

Risk classification of HLA-DQx.5 allele in Celiac Disease HLA genotyping test

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<p>Celiac disease (CD) is a serious lifelong condition, in which the immune system attacks an individual's own tissue when eating gluten. This leads to inflammation and damage to the small intestine. Celiac disease often goes undiagnosed because many of its symptoms are nonspecific. The prevalence of combined undiagnosed and diagnosed CD is estimated to affect 1 in 100 people throughout Europe and USA.</p> <p>CD is a polygenic disease, it is known that the human leukocyte antigen (HLA) system plays a crucial role. HLA-DQ2/DQ8 risk allele genotyping screening test from a whole blood sample (B -HLAKeli) is routinely used to estimate the genetic risk of a patient having CD. HLA genotyping test result is routinely used to rule out celiac disease rather than confirming it; if an individual does not have celiac disease related risk alleles, it is very unlikely that he or she has celiac disease. The Celiac disease diagnosis decision making process is based on the classic triple combination of serological antibody tests, the HLA-DQ2/DQ8 genotyping test and duodenal biopsies.</p> <p>The aim of this master's thesis was to study evaluate how the two different risk classification praxis for HLA-DQx.5 allele used for celiac disease diagnostics in SYNLAB Finland and Estonia central laboratory and in SYNLAB Suomi central laboratory might influence the clinical process and final diagnosis. In SYNLAB Suomi central laboratory HLA-DQx.5 is classified and interpreted as a risk allele predisposing to celiac disease. In SYNLAB Finland and Estonia central laboratory this allele is classified as CD-non-risk-allele based on recommendations in international guideline. In addition, the aim was to get a general understanding of celiac disease prevalence and risk allele distributions among the study population.</p> <p>From the study population of 196 celiac disease suspect patients, 9% had a celiac disease positive laboratory result and the HLA risk genotype distribution among positive cases was well aligned with the expected values described in the literature. Study results indicated that there's no additional clinical value if HLA-DQx.5 is classified as a celiac disease predisposing risk allele; the study data implies that it is very unlikely to find celiac disease positive cases from laboratory test perspective among HLA-DQx.5 carriers. Based on the study, approximately 7% of the celiac disease suspects carry the allele HLA-DQx.5 and therefore probably go through additional celiac disease related laboratory testing if this allele is interpreted as a risk allele. According to the study findings and general recommendations based on international guideline of celiac disease diagnosis, it seems that there is no clear clinical benefit if HLA-DQx.5 is classified as a CD risk allele.</p>			
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<p>Keliakia on vakava elinikäinen autoimmuunisairaus jossa ravintoaineena nautittu gluteeni johtaa elimistön immuunijärjestelmän hyökkäykseen elimistön omia soluja kohtaan. Keliakiassa tämä näkyy ohutsuolen limakalvolla suolinukkaa vaurioittavana tulehdusreaktiona. Keliakia on yleisesti alidiagnosoitu sairaus johtuen pitkälti oireiden monikirjoisuudesta ja yksilötason eroista. Sairauden esiintyvyys Euroopassa ja Pohjois-Amerikassa on 1:100 jos otetaan huomioon sekä diagnosoidut tapaukset että diagnosoimatta jäävien arvioitu osuus.</p> <p>Keliakia on polygeeninen sairaus jossa HLA-molekyyleillä (Human Leukocyte Antigen) on merkittävä asema. Potilaan perinnöllistä keliakiariskiä voidaan arvioida seulontatestinä käytetyllä kokoverestä tehtävällä keliakiaan liittyvien HLA-DQ2/DQ8-riskialleelin genotyyppityksellä (B -HLAKeli). HLA-genotyyppitystä käytetään tyypillisesti keliakin poissulkuun; jos potilaalla ei ole perimässään keliakialleleille tyypillisiä riskialleleita, on hyvin epätodennäköistä että oireiden taustalla olisi keliakia. Keliakian kliininen laboriodiagnosointiprosessi perustuu kolmen eri diagnostisen osa-alueen yhdistelmään. Ensinnäkin määritetään seeruminäytteestä keliakialle tyypilliset vasta-aineet, toiseksi tehdään kokoverinäytteestä HLA-DQ2/DQ8-genotyyppitys ja lopuksi keliakia-diagnosi varmistetaan suolinäytteen mikroskooppisella tutkimuksella.</p> <p>Tämän tutkimuksen aiheena oli arvioida mitä vaikutuksia kahdella toisistaan eroavalla HLA-DQx.5 alleelillä koskevalla riskiluokitusmallilla saattaa olla potilaalle määrättäviin kliinisiin laborioritutumuksiin ja laborioritutumusten perusteella annettavaan keliakia-diagnosiin. SYNLAB Suomen keskuslaboratorio Suomessa luokittelee HLA-DQx.5 alleelin keliakiariskialleeliksi perustuen paikalliseen toimintamalliin ja SYNLAB Finland-Estonian keskuslaboratorio Tallinnassa luokittelee kyseisen alleelin kansainvälisten suositusten mukaisesti keliakian kannalta matalan riskin alleeliksi, jolla ei ole ratkaisevaa merkitystä keliakiaan. Luokitusmallivertailun lisäksi tarkasteltiin keliakin esiintyvyyttä ja alleelijakaumia tutkimuspopulaatiossa.</p> <p>Tutkimukseen valikoituneesta 196 keliakiaepäilypotilaan otannasta laborioritutumusten perusteella 9%:lla voitiin todeta keliakia. Keliakia-positiivisten tapausten keskuudessa HLA-riskigenotyyppijakauma oli hyvin linjassa kirjallisuuden mukaisen odotusjakauman suhteen. Tutkimustulosten perusteella voitiin todeta että HLA-DQx.5-alleelin luokitus keliakiariskialleeliksi ei anna kliinistä lisäarvoa laborioritutumusprosessin kannalta; tulokset osoittivat hyvin epätodennäköiseksi tilanteen missä HLA-DQx.5-alleelin kantajalla diagnosoitaisiin keliakia. Voitiin myös osoittaa että noin 7% keliakiaepäilyistä potilaista kantaa HLA-DQx.5-alleelia, ja jos tämä alleeli luokitellaan keliakiariskialleeliksi, on todennäköistä että heille määrätään keliakia-diagnosiin tarvittavia lisätutkimuksia.</p> <p>Otaen huomioon tutkimuksessa tehdyt havainnot ja yleiset kansainväliset keliakia-diagnosointia koskevat suositukset, näyttää siltä HLA-DQx.5-alleelin luokittelu keliakiariskialleeliksi ei tuo selkeää etua kliinisen päätöksenteon suhteen.</p>			
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ABBREVIATIONS

µl	microlitre
6p21.3	position 21.3 in chromosome 6 short arm
AGA	antigliadin antibody
B-	whole blood
BSA	bovine serum albumin
Cat.	catalog
CD	celiac disease
CLSI	clinical and laboratory standards institute
DGPA	deamidated gliadin peptide antibodies
DGPAbA	deamidated gliadin peptide immunoglobulin A
DGPAbG	deamidated gliadin peptide immunoglobulin G
DNA	deoxyribonucleic acid
ELISA	enzyme-linked immunosorbent assay
EMA	endomysial antibody
EMAbA	endomysial immunoglobulin A
EMAbG	endomysial immunoglobulin G
ISO 15189	International Organization for Standardization, standard 15189 for Medical laboratories — Requirements for quality and competence
ESPHGAN	The European Society for Paediatric Gastroenterology Hepatology and Nutrition
EtOH	ethanol
FAM	Fluorescein amidite dye
g	gravity
g/l	grams per litre
GWAS	genome-wide association study
h	hour
HCl	hydrochloric acid
HE	hematoxylin and eosin
HLA	human leukocyte antigen
HLAKeli	HLA-DQ2/DQ8 risk allele genotyping screening test
IC	internal control
IgA	immunoglobulin A
JOE	xanthene fluorophore dye
K ₂ EDTA	dipotassium ethylenediaminetetraacetic acid, anticoagulant
M	molar concentration, moles per litre
MGP	magnetic glass particles
min	minute
ml	milliliter
mM	molar concentration, millimoles per litre

n	total number of units
Na	sodium
NaN ₃	sodium azide
ng	nanogram
nm	nanometer
No.	number
NPV	negative predictive value
°C	degrees of celcius
PBS	phosphate-buffered saline
PCR	polymerase chain reaction
PEG	polyethylene glycol
PPV	positive predictive value
qPCR	quantitative polymerase chain reaction
RNA	ribonucleic acid
RT-PCR	real-time polymerase chain reaction
S-	serum
SIgAD	selective immunoglobulin A deficiency
SYPL2	synaptophylin-like 2 gene
TCR	T cell receptor
tTG	tissue transglutaminase
tTGAbA	tissue transglutaminase immunoglobulin A
tTGAbG	tissue transglutaminase immunoglobulin G
U/ml	units per millilitre

1 INTRODUCTION OF RESEARCH OBJECTIVES AND QUESTIONS

The main objective of my thesis is to investigate whether two alternative praxis to interpret a celiac disease screening test result lead to significantly different outcomes. Besides the main objective, celiac disease prevalence and allele distribution within the study population were also evaluated and compared against the expected values collected from the literature.

The celiac disease screening test is a genotyping test to analyse if an individual is a carrier of a major histocompatibility complex II class human leukocyte antigen DQ2 and DQ8 celiac disease-associated alleles that predispose to the disorder. This study focused on a certain allele, HLA-DQx.5, which is related to a very low celiac disease risk category according to the internationally recommended risk allele interpretation guideline, and it is generally interpreted as a non-risk allele. The praxis used in SYNLAB Finland and Estonia central laboratory in Tallinn follows the international guideline and the allele HLA-DQx.5 is interpreted as a non-risk allele. This praxis differs from the country specific routine protocol used in SYNLAB Suomi central laboratory in Helsinki, where HLA-DQx.5 is classified and interpreted as a risk allele predisposing to celiac disease. The aim of the study is to investigate how these two genetic test result interpretation scenarios (country-specific praxis versus international recommendation) correlate with celiac disease specific antigen tests and tissue biopsy findings.

This topic has been discussed at great length but there was not a clear understanding what is the impact of these differing risk allele handling protocols, especially if no further testing will be done based on the HLA screening test result, on the celiac disease risk assessment statement. What is the proportion and how big is the risk to miss some potential celiac disease cases if HLA-DQx.5 is interpreted as negative, almost non-risk finding? And, on the other hand, does it cause an extra, unnecessary,

expensive and burdensome confirmatory testing if HLA-DQx.5 is interpreted as a positive, celiac disease risk allele?

2 LITERATURE REVIEW

2.1 Celiac disease

Celiac disease (CD) which is also referred to as gluten-sensitive enteropathy, celiac spruce and non-tropical sprue, is a serious, lifelong multiorgan autoimmune disease associated with the effects of multiple genes (polygenic) in combination with the triggering environmental factor, dietary gluten. Gluten is a group of proteins found in wheat, barley and rye. When individuals with celiac disease eat gluten or related prolamins, it triggers a T cell mediated immune reaction against tissue transglutaminase, which is an extracellular matrix enzyme. This leads to a chronic inflammation of the small intestinal mucosa. This reaction damages intestinal villi and prevents absorption of some nutrients (malabsorption) into the body. At present, the only treatment for celiac disease is a lifelong adherence to a strict gluten-free diet, although there are several ongoing clinical trials of alternative treatments and therapeutic options, such as gluten binding agents, zonulin-inhibitors, oral proteases and desensitization strategies. (Luca, et al., 2015)

Celiac disease can present diverse and non-specific intestinal and extraintestinal symptoms, including abdominal pain, vomiting, chronic diarrhea, constipation, weight loss, anemia, bone or joint pain, skin disorders, bone loss or osteoporosis and many other. In addition to classical, symptomatic celiac disease, many individuals with celiac disease may have an asymptomatic or a mild form of the disease. (Rubio-Tapia, Hill, Kelly, Calderwood, & Murray, 2013)

The prevalence of combined undiagnosed and diagnosed CD is estimated to affect 1 in 100 people in Europe and USA (Megiorni & Pizzuti, 2012). Childhood CD prevalence in Finland is reported to be 1:67. Studies suggest that the incidence rates are increasing but most of these changes are probably explained by availability and

increasing use of high sensitivity serological screening tests, which are able to detect milder or even asymptomatic forms of CD. (Rewers , 2005)

Although celiac disease is a relatively common disease, the clinical heterogeneity makes it difficult to detect. Population-based screening studies indicate that there is a large undiagnosed population. (Mäki, et al., 2003 and Kurppa, et al., 2014) Evidence suggests that even 50-90 % of individuals with celiac disorder do not have a celiac diagnosis (Goddard & Gillett, 2006).

2.2 Diagnosis of celiac disease

2.2.1 Celiac disease diagnostics process today

Today the clinical decision-making protocol of CD diagnosis is based on a combination of patient's symptoms, family history and clinical laboratory test results. Suspected patients are generally screened with two different types of blood tests; serological antibody tests and a major histocompatibility complex II class human leukocyte antigen (HLA) DQ2 and DQ8 genotyping test. Serological antibody test panels are most commonly used as a primary test and the HLA-DQ2/DQ8 genotyping test is a supplementary test to add strength to the diagnosis. Finally, a confirmation gastroscopy by means of duodenal biopsies, is used in most cases as a confirmatory test for the diagnosis of CD. (Husby, et al., 2012)

However, in year 2012 the guidelines published by the European Society for Pediatric Gastroenterology (ESPGHAN) describes an approach to avoid expensive and burdensome confirmatory biopsies from symptomatic children under certain conditions; characteristic symptoms of CD and levels of immunoglobulin A (IgA) against tissue transglutaminase (tTG) 10-fold or more the upper limit of normal and positive HLA-DQ2/DQ8 genotyping result. Even in the absence of clinical symptoms, the screening for CD should be considered among the children and adolescents who have increased risk for celiac disease. Risk groups include those with Down syndrome, Turner syndrome, Williams syndrome, autoimmune liver or thyroid

disease, selective immunoglobulin A deficiency (SIgAD), type-I diabetes mellitus and patients who have first-degree relatives with diagnosed celiac disease. (Husby, et al., 2012) Finnish study among several other studies has revealed that ESPGHAN criteria can be extended and CD can be diagnosed without biopsies both in children and adult population (Kurppa, et al., 2012). Nevertheless, this is not yet a globally approved approach and, for example, American College of Gastroenterology Clinical guidelines for celiac disease diagnosis stated that there are concerns about ESPGHAN criteria, mainly due to poorly standardized antibody tests and the clinical laboratory diagnostics field still strongly leans in the decision making process on the classic triple combination of serological antibody tests, the HLA-DQ2/DQ8 genotyping test and duodenal biopsies. (Rubio-Tapia, Hill, Kelly, Calderwood, & Murray, 2013).

2.2.2 Current challenges and future direction in celiac disease laboratory diagnostics

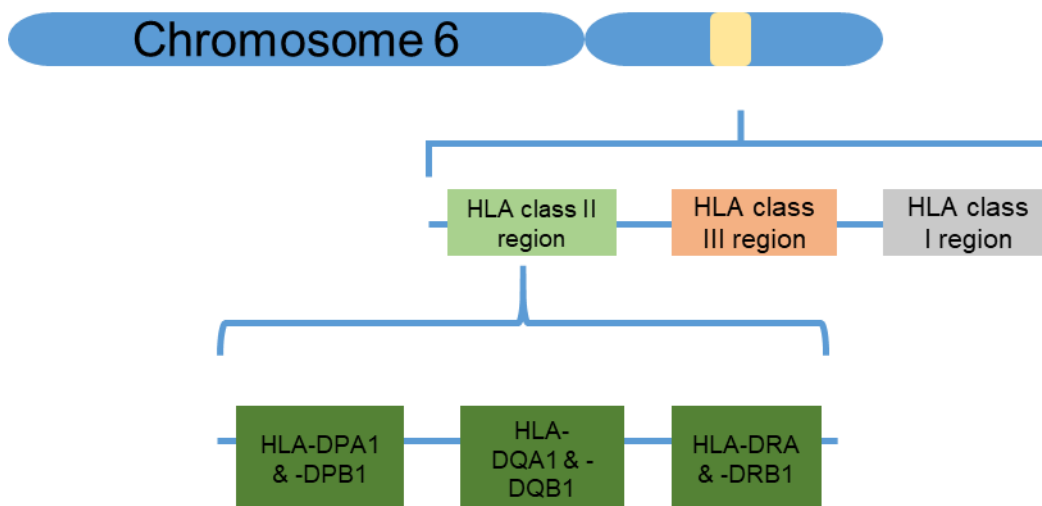
Celiac disease is classified as a polygenic disease, which means that it is caused by a combined action of many various genes. Celiac disease associated genes can contribute the disease phenotype independently or interact with each other and the individual contribution of each existing risk genotype may be very modest. It is widely recognized that particular HLA risk genotypes have an association to celiac disease and most of the patients (up to 95 %) with celiac disease carry HLA-DQ2 and HLA-DQ8 risk alleles. These alleles are, nevertheless, present in general population (up to 35 %) without diagnosed celiac disease. These findings have implied that HLA risk genotype alone is not sufficient factor for CD pathogenesis. (Wijmenga & Gutierrez-Achury, 2014) HLA genotyping based clinical testing has only 12 % positive predictive value (PPV) which means that genotyping should not be used routinely in the initial diagnosis of CD. On the other hand, it has a strong negative predictive value (NPV >99%) which means, that patients who are negative for both risk alleles, are unlikely to suffer from celiac disease. Therefore HLA genotyping is routinely used to rule out the celiac disease rather than confirming the disease in the first stage. (Hadithi, et al., 2007)

The current weakness of the positive predictive value of the HLA-DQ2/DQ8 genotyping test and the polygenic character of CD has led to increasing interest towards genome-wide association studies (GWAS) of which have resulted almost 60 promising CD associated non-HLA loci candidates. These novel risk loci can improve the positive predictive value of genotyping tests and enable more accurate risk classification of patients. This GWAS approach still requires further studies to get a better understanding of the function and role of thousands of genetic variants inside and outside of the coding part of the genome, before the accurate clinical diagnosis and prediction models can rely only on genetic tests. (Wijmenga & Gutierrez-Achury, 2014)

2.3 Celiac disease associated risk alleles

2.3.1 Celiac disease specific HLA risk alleles

Celiac disease is genetically linked to the human leucocyte antigen (HLA) system and the HLA risk allele genotyping screening test from a whole blood sample (B-HLA Keli) is routinely used to estimate the genetic risk of the patient to have CD. Recent GWAS studies have identified several non-HLA genes associated to CD, but, even so, only major histocompatibility complex HLA class II heterodimer coding genes HLA-DQA1 and HLA-DQB1 are genes analysed in the routine clinical diagnosis process for CD. They're located on the short arm of chromosome 6 (6p21.32) in the highly variable HLA-D region which is illustrated in picture 1. The HLA-D-region comprehends HLA-DP (HLA-DPA1 for alpha chain and HLA-DPB1 for beta chain), HLA-DQ (HLA-DQA1 for alpha chain and HLA-DQB1 for beta chain) and HLA-DR (HLA-DRA for alpha chain and HLA-DRB1 for beta chain) genes. (Megiorni & Pizzuti, 2012)



Picture 1 CD associated genes HLA-DQA1 and HLA-DQB1 map on chromosome 6 short arm HLA gene complex on the position 6p21.3 (Sollid & Thorsby, 1993)

The association between CD, HLA-DQ2 and HLA-DQ8 risk alleles is well established, and the disease develops very rarely if these specific risk alleles are not present. European collaboration study regarding HLA risk genotype distribution among celiac disease patients showed that approximately 90% of the patients in Northern Europe (Finland, Sweden, Norway, UK) carry the DQ2 heterodimer encoded by the alleles HLA-DQA1*05 and HLA-DQB1*02 (hereafter called HLA-DQ2.5) either in *cis* or in *trans* configuration. If alleles are present in *cis*, they are inherited together on the same chromosome on DR3 haplotype and, correspondingly, if they are in *trans* configuration, they are inherited separately on DR5/DR7 haplotype on the two homologous chromosomes. The proportion of HLA-DQ2.5 positivity among CD patients in Southern European population (France and Italy) was demonstrated to be lower, varying approximately from 80% in Italy up to 87 % in France, but the proportion of patients carrying more unusual option, one-half of DQ2.5 heterodimer, either DQA1*05 (HLA-DQx.5) or DQB1*02 (HLA-DQ2.x), was instead higher. (Karell, et al., 2003 and Megiorni, et al., 2009) Up to 10% of celiac disease patients carry the DQ8 heterodimer encoded by the alleles HLA-DQB1*03:02 and HLA-DQA1*03 in *cis* (DR4 haplotype) or in *trans* configuration. Only in a very rare case a CD patient

carries a heterodimer without any of formerly mentioned DQA1 or DQB1 variants. (Karell, et al., 2003 and Megiorni & Pizzuti, 2012). Table 1 summarizes the different CD risk alleles and combinations.

