

Product Description SALSA® MLPA® Probemix P482-A1 DICER1

To be used with the MLPA General Protocol.

Version A1. New product.

Catalogue numbers:

- **P482-025R:** SALSA MLPA Probemix P482 DICER1, 25 reactions.
- **P482-050R:** SALSA MLPA Probemix P482 DICER1, 50 reactions.
- **P482-100R:** SALSA MLPA Probemix P482 DICER1, 100 reactions.

To be used in combination with a SALSA MLPA reagent kit and Coffalyser.Net data analysis software. MLPA reagent kits are either provided with FAM or Cy5.0 dye-labelled PCR primer, suitable for Applied Biosystems and Beckman/SCIEX capillary sequencers, respectively (see www.mlpa.com).

Certificate of Analysis: Information regarding storage conditions, quality tests, and a sample electropherogram from the current sales lot is available at www.mlpa.com.

Precautions and warnings: For professional use only. Always consult the most recent product description AND the MLPA General Protocol before use: www.mlpa.com. It is the responsibility of the user to be aware of the latest scientific knowledge of the application before drawing any conclusions from findings generated with this product.

General information: The SALSA MLPA Probemix P482 DICER1 is a **research use only (RUO)** assay for the detection of deletions or duplications in the *DICER1* gene, which is associated with DICER1 syndrome.

DICER1 gene locates on 14q32.13 (hg18), consists of 27 exons and encodes cytoplasmic endoribonuclease (RNase) III enzyme. DICER1 has a central role in the RNA interference pathway, as it cleaves double-stranded RNA molecules into small RNAs including microRNA (miRNA) and small interfering RNA (siRNA). DICER facilitates the incorporation of these RNAs into Argonoute protein, forming the RNA-induced silencing complex (RISC). The activated RISC recognizes a specific mRNA target sequence and can either guide degradation or inhibit translation of the molecule.

DICER1 syndrome or *DICER1*-related pleuropulmonary blastoma cancer predisposition syndrome (OMIM 601200), is a rare pleiotropic tumour predisposition syndrome manifesting usually in children or young adults and it is characterised by benign and malignant tumours in lungs, ovaries, thyroid gland, kidneys and brain (pineal and pituitary glands). *DICER1* syndrome is inherited in an autosomal dominant pattern, but may also arise *de novo* in the germline or in a somatic mosaic manner. It is estimated that 80% of the germline pathogenic variants are inherited from a parent and 20% are *de novo* (see GeneReviews <https://www.ncbi.nlm.nih.gov/books/NBK196157/>). Most of the described mutations in *DICER1* are loss-of-function point or frameshift mutations, however, also deletions of the entire *DICER1* locus and in- or out-of-frame intragenic *DICER1* deletions have been also described (for review see De Kock et al. 2019).

Multinodular goiter-1 (MNG1) with or without Sertoli-Leydig cell tumors (OMIM 138800) is also caused by heterozygous mutations in the *DICER1* gene. Unlike *DICER1* syndrome, MNG1 is a common disorder characterized by nodular enlargement of the thyroid gland and some individuals may also develop Sertoli-Leydig cell tumors, usually of the ovary.

Additionally, mutations in *DICER1* are recurrent in diverse set of cancers e.g. in sporadic pleuropulmonary blastoma, gonadal-, Wilms' and endometrial tumours and anaplastic sarcomas of the kidney. Although miRNAs are required for normal cell fitness, selective inactivation of *DICER1*, especially mutations in the RNase IIIb domain affecting the metal ion-binding residues, can benefit cancer cells (Vedanayagam et al. 2019).

More information is available at <https://www.ncbi.nlm.nih.gov/books/NBK196157/>

This SALSA MLPA Probemix is not CE/FDA registered for use in diagnostic procedures. Purchase of this product includes a limited license for research purposes.

Gene structure and transcript variants:

Entrez Gene shows transcript variants of each gene: <http://www.ncbi.nlm.nih.gov/sites/entrez?db=gene>

For NM_ mRNA reference sequences: <http://www.ncbi.nlm.nih.gov/sites/entrez?db=nucleotide>

Locus Reference Genomic (LRG) database: <http://www.lrg-sequence.org/>

Exon numbering: The *DICER1* exon numbering used in this P482-A1 DICER1 product description is the exon numbering from the RefSeq transcript NM_177438.2, which is identical to the LRG_492 sequence. The exon numbering and NM_177438.2 sequence used have been retrieved on 11/2019. As changes to the NCBI database can occur after release of this product description, exon numbering or ligation site information may not be up-to-date.

