Whole Exome Sequencing
Gene package Noonan syndrome/RASopathies, prenatal
version 1, 31-1-2020

Erasmus MC
University Medical Center Rotterdam

Dept. Clinical Genetics

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. It is not excluded that pathogenic mutations are being missed using this technology. 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

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
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
SHOC2	602775	61	100	99	95
SOS1	182530	71	100	100	95
SOS2	601247	75	100	99	95
SPRED1	609291	57	100	98	92

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