HLA-DQ CD heterodimers	Alpha chain	Beta chain
HLA-DQ2.5	DQA1*05 (α 5)	DQB1*02 (β 2)
HLA-DQ2.x	not α 5	DQB1*02 (β 2)
HLA-DQx.5	DQA1*05 (α 5)	neither β 2 nor β 3:02
HLA-DQ8	DQA1*03 (α 3)	DQB1*03:02 (β 3:02)
HLA-DQx.x	not α 5	neither β 2 nor β 3:02

Table 1 Common CD HLA-DQ alpha and beta chain risk allele combinations and heterodimers. Different risk allele combinations form differently named heterodimers. HLA-DQx.x heterodimer does not contain any typical risk allele and it is very unlikely that CD patients carry this heterodimer.

In summary, all DQ2.5 and DQ8 heterodimers increase the risk of developing CD. However, studies has demonstrated that there is a homozygous effect with DQB1 variant; for DQ2.5 subjects carrying two copies of DQB1*02 allele, the CD risk is approximately three times greater (risk 1:10) than if carrying only one copy (risk 1:35). Similarly, in the case of HLA-DQ2.x condition, individuals homozygous for DQB1*02 allele have a remarkably increased CD risk (risk 1:26) if compared to individuals heterozygous for the same allele (risk 1:210). Homozygosity of DQB1*02 allele is also associated with increased tissue transglutaminase antibody levels and earlier onset of the disease. Moreover, the presence of only single DQB1*02 allele within individuals with DQ8 genotype leads to almost fourfold CD disease risk (1:89 vs. 1:24). (Megiorni, et al., 2009) Table 2 summarizes the evaluated risk of developing CD when individual is carrying certain HLA genotypes. The table 2 also illustrates that the risk allele HLA-DQx.5, which is in the main focus of this thesis, is classified in a very low CD risk category according to the internationally recommended risk allele interpretation guideline.

HLA-DQ CD disease risk genotypes	Alpha chain		Beta-chain		Evaluated risk for CD
HLA-DQ2.5 + HLA-DQ8	$\alpha 5$	$\alpha 3$	$\beta 2$	$\beta 03:02$	1:7 (very high)
HLA-DQ2.5, DQB1*02 homozygosity	$\alpha 5$	$\alpha 5$	$\beta 2$	$\beta 2$	1:10 (very high)
HLA-DQ8 + HLA-DQ2.x, single DQB1*02 allele	$\alpha 3$	not $\alpha 5$	$\beta 2$	$\beta 03:02$	1:24 (high)
HLA-DQ2.x, DQB1*02 homozygosity	not $\alpha 5$	not $\alpha 5$	$\beta 2$	$\beta 2$	1:26 (high)
HLA-DQ2.5, single DQB1*02 allele	$\alpha 5$	not $\alpha 5$	$\beta 2$	not $\beta 2$ /not $\beta 03:02$	1:35 (high)
HLA-DQ8	$\alpha 3$	not $\alpha 5$	$\beta 03:02$	not $\beta 2$ /not $\beta 03:02$	1:89 (high)
HLA-DQ2.x	not $\alpha 5$	not $\alpha 5$	$\beta 2$	not $\beta 2$ /not $\beta 03:02$	1:210 (low)
HLA-DQx.5	$\alpha 5$	not $\alpha 5$	not $\beta 2$ /not $\beta 03:02$	not $\beta 2$ /not $\beta 03:02$	1:1842 (extremely low)
HLA-DQx.x	not $\alpha 5$	not $\alpha 5$	not $\beta 2$ /not $\beta 03:02$	not $\beta 2$ /not $\beta 03:02$	1:2518 (extremely low)

Table 2 HLA-DQ risk genotypes, different combinations of heterodimer alpha and beta chains, and the evaluated disease risk in the case cohort when considering the disease prevalence of 1:100. (Megiorni, et al., 2009 and Megiorni & Pizzuti, 2012)

The fact that majority of patients carry either DQ2.5, DQ8 or half of the DQ2 heterodimer, highlights the role of HLA-DQ molecules as a genetic risk factors for CD and the importance of HLA genotyping test in the CD diagnostics protocol to detect individuals potentially at risk. (Karell, et al., 2003) Since the DQ8 risk allele HLA-DQB1*03:02 is almost always linked to HLA-DR4 allele (HLA-DRB1*04), DRB1*04 is also routinely genotyped together with DQ2 and DQ8 risk alleles and it is used to confirm the DQ8 finding (Megiorni & Pizzuti, 2012).

2.3.2 Mechanism of HLA-heterodimers in humoral response

Protein products of HLA-DQA1 and HLA-DQB1 genes play a critical role in the immune system by presenting foreign peptides to the immune system, which in turn triggers the humoral response. Proteins coded by HLA-DQA1 and HLA-DQB1 genes attach to each other and form together a functional DQ $\alpha\beta$ -heterodimer. This heterodimer has a function as a cell surface receptor on antigen presenting B cells and plasma cells. (Megiorni & Pizzuti, 2012)

Gluten is a mixture of prolamins and its two major components are gliadin and glutenin proteins. Gluten molecules are digested in the gastrointestinal tract to 33-

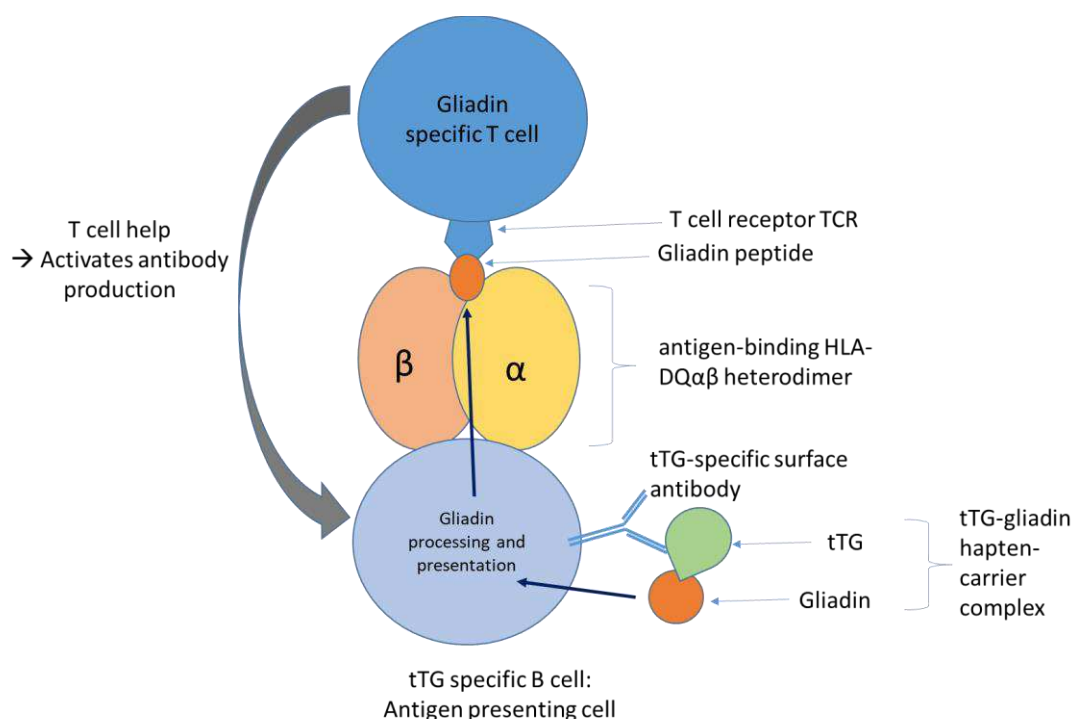
amino acid long gliadin peptides, which are then modified further by tissue transglutaminase (tTG) enzyme in the *lamina propria*, which is a cell rich, thin layer of connective tissue in intestinal *mucosa*. (Russo, Ruchelli, & Piccoli, 2014) Tissue transglutaminase steers an enzymatic deamination which converts glutamine residues in gliadin peptides into negatively charged glutamic acid residues. As HLA-DQ2 and HLA-DQ8 dimers have preference for negatively charged amino acids, these enzymatically modified gluten derived gliadin peptides bind with a high affinity to CD predisposing HLA-DQ2 and HLA-DQ8 dimers. These HLA-DQ dimers then, in turn, present gliadin peptides to CD4+ T cells, which play a major role in the humoral response triggering process. Dietary gluten initiated humoral responses result in cytokine and antibody secretion, in recruitment of other lymphocytes and in damage to the intestinal mucosa. (Koning, 2005)

2.5 Celiac disease specific antibodies

As described in a previous chapter, gluten derived component gliadin is a key activator of the immune system and a driver of CD specific antibody secretion. Many studies have shown that the presence of tissue transglutaminase antibodies and endomysial antibodies (EMA) in blood circulation is a specific indicator of active celiac disease. When a patient has been following a gluten-free diet, these antibody levels decrease. Interestingly, studies have demonstrated that antigliadin antibodies (AGA) against the trigger antigen gliadin itself are less specific for CD: they are present in most CD patients but also in healthy patients. (Picarelli, et al., 1996 and Stenman, et al., 2008)

Antibodies are secreted by B cells and plasma cells. B cells' tTG specific antibody production is dependent on the help of gliadin specific T cells, and therefore a gluten intake activates a parallel immune response against gliadin and tTG. Gliadin acts as a carrier for tTG and together they form a hapten-carrier complex, which is recognized by tTG specific B cells. Gliadin-tTG complex is taken up into the antigen presenting B cell and after degradation and processing, gliadin is in the form which can be

presented by HLA DQ $\alpha\beta$ cell surface receptors to specific CD4⁺ T cells as described in the previous chapter. The T cell triggered humoral response, in turn, stimulates the antibody secreting B cells, leading to the secretion of tTG-specific antibodies. (Lerner, Neidhöfer, & Torsten, 2015) Picture 2 summarizes glute derived gliadin driven tTG antibody production interactions between antigen presenting B cells and gliadin specific CD4⁺ T cells.



Picture 2 HLA-DQA1 and HLA-DQB1 genes code protein subunits, which together form functional DQ $\alpha\beta$ -heterodimers. DQ $\alpha\beta$ -heterodimers are cell surface receptors, which are found on the surface of antigen presenting B cells. They have an ability to present foreign antigens to CD4⁺ T cells, which triggers humoral response. (Koning, 2005) Gluten (carrier) and tTG (hapten) form complexes which are recognized by tTG specific B cells. Gliadin is brought into the cell by endocytosis and processed before the presentation to T cell. This sheds a light why the production and secretion of tTG antibodies are gluten dependent, and why individuals positive for HLA-DQ2 or HLA-DQ8 produce tTG antibodies. (Lerner, Neidhöfer, & Torsten, 2015)

Recently, the routine CD specific antibody test panel used in clinical laboratories has extended with deamidated gliadin peptide antibodies (DGPA) along with more conventional tTG antibodies. DGPA analysis is recommended as an additional test, especially when screening patients are younger than 2 years old. Gliadin peptides are deamidated by tTG when crossing the small intestinal mucosa. Deaminated gliadin peptides are much more immunogenic than unprocessed gliadin peptides and very specific targets for the antibodies against the deaminated peptides. (Husby, et al., 2012 and Hong, 2015)

In a routine CD diagnosis pathway, the initial serological test is an assay to measure a concentration of tissue transglutaminase immunoglobulin A from a serum sample (S -tTGAbA). A total concentration of immunoglobulin A (S -IgA) is also measured as a part of routine test panel, and in the case of low concentration due to primary or secondary humoral IgA deficiency, it is recommended to add a tissue transglutaminase immunoglobulin G (S -tTGAbG) assay to the initial test panel. If S -tTGAb tests are negative, it is recommended to add tests for deamidated gliadin peptide immunoglobulin A and G (S -DGPAAbA and S -DGPAAbG) or for endomysial antibody immunoglobulin A and G (S -EMAbA and S -EMAbG) as additional tests in to the testing panel to increase the sensitivity and specificity of serological diagnostics. (Husby, et al., 2012 and Duodecim, 2018)

Even so, Finnish clinical laboratory praxis follow typically Current Care Guidelines which do not recommend endomysial antibody immunoglobulin tests for screening purposes, because they are laborious from the laboratory analysis perspective. Also deamidated gliadin peptide immunoglobulin tests have not become established in the celiac disease screening program, because tissue transglutaminase antibody tests outperform the deamidated gliadin peptides antibody tests, and therefore they remain the preferred serological test for the diagnosis and/or exclusion of celiac disease. (Duodecim, 2018)

In this study, antibody tests were selected according to the Finnish praxis. Therefore S -tTGAbA and S -IgA were analysed from all patients and results were considered in the final evaluation.

2.6 Celiac disease histopathology

The formalin fixed and hematoxylin and eosin stained small intestine biopsy samples are analysed by clinical pathologists through microscopy diagnosis, which shows characteristic, though not specific, pathological conditions of celiac disease. The inflammatory response causes characteristic mucosal villous atrophy which can be variable and patchy, but the overall thickness of the mucosa is not decreased. Most symptomatic patients having a fully developed stage of celiac disease have a total villous atrophy, which is defined as completely flattened villi. Partial, patchy atrophy is more common in patients having a milder form of celiac disease or in post-treatment patients. The amount of intraepithelial lymphocytes and plasma cells is typically increased. Changes similar to the above, are not specific for celiac disease, and they can be seen in several other conditions, like dermatitis herpetiformis, tropical sprue, kwashiorkor and various autoimmune diseases. (Rosai & Ackerman, 2004)

3 AIMS OF THE STUDY

The specific aims and the structure of the study were:

- To evaluate the local HLA-DQ allele distribution within the study population and compare it to the expected values based on literature
- To get a general understanding of celiac disease prevalence among the study population
- To study the diagnostic value of different HLA-DQ alleles and their risk classification with celiac disease laboratory diagnostics
- To evaluate the differences between two different risk classification scenarios regarding HLA-DQx.5 allele

The study was performed by using routinely received celiac disease test samples collected from patients who were suffering from celiac disease related symptoms and therefore were suspected to have celiac disease.

4 MATERIALS AND METHODS

3.1 Samples

The complete sets of celiac diagnostic panel samples were randomly collected from routine celiac disease testing samples and processing was done anonymously in SYNLAB Finland and Estonia central laboratory in Tallinn, Estonia and in SYNLAB Suomi central laboratory in Helsinki, Finland. Sample sets consist of the following types of sample materials: serum sample (3,5 ml serum gel sample tube, Becton Dickinson Vacutainer SST, Cat. No. 367957, Becton, Dickinson and Company, Plymouth, Devon, UK) for antibody determinations, whole blood sample (3,0 ml K₂EDTA sample tube, Becton Dickinson Vacutainer K₂EDTA, Cat. No. 368856, Becton, Dickinson and Company, Plymouth, Devon, UK) for HLA-DQ risk allele genotyping and tissue biopsy samples (20 ml CellsStor pre-filled specimen container, 10% neutral buffered formalin, Cat. No. BAF-5000-08X or 60 ml CellsStor pre-filled specimen container, 10% neutral buffered formalin, Cat. No. BAF-6000-08U CellPath Ltd, Newtown, Powys, UK) from the upper small intestine for histopathological analysis to check the damage to the villi.

3.1.1 Sample transportation and storage

Samples were transported to the analyzing laboratory in temperature and transportation time controlled conditions, according to the standard ISO 15189. Serum samples were transported in cooled environment +2°C...+8°C and tissue biopsy and whole blood samples in a cooled or in a room temperature +2°C...+25°C. Sample transportation time was varying between 10 to 24 hours. Samples were either analysed immediately after arrival to the analyzing laboratory, or they were stored short term at +4°C (maximum about 3 days).

3.2 Sample preparation methods

3.2.1 Sample preparation for antibody assays

In order to obtain serum, the blood sample collected to serum gel sample tube was let to clot for 30 minutes and after clotting the whole blood samples were centrifuged at 2000 g for 15 minutes. The supernatants were stored on the top of gel during the transportation and the short term storage. This step was performed in several external sample collection centers and therefore the models of centrifuges were unknown. Sample material quality was visually inspected for clots, hemolysis, ictericia and lipemia before analysis and sample tube was decapped manually before analysis. General lab equipment and consumables were used if necessary (disposable Pasteur pipettes, automatic pipettes, disposable pipette tips) to perform sample preparation steps.

3.2.2 DNA extraction for HLA genotyping analysis

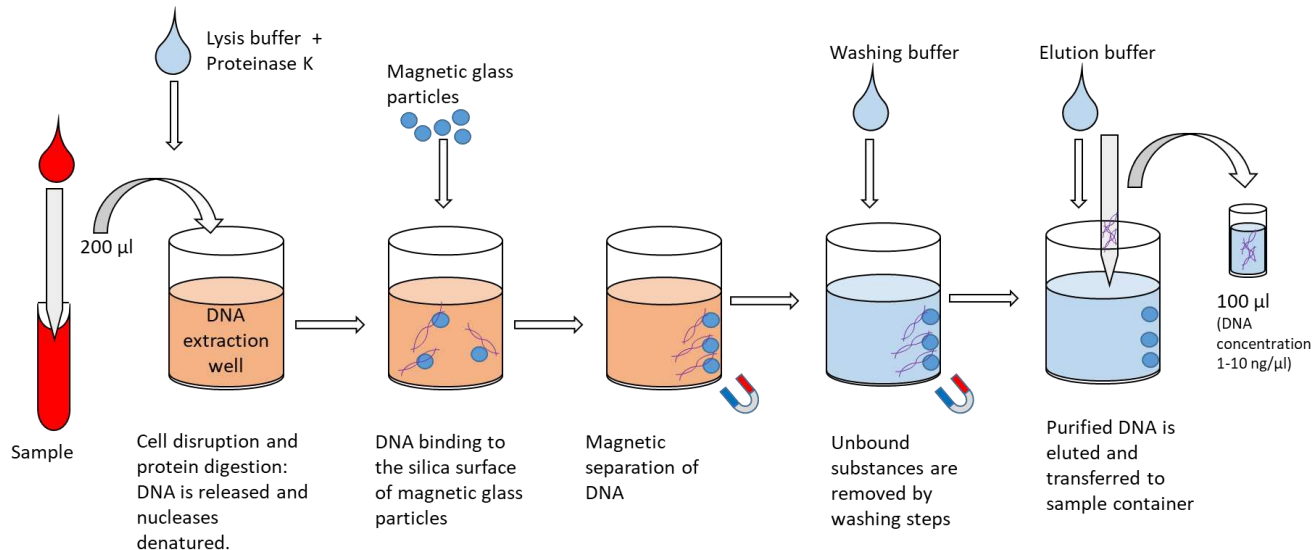
DNA extraction was performed with MagNA Pure96 DNA extraction instrument (Roche Molecular Systems, Pleasanton, California, USA) and MagNA Pure 96 DNA and Viral NA Small Volume Kit (Cat. No. 06 543 588 001, Roche Molecular Systems, Pleasanton, California, USA).

All manual sample preparation steps were performed in a laminar flow cabinet. Standard protective equipment was used (gloves, lab coats) to prevent contamination and safety hazards. General lab equipment and consumables were used (automatic pipettes, disposable DNA/RNA free filter tips, microtubes, vortex, microtube centrifuge) to perform sample preparation steps.

DNA extraction step required 200 µl room temperature primary whole blood sample. Sample material quality was visually inspected for clots. The following process steps are illustrated in a picture 3. Sample material (200 µl whole blood) was pipetted carefully to the bottom of the Magna Pure DNA extraction plate well. The plate was inserted into the DNA extraction instrument for automated extraction processing. The

automated extraction protocol used was “DNA Blood SV”. Lysis/binding buffer (< 6 M guanidine thiocyanate, < 30% Triton X-100, < 60 mM Tris HCl) was added to the reaction wells to initiate cell/virus lysis and binding of nucleic acids. Proteinase K (2% proteinase K, 50% glycerol) addition started the protein digestion. Magnetic glass beads were added to the reaction well (MGP suspension containing isopropanol) for binding DNA.

After DNA binding step, unbound substances were washed away with wash buffers (Wash buffer I: < 6 M guanidine hydrochloride, < 50% EtOH, < 30 mM Tris HCl, Wash buffer III: < 20 mM Na-acetate buffer) by several washing steps. Purified DNA was eluted (elution volume 100 μ l) from magnetic glass particles with elution buffer (< 60 mM Tris-HCl buffer) and transferred to a 96-well sample plate (MagNA Pure 96 Output Plate, Cat. No. 06241611001, Roche Molecular Systems, Pleasanton, California, USA).

