

# IL18RAP GENE CLUSTER G/A POLYMORPHISM

## ORDERING INFORMATION

REF: GEN-033-50 RDM Code: 1768972/R  
 Tests: 50 Reactions: 62  
 CND Code: W0106010499  
 Manufacturer: BioMol Laboratories s.r.l.

## CONTENTS OF THE KIT

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

For in vitro diagnostic use



## PRODUCT CHARACTERISTICS

Detection of G/A polymorphism of the IL18RAP gene cluster by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96, Biorad Opus Dx, Agilent AriaDx.

## SCIENTIFIC BACKGROUND

Susceptibility to celiac disease is largely determined by class II molecules of the major histocompatibility complex (HLA-Human Leukocyte Antigen Complex), in particular by HLA-DQ2 and HLA-DQ8, cell membrane glycoproteins encoded by the HLA-DQA1 genes and HLA-DQB1, located in chromosomal region 6p21.3. The HLA, however, identifies only 30-40% of the genetic risk considering that the presence of DQ2 and DQ8 does not automatically lead to the onset of celiac disease although their absence implies the impossibility of developing the disease. Recent data have demonstrated that IL18RAP rs917997 and CCR3 rs6441961 are potential risk factors for celiac disease in European populations. IL18RAP region polymorphisms are associated with multiple immune-mediated diseases, including atopic dermatitis, celiac disease, and type I diabetes. IL-18RAP interactions with the IL-18R1 receptor mediate signal transduction from IL-18. This interleukin mediates Th1 lymphocyte responses, but also contributes to several biological processes, such as commensal microbiota responses and intestinal epithelial barrier integrity. Thus, decreased response to IL-18 exacerbates experimental colitis and intestinal damage. The rs917997 polymorphism is upstream of in a gene cluster containing IL18RAP, IL18R1, IL1R1, IL1R2, IL1RL1 and IL1RL2. AA rs917997 homozygous subjects express reduced amounts of IL-18RAP, IL-18R1 and IL-1R1 surface proteins and show significant reduction in the activation of IL-1 and IL-18-induced pathways (ERK, p38 and NF- $\kappa$ B) compared to subjects with genotype GG rs917997.

## CLINICAL SIGNIFICANCE

Celiac disease (CD) is a chronic enteropathy, triggered by the presence of gluten proteins contained in wheat, barley and rye. The evidence of a strong genetic component is suggested by a considerable family aggregation: the prevalence of celiac disease is, in fact, 10 times higher in first-degree relatives (10%) than in the rest of the population (1%) and a very high (80%) is present in monozygotic twins. Celiac disease is, therefore, a multifactorial disease in which the genetic predisposition contributes, together with environmental factors, to the onset of the pathology.

§ Improving the estimation of celiac disease sibling risk by non-HLA genes. *PLoS One*. 2011; 6 (11):e26920. doi:10.1371/journal.pone.0026920. Epub 2011 Nov 7.

§ The Inter-Relationship of Platelets with Interleukin-1 $\beta$ -Mediated Inflammation in Humans. *Thromb Haemost*. 2018 Nov 19. doi: 10.1055/s-0038-1675603.

§ The Role of Human Leukocyte Antigen in Celiac Disease Diagnostics. *Clin Lab Med*. 2018 Dec; 38 (4):655-668. doi: 10.1016/j.cll.2018.07.007. Epub 2018 Oct 5.

§ Systematic review and meta-analysis of the association between IL18RAP rs917997 and CCR3 rs6441961 polymorphisms with celiac disease risk. *Expert Rev Gastroenterol Hepatol*. 2015; 9 (10):1327-38. doi: 10.1586/17474124.2015.107588. Epub 2015 Aug 8.

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DESCRIPTION	LABEL	VOLUME GEN-033-50	STORAGE
Mix oligonucleotides and probes	Mix IL18RAP 10X	1 x 170 µl	-20°C
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. GEN-033-50

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
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx e Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
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%