eurofins | Genoma

Nutrinext®

SUMMARY

Sede Legale / Registered Office

Via di Castel Giubileo, 11 - 00138 Roma
C.F. e P.Iva 05402921000
REA 883.995 Iscr. Reg. Impr. 369761/1197

Laboratori e Studi Medici / Laboratories

Rome - Milan
+39 06 16.41.61.500
info@laboratoriogenoma.eu

USEFUL INFORMATION ABOUT THE TEST

WHAT IS NUTRIGENETICS?

The term Nutrigenetics refers to the science that studies the relationships between an individual's specific genetic heritage (genotype) and the molecules in foods, allowing us to predict how ingested substances are assimilated and metabolized every day, based on our DNA.

WHAT DO NUTRIGENETICS TEST INVESTIGATE?

Nutrigenetics tests are based on the analysis of DNA sequence variations (SNV, Single Nucleotide Variant) of genes that are involved in the metabolism of specific nutrients. The presence of one or more genetic variants in these genes may change their functionality and consequently the physiological response to the nutrients themselves.

The Eurofins Genoma Nutrigenetics tests include variants that affect specific traits associated with the investigated condition. For each panel investigated the details and results for each included trait will then be listed.

WHAT IS AN RSNUMBER?

The rsID number is a unique code used by researchers and databases to identify a specific genetic variant. rsID stands for Reference SNP ID and is an international naming convention.

TEST RESULTS

The nutrigenetics tests of the Eurofins Genoma Group are the result of close cooperation between physicians/biologists and bioinformatics experts who have developed a complex algorithm capable of translating genetic data into clear, easy-to-read results.

The "your genotype profile" section contains a table listing the genes analysed for each trait of the investigated panel associated with the investigated rsnumber, and the detected genotype associated with a symbol that will give an initial indication of the value of the individual variant investigated (favourable genotype green, neutral genotype yellow, unfavourable genotype red).

EXAMINED GENE	GENOTYPE	EVALUATION
*MTHFRrs1801133 CT**	CC	

All the data obtained from the analysis will then be processed using a bioinformatics algorithm developed by Eurofins Genoma on the basis of the data currently in the literature and will provide a specific parametric result for each of the traits investigated.

OUTCOME OF THE TRAIT 

TECHNICAL NOTE

DNA is isolated from nucleated cells and then amplified by Real Time PCR technology or NGS analysis.

LIMITATIONS OF THE TEST

The genetic data from nutrigenetics testing is complete only for specific variants investigated by the test. Any other variants that may be present are not detected. Nutrinext is not a diagnostic test, but a predictive test.

PATIENT'S DETAILS

APPLICANT

Full Name

Externa Code

PATIENT

NAME AND SURNAME

Date of Birth

Sex

Address

City

SAMPLE DATA

Internal Code

Collection Date

Acceptance Date

Sample Type

ANALYSIS DATA

Analysis Requested	NUTRIGENETICA - NUTRIFERT
Analysis Start Date	
Aanalysis End Date	
Reporting Date	

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SUMMARY OF YOUR RESULTS

Nutrifert

Recurrent abortion	Your genetic profile is not linked to an increased risk of recurrent abortion.	
Endometriosis	Your genetic profile is not linked to a predisposition to endometriosis.	
GDM	Your genetic profile is not associated with a predisposition to the development of gestational diabetes mellitus.	
PCOS	Your genetic profile is associated with a predisposition to develop polycystic ovary syndrome.	
Response to ovarian stimulation	Your genetic profile is compatible with the condition of a "normal responder" to ovarian stimulation.	
Overweight and obesity	The genetic profile analysed is associated with a high risk of predisposition to obesity.	
Idiopathic infertility: Coeliac disease	Your genetic profile is associated with a predisposition to the development of coeliac disease. DR: DR7-DQ2/DR4-DQ8. Presence only of the beta chain of the DQ2 heterodimer. Presence of the DQ8 heterodimer.	

Direttore del Laboratorio

Eurofins Genoma Group S.r.l.

ROMA (Italia),

EXPLANATION

Your analyzed genotype is favorable	
Your analyzed genotype is slightly favorable	
Your analyzed genotype does not influence	
Your analyzed genotype is slightly unfavorable	
Your analyzed genotype is unfavorable	

NUTRIFERT

TO WHOM IS IT ADDRESSED?

