EUROSPITAL
GENETIC TESTING PRODUCT LINE

KNOWING GENETIC PREDISPOSITION TO HELP DISEASE PREVENTION

XeliGen ***DiabeGen*** ***LactoGen***

EGT EUROSPITAL GENETIC TESTING PRODUCT LINE

Eurospital DIAGNOSTIC

XeliGen - Coeliac disease

XeliGen Lyo is the latest version of Eurospital genetics tests for defining the predisposition to develop coeliac disease. XeliGen Lyo determines all the HLA alleles related to coeliac disease: HLA-DQ2 / HLA-DQ8 heteromers, which have been found in subjects susceptible to coeliac disease. The majority of coeliac patients (90-95%) express the heterodimer DQ2 (HLA-DQA1 * 05 / DQB1 * 022); considering this subjects, those who have the DQ2 homozygosity (HLA-DQB1 * 02 allele in duplicate) have a higher risk of developing the disease. The remaining 10% of non-DQ2 subjects express the DQ8 heterodimer (HLA-DQA1 * 03-DQB1 * 03: 02), or have only either the DQA1 * 05 allele or the DQB1 * 024-5.

The history of the test started with the end point PCR, evolving into a RT PCR kit, finally becoming a kit with **lyophilized reagents**, stable at room temperature.

XeliGen Lyo can be run on the most common thermal cyclers for real time PCR. The test set up is extremely easy thanks to the lyophilized reagents: DNA sample in aqueous solution can now be pipetted directly into the reaction tubes containing the pellet with the reagents and placed directly into the thermal cycler for the amplification reaction.

XeliGen Lyo

(REF. 9186L - 24 TESTS)

- RT PCR test for the determination of DQ2 and DQ8 genotypes involved in the predisposition to develop coeliac disease
- Test can be run on DNA extracted from human peripheral blood
- Single use reagent strips, loadable directly into the thermal cycler
- Lyophilized reagents for an easier use and longer stability at room temperature
- Classification of patients into 5 distinct groups for the stratification of the risk to develop the disease

Main genotypes identified with XeliGen	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

DiabeGen - Type I diabetes

DiabeGen is a unique RT PCR test for the determination of HLA alleles related to either the **predisposition** to or the **protection** against type I diabetes mellitus (T1D). ***DiabeGen*** has been developed from the experience gained on coeliac disease diagnosis. The correlation between type I diabetes and coeliac disease stands in the genetic origin of the predisposition, which can be linked to HLA alleles.

DiabeGen - I step identifies the alleles related to the predisposition to develop type I diabetes (DRB1*04, DRB1*03, DQB1*03:02, DQB1*02), as well as the allele responsible for the protection against the pathology (DQB1*06:02).

DiabeGen - II step can be run on subjects that have been analyzed with ***DiabeGen - I step***, allowing to identify subjects at major risk of developing type I diabetes by determining specific alleles (DR4-DQ8 positives and DRB1*04 variants). Subjects bearing the DRB1*04:01 or the DRB1*04:05 allelic variants will have a higher risk to develop the disease, while the risk will be lower to null in subjects with the DRB1*04:03 or DRB1*04:06 allelic variants. Finally, ***DiabeGen - II step*** identifies with high resolution the DQB1*06:02 protective allele.

DiabeGen can be run on the most common thermal cyclers present on the market. Due to the correlation between coeliac disease and type I diabetes, ***DiabeGen - II step*** can be run on subjects who have undergone ***XeliGen*** analysis, in order to get a complete overview over the predisposition to develop both type I diabetes and coeliac disease.

