Product Description
SALSA® MLPA® Probemix P366-B1 CHM-RP2-RPGR

To be used with the MLPA General Protocol.

Version B1
As compared to version A2, the probemix has been almost completely redesigned. For complete product history see page 8.

Catalogue numbers:
- **P366-025R:** SALSA MLPA Probemix P366 CHM-RP2-RPGR, 25 reactions.
- **P366-050R:** SALSA MLPA Probemix P366 CHM-RP2-RPGR, 50 reactions.
- **P366-100R:** SALSA MLPA Probemix P366 CHM-RP2-RPGR, 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.mrcholland.com).

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

Precautions and warnings
For professional use only. Always consult the most recent product description AND the MLPA General Protocol before use: www.mrcholland.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 P366 CHM-RP2-RPGR is a **research use only (RUO)** assay for the detection of deletions or duplications in the *CHM*, *RP2* and *RPGR* genes, which are associated with X-linked retinitis pigmentosa and choroideremia.

Retinitis pigmentosa (RP) (prevalence 1/4000) is a hereditary degenerative disease of the photoreceptor neurons of the retina. RP is characterized by progressive degeneration of the peripheral retina (leading to night blindness), loss of the peripheral visual field and an abnormal electroretinogram. X-linked Retinitis Pigmentosa (xlRP) accounts for 5-15% of all RP syndromes. Mutations in the *RPGR* (also called *RP3*) and *RP2* genes are the most common causes of xlRP, responsible for 70-90% and 10-20% of the xlRP cases, respectively.

Choroideremia (CHM) is another X-linked recessive retinal degeneration disease which could be confused with X-linked retinitis pigmentosa. CHM is a rare inherited disorder that causes progressive loss of vision due to degeneration of the choroid and retina. This progressive X-linked retinopathy is caused by the deletion of the *CHM* gene which encodes the Rab escort protein1 (REP1). REP1 is involved in the prenylation of Rabs. Under-prenylation of Rabs could affect vesicular trafficking, exocytosis and secretion in peripheral cells of CHM patients.

The *RPGR* gene (19 exons) spans ~58 kb of genomic DNA and is located on Xp11.4, 38 Mb from the p-telomere. The *RP2* gene (5 exons) spans ~45 kb of genomic DNA and is located on Xp11.3, 47 Mb from the p-telomere. The *CHM* gene (16 exons) spans ~186 kb of genomic DNA and is located on Xq21.2, 85 Mb from the p-telomere.

More information is available at https://www.ncbi.nlm.nih.gov/books/NBK1417/ and https://www.ncbi.nlm.nih.gov/books/NBK1337/.

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 *RPGR* exon numbering used in this P366-B1 CHM-RP2-RPGR product description is the exon numbering from the NG_009553.1 sequence. The *RP2* exon numbering used in this product description is the exon numbering from the NG_009107.1 sequence. The *CHM* exon numbering used in this product description is the exon numbering from the LRG_699 sequence. The exon numbering of the NM_ sequence that was used for determining a probe's ligation site does not always correspond to the exon numbering obtained from the LRG sequences. As changes to the databases can occur after release of this product description, the NM_ sequence and exon numbering may not be up-to-date.

Probemix content
The SALSA MLPA Probemix P366-B1 CHM-RP2-RPGR contains 48 MLPA probes with amplification products between 130 and 483 nucleotides (nt). This includes 16 probes for the *RPGR* gene, 5 probes for the *RP2* gene and 18 probes for the *CHM* gene. In addition, nine reference probes are included that detect locations on the X-chromosome. Complete probe sequences and the identity of the genes detected by the reference probes are available online (www.mrcholland.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.mrcholland.com.

Length (nt)	Name
64-70-76-82	Q-fragments (only visible with <100 ng sample DNA)
88-96	D-fragments (low signal 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.mrcholland.com).

MLPA technique validation
Internal validation of the MLPA technique using 16 DNA samples from healthy individuals of the same sex 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, 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
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 different unrelated individuals who are from families without a history of hereditary eye or vision abnormalities. It is recommended to use samples of the same sex to

facilitate interpretation. More information regarding the selection and use of reference samples can be found in the MLPA General Protocol (www.mrcholland.com).

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/) have diverse collections of biological resources which may be used as positive control DNA samples in your MLPA experiments. 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.mrcholland.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 the final ratio (FR) 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 FR of the probes can be used to interpret MLPA results:

Copy Number status: Male samples	Final ratio
Normal	0.80 < FR < 1.20
Deletion	FR = 0
Duplication	1.65 < FR < 2.25
Ambiguous copy number	All other values

Copy Number status: Female samples	Final ratio
Normal	0.80 < FR < 1.20
Homozygous deletion	FR = 0
Heterozygous deletion	0.40 < FR < 0.65
Heterozygous duplication	1.30 < FR < 1.65
Heterozygous triplication/homozygous duplication	1.75 < FR < 2.15
Ambiguous copy number	All other values

Note: The term “dosage quotient”, used in older product description versions, has been replaced by “final ratio” to become consistent with the terminology of the Coffalyser.Net software. (Calculations, cut-offs and interpretation remain unchanged.) Please note that the Coffalyser.Net software also shows arbitrary borders as part of the statistical analysis of results obtained in an experiment. As such, arbitrary borders are different from the final ratio cut-off values shown here above.

