**BACKGROUND**

- The choice between hormonal therapies and chemotherapy is a frequent decision in the care of metastatic breast cancer (mBCa) patients.
- We previously developed quantitative measures of phenotypic CTC heterogeneity in metastatic castration resistant prostate cancer (mCRPC), and found higher heterogeneity was associated with better survival on chemotherapy vs. targeted hormonal therapies, and the reversal was true in low heterogeneity patients (Scher et al. 2017 Cancer Research).
- We sought to apply our previous heterogeneity quantitation methodologies to a cohort of mBCa patient CTCs to ascertain feasibility in mBCa.

**METHODS**

- 295 blood samples from mBCa patients were processed for CTC analysis utilizing the Epic Sciences platform. Following enumeration, multi-dimensional phenotypic characterization analysis was performed utilizing protein expression and digital pathology features.
- Features from each CTC (1760 CTCs from 165 patients, 84 HR+, 19 Her2+, 8 HR+/Her2+, 54 TNBC) were compared by unsupervised clustering, Shannon Index and intra-patient variance analyses to assess the intra-patient heterogeneity among mBCa CTC phenotypes.

**RESULTS**

1. **Epic Sciences Platform**
2. **Single Cell Features**
3. **Unsupervised Clustering**
4. **Single Cell Capture and Sequencing**

**CONCLUSIONS**

- Distinct CTC phenotypes can be visualized reproducibly across patients and associate with specific mBCa subtypes.
- We detected a wide range of inter- and intra-patient heterogeneity in CTC phenotypes.
- Stratification of patients based on heterogeneity levels may help to find better responders to different targeted therapies.
- CTC phenotypes are associated with chromosomal instability and loss/gain of cancer driver genes.
- High CK expression in CTC subtypes D, E and G seem to correlate with higher responders to different targeted therapies.
- Studies linking heterogeneity to therapeutic efficacy and patient outcome are ongoing.