



SALSA® MLPA® is the method of choice for the detection of copy number alterations (CNAs) in cancer. MRC Holland offers over 50 MLPA assays specifically designed to detect CNAs and select point mutations in hundreds of commonly affected cancer genes. For neoplasms in which DNA methylation plays a role, such as glioma and Lynch syndrome-related cancers, we offer MLPA assays that combine genomic analysis with easy bisulfite-free methylation profiling.

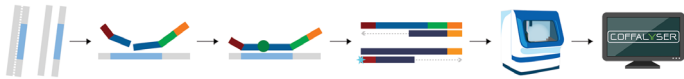
SALSA® digitalMLPA™, a more recent adaptation of the MLPA technology, combines the robustness and simplicity of MLPA with the high throughput of NGS platforms. With our digitalMLPA probemixes, more than 1000 cancer-related DNA sequences can be targeted!

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

- Unparalleled copy number detection.
- High reliability even in complex genetic regions.
- Wide detection range – from chromosomes to single exons.
- Free software, simple analysis and clear-cut results.

MLPA

- ✓ Multiplex PCR-based method for CNA, methylation and targeted mutation detection
- ✓ Needed: thermocycler and capillary electrophoresis device
- ✓ 40-60 targets per reaction
- ✓ 50 ng of DNA input per sample

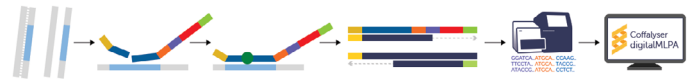


Top-Selling Applications

Colon cancer (Lynch Syndrome)	ME011 Mismatch Repair Genes
Acute Lymphoblastic Leukemia	P335 ALL-IKZF1 P202 IZKF1-ERG P327 iAMP21-ERG P383 T-ALL
Gliomas	P088 Oligodendroglioma ME012 MGMT-IDH-TERT P105 Glioma-2 P370 BRAF-IDH1-IDH2

digitalMLPA

- ✓ NGS-based MLPA for CNA, methylation and targeted mutation detection
- ✓ Needed: thermocycler and Illumina sequencing platform
- ✓ 600-1000 targets per reaction
- ✓ 20 ng of DNA input per sample



Novel developments

Multiple Myeloma	D006 Multiple Myeloma – 1p, 1q, 13q, 17p and trisomies (3, 5, 7, 9, 11, 15, 19, 21)
Acute Lymphoblastic Leukemia	D007 Acute Lymphoblastic Leukemia – 55 genes and regions, and hyper-/hypodiploidy

SALSA® FFPE Solution

for reliable MLPA results on FFPE material

- ✓ Low-cost reagent for extraction, no costly columns
- ✓ Limited hands-on time
- ✓ Simple extraction steps performed in one tube
- ✓ No deparaffinization step with xylene required
- ✓ High DNA yield

SALSA® FFPE Solution (SFS) was created to reduce the challenges that come when working with FFPE material. The SFS method yields DNA that gives reliable MLPA results using crude tissue lysates. When optimal tissue fixation and DNA extraction methods are chosen, FFPE extracted DNA can be well suited for use with many of our MLPA assays and other molecular applications.

General Tumour Profiling

SALSA® MLPA® Probemix	Target genes/regions
ME001 Tumour suppressor mix*	Tumour suppressor gene methylation profiling
ME024 9p21 CDKN2A/2B region*	<i>CDKN2A/2B, MTAP, MIR31, PAX5</i>
P175 Tumour Gain	Multiple genes/regions
P181 Centromere mix 1 P182 Centromere mix 2	Centromeres
P294 Tumour Loss	Multiple genes/regions
P298 BRAF-HRAS-KRAS-NRAS	<i>BRAF, HRAS, KRAS, NRAS</i>
P323 CDK4-HMGA2-MDM2	12p, 12q, <i>GLI1, CDK4, HMGA2, MDM2</i>
P451 Chromosome 16	Chr. 16
P474 CD274-PDCD1LG2-JAK2	<i>CD274 (PD-L1), PDCD1LG2 (PD-L2), JAK2</i>