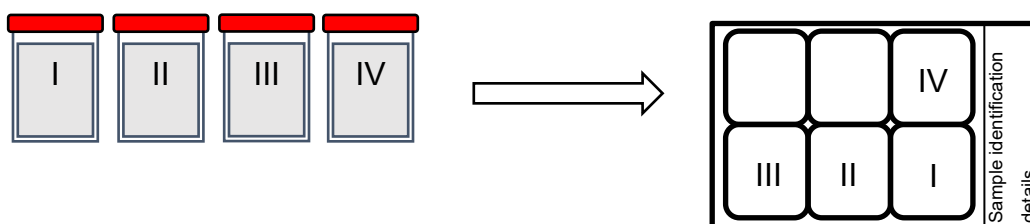


Picture 3. MagNA Pure96 DNA Blood SV protocol is used for HLA genotyping sample preparation. Genotyping analysis is carried out using the isolated, purified DNA sample.

3.2.3 Tissue sample preparation for a biopsy microscopy

3.2.3.1 Tissue sample fixation, embedding and glass slide preparation

Tissue samples were fixed by using immersion fixation technique with 10% neutral buffered formalin, which fixes tissue by cross-linking the proteins. Small pieces of the upper small intestine were let to soak in the fixative solution at a volume of a minimum of 20 times greater than the volume of the tissue and the fixing time was a minimum of 2 hours. Following fixation, tissue pieces from the same patient were transferred to a tissue cassette for processing, as illustrated in a picture 4. The cassette has six separate compartments, each holding one piece of tissue.



Picture 4. Fixed tissue samples are transferred to the tissue cassette for processing. Tissue pieces sampled from different locations are placed to the separate cassette compartments.

Cassettes were placed into the tissue processor cage and the cage was then placed into the tissue processor chamber filled with formalin solution (10% neutral buffered formalin, Alcol Diagnostics Oy, Espoo, Finland). Sample processing was done using the Tissue-Tek VIP 6 system (Sakura Finetek Europe B.V., Alphen aan den Rijn, The Netherlands). Tissue processing program automatically controls the dehydration step which removes the water by immersing tissue in a series of ethanol solutions of increasing concentrations until 100% alcohol concentration is reached (Absolute ethanol ETAX AA, Altia Oyj, Helsinki, Finland, and 96% ethanol ETAX A, Altia Oyj, Helsinki, Finland). During the clearing stage, the ethanol was gradually replaced with Tissue-Tek Tissue-Clear solution (xylene substitute). This stage changes the

appearance of the tissue samples to transparent and clear. It is also a mandatory step before an embedding stage, as the ethanol and a paraffin wax does not mix. The last tissue processing stage was embedding, at which stage the xylene is replaced by the molten paraffin wax (Tissue-Tek III paraffin) during several wax immersion steps. Tissue preparation steps are shown in picture 5.



Picture 5. Tissue sample preparation process steps. Upper left picture: tissue samples in cassette ready for tissue processor. Upper right picture: tissue samples after tissue processor handling. Lower left picture: tissue samples in molten paraffin wax. Lower right picture: tissue samples in paraffin block ready for microtome cutting step.

The samples which were embedded to the paraffin block were cut with a Microm HM 355 S rotary microtome (Microm International GmbH, Thermo Fisher Scientific, Walldorf, Germany) connected to a heated water bath section transfer system Microm STS (Microm International GmbH, Thermo Fisher Scientific, Walldorf, Germany) to

obtain thin sections which were placed to microscopy glass slides. Sections from two different levels were selected to achieve a representative sample. Cut sections from different levels were placed side by side on microscopy glass slides for staining with hematoxylin and eosin (HE).

3.2.3.2 Hematoxylin and eosin staining

Hematoxylin and eosin staining (HE staining) is a common histopathological staining method to reveal different tissue types and morphological changes.

A deep blue-purple color hematoxylin is an alkaline dye and it stains nucleic acids (nuclei of cells). Hematein, a product of oxidation of hematoxylin, is the active dye-metal complex. The hematoxylin solution used was Mayer's hematoxylin, and the oxidizing agent used was potassium iodate. In hematoxylin staining, mordant forms colored dye-mordant-tissue complexes which are often called "lakes" and the color depends on the mordant salt used. In Mayer's hematoxylin solution, the mordant used is potassium aluminium sulfate. During staining the hematoxylin solution first imparts to the nuclei of cells a light transparent red stain. During the differentiation step hydrochloric acid is used to remove excess stain from tissues. The red color then rapidly turns blue on exposure to alkaline solution (tap water). This blueing process step neutralizes the acid and forms an insoluble dark blue aluminum hematein complex.

A pink eosin Y is a fluorescent acidic dye and it stains proteins (basic structure of the tissue; cytoplasm, collagen and muscle fibers). The addition of acetic acid sharpens the staining of the eosin.

Tissue sample staining and film cover-slipping process is done using the Tissue-Tek Prisma and Tissue-Tek Film integrated system (Sakura Finetek Europe B.V., Alphen aan den Rijn, The Netherlands). Reagents and liquids used in the process were 96% ethanol (Absolute ethanol ETAX AA, Altia Oyj, Helsinki, Finland, and 96% ethanol ETAX A, Altia Oyj, Helsinki, Finland), Tissue-Tek xylene, Tissue-Tek Tissue-Clear

solution (xylene substitute), eosin solution (Eosin Solution, Reagen, Toivala, Finland), acetic acid $\geq 90\%$ (Acetic acid $\geq 90\%$, GPR Rectapur, Merck KGaA, Darmstadt, Germany), 0,08% HCl hydrochloric acid solution (Hydrochloric Acid 37-38%, J.T. Baker/Avantor Performance Materials B.V., Arnhem, Netherlands) and Grade 2 laboratory water fulfilling CLSI (Clinical Laboratory Standards Institute) requirements.

Mayer's hematoxylin solution for the staining process was prepared by mixing 750 ml commercial hematoxylin solution (Mayer's hemalum solution, Merck KGaA, Darmstadt, Germany) and 30 ml acetic acid $\geq 90\%$.

The staining protocol was the following:

Preparation

1. Fixing 10 min

Dewaxing step

2. Tissue-Clear 10 min + 10 min

Dehydration step

3. Abs. ethanol 1 min + 1 min
4. 96% ethanol 30 s + 45 s

Wash and hematoxylin treatment

5. Laboratory water 2 min
6. Mayer's hematoxylin solution 7 min

Blueing and differentiation

7. Tap water 2 min
8. 0,08% HCl 10 s
9. Tap water 5 min
10. Laboratory water 1 min

Eosin treatment

11. Eosin 10 min
12. Laboratory water 1 min

Dehydration

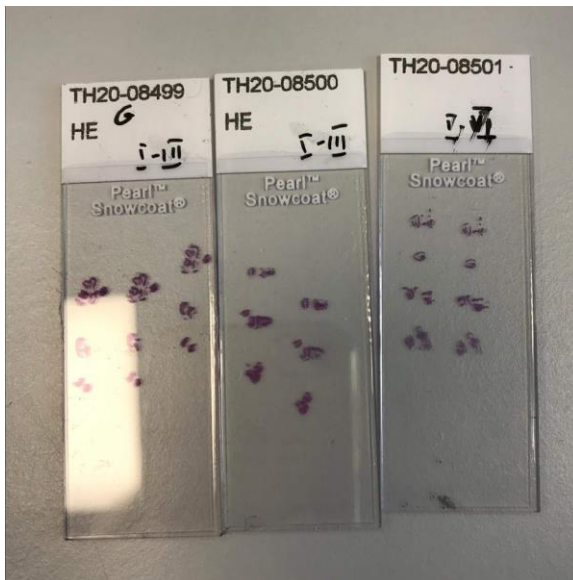
13. 96% ethanol 1 min + 1 min
14. Abs. ethanol 1 min + 1 min + 1 min

Clearing

15. Xylene 2 min + 3 min

Cover-slipping

Prepared microscope slides (examples in picture 6) are analysed by clinical pathologists.



Picture 6. Examples of HE-stained duodenal biopsy sample slides.

3.3 Analytical methods

3.3.1 Serum assays

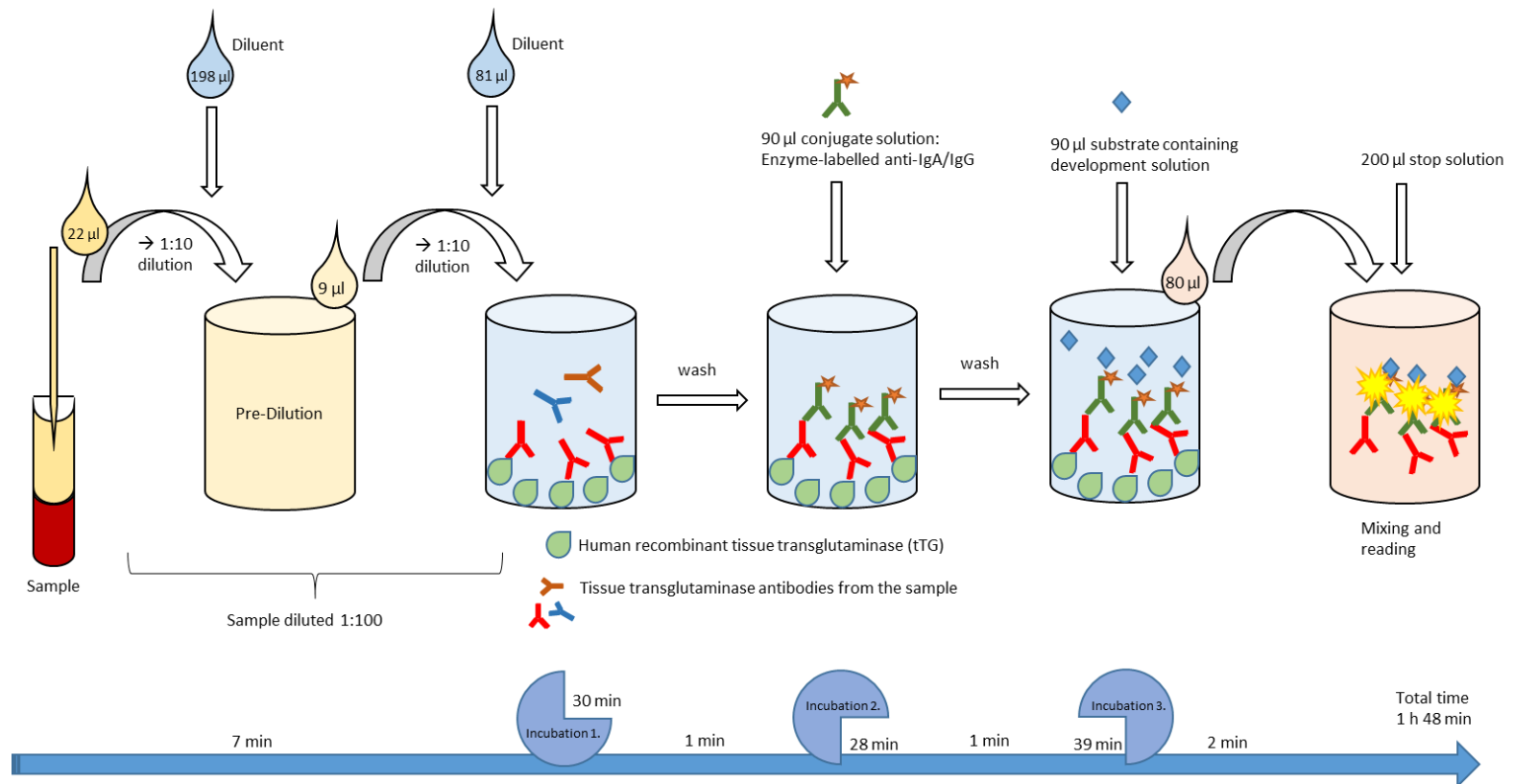
3.3.1.1 Tissue transglutaminase IgA assay from a serum sample

Serological antibody analysis to measure a serum sample S -tTGAbA concentration was done using the Phadia 250 analyser (Thermo Fisher Scientific/Phadia AB, Uppsala, Sweden). The Phadia 250 is a fully automated random-access immunoanalyser

The in vitro measurement of S -tTGAbA in human serum was by the EliA Celikey IgA semi-quantitative fluoroenzyme immunoassay. The assay format is enzyme-linked immunosorbent assay (ELISA) and uses recombinant human tissue transglutaminase as antigen. The Celikey specific reagents are available in a ready to use format in wells.

Celikey IgA microwells are coated with human recombinant tTG. Prior to sampling, the Phadia 250 analyser aspirates 22 μ l of non-diluted sample and automatically dilutes the sample 1:100 with ready for use on-board diluent (PBS containing BSA, detergent and sodium azide (0.095 %)). When the diluted patient sample is added to the microwell, antibodies to tTG bind to antigen in the wells. Incubations are performed at +37°C. After the first incubation, non-bound antibodies are washed away with Phadia phosphate buffer washing solution and enzyme-labeled conjugate antibodies against human IgA (β -galactosidase anti-IgA or anti-IgG, mouse monoclonal antibodies in PBS containing BSA and sodium azide (0.06 %)) are added to form an antibody-conjugate complex. After the second incubation, non-bound conjugate is washed away with Phadia washing solution and the bound complex is incubated with a development solution (0.01 % 4-methylumbelliferyl- β -D-galactoside). β -galactosidase enzyme reacts with the 4-methylumbelliferyl- β -D-galactoside and the enzymatic reaction produces fluorescence.

The reaction is stopped with stopping solution (4 % sodium carbonate) and the fluorescence in the reaction mixture is measured. The higher the fluorescence signal, the more specific IgA is present in the specimen. Calibration of the assays is completed whenever a new kit lot is taken into use and analyser software converts the measured signal automatically to EliA U/ml using the calibration curve. Detailed description of assay format and steps are described in picture 7.



Picture 7. Phadia Celikey IgA assay format.

3.3.1.2 Total IgA assay from a serum sample

Concentration of total serum IgA (S -IgA) was measured by using the Siemens ADVIA Chemistry XPT system (Siemens Healthcare GmbH, Erlangen, Germany). The ADVIA XPT is a fully automated random-access clinical chemistry analyser.

The in vitro measurement of S -IgA in human serum was done using the ADVIA Chemistry XPT IGA_2 assay reagent which is available as a ready to use format and the test principle is a PEG-enhanced immunoturbidimetric method.

The analyser aspirates 30 µl of the primary serum sample and automatically dilutes the sample 1:5 with saline. 4 µl of diluted sample is aspirated to a reaction cuvette which contains 80 µl of Reagent 1 (Polyethylene glycol (6%), Tris/HCL buffer, pH 7.4 (20 mmol/L), sodium chloride (150 mmol/L) and NaN₃ (0.09%)). After stirring and incubation at +37°C, 16 µl of Reagent 2 (Polyethylene glycol (6%), Antihuman IgA (goat), Tris/HCL buffer, pH 7.4 (20 mmol/L), sodium chloride (150 mmol/L), NaN₃ (0.09%)) is added to the reaction cuvette. Sample is left to react with the Reagent 2 containing the analyte specific antiserum to form a precipitate. After the second stirring and incubation steps, sample absorbance is measured turbidimetrically at 340/694 nm. The analyser software converts the measured absorbance automatically to the concentration of IgA (g/l) using a standard curve from the absorbances of standards.

3.3.2 HLA genotyping method

HLA genotype is analysed from isolated DNA sample using EliGene Coeliac RT kit (Elizabeth Pharmacon, Brno-Zidenice, Czech Republic) which is based on real-time polymerase chain reaction (RT-PCR) method. The kit consists of primers and labeled probes for the detection of HLA-DQ2 (DQA1*05, DQB1*02), HLA-DQ8 (DQA1*03, DQB1*03:02) and HLA-DR4 (DRB1*04) alleles. Synaptophysin-like 2 gene (SYPL2) is used as an internal control (IC) which monitors if RT-PCR processes are working as

expected. RT-PCR technique monitors the amplification reaction of a targeted DNA molecule using fluorescence during each amplification cycle in the PCR reaction.

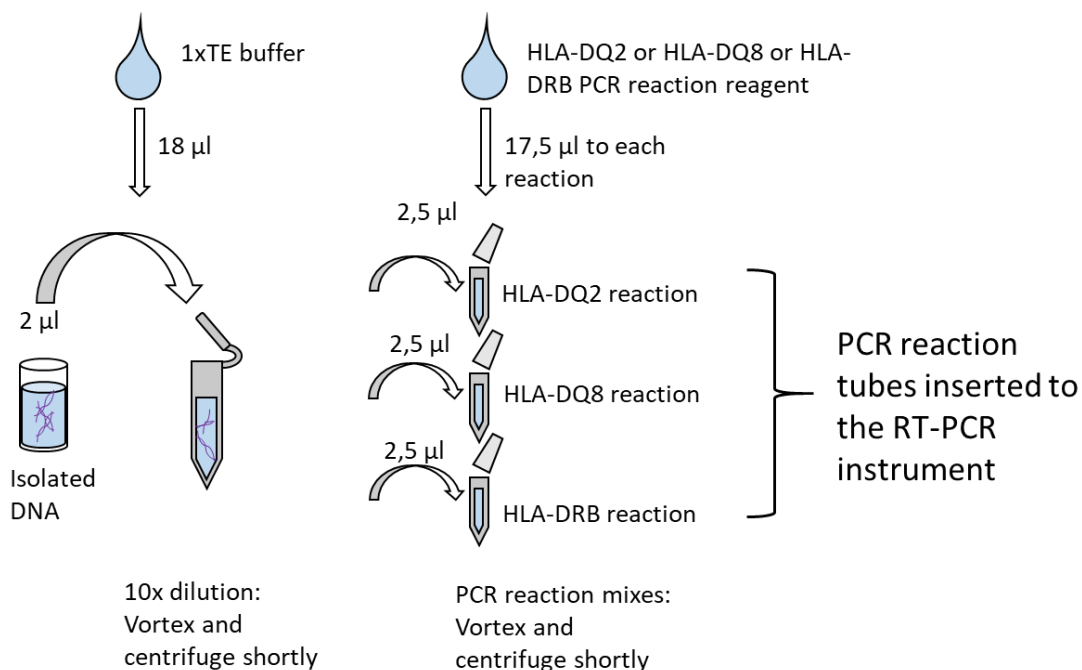
Probes used for detection are labelled with 2 different type of fluorescent dye labels to separate different alleles within the same reaction. RT-PCT instrument runs 3 reactions and the details of each reaction are listed in the table 3 below.

	FAM labeled probe (6-fluorescein amidite (6-FAM))	JOE labeled probe (4-5-Dichloro carboxy fluorescein)
HLA-DQ2 reaction	DQA1*05	DQB1*02
HLA-DQ8 reaction	DQB1*03:02	DQA1*03
HLA-DRB reaction	DRB1*04	IC

Table 3. HLA genotyping method RT-PCR run consists of 3 reactions. Probes are labelled either with FAM or with JOE to detect different alleles within the same reaction.

RT-PCR reaction was with Mic qPCR (Bio Molecular Systems, Upper Coomera, Australia) thermocycler and PCR tubes (Mic-Tubes and Caps strip PCR tube, total reaction volume 10 - 25 μ L, Bio Molecular Systems, Upper Coomera, Australia, Cat. No. 60655). All manual sample preparation steps were performed in a laminar flow cabinet. Standard protective equipment was used (gloves, lab coats) to prevent contamination and safety hazards. General lab equipment and consumables were used (automatic pipettes, disposable DNA/RNA free filter tips, microtubes, PCR tubes, vortex, microtube centrifuge) to perform sample preparation steps. Liquids used were Grade 2 laboratory water fulfilling CLSI (Clinical Laboratory Standards Institute) requirements and Tris-EDTA buffer solution (1xTris-EDTA, pH 8,0, diluted from 100x concentrate, Sigma-Aldrich, St. Louis, MO, USA).

DNA extract was diluted 10x with 1xTris-EDTA buffer (18 μl 1xTris-EDTA and 2 μl DNA extract). All reaction runs included positive (SYPL2) and negative ($mQ\text{H}_2\text{O}$ sterile water) controls. Reaction preparation steps are described in a picture 8.



Picture 8. Reaction preparation for HLA genotyping RT-PCR method. DNA extract is diluted 10x and 2,5 μl of diluted DNA sample is used per each PCR reaction.

RT-PCR protocol has a holding stage (initial denaturation) at 95°C for 3 minutes and a cycling stage, which consists of a denaturation step at 95°C for 15 seconds and an annealing step at 58°C for 40 seconds. The cycling stage is repeated 40 times.

