Molecular inversion probe technology generates high-quality HER2 copy number data in formalin-fixed paraffin-embedded breast cancer tissue

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Background: Molecular inversion probe (MIP) technology has proven successful in overcoming the challenges of generating high-quality copy number (CN) data from formalin-fixed paraffin-embedded (FFPE) samples, requiring a minimal amount of DNA. HER2 status is currently assessed by a variety of qualitative and semi-quantitative methods, including immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH). We hypothesized that MIP technology can provide accurate and quantitative HER2 assessment, which is especially important with emerging novel anti-HER2 therapies. Applying MIP technology on FFPE breast cancer (BC) tissue, we generated HER2 and pericentromeric 17 CN data by MIP and correlated them with HER2 and chromosome 17 centromere (CEP17) CN data by FISH.

Methods: We selected 27 tumor blocks from 26 female patients with invasive BCs (17 with, 8 without and 2 equivocal for HER2 amplification by FISH). For each tumor, we had cut 5-μm sections from a representative FFPE tissue block for IHC, FISH, and MIP array studies. We performed IHC with monoclonal HER2/neu Ab-8 antibody and FISH with PathVysion HER2/CEP17 dual-probe. After manual microdissection, we extracted genomic DNA and subjected DNA samples to genome-wide CN analysis with focus on HER2 and chromosome 17’s pericentromeric region. Data were analyzed by Nexus Express for OncoScan.

Results: With a designated cut-off of 4.0 for CN gains, 15 of 17 HER2+ BC by FISH had HER2 CN gains (4.0-28.0) on MIP analysis. Two of 17 HER2+ BC by FISH had a HER2 CN of 2.5 and 2.3 by MIP, likely due to tumor heterogeneity. All 8 HER2-BC by FISH also had a HER2 CN <4.0 by MIP. All 27 samples displayed excellent correlation between CEP17 CN by FISH and pericentromeric 17 CN by MIP.

Conclusion: Our findings show a robust correlation between MIP and FISH results, with 25 of 27 samples showing similar CN data by both methods. With minimal DNA requirements using FFPE tissue, MIP array technology shows promise as a quantitative measure of HER2 CN. A larger prospective study is required to assess whether MIP array is a more accurate representation of the tumor’s HER2 status than FISH. By allowing genome-wide CN profiling, MIP technology may improve our understanding of BC biology and behavior and potentially be critical in guiding clinical decisions regarding targeted therapy.

Biography
Alexis Bousamra has completed his Breast Pathology fellowship at MD Anderson Cancer Center in June 2015, following a 4-year residency at UAMS in Little Rock, Arkansas and medical studies at American University of Beirut, Lebanon. Currently, he is a staff pathologist at Allegheny Health Network. He is also the program director of the Surgical Pathology Fellowship alexbousamramd@gmail.com