utility in a larger disease range

References


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