Inhibition of abnormal HER2-driven signaling by two HER2 targeted antibody drugs tested ex vivo in live primary HER2+ breast cancer cell lines and HER2+ cell lines

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Background
HER2 gene (ERBB2) amplification and/or HER2 protein overexpression is frequently present in breast cancer. HER2 amplification is associated with a more aggressive disease progression, resistance to and failure of standard therapies, and a poorer overall survival. The use of HER2-targeting small-molecule and/or antibody drugs (trastuzumab, pertuzumab, and ado-trastuzumab emtansine) has significantly improved the outcome of patients with HER2+ breast cancer. However, the development of resistance to HER2-targeting agents (e.g., trastuzumab) has resulted in the emergence of pharmacologically defined subgroups of HER2+ breast cancer samples with a poor prognosis.

Methods
Specimens and Cell Cultures: Primary tumor samples were obtained from patients treated with trastuzumab (n=10) and pertuzumab (n=6). Cell lines were maintained according to ATCC recommendations and authenticated by ATCC in March 2016.

Results
Figure 1. Impedance Platform Sensitivity Enables Qualification of HER2 Signaling

Figure 2. Characterization of Primary Epithelial Cells Derived from Patient Tissue

Figure 3. CELx Test Identifies Four Different Subgroups for HER2 Signaling

Figure 4. Examples of HER2-driven HER2 Signaling Inhibition by Trastuzumab (Tz) or Pertuzumab (Pz) Alone or in Combination

Table 1. Antibodies Used in Flow Cytometry

Table 2. Examples of HER2-Negative (HER2) Patient Samples with Alternatively High HER2 Dependent Signaling (HER2+) Identification by CELx Test

Table 3. Comparison of Inhibition of HER2-driven HER2 Signals by Trastuzumab (Tz) or Alone in Combination

Conclusions
These findings support clinical evidence that both HER2-targeted antibody drugs can be effective for blocking HER2-driven signaling in HER2+ breast cancer cell lines, but trastuzumab may have a more significant effect than pertuzumab for HER2+ breast cancer cell lines.

Additional studies to confirm these findings are currently underway.