Whole Exome Sequencing
Gene package Noonan syndrome/RASopathies, postnatal
version 1.1, 30-9-2020

Technical information
DNA was enriched using Agilent SureSelect DNA + 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 Alissa Interpret 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).

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HGNC approved gene symbol	OMIM gene ID (active link to omim.org)	median depth	% covered >10x	% covered >20x	% covered >30x
A2ML1	610627	128	100	100	100
BRAF	164757	84	100	99	94
CBL	165360	130	100	100	99
HRAS	190020	426	100	100	100
KRAS	190070	59	90	78	77
LZTR1	600574	242	100	100	100
MAP2K1	176872	148	100	100	99
MAP2K2	601263	276	100	100	100
MRAS	608435	160	100	100	100
NF1	613113	88	97	91	85
NRAS	164790	107	100	100	99
PPP1CB	600590	90	100	100	97
PTPN11	176876	80	98	94	89
RAF1	164760	124	100	98	97
RIT1	609591	123	100	100	100
RRAS2	600098	90	100	90	82
SHOC2	602775	74	100	100	96
SOS1	182530	74	94	89	79
SOS2	601247	64	95	80	67
SPRED1	609291	108	100	100	98

- 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