Hematologic Disorders and Neoplasms

SALSA® MLPA® is the technique of choice for the determination of copy number (CN) status in genes associated with blood disorders. MRC Holland offers over 50 MLPA assays specifically designed to detect CN changes as well as selected SNVs and point mutations in hematologic disorders and neoplasms.

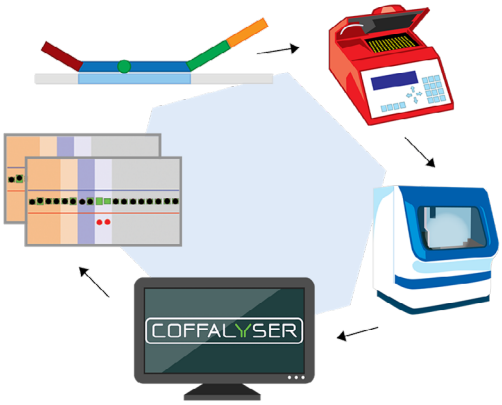
digitalMLPA™, our more recent technique, combines the robustness and simplicity of MLPA with the high throughput of NGS platforms. With our digitalMLPA assays, up to 1600 DNA sequences can be targeted.

Both technologies share features that makes them well-suited for hematologic applications:

- Unparalleled copy number detection.
- Wide CN detection range – from whole chromosomes to single exons.
- High reliability even in complex genetic regions such as *PTEN* and *HBA1*/*HBA2*.
- Simple analysis and clear-cut results with our free software.

MLPA

- ✓ Multiplex PCR-based method for CN and methylation status determination
- ✓ Selected single nucleotide changes detection
- ✓ Needed: thermocycler and capillary electrophoresis device
- ✓ 40-60 targets per reaction
- ✓ 50 ng of DNA input per sample



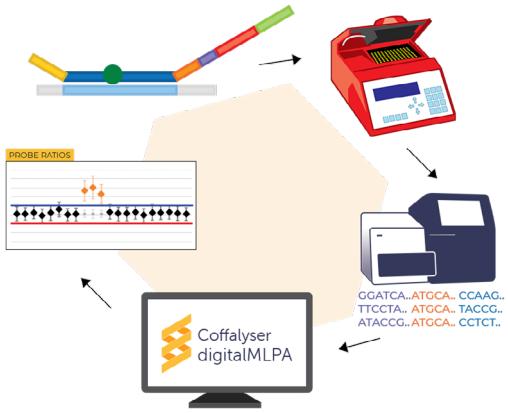
Highlights

Top-selling MLPA Applications

Thalassemia	**P140** HBA **P102** HBB
Acute Lymphoblastic Leukemia	**P335** ALL-IKZF1 **P202** IKZF1-ERG **P327** iAMP21-ERG **P383** T-ALL
Ataxia-telangiectasia	**P041** ATM-1 **P042** ATM-2
Myeloproliferative Neoplasms	**P420** MPN mix 1 **P520** MPN mix 2

digitalMLPA

- ✓ NGS-based MLPA for CN status determination
- ✓ Selected single nucleotide changes detection
- ✓ Needed: thermocycler and NGS platform
- ✓ Up to 1600 targets per reaction
- ✓ 20 ng of DNA input per sample
- ✓ Combine digitalMLPA with other libraries to maximise sequencing capacity



Highlights

New releases

Acute Lymphoblastic Leukemia	**NXtec D007 Acute Lymphoblastic Leukemia** – 73 ALL-related genes and 8 ALL-related regions; hyperdiploidy and hypodiploidy
Carrier Status	**NXtec D028 Carrier Panel 1** – HBA and HBB regions. Also detects *SMN1*, *DMD*, *CYP21A2*, *CFTR*, *CLN3*, DFNB1 region and *CTNS*.

Hereditary Hematologic Disorders

digitalMLPA assay	Target genes/regions
NXtec D028 Carrier Panel 1	HBA and HBB regions. Also detects *SMN1*, *DMD*, *CYP21A2*, *CFTR*, *CLN3*, DFNB1 region and *CTNS*.

SALSA® MLPA® Probemix	Target genes/regions
P011 VWF mix 1 **P012** VWF mix 2	*VWF*
P013 ATRX	*ATRX*
P102 HBB	*HBB* cluster
P140 HBA	*HBA* cluster
P031 FANCA mix 1 **P032** FANCA mix 2	*FANCA*
P057 FANCD2-PALB2	*FANCD2, PALB2*
P113 FANCB	*FANCB*
P260 PALB2-RAD50-RAD51C-RAD51D	*PALB2, RAD50, RAD51C, RAD51D*
P236 CFH Region	*CFH, CFHR1, CFHR2, CFHR3, CFHR4, CFHR5*
P240 BRIP1/CHEK1	*BRIP1/CHEK1*
P296 aHUS	*CFI, CD46*
P178 F8	*F8*
P207 F9	*F7, F8, F9*
P440 F10 + F11	*F10, F11*
P469 F5	*F5*
P203 PKLR	*PKLR*
P210 BTK	*BTK*
P112 PROS1	*PROS1*
P212 DBA	*RPL11, RPL35A, RPS17, RPS19, RPS26, RPL5*
P227 SERPINC1	*SERPINC1*
P257 TERT-DKC1	*DKC1, TERT, TERC*
P265 PROC	*PROC*
P432 MYH9	*MYH9*
P490 ADA2	*ADA2*

Leukemia & Lymphoma
Predisposition

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*
NXtec D007 Acute Lymphoblastic Leukemia	*CDKN2A, ETV6, IKZF1, PAX5, PTEN, TP53*