The Nutrifert genetic test is indicated for women who are planning to become pregnant and women with difficulty conceiving without them being given a clear diagnosis or one linked to the reproductive sphere.

WHAT DOES THE TEST INVESTIGATE?

The Nutrifert genetic test offered by Eurofins Genoma is based on a careful study of the latest scientific and nutrigenetic publications in the field of fertility, using the PUBMED search engine. The genes that in the literature have been related to disorders that may have important consequences on fertility were selected from this investigation. The variants investigated with the Nutrifert test involve:

- genetic predisposition to gestational diabetes mellitus (GDM);
- genetic predisposition to endometriosis;
- failure to respond to repeated ovarian stimulation treatments;
- predisposition to polycystic ovary syndrome (PCOS);
- predisposition to recurrent abortion;
- increased risk compared to the general population of developing overweight or obesity;
- genetic predisposition to coeliac disease as it was found 3 times more frequently in women with unexplained infertility than in the general population.

Please go to https://www.nutrinext.it to view supporting bibliography for your test.

TRAITS ANALIZED	INVOLVED GENES
Recurrent abortion	MTHFR - VDR
Endometriosis	ESR2 - CYP19A1
GDM	CDKAL1 - TCF7L2 - MTNR1B
PCOS	PON1 - MTHFR - FTO
Response to ovarian stimulation	FSHR
Overweight and obesity	FTO
Idiopathic infertility: Coeliac disease	DQA1 - DQB1 - DRB1

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RECURRENT ABORTION

Recurrent abortion is defined as the failure of two or more clinical pregnancies and affects approximately 2.5% of women seeking pregnancy. The most common causes are chromosomal errors, uterine anatomical defects, autoimmune diseases and endometrial dysfunction. Recent studies have shown that some genetic variants may also be linked to an increased risk of abortion, in particular those coding for the vitamin D receptor (VDR) and those for the enzyme methylene-tetrahydrofolate reductase (MTHFR), which is responsible for homocysteine metabolism.

Vitamin D deficiency is extremely common. Vitamin D deficiency during pregnancy has been associated with various reproductive and obstetric complications including an increased risk of abortion. In particular, it has been shown that some genetic variants can modulate the activity of the vitamin D receptor thus predisposing more to the risk of spontaneous and recurrent abortion. The importance of genetic variants of the vitamin D receptor has also been demonstrated in other complications of pregnancy such as preeclampsia, gestational diabetes and premature birth. It is not known, however, whether pre-conception vitamin D supplementation can protect against loss of pregnancy in women at increased risk of abortion. Homocysteine is a non-protein amino acid and is produced from another essential amino acid, methionine, which is introduced into our body through the diet. Transformation from methionine to homocysteine takes place through a biochemical process, known as methylation, which requires an enzyme called methylene-tetrahydrofolate reductase (MTHFR). Under normal conditions, homocysteine is then transformed back into methionine or other simple amino acids that are then eliminated by urine. When there are some mutations of the MTHFR gene, there may be a reduction in the activity of the methylene-tetrahydrofolate reductase enzyme leading to an inefficiency in the metabolism of homocysteine and its subsequent accumulation in the blood, known as hyperhomocysteinemia. Hyperhomocysteinemia has also been associated with an increased risk of abortion.

YOUR GENETIC PROFILE

EXAMINED GENE	GENOTYPE	EVALUATION
MTHFR : rs1801133	C/T	
VDR : rs2228570	C/T	
VDR : rs2228570, rs1544410, rs731236, rs7975232	C/T, A/A, C/C, T/T	

OUTCOME OF THE TRAIT 

Your genetic profile is not linked to an increased risk of recurrent abortion.

