



1. LÉKAŘSKÁ FAKULTA
UNIVERZITY KARLOVY V PRAZE



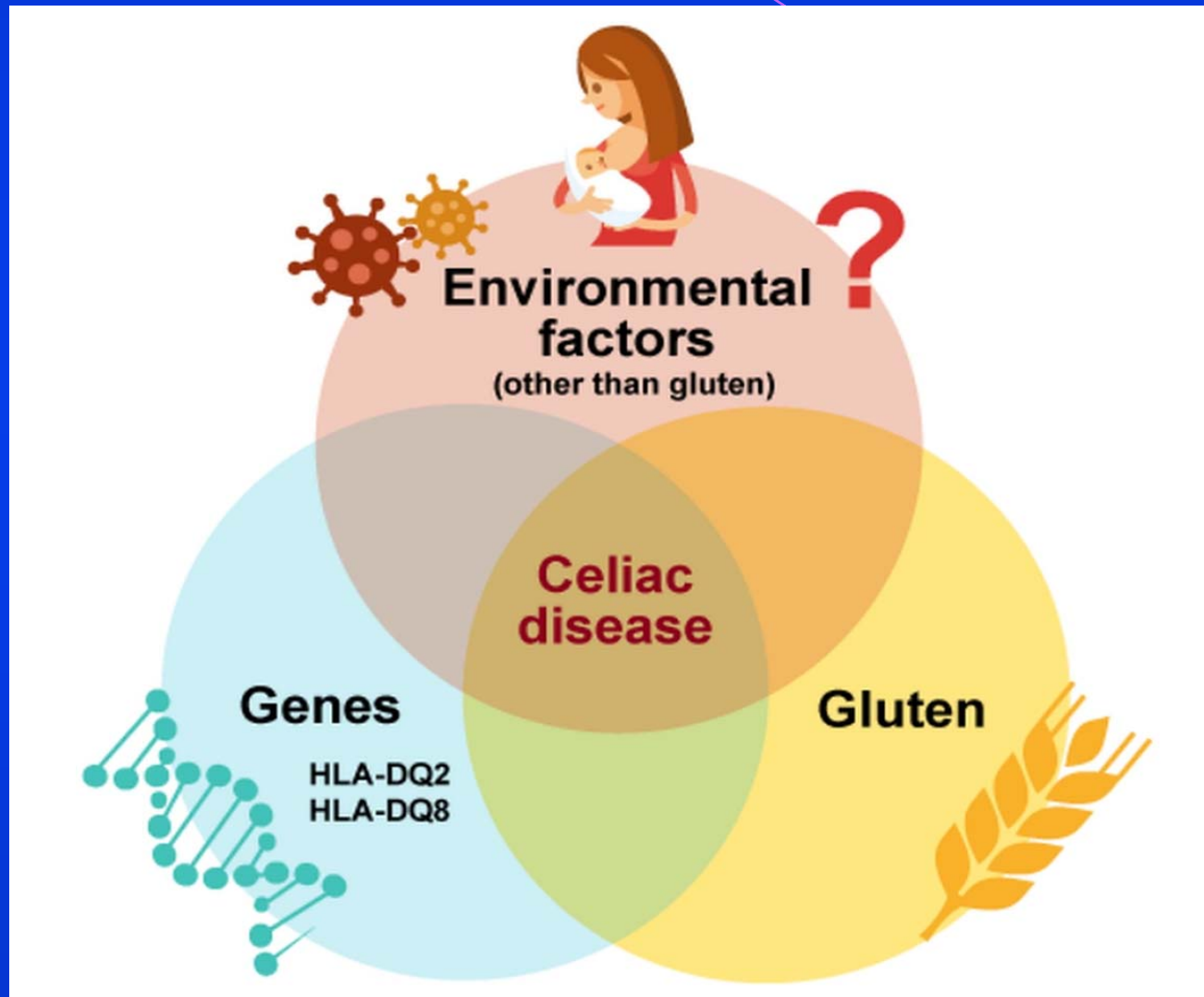
COELIAC DISEASE DIAGNOSIS, MONITORING AND THERAPY