- 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. Sequence changes (e.g. SNVs, point mutations) in the target sequence detected by a probe can be one cause. Incomplete DNA denaturation (e.g. due to salt contamination) can also 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 (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.
- 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: a lower injection voltage or a shorter injection time, 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 *RPGR*, *RP2* and *CHM* genes are small (point) mutations, none of which will be detected by using SALSA MLPA Probemix P366 CHM-RP2-RPGR.
- 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. SNVs, point mutations) in the target sequence detected by a probe can cause false positive results. Mutations/SNVs (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.

***RPGR*, *RP2* and *CHM* mutation databases**

https://databases.lovd.nl/shared/genes/RPGR,
https://databases.lovd.nl/shared/genes/RP2
https://databases.lovd.nl/shared/genes/CHM.

We strongly encourage users to deposit positive results in the 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 copy number changes detected by the reference probes, false positive results due to SNVs and unusual results (e.g., a duplication of *CHM* exons 2 and 4 but not exon 3) to MRC Holland: info@mrcholland.com.

Table 1. SALSA MLPA Probemix P366-B1 CHM-RP2-RPGR

Length (nt)	SALSA MLPA probe	Chromosomal position (hg18)[a]			
		Reference	*RPGR*	*RP2*	*CHM*
64-105	Control fragments – see table in probemix content section for more information				
130 *	Reference probe 14408-L16113	Xq			
136 *	**CHM** probe 23160-L32762				**Exon 1**
144 ¥	**CHM** probe 13085-L32731				**Exon 13**
149 ¥	**RP2** probe 13086-L32732			**Exon 5**	
155 ¥	**CHM** probe 13087-L32733				**Exon 3**
160 *	Reference probe 21139-L29421	Xp			
166	**CHM** probe 13089-L14308				**Exon 16**
172 *	**CHM** probe 23162-L32764				**Exon 6**
180	**CHM** probe 13090-L14309				**Exon 2**
185 *	**CHM** probe 23159-L32761				**Exon 1**
192	**CHM** probe 13091-L14310				**Exon 15**
197 *	**RPGR** probe 23171-L32773		**Exon 2**		
202 *	Reference probe 15346-L17180	Xq			
208 *	**RPGR** probe 23173-L32775		**Exon 4**		
216 *	**CHM** probe 23168-L32770				**Exon 14**
220 *	**RPGR** probe 23176-L32778		**Exon 9**		
226 *	**CHM** probe 23163-L32765				**Exon 7**
234 *	**RPGR** probe 23174-L32776		**Exon 6**		
239 *	**RPGR** probe 23177-L32779		**Exon 11**		
244 Ø	**CHM** probe 13096-L14315				Intron 10
250 *	Reference probe 15552-L18326	Xq			
258 ¥	**RPGR** probe 13520-L32736		**Exon 5**		
265	**CHM** probe 13101-L14320				**Exon 1**
274 ¥	**RPGR** probe 13102-L21002		**Exon 10**		
283 *	**CHM** probe 23161-L32763				**Exon 4**
288 *	**RPGR** probe 23225-L32782		**Exon 14**		
301 *	**CHM** probe 23158-L32760				Upstream
311 *	**RPGR** probe 23178-L32780		**Exon 12**		
319 *	Reference probe 07650-L08159	Xp			
328 *	**RPGR** probe 23181-L32783		**Exon 15**		
340 *	**CHM** probe 23167-L32769				**Exon 12**
346 *	**RPGR** probe 23172-L32774		**Exon 3**		
356 *	**CHM** probe 23164-L32766				**Exon 8**
364 *	Reference probe 02906-L02300	Xp			
373 *	**RPGR** probe 23170-L32772		**Exon 1**		
384 ¥	**RP2** probe 13523-L14328			**Exon 1**	
394 *	**CHM** probe 23165-L32767				**Exon 9**
402 *	**RPGR** probe 23179-L32781		**Exon 13**		
411 *	Reference probe 17688-L21770	Xq			
418 *	**RP2** probe 23169-L32771			**Exon 3**	
427 *	**RPGR** probe 23175-L32777		**Exon 8**		
432 ¥	**RP2** probe 13117-L32738			**Exon 4**	
440 *	**CHM** probe 23166-L32768				**Exon 11**
449 ¥	**RP2** probe 13119-L32881			**Exon 2**	
456 *	Reference probe 22641-L31848	Xq			
463 *	**RPGR** probe 23182-L32784		**Exon 19**		
474 ¥	**RPGR** probe 23154-L32740		**Exon 7**		
483 *	Reference probe 10764-L11368	Xq			

[a] See section Exon numbering on page 2 for more information.