ENDOMETRIOSIS

Endometriosis is a frequent gynaecological condition characterized by the presence outside the uterus of endometrium, the mucosa that covers its internal cavity. In women with this disease, clusters of endometrial tissue can be found in different areas of the pelvis: ovaries, uterine ligaments, rectum-vaginal septum, bladder, tubes, etc. Endometriosis is quite common and may start to occur from the first menstrual period and last throughout fertile life. Some cases of endometriosis lasting after menopause have also been reported. It is estimated that it may affect at least 10% of women of childbearing age. Endometrial tissue found in endometriosis has the same oestrogen receptors as in the uterine endometrium and therefore responds to the hormonal stimuli of the menstrual cycle. For this reason, symptoms are often amplified: excessive blood loss, pelvic pain, pain during sexual intercourse, during evacuation and urination, asthenia, inflammation and infertility are possible. Depending on the size and number of lesions and whether or not there are ovarian cysts, the disease is divided into four stages, increasing in severity as the disease passes from the first to the fourth. The causes of endometriosis are not yet fully known. It has been suggested that it may be due to abnormal blood reflux from the tubes into the abdominal cavity, the presence of residual embryonic cells, or surgical dissemination. In recent years, particular attention has been paid to genetic variants which may be of particular importance for increasing rates of incidence of endometriosis. In particular, the Estrogen Receptor 2 (ESR2) and CYP19A1 genes appear to be related to potential infertility risk factors associated with endometriosis. Early diagnosis enables timely treatment, reducing disease progression, improving quality of life and preventing infertility. Knowing your genetic predisposition can therefore help. Drug therapy supported by anti-inflammatory nutrition and targeted supplementation can be extremely effective in disease management.

YOUR GENETIC PROFILE

EXAMINED GENE	GENOTYPE	EVALUATION
ESR2 : rs17179740	A/G	
CYP19A1 : rs2899470	G/G	

OUTCOME OF THE TRAIT 

Your genetic profile is not linked to a predisposition to endometriosis.

GDM

Gestational diabetes mellitus is a disorder of blood glucose regulation, characterized by an increase in maternal and foetal glucose, due to a reduced sensitivity of maternal tissues to insulin. It is diagnosed during pregnancy and in most cases regresses after childbirth. It is one of the most common complications during pregnancy and can cause significant short- and long-term risks to both mother and offspring. In women, gestational diabetes is associated with an increased risk of pre-eclampsia and an increased predisposition to develop type 2 diabetes a few years after delivery. Babies born to mothers with gestational diabetes are more likely to be born with a higher weight than 90% of babies of the same gestational age and therefore have a higher risk of birth trauma. They are also predisposed to obesity, type 2 diabetes and cardiovascular disease. It is also known that inadequate nutrition and lifestyle can increase the risk of developing this disease during pregnancy, as well as familiality for type 2 diabetes, a previous pregnancy with gestational diabetes, a previous delivery with a child born with macrosomia, an advanced maternal age, polycystic ovary syndrome, hypothyroidism, overweight and obesity. There is also a genetic susceptibility that can predispose to gestational diabetes. In particular, variants of the melatonin receptor 1B (MTNR1B) gene, the transcription factor TCF7L2 and the gene coding for a protein in the methylthiotransferase family (CDKAL1) have been associated with a genetic predisposition to develop gestational diabetes. In the presence of such variants, it is even more important to intervene on modifiable factors, such as nutrition and lifestyle, in order to prevent the consequences of this disease and to avoid predisposition to metabolic diseases in future generations. The first-line treatment of gestational diabetes is therefore nutritional therapy, along with weight management and physical activity.

YOUR GENETIC PROFILE

EXAMINED GENE	GENOTYPE	EVALUATION
CDKAL1 : rs7756992	A/A	
CDKAL1 : rs7754840	G/G	
TCF7L2 : rs7903146	C/C	
TCF7L2 : rs7901695	T/T	
MTNR1B : rs1387153	C/C	
MTNR1B : rs10830963	C/C	

OUTCOME OF THE TRAIT

Your genetic profile is not associated with a predisposition to the development of gestational diabetes mellitus.

