Enabling detection of HER2 and AR protein expression and localization in circulating tumor cells (CTCs) of metastatic breast cancer (MBC) patients (pts)

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Background

- Upregulation of HER2 and androgen receptor (AR) are mechanisms of acquired resistance to endocrine therapy
- Measurement of these proteins and their localization requires metastatic biopsies, which are costly, invasive, and prone to under-sampling
- A CTC-based test could expand the clinical utility of these biomarkers
- MBC blood samples were characterized for CTC prevalence, HER2 and AR expression on treatment and at time of disease progression using the Epic Sciences platform

Methods

A. The Epic Sciences CTC Platform

1. Epic Sciences Platform
   - CK, CD45, DAPI

2. Single Cell Capture and Sequencing
   - IDENTIFIED CTC
   - SINGLE CTC ISOLATION
   - SINGLE CELL WGA

3. Genomic Amplification
   - Whole Genome Sequencing & Bioinformatics
   - Library Preparation

B. Example Cell images

C. Consort

- 914 blood samples from 82 MBC Pts:
  - 62 ER/PR+, HER2-
  - 28 ER/PR, HER2-
  - 18 ER/PR+, HER2+
  - 6 ER/PR, HER2+

- 914 Samples tested for HER2 expression
- 910 samples tested for AR expression

HER2+ CTCs Are Identified in Tissue HER2- Pts

CTC Counts Are Mostly Independent of MBC Subtypes

Case Study: HER2+ and AR+ CTCs Disappear Post Trastuzumab in a Tissue HER2- Pt

- HER2+ by Tissue
- CTC HER2+ and AR+ at draw 1
- Started Trastuzumab right after draw 1 and continued for 155 days
- CTC HER2- and AR- at draw 2 (80 days after start)
- Started CDK4+ aromatase inhibitor 184 days after draw 1
- Patient deceased 247 days after draw 1

Single Cell CTC Genomics Confirm HER2 Amplification in Tissue HER2- Pts

Heterogeneous Genome Profiles Are Observed Across Multiple Patients

Conclusions

- The majority (76.3%) of metastatic breast cancer patients had detectable CTCs
- Diverse expression of HER2 and AR were observed and these endocrine therapy resistance markers could potentially guide subsequent therapy selection
- Prospective evaluation of HER2 and AR on MBC pts’ CTCs as predictive biomarkers of benefit from inhibitors of these proteins is needed