

# GENETIC VARIANTS 197 G>T, (C8092A, rs3212986) and 19007 T>C (rs11615) OF THE ERCC1 GENE

## ORDERING INFORMATIONS

REF: FGC-012-25  
 RDM Code: 2259502/R  
 CND Code: W0106010499  
 Tests: 25 Reactions: 31  
 Manufacturer: BioMol Laboratories s.r.l.

## CONTENTS OF THE KIT

The kit consists of: reagents for Real-Time PCR amplification  
 \*the reagents for the extraction of genomic DNA are not supplied in the kit.

For in vitro diagnostic use



## PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUALITATIVE PCR-TESTS IN PHARMACOGENETICS**. Determination of the genetic variants 197 G>T (rs3212986) and 19007 T>C (rs11615) of the ERCC1 gene by amplification with oligonucleotides and specific probes (allele-specific genotyping) and subsequent detection with qPCR-Real-time. Kit optimized for Real-Time PCR instrumentation Biorad CFX96, Biorad Opus Dx, Agilent AriaDx.

## SCIENTIFIC BACKGROUND

DNA repair systems play a critical role in maintaining the integrity and fidelity of the genome, and DNA repair capacity is an important source of interindividual variability in relation to cancer development. In particular, polymorphisms in DNA repair genes can influence repair capacity.

The ERCC1 (Excision repair cross-complementation group 1) protein is a 297 amino acid protein encoded by a gene located on chromosome 19q13.

ERCC1 contributes to the elimination of DNA adducts, altered forms of DNA that result from exposure to chemical carcinogens (UV light, ROS, environmental mutagens, and chemotherapy drugs). Furthermore, the protein also plays a role in preserving chromosomal stability and telomere integrity. High levels of ERCC1 have been associated with resistance to therapy with platinum derivatives, while cells deficient in this protein appear to be highly sensitive to alkylating agents.

The best characterized single nucleotide polymorphisms (SNPs) of ERCC1 include the T19007C variant (Asn118Asn; rs11615) and the HGVS variant: c.\*197G>T, SNP n.8092 C>A (3' UTR; rs3212986).

## CLINICAL SIGNIFICANCE

The ERCC1 T19007C variant, although it does not cause a change at the amino acid level, results in reduced stability of the protein. On the other hand, reduced expression of ERCC1, as a result of the C allele, has been shown to correlate with better responses to platinum-based therapies, such as FOLFOX (chemotherapeutic combination composed of folinic acid, fluorouracil and oxaliplatin), in NSCLC (non-small cell lung cancer) patients, while the T allele was found to be more correlated with platinum resistance in gastric, ovarian and cervical cancers. Furthermore, the presence of the C allele increases genotoxicity to platinum derivatives. Another ERCC1 variant is C8092A, located in the 3'UTR of the gene and can alter polyadenylation, translation efficiency, localization and stability of the mRNA. In particular, the presence of the A allele reduces the stability of the mRNA causing a lower expression of the protein, and an increase in sensitivity to genotoxic chemotherapies.

In a recent study, it was demonstrated that, in NSCLC patients treated with platinum-based chemotherapy, AA/CA genotypes of the C8092A variant were associated with increased genotoxicity.

§ SNPs in predicting clinical efficacy and toxicity of chemotherapy: walking through the quicksand. *Oncotarget*, 2018, Vol. 9, (No. 38), pp: 25355-25382

§ ERCC1 rs11615 polymorphism increases susceptibility to breast cancer: a meta-analysis of 4547 individuals. *Bioscience Reports* (2018) 38 BSR20180440 <https://doi.org/10.1042/BSR20180440>

§ PHARMACOVIGILANCE, DRUG INTERACTIONS, PHARMACOGENETICS AND THERAPEUTIC DRUG MONITORING OF ANTICANCER AGENTS: A VALUABLE SUPPORT FOR CLINICAL PRACTICE. *Volume 3, issue 3, 2021: 548-67* Doi: 10.36118/pharmadvances.2021.15

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DESCRIPTION	LABEL	VOLUME	STORAGE
		<b>FGC-012-25</b>	
Mix oligonucleotides and probes	Mix 10X 197 G>T ERCC1	1 x 85 µl	-20°C
Mix oligonucleotides and probes	Mix 10X 19007 T>C ERCC1	1 x 85 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 850 µl	-20°C
Deionized H <sub>2</sub> O	Deionized H <sub>2</sub> O	2 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control +1	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control +2	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control +3	1 x 22 µl	-20°C

## TECHNICAL CHARACTERISTICS

COD. FGC-012-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissue, cells
POSITIVE CONTROL	Recombinant DNA for at least 3 analytical sessions
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx e Agilent AriaDx
RUNNING TIME	85 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 45 cycles at 95 °C (15 sec) + 60 °C (60 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
ANALYTICAL SENSITIVITY : LIMIT OF DETECTION (LOD)	≥ 0,016 ng of DNA
ANALYTICAL SENSITIVITY : LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%