Product Description SALSA® MLPA® Probemix P089-B2 TK2

To be used with the MLPA General Protocol.

Version B2. As compared to version B1, three reference probes have been replaced and four probe lengths have been adjusted. For complete product history see page 8.

Catalogue numbers:
- **P089-025R:** SALSA MLPA Probemix P089 TK2, 25 reactions.
- **P089-050R:** SALSA MLPA Probemix P089 TK2, 50 reactions.
- **P089-100R:** SALSA MLPA Probemix P089 TK2, 100 reactions.

To be used in combination with a SALSA MLPA reagent kit, available for various number of reactions. MLPA reagent kits are either provided with FAM or Cy5.0 dye-labelled PCR primer, suitable for Applied Biosystems and Beckman 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 P089 TK2 is a **research use only (RUO)** assay for the detection of deletions or duplications in *MPV17*, *DGUOK*, *SUCLG1*, *RRM2B*, *SUCLA2* and *TK2* genes, which are associated with Mitochondrial DNA depletion syndromes.

Mitochondrial DNA (mtDNA) depletion syndromesare a clinically and genetically heterogeneous group of autosomal recessive disorders, characterized by a severe reduction in mtDNA content, which leads to decreased energy production in the affected tissues (El-Hattab and Scaglia 2013). The myopathic form, mtDNA depletion syndrome-2 (MTDPS2; OMIM # 609560) is associated with defects in the *TK2* gene. This syndrome is characterized by muscle weakness with childhood onset, associated with depletion of mtDNA in skeletal muscle.
The encephalomyopathic form with methylmalonic aciduria, mtDNA depletion syndrome-9 (MTDPS9; OMIM # 245400) is caused by defects in the *SUCLG1* gene, and it is characterized by hypotonia, muscle atrophy, feeding difficulties, lactic acidosis, and development delay, among other symptoms. Defects in the *SUCLA2* gene causes mtDNA depletion syndrome-5 (MTDPS5; OMIM # 612073), which is difficult to distinguish from the MTDPS-9, being both associated with elevated methylmalonic aciduria.
A severe form with renal tubulopathy, mtDNA depletion syndrome-8A (MTDPS8A; OMIM # 612075) is linked to defects in the *RRM2B* gene. This syndrome is characterized by neonatal hypotonia, lactic acidosis, neurologic deterioration, and renal tubular involvement.
The hepatocerebral form, mtDNA depletion syndrome-3 (MTDPS3; OMIM # 251880) is linked to defects in the *DGUOK* gene, and it is characterized by progressive liver failure and neurological abnormalities with infancy onset, hypoglicemia, and increased lactate in body fluids. mtDNA depletion and decrease activity of the mtDNA-enconded respiratory chain complexes (I, II, IV and V) are present in the affected tissues. mtDNA depletion syndrome-6 (MTDPS6; OMIM # 256810), another hepatocerebral form, is caused by defects in the *MPV17* gene. MTDPS6 is characterized by infantile onset of progressive liver failure, frequently leading to death in the first year of live, progressive neurologic involvement, including ataxia, hypotonia, dystonia and psychomotor regression is present in the infants that survive.

More information is available at: https://www.ncbi.nlm.nih.gov/books/NBK425223/;
https://www.omim.org/entry/609560 (*TK2*);
https://www.omim.org/entry/612073 (*SUCLA2*);
https://www.omim.org/entry/245400 (*SUCLG1*);
https://www.omim.org/entry/256810 (*MPV17*);

https://www.omim.org/entry/612075 (*RRM2B*);
https://www.omim.org/entry/251880 (*DGUOK*).

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/

Probemix content: The SALSA MLPA Probemix P089-B2 TK2 contains 49 MLPA probes with amplification products between 130 and 500 nt. This includes eight probes for the *MPV17* gene, four probes for the *DGUOK* gene, four probes for the *SUCLG1* gene, nine probes for the *RRM2B* gene, five probes for the *SUCLA2* gene, ten probes for the *TK2* gene. In addition, nine reference probes are included and detect nine different autosomal chromosomal locations. Complete probe sequences and the identity of the genes detected by the reference probes is available 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 and 88 and 96 fragment indicates incomplete denaturation)
92	Benchmark fragment
100	X-fragment (X chromosome specific)
105	Y-fragment (Y chromosome specific)

No DNA controls results in only five major peaks shorter than 121 nucleotides (nt): four Q-fragments at 64, 70, 76 and 82 nt, and one 19 nt peak corresponding to the unused portion of the fluorescent PCR primer. Non-specific peaks longer than 121 nt AND with a height >25% of the median of the four Q-fragments should not be observed. Note: peaks below this 25% threshold are not expected to affect MLPA reactions when sufficient amount of sample DNA (50-200 ng) is used.

