EUROSPITAL
COELIAC DISEASE PRODUCT LINE

THE MOST COMPLETE AND RELIABLE PANEL OF PRODUCTS FOR THE IN VITRO DIAGNOSIS OF COELIAC DISEASE

From early identification through the most comprehensive definition of the coeliac patient and prevention of the disease

ECD EUROSPITAL COELIAC DISEASE PRODUCT LINE

Eurospital DIAGNOSTIC

Why Eurospital

Eurospital is a family company with more than 30 years of experience in the identification of both symptomatic and asymptomatic coeliac disease patients, owner of the European Patent (EP 0912898) for the use of the tissue transglutaminase (tTG) as a marker for the *in vitro* determination of the coeliac disease.

What is coeliac disease

DEFINITION OF THE DISEASE

Coeliac disease is a chronic inflammatory autoimmune disorder of the small intestine, deriving from an aberrant immune response against the intestinal mucosa after gluten ingestion. This pathology is found prevalently in susceptible individuals expressing the HLA-DQ2/-DQ8 haplotype of the major histocompatibility complex (MHC) human proteins, resulting in damage of the intestinal villi and consequently in anomalous absorption of nutrients.

A MULTIFACTORIAL DISORDER

Coeliac disease is a very complex pathology and can be defined as a classic example of multifactorial disorder, in which a strict interplay between different contributing factors (*e.g.*, environmental, genetic and immunological) makes the diagnosis difficult because of a broad range of symptoms and variations in its clinical expression.

GLUTEN

The term gluten defines a mix of gliadin and glutenin proteins present in wheat and other cereals like rye and barley. Gluten is the glue that holds dough together, helps it rise by trapping gas bubbles during fermentation, thus giving it its peculiar malleability. Gluten could be considered the essential driving factor in the pathogenesis of the coeliac disease.

TISSUE TRANSGLUTAMINASE

A second key player in this scenario is the tissue transglutaminase (tTG), a ubiquitous enzyme catalysing, among other functions, the deamidation of glutamine residues to glutamic acid in the presence of water. Among all the suitable substrates for this enzymatic reaction there are undigested gluten peptides, in particular glutamine-rich gliadin, which crosses the epithelial barrier of the intestinal lamina propria.

HLA INVOLVEMENT

HLAs (Human Leukocyte Antigens) are cell-surface proteins responsible for the regulation of the immune system in humans. A strong association of HLAs and autoimmune diseases has been established for over fifty years. In genetically predisposed individuals, the deamidation catalysed by tTG gives gliadin a much higher affinity for the HLA-DQ2 and HLA-DQ8 molecules, therefore triggering an autoimmune response.

AUTOIMMUNE RESPONSE

Specific HLA-DQ2 and HLA-DQ8 molecules present gliadin to CD4+ T lymphocytes of the lamina propria of the intestinal mucosa. Once activated, these CD4 cells drive a typical T helper cell type 1 response with the consequent release of pro-inflammatory cytokines that leads to the onset of typical coeliac lesions. In addition, activated CD4 cells cause not only a clonal expansion of B lymphocytes that subsequently differentiate in plasma cells secreting antibodies against tTG, gliadin and endomysium, but also an augmented density of CD8+ T lymphocytes, which in turn increase the extent of lesions.

CLINICAL MANIFESTATIONS

The exacerbated tissue damage is characterised by villous atrophy, together with intraepithelial and lamina propria infiltration of inflammatory cells. Typical clinical manifestations include weight loss, diarrhoea, mood swings, lack of appetite, abdominal pain, constipation, mouth and skin diseases and/or children failure to grow normally. In children the onset of symptoms is gradual and usually characterised by a time lag of some months after weaning. In adults the diagnosis is often only suspected from abnormalities found on routine blood tests. Some cases are identified from family studies or screening programs.

EPIDEMIOLOGY

Coeliac disease has an estimated global prevalence of 1%. It is an extremely heterogeneous pathology, at least in part depending on the patient's age, the duration and extent of the disease, and the presence of extra-intestinal comorbidities. It can develop at any age in genetically predisposed people after gluten ingestion. The susceptibility can be inherited, but not the disease itself. People with first-degree relatives (parent, child, sibling) with coeliac disease have a 1 out of 10 risk to develop the same pathology.

COMPLICATIONS

Left untreated, coeliac disease can lead to additional serious health problems such as malnutrition, bone weakening, infertility and miscarriage, lactose intolerance, nervous system problems and cancer. Studies demonstrated that coeliac patients develop more frequently (~5%) concurrent autoimmune diseases compared to healthy individuals. In fact, the abnormal immunological response elicited by gluten can lead to the production of several autoantibodies, which in turn affect different organ systems. Moreover, patients with autoimmune diseases such as diabetes, thyroid and liver disease, Inflammatory Bowel Disease (IBD), Sjögren's syndrome, often have coeliac disease, due to genetic overlap. In addition, conditions such as dermatitis herpetiformis, anaemia, infertility, recurrent abortions and alopecia have all been associated with coeliac disease.