MUDr. Petr Kocna CSc.
<http://gweb.zde.cz>

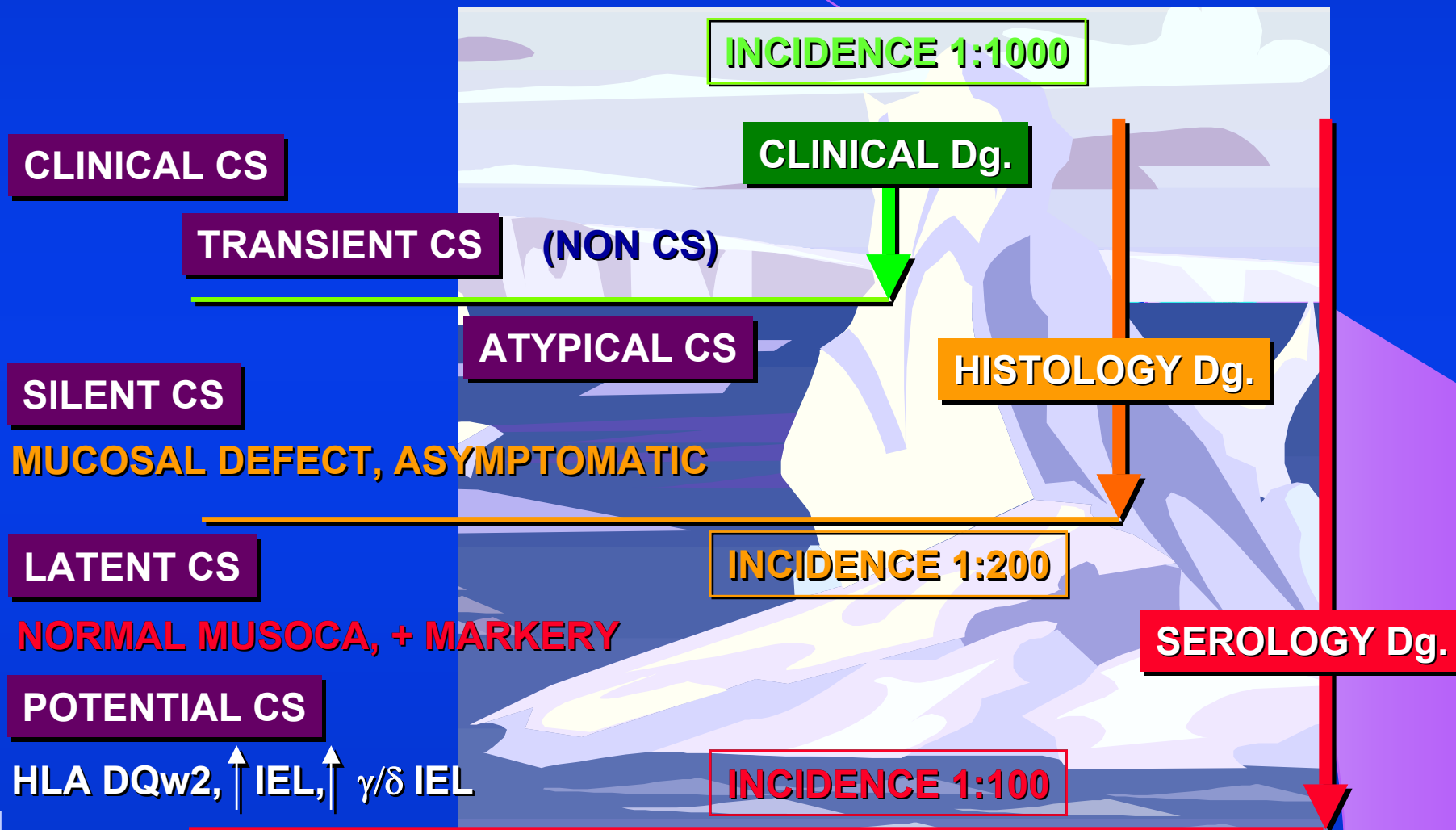


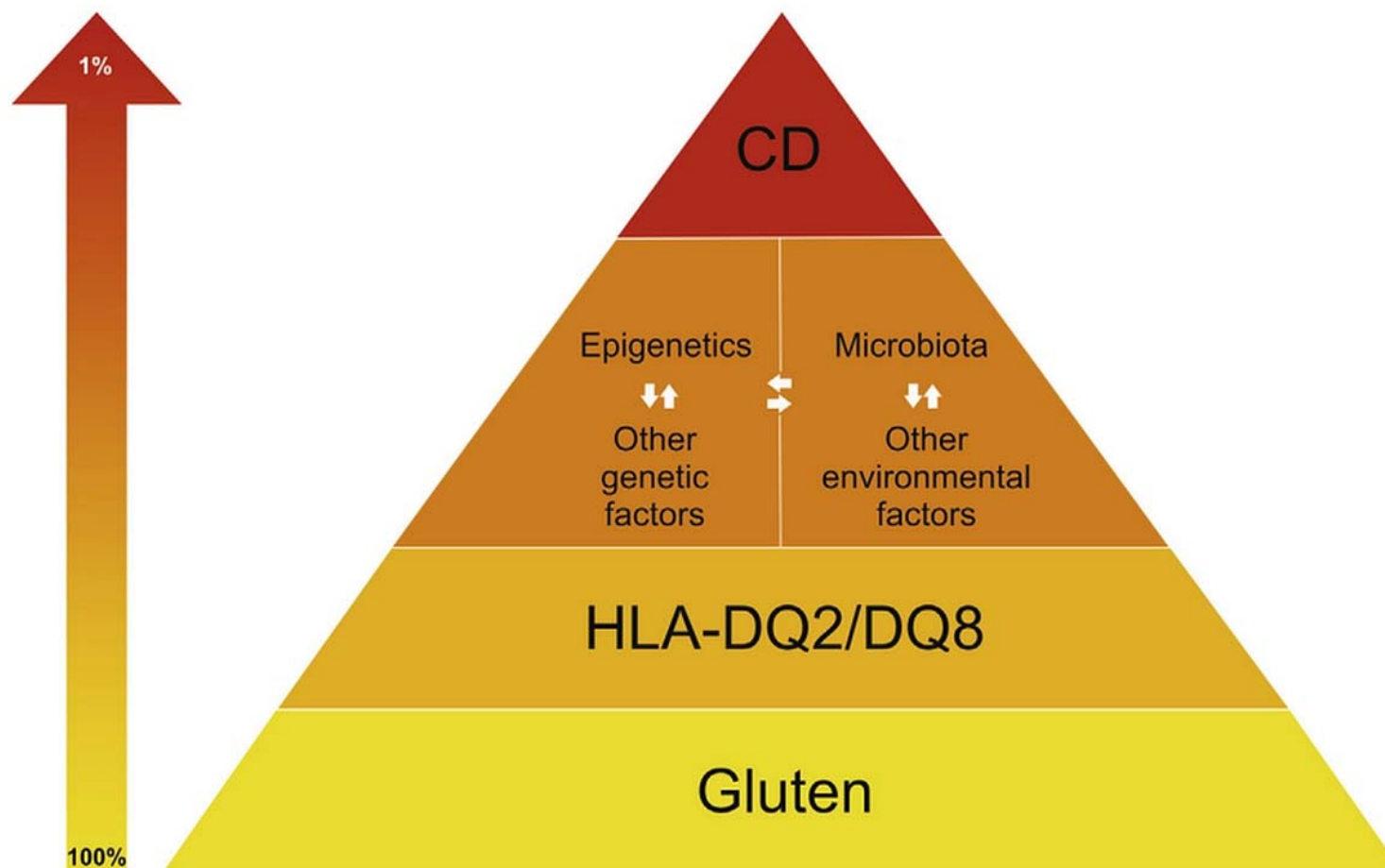
1.LF UK tutorial, July 2025