Intensity of FAM and JOE reporter probes' fluorescence was read by using two different channels, FAM channel (green: absorbance 494 nm – emission 518 nm) and JOE channel (yellow: absorbance 525 nm – emission 548 nm).

3.4 Result interpretations

3.4.1 Serum tissue transglutaminase IgA assay results

S -tTGAbA assay's reference value of healthy individuals is <7 EliA U/ml. Results between 7 and 10 EliA U/ml are intermediate and further investigation is recommended. Typically biopsy samples are collected to confirm the diagnosis or exclude CD. If S -tTGAbA result is >10 EliA U/ml, it is interpreted as a positive result and if S -tTGAbA result is 10 x upper limit of normal value (≥ 70 EliA U/ml) it is a strong predictor of subsequent celiac disease even in patients with normal villi. Increased values are highly specific for villous atrophy and therefore used as a specific indicator of active celiac disease. When the patient has been on a gluten-free diet, antibody levels decrease.

3.4.2 Serum total IgA test results

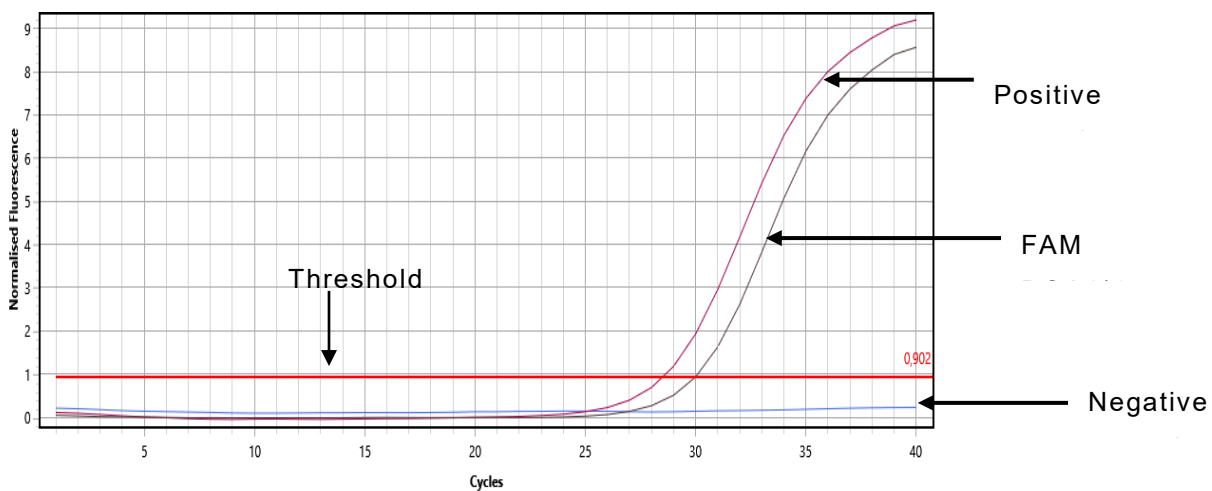
Total IgA reference values for healthy individuals vary by age. Reference values are listed in a table 4 below.

Total Serum IgA concentration	
Age group	Reference range (g/l)
<2 years	0-0,8
2-3 years	0,2-1
4-6 years	0,3-2
7-9 years	0,3-3
10-11 years	0,5-2
12-13 years	6-3,6
14-15 years	5-2,5
16-19 years	6-3,5
≥ 20 years	0,7-4

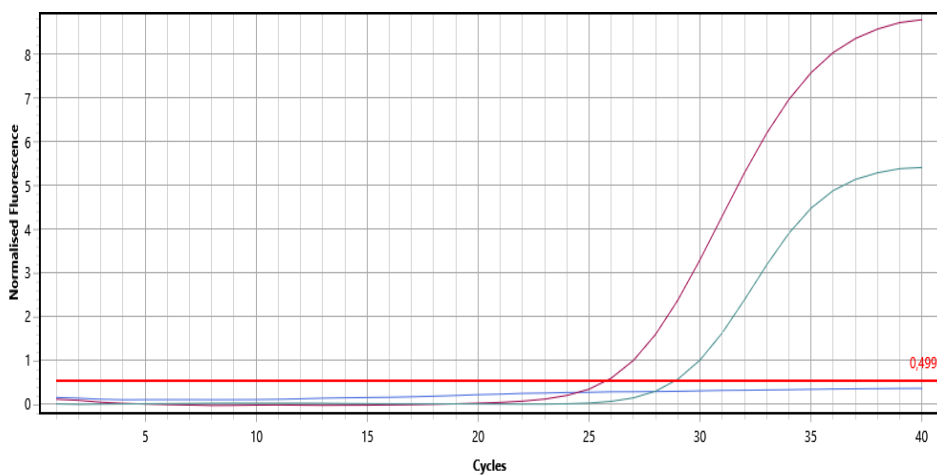
Table 4. Age specific reference values of serum total IgA (S -IgA).

3.4.3 HLA genotyping results

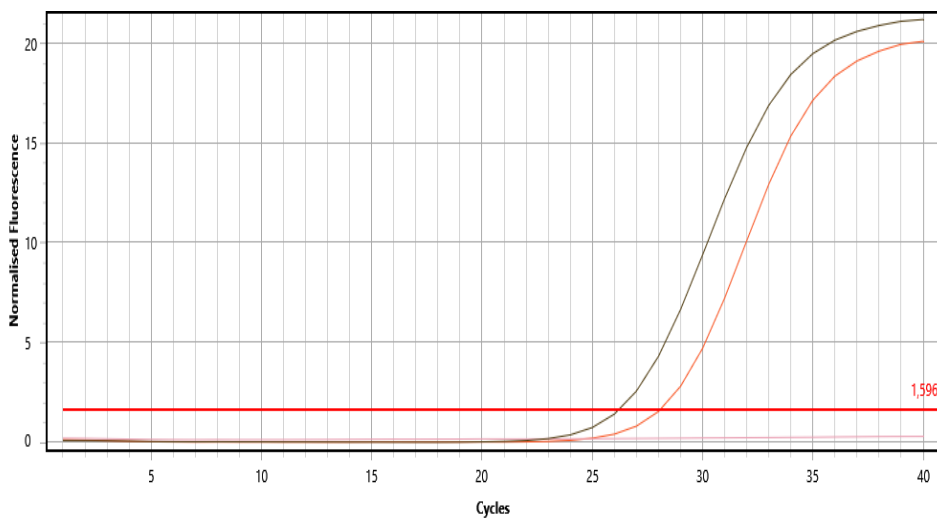
B -HLAKeli results are read from the Mic qPCR interface. Mic qPCR system sets a threshold value automatically to eliminate false positivity due to very faint increase of signal. In a successful analysis the positive, negative and internal controls are passed, and the internal control amplification signal is exponential. In the case of a positive genotype result, the positive control has the highest amplification signal and the positive genotype has a slightly lower amplification signal than the positive control. Both amplification signals increase exponentially before cycle number 35 and the negative control amplification signal remains below the threshold value. Examples of positive findings are shown in pictures 9, 10 and 11.



Picture 9. HLA-DQ2 reaction example. Sample is positive for DQA1*05.



Picture 10. HLA-DQ2 reaction example. Sample is positive for DQB1*02.



Picture 11. HLA-DRB reaction example. Sample is positive for DRB1*04.

Results are interpreted following the rules described in tables 5 and 6.

Genotype	HLA-DQ2 reaction		HLA-DRB reaction	
	FAM DQA1*05	JOE DQB1*02	FAM DRB1*04	JOE IC
HLA-DQ2.5	+	+	+/-	+
HLA-DQ2.x	-	+	+/-	+
HLA-DQx.5	+	-	+/-	+
No DQ2 risk alleles	-	-	+/-	+

Genotype	HLA-DQ8 reaction		HLA-DRB reaction	
	FAM DQB1*03:02	JOE DQA1*03	FAM DRB1*04	JOE IC
HLA-DQ8	+	+	+	+
No DQ8 risk alleles	-	+	+/-	+
No DQ8 risk alleles	+	-	+/-	+
No DQ8 risk alleles	-	-	+/-	+

Table 5. HLA genotyping results are interpreted by combining results from HLA-DQ2, HLA-DQ8 and HLA-DRB (control) reactions. Plus (+) symbol means that the allele is present (positive result) and in the sample and minus (-) symbol means that the allele cannot be detected (negative result) from the sample. Internal control's (IC) positive result confirms that the reaction was successful and DRB1*04 allele should be positive together with a positive HLA-DQ8 finding.

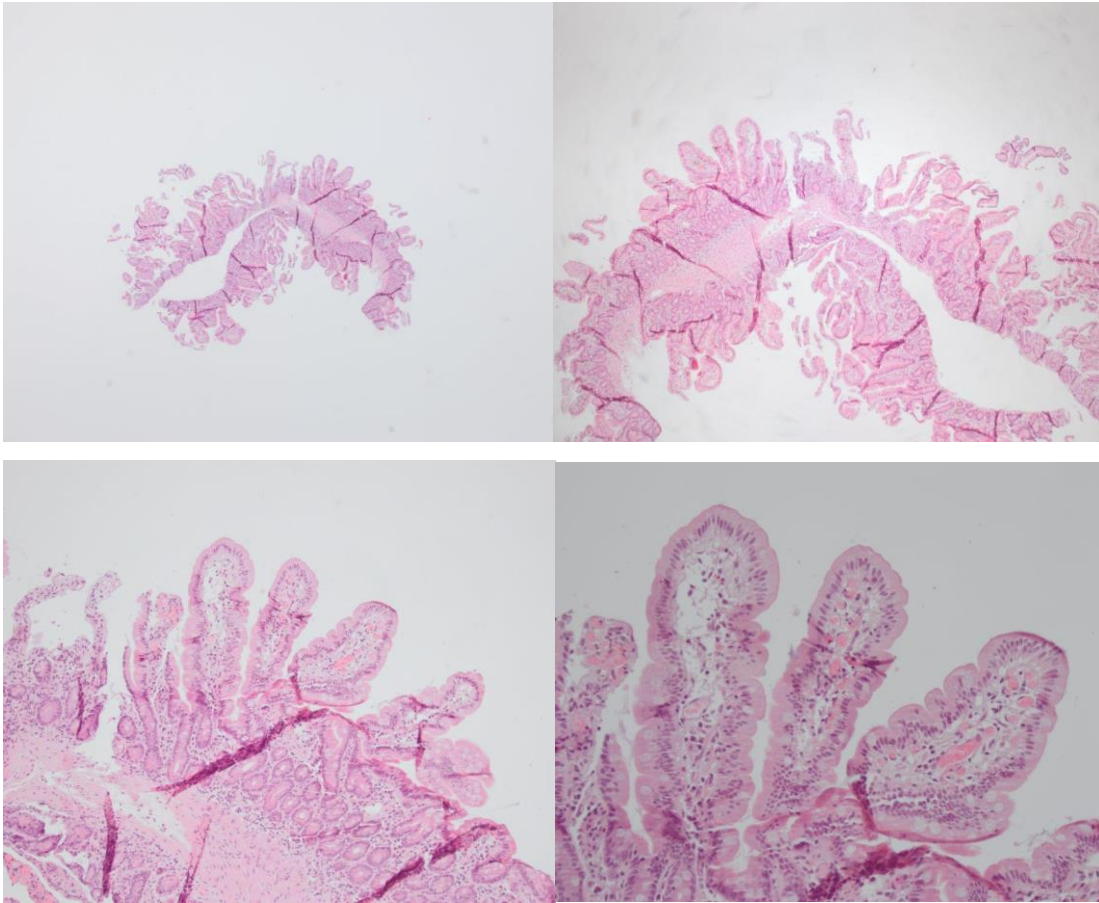
Genotype	CD risk classification	Alleles found	Result statement in SYNLAB Finland and Estonia central laboratory	Result statement in SYNLAB Suomi central laboratory
HLA-DQ2.5 + HLA-DQ8	1:7 (very high)	HLA-DQA1*05, HLA-DQB1*02, HLA-DQB1*03:02, HLA-DQA1*03	HLA-analysis: HLA-DQ2.5 and HLA-DQ8 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05, HLA-DQB1*02 and HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-analysis: HLA-DQ2.5 and HLA-DQ8 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05, HLA-DQB1*02 and HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.
HLA-DQ8 + HLA-DQ2.x, single DQB1*02 allele	1:24 (high)	HLA-DQB1*02, HLA-DQB1*03:02, HLA-DQA1*03	HLA-analysis: HLA-DQ2 and HLA-DQ8 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQB1*02 and HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-analysis: HLA-DQ2 and HLA-DQ8 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQB1*02 and HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.
HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	HLA-DQA1*05, HLA-DQB1*02	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.
HLA-DQ2.x, DQB1*02 homozygosity or single DQB1*02 allele	1:26 (high) or 1:210 (low)	HLA-DQB1*02	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.
HLA-DQ8	1:89 (high)	HLA-DQB1*03:02, HLA-DQA1*03	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.
HLA-DQx.5	1:1842 (extremely low)	HLA-DQA1*05	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-analysis: HLA-DQx.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.
HLA-DQx.x	1:2518 (extremely low)	no risk alleles found	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.

Table 6. HLA genotyping result statements and celiac disease risk classification are given by combining HLA-DQ2 and HLA-DQ8 genotype findings. The method cannot make a difference between DQB1*02 homozygosity or heterozygosity if a sample result is HLA-DQ2 or HLA-DQ2.5 positive but HLA-DQ8 negative. The genotype HLA-DQx.5, which has a different result statement protocols between SYNLAB Suomi and SYNLAB Finland and Estonia central laboratories, is highlighted with red borders.

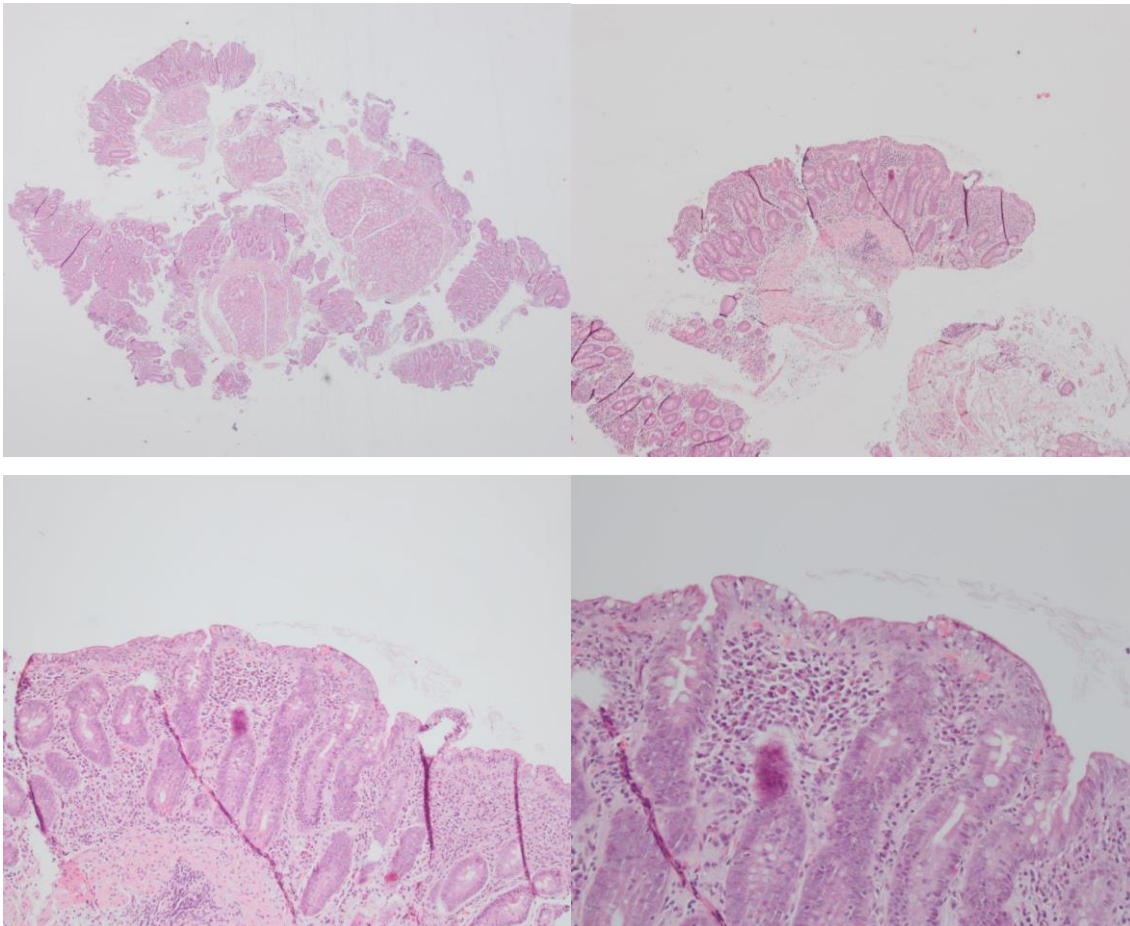
3.4.4 Histological results

Histological microscopy examination of the duodenal biopsy sample is performed by clinical pathologists under microscopy using 2X, 4X, 10X and 40X magnification.

Examples of normal duodenal tissue morphology and villous atrophy findings are shown in pictures 12 and 13.



Picture 12. Examples of duodenal tissue morphology of a normal duodenal tissue. The tissue has normal villous architecture – villi are long, finger-like tentacles and separated with crypts. Magnifications used: 2X, 4X, 10X and 40X.



Picture 13. Examples of duodenal tissue morphology of a CD patient duodenal tissue. Tissue architecture represents a severe villous atrophy – villi have eroded away, leaving a virtually flat surface missing visible crypts. Magnifications used: 2X, 4X, 10X and 40X.

There are several different grading systems available to classify the duodenal histological findings, for example Oberhuber's grading system based on Marsh Classification of histologic findings (Oberhuber, Granditsch, & Vogelsang, 1999) or Corazza's, Roberts' & Ensari's simplified celiac disease grading systems (Ensari, 2010). In this study the duodenal tissue morphology grading conforms to the Ensari's and Chief Pathologist Medical Doctor Tuula Kuukasjärvi's recommendations (Kuukasjärvi, 2019) and it is described in the table 7.

Grade	Description/clinical statement
-	Normal tissue, celiac disease highly unlikely
+	Inflammation, increased intraepithelial lymphocytes but no villous atrophy. Not specific, may be seen in infections
++	Villi still present but shortened. Spectrum of changes seen in symptomatic celiac disease.
+++	Severe/complete villous atrophy. Spectrum of changes seen in symptomatic celiac disease.

Table 7. Histological findings and grading system. Histological findings through microscopy examination are classified based on the level of villous atrophy and/or inflammation.

4 RESULTS AND DISCUSSION

4.1 Validation of study population

The total number of 199 celiac diagnostic panel sample sets (serum, whole blood and tissue biopsy) were studied. One celiac diagnostics sample set represents one patient. SYNLAB laboratories do not have access to detailed clinical patient data, but a common reason for a such a detailed celiac disease test requested by clinician is that a patient has gastrointestinal symptoms and is suspected to have a celiac disease or another condition with similar symptoms.

Three sets of samples were omitted from the final comparisons because they were known to be disease treatment monitoring samples collected from patients formerly diagnosed with celiac disease. The remaining 196 sample sets were estimated to be eligible based on the clinical patient data available and included in a final data analysis.

4.2 Combined serological, genotyping and histological laboratory results

Clinical diagnostics tests were completed on all samples including B -HLAKeli test from a whole blood sample, S -tTGAbA analysis from a serum sample and a histological examination of a duodenal biopsy sample. Total serum IgA levels were also measured to rule out the possibility of IgA deficiency. None of the samples had abnormally low concentration of S -IgA and hence no further investigation such as S -tTGAbG analysis was required. Appendix 1. has a detailed list of clinical laboratory results.

Sample set results were first divided into groups based on the diagnosed HLA genotype. After that results were subdivided into groups representing the outcome of histological and serum tissue transglutaminase antibody results. Data is shown in the table 8.