MLPA technique: The principles of the MLPA technique (Schouten et al. 2002) are described in the MLPA General Protocol (www.mlpa.com).

Required specimens: Extracted DNA, 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.

Reference samples: 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 Mitochondrial DNA depletion syndromes. 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 Biobank (https://catalog.coriell.org) and 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 numbers NA10401, NA02030, NA03330, NA02718 and NA19401 from the Coriell Institute have been tested at MRC-Holland and can be used as

positive control samples (see table below). The quality of cell lines can change, therefore samples should be validated before use.

Sample ID Coriell	Genotype	Probes affected	Expected DQ
NA10401	Heterozygous duplication of *MPV17*, *DGUOK*, *SUCLG1* genes	All MPV17, DGUOK and SUCLG1 probes	1.5
NA02030	Heterozygous duplication of *RRM2B* gene	All RRM2B probes (including reference probe in 8q12)	1.5
NA03330	Heterozygous duplication of *SUCLA2* gene	All SUCLA2 probes	1.5
NA02718	Heterozygous deletion of *SUCLA2* gene	All SUCLA2 probes	0.5
NA19401	Heterozygous deletion of exon 1 and 2 of *TK2* gene	TK2 exon 1 and exon 2 probes	0.5

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 all probes in the reference samples should be <0.10 and the dosage quotient (DQ) of the reference probes 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 or pseudo-autosomal chromosomes:

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

- 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.
- 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. 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 (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 are unlikely to have any relation to the condition tested for.

Limitations of the procedure:

- In most populations, the major cause of genetic defects in these gene are small (point) mutations, most of which will not be detected by using SALSA MLPA Probemix P089 TK2.
- 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.

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.

***MPV17, DGUOK, SUCLG1, RRM2B, SUCLA2* and *TK2* mutation database:**
https://databases.lovd.nl/shared/genes/MPV17;
https://databases.lovd.nl/shared/genes/DGUOK;
https://databases.lovd.nl/shared/genes/SUCLG1.
https://databases.lovd.nl/shared/genes/RRM2B;
https://databases.lovd.nl/shared/genes/SUCLA2;
https://databases.lovd.nl/shared/genes/TK2;
We strongly encourage users to deposit positive results in the LOVD Database. Recommendations for the nomenclature to describe deletions/duplications of one or more exons can be found on http://varnomen.hgvs.org/.

Please report copy number changes detected by the reference probes, false positive results due to SNPs and unusual results (e.g., a duplication of *MPV17* exons 6 and 8 but not exon 7) to MRC-Holland: info@mlpa.com.