COELIAC INCIDENCE - THREE MAIN CONDITIONS



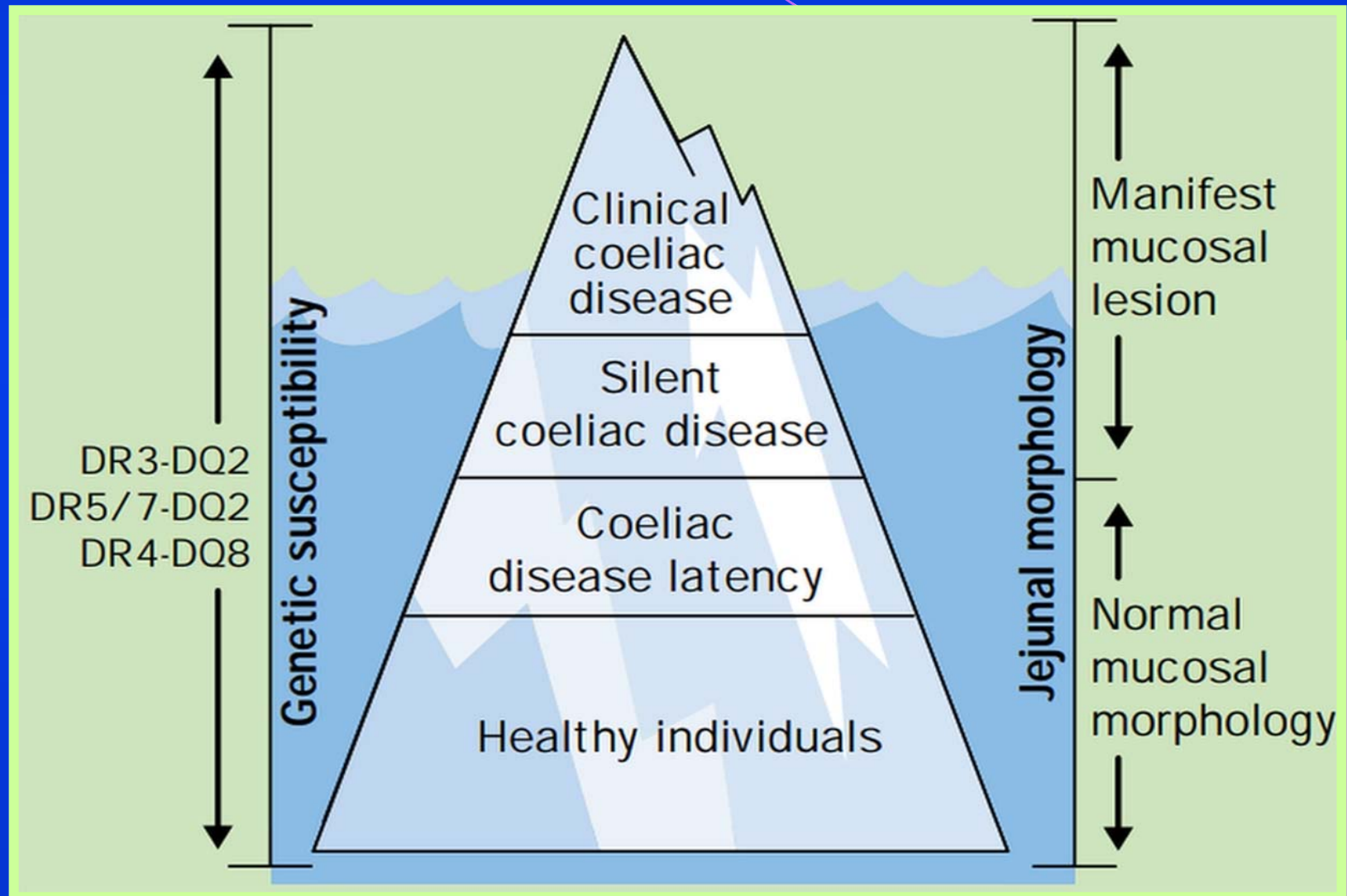
ICEBERG HYPOTHESIS OF COELIAC INCIDENCE



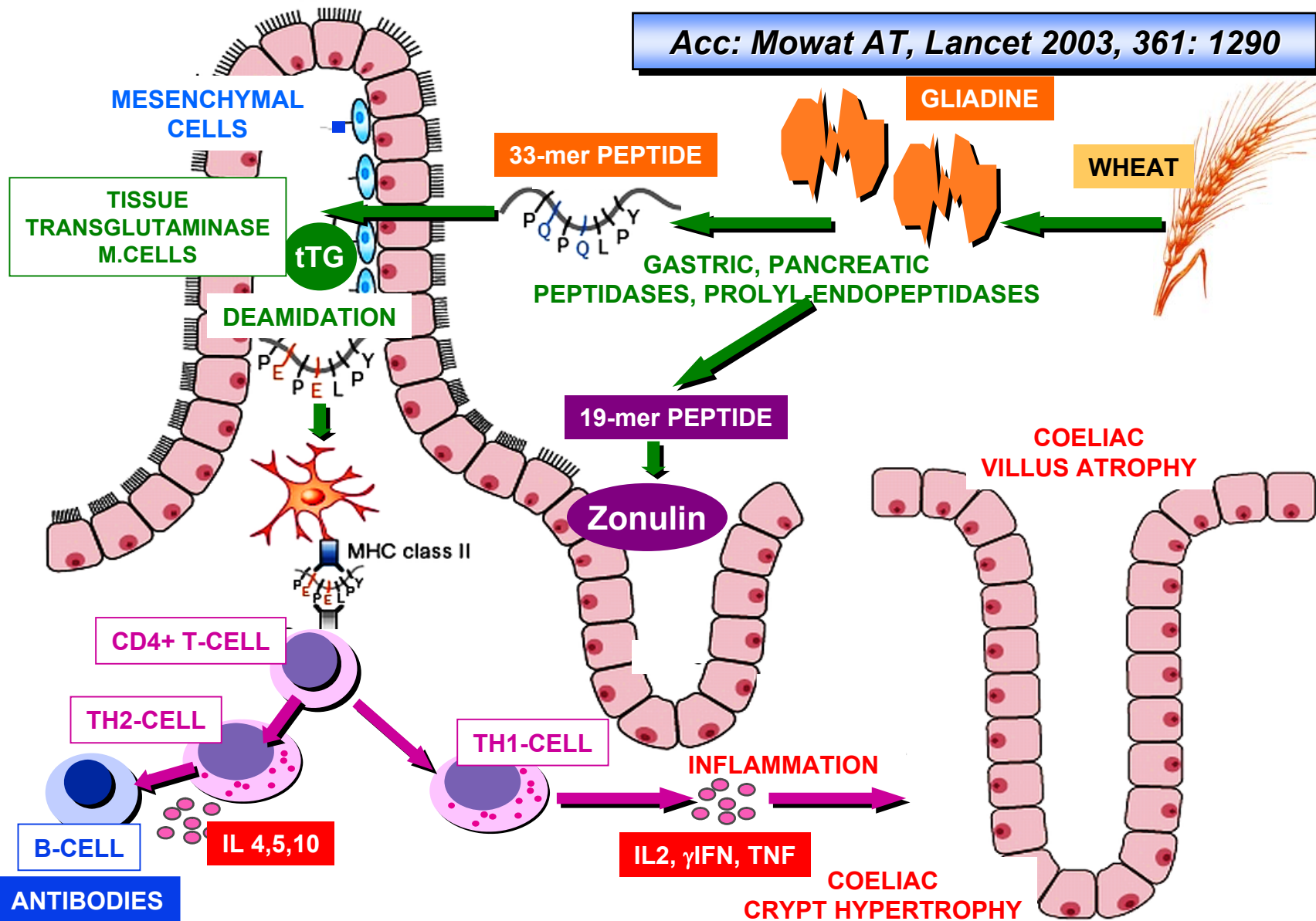


