Specifications Sanquin Molecular diagnostics for TP53 (X023)

Sanquin diagnostics is a certified center by the European Research Initiative on CLL (ERIC) for analysis of TP53 gene mutations.

Design TP53 Panel
The Ion AmpliSeq TP53 panel (TP53.20140108) exists of 24 amplicons and is covering 100% of submitted areas (all coding regions (exons)) and is able to analyze variants in TP53. Indicated exons (Table 1) include flanking intronic regions based on 5 base exon padding. For exon 2 and 3 the 5 base exon padding is not achieved. See Table 2 for detailed coverage information.

Table 1. Design TP53 panel

Gene	Chromosome	NCBI Transcript	Exon	Coverage %
TP53	chr17	NM_000546.5	2-11 (full)	100
TP53β	chr17	NM_001126114.2	alt 10	100
TP53γ	chr17	NM_001126113.2	alt 10	100

Table 2. Aberrant covered regions TP53 panel

Gene	Exon	Coding region
TP53	2	c.-5 - c.74+2
TP53	3	c.75-5 - c.96+2

Coverage of the NGS TP53 Panel
Coverage is the number of times a base is sequenced. The deeper the coverage of each base the greater the reliability and sensitivity of the sequencing assay. The minimum depth of coverage required for detection of somatic variants with the TP53 Panel is 500X. The percentage of Target Base coverage (%Base500x) is the percentage of target bases in a panel that is covered at least 500 times.

Coverage for the NGS TP53 panel is in silico validated and is 100% for all amplicons. The percentage of target bases that is covered at least 500 times (%Base500x) is 100% at 200.000 Mapped Reads and no amplicons are encountered below 500x coverage.

Reporting: addition hematological malignancies variants
This test does not distinguish between somatic and germ line alterations in analyzed gene regions, particularly when variant allele frequencies (VAF) are near 50% or 100%. If nucleotide alterations in genes associated with germline mutation syndromes are present and there is also a strong clinical suspicion or family history of malignant disease predisposition, appropriate genetic counselling may be indicated.

Correlation with clinical, histopathologic and additional laboratory findings is required for final interpretation of the results. The final interpretation of results for clinical management of the patient is the responsibility of the managing physician.

NGS data are interpreted with the current knowledge concerning variants in relation to disease or as explanation of a phenotype. For reporting variants, the following guidelines will be followed: 'Best Practice Guidelines for Reporting Molecular Genetics results' written by R.J.L. Treacy and D.O. Robinson. The authorization of the results is done by a recognized Clinical molecular geneticist. All variants are annotated and reported as designated by the Human Genome Variation Society (HGVS) nomenclature, as described at their website.