HLA-DQx.x (total 45 samples)	Histology grade -	Histology grade +	Histology grade ++	Histology grade +++
S -tTGAbA positive >10 EliA U/ml	0	0	0	0
S -tTGAbA intermediate 7-10 EliA U/ml	0	0	0	0
S -tTGAbA normal <7 EliA U/ml	34	8	3	0

HLA-DQx.5 (total 13 samples)	Histology grade -	Histology grade +	Histology grade ++	Histology grade +++
S -tTGAbA positive >10 EliA U/ml	0	0	0	0
S -tTGAbA intermediate 7-10 EliA U/ml	0	0	0	0
S -tTGAbA normal <7 EliA U/ml	9	3	1	0

HLA-DQ8 (total 39 samples)	Histology grade -	Histology grade +	Histology grade ++	Histology grade +++
S -tTGAbA positive >10 EliA U/ml	0	0	1	1
S -tTGAbA intermediate 7-10 EliA U/ml	0	0	0	0
S -tTGAbA normal <7 EliA U/ml	33	4	0	0

HLA-DQ2.x, single DQB1*02 allele or DQB1*02 homozygosity (total 20 samples)	Histology grade -	Histology grade +	Histology grade ++	Histology grade +++
S -tTGAbA positive >10 EliA U/ml	0	0	1	0
S -tTGAbA intermediate 7-10 EliA U/ml	0	0	1	0
S -tTGAbA normal <7 EliA U/ml	15	2	1	0

HLA-DQ2.5, single DQB1*02 allele or DQB1*02 homozygosity (total 71 samples)	Histology grade -	Histology grade +	Histology grade ++	Histology grade +++
S -tTGAbA positive >10 EliA U/ml	0	1	9	4
S -tTGAbA intermediate 7-10 EliA U/ml	0	3	3	1
S -tTGAbA normal <7 EliA U/ml	39	6	5	0

HLA-DQ8 + HLA-DQ2.x, single DQB1*02 allele (total 3 samples)	Histology grade -	Histology grade +	Histology grade ++	Histology grade +++
S -tTGAbA positive >10 EliA U/ml	0	0	0	0
S -tTGAbA intermediate 7-10 EliA U/ml	0	0	0	0
S -tTGAbA normal <7 EliA U/ml	2	0	1	0

HLA-DQ2.5 + HLA-DQ8 (total 5 samples)	Histology grade -	Histology grade +	Histology grade ++	Histology grade +++
S -tTGAbA positive >10 EliA U/ml	0	0	0	0
S -tTGAbA intermediate 7-10 EliA U/ml	0	0	0	0
S -tTGAbA normal <7 EliA U/ml	4	1	0	0

Table 8. B -HLAkel test data from 199 patients divided to individual tables representing different genotypes. All cases in each table are then subdivided by severity grade of histological findings and S -tTGAbA results (number represents the amount of cases falling in each category).

4.3 Celiac disease likelihood

Given that SYNLAB laboratories do not have access to the clinician's final clinical decision and patient data, the classification of celiac disease likelihood was defined together with SYNLAB laboratories' clinical specialists, considering both the serum antibody test results and histological findings. The clinical test result classification matrix is shown in the table 9. Celiac disease laboratory test results shown in the table 8 were then classified according to the classification matrix and the final summary is shown in table 10.

Probability - how likely is it that patient has a CD?	Histology grade -	Histology grade +	Histology grade ++	Histology grade +++
S -tTGAbA positive ≥ 70 EliA U/ml (10 x upper limit of normal value)	Positive	Positive	Positive	Positive
S -tTGAbA positive >10 and <70 EliA U/ml	Intermediate	Intermediate	Positive	Positive
S -tTGAbA intermediate 7-10 EliA U/ml	Low	Intermediate	Intermediate	High
S -tTGAbA normal <7 EliA U/ml	Low	Low	Intermediate	Intermediate

Table 9. Sample set results were classified by the likelihood of celiac disease diagnosis matrix set by SYNLAB laboratories' clinical specialists Medical Doctor Glöckmann and Medical Doctor Kuukasjärvi according to the guidelines (Glöckmann, 2020 and Kuukasjärvi, 2019).

Genotype	CD risk classification	n	% from total	Negative	% from the genotype	Intermediate	% from the genotype	Positive	% from the genotype
HLA-DQ2.5 + HLA-DQ8	1:7 (very high)	5	3 %	5	100 %	0	0 %	0	0 %
HLA-DQ8 + HLA-DQ2.x, single DQB1*02 allele	1:24 (high)	3	2 %	2	67 %	1	33 %	0	0 %
HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	71	36 %	45	63 %	12	17 %	14	20 %
HLA-DQ2.x, DQB1*02 homozygosity or single DQB1*02 allele	1:26 (high) or 1:210 (low)	20	10 %	17	85 %	2	10 %	1	5 %
HLA-DQ8	1:89 (high)	39	20 %	37	95 %	0	0 %	2	5 %
HLA-DQx.5	1:1842 (extremely low)	13	7 %	12	92 %	1	8 %	0	0 %
HLA-DQx.x	1:2518 (extremely low)	45	23 %	42	93 %	3	7 %	0	0 %
Total		196		160	82 %	19	10 %	17	9 %

Table 10. The laboratory test result data classified regarding the celiac disease likelihood. 160 sample sets out of 196 were negative and only 17 sample sets were positive. 19 sample sets were intermediate, which means that the celiac disease cannot be confirmed based on clinical laboratory test results. The allele HLA-DQx.5, which's interpretation varies between SYNLAB Suomi and SYNLAB Finland and Estonia central laboratories, is marked in the table with red frames.

4.4 Positive predictive value of B -HLAKeli screening test

The observed positive predictive value (PPV, the proportion of those with positive B -HLAKeli screening test result who have the disease) was calculated by using the genotype risk classifications from the perspective of two alternative scenarios:

- the first scenario which considers HLA-DQx.5 and HLA-DQx.x both as negative, almost non-risk findings and all the rest of the analysed genotypes as positive, celiac disease risk genotype results. This scenario is aligned with the interpretation protocol used in SYNLAB Finland and Estonia central laboratory.
- the second scenario which considers only HLA-DQx.x as a negative result and all the rest of the analysed genotypes, also HLA-DQx.5, as positive, celiac disease risk genotype results. This scenario follows the interpretation protocol used in SYNLAB Suomi central laboratory.

The algorithm to calculate positive predictive value is

$$PPV = \frac{\text{number of true positives}}{(\text{number of true positives} + \text{number of false positives})}$$

Given that SYNLAB laboratories do not have access to the clinician's final clinical decision or the patient diagnosis data, the following definition of true positives and false positives were made:

Number of true positives = positive B-HLAkeli screening cases (carriers of risk genotype) which were confirmed to have a high likelihood for celiac disease by duodenal biopsy examination and S -tTGAbG serological test (according to the celiac disease likelihood diagnosis matrix, table 9).

Number of false positives = positive B-HLAkeli screening cases (carriers of risk genotype) which were confirmed to have a medium or low likelihood for celiac disease by duodenal biopsy examination and S -tTGAbG serological test (according to the celiac disease likelihood diagnosis matrix, table 9).

Calculated positive predictive values are shown in table 11. PPV 1 demonstrates the value of scenario 1 and, accordingly, PPV 2 demonstrates the value of scenario 2.

PPV scenario 1	
Number of true positives (n)	17
Number of true positives + number of false positives (n)	138
PPV 1 (%)	12,3 %

PPV scenario 2	
Number of true positives (n)	17
Number of true positives + number of false positives (n)	151
PPV 2 (%)	11,3 %

table 11. Positive predictive values regarding scenario 1 (HLA-DQx.5 and HLA-DQx.x both interpreted as CD negative results) and scenario 2 (only HLA-DQx.x interpreted as a CD negative result and all the rest of the analysed genotypes, also HLA-DQx.5, are considered as positive, risk genotype results).

4.5 Negative predictive value of B -HLAKeli screening test

The observed negative predictive value (NPV, the proportion of those with negative B -HLAKeli screening test result who do not have the disease) was calculated in the similar manner by using the differing genotype risk classifications from two alternative scenarios.

The algorithm to calculate negative predictive value is

$$NPV = \frac{\text{number of true negatives}}{(\text{number of true negatives} + \text{number of false negatives})}$$

Given that SYNLAB laboratories do not have access to the clinician's final clinical decision or the patient diagnosis data, the following definition of true negatives and false negatives was made:

Number of true negatives = negative B-HLAKeli screening cases (carriers of very low risk genotype) which were confirmed to have a low likelihood for celiac disease by duodenal biopsy examination and S -tTGAbG serological test (according to the celiac disease likelihood diagnosis matrix, table 9).

Number of false negatives = negative B-HLAKeli screening cases (carriers of very low risk genotype) which were confirmed to have a medium or high likelihood for celiac disease by duodenal biopsy examination and S -tTGAbG serological test (according to the celiac disease likelihood diagnosis matrix, table 9).

Calculated negative predictive values are shown in table 12. NPV 1 demonstrates the value of scenario 1 and, accordingly, NPV 2 demonstrates the value of scenario 2.

NPV scenario 1	
Number of true negatives (n)	54
Number of true negatives + number of false negatives (n)	58
NPV 1 (%)	93,1 %

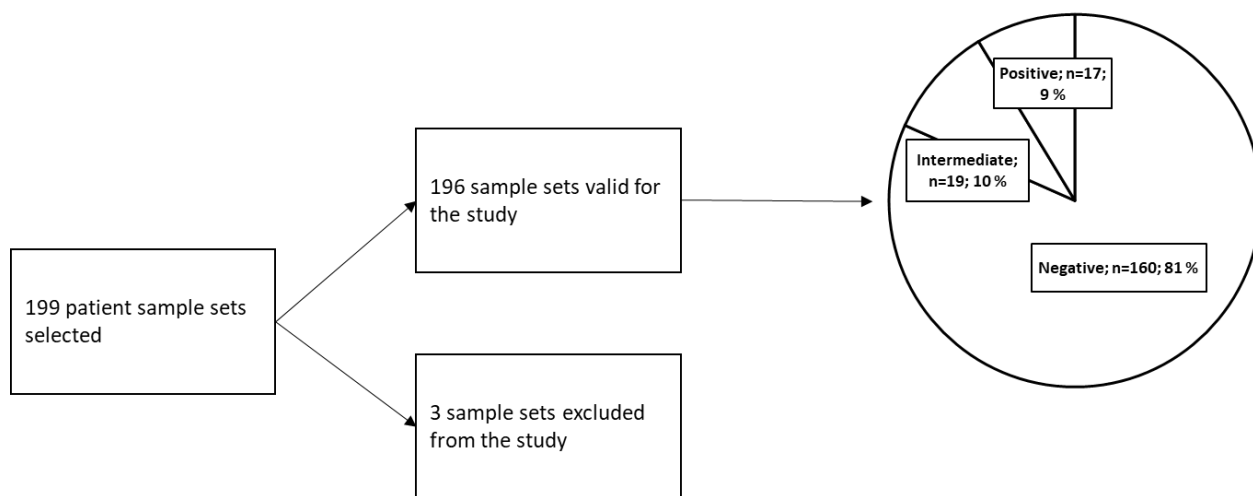
NPV scenario 2	
Number of true negatives (n)	42
Number of true negatives + number of false negatives (n)	45
NPV 2 (%)	93,3 %

Table 12. Negative predictive values regarding scenario 1 (HLA-DQx.5 and HLA-DQx.x both interpreted as CD negative results) and scenario 2 (only HLA-DQx.x interpreted as a CD negative result and all the rest of the analysed genotypes, also HLA-DQx.5, are considered as positive, risk genotype results).

6 CONCLUSIONS

6.1 Test result distribution of the study population

Sample materials used in this study were collected from a selected population of almost 200 patients referred for symptoms, signs and for screening of celiac disease. Nevertheless 82% of the cohort tested negative for CD by the clinical laboratory tests, and 10% of results were classified as intermediate, which typically suggests further testing and clinical examination is needed for a final diagnosis. Only 9% of the clinical laboratory tests pointed out a clear indication of celiac disease. The result distribution is illustrated in picture 14. The primary aim behind the laboratory test request is to exclude celiac disease from the pool of possible diseases causing patient's symptoms. These study findings demonstrated the complexity of celiac disease nature and diagnostics; symptoms are diverse and non-specific and celiac disease is only one of the possible causes for the patient's condition.



Picture 14. Sample sets selected to the study. Three sample sets were excluded because they were collected from the patients formerly diagnosed for celiac disease and were probably collected for treatment monitoring purposes. Out of 196 sample sets only 9% resulted in a positive celiac disease test result.

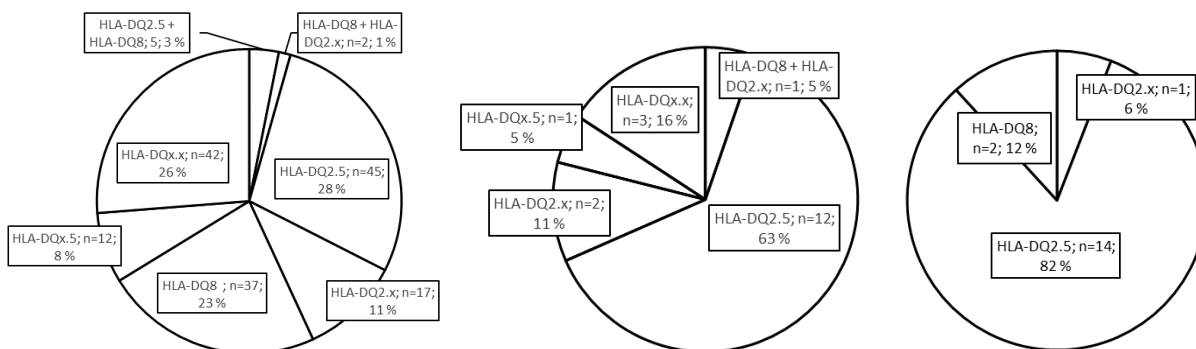
6.2 HLA-DQ allele distribution of the study population and result comparison to the literature

The majority of celiac disease positive subjects present HLA-DQ2.5 heterodimer. Most of the remaining CD positive subjects carry HLA-DQ8 heterodimer and one subject was homozygous or heterozygous for DQB1*02 allele. The genotype distribution of CD positive findings is very well aligned with the expected values described in the literature (Karell, et al., 2003 and Megiorni, et al., 2009). These values are shown in the table 13. Only the amount of HLA-DQ8 heterodimers among all CD positive cases was slightly elevated. However, the data was prone for bias due to a limited number of positive cases; there were only two HLA-DQ8 carriers and one HLA-DQ2.x carrier among only 17 positive cases. If this is taken in consideration, the distribution of CD positive genotypes demonstrated in the study aligned well with expected values based on literature.

Genotype	positive (n)	positive (%)	Expected values (%)
HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	14	82 %	78-90%
HLA-DQ2.x, DQB1*02 homozygosity or single DQB1*02 allele	1	6 %	Appr. 6%
HLA-DQ8	2	12 %	5-10%

Table 13. Genotype distribution of CD positive subjects. Majority of cases carry HLA-DQ2.5 heterodimer as expected.

When allele distribution was compared between positive, intermediate and negative results, the largest variation was seen among celiac disease negative subjects (picture 15). All alternative allele types which can be detected by the used method were present. An interesting point was that the allele combination HLA-DQ2.5 + HLA-DQ8, which has the highest celiac disease predisposing risk, gave neither positive nor intermediate final outcomes, but all five cases were negative. The highest proportion of celiac disease positive subjects were HLA-DQ2.5 carriers. The method used in this study for HLA genotyping was not capable to differentiate between homozygosity and heterozygosity of DQB1*02 allele, so the increased celiac disease risk impact of homozygosity within the HLA-DQ2.5 or HLA-DQ2.x carriers cannot be evaluated in this study.



Picture 15. Allele distribution among positive, intermediate and negative celiac disease test results.

6.3 Differences in HLAkeli test results between SYNLAB laboratories

The main objective of the study was to compare whether the SYNLAB Suomi central laboratory's genetic test result interpretation praxis regarding HLA-DQx.5 allele (scenario 2) gives a clinically different result when compared to SYNLAB Finland and Estonia central laboratory's praxis (scenario 1).

HLA genotyping test's positive predictive value varied from 11,3% to 12,3%, depending on the scenario used. These measured PPV's were well aligned with the 12% PPV described by Hadithi in his study of HLA-DQ typing accuracy (Hadithi, et al., 2007). Scenario 1 showed a slightly better PPV because of less false positives. These additional false positives in scenario 2 are HLA-DQx.5 allele results which are interpreted as positive, risk genotype results, but none of these cases were confirmed CD positive when combined with S -tTGAbA results and histological findings.

Negative predictive values from scenario 1 (93,1%) and scenario 2 (93,3%) were almost identical. There were no positive results among false negatives, and only 4 intermediate cases within scenario 1 and 3 intermediate cases within scenario 2. This shows that patients who do not carry risk alleles are unlikely to have CD and, furthermore, that B-HLAkeli genotyping test can be used to rule out CD diagnosis. Nevertheless the measured negative predictive values were strong and somehow aligned with expectations, they were still lower than NPV (>99%) published by Hadithi (Hadithi, et al., 2007). Our study has some limitations regarding the conclusion of intermediate cases, which were handled as false negatives, as we were not able to confirm them as negative or positive with the limited extent of the data we had. Further examination, more detailed patient data and additional testing after gluten free diet might shed a light to the final result and diagnosis. This might change the B-HLAkeli test NPV value closer to the expected >99%, but unfortunately additional information was not available for SYNLAB laboratories.

Overall, the number of patients carrying HLA-DQx.5 allele was 13 which was 7% of the study population. After S -tTGAbA tests and histological examination, none of

these 13 cases were classified positive for celiac disease. One patient was classified intermediate and 12 were classified negative for celiac disease. In other words, 92% of patients carrying HLA-DQx.5 were diagnosed as very unlikely to have celiac disease and 0% were diagnosed as having a strong likelihood of celiac disease. Percentage of negative, intermediate and positive cases were almost identical if HLA-DQx.5 carrier results are compared to the HLA-DQx.x carrier results; 92% of HLA-DQx.5 and 93% of HLA-DQx.x carriers were diagnosed very unlikely to have a celiac disease and 0% were diagnosed to have a strong likelihood of celiac disease regarding both alleles.

If HLA-DQx.5 is classified as a CD risk allele, it is very likely to cause increasing amounts of, probably unnecessary, laboratory testing and confirmatory biopsies; the data from this study shows that additional 7% of the celiac disease suspects carry the allele HLA-DQx.5 and therefore probably go through additional celiac disease related laboratory testing. On the other hand, if HLA-DQx.5 is classified as a CD non-risk allele, the study data implies that it is very unlikely to miss positive cases from laboratory test perspective. According to the study findings and general recommendations based on international guidelines, it seems that there is no clear clinical benefit if HLA-DQx.5 is classified as a CD risk allele.

6.4 Limitations of the study

Our study has some limitations and the potential for bias because of the lack of direct contact to the clinician and patient. SYNLAB is a commercial clinical laboratory providing clinical laboratory testing and consultation services to medical clinics who are treating patients. SYNLAB laboratories receive only the minimum required information to perform the requested laboratory testing and hence the patient background information available was limited. Patient's final diagnosis was not available for SYNLAB.

This study material was observed only from SYNLAB laboratory diagnostics point of view and intermediate cases were not analysed any deeper than originally requested

by clinicians. This naturally creates limitations to the number of cases selected to this study. Only full sets of samples including whole blood sample for genotyping, serum sample for antibody testing and biopsy sample for histopathological analysis were selected in this study. HLA genotyping test B -HLAKeli should be requested only once in a lifetime per patient because the genetic result does not change. Assumption was made that B -HLAKeli test request should work as a good marker to filter out the celiac disease primary screening cases from all celiac disease related test requests. Even so, there were three clear cases, when the clinician mistakenly repeatedly requested the genotyping test for the celiac disease diagnosed patient during the treatment monitoring phase. These three cases were excluded from the final study data, however, there is a risk that the data could contains similar cases. This finding also highlights the need for additional information to be shared with clinicians regarding celiac disease laboratory diagnostics.

6.5 Suggestions for further research

As pointed out before, the limited number of positive cases, incomplete outcomes of intermediate cases and inadequate patient background information means that this study can be seen as a promising starting material and prelude for a more detailed study regarding the deeper insight to the nature of the HLA-DQx.5 allele under interest. The primary results can be shared with clinicians and discussed if this study could be continued in co-operation with medical clinics and hospitals.