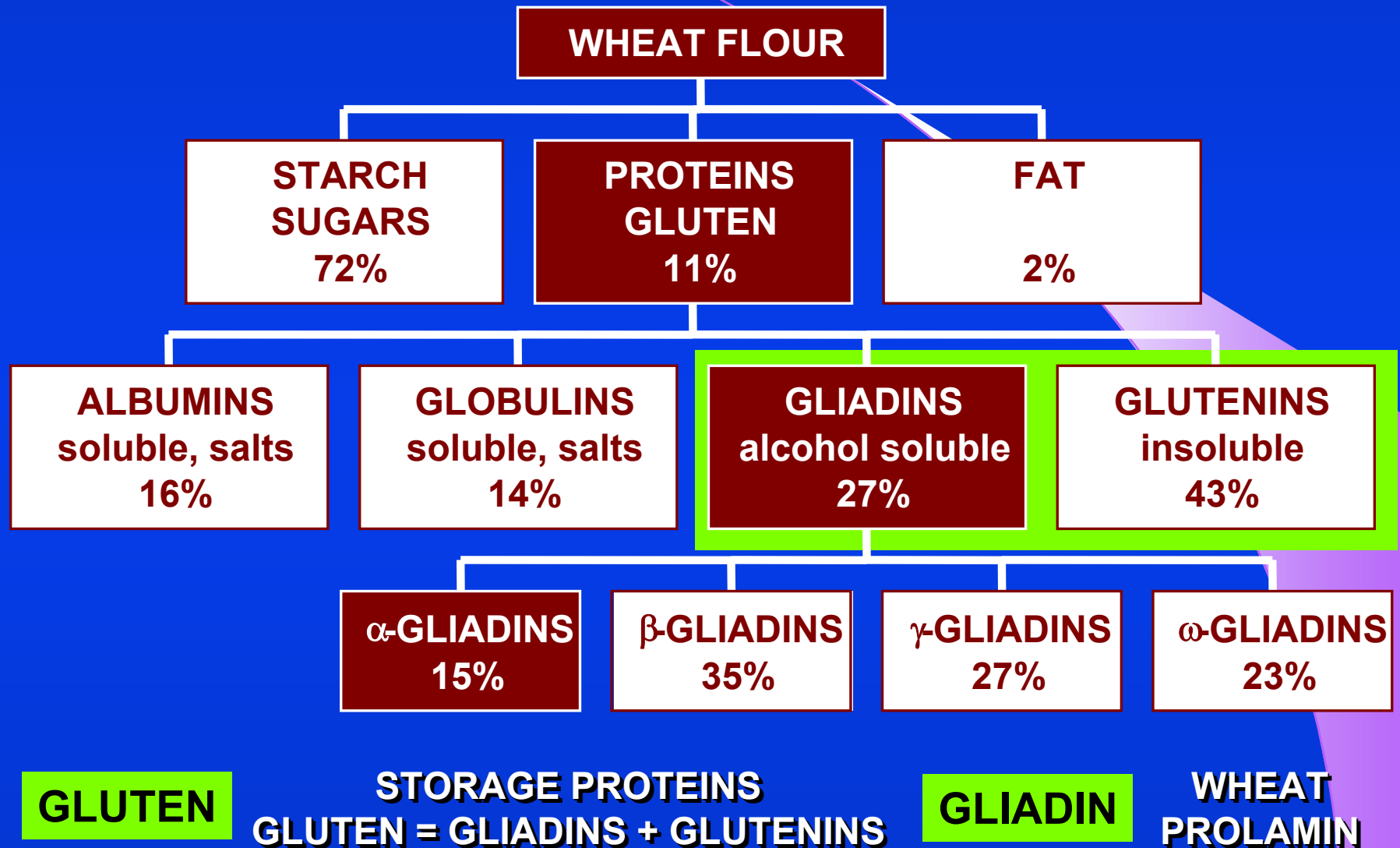
***Dieli-Crimi R, Cénit MC, Núñez C. The genetics of celiac disease:
A comprehensive review of clinical implications. J Autoimmun. 2015; 64:26-41***

