Pediatric Oncology

SALSA® MLPA® is the preferred method for determining copy number (CN) status in genes linked to childhood cancers. MRC Holland provides over 60 MLPA assays specifically designed to detect CN changes, selected variants, and methylation profiles in germline and somatic pediatric oncology applications.

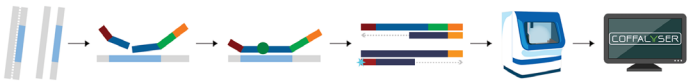
digitalMLPA™, a more recent adaptation of the MLPA technology, combines the robustness and simplicity of MLPA with the high throughput of NGS platforms. Our digitalMLPA NXtec™ assays can analyse a greater number of genomic targets in a single reaction, providing a comprehensive cancer genetic profile.

Both technologies share features that make them well-suited for cancer applications:

- Unparalleled copy number detection.
- High reliability even in complex genomic regions such as *PTEN* and *PMS2*.
- Quick turnaround time.
- Wide CN detection range – from chromosomes to single exons.
- Free software, simple analysis and clear-cut results.

MLPA

- ✓ Multiplex PCR-based method for targeted CN, methylation status, and selected single nucleotide changes determination
- ✓ Required equipment: thermocycler and capillary electrophoresis device
- ✓ 40-60 targets per reaction
- ✓ 50 ng of DNA input per sample

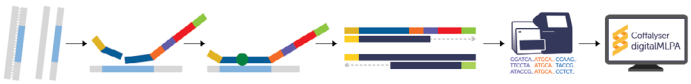


Highlighted Applications

Acute Lymphoblastic Leukemia (ALL)	**P335** ALL-IKZF1 **P202** IKZF1-ERG **P327** iAMP21-ERG **P383** T-ALL
Neuro-oncology	**P088** Oligodendroglioma 1p-19q **P105** Glioma **P370** BRAF-IDH1-IDH2 **ME012** MGMT-IDH-TERT
Li-Fraumeni Syndrome	**P056** TP53 **P190** CHEK2

digitalMLPA

- ✓ NGS-based MLPA for targeted CN status and selected single nucleotide changes determination
- ✓ Required equipment: thermocycler and Illumina sequencing platform
- ✓ 600-1200 targets per reaction
- ✓ 20 ng of DNA input per sample



Highlighted Applications

Predisposition to Cancer	**NXtec D002 Hereditary Cancer Panel 2** Broad panel targeting a wide range of genes associated with a hereditary predisposition to various types of cancer.
Acute Lymphoblastic Leukemia (ALL)	**NXtec D007 Acute Lymphoblastic Leukemia** – 73 ALL-related genes and 8 ALL-related regions; hyperdiploidy and hypodiploidy.

MRC Holland

Confidence in Copy Number Determination

www.mrcholland.com | info@mrcholland.com | tel +31 88 865 7200

F-PO-0021D

GERMLINE

digitalMLPA assay	Target genes/regions
NXtec D001 Hereditary Cancer Panel 1	*APC, ATM, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, MITF* (p.E318K), *MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, POLE, PTEN, RAD51C, RAD51D, SCG5/GREM1, SMAD4, STK11, TP53*
NXtec D002 Hereditary Cancer Panel 2	All D001 targets + *CEBPA, DICER1, FH, FLCN, HOXB13, MAX, MEN1, MET, NF1, NF2, NTHL1, PHOX2B, POLD1, PTCH1, RB1, RUNX1, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMARCB1, SUFU, TMEM127, TSC1, TSC2, VHL, WT1*

Hematologic Malignancies

SALSA® MLPA® Probemix	Target genes/regions
P327 iAMP21-ERG	*iAMP21, RUNX1, ERG*
P437 Familial MDS-AML	*GATA2* (+p.R398W, p.T354M), *TERC, TERT* (+p.A1062T), *CEBPA, RUNX1*

DNA Instability Syndromes

P031 FANCA mix 1 **P032** FANCA mix 2	*FANCA*
P041 ATM-1 **P042** ATM-2	*ATM*
P057 FANCD2-PALB2	*FANCD2, PALB2*
P113 FANCB	*FANCB*
P212 DBA	*RPL11, RPL35A, RPS17, RPS19, RPS26, RPL5*
P260 PALB2-RAD50-RAD51C-RAD51D	*PALB2, RAD50, RAD51C, RAD51D*
P494 NBN	*NBN*