DiabeGen – I step

(REF. 9192 - 12 TESTS)

- RT PCR test for defining genetic predisposition to the development of or protection against type I diabetes
- Test can be run on DNA extracted from human blood
- Determined alleles: DRB1*04, DRB1*03, DQB1*03:02, DQB1*02
- Determination of the protective allele DQB1*06:02

DiabeGen – II step

(REF. 9193 - 12 TESTS)

- RT PCR test for the high resolution determination of the DRB1*04 allele in subjects resulting at risk to develop type I diabetes after DiabeGen I step analysis
- Test can be run on DNA extracted from human blood
- To be run on subjects underwent the analysis with DiabeGen I step or XeliGen

Case	Alleles present on both chromosome of DQA1 and DQB1 loci	Alleles of DRB1 locus	Susceptibility to T1D
1	DQA1* 03 - DQB1* 03:02 DQA1* 01 - DQB1* 06:02	DRB1* 04 DR2	Protected whichever DRB1* 04 allele is present
2	DQA1* 03 - DQB1* 03:02 DQA1* X - DQB1* X	DRB1* 04:01 DRX	High predisposition
3	DQA1* 03 - DQB1* 03:02 DQA1* X - DQB1* X	DRB1* 04:02 DRX	Medium predisposition
4	DQA1* 03 - DQB1* 03:02 DQA1* X - DQB1* X	DQB1* 04:03 DRX	Protected
5	DQA1* 03 - DQB1* 03:02 DQA1* X - DQB1* X	DRB1* 04:04 DRX	Medium predisposition
6	DQA1* 03 - DQB1* 03:02 DQA1* X - DQB1* X	DRB1* 04:05 DRX	High predisposition
7	DQA1* 03 - DQB1* 03:02 DQA1* X - DQB1* X	DQB1* 04:06 DRX	Protected
8-20	DQA1* 03 - DQB1* 03:02 DQA1* X - DQB1* X	DRB1* 04:07 a 04:19 DRX	Medium predisposition

LactoGen - Lactose intolerance

LactoGen is an easy to run RT PCR genetic test that can be performed on DNA samples extracted from both human blood samples and buccal swabs, making this test the **less invasive on the market** for subjects that may suffer from lactose intolerance. Running ***LactoGen*** just once in a lifetime defines once and forever the lactase genotype (LP, lactase persistence or LNP, lactase non persistence), avoiding to undergo painful and uncomfortable assessment tests like the breath test.

LactoGen identifies the two different alleles that define either the **lactase persistence** (LP, lactase synthesis also after childhood) or **non persistence** (LNP, lactase synthesis stopped during adulthood), providing 3 possible genetic scenarios:

- **Homozygosis C/C-13910 Genotype:** associated to a genetic lactose intolerance due to lactase synthesis non persistence (LNP)
- **Heterozygosis C/T-13910 Genotype:** associated to normal lactase activity due to lactase synthesis persistence also during adulthood (LP)
- **Homozygosis T/T-13910 Genotype:** associated to normal lactase activity due to lactase synthesis persistence also during adulthood (LP)

LactoGen

(REF. 9241 - 32 TESTS)

- RT PCR test for the determination of the alleles responsible for the lactose intolerance
- Test can be run on DNA extracted from human blood or buccal swabs
- No pain for the analyzed subject
- Easy and fast
- No need for further analysis

LNP lactase non-persistence phenotype	LCT 13910
Lactose intolerance (ancestral condition)	C / C

LP lactase persistence phenotype	LCT 13910
Lactose tolerance (mutation C > T heterozygosis)	C / T

LP lactase persistence phenotype	LCT 13910
Lactose tolerance (mutation C > T homozygosis)	T / T

Easy-NAT: Software for an easier handling and interpretation of genetic tests

Easy-NAT is a proprietary software developed by Eurospital with the aim of easing the management of Eurospital genetic tests. ***Easy-NAT*** not only receives patients' data from the LIS and associates the requested genetic analysis, but also sends the program to the PCR thermal cycler and retrieves the data at the end of the run. The biggest advantage of using ***Easy-NAT*** is having a tool that automatically analyses the results and provides a report with their interpretation. Results can be finally sent back to the LIS.