How to define a coeliac patient

The guidelines of the European Society for Paediatric Gastroenterology Hepatology and Nutrition (***ESPGHAN***) aimed at easily and correctly guiding physicians to an accurate diagnosis of coeliac disease with different laboratory tests. Based on several evidences collected during years of observations, the below algorythm pictures an example of a way to follow the ***ESPGHAN*** guidelines using Eurospital tests to confirm or exclude the pathology.

Eurospital Tests

SEROLOGICAL TESTS

Xeliac Test (9124, 9127)

Eu-tTG IgA (9105)
Eu-tTG IgG (9106)

α-Glia-Pep IgA (9137)
α-Glia-Pep IgG (9138)
α-Gliatest IgA (9107)
α-Gliatest IgG (9108)

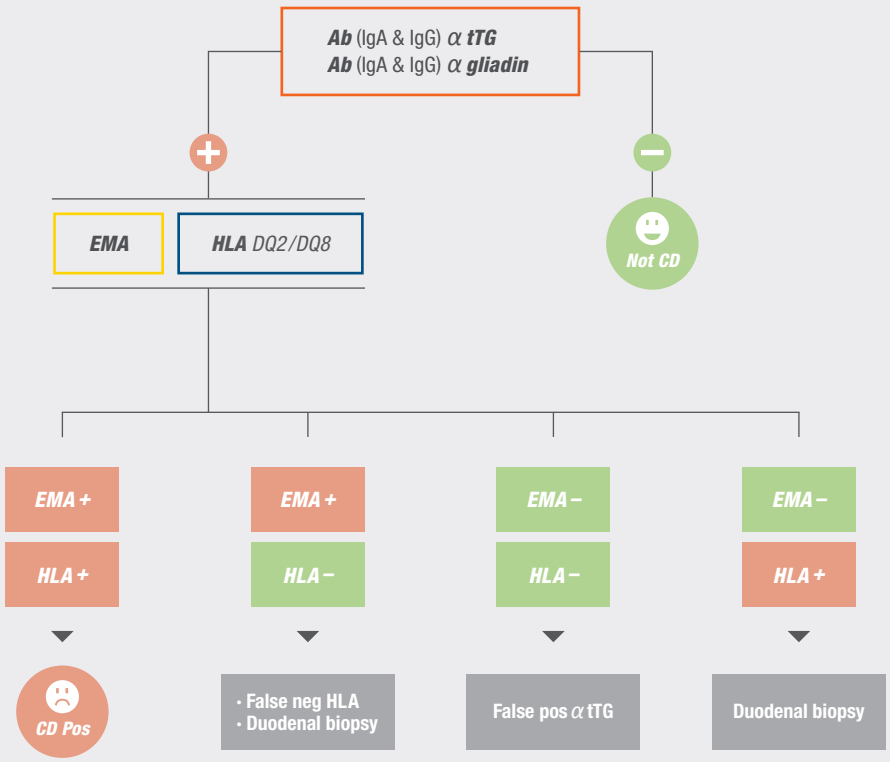
Antiendomysium IgA (8734)

GENETIC TEST

XeliGen (9136)

Legend

- Test is positive
- Test is negative
- **CD Pos:** Coeliac disease patient
- **Not CD:** Not coeliac disease patient



Eurospital portfolio of tests for the diagnosis of coeliac disease

XeliacTest

(REF. 9124 AND 9127)

- **Lateral flow detection** of IgA, IgG and IgM anti-tissue transglutaminase (tTG) antibodies from human whole blood or serum samples.
- Simple, rapid and reliable rapid test (self test).
- The perfect first approach to identify suspected coeliac patients.
- The cheapest and fastest tool for population screenin and rapid identification of anti-tTG antibodies.
- Test configuration for pharmacies or laboratories.

Eu-tTG

(REF. 9105 AND 9106)

- **ELISA test** for the identification and quantification of bot IgA and IgG anti-tissue transglutaminase antibodies (tTG).
- The gold standard for the identification of coeliac patients, with very high sensitivity and specificity.
- Eurospital held a 20 years worldwide patent on the use of tTG in the diagnosis of coeliac disease.

α-GliaPep

(REF. 9137 AND 9138)

- **ELISA test** for the identification and quantification of both IgA and IgG anti-deamidated gliadin peptide antibodies (DGP).
- Anti-DGPs may be used in case of suspected coeliac disease, particularly in < 2 years old children.
- Anti-DGPs may appear earlier than IgA anti-tTG in very young children with coeliac disease.
- IgG anti-DGP detection can be used in support to tTG test when there is a deficit of IgA.
- Anti-tTG IgA together with anti-DPG IgG is the best screening tool in suspected coeliac patients.