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APPENDIX 1 – Clinical laboratory diagnostics results

(12 pages)

Internal ID	Mnemonic	Test Shortname	B-HLAKeil ValTime	Result external comment (B-HLAKeil)	HLADQ2_DQB genotype	RISK	PADGAST statement	Histology grade	tTGAbA result U/ml	tTGAbA result interpretation	IgA result gl	IgA reference range (age dependent)	IgA result interpretation
19740713N	B-HLADQ2_DQB-PCR	B-HLAKeil	26.07.2018 15:06	HLA-analysis: HLA-DQ2.5 and HLA-DQB1*02:01 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05, HLA-DQB1*02 and HLA-DQB1*03:02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5 + HLA-DQB1*02	1.7 (very high)	T64300 DUODENUM M43000 CHRONIC INFLAMMATION T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS T62350 CARDIO-ESOPHAGEAL JUNCTION M43000 CHRONIC INFLAMMATION	+	<0.6	neg	1.17	0.7-4	normal
19740219A	B-HLADQ2_DQB-PCR	B-HLAKeil	13.09.2018 15:15	HLA-analysis: HLA-DQ2.5 and HLA-DQB1*02:01 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05, HLA-DQB1*02 and HLA-DQB1*03:02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5 + HLA-DQB1*02	1.7 (very high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M43000 CHRONIC GASTRITIS	-	<0.6	neg	1.84	0.7-4	normal
19720708H	B-HLADQ2_DQB-PCR	B-HLAKeil	07.11.2018 15:55	HLA-analysis: HLA-DQ2.5 and HLA-DQB1*02:01 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05, HLA-DQB1*02 and HLA-DQB1*03:02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5 + HLA-DQB1*02	1.7 (very high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M40000 GASTRITIS REACTIVE T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M40000 ESOPHAGITIS T62350 GASTROESOPHAGEAL JUNCTION M40000 INFLAMMATION ACTIVE T62350 GASTROESOPHAGEAL JUNCTION M73320 INTESTINAL METAPLASIA	-	<0.6	neg	1.71	0.7-4	normal
19730508T	B-HLADQ2_DQB-PCR	B-HLAKeil	16.11.2018 15:40	HLA-analysis: HLA-DQ2.5 and HLA-DQB1*02:01 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05, HLA-DQB1*02 and HLA-DQB1*03:02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5 + HLA-DQB1*02	1.7 (very high)	T64300 DUODENUM M73330 GASTRIC METAPLASIA T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	2.90	0.7-4	normal
19600904H	B-HLADQ2_DQB-PCR	B-HLAKeil	06.06.2019 15:42	HLA-analysis: HLA-DQ2.5 and HLA-DQB1*02:01 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05, HLA-DQB1*02 and HLA-DQB1*03:02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5 + HLA-DQB1*02	1.7 (very high)	T64300 DUODENUM: M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM AND CORPUS: M43000 CHRONIC GASTRITIS ACTIVE (HP+)	-	<0.6	neg	3.43	0.7-4	normal
19850303P	B-HLADQ2_DQB-PCR	B-HLAKeil	18.09.2019 16:37	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1.10 (very high) or 1.35 (high)	T64300 DUODENUM M08350 MORPHOLOGICAL DESCRIPTION ONLY (LIEVA INTRAEPITELIAALINEN LYMFOSYTOOSI) T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62350 GASTROESOPHAGEAL JUNCTION M00100 NORMAL TISSUE MORPHOLOGY	+	8.5	intermediate	3.77	0.7-4	normal
19890410K	B-HLADQ2_DQB-PCR	B-HLAKeil	16.01.2018 15:25	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1.10 (very high) or 1.35 (high)	1-3: T64300 DUODENUM AND STOMACH M00100 NORMAL TISSUE MORPHOLOGY	-	0.6	neg	2.82	0.7-4	normal
19700612K	B-HLADQ2_DQB-PCR	B-HLAKeil	17.01.2018 16:18	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1.10 (very high) or 1.35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS ACTIVE HELICOBACTER+++ T63600 GASTRIC ANTRUM M73320 INTESTINAL METAPLASIA AND ATROPHY MILD T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS ACTIVE HELICOBACTER+++	-	<0.6	neg	1.70	0.7-4	normal
19640626V	B-HLADQ2_DQB-PCR	B-HLAKeil	21.01.2018 20:23	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1.10 (very high) or 1.35 (high)	1: T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY 2-3: T63000 STOMACH M43000 CHRONIC GASTRITIS 4: T62000 ESOPHAGUS M43000 CHRONIC INFLAMMATION	-	<0.6	neg	1.97	0.7-4	normal
19610615S	B-HLADQ2_DQB-PCR	B-HLAKeil	31.01.2018 16:00	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1.10 (very high) or 1.35 (high)	T64300 DUODENUM M00100 NO DIAGNOSTIC ABNORMALITY	- CD diagnosed, control test, EXCLUDED	28.0	pos	2.53	0.7-4	normal
19800906K	B-HLADQ2_DQB-PCR	B-HLAKeil	01.02.2018 16:35	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1.10 (very high) or 1.35 (high)	I T64300 DUODENUM M00100 NORMAL FINDING II T63600 GASTRIC ANTRUM, JA CORPUS M00100 NORMAL FINDING IV T62000 ESOPHAGUS M73330 GASTRIC METAPLASIA	-	<0.6	neg	1.19	0.7-4	normal
19970324K	B-HLADQ2_DQB-PCR	B-HLAKeil	09.02.2018 15:55	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1.10 (very high) or 1.35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.48	0.7-4	normal
19820329J	B-HLADQ2_DQB-PCR	B-HLAKeil	09.02.2018 15:56	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1.10 (very high) or 1.35 (high)	T64300 DUODENUM M58000 ATROPHY, MODERATE T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M40000 GASTRITIS, CHRONIC, MILD	++	31.0	pos	1.60	0.7-4	normal
19620508P	B-HLADQ2_DQB-PCR	B-HLAKeil	07.03.2018 16:25	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1.10 (very high) or 1.35 (high)	1-3:T64300 DUODENUM AND STOMACH M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.61	0.7-4	normal
19650612V	B-HLADQ2_DQB-PCR	B-HLAKeil	07.03.2018 16:25	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1.10 (very high) or 1.35 (high)	T64300 DUODENUM M40000 INFLAMMATION MILD T63000 STOMACH M43000 CHRONIC GASTRITIS T62000 ESOPHAGUS M00100 NO PATHOLOGIC DIAGNOSIS	+	56.0	pos	2.40	0.7-4	normal
19750210L	B-HLADQ2_DQB-PCR	B-HLAKeil	11.03.2018 18:38	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isotypes may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1.10 (very high) or 1.35 (high)	I T64300 DUODENUM M58000 ATROPHY, MILD II T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY III T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY IV T62000 ESOPHAGUS M09350 MORPHOLOGICAL DESCRIPTION ONLY	++	6.5	neg	3.26	0.7-4	normal

Internal ID	Mnemonic	Test Shortname	B-HLAKeil ValTime	Result external comment (B-HLAKeil)	HLADQ2_DQB genotype	RISK	PADGAST statement	Histology grade	tTGAb result U/ml	tTGAb result interpretation	IgA result g/l	IgA reference range (age dependent)	IgA result interpretation
1954121L	B-HLADQ2_DQB-PCR	B-HLAKeil	21.03.2018 16:43	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY, MODERATE T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, MILD T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	++	8.7	intermediate	2.21	0.7-4	normal
19600819R	B-HLADQ2_DQB-PCR	B-HLAKeil	22.03.2018 15:36	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M43000 CHRONIC GASTRITIS	-	<0.6	neg	1.56	0.7-4	normal
19530926A	B-HLADQ2_DQB-PCR	B-HLAKeil	25.03.2018 20:43	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 PYLORIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M42000 SUPERFICIAL GASTRITIS	-	<0.6	neg	1.79	0.7-4	normal
20010305H	B-HLADQ2_DQB-PCR	B-HLAKeil	05.04.2018 15:22	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NO PATHOLOGIC DIAGNOSIS T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M00100 NO PATHOLOGIC DIAGNOSIS	-	<0.6	neg	1.44	0.6-3.5	normal
19621009H	B-HLADQ2_DQB-PCR	B-HLAKeil	08.04.2018 23:48	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 PARTIAL VILLOUS ATROPHY	++	8.5	intermediate	1.69	0.7-4	normal
19791015H	B-HLADQ2_DQB-PCR	B-HLAKeil	12.04.2018 14:47	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M09350 MORPHOLOGICAL DESCRIPTION ONLY	-	<0.6	neg	1.53	0.7-4	normal
19861211K	B-HLADQ2_DQB-PCR	B-HLAKeil	27.04.2018 15:02	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 PYLORIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M42000 SUPERFICIAL GASTRITIS	-	<0.6	neg	1.79	0.7-4	normal
19780321H	B-HLADQ2_DQB-PCR	B-HLAKeil	27.04.2018 15:02	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	1: T64300 DUODENUM M82611 VILLOUS ADENOMA 2: T64400 DUODENAL BULBUS M09350 MORPHOLOGICAL DESCRIPTION ONLY 3-4: T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY	++	>128.0	pos	3.23	0.7-4	normal
19470221C	B-HLADQ2_DQB-PCR	B-HLAKeil	29.04.2018 17:25	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T64400 DUODENAL BULBUS M14110 EROSION T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	2.89	0.7-4	normal
19880825K	B-HLADQ2_DQB-PCR	B-HLAKeil	24.05.2018 14:36	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS, MILD T63600 GASTRIC ANTRUM M73320 INTESTINAL METAPLASIA AND ATROPHY MILD T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	3.1	neg	1.12	0.7-4	normal
19990111P	B-HLADQ2_DQB-PCR	B-HLAKeil	25.05.2018 15:46	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY MODERATE T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS MILD T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	++	15.0	pos	2.58	0.6-3.5	normal
19691023L	B-HLADQ2_DQB-PCR	B-HLAKeil	25.05.2018 15:46	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY MILD T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS MILD T62000 ESOPHAGUS M73320 INTESTINAL METAPLASIA	++	11.0	pos	1.80	0.7-4	normal
19560527K	B-HLADQ2_DQB-PCR	B-HLAKeil	27.05.2018 16:16	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY SEVERE T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NO DIAGNOSTIC ABNORMALITY	+++	8.8	intermediate	1.10	0.7-4	normal
19750519B	B-HLADQ2_DQB-PCR	B-HLAKeil	27.05.2018 16:16	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	I T64300 DUODENUM M440000 INFLAMMATION, SEE TEXT II-III T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY IV T62000 ESOPHAGUS M40000 ESOPHAGITIS, MILD	+	0.6	neg	4.42	0.7-4	elevated
19560502C	B-HLADQ2_DQB-PCR	B-HLAKeil	31.05.2018 16:32	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.98	0.7-4	normal
19661124L	B-HLADQ2_DQB-PCR	B-HLAKeil	08.06.2018 16:05	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	1.4	neg	2.17	0.7-4	normal
19640505M	B-HLADQ2_DQB-PCR	B-HLAKeil	11.06.2018 07:07	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 PARTIAL VILLOUS ATROPHY WITH INFLAMMATION T63000 STOMACH M43000 CHRONIC GASTRITIS helicost ++	++	23.0	pos	2.94	0.7-4	normal
19730722I	B-HLADQ2_DQB-PCR	B-HLAKeil	11.06.2018 07:06	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS, MILD T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, MILD	-	<0.6	neg	1.73	0.7-4	normal

Internal ID	Mnemonic	Test Shortname	B-HLAKeil ValTime	Result external comment (B-HLAKeil)	HLADQ2_DQB1*02 genotype	RISK	PADGAST statement	Histology grade	tTGAb result U/ml	tTGAb result interpretation	IgA result g/l	IgA reference range (age dependent)	IgA result interpretation	
19921130K	B-HLADQ2_DQB-PCR	B-HLAKeil	13.06.2018 16:26	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS	-	<0.6	neg	2.00	0.7-4	normal	
19730617I	B-HLADQ2_DQB-PCR	B-HLAKeil	26.06.2018 15:57	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NO DIAGNOSTIC ABNORMALITY T63500 GASTRIC CORPUS M00100 NO DIAGNOSTIC ABNORMALITY T62000 ESOPHAGUS M40000 ESOPHAGITIS MILD	-	<0.6	neg	1.93	0.7-4	normal	
19610327K	B-HLADQ2_DQB-PCR	B-HLAKeil	06.07.2018 15:46	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T64400 DUODENAL BULBUS M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS ACTIVE, HELICOBACTER +++ T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS ACTIVE, HELICOBACTER +++ T62000 ESOPHAGUS M58000 ATROPHY MILD	-	0.8	neg	2.32	0.7-4	normal	
19760726S	B-HLADQ2_DQB-PCR	B-HLAKeil	02.08.2018 17:06	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY, MODERATE/SEVERE T63000 STOMACH M43000 CHRONIC GASTRITIS T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	+++	129.0	pos	3.35	0.7-4	normal	
2002020O	B-HLADQ2_DQB-PCR	B-HLAKeil	07.08.2018 15:16	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY, MODERATE T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, MILD T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	++	2.1	neg	1.18	0.6-3.5	normal	
19650112M	B-HLADQ2_DQB-PCR	B-HLAKeil	10.08.2018 15:30	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58007 TOTAL VILLOUS ATROPHY WITH INFLAMMATION T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS T62000 ESOPHAGUS M00100 NO DIAGNOSTIC ABNORMALITY	+++	118.0	pos	1.30	0.7-4	normal	
19860906P	B-HLADQ2_DQB-PCR	B-HLAKeil	10.08.2018 15:31	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58005 SUBTOTAL VILLOUS ATROPHY T63600 GASTRIC ANTRUM M03550 REACTIVE CHANGES T63500 GASTRIC CORPUS M00100 NO DIAGNOSTIC ABNORMALITY	++	78.0	pos	1.50	0.7-4	normal	
19770818K	B-HLADQ2_DQB-PCR	B-HLAKeil	19.08.2018 18:25	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M40000 ESOPHAGITIS	-	<0.6	neg	1.60	0.7-4	normal	
19730619R	B-HLADQ2_DQB-PCR	B-HLAKeil	26.08.2018 14:40	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M78000 POLYP, CYSTIC T62000 ESOPHAGUS M40000 ESOPHAGITIS (EOSINOPHILIC ESOPHAGITIS?)	-	<0.6	neg	0.82	0.7-4	normal	
19800416M	B-HLADQ2_DQB-PCR	B-HLAKeil	02.09.2018 14:50	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M09350 MORPHOLOGICAL DESCRIPTION ONLY, IEA +, SEE THE STATEMENT T63000 STOMACH M00100 NO DIAGNOSTIC ABNORMALITY T62000 ESOPHAGUS M40000 ESOPHAGITIS, MILD	+	5.6	neg	4.54	0.7-4	elevated	
19700925I	B-HLADQ2_DQB-PCR	B-HLAKeil	06.09.2018 15:51	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY MODERATE T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M80001 SUSPECTED MALIGNANCY, SEVERE T62000 ESOPHAGUS M40000 ESOPHAGITIS	++	5.7	neg	3.72	0.7-4	normal	
19770211K	B-HLADQ2_DQB-PCR	B-HLAKeil	26.09.2018 15:56	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M09350 MORPHOLOGICAL DESCRIPTION ONLY (mild intraepithelial lymphosytosis) T64400 DUODENAL BULBUS M58000 ATROPHY, MILD T63600 GASTRIC ANTRUM M00100 NO DIAGNOSTIC ABNORMALITY T62350 GASTRO-ESOPHAGEAL JUNCTION M73320 INTESTINAL METAPLASIA?	+	CD diagnosed, control test, EXCLUDED	8.3	intermediate	2.37	0.7-4	normal
19870707N	B-HLADQ2_DQB-PCR	B-HLAKeil	30.09.2018 12:50	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	0.96	0.7-4	normal	
19710205V	B-HLADQ2_DQB-PCR	B-HLAKeil	04.10.2018 15:26	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NO DIAGNOSTIC ABNORMALITY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M58010 ATROPHIC GASTRITIS	-	<0.6	neg	1.98	0.7-4	normal	
19911106T	B-HLADQ2_DQB-PCR	B-HLAKeil	04.10.2018 15:25	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M43000 CHRONIC GASTRITIS T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	0.71	0.7-4	normal	
19690809V	B-HLADQ2_DQB-PCR	B-HLAKeil	26.10.2018 16:30	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, MILD	-	1.4	neg	4.34	0.7-4	elevated	
19850723K	B-HLADQ2_DQB-PCR	B-HLAKeil	08.11.2018 16:30	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS MILD	-	0.6	neg	3.10	0.7-4	normal	

Internal ID	Mnemonic	Test Shortname	B-HLAKelI ValTime	Result external comment (B-HLAKelI)	HLADQ2_DQB1*02 genotype	RISK	PADGAST statement	Histology grade	tTGAbA result U/ml	tTGAbA result interpretation	IgA result g/l	IgA reference range (age dependent)	IgA result interpretation
19550325K	B-HLADQ2_DQB1-PCR	B-HLAKelI	09.11.2018 15:25	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY SEVERE T63000 STOMACH M43000 CHRONIC GASTRITIS MILD	+++	60.0	pos	2.75	0.7-4	normal
19630208L	B-HLADQ2_DQB1-PCR	B-HLAKelI	09.11.2018 15:25	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY SEVERE T63000 STOMACH M43000 CHRONIC GASTRITIS MILD T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	+++	33.0	pos	3.04	0.7-4	normal
20000625Y	B-HLADQ2_DQB1-PCR	B-HLAKelI	16.11.2018 15:41	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	I T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY II T63600 PYLORIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY	-	<-0.6	neg	0.65	0.6-3.5	normal
19700323K	B-HLADQ2_DQB1-PCR	B-HLAKelI	28.11.2018 16:35	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M40000 ESOPHAGITIS T62000 ESOPHAGUS M69700 ATYPIA, REGENERATIVE, SEE TEXT	-	<-0.6	neg	1.98	0.7-4	normal
19820510K	B-HLADQ2_DQB1-PCR	B-HLAKelI	06.12.2018 15:35	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY MILD T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	++	4.8	neg	1.43		
19700409A	B-HLADQ2_DQB1-PCR	B-HLAKelI	23.12.2018 12:15	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M76800 POLYP CYSTIC T62350 CARDIO-ESOPHAGEAL JUNCTION M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	- CD diagnosed, control test, EXCLUDED	<-0.6	neg	0.95	0.7-4	normal
19590408E	B-HLADQ2_DQB1-PCR	B-HLAKelI	27.01.2019 12:10	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY MILD T63600 GASTRIC ANTRUM M40000 GASTRITIS REACTIVE T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	+	10.0	intermediate	1.42	0.7-4	normal
19760319L	B-HLADQ2_DQB1-PCR	B-HLAKelI	10.02.2019 19:26	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M76800 POLYP, CYSTIC	-	<-0.6	neg	2.65	0.7-4	normal
19521213Y	B-HLADQ2_DQB1-PCR	B-HLAKelI	13.02.2019 16:00	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M40000 INFLAMMATION, see text T63000 STOMACH M00100 NO DIAGNOSTIC ABNORMALITY T62000 ESOPHAGUS M43000 CHRONIC ESOPHAGITIS	+	4.6	neg	2.82	0.7-4	normal
19550925T	B-HLADQ2_DQB1-PCR	B-HLAKelI	14.02.2019 14:45	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M40000 INFLAMMATION ACTIVE, MILD T64300 DUODENUM M58000 ATROPHY, FOKAALINEN T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS MILD T63500 GASTRIC CORPUS M76800 POLYP, CYSTIC T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS MILD T62000 ESOPHAGUS M09350 MORPHOLOGICAL DESCRIPTION ONLY	++	<-0.6	neg	1.60	0.7-4	normal
20001103T	B-HLADQ2_DQB1-PCR	B-HLAKelI	20.02.2019 15:35	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M40000 INFLAMMATION, MILD T63600 GASTRIC ANTRUM M00100 NO DIAGNOSTIC ABNORMALITY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, MILD	+	<-0.6	neg	0.81	0.6-3.5	normal
19631214N	B-HLADQ2_DQB1-PCR	B-HLAKelI	20.02.2019 15:35	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NO DIAGNOSTIC ABNORMALITY	-	<-0.6	neg	1.34	0.7-4	normal
19731216M	B-HLADQ2_DQB1-PCR	B-HLAKelI	13.03.2019 15:41	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY, MILD T63600 GASTRIC ANTRUM M00100 NORMAL FINDING T63500 GASTRIC CORPUS M00100 NORMAL FINDING	++	10.0	intermediate	1.98	0.7-4	normal
19710603T	B-HLADQ2_DQB1-PCR	B-HLAKelI	27.03.2019 16:01	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 VILLOUS ATROPHY T64300 DUODENUM M40000 INFLAMMATION T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	++	25.0	pos	1.92	0.7-4	normal
20090113O	B-HLADQ2_DQB1-PCR	B-HLAKelI	29.03.2019 15:51	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 PYLORIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M42000 SUPERFICIAL GASTRITIS	-	<-0.6	neg	1.79	0.7-4	normal
19770510S	B-HLADQ2_DQB1-PCR	B-HLAKelI	29.03.2019 15:51	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M40000 INFLAMMATION MILD, SEE TEXT T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	+	5.0	neg	1.47	0.7-4	normal
19920221L	B-HLADQ2_DQB1-PCR	B-HLAKelI	09.05.2019 15:02	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQB1 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M40000 ESOPHAGITIS, SEE TEXT	-	0.9	neg	2.78	0.7-4	normal