PCOS

Polycystic ovary syndrome (PCOS) is a very common endocrine disorder in women of reproductive age and can have important metabolic and fertility consequences. The aetiology of this disease is quite complex and is associated with various clinical manifestations such as: insulin resistance, hyperinsulinemia, obesity, type 2 diabetes, hyperandrogenism, multiple ovarian cysts, menstrual disorders, anovulation, cardiometabolic disorders, hirsutism, androgenetic alopecia. It has recently been shown that both environmental and genetic factors can have a marked influence on the progression of this syndrome. Oxidative stress in particular has been found to be an environmental factor that plays an important role in the pathogenesis of PCOS. This is why analysis of genes coding for antioxidant proteins may provide indications of the risk of developing this syndrome. The glycoprotein Paraoxonase 1 coded by the PON-1 gene is synthesized in the liver and secreted into the bloodstream and has important antioxidant and anti-inflammatory properties. Some variants of this gene may therefore be associated with a genetic predisposition to PCOS. Another gene associated with PCOS is the Fat Mass and Obesity-Associated (FTO) gene involved in energy metabolism and associated with body mass index and obesity. Finally, variants of the MTHFR gene coding for the methylenetetrahydrofolate reductase protein, an enzyme involved in the metabolism of folic acid and group B vitamins, have proved to be associated with the risk of developing PCOS. The diagnosis of PCOS can be complicated precisely because of the multiplicity of symptoms associated with it. The primary treatment for PCOS, especially in the presence of overweight or obesity, is targeted and personalized intervention on nutrition and lifestyle.

YOUR GENETIC PROFILE

EXAMINED GENE	GENOTYPE	EVALUATION
PON1 : rs662	A/G	
PON1 : rs705379	T/T	
MTHFR : rs1801133	C/T	
MTHFR : rs1801131	A/C	
FTO : rs9939609	A/T	

OUTCOME OF THE TRAIT 

Your genetic profile is associated with a predisposition to develop polycystic ovary syndrome.

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RESPONSE TO OVARIAN STIMULATION

Every woman is born with her own ovarian reserve, that is, with a certain number of primordial follicles present in the ovary, which constitutes her reproductive potential. From the first menstrual period and during each monthly cycle, a small portion of these follicles are brought to maturity by the action of the glycoprotein follicle-stimulating hormone (FSH) secreted by the pituitary gland. The ovarian reserve decreases as women age to deplete at the end of their childbearing period. During a medically assisted procreation treatment, ovarian stimulation is carried out, i.e. the administration of variable doses of exogenous FSH in order to obtain a higher number of follicles, and then oocytes (egg cells), to be used during the treatment. The chances of success are strongly dependent on the number and quality of the oocytes that are recovered. In this scenario, ovarian response to stimulation is critical to the success of the entire procedure. There are several protocols that can be used, but standardizing effective ovarian stimulation is very complicated as the individual response of patients is extremely heterogeneous. The ovarian response is influenced by many factors, including certainly maternal age, but basal hormonal values and antral follicle counts are also decisive. It is therefore difficult to identify the dose of gonadotropins to be administered in advance to achieve an optimal response. It has recently been shown that variants of the FSH hormone and its receptor may affect the outcome of an ovarian response, in particular with regard to the number of oocytes recovered and the duration of the stimulation. Knowing these variants in advance may help to better calibrate ovarian stimulation. Depending on the genotype, the ovarian response to gonadotropin administration may be reduced, normal or excessive. This makes it possible to start by assessing the optimal dose of FSH to be used, avoiding too low stimulation (hypostimulation) or too high stimulation (hyperstimulation).

YOUR GENETIC PROFILE

EXAMINED GENE	GENOTYPE	EVALUATION
FSHR : rs6165	A/G	
FSHR : rs6166	A/G	

OUTCOME OF THE TRAIT 

Your genetic profile is compatible with the condition of a “normal responder” to ovarian stimulation.

OVERWEIGHT AND OBESITY

In addition to a number of gynaecological and systemic diseases affecting a woman's fertility, lifestyle factors and environmental conditions such as stress, environmental pollution, alteration of circadian rhythms, unbalanced nutrition, alcohol and drug abuse, drug use, cigarette smoking and physical inactivity interfere with reproductive safety. It has been shown that overweight and obesity, as well as underweight, are conditions that adversely affect male and female fertility resulting in a reduction in the quality of gametes and embryos, a poor response to ovarian stimulation, reduced embryonic development, a reduction in the rate of implantation and pregnancy and an increase in the rate of abortion.

In the case of overweight and obesity, excess fat acts as an actual endocrine organ, interfering with hormonal balance and thus altering reproductive function. Recent studies have found an increase in the rate of spontaneous pregnancy following a loss of as little as 10% of body weight, though without reaching the ideal weight. Underweight, too, has been correlated with a reduced chance of pregnancy, due to the resulting nutritional deficiencies and limited nutrient intake. Fertility and body weight are associated according to a U-curve: the time of conception is longer in women with a body mass index (BMI) above 25 kg/m2 or below 19 kg/m2. A high body mass index is also associated with adverse pregnancy outcomes such as gestational diabetes, hypertension, pre-eclampsia, premature births and neonatal death.