Table 1. SALSA MLPA Probemix P089-B2 TK2

Length (nt)	SALSA MLPA probe	Chromosomal position (hg18)						
		Ref	*MPV17*	*DGUOK*	*SUCLG1*	*RRM2B*	*SUCLA2*	*TK2*
64-105	Control fragments – see table in probemix content section for more information							
130	Reference probe 00797-L13645	5q31						
136	**TK2** probe 11564-L12311							**Exon 4**
142	**RRM2B** probe 11565-L12312					**Exon 3**		
148	**MPV17** probe 11566-L15809		**Exon 2**					
154 ¥	**TK2** probe 22233-L31533							**Exon 9**
160	**RRM2B** probe 11568-L12315					**Exon 6**		
166	**SUCLA2** probe 11569-L12316						**Exon 2**	
172	**DGUOK** probe 11570-L12317			**Exon 7**				
178	**TK2** probe 11571-L12318							**Exon 10**
184 *	Reference probe 19450-L25864	14q31						
190	**SUCLA2** probe 11572-L21178						**Exon 1**	
196	**SUCLG1** probe 11573-L12320				**Exon 2**			
200 ¥	**DGUOK** probe 21832-L31603			**Exon 2**				
208	**TK2** probe 11575-L12322							**Exon 1**
214	**RRM2B** probe 11576-L12323					**Exon 2**		
220	**MPV17** probe 11577-L12324		**Exon 1**					
226	**TK2** probe 17276-L21179							**Exon 3**
232	**TK2** probe 11579-L21180							**Exon 5**
238	Reference probe 12492-L13536	1q32						
244	**RRM2B** probe 11580-L12327					**Exon 7**		
250 ¥	**MPV17** probe 22340-L31605		**Exon 4**					
256	**RRM2B** probe 11582-L12329					**Exon 5**		
265	**SUCLA2** probe 17499-L21182						**Exon 11**	
274	**SUCLG1** probe 11584-L12331				**Exon 1**			
283	**DGUOK** probe 11585-L12332			**Exon 1**				
292 *	Reference probe 18469-L23646	6p22						
301	**SUCLA2** probe 11587-L12334						**Exon 6**	
310	**TK2** probe 11589-L21183							**Exon 6**
321	**MPV17** probe 11586-L12333		**Exon 5**					
330	**SUCLG1** probe 11588-L15811				**Exon 6**			
338	**RRM2B** probe 11590-L15225					**Exon 4**		
346	**MPV17** probe 11591-L21184		**Exon 7**					
355	Reference probe 10134-L10596	18q11						
364	**TK2** probe 11592-L12339							**Exon 8**
373	**RRM2B** probe 11593-L12340					**Exon 1a**		
382	**MPV17** probe 11594-L12341		**Exon 6**					
391	**TK2** probe 11595-L12342							**Exon 7**
400 *	Reference probe 18497-L24542	3p14						
409	**RRM2B** probe 11596-L12343					**Exon 8**		
418	**MPV17** probe 11597-L12344		**Exon 8**					
427 ¥	**TK2** probe 21831-L31602							**Exon 2**
436	**RRM2B** probe 11599-L12346					**Exon 9**		
445	**DGUOK** probe 17277-L21339			**Exon 4**				
454	Reference probe 10635-L11183	8q12						
465	**SUCLG1** probe 17432-L21188				**Exon 8**			
475	**MPV17** probe 11602-L12349		**Exon 3**					
484	**SUCLA2** probe 11603-L12350						**Exon 9**	
490	Reference probe 12463-L21340	9q31						
500	Reference probe 10218-L14675	7q22						

* New in version B2 (from lot B2-0219 onwards).

¥ Changed in version B2 (from lot B2-0219 onwards). Small change in length, no change in sequence detected.

Note: The exon numbering used in this P089-B2 TK2 product description for the *TK2* gene is the exon numbering from the RefSeq transcript NM_004614.4. For the *SUCLA2* gene the exon numbering used is from the RefSeq transcript NM_003850.2. For the *RRM2B* gene the exon numbering used is from the RefSeq transcript NM_015713.4. For the *MPV17* gene the exon numbering used is from the RefSeq transcript NM_002437.5. For the *DGUOK* gene the exon numbering used is from the RefSeq transcript NM_080916.3. For the *SUCLG1* gene the exon numbering used is present in from the RefSeq transcript NM_003849.3. The exon numbering and NM sequence used are from 04/2019, but can be changed (by NCBI) after the release of the product description. Please notify us of any mistakes: info@mlpa.com.

Table 2. P089 probes arranged according to chromosomal location

Table 2a. *MPV17* gene

Length (nt)	SALSA MLPA probe	*MPV17* exon	Ligation site NM_002437.5	Partial sequence (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*52-54 (exon 2)*		
220	11577-L12324	Exon 1	21-22	GCCAGCCTGTCA-CGTGGGAGGGAG	0.6 kb
148	11566-L15809	Exon 2	2 nt after exon 2	CTGACAGCTGGT-GAGTGTCCCTCT	9.4 kb
475	11602-L12349	Exon 3	161-162	CTCACAGCAGCT-GGTGGAGAGGCG	0.3 kb
250 ¥	22340-L31605	Exon 4	256-255 reverse	AACCTTGTACCA-GCCTCCTACCAC	0.2 kb
321	11586-L12333	Exon 5	407-408	AGCCCAGGACAA-CTGGGCCAAACT	0.2 kb
382	11594-L12341	Exon 6	45 nt before exon 6	GAAGTGGGAGCT-GCTTGGAGGCGC	0.4 kb
346	11591-L21184	Exon 7	488-489	GTTAGCCAACTT-CTACCTGGTCCC	2.0 kb
418	11597-L12344	Exon 8	541-542	GTGTTGCTGTTA-TCTGGAACTCCT	
		stop codon	*580-582 (exon 8)*		

¥ Changed in version B2 (from lot B2-0219 onwards). Small change in length, no change in sequence detected.