Internal ID	Mnemonic	Test Shortname	B-HLAKeil ValTime	Result external comment (B-HLAKeil)	HLADQ2_DQB1 genotype	RISK	PADGAST statement	Histology grade	tTGAbA result U/ml	tTGAbA result interpretation	IgA result g/l	IgA reference range (age dependent)	IgA result interpretation
19590526M	B-HLADQ2_DQB1-PCR	B-HLAKeil	10.05.2019 15:45	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M40000 INFLAMMATION MILD T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	+	3.6	neg	2.71	0.7-4	normal
19810727L	B-HLADQ2_DQB1-PCR	B-HLAKeil	23.05.2019 15:35	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	1. T64300 DUODENUM M58000 VILLOUS ATROPHY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	++	15.0	pos	1.62	0.7-4	normal
19670507M	B-HLADQ2_DQB1-PCR	B-HLAKeil	24.05.2019 17:15	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 PARTIAL VILLOUS ATROPHY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	++	8.0	intermediate	1.43	0.7-4	normal
19610717V	B-HLADQ2_DQB1-PCR	B-HLAKeil	03.07.2019 15:38	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62350 CARDIO-ESOPHAGEAL JUNCTION M00100 NO DIAGNOSTIC ABNORMALITY	-	<0.6	neg	3.27	0.7-4	normal
19830505M	B-HLADQ2_DQB1-PCR	B-HLAKeil	04.07.2019 14:21	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS	-	0.9	neg	1.76	0.7-4	normal
19870530V	B-HLADQ2_DQB1-PCR	B-HLAKeil	04.07.2019 14:21	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M58000 ATROPHY, MODERATE T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M40000 ESOPHAGITIS	++	>128.0	pos	1.15	0.7-4	normal
19690321R	B-HLADQ2_DQB1-PCR	B-HLAKeil	25.09.2019 15:56	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M58010 ATROPHIC GASTRITIS	-	0.7	neg	1.43	0.7-4	normal
19600515M	B-HLADQ2_DQB1-PCR	B-HLAKeil	04.10.2019 16:57	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M76800 POLYP, CYSTIC	-	<0.6	neg	2.25	0.7-4	normal
19850303P	B-HLADQ2_DQB1-PCR	B-HLAKeil	11.10.2019 15:52	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M08350 MORPHOLOGICAL DESCRIPTION ONLY (MILD INTRAEPITHELIAL LYMPHOCYTOXIS) T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62350 GASTROESOPHAGEAL JUNCTION M00100 NORMAL TISSUE MORPHOLOGY	+	8.5	intermediate	3.77	0.7-4	normal
19880101A	B-HLADQ2_DQB1-PCR	B-HLAKeil	17.10.2019 15:20	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 PYLORIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M42000 SUPERFICIAL GASTRITIS	-	<0.6	neg	1.79	0.7-4	normal
20140612D	B-HLADQ2_DQB1-PCR	B-HLAKeil	27.06.2019 15:58	HLA-analysis: HLA-DQ2.5 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQA1*05 and HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.5, DQB1*02 homozygosity or single DQB1*02 allele	1:10 (very high) or 1:35 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 PYLORIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M42000 SUPERFICIAL GASTRITIS	-	<0.6	neg	1.79	0.7-4	normal
19760607H	B-HLADQ2_DQB1-PCR	B-HLAKeil	14.02.2018 15:43	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygosity or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NO DIAGNOSTIC ABNORMALITY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	0.6	neg	2.23	0.7-4	normal
19950123M	B-HLADQ2_DQB1-PCR	B-HLAKeil	01.03.2018 16:32	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygosity or single DQB1*02 allele	1:26 (high) or 1:210 (low)	1. T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY 2-3. T63000 STOMACH M43000 CHRONIC GASTRITIS, MILD 4. T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	0.70	0.7-4	normal
19840421P	B-HLADQ2_DQB1-PCR	B-HLAKeil	05.04.2018 15:22	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygosity or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.89	0.7-4	normal
19660410T	B-HLADQ2_DQB1-PCR	B-HLAKeil	15.04.2018 19:11	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygosity or single DQB1*02 allele	1:26 (high) or 1:210 (low)	I T64300 DUODENUM M40000 DUODENITIS, see text II - III T63000 STOMACH M00120 NORMAL CELLULAR MORPHOLOGY IV T63500 GASTRIC CORPUS M75630 FUNDIC GLAND POLYP V T62000 ESOPHAGUS M00100 NO DIAGNOSTIC ABNORMALITY	+	<0.6	neg	1.32	0.7-4	normal
19610123J	B-HLADQ2_DQB1-PCR	B-HLAKeil	27.04.2018 15:02	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygosity or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M40000 GASTRITIS REACTIVE T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M40000 ESOPHAGITIS	-	1.0	neg	5.01	0.7-4	elevated
19660129S	B-HLADQ2_DQB1-PCR	B-HLAKeil	26.04.2018 14:16	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygosity or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M43000 CHRONIC GASTRITIS	-	<0.6	neg	2.27	0.7-4	normal
19760323A	B-HLADQ2_DQB1-PCR	B-HLAKeil	01.06.2018 16:26	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygosity or single DQB1*02 allele	1:26 (high) or 1:210 (low)	1. T64300 DUODENUM M58000 PARTIAL VILLOUS ATROPHY 2-3. T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY 4. T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	++	9.4	intermediate	3.63	0.7-4	normal

Internal ID	Mnemonic	Test Shortname	B -HLAKeil ValTime	Result external comment (B-HLAKeil)	HLADQ2_DQB genotype	RISK	PADGAST statement	Histology grade	tTGAbA result U/ml	tTGAbA result interpretation	IgA result gl	IgA reference range (age dependent)	IgA result interpretation
19950918R	B-HLADQ2_DQB-PCR	B -HLAKeil	20.06.2018 15:51	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NO DIAGNOSTIC ABNORMALITY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	2.95	0.7-4	normal
19920906T	B-HLADQ2_DQB-PCR	B -HLAKeil	22.06.2018 14:51	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS, HELICOBACTER ++ T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, HELICOBACTER +	-	0.6	neg	1.97	0.7-4	normal
19750829A	B-HLADQ2_DQB-PCR	B -HLAKeil	29.06.2018 17:01	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M09350 MORPHOLOGICAL DESCRIPTION ONLY	-	1.0	neg	3.29	0.7-4	normal
19951229F	B-HLADQ2_DQB-PCR	B -HLAKeil	16.07.2018 15:50	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS MILD T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NO DIAGNOSTIC ABNORMALITY	-	<0.6	neg	2.03	0.7-4	normal
19870609K	B-HLADQ2_DQB-PCR	B -HLAKeil	06.08.2018 15:41	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NO DIAGNOSTIC ABNORMALITY T63600 GASTRIC ANTRUM M00100 NO DIAGNOSTIC ABNORMALITY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS	-	<0.6	neg	2.10	0.7-4	normal
19650429I	B-HLADQ2_DQB-PCR	B -HLAKeil	02.09.2018 14:50	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M43000 CHRONIC INFLAMMATION T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M00100 NO DIAGNOSTIC ABNORMALITY	+	<0.6	neg	2.26	0.7-4	normal
19710226K	B-HLADQ2_DQB-PCR	B -HLAKeil	26.10.2018 16:30	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS ACTIVE	-	<0.6	neg	2.32	0.7-4	normal
19950122V	B-HLADQ2_DQB-PCR	B -HLAKeil	02.11.2018 14:45	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS MILD	-	<0.6	neg	2.01	0.7-4	normal
20000831V	B-HLADQ2_DQB-PCR	B -HLAKeil	30.11.2018 16:16	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M58000 PARTIAL VILLOUS ATROPHY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M00100 NO DIAGNOSTIC ABNORMALITY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	++	34.0	pos	1.88	0.6-3.5	normal
19661014L	B-HLADQ2_DQB-PCR	B -HLAKeil	02.12.2018 13:35	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS, MILD T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS	-	2.0	neg	2.20	0.7-4	normal
19960214A	B-HLADQ2_DQB-PCR	B -HLAKeil	14.12.2018 16:25	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS, MILD T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, MILD	-	<0.6	neg	1.78	0.7-4	normal
19770715T	B-HLADQ2_DQB-PCR	B -HLAKeil	10.05.2019 15:45	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M40000 GASTRITIS, REACTIVE T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	1.5	neg	4.89	0.7-4	elevated
19650624J	B-HLADQ2_DQB-PCR	B -HLAKeil	09.10.2019 16:26	HLA-analysis: HLA-DQ2 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*02. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ2.x, DQB1*02 homozygoty or single DQB1*02 allele	1:26 (high) or 1:210 (low)	I T64300 DUODENUM M58000 PARTIAL VILLOUS ATROPHY, WITH INFLAMMATION II-IV T50100 GASTROSCOPIC BIOPSY SPECIMEN M00100 NO DIAGNOSTIC ABNORMALITY	++	<0.6	neg	1.10	0.7-4	normal
19920414M	B-HLADQ2_DQB-PCR	B -HLAKeil	15.01.2018 07:07	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	0.85	0.7-4	normal
19781202R	B-HLADQ2_DQB-PCR	B -HLAKeil	17.01.2018 16:18	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	0.9	neg	3.36	0.7-4	normal
19941121N	B-HLADQ2_DQB-PCR	B -HLAKeil	18.01.2018 16:26	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M43000 CHRONIC GASTRITIS, MILD	-	<0.6	neg	1.76	0.7-4	normal
19870304M	B-HLADQ2_DQB-PCR	B -HLAKeil	26.02.2018 07:07	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL FINDING T63000 STOMACH M43000 CHRONIC GASTRITIS, helicobacter + T62000 ESOPHAGUS M00100 NORMAL FINDING	-	0.8	neg	5.55	0.7-4	elevated
19620510L	B-HLADQ2_DQB-PCR	B -HLAKeil	15.03.2018 16:25	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	I T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY II - III T63000 STOMACH M43000 CHRONIC GASTRITIS, HELIKOT + IV T62000 ESOPHAGUS M43000 CHRONIC INFLAMMATION IV T62000 ESOPHAGUS M72000 HYPERPLASIA, SEE TEXT	-	<0.6	neg	1.01	0.7-4	normal

Internal ID	Mnemonic	Test Shortname	B-HLAKeil ValTime	Result external comment (B-HLAKeil)	HLADQ2_DQ8 genotype	RISK	PADGAST statement	Histology grade	tTGAbA result U/ml	tTGAbA result interpretation	IgA result gl	IgA reference range (age dependent)	IgA result interpretation
19590407T	B-HLADQ2_DQ8-PCR	B-HLAKeil	28.03.2018 16:11	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 GASTRITIS CHRONIC T63500 GASTRIC CORPUS M76800 POLYP. CYSTIC T62000 ESOPHAGUS M40000 ESOPHAGITIS	-	0.8	neg	4.52	0.7-4	elevated
20000816S	B-HLADQ2_DQ8-PCR	B-HLAKeil	25.04.2018 16:03	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	0.98	0.6-3.5	normal
19820213L	B-HLADQ2_DQ8-PCR	B-HLAKeil	25.04.2018 16:03	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M40000 ESOPHAGITIS MILD	-	<0.6	neg	1.50	0.7-4	normal
19980926K	B-HLADQ2_DQ8-PCR	B-HLAKeil	29.04.2018 17:25	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	1. T64300 DUODENUM M40000 INFLAMMATION, MILD 2-3. T63000 STOMACH M43000 CHRONIC GASTRITIS, MILD	+	0.9	neg	2.72	0.6-3.5	normal
19621008L	B-HLADQ2_DQ8-PCR	B-HLAKeil	29.04.2018 17:25	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M40000 GASTRITIS REACTIVE T63500 GASTRIC CORPUS M00100 NO DIAGNOSTIC ABNORMALITY	-	<0.6	neg	1.39	0.7-4	normal
19580428P	B-HLADQ2_DQ8-PCR	B-HLAKeil	04.05.2018 15:50	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	I T64300 DUODENUM M00100 NO DIAGNOSTIC ABNORMALITY II T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS, INACTIVE III T63600 GASTRIC ANTRUM M73320 INTESTINAL METAPLASIA IT63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, ACTIVE, HELICOBACTER +	-	<0.6	neg	3.93	0.7-4	normal
19820606H	B-HLADQ2_DQ8-PCR	B-HLAKeil	25.05.2018 15:46	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.78	0.7-4	normal
19890810T	B-HLADQ2_DQ8-PCR	B-HLAKeil	07.06.2018 15:26	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M73330 GASTRIC METAPLASIA, FOCAL T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.28	0.7-4	normal
19590906A	B-HLADQ2_DQ8-PCR	B-HLAKeil	11.06.2018 07:07	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T64400 DUODENAL BULBUS M72040 HYPERPLASTIC POLYP T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.51	0.7-4	normal
19670922K	B-HLADQ2_DQ8-PCR	B-HLAKeil	06.07.2018 15:46	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M09350 MORPHOLOGICAL DESCRIPTION ONLY, BULBITIS T63000 STOMACH M09350 REACTIVE CHANGES T62000 ESOPHAGUS M73330 GASTRIC METAPLASIA	-	<0.6	neg	2.35	0.7-4	normal
19801205T	B-HLADQ2_DQ8-PCR	B-HLAKeil	06.08.2018 16:35	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS, ACTIVE T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	3.2	neg	2.52	0.7-4	normal
19730612H	B-HLADQ2_DQ8-PCR	B-HLAKeil	09.08.2018 15:55	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M40000 GASTRITIS, CHRONIC, MILD	-	<0.6	neg	2.77	0.7-4	normal
19790430R	B-HLADQ2_DQ8-PCR	B-HLAKeil	04.09.2018 15:56	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M43000 CHRONIC GASTRITIS ACTIVE (HELICOBACTER PYLORI) T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.66	0.7-4	normal
20040520P	B-HLADQ2_DQ8-PCR	B-HLAKeil	05.09.2018 16:40	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NO DIAGNOSTIC ABNORMALITY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.71	0.5-2.5	normal
19571117J	B-HLADQ2_DQ8-PCR	B-HLAKeil	14.09.2018 15:55	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, MILD	-	<0.6	neg	1.58	0.7-4	normal
19591230T	B-HLADQ2_DQ8-PCR	B-HLAKeil	19.09.2018 16:11	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	I T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY II T63600 GASTRIC ANTRUM M40000 GASTRITIS, CHRONIC, MILD III T63500 GASTRIC CORPUS M58010 ATROPHIC GASTRITIS	-	0.8	neg	4.16	0.7-4	elevated
19950927M	B-HLADQ2_DQ8-PCR	B-HLAKeil	12.10.2018 09:40	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NO PATHOLOGIC DIAGNOSIS T63600 GASTRIC ANTRUM M79900 REGENERATION T63600 GASTRIC ANTRUM M73320 INTESTINAL METAPLASIA T63500 GASTRIC CORPUS M00100 NO PATHOLOGIC DIAGNOSIS	-	0.6	neg	3.88	0.7-4	normal
19620116A	B-HLADQ2_DQ8-PCR	B-HLAKeil	17.10.2018 16:10	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	1,2. T64300 DUODENUM M09350 MORPHOLOGICAL DESCRIPTION ONLY 3. T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS (HELICOBACTER +) 4. T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS	-	0.8	neg	3.82	0.7-4	normal

Internal ID	Mnemonic	Test Shortname	B -HLAKeII ValTime	Result external comment (B -HLAKeII)	HLADQ2_DQ8 genotype	RISK	PADGAST statement	Histology grade	tTGAbA result U/ml	tTGAbA result interpretation	IgA result gl	IgA reference range (age dependent)	IgA result interpretation
19530113P	B-HLADQ2_DQ8-PCR	B -HLAKeII	22.10.2018 09:45	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M09350 MORPHOLOGICAL DESCRIPTION ONLY T63000 STOMACH M00100 NO DIAGNOSTIC ABNORMALITY	+	<0.6	neg	4.11	0.7-4	elevated
19790711H	B-HLADQ2_DQ8-PCR	B -HLAKeII	22.10.2018 09:45	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, LEVIS	-	<0.6	neg	2.97	0.7-4	normal
19641117P	B-HLADQ2_DQ8-PCR	B -HLAKeII	11.11.2018 15:30	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	1 T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY 2-4 T63000 STOMACH M43000 CHRONIC GASTRITIS	-	<0.6	neg	1.12	0.7-4	normal
19780608N	B-HLADQ2_DQ8-PCR	B -HLAKeII	21.11.2018 16:00	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M76800 POLYP T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.75	0.7-4	normal
19770118N	B-HLADQ2_DQ8-PCR	B -HLAKeII	20.12.2018 16:40	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS, LEVIS T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, LEVIS T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.76	0.7-4	normal
19840317G	B-HLADQ2_DQ8-PCR	B -HLAKeII	10.01.2019 16:07	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M58000 VILLOUS ATROPHY T64300 DUODENUM M40000 DUODENITIS T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY ADD. STATEMENT PAD: T64300 DUODENUM M58000 PARTIAL VILLOUS ATROPHY T64300 DUODENUM M40000 DUODENITIS T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS	++	23.0	pos	1.99	0.7-4	normal
19930414H	B-HLADQ2_DQ8-PCR	B -HLAKeII	23.01.2019 15:14	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL FINDING T63600 GASTRIC ANTRUM M00100 NORMAL FINDING T63500 GASTRIC CORPUS M00100 NORMAL FINDING	-	<0.6	neg	0.96	0.7-4	normal
19790711H	B-HLADQ2_DQ8-PCR	B -HLAKeII	27.01.2019 12:10	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, LEVIS	-	<0.6	neg	2.97	0.7-4	normal
19931121R	B-HLADQ2_DQ8-PCR	B -HLAKeII	14.02.2019 14:45	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NO DIAGNOSTIC ABNORMALITY T62000 ESOPHAGUS M09350 MORPHOLOGICAL DESCRIPTION ONLY	-	<0.6	neg	1.58	0.7-4	normal
19490701M	B-HLADQ2_DQ8-PCR	B -HLAKeII	22.04.2019 16:55	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M40000 INFLAMMATION, MILD T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS T62000 ESOPHAGUS M00100 NO DIAGNOSTIC ABNORMALITY	+	0.8	neg	2.56	0.7-4	normal
19720122O	B-HLADQ2_DQ8-PCR	B -HLAKeII	20.05.2019 15:41	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	1: T64300 DUODENUM M09350 MORPHOLOGICAL DESCRIPTION ONLY 2-4: STOMACH M00100 NO DIAGNOSTIC ABNORMALITY	+	<0.6	neg	2.49	0.7-4	normal
19840714B	B-HLADQ2_DQ8-PCR	B -HLAKeII	19.07.2019 15:00	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NO DIAGNOSTIC ABNORMALITY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, MILD T62000 ESOPHAGUS M00100 NO DIAGNOSTIC ABNORMALITY	-	0.7	neg	5.92	0.7-4	elevated
19881014P	B-HLADQ2_DQ8-PCR	B -HLAKeII	16.08.2019 15:50	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M09350 MORPHOLOGICAL DESCRIPTION ONLY, SEE THE ADDITIONAL STATEMENT T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY ADD. STATEMENT PAD: T64300 DUODENUM M58000 ATROPHY, SEE TEXT T63600 GASTRIC ANTRUM M40000 GASTRITIS REACTIVE T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	+++	27.0	pos	2.14	0.7-4	normal
19820518V	B-HLADQ2_DQ8-PCR	B -HLAKeII	28.08.2019 16:19	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M58010 ATROPHIC GASTRITIS	-	<0.6	neg	1.14	0.7-4	normal
19911120V	B-HLADQ2_DQ8-PCR	B -HLAKeII	09.09.2019 15:28	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	1 T64300 DUODENUM M00100 NORMAL FINDING 2-3 T63000 STOMACH M43000 CHRONIC GASTRITIS, helicobacter + 4 T64400 DUODENAL BULBUS M40000 INFLAMMATION, active	-	0.8	neg	2.11	0.7-4	normal
19500518H	B-HLADQ2_DQ8-PCR	B -HLAKeII	06.06.2019 15:42	HLA-analysis: HLA-DQ8 positive. The analysis detected the following risk allele related to celiac disease: HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8	1:89 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 PYLORIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M42000 SUPERFICIAL GASTRITIS	-	<0.6	neg	1.79	0.7-4	normal