Li-Fraumeni Syndrome

P056 TP53	*TP53, CHEK2* (+c.del1100C)
P190 CHEK2	*CHEK2* (+c.del1100C), *ATM, TP53*

Familial Adenomatous Polyposis

P043 APC	*APC*
P378 MUTYH	*MUTYH* (+c.536A>G, c.1187G>A), *SCG5/GREM1*

Neurofibromatoses

P081 NF1 mix 1 **P082** NF1 mix 2	*NF1*
P044 NF2	*NF2*
P122 NF1-area	*NF1* area on 17q11.2
P258 SMARCB1	*SMARCB1*
P295 SPRED1	*SPRED1*
P455 LZTR1	*LZTR1*
P478 SMARCE1	*SMARCE1*

Neural Tumour Syndromes

P047 RB1#	*RB1+* flanking region and methylation profiling of *RB1*
P067 PTCH1	*PTCH1*
P472 SUFU	*SUFU*

Neuroendocrine Syndromes

P016 VHL	*VHL*
P017 MEN1	*MEN1*
P226 SDH	*SDHB, SDHC, SDHD, SDHAF1, SDHAF2*
P244 AIP-MEN1-CDKN1B	*AIP, MEN1, CDKN1B*
P429 SDHA-MAX-TMEM127	*SDHA, MAX, TMEM127*
P466 CDC73	*CDC73, B3GALT2*

Mismatch Repair Deficiency

P003 MLH1/MSH2	*MLH1, MSH2, EPCAM*
P008 PMS2	*PMS2, PMS2CL*
P072 MSH6-MUTYH	*MSH2, MSH6, EPCAM, MUTYH* (+c.536A>G, c.1187G>A)
P248 MLH1-MSH2 Confirmation	*MLH1, MSH2*
ME011 Mismatch Repair Genes#	*MLH1* methylation, *BRAF* p.V600E point mutation and associated Lynch syndrome genome changes profiling

Other

ME030 BWS/RSS#	Copy number analysis and methylation profiling of *KCNQ1OT1*:TSS (IC2), *H19/IGF2*:IG (IC1), *IGF2*:alt-TSS
P101 STK11	*STK11*
P118 WT1	*WT1, AMER1*
P225 PTEN	*PTEN, PTENP1*
P257 TERT-DKC1	*DKC1, TERT, TERC*
P481 PRKAR1A-ARMC5	*PRKAR1A, ARMC5*
P482 DICER1	*DICER1*

SOMATIC

Hematologic Malignancies

digitalMLPA assay	Target genes/regions
NXtec D007 Acute Lymphoblastic Leukemia	*ADD3, BACH2, BCL2L1, BTG1, BTLA, CASP8AP2, CD200, CDKN1B, CDKN2A, CDKN2B, CDX2, CREBBP, CTCF, DMD, DNMT3A, DNMT3B, EPHA1, EPHA7, EPOR, ERG, ETV6, EZH2, FHIT, FLT1, FLT3, IGHM, IKZF1, IKZF2, IKZF3, JAK2, KRAS, LEF1, LMO1, MAP3K7, MEF2C, MLLT3, MTAP, MYB, NF1, NOTCH1, NR3C1, NR3C2, PAN3, PAX5, PHF6, PRAMENP, PTEN, PTPN2, RB1, RUNX1, SPRED1, SUZ12, TBL1XR1, TOX, TP53, VPREB1,* 5q, 6q15-q16.1, 13q12.2-q12.3, 17q21, 20q11.21 (dic(9:20) breakpoint), 21q (iAMP21), 22q11.22, PAR1 region and fusion indications (*MEF2D-BCL9, MEF2D-HNRNPH1, MEF2D-NRNPUL1, MEF2D-DAZAP1, NUP214-ABL1, PDGFRB-EBF1, RAG2-LMO2, STIL-TAL1, TCF3-HLF, TCF3-PBX1, UBTF-ATXN7L3*)

