Published OnlineFirst February 21, 2019; DOI: 10.1158/1940-6207.CAPR-18-0492

Letter to the Editor

Cancer Prevention Research

HER2 Expression in NF1 Breast Cancer—Response

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We thank Gambini and colleagues for the thoughtful letter (1) regarding our article "*NF1* alterations are linked to increased HER2 expression in breast cancer" published in *Cancer Prevention Research* in November 2018 (2).

In the letter, Gambini and colleagues pointed out that breast ductal carcinoma *in situ* (DCIS) has a higher probability of being HER2 positive than invasive ductal carcinoma (IDC). Moreover, because DCIS HER2-positive status does not affect treatment options, the American Society of Clinical Oncology (ASCO) and the College of American Pathologists (CAP) do not recommend HER2 evaluation for DCIS. Gambini and colleagues' letter also brought into question whether the higher rate of HER2 positivity in our NF1 breast cancer specimens was due to the fact that IHC results were derived from DCIS portions instead of IDC portions of the samples. Indeed, in clinical practice, we follow ASCO/CAP guidelines for reporting HER2 IHC status. In the clinical setting, we perform HER2 IHC analysis only in cases of invasive breast cancer. No further testing is performed if the IHC score is defined as strongly positive (3+) or negative (0, 1+). *In situ* hybridization (ISH) is only performed in equivocal cases when the IHC score is 2+. For the purpose of this research study, all the tumors, invasive or *in situ*, were sectioned and stained for HER2 using antibodies from Cell Signaling Technology. For tumors with components of both IDC and DCIS, HER2 status was scored and reported for only the IDC portion of the tumor. Among IDC samples, 7 of 11 (63.6%) were strongly positive. Meanwhile, three tumors with a DCIS component only were stained for HER2 and all were strongly positive. All HER2 3+ samples, as determined by IHC, met the current ASCO/CAP criteria, with complete and strong membranous staining in more than 10% of tumor cells. Because whole tissue sections were used in our study for IHC scoring, the results may not be directly comparable with the results of other publications such as that of Borgquist and colleagues (2015), where only two cores of 1 mm were selected from the DCIS tumor blocks to generate a tissue microarray for IHC analysis (3).

For a study with a limited sample size such as ours, we refrain from making a direct comparison with the data of those unselected breast tumors. Therefore, we strongly support the suggestions by Gambini and colleagues that a multicenter, synergistic data collection among different centers with expertise in NF1 and breast cancer would achieve the goal of characterizing these rare conditions.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Received December 17, 2018; revised January 3, 2019; accepted January 15, 2019; published first February 21, 2019.

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doi: 10.1158/1940-6207.CAPR-18-0492

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Cancer Prev Res 2019;12:197-198. Published OnlineFirst February 21, 2019.