* New in version B1.

¥ Changed in version B1. Minor alteration, no change in sequence detected.
Ø 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.

SNVs located in the target sequence of a probe can influence probe hybridization and/or probe ligation. Single probe aberration(s) must be confirmed by another method.

Table 2. P366-B1 probes arranged according to chromosomal location

Table 2a. *RPGR* gene

Length (nt)	SALSA MLPA probe	*RPGR* exon[a]	Ligation site NM_000328.3	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*143-145 (Exon 1)*		
373	23170-L32772	Exon 1	142-143	ACTGCCCGTGGC-ATGAGGGAGCCG	3.9 kb
197 #	23171-L32773	Exon 2	258-259	TGTCCCTGTACA-TCTTTCATGTGG	0.5 kb
346	23172-L32774	Exon 3	344-345	GGGGTCAGTTAG-GATTAGGATCAA	1.8 kb
208	23173-L32775	Exon 4	427-426 *reverse*	GTGTGGTTCCTT-CCACAGGCAGCT	2.1 kb
258	13520-L32736	Exon 5	482-483	CAACTGGTGGAA-ATAATGAAGGAC	1.6 kb
234	23174-L32776	Exon 6	733-734	TGGATCTCTTGT-GGATATTACCAT	6.7 kb
474	23154-L32740	Exon 7	912-913	GCATACTGTGGT-TCTCACGGGTAT	5.9 kb
427	23175-L32777	Exon 8	956-957	TGTGACAATTTG-GTCAGCTGGGTC	3.5 kb
220	23176-L32778	Exon 9	1157-1158	CCAATCACTTCA-TTCCTACTTTGT	2.3 kb
274	13102-L21002	Exon 10	1381-1382	ATGCGGCGAAGA-GAGAGGGTACAA	1.6 kb
239	23177-L32779	Exon 11	1483-1484	AATTCAGTCTTT-CCACGATGTTCT	5.9 kb
311	23178-L32780	Exon 12	1611-1610 *reverse*	CAAGGCTTTCTA-CAGTTGAAGAAT	0.4 kb
402	23179-L32781	Exon 13	1672-1673	AGCCTGAATTCC-AATGAAAAGTCA	3.1 kb
288	23225-L32782	Exon 14	1883-1884	AAGCATTTTCAG-ATGAGGAAGTAG	0.8 kb
328	23181-L32783	Exon 15	2031-2032	ATCAGATGACCT-TACAGACAAAGC	17.4 kb
463	23182-L32784	Exon 19	2456-2457	CGCTCCCAGAGA-TAAAATCCATAG	
		stop codon	*2588-2590 (Exon 19)*		

Table 2b. *RP2* gene

Length (nt)	SALSA MLPA probe	*RP2* exon[a]	Ligation site NM_006915.3	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*59-61 (Exon 1)*		
384	13523-L14328	Exon 1	148-147 *reverse*	TTCTCGCGCTGA-TCCCAGCTGTAC	16.3 kb
449	13119-L32881	Exon 2	182-183	AAGACTACATGT-TCAGTGGACTGA	6.5 kb
418	23169-L32771	Exon 3	850-851	GGCTTTTTCCTA-GTTCAGACAAAG	17.5 kb
432	13117-L32738	Exon 4	979-980	GGGGATGGTGCT-GTAGAAGTATGT	2.2 kb
149	13086-L32732	Exon 5	1133-1134	GGAACCAGGACT-TGGTATTAAGCC	
		stop codon	*1109-1111 (Exon 5)*		

Table 2c. *CHM* gene

Length (nt)	SALSA MLPA probe	*CHM* exon[a]	Ligation site NM_000390.4	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
		start codon	*27-29 (Exon 1)*		
301	23158-L32760	Upstream	1590 nt before exon 1	CTGAACATCTTC-TAAATATAAGAC	1.0 kb
185	23159-L32761	Exon 1	557 nt before exon 1	GCTGTCTGGACT-AACTGGAACAAA	0.6 kb
136	23160-L32762	Exon 1	6 nt before exon 1	CTCATTTCCACA-AGTAATAGTCAC	0.1 kb
265	13101-L14320	Exon 1	3 nt after exon 1	TAGGGACGGGTA-TGTGTAGCCTGG	19.8 kb
180	13090-L14309	Exon 2	102 nt before exon 2	GATGGGTCTCTT-TGGTGGTTAAAC	45.9 kb
155	13087-L32733	Exon 3	12 nt after exon 3	GTAAAGTTTGTA-TCTGACCTTTTA	2.9 kb
283	23161-L32763	Exon 4	251-252	AGTCCAGTGTGG-CAAGACCAGATC	15.1 kb
172	23162-L32764	Exon 6	611-612	TCAGCAGAAGAC-ATGAGTGAAAAT	4.9 kb
226	23163-L32765	Exon 7	774-775	TAATCAAATCTA-ATGTTAGTCGAT	1.0 kb

