Mitochondrial DNA mutations in Malaysian female breast cancer patients

ABSTRACT

Cancer development has been ascribed with diverse genetic variations which are identified in both mitochondrial and nuclear genomes. Mitochondrial DNA (mtDNA) alterations have been detected in several tumours which include lung, colorectal, renal, pancreatic and breast cancer. Several studies have explored the breast tumour-specific mtDNA alteration mainly in Western population. This study aims to identify mtDNA alterations of 20 breast cancer patients in Malaysia by next generation sequencing analysis. Twenty matched tumours with corresponding normal breast tissues were obtained from female breast cancer patients who underwent mastectomy. Total DNA was extracted from all samples and the entire mtDNA (16.6kb) was amplified using long range PCR amplification. The amplified PCR products were sequenced using mtDNA next-generation sequencing (NGS) on an Illumina Miseq platform. Sequencing involves the entire mtDNA (16.6kb) from all pairs of samples with high-coverage (~ 9,544 reads per base). MtDNA variants were called and annotated using mtDNA-Server, a web server. A total of 18 of 20 patients had at least one somatic mtDNA mutation in their tumour samples. Overall, 65 somatic mutations were identified, with 30 novel mutations. The majority (59%) of the somatic mutations were in the coding region, whereas only 11% of the mutations occurred in the D-loop. Notably, somatic mutations in protein-coding regions were non-synonymous (49%) in which 15.4% of them are potentially deleterious. A total of 753 germline mutations were identified and four of which were novel mutations. Compared to somatic alterations, less than 1% of germline missense mutations are harmful. The findings of this study may enhance the current knowledge of mtDNA alterations in breast cancer. To date, the catalogue of mutations identified in this study is the first evidence of mtDNA alterations in Malaysian female breast cancer patients.