SALSA® MLPA® Probemix	Target genes/regions
ME024 9p21 CDKN2A/2B region#	*CDKN2A/2B, MTAP, MIR31, PAX5* and methylation profiling of *CDKN2A/2B*
P202 IKZF1-ERG	*IKZF1, ERG, CDKN2A/2B,* 14q32
P327 iAMP21-ERG	iAMP21, *RUNX1, ERG*
P329 CRLF2-CSF2RA-IL3RA	Xp22.33 PAR1 region (*SHOX, CRLF2, CSF2RA, IL3RA*)
P335 ALL-IKZF1	*IKZF1, PAX5, ETV6, RB1, BTG1, EBF1,* 9p21.3 (*CDKN2A/2B*), Xp22.33, PAR1 region
P377 Hematologic malignancies	*ALK, ATM, CDKN2A/2B, DLEU1/2, EBF1, ETV6, IKZF1, MIR15A, MIR145, MIR146A, MTAP, MYC, MYCN, PAX5, PTEN, RB1, RUNX1, TP53,* 6q, 7q, 12q, 17q, chr. 18, chr. 19, *JAK2* (p.V617F)
P383 T-ALL	*STIL-TAL1, LEF1, CASP8AP2, MYB, EZH2, CDKN2A/2B, MTAP, MLLT3, NUP214-ABL1, PTEN, LMO1, LMO2, NF1, SUZ12, PTPN2, PHF6*
P437 Familial MDS-AML	*GATA2* (+p.R398W, p.T354M), *TERC, TERT* (+p.A1062T), *CEBPA, RUNX1*
P496 KMT2A	*5q (CTNNA1, NPM1), 7p (IKZF1), 7q (CUX1, KMT2E, EZH2), 11q (ATM and KMT2A PTDs), 17p (TP53, NF1), ASXL1 (c.1934dupG)*

Gliomas

ME012 MGMT-IDH-TERT#	Methylation profiling of *MGMT, IDH1* (p.R132H/C), *IDH2* (p.R172K/M), *TERT* (C228T, C250T)
P088 Oligodendroglioma 1p-19q	1p, 9p21 (*CDKN2A/2B*), 19q, *IDH1* (p.R132H/C), *IDH2* (p.R172K/M)
P105 Glioma	*TERT* (C228T, C250T), chr. 7 (*EGFR*), chr. 10 (*PTEN*), *CDKN2A, CDK4, MIR26A2, MDM2, NFKBIA, PDGFRA, TP53*
P370 BRAF-IDH1-IDH2	3p (*SRGAP3-RAF1*), 6q (*MYB*), 7q (*KIAA1549-BRAF*), 8p (*FGFR1-TACC1*), 8q (*MYBL1*), 9p21, *IDH1* (p.R132H/C), *IDH2* (p.R172K/M), *BRAF* (p.V600E)

Neuroblastoma

P251 NB mix 1 **P252** NB mix 2 **P253** NB mix 3	Chr. 1, 2 (*NBAS, DDX1, MYCN, ALK, BMPR2*), 3, 4, 7, 9 (*PTPRD, CDKN2A*), 11, 12, 14q, 17 (*TP53, WSB1*)

Medulloblastoma

P301 Medulloblastoma mix 1 **P302** Medulloblastoma mix 2 **P303** Medulloblastoma mix 3	Chr. 1, 2, 3, 4q, 5q, 6, 7, 8, 9, 10, 14q, 16, 17, 20

Other

P056 TP53	*TP53, CHEK2* (+c.del1100C)
P258 SMARCB1	*SMARCB1*
P308 MET	*MET, PTEN, LRRK2*
P380 Wilms' tumour	1p/q, 2p (*MYCN*), 2q, 4q (*FBXW7*), 11p (*WT1*), 16p/q, 17p (*TP53*), Xq11 (*AMER1*)
P419 CDKN2A/2B-CDK4	*CDKN2A/2B, CDK4, MITF* (p.E318K)
P433 ARID1A-ARID1B	*ARID1A, ARID1B*
P482 DICER1	*DICER1*

This probemix also includes probes that determine the methylation status of a target.