BRCA1/2 gene mutation detection in 2686 Chinese clinical samples based on NGS HANDLE technology

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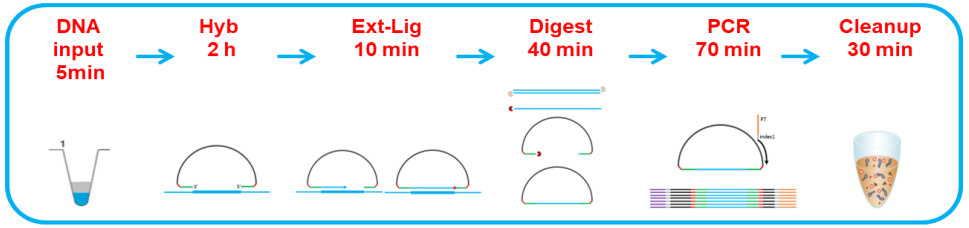
Background

BRCA1 and BRCA2 are tumor suppressor genes that play an important role in prevention, monitoring, and use of targeted therapy in cancer. The mutation types include single-nucleotide variation (SNV), small insertions and deletions (InDel) and copy number variations (CNV). Traditional methods for SNV and InDel detection are multiplex polymerase chain reaction (PCR) plus Sanger sequencing or Next Generation Sequencing (NGS). For CNV detection, the gold standard method is Multiplex Ligation-dependent Probe Amplification (MLPA). A new NGS method based on Halo-shape ANnealing and Defer-Ligation Enrichment (HANDLE) technology developed by AmoyDx can detect all mutation types within one reaction tube, and a turn-around time of 5 h for library preparation with hands-on time of 1 hour.

Methods

There were 2686 samples from Chinese patients (2563 whole blood samples and 123 FFPE tissue samples) detected in AmoyDx Medical Institute, including 1357 breast, 754 ovarian, and 575 other samples (prostate, pancreatic, patients of unknown cancer types and family members of cancer patients). All samples were tested following the instructions of the AmoyDx BRCA1 and BRCA2 gene mutation detection kit combined with the automatic AmoyDx NGS Data Analysis System (ANDAS). The MLPA method was used for confirmation of CNV results of whole blood samples.



One-tube, One PCR, Turn-Around Time: 5h, Hands-on Time: 1h

Results

In total, there were 476 samples detected with a pathogenic or likely pathogenic BRCA mutation. The mutation rate was 17.7% for all samples, 12.2% in breast and 26.4% in ovarian cancer samples. There were 11 samples with multiple breast cancer types or combined breast cancer and other cancer types, 6 of which were detected with pathogenic or likely pathogenic mutations. There were 20 out of 476 (4.2%) samples that demonstrated pathogenic or likely pathogenic BRCA CNVs by MLPA. 18 (90%) of these CNVs were from BRCA1 gene, and 19 (95%) of them were concordant with the BRCA mutation detection according to the AmoyDx NGS test kit based on HANDLE technology.

Conclusions

1. BRCA1/2 gene mutations were detected in multiple cancer types.
2. CNVs of BRCA1 were much more frequent than CNVs of BRCA2 in Chinese cancer patients.
3. Testing of BRCA 1/2 by NGS based on HANDLE technology is a valid and fast solution for detection of BRCA1/2 mutations.