Length (nt)	SALSA MLPA probe	*CHM* exon[a]	Ligation site NM_000390.4	Partial sequence[b] (24 nt adjacent to ligation site)	Distance to next probe
356	23164-L32766	Exon 8	933-934	TTACATTTTGTA-TGGAATATGAGA	1.6 kb
394	23165-L32767	Exon 9	1051-1052	GCATTCAATTGC-AATGACATCAGA	45.5 kb
244 Ø	13096-L14315	Intron 10	439 nt after exon 10	TGATTTTCATCA-GATGACAACAAA	9.7 kb
440	23166-L32768	Exon 11	1352-1351 *reverse*	CGTGAGCACATG-TTCTCAGGAAAG	0.4 kb
340	23167-L32769	Exon 12	1415-1414 *reverse*	TCTGTTTTTAGG-ACAGATCTATCT	6.4 kb
144	13085-L32731	Exon 13	1496-1495 *reverse*	GAACATAACTCA-ATGACCCGAACA	15.2 kb
216	23168-L32770	Exon 14	1599-1598 *reverse*	AAACAATTTCTG-CACAACTGATTC	6.0 kb
192	13091-L14310	Exon 15	1792-1793	TAATGCAGTCAA-ACAGGTAAGGCT	8.5 kb
166	13089-L14308	Exon 16	2017-2018	GGATACCCAACT-TTGGAAATTCTG	
		stop codon	*1986-1988 (Exon 16)*		

[a] See section Exon numbering on page 2 for more information.
[b] Only partial probe sequences are shown. Complete probe sequences are available at www.mrcholland.com. Please notify us of any mistakes: info@mrcholland.com.

Ø 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.

SNVs located in the target sequence of a probe can influence probe hybridization and/or probe ligation. Single probe aberration(s) must be confirmed by another method.

Related SALSA MLPA probemixes

- P235 Retinitis: Contains probes for *RHO*, *IMPDH1*, *PRPF31* and *RP1*.
- P328 EYS: Contains probes for the *EYS* gene, involved in Retinitis Pigmentosa 25.
- P361 & P362 USH2A: Contains probes for the *USH2A* gene, involved in Usher Syndrome.

References

- 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.
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- Ezquerra-Inchausti M et al. (2018). A new approach based on targeted pooled DNA sequencing identifies novel mutations in patients with Inherited Retinal Dystrophies. *Sci Rep*. 8:1-12.
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- Liu X et al. (2021). Molecular diagnosis based on comprehensive genetic testing in 800 Chinese families with non-syndromic inherited retinal dystrophies. *Clin Exp Ophthalmol*. 49:46-59.
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- Ramsden SC et al. (2013). A clinical molecular genetic service for United Kingdom families with choroideraemia. *Eur J Med Genet*. 56:432-438.

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- Shah M et al. (2020). Next generation sequencing using phenotype-based panels for genetic testing in inherited retinal diseases. *Ophthalmic Genet*. 41:331-337.
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- Wu S et al. (2021). Novel variants in PNPLA6 causing syndromic retinal dystrophy. *Exp Eye Res*. 202:108327.
- Zhou Q et al. (2017). Rep1 copy number variation is an important genetic cause of choroideremia in Chinese patients. *Exp Eye Res*. 164:64-73.

P366 product history	
Version	*Modification*
B1	Probemix almost completely redesigned.
A2	Three reference probes have been replaced and the control fragments have been adjusted (QDX2).
A1	First release.

Implemented changes in the product description

Version B1-01 – 20 May 2022 (04P)
- Product description adapted to a new product version (version number changed, changes in Table 1 and Table 2).
- Various minor textual or layout changes.
- Small changes of probe lengths in Table 1 and 2 in order to better reflect the true lengths of the amplification products.

Version A2-01 – 14 September 2021 (04P)
- Product description rewritten and adapted to a new template.
- Ligation sites of the probes targeting the RPGR, RP2 and CHM genes updated according to new versions of the NM_ reference sequences.
- Small changes of probe lengths in Table 1 and 2 in order to better reflect the true lengths of the amplification products.

Version 07 – 12 December 2017 (55)
- Product description adapted to a new product lot (lot number changed, small changes in Table 1 and Table 2, new pictures included).

Various minor textual changes.

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