Whole Exome Sequencing
Gene package Noonan syndrome/RASopathies, postnatal
version 1.2, 26-2-2021

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/). Sequence variant detection is performed by the Genome Analysis Toolkit HaplotypeCaller (reference: http://www.broadinstitute.org/gatk/). The detected sequence variants are filtered and annotated with Alissa Interpret software and classified with Alamut Visual. Copy variant detection is performed using the BAM multiscale reference method using depth of coverage analysis and dynamical bins in NexusClinical. The detected copy number variants are filtered and annotated with the NexusClinical software and classified using UCSC Genome Browser (NCBI37/hg19). 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). It is not excluded that pathogenic variants 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 changes).

Erasmus MC
University Medical Center Rotterdam

Dept. Clinical Genetics

HGNC approved gene symbol	OMIM gene ID (active link to omim.org)	% covered ≥10x	% covered ≥20x	% covered ≥30x	% covered ≥50x
A2ML1	610627	100	99.92	99.35	96.69
BRAF	164757	100	99.25	98.19	92.07
CBL	165360	100	100	100	97.75
HRAS	190020	100	100	100	100
KRAS	190070	100	100	100	100
LZTR1	600574	100	100	100	96.12
MAP2K1	176872	100	100	99.21	93.07
MAP2K2	601263	100	99.89	96.23	84.15
MRAS	608435	100	100	100	99.79
NF1	613113	100	99.31	97.66	91.70
NRAS	164790	100	100	100	99.07
PPP1CB	600590	100	100	100	93.69
PTPN11	176876	98.37	98.37	98.37	98.28
RAF1	164760	100	100	97.97	93.07
RIT1	609591	100	100	100	100
RRAS2	600098	100	100	98.16	82.51
SHOC2	602775	100	100	100	97.82
SOS1	182530	100	97.71	97.35	91.97
SOS2	601247	99.08	97.55	95.49	87.28
SPRED1	609291	100	100	100	99.18

- OMIM release used: 18-2-2021
- The statistics above are based on a set of 100 samples
- % Covered 10x , 20x, 30x and 50x describes the percentage of a gene's coding sequence (±10bp flanking introns) that is covered at least 10x, 20x, 30x or 50x