

Whole Exome Sequencing

Gene package Noonan syndrome/RASopathies, postnatal

version 1, 9-3-2020



Technical information

DNA was enriched using Agilent SureSelect DNA + SureSelect OneSeq 300kb CNV Backbone + Human All Exon V7 capture and paired-end sequenced on the Illumina platform (outsourced). The aim is to obtain 10 Giga base pairs per exome with a mapped fraction of 0.99. The average coverage of the exome is ~50x. Duplicate and non-unique reads are excluded. Data are demultiplexed with bcl2fastq Conversion Software from Illumina. Reads are mapped to the genome using the BWA-MEM algorithm (reference: <http://bio-bwa.sourceforge.net/>). Variant detection is performed by the Genome Analysis Toolkit HaplotypeCaller (reference: <http://www.broadinstitute.org/gatk/>). The detected variants are filtered and annotated with Cartagenia software and classified with Alamut Visual. Additionally, MPLA analysis was performed for NF1 (P081, versie D1 en P082, versie C2; MRC-Holland), SPRED1 (P295, versie B3; MRC-Holland), LZTR1 (P455, versie A1; MRC-Holland) and BRAF-HRAS-KRAS-NRAS (P298, versie A1; MRC-Holland). 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 5 nucleotides and of somatic mosaic mutations (all types of sequence changes).



Dept. Clinical Genetics

HGNC approved gene symbol	OMIM gene ID (active link to omim.org)	median depth	% covered >10x	% covered >20x	% covered >30x
A2ML1	610627	66	100	100	96
BRAF	164757	68	100	100	94
CBL	165360	78	100	100	100
HRAS	190020	179	100	100	100
KRAS	190070	83	100	100	87
LZTR1	600574	117	100	100	100
MAP2K1	176872	79	100	100	96
MAP2K2	601263	117	100	100	95
MRAS	608435	87	100	100	100
NF1	613113	55	97	90	79
NRAS	164790	63	100	100	98
PPP1CB	600590	54	100	100	95
PTPN11	176876	77	100	99	90
RAF1	164760	78	100	99	95
RIT1	609591	72	100	100	100
RRAS2	600098	68	100	99	86
SHOC2	602775	61	100	99	95
SOS1	182530	71	100	100	95
SOS2	601247	75	100	99	95
SPRED1	609291	57	100	98	92

- OMIM release used: 8-9-2019

- The statistics above are based on a set of 100 samples

- Median depth is the median of the mean sequence depth over the protein coding exons (± 10 bp flanking introns) of the longest transcript

- % Covered 10x, 20x and 30x describes the percentage of a gene's coding sequence (± 10 bp flanking introns) that is covered at least 10x, 20x or 30x