SALSA® MLPA® Probemix	Target genes/regions
P031 FANCA mix 1 / **P032** FANCA mix 2	*FANCA*
P057 FANCD2-PALB2	*FANCD2, PALB2*
P113 FANCB	*FANCB*
P260 PALB2-RAD50-RAD51C-RAD51D	*PALB2, RAD51C, RAD51D, RAD50*
P041 ATM-1 / **P042** ATM-2	*ATM*
P056 TP53	*TP53, CHEK2* (+c.del1100C)
P212 DBA	*RPL11, RPL35A, RPS17, RPS19, RPS26, RPL5*
P202 IKZF1-ERG	*IKZF1, ERG, CDKN2A/2B,* 14q32
P327 iAMP21-ERG	iAMP21, *RUNX1, ERG*
P335 ALL-IKZF1	*IKZF1, PAX5, ETV6, RB1, BTG1, EBF1,* 9p21.3 (*CDKN2A/2B*), Xp22.33, PAR1 region
P437 Familial MDS-AML	*GATA2* (+p.R398W, p.T354M), *TERC, TERT* (+p.A1062T), *CEBPA, RUNX1*

Leukemia & Lymphoma
Somatic

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*)
NXtec D006 Multiple Myeloma	1p (*FAF1, CDKN2C, DAB1, EVI5, RPL5, CDC14A, TENT5C*), 1q (*ANP32E, MCL1, ADAR, CKS1B, SLAMF7, PBX1*),4p (*FGFR3, NSD2*), 11q (*CCND1, BIRC2/3, ATM*), 12p, 13q, 14q, 16q (*CYLD, WWOX*), 17p (*TP53*), 20q (*MAFB*), Xp (*KDM6A*), *BCMA, CRBN, GPRC5D, FcRH5, IKZF1/3, IRF4, MYC, RPL5, SLAMF7,* trisomies and *BRAF* (p.V600E)

SALSA® MLPA® Probemix	Target genes/regions
P202 IKZF1-ERG	*IKZF1, ERG, CDKN2A/2B,* 14q32
P327 iAMP21-ERG	iAMP21, *RUNX1, ERG*
P329 CRLF2-CSF2RA-IL3RA	p22.33 PAR1 region (*SHOX, CRLF2, CSF2RA, IL3RA*)
P335 ALL-IKZF1	*IKZF1, PAX5, ETV6, RB1, BTG1, EBF1,* 9p21.3 (*CDKN2A/2B*), Xp22.33, PAR1 region
P383 T-ALL	*STIL-TAL1, LEF1, CASP8AP2, MYB, EZH2, CDKN2A/2B, MTAP, MLLT3, NUP214-ABL1, PTEN, LMO1, LMO2, NF1, SUZ12, PTPN2, PHF6*
ME024 9p21 CDKN2A/2B region	*CDKN2A/2B, MTAP, MIR31, PAX5* and methylation profiling of *CDKN2A/2B*
P414 MDS	Chr. 3, 5q, 7q, 8q, 11q (*KMT2A*), 12p (*ETV6*), chr. 17 (*TP53*), chr. 19, 20q, chr. Y, *JAK2* (p.V617F)
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)
P037 CLL-1	2p (*MYCN, ALK, REL*), 6q (*TNFAIP3*), 8p (*TNFRSF10A/B*), 8q (*EIF3H, MYC*), 9p21 (*CDKN2A/B*), 11q (*ATM*), chromosome 12, 13q14 (*MIR15A, DLEU2/7*), 17p (*TP53*)
P038 CLL-2	10q23 (*PTEN*), 11q (*ATM*), chromosome 12, 13q14 (*RB1, DLEU1/2*), 14q, 17p13 (*TP53*), chr. 19 and *NOTCH1* (p.P2514Rfs*4), *SF3B1* (p.K700E), *MYD88* (p.L265P)
P040 CLL	11q13-q25, chr. 12, 13q14, 17p13 (*TP53*)
P425 Multiple Myeloma	1p12-p32, 1q21-q23, 5q31, chr. 9, 12p13, 13q14, 14q32 (*TRAF3*), chr. 15, 16q12-q23 (*CYLD, WWOX*), 17p13 (*TP53*)
P420 MPN mix 1	Point mutation detection with only >10% mutation burden for *JAK2* (p.V617F, p.E543_D544del, p.N542_E543del), *MPL* (p.W515L, p.W515K), *KIT* (p.D816V), *CALR* (p.L367fs*46, p.K385fs*47)
P520 MPN mix 2	Point mutation detection with only >1% mutation burden for *JAK2* (p.V617F, p.E543_D544del, p.N542_E543del), *MPL* (p.W515L, p.W515K), *KIT* (p.D816V), *CALR* (p.L367fs*46, p.K385fs*47)
P377 Hematologic Malignancies	2p (*MYCN, ALK*), 5q (*MIR145, EBF1, MIR146A*), 6q, 7p12 (*IKZF1*), 7q, 8q24 (*MYC*), 9p (*MTAP, CDKN2A/2B, PAX5*), 10q23 (*PTEN*), 11q22.3 (*ATM*), 12p (*ETV6*), 12q, 13q (*RB1, MIR15A, DLEU1/2*), 17p (*TP53*), 17q, chr. 18, chr. 19, 21q (*RUNX1*), *JAK2* (p.V617F)
P047 RB1	*RB1*+ flanking, *RB1* methylation profiling
P056 TP53	*TP53, CHEK2* (+c.del1100C)
P323 CDK4-HMGA2-MDM2	12p, 12q, *GLI1, CDK4, HMGA2, MDM2*
P419 CDKN2A/2B-CDK4	*CDKN2A/2B, CDK4, MTAP, MITF* (p.E318K)

MRC Holland

Confidence in Copy Number Determination

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

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