Genetic susceptibility, i.e. individual predisposition leading to an increased risk of overweight or obesity, has been confirmed in numerous clinical studies showing that genetics also affects the amount and distribution of body fat. In addition, hereditary factors affect 70% of BMI. So far, numerous genes associated with obesity have been identified. Those in scientific literature that bear witness to an association with eating habits and lifestyle are important in order to be able to draw up individual nutritional plans. In order to optimize nutrition for reproductive purposes, it is extremely important to focus on the quality of raw materials, avoiding inflammatory foods and ensuring that all the necessary nutrients are provided. In addition, the use of foods from intensive farming, preserved products, packaged products and big industry should be kept to a minimum as far as possible, since several studies have shown the negative effect on the fertility of multiple substances (plastics, pesticides, additives, phthalates, bisphenols, pharmaceutical products), which act as endocrine disruptors altering the physiological hormonal balance.

YOUR GENETIC PROFILE

EXAMINED GENE	GENOTYPE	EVALUATION
FTO : rs9939609	A/T	

OUTCOME OF THE TRAIT

The genetic profile analysed is associated with a high risk of predisposition to obesity.

IDIOPATHIC INFERTILITY: COELIAC DISEASE

Coeliac disease is a chronic immune-mediated disease of the intestine triggered by exposure to dietary gluten in genetically predisposed individuals. Many genes involved in the pathogenesis have been identified and it is known that a crucial role is played by the human leukocyte antigen (HLA) system and in particular the HLA-DQA1 and HLA-DQB1 genes that code for the HLA-DQ2 and HLA-DQ8 molecules. In a coeliac subject, gluten exposure causes a major inflammatory response in the small intestine. The resulting immune response leads to a chronicisation of the inflammation, resulting in tissue damage as far as the disappearance of the intestinal villi, indispensable structures for the absorption of nutrients. The symptoms of coeliac disease are often confused and overlapping with other diseases, so the diagnosis of coeliac disease is not always immediate. Some studies show an association between infertility and undiagnosed coeliac disease, while there appears to be no relationship between previously diagnosed coeliac disease and the onset of infertility. Early detection and intervention are therefore of fundamental importance in women seeking pregnancy. Presence of the DQ2/DQ8 heterodymer in women with idiopathic infertility is 3 times higher compared with the general population.

YOUR GENETIC PROFILE

EXAMINED GENE	GENOTYPE	EVALUATION
DQA1	02; 03	
DQB1	02; 0302	
DRB1	04; 07	

OUTCOME OF THE TRAIT

Your genetic profile is associated with a predisposition to the development of coeliac disease. DR: DR7-DQ2/DR4-DQ8. Presence only of the beta chain of the DQ2 heterodimer. Presence of the DQ8 heterodimer.

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EXPERT ADVICE BASED ON YOUR GENETIC PROFILE

Nutrifert

RECURRENT ABORTION

Your genetic profile is not linked to an increased risk of recurrent abortion. You don't have to do anything special. However, it is important to stress that abortion has a multifactorial aetiology and therefore this result does not rule out the possibility of it occurring. It is specified that a vitamin D deficiency and elevated homocysteine values may still be present in non-genetically predisposed individuals. It should be remembered that during pregnancy it is of the utmost importance to maintain a diet and a healthy lifestyle that provides all the necessary nutrients and micronutrients to best support the development of the fetus and protect the health of the mother. It is therefore recommended that you consult your gynaecologist for an overall assessment.

ENDOMETRIOSIS

Your genetic profile is not linked to a predisposition to endometriosis. You don't have to do anything special. However, it is recommended to perform a gynaecological examination to exclude the presence of initial or asymptomatic forms of endometriosis. If you are seeking a pregnancy, an anti-inflammatory diet and a healthy lifestyle can in any case promote natural fertility.

