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**THE MOST ADVANCED SOLUTION FOR THE IDENTIFICATION OF HLA
PREDISPOSITION TO DEVELOP COELIAC DISEASE**

HLA PREDISPOSITION TO DEVELOP COELIAC DISEASE AND RISK ASSESSMENT.

DETECTION OF MAIN HLA GENOTYPES PREDISPOSING TO CELIAC DISEASE

Recently, research in the genetic field of celiac disease had made more progress. The introduction of **XeliGen RT**, identifying main HLA genotypes, allows to detect the “HLA-related risk” of developing celiac disease. Previous systems, based on the sole determination of the alleles encoding DQ2 and DQ8 heterodimers, do not detect their quantity, but allow only to exclude the risk of developing the disease.

FIELD OF APPLICATION

Celiac Disease is an autoimmune multifactorial disease, where many genetic and environmental factors are involved.

- The genetic factors involved are about 40% related to the HLA system, while the others are linked to various genes distributed in different chromosomes⁽¹⁾. The presence of specific “HLA genotypes” in the short arm of chromosome 6 determines the encoding of heterodimers, responsible for the abnormal activation of the immune-system. The presence of these heterodimers, does not imply the development of the disease, but shows the presence of risk factors. However, their absence allows to exclude the disease almost certainly.
- In order to help customers in the identification of these genotypes, Eurospital created a line of unique and innovative products such as Eu-Gen, Eu-Gen Risk and the most recent and advanced product **XeliGen RT**.

Recent studies^(1,2) proved that the genetic risk associated with genotypes encoding the DQ2/DQ8 heterodimers is not the same for all patients. The genetic risk of developing celiac disease may be stratified into 5 classes, G1 to G5, depending on the different genotypes.

- By using **XeliGen RT** and Eu-Gen-RT it is possible to identify the main HLA genotypes predisposing to coeliac disease and, therefore, patients at highest risk.
- It is possible to identify a genetic risk stratification, from those having the highest probability of developing the condition to those with no or minimal risk.

XeliGen RT-PCR is the only system Real Time, which can determine all HLA genotypes characterising the 5 risk classes predisposing to celiac disease.

WHEN TO USE

XeliGen RT can be used as an additional tool in the diagnosis of celiac disease:

- Excluding the disease in case of negative results.
- Defining the “risk” of developing celiac disease.
- Supporting complex diagnosis in case discrepancy between serologic and biopsy data.
- Confirming previous diagnosis.
- Determining the HLA profile in relatives of coeliac patients.
- Finding a proper preventive approach.

ADVANCED TECHNOLOGY

Developing Eu-GEN, Eu-GEN-Risk and **XeliGen RT**, Eurospital had put a lot of efforts in order to provide its customers with high technology and innovative products, from standard PCR method (Eu-Gen and Eu-GEN Risk), to **XeliGen RT** (advanced Real Time PCR).

- Higher precision.
- Higher resolution.
- Improved dynamic range.
- Higher sensitivity.
- Full automation.

FULL AUTOMATION

XeliGen RT has been validated on the most common RT thermal cyclers present in the market (AB7300-7500-7900 StepOne; Rotorgene 3000-6000; BioRad MiniOpticon - CFX Connect/Touch 96 and/or 384 wells; Eppendorf RealPlex).

Once the amplification process is completed for each patients and allele assayed, a fluorescence signal is generated, which shall be interpreted according to the assay specifications. Eventually all results will be transferred as a file in a PC for the final data interpretation.

INTERPRETATION OF RESULTS

The data generated by **XeliGen RT** will be interpreted according to the table below. The following information will be available for each patient:

- DR and DQ Genotypes.
- Complete Haplotypes.
- Status of the DQB1*02 allele.
- Risk Class (from G1, highest, to G5, lowest or absent).

Main genotypes identified with XeliGen RT	DQ Genotype	DR Genotype	DQB1*02 Status	Risk Group
DQA1*05 - DQB1*02 / DQA1*05 - DQB1*02	DQ2 / DQ2	DR3 / DR3	Homozygosis	Group G1
DQA1*05 - DQB1*02 / DQA1*02:01 - DQB1*02	DQ2 / DQ2	DR3 / DR7	Homozygosis	Group G1
DQA1*05 - DQB1*03:01 / DQA1*02:01 - DQB1*02	DQ7 / DQ2	DR5 / DR7	Heterozygosis	Group G2
DQA1*05 - DQB1*02 / DQA1*05- DQB1*03:01	DQ2 / DQ7	DR3 / DR5	Heterozygosis	Group G3
DQA1*05 - DQB1*02 / DQA1*03 - DQB1*03:02	DQ2 / DQ8	DR3 / DR4	Heterozygosis	Group G3
DQA1*05 - DQB1*02 / DQAX - DQBX	DQ2 / DQX	DR3 / DRX	Heterozygosis	Group G3
DQA1*02:01 - DQB1*02 / DQA1*02:01 - DQB1*02	DQ2 / DQ2	DR7 / DR7	Homozygosis	Group G4
DQA1*02:01 - DQB1*02 / DQA1*03 - DQB1*03:02	DQ2 / DQ8	DR7 / DR4	Heterozygosis	Group G4
DQA1*03 - DQB1*03:02 / DQA1*03 - DQB1*03:02	DQ8 / DQ8	DR4 / DR4	Heterozygosis	Group G4
DQA1*02:01 - DQB1*02 / DQAX - DQBX	DQ2 / DQX	DR7 / DRX	Heterozygosis	Group G5
DQA1*05 - DQB1*03 / DQA1*05 - DQB1*03	DQ7 / DQ7	DR5 / DR5	Not Present	Group G5
DQA1*05 - DQB1*03 / DQA1*03 - DQB1*03:02	DQ7 / DQ8	DR5 / DR4	Not Present	Group G5
DQA1*05 - DQB1*03 / DQAX - DQBX	DQ7 / DQX	DR5 / DRX	Not Present	Group G5
DQA1*03 - DQB1*03:02 / DQAX - DQBX	DQ8 / DQX	DR4 / DRX	Not Present	Group G5
DQAX - DQBX / DQAX - DQBX	DQX / DQX	DRX / DRX	Not Present	Group G5

Literature:

1. Petronezelli F. *Ann Hum Genet.* 1997; 61: 307-17;

2. Margarite-Jeannine et Al. in “HLA relative risks for coeliac disease in European populations: a study of the Genetics Cluster on Coeliac Disease” *Tissue Antigens* 2004; 63: 562-567;

3. Bourgey M, et Al. in “HLA related risk for coeliac disease” *Gut* 2007; 56: 1054-1059.