Probemix content: The SALSA MLPA Probemix P482-A1 DICER1 contains 50 MLPA probes with amplification products between 124 and 500 nucleotides (nt). This includes 31 probes for the *DICER1* gene, and four probes centromeric and three probes telomeric to *DICER1* gene. In addition, 12 reference probes are included that detect target relatively copy number stable regions in various cancer types. Complete probe sequences and the identity of the genes detected by the reference probes are available in Table 2b and online (www.mlpa.com).

This probemix contains nine quality control fragments generating amplification products between 64 and 105 nt: four DNA Quantity fragments (Q-fragments), two DNA Denaturation fragments (D-fragments), one Benchmark fragment, and one chromosome X and one chromosome Y-specific fragment (see table below). More information on how to interpret observations on these control fragments can be found in the MLPA General Protocol and online at www.mlpa.com.

Length (nt)	Name
64-70-76-82	Q-fragments (only visible with <100 ng sample DNA)
88-96	D-fragments (low signal of 88 nt and 96 nt fragment indicates incomplete denaturation)
92	Benchmark fragment
100	X-fragment (X chromosome specific)
105	Y-fragment (Y chromosome specific)

MLPA technique: The principles of the MLPA technique (Schouten et al. 2002) are described in the MLPA General Protocol (www.mlpa.com). More information on the use of MLPA in tumour applications can be found in Hömig-Hölzel and Savola (2012).

MLPA technique validation: Internal validation of the MLPA technique using 16 DNA samples from healthy individuals is required, in particular when using MLPA for the first time, or when changing the sample handling procedure, DNA extraction method or instruments used. This validation experiment should result in a standard deviation ≤ 0.10 for all probes over the experiment.

Required specimens: Extracted DNA, which includes DNA derived from paraffin-embedded tissues, free from impurities known to affect MLPA reactions. For more information please refer to the section on DNA sample treatment found in the MLPA General Protocol. More information on the use of FFPE tissue samples for MLPA can be found in Atanesyan et al. (2017).

Reference samples: A sufficient number (≥ 3) of reference samples should be included in each MLPA experiment for data normalisation. All samples tested, including reference DNA samples, should be derived from the same tissue type, handled using the same procedure, and prepared using the same DNA extraction method when possible. Reference samples should be derived from unrelated individuals who are from families without a history of *DICER1*-related disorders. More information regarding the selection and use of reference samples can be found in the MLPA General Protocol.

Positive control DNA samples: MRC-Holland cannot provide positive DNA samples. Inclusion of a positive sample in each experiment is recommended. Coriell Institute (<https://catalog.coriell.org>) and Leibniz Institute DSMZ (<https://www.dsmz.de/home.html>) have a diverse collection of biological resources which may be used as a positive control DNA sample in your MLPA experiments. Sample ID number NA13410 from the Coriell Institute has been tested with this P482-A1 probemix at MRC-Holland and can be used as a positive control sample to detect gain of *DICER1* and flanking genes (except *RPGRIP1* gene), and L-363 cell line (ACC-49) from DSMZ can be used as a positive control sample to detect loss of *DICER1* and flanking genes (except *RPGRIP1* gene). The quality of cell lines can change; therefore samples should be validated before use.

Data analysis: Coffalyser.Net software should be used for data analysis in combination with the appropriate lot-specific MLPA Coffalyser sheet. For both, the latest version should be used. Coffalyser.Net software is freely downloadable at www.mlpa.com. Use of other non-proprietary software may lead to inconclusive or false results. For more details on MLPA quality control and data analysis, including normalisation, see the Coffalyser.Net Reference Manual.

Interpretation of results: The standard deviation of each individual probe over all the reference samples should be ≤ 0.10 and for germline analysis the dosage quotient (DQ) of each individual reference probe in the patient samples should be between 0.80 and 1.20. When these criteria are fulfilled, the following cut-off values for the DQ of the probes can be used to interpret MLPA results for autosomal chromosomes or pseudo-autosomal regions:

Copy number status	Dosage quotient
Normal	$0.80 < DQ < 1.20$
Homozygous deletion	$DQ = 0$
Heterozygous deletion	$0.40 < DQ < 0.65$
Heterozygous duplication	$1.30 < DQ < 1.65$
Heterozygous triplication/Homozygous duplication	$1.75 < DQ < 2.15$
Ambiguous copy number	All other values

Please note that these above mentioned dosage quotients are only valid for germline testing. Dosage quotients are affected both by percentage of tumour cells and by possible subclonality.