Leukemia & Lymphoma

SALSA® digitalMLPA™ Probemix	Target genes/regions
D006 Multiple Myeloma	1p (<i>FAF1, CDKN2C, DAB1, EVI5, RPL5, CDC14A, TENT5C</i>), 1q (<i>ANP32E, MCL1, ADAR, CKS1B, SLAMF7, PBX1</i>), 4p (<i>FGFR3, NSD2</i>), 11q (<i>CCND1, BIRC2/3, ATM</i>), 12p, 13q, 14q, 16q (<i>CYLD, WWOX</i>), 17p (<i>TP53</i>), 20q (<i>MAFB</i>), Xp (<i>KDM6A</i>), trisomies, <i>BCMA, CRBN, GPRC5D, FcRH5, IKZF1/3, IRF4, MYC, RPL5, SLAMF7, BRAF (V600E)</i>
D007 Acute Lymphoblastic Leukemia	5q (terminal) deletion region, <i>ADD3, BTG1, BTLA, CASP8AP2, CDKN2A/2B, CD200, CREBBP, CTCF, DMD, EBF1-PDGFRB, EPHA1, ETV6, EZH2, FHIT</i> , Hyperdiploidy, Hypodiploidy, iAMP21 region (including <i>RUNX1, ERG</i>), <i>IGHM, IKZF1, IKZF2, IKZF3, JAK2, LEF1, LMO1, MLLT3, MTAP, MYB, NF1, NOTCH1, NR3C1, NR3C2, NUP214-ABL1, PAR1</i> region, <i>PAX5, PDGFRB, PHF6, PTEN, PTPN2, RAG2-LMO2, RB1, SPRED1, STIL-TAL1, SUZ12, TBL1XR1, TOX, TP53, VPREB1</i>

SALSA® MLPA® Probemix	Target genes/regions
P037 CLL-1	11q22.3 (<i>ATM</i>), chr. 12, 13q14, 17p13 (<i>TP53</i>), 2p, 6q, 8, 9p21
P038 CLL-2	11q22-q23, chr. 12, 13q14, 17p13 (<i>TP53</i>), 10q23, 14q32, chr. 19, <i>NOTCH1 (7541_7542delCT), SF3B1 (K700E), MYD88 (L265P)</i>
P040 CLL	11q13-q25, chr. 12, 13q14, 17p13 (<i>TP53</i>)
P041 ATM-1 / P042 ATM-2	<i>ATM</i>
P047 RB1*	<i>RB1</i>
P056 TP53	<i>TP53, CHEK2 (+del1100C)</i>
P202 IKZF1-ERG	<i>IKZF1, ERG, CDKN2A/2B, 14q32</i>
P323 CDK4-HMGA2-MDM2	12p, 12q (<i>GLI1, CDK4, HMGA2, MDM2</i>)
P327 iAMP21-ERG	<i>iAMP21, RUNX1, ERG</i>
P329 CLR2-CSF2RA-IL3RA	Xp22.33 PAR1 region (<i>SHOX, CRLF2, CSF2RA, IL3RA</i>)
P335 ALL-IKZF1	<i>IKZF1, PAX5, ETV6, RB1, BTG1, EBF1, 9p21.3 (CDKN2A/2B), Xp22.33 PAR1 region</i>
P377 Hematologic Malignancies	2p (<i>MYCN, ALK</i>), 5q (<i>MIR145, EBF1, MIR146A</i>), 6q, 7p12 (<i>IKZF1</i>), 7q, 8q24 (<i>MYC</i>), 9p (<i>JAK2 (V617F), MTAP, CDKN2A/2B, PAX5</i>), 10q23 (<i>PTEN</i>), 11q22.3 (<i>ATM</i>), 12p (<i>ETV6</i>), 12q, 13q (<i>RB1, MIR15A, DLEU1/2</i>), 17p (<i>TP53</i>), 17q, chr. 18, chr. 19, 21q (<i>RUNX1</i>)
P383 T-ALL	<i>STIL-TAL1, LEF1, CASP8AP2, MYB, EZH2, CDKN2A/2B, MTAP, MLLT3, NUP214-ABL1, PTEN, LMO1, LMO2, NF1, SUZ12, PTPN2, PHF6</i>
P414 MDS	Chr. 3, 5q, 7q (<i>EZH2</i>), 8q (<i>MYC</i>), 11q (<i>KMT2A</i>), 12p (<i>ETV6</i>), chr. 17 (<i>TP53, NF1, SUZ12</i>), chr. 19, 20q, chr. Y, <i>JAK2 (V617F)</i>
P419 CDKN2A/2B-CDK4	<i>CDKN2A/2B, CDK4, MITF (E318K)</i>
P420 MPN mix 1	Point mutation detection with only >10% mutation burden for <i>JAK2 (V617F, E543_D544del, N542_E543del), CALR (52-bp deletion, 5-bp insertion), MPL (W515L, W515K), KIT (D816V)</i>
P425 Multiple Myeloma	1p12-p32, 1q21-q23, 5q31, chr. 9, 12p13, 13q14 (<i>RB1, DLEU1/2</i>), 14q32 (<i>TRAF3</i>), 16q12-q23 (<i>CYLD, WWOX</i>), 17p13 (<i>TP53</i>)
P437 Familial MDS-AML	<i>GATA2 (+R398W, T354M), TERC, TERT (+A1062T), CEBPA, RUNX1</i>
P520 MPN mix 2	Point mutation detection with only >1% mutation burden for <i>JAK2 (V617F, E543_D544del, N542_E543del), CALR (52-bp deletion, 5-bp insertion), MPL (W515L, W515K), KIT (D816V)</i>