Internal ID	Mnemonic	Test Shortname	B-HLAkell ValTime	Result external comment (B-HLAkell)	HLADQ2_DQ8 genotype	RISK	PADGAST statement	Histology grade	tTGAbA result U/ml	tTGAbA result interpretation	IgA result g/l	IgA reference range (age dependent)	IgA result interpretation
19870930V	B-HLADQ2_DQ8-PCR	B-HLAkell	02.02.2018 15:41	HLA-analysis: HLA-DQ2 and HLA-DQ8 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQB1*02 and HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8 + HLA-DQ2.x, single DQB1*02 allele	1:24 (high)	T64300 DUODENUM M00100 NO DIAGNOSTIC ABNORMALITY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	2.08	0.7-4	normal
19790314H	B-HLADQ2_DQ8-PCR	B-HLAkell	04.02.2018 15:56	HLA-analysis: HLA-DQ2 and HLA-DQ8 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQB1*02 and HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8 + HLA-DQ2.x, single DQB1*02 allele	1:24 (high)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M40000 ESOPHAGITIS (EOSINOPHILINEN ESOFAGIIT?)	-	<0.6	neg	2.08	0.7-4	normal
19510826O	B-HLADQ2_DQ8-PCR	B-HLAkell	04.10.2019 16:49	HLA-analysis: HLA-DQ2 and HLA-DQ8 positive. The analysis detected the following risk alleles related to celiac disease: HLA-DQB1*02 and HLA-DQB1*0302. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQ8 + HLA-DQ2.x, single DQB1*02 allele	1:24 (high)	T64300 DUODENUM M58000 ATROPHY, MILD T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS, MILD T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, MILD T63500 GASTRIC CORPUS M58000 ATROPHY, MILD	++	<0.6	neg	1.08	0.7-4	normal
19650517R	B-HLADQ2_DQ8-PCR	B-HLAkell	18.02.2018 18:27	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease OR HLA-analysis: HLA-DQX.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T63000 GASTRIC CARDIA M76900 POLYP T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	2.65	0.7-4	normal
19600428L	B-HLADQ2_DQ8-PCR	B-HLAkell	09.03.2018 15:16	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease OR HLA-analysis: HLA-DQX.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M09350 MORPHOLOGICAL DESCRIPTION ONLY, SEE THE STATEMENT T63000 STOMACH M00100 NO DIAGNOSTIC ABNORMALITY T62000 ESOPHAGUS M73320 INTESTINAL METAPLASIA T62000 ESOPHAGUS M73330 GASTRIC METAPLASIA	+	<0.6	neg	2.10	0.7-4	normal
19800327K	B-HLADQ2_DQ8-PCR	B-HLAkell	01.04.2018 17:53	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease OR HLA-analysis: HLA-DQX.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	2.64	0.7-4	normal
19580625M	B-HLADQ2_DQ8-PCR	B-HLAkell	05.04.2018 15:21	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease OR HLA-analysis: HLA-DQX.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M00100 NO DIAGNOSTIC ABNORMALITY T63000 STOMACH M00100 NO DIAGNOSTIC ABNORMALITY T62000 ESOPHAGUS M09350 MORPHOLOGICAL DESCRIPTION ONLY	-	<0.6	neg	3.35	0.7-4	normal
19551001S	B-HLADQ2_DQ8-PCR	B-HLAkell	06.05.2018 21:10	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease OR HLA-analysis: HLA-DQX.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	1: T64300 DUODENUM M43000 CHRONIC INFLAMMATION 1-2: T63000 STOMACH M43000 CHRONIC GASTRITIS 1: T63500 GASTRIC CORPUS M75630 FUNDIC GLAND POLYP	+	0.9	neg	3.71	0.7-4	normal
19810316S	B-HLADQ2_DQ8-PCR	B-HLAkell	13.05.2018 18:22	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease OR HLA-analysis: HLA-DQX.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M58000 VILLOUS ATROPHY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M76900 POLYP	++	<0.6	neg	1.26	0.7-4	normal
19590106R	B-HLADQ2_DQ8-PCR	B-HLAkell	14.06.2018 16:26	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease OR HLA-analysis: HLA-DQX.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M09350 MORPHOLOGICAL DESCRIPTION ONLY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62350 CARDIO-ESOPHAGEAL JUNCTION M00100 NORMAL TISSUE MORPHOLOGY	+	<0.6	neg	2.44	0.7-4	normal
19780609R	B-HLADQ2_DQ8-PCR	B-HLAkell	19.08.2018 18:25	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease OR HLA-analysis: HLA-DQX.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 PYLORIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M75630 FUNDIC GLAND POLYP T62000 ESOPHAGUS M09350 CHANGES NOT DIAGNOSTIC	-	<0.6	neg	2.50	0.7-4	normal
19640414N	B-HLADQ2_DQ8-PCR	B-HLAkell	05.10.2018 16:31	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease OR HLA-analysis: HLA-DQX.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS T62000 ESOPHAGUS M09370 NO ORGANOID TISSUE RECEIVED	-	<0.6	neg	3.15	0.7-4	normal
19560601A	B-HLADQ2_DQ8-PCR	B-HLAkell	05.10.2018 16:30	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease OR HLA-analysis: HLA-DQX.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	2.00	0.7-4	normal
19730923K	B-HLADQ2_DQ8-PCR	B-HLAkell	31.10.2018 15:10	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease OR HLA-analysis: HLA-DQX.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS T62000 ESOPHAGUS M26000 HETEROPTOPHY, SAMPLE IV T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY, SAMPLE V	-	1.0	neg	4.05	0.7-4	elevated

Internal ID	Mnemonic	Test Shortname	B-HLAKeil ValTime	Result external comment (B-HLAKeil)	HLADQ2_DQ8 genotype	RISK	PADGAST statement	Histology grade	tTGAbA result U/ml	tTGAbA result interpretation	IgA result g/l	IgA reference range (age dependent)	IgA result interpretation
19590919L	B-HLADQ2_DQ8-PCR	B-HLAKeil	22.11.2018 15:45	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease. OR HLA-analysis: HLA-DQx.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.96	0.7-4	normal
19500413L	B-HLADQ2_DQ8-PCR	B-HLAKeil	30.01.2019 15:20	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease. OR HLA-analysis: HLA-DQx.5 positive. The analysis detected the following low-risk allele related to celiac disease: HLA-DQA1*05. The risk alleles are not sufficient for the diagnosis as HLA-DQ2 or DQ8 isoforms may occur in up to 30% of healthy individuals. The finding of the risk haplotype supports the diagnosis of celiac disease if the patient has symptoms similar to celiac disease and if the disease-associated antibodies are also found.	HLA-DQx.5	1:1842 (extremely low)	T64300 DUODENUM M00100 NORMAL FINDING T63000 STOMACH M58010 ATROPHIC GASTRITIS	-	<0.6	neg	1.57	0.7-4	normal
19630917H	B-HLADQ2_DQ8-PCR	B-HLAKeil	10.01.2018 17:42	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NO DIAGNOSTIC ABNORMALITY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS INACTIVE T63600 GASTRIC ANTRUM M73320 INTESTINAL METAPLASIA T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS INACTIVE T63500 GASTRIC CORPUS M58000 ATROPHY T62000 ESOPHAGUS M73330 BARRETT'S SYNDROME	-	0.7	neg	4.52	0.7-4	elevated
19830319P	B-HLADQ2_DQ8-PCR	B-HLAKeil	21.01.2018 20:23	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M09350 MORPHOLOGICAL DESCRIPTION ONLY	-	0.6	neg	1.99	0.7-4	normal
19830310P	B-HLADQ2_DQ8-PCR	B-HLAKeil	23.01.2018 15:35	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	1-3: T64300 DUODENUM AND STOMACH M00100 NORMAL TISSUE MORPHOLOGY 4: T62000 ESOPHAGUS M43000 CHRONIC INFLAMMATION, MILD	-	<0.6	neg	2.76	0.7-4	normal
19590613H	B-HLADQ2_DQ8-PCR	B-HLAKeil	11.02.2018 20:52	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	1: T64300 DUODENUM M40000 DUODENITIS, SEE TEXT 2: T50100 GASTROSCOPIC BIOPSY SPECIMEN M00100 NO DIAGNOSTIC ABNORMALITY 5: T63500 GASTRIC FUNDUS M09350 MORPHOLOGICAL DESCRIPTION ONLY	+	<0.6	neg	2.46	0.7-4	normal
19780202B	B-HLADQ2_DQ8-PCR	B-HLAKeil	21.02.2018 16:11	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	2.77	0.7-4	normal
19530610L	B-HLADQ2_DQ8-PCR	B-HLAKeil	26.02.2018 07:07	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	1 T64300 DUODENUM M43000 INFLAMMATION CHRONIC, SEE TEXT 2 T63600 GASTRIC ANTRUM M00100 NO DIAGNOSTIC ABNORMALITY 3-4 T63500 GASTRIC CORPUS M00100 NO DIAGNOSTIC ABNORMALITY 5 T62000 ESOPHAGUS M43000 INFLAMMATION CHRONIC T62000 ESOPHAGUS M09350 REACTIVE CHANGES (HYPERPLASY)	+	<0.6	neg	2.30	0.7-4	normal
19580406R	B-HLADQ2_DQ8-PCR	B-HLAKeil	02.10.2019 15:53	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M40000 INFLAMMATION, mild T63600 GASTRIC ANTRUM M00100 NO DIAGNOSTIC ABNORMALITY T63500 GASTRIC CORPUS M00100 NO DIAGNOSTIC ABNORMALITY	+	<0.6	neg	2.43	0.7-4	normal
19850426K	B-HLADQ2_DQ8-PCR	B-HLAKeil	07.03.2018 16:26	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62350 GASTROESOPHAGEAL JUNCTION M00100 NO DIAGNOSTIC ABNORMALITY	-	<0.6	neg	0.78	0.7-4	normal
19560514K	B-HLADQ2_DQ8-PCR	B-HLAKeil	14.03.2018 15:32	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M00100 NO DIAGNOSTIC ABNORMALITY	-	<0.6	neg	2.27	0.7-4	normal
19921030R	B-HLADQ2_DQ8-PCR	B-HLAKeil	22.03.2018 15:36	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	1.97	0.7-4	normal
19820220T	B-HLADQ2_DQ8-PCR	B-HLAKeil	29.03.2018 15:11	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	1. T64300 DUODENUM M09350 MORPHOLOGICAL DESCRIPTION ONLY 1-2. T63000 STOMACH M00100 NO DIAGNOSTIC ABNORMALITY 3. T62350 CARDIO-ESOPHAGEAL JUNCTION M43000 CHRONIC INFLAMMATION, SEE TEXT 3. T62350 CARDIO-ESOPHAGEAL JUNCTION M72000 HYPERPLASIA, SEE TEXT	+	<0.6	neg	1.69	0.7-4	normal
19770504K	B-HLADQ2_DQ8-PCR	B-HLAKeil	06.04.2018 16:35	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	2.16	0.7-4	normal
19760727N	B-HLADQ2_DQ8-PCR	B-HLAKeil	26.04.2018 14:11	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	I T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY II T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY III T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	3.17	0.7-4	normal
19980328A	B-HLADQ2_DQ8-PCR	B-HLAKeil	10.05.2018 15:30	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 PYLORIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M42000 SUPERFICIAL GASTRITIS	-	<0.6	neg	1.79	0.7-4	normal
19760410K	B-HLADQ2_DQ8-PCR	B-HLAKeil	18.05.2018 10:13	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NO PATHOLOGIC DIAGNOSIS T63000 STOMACH M43000 CHRONIC GASTRITIS	-	<0.6	neg	2.44	0.7-4	normal
19630119Y	B-HLADQ2_DQ8-PCR	B-HLAKeil	23.05.2018 16:05	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M58000 VILLOUS ATROPHY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M76800 POLYP T62000 ESOPHAGUS M73330 BARRETT'S SYNDROME	++	<0.6	neg	1.80	0.7-4	normal
19691115K	B-HLADQ2_DQ8-PCR	B-HLAKeil	31.05.2018 16:32	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M76800 POLYP, CYSTIC	-	<0.6	neg	3.03	0.7-4	normal
19831219K	B-HLADQ2_DQ8-PCR	B-HLAKeil	30.05.2018 16:36	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M40000 ESOPHAGITIS MILD	-	0.6	neg	3.07	0.7-4	normal
19691113R	B-HLADQ2_DQ8-PCR	B-HLAKeil	04.06.2018 07:06	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	1: T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY 2: T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY 3: T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY 4: T63500 GASTRIC CORPUS M76800 FUNDIC GLAND POLYP	-	<0.6	neg	1.76	0.7-4	normal

Internal ID	Mnemonic	Test Shortname	B -HLAKeII ValTime	Result external comment (B -HLAKeII)	HLADQ2_DQ8 genotype	RISK	PADGAST statement	Histology grade	tTGAbA result U/ml	tTGAbA result interpretation	IgA result gl	IgA reference range (age dependent)	IgA result interpretation
19580116F	B-HLADQ2_DQ8-PCR	B -HLAKeII	25.07.2018 14:31	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	1. T64300 DUODENUM M40000 INFLAMMATION, SEE TEXT 2. T64400 DUODENAL BULBUS M09350 MORPHOLOGICAL DESCRIPTION ONLY 3. T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY 4. T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY 5. T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY*	+	<0.6	neg	2.34	0.7-4	normal
19920804V	B-HLADQ2_DQ8-PCR	B -HLAKeII	30.07.2018 16:17	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T63000 STOMACH M43000 CHRONIC GASTRITIS	-	<0.6	neg	1.39	0.7-4	normal
19830730K	B-HLADQ2_DQ8-PCR	B -HLAKeII	07.09.2018 16:21	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	I T64300 DUODENUM M09350 MORPHOLOGICAL DESCRIPTION ONLY II T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY III T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY IV T62350 GASTROESOPHAGEAL JUNCTION (VENTRIKELITYYPINEN LIMAKALVO) M43000 CHRONIC INFLAMMATION, MILD	+	<0.6	neg	1.56	0.7-4	normal
19850907G	B-HLADQ2_DQ8-PCR	B -HLAKeII	07.09.2018 16:20	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS, ACTIVE, helicobacter + + +	-	<0.6	neg	0.72	0.7-4	normal
19760322L	B-HLADQ2_DQ8-PCR	B -HLAKeII	23.09.2018 16:20	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M43000 CHRONIC GASTRITIS	-	<0.6	neg	2.05	0.7-4	normal
19590724O	B-HLADQ2_DQ8-PCR	B -HLAKeII	23.09.2018 16:20	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NO DIAGNOSTIC ABNORMALITY	-	2.9	neg	1.80	0.7-4	normal
19930823A	B-HLADQ2_DQ8-PCR	B -HLAKeII	30.09.2018 12:50	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 PYLORIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M42000 SUPERFICIAL GASTRITIS	-	<0.6	neg	1.79	0.7-4	normal
19550603H	B-HLADQ2_DQ8-PCR	B -HLAKeII	09.11.2018 15:25	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS MILD	-	<0.6	neg	2.48	0.7-4	normal
19831011J	B-HLADQ2_DQ8-PCR	B -HLAKeII	11.11.2018 15:30	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M09350 MORPHOLOGICAL DESCRIPTION ONLY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	2.21	0.7-4	normal
19550819F	B-HLADQ2_DQ8-PCR	B -HLAKeII	15.11.2018 15:46	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	1-2 T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY 3-4 T63000 STOMACH M43000 CHRONIC GASTRITIS, helicobacter + 5 T62000 ESOPHAGUS M00100 NO DIAGNOSTIC ABNORMALITY	-	<0.6	neg	2.89	0.7-4	normal
19790508V	B-HLADQ2_DQ8-PCR	B -HLAKeII	16.11.2018 15:40	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63000 STOMACH M43000 CHRONIC GASTRITIS T62000 ESOPHAGUS M43000 CHRONIC ESOPHAGITIS	-	<0.6	neg	1.61	0.7-4	normal
19770512V	B-HLADQ2_DQ8-PCR	B -HLAKeII	18.11.2018 15:20	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M58010 ATROPHIC GASTRITIS	-	<0.6	neg	1.12	0.7-4	normal
19700529K	B-HLADQ2_DQ8-PCR	B -HLAKeII	18.11.2018 15:20	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	-	<0.6	neg	2.99	0.7-4	normal
19830714H	B-HLADQ2_DQ8-PCR	B -HLAKeII	06.12.2018 15:35	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS MILD T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS MILD T62350 CARDIO-ESOPHAGEAL JUNCTION M40000 INFLAMMATION CHRONIC ACTIVE T62000 ESOPHAGUS M09350 MORPHOLOGICAL DESCRIPTION ONLY (FUNGUS+)	-	0.6	neg	2.95	0.7-4	normal
19981225K	B-HLADQ2_DQ8-PCR	B -HLAKeII	09.12.2018 15:25	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS, MILD T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS, MILD	-	<0.6	neg	1.92	0.6-3.5	normal
19750516R	B-HLADQ2_DQ8-PCR	B -HLAKeII	20.12.2018 16:40	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	I T64300 DUODENUM M58000 VILLOUS ATROPHY II T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY III T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY	++	<0.6	neg	2.26	0.7-4	normal
19650924T	B-HLADQ2_DQ8-PCR	B -HLAKeII	31.01.2019 15:55	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS MILD	-	<0.6	neg	1.69	0.7-4	normal
19560521I	B-HLADQ2_DQ8-PCR	B -HLAKeII	15.02.2019 15:51	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M42000 SUPERFICIAL GASTRITIS	-	<0.6	neg	1.99	0.7-4	normal
19750311H	B-HLADQ2_DQ8-PCR	B -HLAKeII	31.03.2019 18:05	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M43000 CHRONIC INFLAMMATION, mild T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T67000 COLON M00100 NORMAL TISSUE MORPHOLOGY	+	<0.6	neg	2.67	0.7-4	normal
19790102T	B-HLADQ2_DQ8-PCR	B -HLAKeII	12.06.2019 15:59	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M40000 DUODENITIS, LEVIS T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	+	<0.6	neg	1.42	0.7-4	normal
19941125R	B-HLADQ2_DQ8-PCR	B -HLAKeII	24.07.2019 15:18	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NO DIAGNOSTIC ABNORMALITY T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS T62000 ESOPHAGUS M43000 CHRONIC INFLAMMATION	-	<0.6	neg	0.90	0.7-4	normal
19830101M	B-HLADQ2_DQ8-PCR	B -HLAKeII	22.08.2019 16:31	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M00100 NORMAL TISSUE MORPHOLOGY T63500 GASTRIC CORPUS M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	-	0.8	neg	3.80	0.7-4	normal
19620917H	B-HLADQ2_DQ8-PCR	B -HLAKeII	28.08.2019 16:19	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	1. T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY 2. T64400 DUODENAL BULBUS M73330 GASTRIC METAPLASIA 3,4. T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY 5. T63500 GASTRIC CORPUS M82110 TUBULAR ADENOMA, LOW GRADE	-	<0.6	neg	1.45	0.7-4	normal

Internal ID	Mnemonic	Test Shortname	B-HLAKeil ValTime	Result external comment (B-HLAKeil)	HLADQ2_DQ8 genotype	RISK	PADGAST statement	Histology grade	tTGAbA result U/ml	tTGAbA result interpretation	IgA result g/l	IgA reference range (age dependent)	IgA result interpretation
19830320H	B-HLADQ2_DQ8-PCR	B-HLAKeil	02.09.2019 17:06	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 PYLORIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M42000 SUPERFICIAL GASTRITIS	-	<0.6	neg	1.79	0.7-4	normal
19661115V	B-HLADQ2_DQ8-PCR	B-HLAKeil	30.09.2019 16:54	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M00100 NORMAL TISSUE MORPHOLOGY T63600 GASTRIC ANTRUM M43000 CHRONIC GASTRITIS T63500 GASTRIC CORPUS M43000 CHRONIC GASTRITIS T62350 CARDIO-ESOPHAGEAL JUNCTION M00100 NO DIAGNOSTIC ABNORMALITY T62000 ESOPHAGUS M00100 NO DIAGNOSTIC ABNORMALITY	-	0.8	neg	4.27	0.7-4	elevated
19821125J	B-HLADQ2_DQ8-PCR	B-HLAKeil	16.10.2019 16:06	HLA-analysis: negative. No association was found between the risk haplotypes HLA-DQ2 and HLA-DQ8 and celiac disease. The patient has no increased risk of developing celiac disease.	HLA-DQx.x	1:2518 (extremely low)	T64300 DUODENUM M40000 INFLAMMATION (SEE ADDITIONAL STATEMENT) T64300 DUODENUM M58000 ATROPHY, LEVIS T63000 STOMACH M00100 NORMAL TISSUE MORPHOLOGY T62000 ESOPHAGUS M00100 NORMAL TISSUE MORPHOLOGY	++	<0.6	neg	2.31	0.7-4	normal