- Arranging probes according to chromosomal location facilitates interpretation of the results and may reveal more subtle changes such as those observed in mosaic cases. Analysis of parental samples may be necessary for correct interpretation of complex results when analysing germline samples.
- False positive results: Please note that abnormalities detected by a single probe (or multiple consecutive probes) still have a considerable chance of being a false positive result. Incomplete DNA denaturation (e.g. due to salt contamination) can lead to a decreased probe signal, in particular for probes located in or near a GC-rich region or in or near the *CLMN* gene. The use of an additional purification step or an alternative DNA extraction method may resolve such cases. Additionally, contamination of DNA samples with cDNA or PCR amplicons of individual exons can lead to an increased probe signal (Varga et al. 2012). Analysis of an independently collected secondary DNA sample can exclude these kinds of contamination artefacts.
- Normal copy number variation in healthy individuals is described in the database of genomic variants: <http://dgv.tcag.ca/dgv/app/home>. Users should always consult the latest update of the database and scientific literature when interpreting their findings.
- Not all abnormalities detected by MLPA are pathogenic. In some genes, intragenic deletions are known that result in very mild or no disease (as described for *DMD* by Schwartz et al. 2007). For many genes, more than one transcript variant exists. Copy number changes of exons that are not present in all transcript variants may not have clinical significance. Duplications that include the first or last exon of a gene (e.g. exons 1-3) might not result in inactivation of that gene copy.
- Copy number changes detected by reference probes or flanking probes are unlikely to have any relation to the condition tested for.
- When running MLPA products, the capillary electrophoresis protocol may need optimization. False results can be obtained if one or more peaks are off-scale. For example, a duplication of one or more exons can be obscured when peaks are off-scale, resulting in a false negative result. The risk on off-scale peaks is

higher when probemixes are used that contain a relatively low number of probes. Coffalyser.Net software warns for off-scale peaks while other software does not. If one or more peaks are off-scale, rerun the PCR products using either: lower injection voltage / injection time settings, or a reduced amount of sample by diluting PCR products.

Limitations of the procedure:

- In most populations, the major cause of genetic defects in the *DICER1* gene are small (point) mutations, most of which will not be detected by using SALSA MLPA Probemix P482 DICER1.
- MLPA cannot detect any changes that lie outside the target sequence of the probes and will not detect copy number neutral inversions or translocations. Even when MLPA did not detect any aberrations, the possibility remains that biological changes in that gene or chromosomal region *do* exist but remain undetected.
- Sequence changes (e.g. SNPs, point mutations, small indels) in the target sequence detected by a probe can cause false positive results. Mutations/SNPs (even when >20 nt from the probe ligation site) can reduce the probe signal by preventing ligation of the probe oligonucleotides or by destabilising the binding of a probe oligonucleotide to the sample DNA.
- MLPA analysis on tumour samples provides information on the *average* situation in the cells from which the DNA sample was purified. Gains or losses of genomic regions or genes may not be detected if the percentage of tumour cells is low. In addition, subclonality of the aberration affects the final ratio of the corresponding probe. Furthermore, there is always a possibility that one or more reference probes *do* show a copy number alteration in a patient sample, especially in solid tumours with more chaotic karyotypes.

Confirmation of results: Copy number changes detected by only a single probe always require confirmation by another method. An apparent deletion detected by a single probe can be due to e.g. a mutation/polymorphism that prevents ligation or destabilises the binding of probe oligonucleotides to the DNA sample. Sequence analysis can establish whether mutations or polymorphisms are present in the probe target sequence. The finding of a heterozygous mutation or polymorphism indicates that two different alleles of the sequence are present in the sample DNA and that a false positive MLPA result was obtained.

Copy number changes detected by more than one consecutive probe should be confirmed by another independent technique such as long range PCR, qPCR, array CGH or Southern blotting, whenever possible. Deletions/duplications of more than 50 kb in length can often be confirmed by FISH.

DICER1 mutation database: <https://www.LOVD.nl/DICER1>. We strongly encourage users to deposit positive results in the LOVD (Leiden Open Variation Database). Recommendations for the nomenclature to describe deletions/duplications of one or more exons can be found on <http://varnomen.hgvs.org/>.

Please report false positive results due to SNPs and unusual results (e.g., a duplication of *DICER1* exons 10 and 12 but not exon 11) to MRC-Holland: info@mlpa.com.

