Background

Breast cancers other than HER2-positive tumors, such as v-HER2 and HER2-negative breast cancer, may be important to measure when identifying patients eligible for HER2-targeted therapies. A new assay using an impedance biosensor and live cells derived from each patient’s tumor, the CELx MP test, was developed. Currently, a patient’s eligibility for HER2 targeted therapies is determined using IHC or FISH HER2 tests. However, clinical trials have indicated a weak correlation between HER2 signaling and who will respond to these therapies. Clinical pathology diagnostic marker fails to identify a population responsive to c-Met targeted therapies, an alternative approach is required to identify patients with dysfunctional c-Met signaling.

Methods

**Specimens:** A test set of 172 breast cancer specimens was obtained from 114 patients diagnosed with HER2-negative breast cancer. See Summary of relevant cell/tumour samples per target. The samples were either primary tumors or metastases collected from any of the 79 patients, including 22 with HER2-positive breast cancer.

**Cell Culture:** Methods to focus on any one or all of the following: (a) medium/condition need; (b) cell medium; (c) processing/treatment requirements; (d) cell labelling requirements

**Flow Cytometry:** Flow cytometry was performed on whole cell samples from breast cancers with abnormally amplified HER2 signaling activity. A combination of pan-HER and c-Met TKI inhibits the functional signaling in HER2-negative breast cancer cells.

**Statistical Analyses:** A table of 79 breast cancer specimens from 79 HER-negative patient samples collected between July 2015 and March 2017 and used in 2017 was conducted. 

**Results:** A clinical trial to evaluate treatment response of this patient subset to combine c-Met and pan-HER inhibitors is warranted.

Conclusions

The CELx MP test identified 19 of 79 HER2-negative patient samples for identifying pathway dysfunction in HER2-negative breast cancer. The CELx MP test identified 19 of 79 HER2-negative patient samples and identified a population responding to c-Met targeted therapies. The CELx MP test identified 19 of 79 HER2-negative patient samples for identifying pathway dysfunction in HER2-negative breast cancer.

Sub-group of HER2-negative breast cancer patients with hyperactive and co-involved c-Met and HER (Erbb2) pathways identified: functional signaling profiling test identifies patient group that may benefit from c-Met and pan-HER combination therapy


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Figure 1. Pattern-Behavior Sensing Enables Quantitation of HER and c-MET Signaling Real-Time in Live Cells

**Figure 2. CELx MP Assay Identifies HER2-Positive Breast Cancer Cell Line SKBr3**

**Figure 3. Representative CELx Time-Course Curves**

**Table 1. Summary of Patient Characteristics**

<table>
<thead>
<tr>
<th>Breast Cancer Metastatic Site</th>
<th>ER+</th>
<th>PR+</th>
<th>HER2</th>
<th>Stage</th>
<th>pNX or N/A</th>
<th>Density</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive ductal/DCIS mixed</td>
<td>45</td>
<td>57%</td>
<td>51%</td>
<td>51%</td>
<td>94%</td>
<td>6.80E-24</td>
</tr>
<tr>
<td>Invasive ductal/DCIS mixed</td>
<td>3</td>
<td>4%</td>
<td>51%</td>
<td>51%</td>
<td>94%</td>
<td>6.80E-24</td>
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<td>Invasive ductal/DCIS mixed</td>
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<td>15%</td>
<td>51%</td>
<td>51%</td>
<td>94%</td>
<td>6.80E-24</td>
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<tr>
<td>Invasive ductal/DCIS mixed</td>
<td>15</td>
<td>19%</td>
<td>51%</td>
<td>51%</td>
<td>94%</td>
<td>6.80E-24</td>
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<tr>
<td>Invasive ductal/DCIS mixed</td>
<td>69</td>
<td>87%</td>
<td>51%</td>
<td>51%</td>
<td>94%</td>
<td>6.80E-24</td>
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</tbody>
</table>

References


