Targeted next-generation sequencing enables reliable detection of HER2 (ERBB2) status in breast cancer and provides ancillary information of clinical relevance.

Abstract:
HER2-positive breast cancers are a heterogeneous group of tumors, which share amplification and overexpression of HER2. In routine diagnostics, the HER2 (ERBB2) status is currently assessed by immunohistochemistry (IHC) and in situ hybridization (ISH). Data on targeted next-generation sequencing (NGS) approaches that could be used to determine the HER2 status are sparse. Employing two breast cancer-related gene panels, we performed targeted NGS of 41 FFPE breast cancers for which full pathological work-up including ISH and IHC results was available. Selected cases were analyzed by qPCR. Of the 41 cases, the HER2 status of the 4 HER2-positive and 6 HER2-negative tumors was independently detected by our NGS approach achieving a concordance rate of 100%. The remaining 31 cases were equivocal HER2 cases by IHC of which 5 showed amplification of HER2 by ISH. Our NGS approach classified all non-amplified cases correctly as HER2 negative and corroborated all but one of the 5 cases with amplified HER2 as detected by ISH. For the overall cohort, concordance between
the gold standard and NGS was 97.6% (sensitivity 88.9% and specificity 100%). Additionally, we observed mutations in PIK3CA (44%), HER2 (8%), and CDH1 (6%) among others. Amplifications were found in CCND1 (12%), followed by MYC (10%) and EGFR (2%) and deletions in CDKN2A (10%), MAP2K4 and PIK3R1 (2% each). We here show that targeted NGS data can be used to interrogate the HER2 status with high specificity and high concordance with gold standard methods. Moreover, this approach identifies additional genetic events that may be clinically exploitable. © 2016 Wiley Periodicals, Inc.