Table 1. SALSA MLPA Probemix P482-A1 DICER1

Length (nt)	SALSA MLPA probe	Chromosomal position (hg18) ^a			Location (hg18) in kb
		Reference	DICER1	Flanking	
64-105	Control fragments – see table in probemix content section for more information				
124	Reference probe 19616-L26275	4p13			04-042.278
130	Reference probe 13867-L15385	16p13			16-008.765
136 ∅	DICER1 probe 22501-L31650		Upstream		14-094.694
143	DICER1 probe 22504-L31653		Exon 18		14-094.642
148 ↖	GSC probe 22523-L31672			14q32.13	14-094.305
155	DICER1 probe 22507-L31656		Exon 11		14-094.652
160	DICER1 probe 22518-L31981		Exon 26		14-094.627
166	Reference probe 13816-L30646	2q13			02-108.906
170	DICER1 probe 22522-L31671		Exon 1		14-094.693
179	DICER1 probe 22511-L31660		Exon 16		14-094.644
185 ↖	BTBD7 probe 22490-L31982			14q32.12	14-092.800
190	DICER1 probe 22509-L31658		Exon 23		14-094.632
196	Reference probe 22483-L31204	21q22			21-037.920
202 ∅	DICER1 probe 22512-L31661		Intron 1		14-094.673
208	DICER1 probe 22492-L31983		Exon 8		14-094.661
215	DICER1 probe 22513-L31662		Exon 25		14-094.627
220	DICER1 probe 22515-L31984		Exon 2		14-094.670
227	Reference probe 22485-L09033	11p15			11-020.596
232	DICER1 probe 22514-L31663		Exon 13		14-094.648
238 ↖	SERPINA3 probe 22524-L31673			14q32.13	14-094.155
245	DICER1 probe 22508-L31657		Exon 27		14-094.627
250 ∅	DICER1 probe 22510-L31659		Intron 1		14-094.678
258	Reference probe 09064-L16631	19p13			19-013.302
266	DICER1 probe 22520-L31985		Exon 10		14-094.653
274	DICER1 probe 22521-L31670		Exon 4		14-094.668
283 ↖	ATG2B probe 22489-L31638			14q32.2	14-095.858
292	DICER1 probe 22517-L31666		Exon 17		14-094.644
301 ∅	DICER1 probe 22516-L31665		Intron 1		14-094.677
310	DICER1 probe 22519-L31668		Exon 20		14-094.641
320	Reference probe 14346-L16015	2q32			02-190.146
328 ↖	RPGRIP1 probe 22484-L20663			14q11.2	14-020.839
337	DICER1 probe 22496-L31645		Exon 9		14-094.654
346	DICER1 probe 22495-L31644		Exon 15		14-094.644
356	Reference probe 22486-L06313	15q24			15-070.425
365	DICER1 probe 22498-L31647		Exon 3		14-094.669
373	DICER1 probe 22497-L31986		Exon 24		14-094.630
383	DICER1 probe 22494-L31643		Exon 12		14-094.649
392	DICER1 probe 22493-L31642		Exon 6		14-094.666
400	Reference probe 14839-L16547	1p34			01-045.253
409	DICER1 probe 22505-L31654		Exon 22		14-094.636
418 « ↖	CLMN probe 22491-L31989			14q32.13	14-094.856
427	DICER1 probe 22506-L31655		Exon 14		14-094.647
436	DICER1 probe 22500-L31649		Exon 19		14-094.642
445	Reference probe 22487-L31637	10q21			10-055.296
454	DICER1 probe 22502-L31651		Exon 7		14-094.663
462	DICER1 probe 22503-L31987		Exon 21		14-094.640
472 ↖	TCL1A probe 22525-L31674			14q32.13	14-095.248
481	DICER1 probe 22499-L31988		Exon 5		14-094.666
495	Reference probe 22488-L24472	12q21			12-084.219
500	Reference probe 19555-L27674	2p13			02-071.750

^a) See above section on exon numbering for more information.

« Probe located in or near a GC-rich region. A low signal can be caused by salt contamination in the DNA sample leading to incomplete DNA denaturation, especially of GC-rich regions.

↖ Flanking probe. Included to help determine the extent of a deletion/duplication. Copy number alterations of only the flanking or reference probes are unlikely to be related to the condition tested.

∅ Intron probe. Only included to help determine the extent of a deletion/duplication. Copy number alterations of only this probe are of unknown clinical significance.

