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Oral Presentation

The Transition to Next Generation Sequencing from Conventional Sanger Sequencing for Breast Cancer Genetic Study

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Background/Purpose: The incidence of breast cancer is on the rise in Asia including Hong Kong. 40% of the breast cancer patients are diagnosed before age of 50 in Hong Kong. From clinical aspect, it is important to distinguish patients with inherited predisposition to breast cancer from sporadic cases, particularly in early-onset patients (< 45 years old). *BRCA*1/2 have been widely investigated and frequently implicated in familial predisposition to breast cancer. Conventional Sanger sequencing has long been used and proved to be a reliable method, although it is relatively labour intensive and expensive.

Methods: An alternative high efficiency method is much desired, thus more patients will benefit from screening. Harnessing the advantage of Polymerase Chain Reaction (PCR) array and next generation sequencing (NGS), we expand the *BRCA* gene panel to include *TP53* and *PTEN*. The sensitivity of the NGS platform was validated by over hundred Sanger detectable mutations. We have also provided a solution to overcome the challenges in the analysis of homopolymer regions by in-house bioinformatics algorithm.

Results: The NGS approach to mutation detection was applied to 464 high-risk index patients. Altogether 1,092 index patients were examined by either Sanger or NGS approach, germline mutation has been identified in 10% of the families. Overall, 24.1%, 19.4% and 17% of the mutation carriers presented with multiple cancers, triple negative breast cancer and family history of breast and/or ovarian cancer respectively.

Conclusion: These findings may provide information for adaptation of NGS in the diagnostic molecular pathology service and revolutionize laboratory strategies for mutation screening.