Next Generation Sequencing - targeted panel
Hereditary breast cancer, version 1, 26-2-2021

Erasmus MC
University Medical Center Rotterdam

Dept. Clinical Genetics

Technical information

DNA was enriched using Agilent SureSelect Custom Capture (ELID 3293151) and paired-end sequenced on the Illumina platform (outsourced). Data are demultiplexed with bcl2fastq Conversion Software from Illumina. Reads are mapped to the genome using the BWA-MEM algorithm. The aim is to obtain a unique coverage of the coding regions (CDS) +/- 10 basepairs for the indicated transcripts of at least 20x*. When unique coverage is between 10x and 20x, regions are manually checked in the BAM file. When below 10x, Sanger sequencing is deployed for those regions. Variant detection is performed by the Genome Analysis Toolkit HaplotypeCaller. The detected variants are filtered and annotated with Alissa Interpret software and classified with Alamut Visual. As no technique has a 100% sensitivity, we cannot exclude that pathogenic variants remain undetected. At this moment, there is not enough information about the sensitivity of this technique with respect to the detection of deletions and duplications of more than 15 nucleotides and of somatic mosaic variants (all types of sequence changes).

HGNC approved gene symbol	OMIM gene ID (active link to omim.org)	Transcript	median depth	% covered >10x	% covered >20x
ATM	607585	NM_000051.3	2290	100,00	100,00
BRCA1	113705	NM_007294.3	3496	100,00	100,00
BRCA2	600185	NM_000059.3	2892	100,00	100,00
CHEK2*	604373	NM_007194.4	2674	100,00	100,00*
PALB2	610355	NM_024675.3	3435	100,00	100,00

- OMIM release used: 18-2-2021
- The statistics above are based on a set of 44 samples
- Median depth is the median of the mean sequence depth over the protein coding exons (±10bp flanking introns)
- % Covered 10x and 20x describes the percentage of a gene's coding sequence (±10bp flanking introns) that is covered at least 10x or 20x

* Due to technical reasons exon 7 of the CHEK2 gene (amino acids 265-282) is covered suboptimal in this capture design and therefore excluded from the minimal coverage QC