GDM

Your genetic profile is not associated with a predisposition to the development of gestational diabetes mellitus. You don't have to do anything special. It should be remembered, however, that during pregnancy it is of the utmost importance to maintain a healthy lifestyle and a diet that provides all the necessary nutrients to best support the development of the fetus and protect the health of the mother. In particular, it is recommended to follow a Mediterranean-style diet that is healthy and balanced for the distribution of macro and micronutrients. It is therefore recommended that you consult your gynaecologist.

PCOS

Your genetic profile is associated with a predisposition to develop polycystic ovary syndrome. It is important to perform a gynaecological examination in order to have a diagnosis of PCOS. In fact, the gynaecologist will evaluate the diagnostic tests needed and any therapy. It should be remembered that an anti-inflammatory diet, a healthy lifestyle and proper supplementation can help in the management of PCOS and its associated symptoms. In the case of being overweight or obesity, a low-calorie diet promoting weight loss would be recommended. It is recommended to reduce the intake of sugar (including those in beverages) and to avoid an excessive consumption of simple carbohydrates favouring those with a low glycaemic index to counter insulin resistance. Limit the consumption of dairy products. Eliminate alcohol consumption and reduce coffee consumption. Avoid packaged foods. Ensure a proper supply of fibre. Prefer seasonal fruits and vegetables. It is advisable to eat healthy fats such as extra virgin olive oil, avocado, clarified butter, nuts and oil seeds. In some studies, the distribution of macronutrients during the day has also proved to be important. In particular, the intake of a larger share of the daily quantity of carbohydrates during the first part of the day appears to be associated with a significant reduction in blood glucose and insulin levels. Supplementation based on Inositol (Myo-inositol and D-chiro-inositol), Omega-3, vitamins (especially B12, C, and D), folic acid and coenzyme Q10 may be of great benefit and should be assessed specifically for each individual patient. We recommend consulting a specialist. Exercise that promotes weight loss and improves insulin resistance is recommended.

RESPONSE TO OVARIAN STIMULATION

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Your genetic profile is compatible with the condition of a “normal responder” to ovarian stimulation. Genetic analysis shows that this variant is not associated with a particular predisposition to a high response (high responder) or low response (low responder) to ovarian stimulation. It is recommended that you contact your gynaecologist who will be able to evaluate the most suitable ovarian stimulation protocol.

OVERWEIGHT AND OBESITY

Genetic analysis has shown a high risk of predisposition to obesity. Such a predisposition combined with an effective high body mass index, according to several studies in the scientific literature, may contribute to an infertility condition.

We recommend contacting a specialist who, in addition to the genetic data, can possibly add anthropometric and blood-chemical parameters in order to assess the development of an appropriate personalised nutritional plan to be able to limit and keep under control the effects of the genetic predisposition to obesity. However, it is recommended to limit the consumption of simple sugars and fats of animal origin, preferring high-quality vegetable fats (such as extra virgin olive oil, avocado, oil seeds, skinless nuts). It is recommended to prefer eating seasonal fruits and vegetables, avoiding greenhouse produce and preserved products. The consumption of pulses should be encouraged, taking any intestinal disorders into account. Prefer eating complex carbohydrates. An adequate supply of quality proteins is recommended: in particular eggs, fish (especially small oily fish), white meat. Limit the consumption of dairy products and red meat. Avoid alcohol consumption and reduce consumption of caffeine. Avoid cigarette smoke. It is recommended to assess a correct supplementation of micronutrients with a specialist. It is lastly recommended to exercise moderately: approximately 2-3 hours a week as reported in "Guidelines for Healthy Eating" drawn up by the Research Centre on Food and Nutrition and available on the website of the Italian Ministry of Health ([link])

IDIOPATHIC INFERTILITY: COELIAC DISEASE

You have proved to be at risk of developing coeliac disease. Coeliac disease is a multifactorial disease, for which environmental and food factors are an important joint cause associated with genetic predisposition. It is known that only a part of the world's population carrying predisposing variants will develop the disease. The triggers for the disease are not yet fully known. The only possible treatment for coeliac disease is the total exclusion of gluten from the diet. It is therefore recommended that you contact your gynaecologist who will evaluate the necessary diagnostic investigations. It is recommended to follow the guidelines of the Italian Association of Coeliac patients (AIC, https://www.celiachia.it/) and the National Register of the Italian Ministry of Health ([link]).

Biologo Nutrizionista

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