Table 2a. *DICER1* probes arranged according to chromosomal location

Length (nt)	SALSA MLPA probe	Gene / Exon	Location (hg18) / Ligation site on NM_177438.2 (unless otherwise noted)	Partial sequence (24 nt adjacent to ligation site)	Distance to next probe
328 ↯	22484-L20663	RPGRIP1	14q11.2	TCTATTTGTCCA-CAGGCTGAGGAC	72.0 Mb
185 ↯	22490-L31982	BTBD7	14q32.12	CTCATCCATATG-GCTCTAAATGGG	1.4 Mb
238 ↯	22524-L31673	SERPINA3	14q32.13	AAAAGTGGGTAA-TGGTGCCCATGA	149.8 kb
148 ↯	22523-L31672	GSC	14q32.13	AGGTTCTCGAGA-GCTTCGAGCTGC	321.5 kb
<i>Centromeric</i>					
		<i>stop codon</i>	<i>6005-6007 (exon 27)</i>		
245 #	22508-L31657	DICER1, exon 27	5927-5926 reverse	GGCAATCCTGTA-ACTTCGACCAAC	0.5 kb
160	22518-L31981	DICER1, exon 26	5778-5777 reverse	GGGGTACATTTG-CAGAAAACTTTT	0.2 kb
215	22513-L31662	DICER1, exon 25	5705-5706	TTTACATGGATA-GTGGGATGTCAC	2.7 kb
373	22497-L31986	DICER1, exon 24	5512-5513	CACAAGTACTTC-AAAGCTGTCTCT	2.3 kb
190	22509-L31658	DICER1, exon 23	4879-4880	ATTTCTTACGAC-TTGCACTGAG	3.5 kb
409	22505-L31654	DICER1, exon 22	4403-4404	ATGTAGTAAATC-AAGACAAAAGCA	4.1 kb
462	22503-L31987	DICER1, exon 21	3707-3708	GCAGAACGTTGC-TCAGCGAGTCCC	1.3 kb
310	22519-L31668	DICER1, exon 20	3394-3395	AGAAAAGCTGTT-TGTCCTCCACGC	0.5 kb
436	22500-L31649	DICER1, exon 19	3317-3318	AATGGGAAAGTC-TGCAGAATAAAC	0.5 kb
143	22504-L31653	DICER1, exon 18	3086-3087	ATGTAGCTGATG-TGTACACTGATC	1.5 kb
292	22517-L31666	DICER1, exon 17	2944-2943 reverse	CGAGCTTCAGAC-TTCTCAATATCT	0.3 kb
179	22511-L31660	DICER1, exon 16	2740-2741	TTGAAGAAGTCT-GGTTTCATGTTG	0.3 kb
346	22495-L31644	DICER1, exon 15	2645-2646	CAAGATGCTTTG-GAATACTGACGG	3.1 kb
427	22506-L31655	DICER1, exon 14	2377-2378	GACCATTTGATG-CCAGTTGGGAAA	0.8 kb
232	22514-L31663	DICER1, exon 13	2306-2307	GTGTACGATTGG-CTGAAAGAGTTG	0.9 kb
383	22494-L31643	DICER1, exon 12	2212-2213	ACCCGAGAGTTG-CCTGATGGTACA	2.6 kb
155	22507-L31656	DICER1, exon 11	2019-2020	TTCCAAGTCGGT-TGTAATCTGGTA	0.8 kb
266	22520-L31985	DICER1, exon 10	1876-1877	TATCGATCCTAT-GTTCAACTTAAA	1.1 kb
337	22496-L31645	DICER1, exon 9	1694-1695	ATGGCATTGGGA-AGAATCAGCCTC	6.9 kb
208	22492-L31983	DICER1, exon 8	1217-1218	GAATGATGGTAA-GAGAACTACAGA	2.1 kb
454	22502-L31651	DICER1, exon 7	1027-1028	TTTACTGACAGA-AGTGGGCTTTAT	2.8 kb
392	22493-L31642	DICER1, exon 6	958-959	GCAACTGACCTG-GTGGTCTTAGAC	0.6 kb
481	22499-L31988	DICER1, exon 5	767-768	TGTTTGATGAGT-GTCATCTTGCAA	1.4 kb
274	22521-L31670	DICER1, exon 4	637-636 reverse	CTCTCTTTTGTC-CAAGATGCATTT	1.0 kb
365	22498-L31647	DICER1, exon 3	479-478 reverse	CTGATAGGACAG-CTCTTTAGTGAG	0.9 kb
220	22515-L31984	DICER1, exon 2	247-248	TGAATGAAAAGC-CCTGCTTTGCAA	3.3 kb
		<i>start codon</i>	<i>239-241 (exon 2)</i>		
202 ∅	22512-L31661	DICER1, intron 1	3.2 kb before exon 2 reverse (NM_001271282.3; 95-94 reverse)	AAGCAGTTGTCT-TTCTTCCCTCT	4.0 kb
301 ∅	22516-L31665	DICER1, intron 1	7.2 kb before exon 2 (NM_030621.4; 215-216)	GCAGTTCAGACA-AGAGCAACACAG	1.0 kb
250 ∅	22510-L31659	DICER1, intron 1	8.2 kb before exon 2 (NM_030621.4; 111-112)	AATACAGACTTG-GAAACTCTGAAA	15.7 kb
170	22522-L31671	DICER1, exon 1	39-40	CCCAGGTGAATG-GAGTAACCTGAC	0.6 kb
136 ∅	22501-L31650	DICER1, upstream	555 nt before exon 1 (NM_030621.4; 33-34)	TTCCCAAATGC-GGAGGCCCTGC	161.7 kb
<i>Telomeric</i>					
418 « ↯	22491-L31989	CLMN	14q32.13	CCTTGCAGGTTT-TGCACTCGGATG	392.6 kb
472 ↯	22525-L31674	TCL1A	14q32.13	CGGTATCGTCCA-TCAGGGTAGAGC	609.9 kb
283 ↯	22489-L31638	ATG2B	14q32.2	TAGTGAGAATTG-CTGATTGCTTTA	-