ICEBERG HYPOTHESIS OF COELIAC INCIDENCE

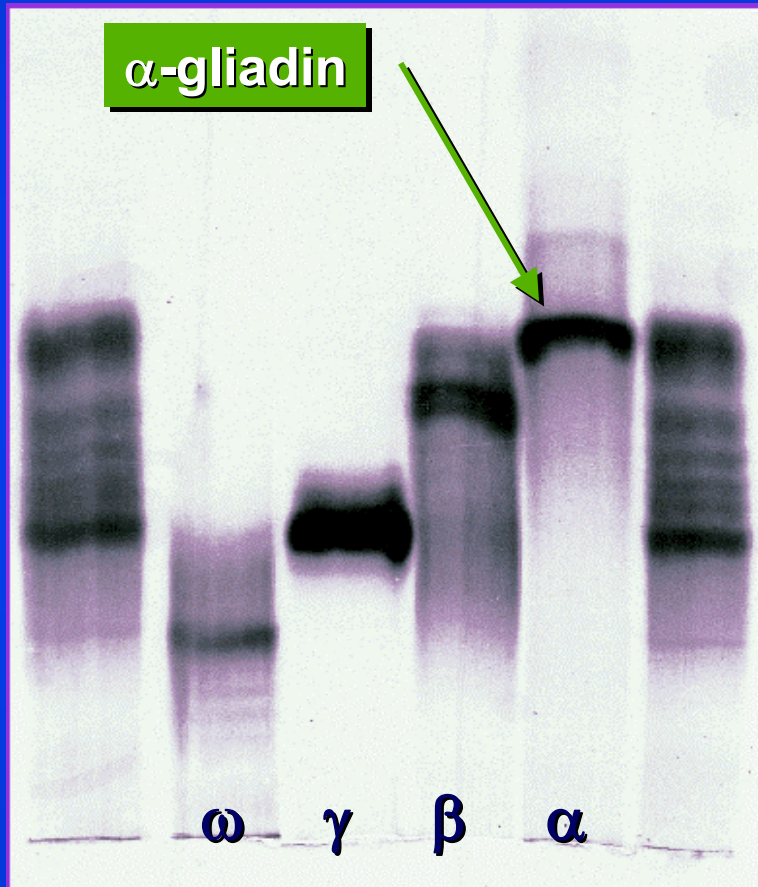


Acc: Mowat AT, Lancet 2003, 361: 1290





GLIADINS – PROTEIN SEPARATION



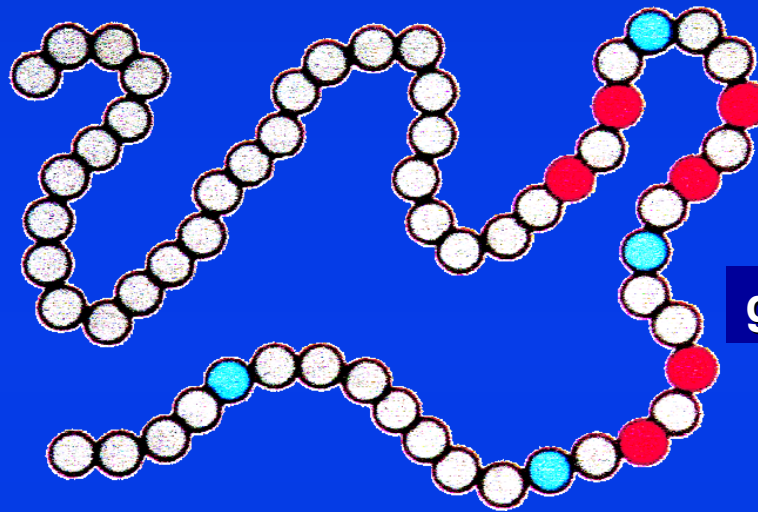
STARCH GEL
ELECTROPHORESIS
(SGE)

PROTEIN SEPARATION
GLIADIN CLASSIFICATION
FOUR GROUPS

$\alpha - \beta - \gamma - \omega$

Kocna, P.; Holáková-Kočová, M.; Šásek, A., Simple starch-gel electrophoresis of gliadin proteins using the LKB-Multiphor system. Z.Lebens.Unters.Forsch., 1983, 177, 454-456

SEQUENCE OF RESISTANT GLIADIN 33 mer PEPTIDE

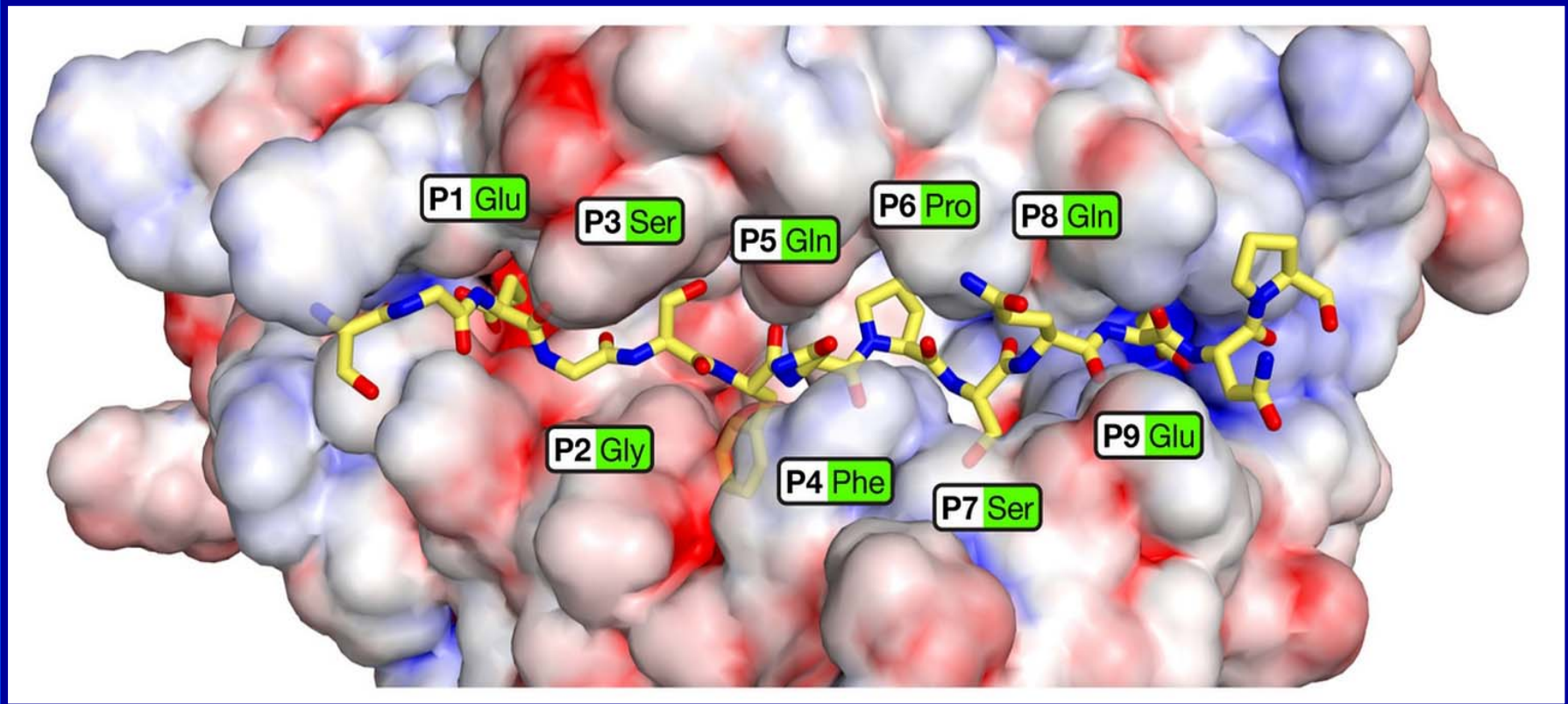


gliadine sequence

33-mer resistant peptide

LQLQPFPPQPQLPYPPQPQLPYPPQPQPF

BINDING OF GLIADIN PEPTIDE TO HLA-DQ8



Celiac Disease. in The Autoimmune Diseases ed. Rose NR, Mackay IR, Sollid LM., Lundin KAE. Academic Press, 2014: 1247-1267