Table 2b. *DGUOK* gene

Length (nt)	SALSA MLPA probe	*DGUOK* exon	Ligation site NM_080916.3	Partial sequence (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*32-34 (exon 1)*		
283	11585-L12332	Exon 1	20-21	TCGCTGTGTGAA-TCGTGGGTGGGA	12.1 kb
200 ¥	21832-L31603	Exon 2	253-254	CCTGTAGCAACA-TGGCAGAATATC	11.7 kb
445	17277-L21339	Exon 4	597-598	ATTACATGGCTT-CATCTACCTCCA	8.1 kb
172	11570-L12317	Exon 7	913-914	CTGACTTTCTGA-AGCTAGAAAAAT	
		stop codon	*863-865 (exon 7)*		

¥ Changed in version B2 (from lot B2-0219 onwards). Small change in length, no change in sequence detected.

Table 2c. *SUCLG1* gene

Length (nt)	SALSA MLPA probe	*SUCLG1* exon	Ligation site NM_003849.3	Partial sequence (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*194-196 (exon 1)*		
274	11584-L12331	Exon 1	109-110	AGGGAAATTTGT-TCAGGCGACTGC	9.7 kb
196	11573-L12320	Exon 2	327-328	TTCCTACACAGC-TTCTCGGCAACA	16.3 kb
330	11588-L15811	Exon 6	796-797	ATTGTGTCCAGA-TCTGGCACCCTG	8.0 kb
465	17432-L21188	Exon 8	1162-1163	AGTGCAGGAGTT-GTGGTCAGTATG	
		stop codon	*1232-1234 (exon 9)*		

Table 2d. *RRM2B* gene

Length (nt)	SALSA MLPA probe	*RRM2B* exon	Ligation site NM_015713.4	Partial sequence (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*245-247 (exon 1)*		
373	11593-L12340	Exon 1a	4 nt after exon 1a	AGGATGAGGTAA-ATGTTGCTGTTG	6.6 kb
214	11576-L12323	Exon 2	349-350	GAGCCACTCCTA-AGAAAGAGTTCT	6.2 kb
142	11565-L12312	Exon 3	483-484	TCACTGGAACAA-GCTTAAAGCAGA	1.0 kb
338	11590-L15225	Exon 4	629-630	GCTTTCAAATTC-TCATCGAGAATG	0.9 kb
256	11582-L12329	Exon 5	735-736	AACCATGCCCTA-TGTTAAGAAAAA	5.2 kb
160	11568-L12315	Exon 6	853-854	GGATCTTTTGCT-GCTATATTCTGG	4.8 kb
244	11580-L12327	Exon 7	970-971	TTCCAATACTTA-GTAAATAAGCCT	1.4 kb
409	11596-L12343	Exon 8	6 nt after exon 8	TCAAAGGTAATG-TGTTTAAAAATG	4.8 kb
436	11599-L12346	Exon 9	1493-1494	GACCTAAATGCT-TTTGTCTTGTCA	
		stop codon	*1298-1300 (exon 9)*		

Table 2e. *SUCLA2* gene

Length (nt)	SALSA MLPA probe	*SUCLA2* exon	Ligation site NM_003850.2	Partial sequence (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*58-60 (exon 1)*		
190	11572-L21178	Exon 1	10 nt before exon 1	TGCAGAGAGGCT-GCGCCTTGGGCC	4.3 kb
166	11569-L12316	Exon 2	156-157	TAGGTTCTGGGA-AGTTCTGGATTG	28.4 kb
301	11587-L12334	Exon 6	4 nt after exon 6	TGGAGCTGGTAA-AGTATCTTCTTT	19.1 kb
484	11603-L12350	Exon 9	4 nt after exon 9	GTTACAAGGTGA-GTATAAAAGGTA	6.3 kb
265	17499-L21182	Exon 11	1595-1596	AGGATTTGGACT-GCATTTAATTGT	
		stop codon	*1447-1449 (exon 11)*		

