Letter to the Editor

Reply to Commentary on 'HER2 immunohistochemical and fluorescence *in situ* hybridization discordances in invasive breast carcinoma with micropapillary features'

Modern Pathology (2018) **31,** 686; doi:10.1038/modpathol.2018.28

To the Editor: We appreciate the comments of Dr Sorscher regarding our study of HER2 testing discordances in invasive breast carcinoma with micropapillary features.[1] While we agree that clinical trials are the optimal means to define response to HER2 targeted therapy, it is notable that four out of nine cases in our study that were scored 1+ by immunohistochemistry (IHC) would have met criteria for HER2 amplification based on both the 2007 and 2013 ASCO/CAP guidelines.[2,3] We are not suggesting that the definition of HER2 positivity be expanded, but rather, we would like to make pathologists aware of the potential for discordance between IHC and FISH results in this morphologic subtype. Specifically, our results support the 2013 ASCO/CAP recommendation that pathologists consider reporting IHC in micropapillary carcinomas as equivocal, and perform reflex testing using *in situ* hybridization, as this method better reflects the HER2 status in this morphologic subtype. Micropapillary carcinomas display unusual cell membrane architecture, and in some instances, may be scored 1+ by IHC because of the strict requirement for circumferential staining. Because tumors of this histologic subtype can demonstrate HER2 staining that deviates from the typical circumferential staining pattern, it is possible that cases that are HER2-amplified (by both 2007 and 2013 criteria), and that are likely to respond to anti-HER2 directed therapy, could be missed and interpreted as HER2-negative. We agree that ASCO/CAP guidelines should 'ensure that the right patient receives the right treatment,' and therefore highlight a potential pitfall that could impact treatment decisions for patients with invasive carcinomas with micropapillary features.

Disclosure/conflict of interest

The authors declare no conflict of interest.

Rachel L Stewart[1], Evin H Gulbahce[1], Katherine B Geiersbach[2] and Erinn Downs-Kelly[3]
[1]Department of Pathology, ARUP Laboratories, University of Utah Medical Center, University of Utah, Salt Lake City, UT, USA; [2]Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA; [3]Robert J. Tomsich Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH, USA
E-mail: rachel.stewart@aruplab.com

References

1 Stewart RL, Caron JE, Gulbahce EH, *et al.* HER2 immunohistochemical and fluorescence in situ hybridization discordances in invasive breast carcinoma with micropapillary features. Mod Pathol 2017;30:1561.
2 Wolff AC, Hammond ME, Schwartz JN, *et al.* American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. Arch Pathol Lab Med 2007;131:18–43.
3 Wolff AC, Hammond ME, Hicks DG, *et al.* Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Update. J Clin Oncol 2013;31: 3997–4013.