BINDING OF GLIADIN PEPTIDE TO HLA-DQ2

LQPFPQP^QLPY

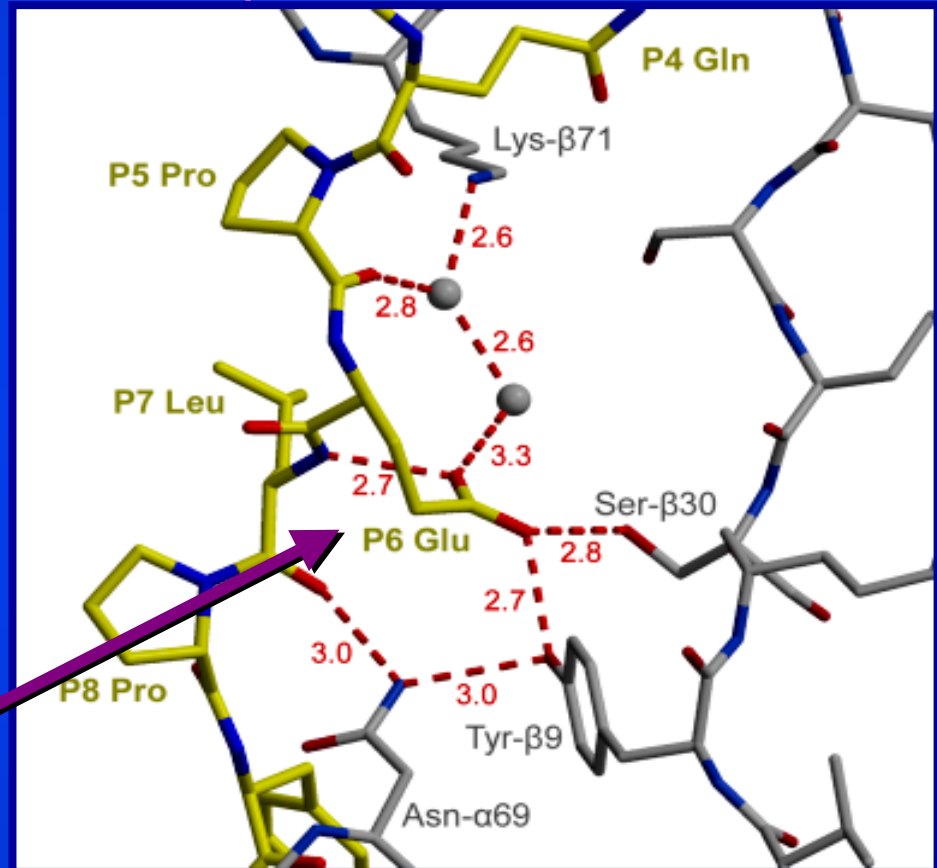
IC₅₀: 103 μM

DEAMIDATION - TG2
TISSUE TRANSGLUTAMINASE

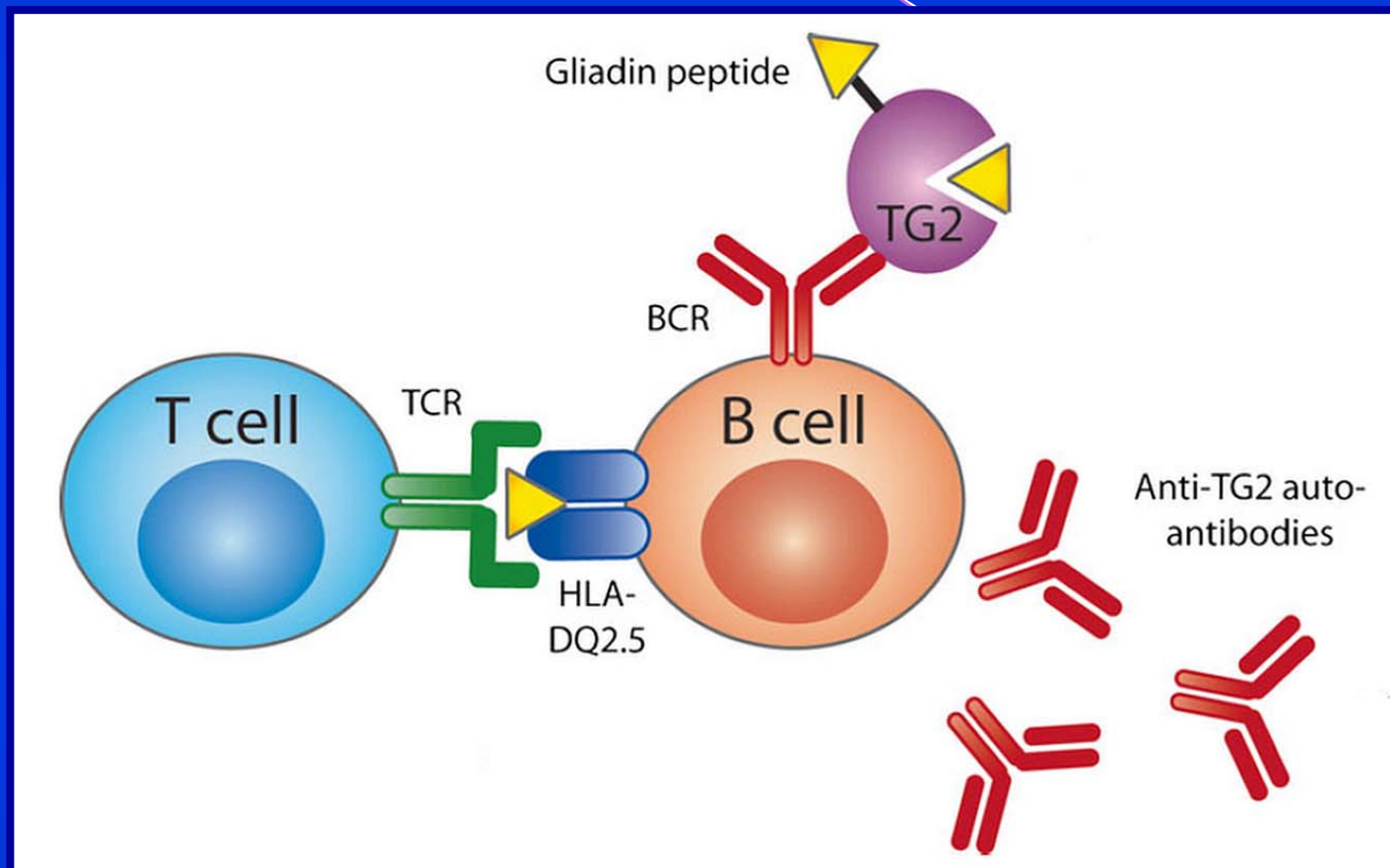
LQPFPQP^ELPY

IC₅₀: 4 μM

AFFINITY LINKS TO POSITION P6
INCREASE 25x



GLIADIN PEPTIDE BINDING TO T-CELLS and B-CELLS



Qiao SW, Iversen R, Ráki M, Sollid LM. The adaptive immune response in celiac disease. *Semin Immunopathol.* 2012 Jul;34(4):523-540