Table 2f. *TK2* gene

Length (nt)	SALSA MLPA probe	*TK2* exon	Ligation site NM_004614.4	Partial sequence (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*352-354 (exon 1)*		
208	11575-L12322	Exon 1	23-24	CATCATGAGTGT-GTGCCAGGTGTC	1.4 kb
427 ¥	21831-L31602	Exon 2	506-505 reverse	AGGGACTTACCA-CTGATTTTTTCT	7.1 kb
226	17276-L21179	Exon 3	5 nt after exon 3	CGTCGAGGTACA-GCCTCTATGCTA	4.9 kb
136	11564-L12311	Exon 4	604-605	AGCCTGTGTCCA-AGTGGAGAAATG	5.6 kb
232	11579-L21180	Exon 5	700-701	TGCAGCTCACCA-TGCTGGACAGGC	2.4 kb
310	11589-L21183	Exon 6	759-760	GAGAGGTCGATT-CACAGCGCAAGA	11.2 kb
391	11595-L12342	Exon 7	840-841	GTTCTGTCGGAA-TGGTTTGACTGG	0.7 kb
364	11592-L12339	Exon 8	950-949 reverse	TGACCTTCTCCT-CTTCCCTGCATC	3.4 kb
154 ¥	22233-L31533	Exon 9	1015-1016	AGTGGCTCATCA-AAGGCAGCCTTT	1.8 kb
178	11571-L12318	Exon 10	1155-1156	CCATAGGAGGCA-AAAGGTCTATGG	
		stop codon	*1147-1149 (exon 10)*		

¥ Changed in version B2 (from lot B2-0219 onwards). Small change in length, no change in sequence detected.

Note: The exon numbering used in this P089-B2 TK2 product description for the *TK2* gene is the exon numbering from the RefSeq transcript NM_004614.4. For the *SUCLA2* gene the exon numbering used is from the RefSeq transcript NM_003850.2. For the *RRM2B* gene the exon numbering used is from the RefSeq transcript NM_015713.4. For the *MPV17* gene the exon numbering used is from the RefSeq transcript NM_002437.5. For the *DGUOK* gene the exon numbering used is from the RefSeq transcript NM_080916.3. For the *SUCLG1* gene the exon numbering used is present in from the RefSeq transcript NM_003849.3. The exon numbering and NM sequence used are from 04/2019, but can be changed (by NCBI) after the release of the product description. Please notify us of any mistakes: info@mlpa.com.

Related SALSA MLPA probemixes

- P010 POLG Contains probes for the *POLG*, *C10orf2 (PEO1)*, *SLC25A4* and *POLG2* genes.

References

- El-Hattab AW et al. (2013). Mitochondrial DNA depletion syndromes: review and updates of genetic basis, manifestations, and therapeutic options. *Neurotherapeutics.* 10:186-198.
- Schouten JP et al. (2002). Relative quantification of 40 nucleic acid sequences by multiplex ligation-dependent probe amplification. *Nucleic Acids Res.* 30:e57.
- Schwartz M et al. (2007). Deletion of exon 16 of the dystrophin gene is not associated with disease. *Hum Mutat.* 28:205.
- Varga RE et al. (2012). MLPA-based evidence for sequence gain: pitfalls in confirmation and necessity for exclusion of false positives. *Anal Biochem.* 421:799-801.

Selected publications using SALSA MLPA Probemix P089 TK2

- Carrozzo R et al. (2016). Succinate-CoA ligase deficiency due to mutations in SUCLA2 and SUCLG1: phenotype and genotype correlations in 71 patients. *J Inherit Metab Dis.* 39:243-52.
- Iwanicka-Pronicka K et al. (2019). Congenital cochlear deafness in mitochondrial diseases related to RRM2B and SERAC1 gene defects. A study of the mitochondrial patients of the CMHI hospital in Warsaw, Poland. *Int J Pediatr Otorhinolaryngol.* 121:143-9.
- Uusimaa J et al. (2014). Clinical, biochemical, cellular and molecular characterization of mitochondrial DNA depletion syndrome due to novel mutations in the MPV17 gene. *Eur J Hum Genet.* 22:184-91.

P089 Product history	
Version	*Modification*
B2	Three reference probes have been replaced and four probe lengths have been adjusted.
B1	Five new probes have been included. All *TK2*, *MPV17* and *RRM2B* exons are now covered.
A1	First release.

Implemented changes in the product description

Version B2-01- 11 April 2019 (01P)
- Product description restructured, adapted to a new template and to a new product version (version number changed).
- Small changes of probe lengths in Table 1 and 2 in order to better reflect the true lengths of the amplification products.
- Ligation sites of the probes targeting the *MPV17* and *DGUOK* genes updated according to new versions of the NM_reference sequences.
- One reference was added to the section of selected publications.

Version 06 – 04 December 2015 (55)
- Product description adapted to a new lot (lot number added, new picture included).
- References added.

Version 05 – 12 August 2015 (54)
- Various minor textual changes.
- Figure(s) based on the use of old MLPA buffer (replaced in December 2012) removed.
- "Peak area" replaced with "peak height".

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