« Probe located in or near a GC-rich region. A low signal can be caused by salt contamination in the DNA sample leading to incomplete DNA denaturation, especially of GC-rich regions.

↯ Flanking probe. Included to help determine the extent of a deletion/duplication. Copy number alterations of only the flanking or reference probes are unlikely to be related to the condition tested.

∅ Intron probe. Only included to help determine the extent of a deletion/duplication. Copy number alterations of only this probe are of unknown clinical significance.

This probe's specificity relies on a single nucleotide difference compared to a related gene or pseudogene. As a result, an apparent duplication of only this probe can be the result of a non-significant single nucleotide sequence change in the related gene or pseudogene.

Only partial probe sequences are shown. Complete probe sequences are available at www.mlpa.com. Please notify us of any mistakes: info@mlpa.com.

Table 2b. Reference probes arranged according to chromosomal location.

Length (nt)	SALSA MLPA probe	Gene	Location (hg18)	Partial sequence (24 nt adjacent to ligation site)	Location (hg18) in kb
400	14839-L16547	UROD	1p34	GGCTATGAGGTG-GTTGGGCTTGAC	01-045.253
500	19555-L27674	DYSF	2p13	CCATTGCCAAGA-AGGTGAGTGTCC	02-071.750
166	13816-L30646	EDAR	2q13	CTCACATTCCTT-GGTGTTGGGGGG	02-108.906
320	14346-L16015	SLC40A1	2q32	TCGCTGGTGGTA-CAGAATGTTTCA	02-190.146
124	19616-L26275	ATP8A1	4p13	CAGATTCTTCTT-CGAGGAGCTCAG	04-042.278
445	22487-L31637	PCDH15	10q21	TGAGGAGATCCT-ACCTCAAGTTTC	10-055.296
227	22485-L09033	SLC6A5	11p15	TTTCTGCAGGGA-TTGAATATCCTG	11-020.596
495	22488-L24472	ALX1	12q21	ATGACACCTTAT-TCTCACTCGCCT	12-084.219
356	22486-L06313	HEXA	15q24	AGTTGACATCTG-ACCTGACATTTG	15-070.425
130	13867-L15385	ABAT	16p13	ACTTTGTGGAGA-AGCTCCGGCAGT	16-008.765
258	09064-L16631	CACNA1A	19p13	CACCATAAAGAA-AAGCAAGACAGA	19-013.302
196	22483-L31204	KCNJ6	21q22	AGCTCCTACATC-ACCAGTGAGATC	21-037.920

Complete probe sequences are available at www.mlpa.com.

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P482 Product history

Version	Modification
A1	First release.

Implemented changes in the product description

Version A1-01— 10 December 2019 (02P)
- Not applicable, new document.

More information: www.mlpa.com ; www.mlpa.eu	
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