CASE STUDY, WOMAN 33 YEARS: 12-02

Woman - L.J. - born 1972

in childhood **anemic, asthenic**, often in sanatoria,

mother and sister followed for **thyreopathy**

astheny, height 171 cm, weight 52 kg

menarche at 15 years, married,

at the time of diagnosis (2005) after **1 spont. abortion** 1994

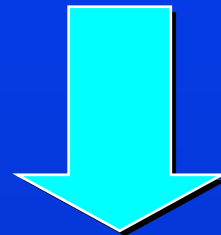


CASE STUDY, WOMAN 33 YEARS: 12-02

**2005 admitted to gastroenterology clinic
with required of colonoscopy for **hypochrome anemia****

Colonoscopy - normal findings

Histology of bioptical samples - normal findings



Routine laboratory test indicated



CASE STUDY, WOMAN 33 YEARS: 12-02

haemoglobin 117 g/l, haematocrit 0.352

albumin 46.6 g/l

alkaline phosphatase 1.54 ukat/l

alanine aminotransferase 0.52 ukat/l

aspartate aminotransferase 0.43 ukat/l

gamma-glutamyl transpeptidase 0.16 ukat/l

calcium 2.35 mmol/l

phosphate 1.22 mmol/l

ferrum 22.9 mmol/l

total cholesterol 3.19 mmol/l

triglycerides 0.65 mmol/l



CASE STUDY: 12-02 - laboratory data

coeliac screening markers - 11/4/05:

IgA anti-transglutaminase 132 U/ml

IgA anti-gliadin 30 U/ml

IgG anti-gliadin 132 U/ml

IgA anti-endomysium - positive



**Histology - small bowel biopsy:
active coeliac, subtotal atrophy,
decreased lactase, IEL 50/100**



CASE STUDY: 12-02 - therapy

since 11/2005 **complete gluten-free diet**
2008 gave birth to a **healthy daughter**, who has not coeliac,
follows the diet - is on remission

CASE STUDY: 12-02 - laboratory data

coeliac specific antibodies - 24/4/06:

IgA anti-transglutaminase 2 U/ml

IgA anti-gliadin 7 U/ml

IgG anti-gliadin 29 U/ml

IgA anti-endomysium - negative



CASE STUDY: 12-02 - laboratory data

immunological markers - 24/7/12:

interferron gamma, **IFN γ 57,7** (normal up to 31 %)

tumor necrosis factor, **TNF α 74,7** (normal up to 44 %)

interleukin, **IL2 - 47,9** (normal up to 28 %)