α-Gliatest

(REF. 9107 AND 9108)

- **ELISA test** for the identification and quantification of both IgA and IgG anti-gliadin antibodies (AGA).
- Test directed against the the most immunogenic fraction of gliadin (alpha).
- Preferred option when intestinal symptoms are not clear: coeliac disease, gluten sensitivity or intestinal malabsorption?
- The best marker for the monitoring of diet compliance.

Antiendomysium

(REF. 8734, 8721 AND 8726)

- **Indirect immunofluorescence test** for the identification of both IgA and IgG anti-endomysium antibodies (EMA).
- The confirmation test for patients with a positive serology.
- Test for IgA and IgG seric detection available on either low third monkey oesophagus or jejunal bioptic fragments.
- Identification of IgA antibodies in vitro synthesized from intestinal biopsy culture and analysed on low third monkey oesophagus substrate.
- Whole sections of the low third monkey oesophagus for a simplified test interpretation.

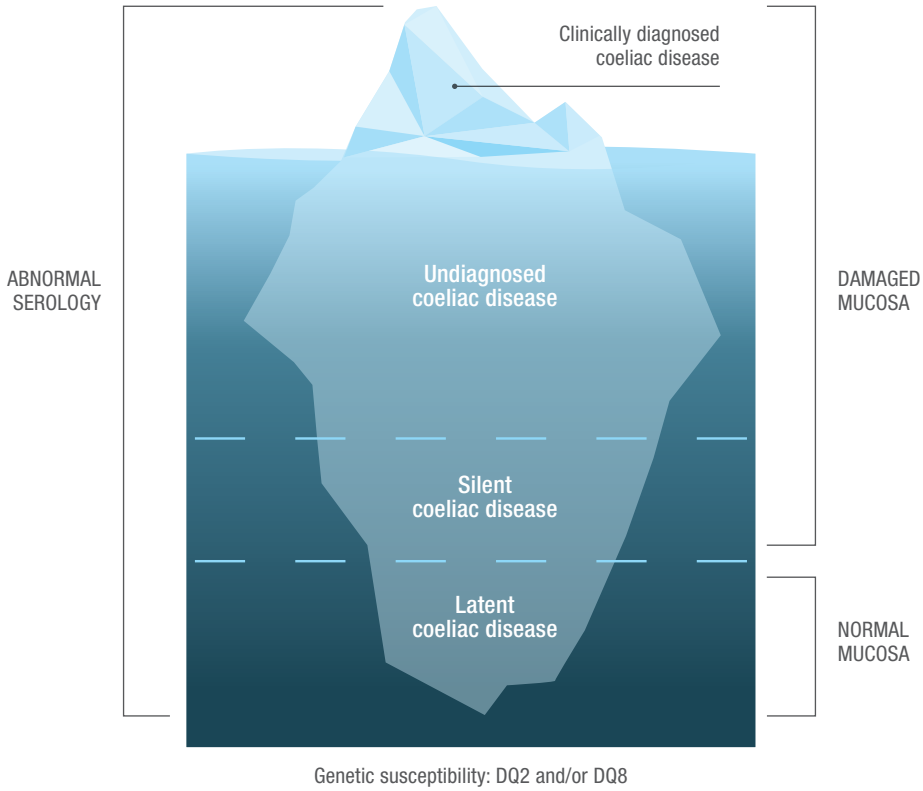
XeliGen XL

(REF. 9186)

- **Real Time PCR test** for the determination of all the HLA alleles codifying DQ2 and DQ8 antigens involved in the susceptibility to coeliac disease.
- Identification of about 300 genotypes, including the rarest ones.
- Classification of patients into 5 distinct groups for the stratification of the risk to develop the disease.
- Allows the identification of DQ2 and DQ8 homozygosis.
- Easy-to-use software (***Easy-NAT***) for a simpler test set up, patient data interpretation and management, together with LIS communication.

The coeliac iceberg

Coeliacs could manifest a wide plethora of clinically established symptoms, as well as being silent or latent patients. The current state of coeliac disease penetration in the population can be pictured with an iceberg, as revealed by several multicentre studies. The tip of the iceberg identifies the patients who are clinically diagnosed, usually because they are sick, showing evident symptoms. A far bigger submerged portion of the iceberg represents all individuals who remain undiagnosed or misdiagnosed, mostly because of atypical signs or lack of symptoms. The most submerged part of the iceberg depicts the large number of both silent and latent patients who present an abnormal serology, together with a damaged or a normal mucosa, respectively. Especially these last two groups should be identified timely in order to prevent the insurgence of the pathology.



Performance of Eurospital serogical tests

Test	Sensitivity		Specificity	
	IgA	IgG	IgA	IgG
Xeliac (rapid test for tTG)	97%		97%	
Eu-tTG (tTG in ELISA)	99%	59%	99%	95%
α-GliaPep (DGP in ELISA)	82%	82%	97%	97%
α-Gliatest (AGA in ELISA)	69%	81%	95%	89%
Antiendomysium (EMA in IFI)	94%	> 99%	98%	> 99%
EMA Biopsy (EMA in IFI)	96%		>99%	

More information and scientific references on:
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