

PML-RAR α t (15; 17) (q22; q21) ONE-STEP RT-PCR QUALITATIVE DETECTION (bcr1, bcr2, bcr3)

ORDERING INFORMATIONS

REF: *ONC-030-25*
CND Code: *W01060299*
RDM Code: *2256789/R*
Tests: *25 Reactions: 31 x 3*
Manufacturer: *BioMol Laboratories s.r.l.*

CONTENTS OF THE KIT

The kit consists of reagents for reverse transcription and Real-Time PCR amplification
*the reagents for RNA extraction are not supplied in the kit.

For in vitro diagnostic use



PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro **REAL-TIME QUALITATIVE PCR-SOMATIC MUTATIONS** medical devices.

Qualitative determination of the t(15; 17) PML-RAR α translocation (bcr1, bcr2 and bcr3) by RT-PCR (Reverse transcriptase-polymerase chain reaction) technique and subsequent detection in PCR-Real-time.

Optimized kit for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

SCIENTIFIC BACKGROUND

PML- RAR α transcripts derive from the t (15; 17) (q22; q21) translocation and are associated with most cases of acute promyelocytic leukemia (APL).

The two genes fused in the t (15; 17) translocation are the PML (Promyelocytic leukemia) gene, located on chromosome 15, and the retinoic acid receptor α (RAR α) gene located on chromosome 17. The chimeric protein PML- RAR α it is a transcriptional repressor. In the absence of the ligand (retinoic acid, RA), it binds to DNA together with the co-repressors SMRT (silencing mediator for RAR and TR) and N-CoR (nuclear receptor corepressor) making chromatin inaccessible to transcriptional activators or various machinery for basal transcription.

§ Oncol Lett. 2024 Jan 22;27(3):114. doi: 10.3892/ol.2024.14246. eCollection 2024 Mar. Acute promyelocytic leukemia with PML/RARA (bcr1, bcr2 and bcr3) transcripts in a pediatric patient

§ Transl Immunol. 2023 Dec;8(1):101919. doi: 10.1016/j.trim.2023.101919. Epub 2023 Aug 19. PML/RARA leukemia induced murine model for immunotherapy evaluation

§ Leukemia. 2003 Dec;17(12):2318-57. doi: 10.1038/sj.leu.2403135. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia - a Europe Against Cancer program.

§ Reiter A, Saubele S, Grimwade D, Wiesmels JL, Segal M, Lafage-Pochitaloff M et al. Genomic anatomy of the reciprocal translocation t(15;17) in acute promyelocytic leukemia. *Gene Chromosome Cancer* 2003; 36: 175-188.

§ Zelent A, Guidez F, Melnick A, Waxman S, Licht JD. Translocations of the RARalpha gene in acute promyelocytic leukemia. *Oncogene* 2001; 20: 7186-7203.

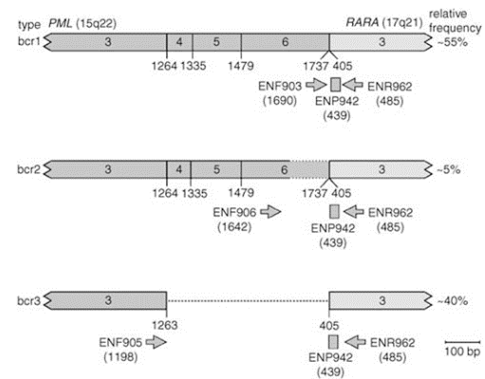
§ Grimwade D. The pathogenesis of acute promyelocytic leukaemia: evaluation of the role of molecular diagnosis and monitoring in the management of the disease. *Br J Haematol* 1999; 106: 591-613.

§ Longo L, Pandolfi PP, Biondi A, Rambaldi A, Mencarelli A, Lo Coco F et al. Rearrangements and aberrant expression of the retinoic acid receptor alpha gene in acute promyelocytic leukemias. *J Exp Med* 1990; 172: 1571-1575.

§ Lemons RS, Eilender D, Waldmann RA, Rebentisch M, Frej AK, Ledbetter DH et al. Cloning and characterization of the t(15;17) translocation breakpoint region in acute promyelocytic leukemia. *Genes Chromosomes Cancer* 1990; 2: 79-87.

CLINICAL SIGNIFICANCE

RAR α breakpoints always occur in intron 2 which is 17 kb long while for the PML locus, in the t(15;17) translocation breakpoints three regions are involved: intron 6 (bcr1; 55% of cases), exon 6 (bcr2; 5% of cases) and intron 3 (bcr3; 40% of cases). As a result, therefore, there are three possible PML- RAR α isoforms: the long isoform **L** (bcr1), the variant isoform **V** (bcr2), and the short isoform **S** (bcr3).



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DESCRIPTION	LABEL	VOLUME	STORAGE
		ONC-030-25	
Mix oligonucleotides and probes	Mix PCR PML-RAR α bcr1 4X	1 x 155 μ l	- 20 °C
Mix oligonucleotides and probes	Mix PCR PML-RAR α bcr2 4X	1 x 155 μ l	- 20 °C
Mix oligonucleotides and probes	Mix PCR PML- RAR α bcr3 4X	1 x 155 μ l	- 20 °C
Mix buffer and Taq-polymerase	Mix RT-PCR 4X	1 x 465 μ l	- 20 °C
Deionized H ₂ O	Deionized H ₂ O	1 x 1 ml	- 20 °C
Recombinant RNA Positive control	Positive control bcr1 - bcr2- bcr3- abl	1 x 90 μ l	- 20 °C
Recombinant RNA Negative control	Negative control	1 x 90 μ l	- 20 °C

TECHNICAL CHARACTERISTICS

COD. **ONC-030-25**

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Total RNA extracted from white blood cells from whole blood or bone marrow aspirate.
CONTROLS	Recombinant RNA for at least 3 analytical sessions; single positive control for bcr1, bcr2, bcr3; negative control for abl
TECHNOLOGY	RT-PCR ONE STEP in Real-time; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels.
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP
RUNNING TIME	100 min
THERMAL CYCLING PROFILE	1 cycle at 50 °C (25 min); 1 cycle at 95 °C (2 min); 45 cycles at 95 °C (5 sec) + 60 °C (45 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	$\geq 0,025$ ng of RNA; $\geq 1\%$
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%