Other Solid Tumours

SALSA® MLPA® Probemix	Target genes/regions
ME011 Mismatch Repair Genes*	<i>MLH1</i> methylation, <i>BRAF p.V600E</i> point mutation and associated Lynch syndrome genome changes profiling
ME012 MGMT-IDH-TERT*	Methylation profiling of <i>MGMT, IDH1 (R132H/C), IDH2 (R172K/M), TERT (C228T, C250T)</i>
ME042 CIMP*	Methylation profiling of <i>CACNA1G, CDKN2A, CRABP1, IGF2, MLH1, NEUROG1, RUNX3, SOCS1</i>
ME053 BRCA1-BRCA2-RAD51C	Methylation profiling of <i>BRCA1, BRCA2, RAD51C</i>
P027 Uveal melanoma	1p, chr. 3, chr. 6, chr. 8
P044 NF2	<i>NF2</i>
P047 RB1*	<i>RB1</i>
P056 TP53	<i>TP53, CHEK2 (+del1100C)</i>
P078 Breast tumour	6q (<i>ESR1</i>), 7p (<i>EGFR</i>), 8p (<i>ZNF703, FGFR1, IKBKB</i>)/8q (<i>MTDH, MYC</i>), 11q13 (<i>CCND1, EMSY</i>), 16q (<i>CDH1</i>), 17q12-q25 (<i>ERBB2, TOP2A, BIRC5</i>), 19q (<i>CCNE1</i>), 20q (<i>AURKA</i>)
P088 Oligodendroglioma 1p-19q	1p/q, 9p21, 19p/q, <i>IDH1 (R132H/C), IDH2 (R172K/M)</i>
P105 Glioma-2	<i>EGFR, PTEN, CDKN2A, TP53, PDGFRA, NFKBIA, CDK4, MIR26A2, MDM2</i>
P225 PTEN	<i>PTEN, PTENP1</i>
P244 AIP-MEN1-CDKN1B	<i>AIP, MEN1, CDKN1B</i>
P251 NB mix 1 P252 NB mix 2 P253 NB mix 3	Chr. 1, 2 (<i>NBAS, DDX1, MYCN, ALK, BMPR2</i>), 3, 4, 7, 9 (<i>PTPRD, CDKN2A</i>), 11, 12, 14q, 17 (<i>TP53, WSB1</i>)
P258 SMARCB1	<i>SMARCB1</i>
P298 BRAF-HRAS-KRAS-NRAS	<i>BRAF, HRAS, KRAS, NRAS</i>
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
P308 MET	<i>MET, PTEN, LRRK2</i>
P315 EGFR	<i>EGFR (+L858R, T790M)</i>
P323 CDK4-HMGA2-MDM2	12p, 12q (<i>GLI1, CDK4, HMGA2, MDM2</i>)
P370 BRAF-IDH1-IDH2	3p (<i>SRGAP3-RAF1</i>), 6q (<i>MYB</i>), 7q (<i>KIAA1549-BRAF</i>), 8p (<i>FGFR1-TACC1</i>), 8q (<i>MYBL1</i>), 9p21, <i>IDH1 (R132H/C), IDH2 (R172K/M), BRAF (V600E)</i>
P378 MUTYH	<i>MUTYH, SCG5, GREM1</i>
P380 Wilms' tumour	1p/q, 2p (<i>MYCN</i>), 2q, 4q (<i>FBXW7</i>), 11p (<i>WT1</i>), 16p/q, 17p (<i>TP53</i>), Xq11 (<i>AMER1</i>)
P417 BAP1	<i>BAP1</i>
P419 CDKN2A/2B-CDK4	<i>CDKN2A/2B, CDK4, MITF (E318K)</i>
P429 SDHA-MAX-TMEM127	<i>SDHA, MAX, TMEM127</i>
P433 ARID1A-ARID1B	<i>ARID1A, ARID1B</i>
P451 Chromosome 16	Chr. 16
P455 LZTR1	<i>LZTR1</i>
P466 CDC73	<i>CDC73</i>
P472 SUFU	<i>SUFU</i>
P476 ZNRF3	<i>ZNRF3</i>
P478 SMARCE1	<i>SMARCE1</i>
P481 PRKAR1A-ARMCS	<i>PRKAR1A, ARMCS</i>
P482 DICER1	<i>DICER1</i>
P483 HER gene family	<i>EGFR, ERBB2, ERBB3, ERBB4</i>

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