

THE SPATIALLY-RESOLVED PROTEOMIC ATLAS OF THE TUMOR IMMUNE ARCHITECTURE OF HER2-POSITIVE BREAST CANCER AND RESPONSE TO NEOADJUVANT ANTI-HER2 THERAPY-BASED CHEMOTHERAPY

¹Saranya Chumsri*, ¹Jennifer Kachergus, ¹Ji Shi, ¹Yi Liu, ¹Yaohua Ma, ²Alyssa Rosenbloom, ²Shilah Bonnett, ²Mark Conner, ²Erin Piazza, ²Brian Filanoski, ²Rhonda Meredith, ²Christine Kang, ²Lesley Isgur, ²Margaret Hoang, ²Gary Geiss, ²Joseph Beechem, ¹EA Thompson. ¹Mayo Clinic, Jacksonville, FL, USA; ²NanoString Technologies, Seattle, WA, USA

Background The standard of care for early-stage HER2-positive (HER2+) breast cancer is neoadjuvant anti-HER2 therapy-based chemotherapy, with the preferred regimen being TCHP (docetaxel, carboplatin, trastuzumab, and pertuzumab). Approximately half of such patients have a pathological complete response (pCR) with this regimen. There is a compelling need to understand the biology that underlies response or failure to respond. Such an understanding is central to the development of alternative therapeutic strategies. To this end, we carried out a proteomic investigation of the stromal and intratumoral compartments of early-stage HER2+/ER- tumors using the GeoMx[®] Digital Spatial Profiling (DSP) and the novel human Immuno-oncology Proteome Atlas (IPA) 500, featuring >500 antibodies coupled to photocleavable DNA barcodes with NGS sequencing readout.

Methods We used the human GeoMx IPA 500 panel to evaluate the proteomic architecture in the tumor and stroma niches in early-stage HER2+(IHC3+)/ER- tumors. We analyzed 12 samples, 4 that underwent pCR in response to TCHP, 4 that did not undergo pCR, plus residual disease from the 4 non-responders. Differential expression of proteins, using the linear mixed model, was used to identify features that are associated with response to TCHP and to evaluate the immune microenvironment of those samples that retained residual cancer burden after therapy.

Results The 500-plex Immuno-oncology Proteome Atlas (IPA) demonstrates the ability to interrogate the spatial distribution of protein abundance at a depth that has heretofore been unobtainable. This pilot analysis provides novel insight into proteomic features that are associated with favorable responses to the standard-of-care therapy in HER2+ breast cancer. Such features may inform prognostic or predictive indicators of outcome and may identify potential therapeutic targets that can be exploited to maximize the benefit of neoadjuvant TCHP.

Conclusions Analysis of the spatial distribution of protein expression at an unobtainable depth heretofore provides novel insight into the baseline biology of early-stage HER2+ cancer. We further demonstrate the power of the combination of the GeoMx DSP and curated human IPA 500 to enable more holistic discovery biology by rapidly evaluating 100s of critical potential therapeutic targets on individual tumor and stromal niches.

Supported in part by grants from the Breast Cancer Research Foundation (BCRF 22-161) and the Florida Department of Health (Bankhead Coley 22B08).

<http://dx.doi.org/10.1136/jitc-2023-SITC2023.0207>