Main features:

- Set up with all the EGT tests: XeliGen, DiabeGen I and II, LactoGen
- Bidirectional communication with LIS for patient's data and results
- Specific test plate set up
- Bidirectional communication with thermal cyclers
- Data retrieval after reactions
- Data analysis and interpretation
- Test report

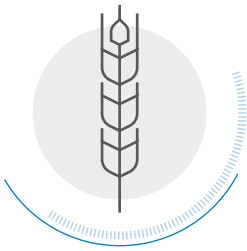
What is genetic predisposition

The human genome is made of more than 20,000 genes, each of them harboring the information necessary to determine specific phenotypic traits of the organism. Each gene can have small variants that bring diversity to the genome albeit keeping its funcionality, but sometimes they can also determine a genetic predisposition to a dysfunction that can lead to a pathological condition. The onset of the pathology is usually caused by an external trigger like diet, environment, bad habits or severe illness. The majority of subjects genetically predisposed to certain pathological conditions are generally unaware of their situation.

In order to determine genetic predisposition to certain pathologies, like coeliac disease, type I diabetes mellitus (T1D) and lactose intolerance, genetic testing represents an easy and non-invasive solution. Coeliac disease is a chronic inflammation of the intestine that affects about 1% of the population, triggered by the ingestion of food containing gluten, in subjects that have specific HLA alleles. Individuals genetically predisposed to develop coeliac disease develop an autoimmune response against a self-enzyme (tTG) resulting in a chronic inflammation. Type I diabetes is also correlated to HLA alleles, which in this case can either protect or predispose to the disease, that is characterized by a high concentration of glucose in the blood after food ingestion, due to an insulin deficiency. Type I diabetes usually occurs in children with an incidence of 5-10% of the total worldwide cases of diabetes. A less life threatening condition, nonetheless very unpleasant, is lactose intolerance, which affects more than half of the world population, although the incidence may vary according to ethnicity. Lactose intolerance is characterized by gastrointestinal disorders that arise following the ingestion of lactose, which is not metabolized due to a lack of the lactase enzyme, not synthesized in subjects bearing the lactase non persistence allele.

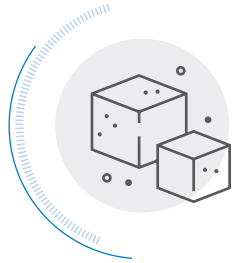
An early diagnosis with genetic testing would make the subject aware of the genetic predisposition, allowing to take steps to adapt the daily habits and improve the life standard so to delay or even prevent the development of the most severe symptoms and the onset of the disease. A genetic predisposition is not a death sentence or guarantee that someone will become sick. The diagnosis is an indicator that the disease can be triggered. Millions of people with genetic predispositions go on to live long, healthy, disease-free lives.

COELIAC DISEASE



XeliGen Lyo

TYPE I DIABETES



DiabeGen Step I
DiabeGen Step II

LACTOSE INTOLERANCE

LactoGen

Eurospital solution

Eurospital Genetic Testing Product Line (EGT) provides a portfolio of **genetic tests in Real Time PCR (RT PCR)** that can be adapted to any open platform real time thermal cycler. Decades of experience in the identification and diagnosis of coeliac patients allowed Eurospital to develop ***XeliGen***, the only genetic test on the market able not only to identify the individuals bearering the alleles for coeliac disease, but also to stratify the risk to develop the pathology.

Since the HLA alleles responsible for coeliac disease are linked to those of type I diabetes, Eurospital has further developed ***DiabeGen***, the genetic test for the identification of alleles that either predispose to or protect against type I diabetes.

Eurospital portfolio of genetic tests related to gastroenterology diseases is completed with ***LactoGen***, the easy and non-invasive genetic test with the highest specificity for the identification of lactose intollerant subjects.

More information and scientific references on:
www.eurospital.com

Eurospital SpA
Via Flavia 122, 34147 Trieste, Italy
Phone +39 040 8997.1 - Fax +39 040 280944
www.eurospital.com - info@eurospital.it

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