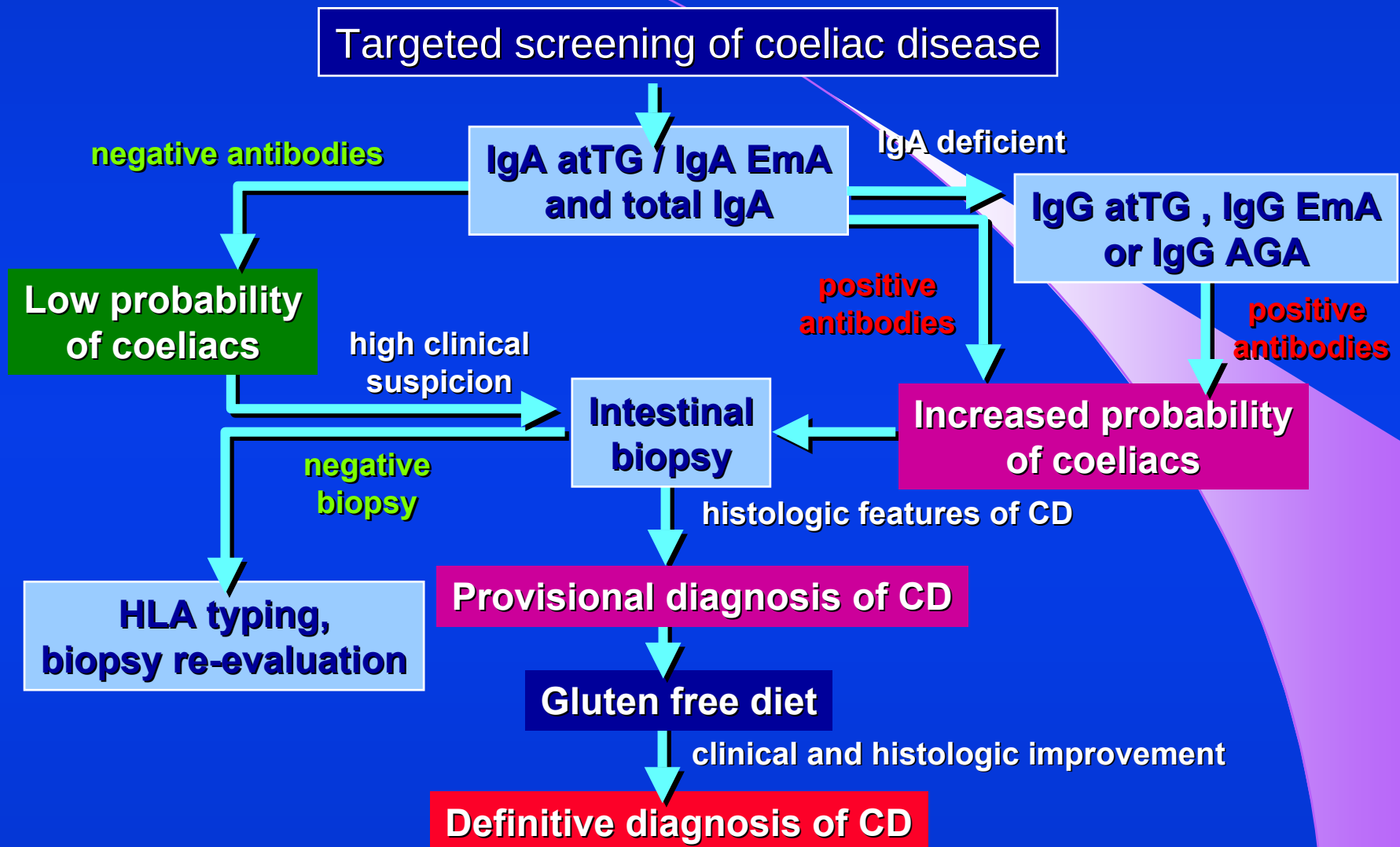
TARGETED COELIAC SCREENING

- ❑ Dermatitis herpetiformis
- ❑ Osteoporosis, unexplained fractures
- ❑ **Unexplained anaemia**
- ❑ Chronic fatigue syndrome
- ❑ Resistent irritable bowel syndrome
- ❑ **Spont. abortion and fetal growth retardation**
- ❑ Unexplained anaemia (iron, folic acid)
- ❑ Hypertransaminasemia
- ❑ Recurrent aphthous stomatitis
- ❑ Dental enamel hypoplasia
- ❑ Diabetes mellitus type 1.
- ❑ **Autoimmune thyroiditis**
- ❑ Autoimmune liver disease
- ❑ Systemic lupus erythematosus
- ❑ Sjögren syndrome
- ❑ Primary biliary cirrhosis or sclerosing cholangitis

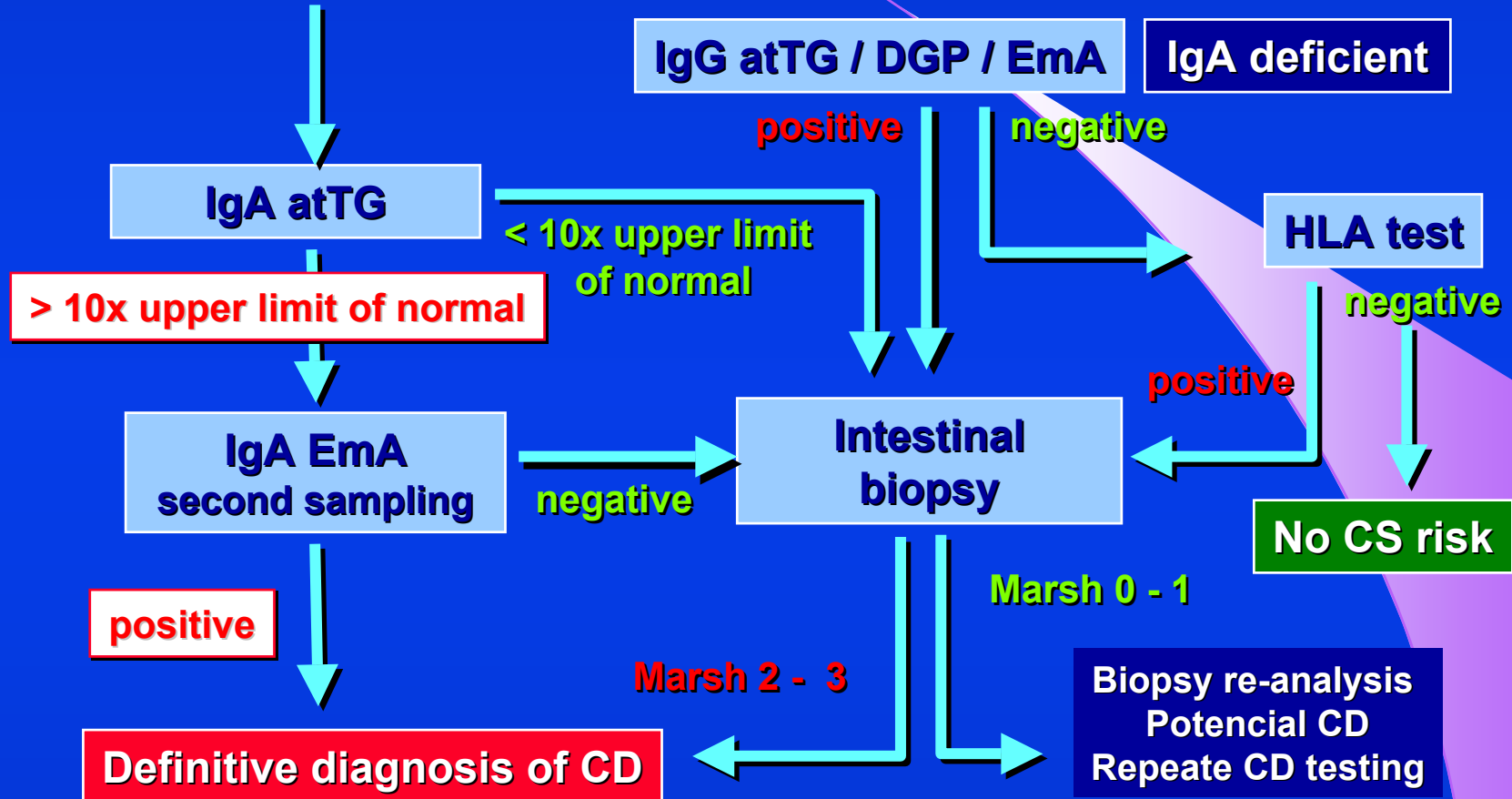
MAIN RISK GROUPS

CD SUSPECTED SYMPTOMS

AUTOIMUNNE DISEASES



Screening of coeliac disease in children





**ACTUAL PROTOCOL
ANTIBODIES DETERMINATION
(EVIDENCE - BASED)**

IgA atTG

+ IgA

+ IgA EmA

INCREASE OF IgA atTG SPECIFICITY

+ IgG atTG

**COELIAC DETECTION WITH
IgA DEFICIENCY**

+ IgA AGA

**COELIAC DETECTION
IN CHILDRENS < 2 YR**

**PERSPECTIVE PROTOCOL
ANTIBODIES DETERMINATION
(WORKING HYPOTHESIS)**

IgA atTG

+ IgG DGP

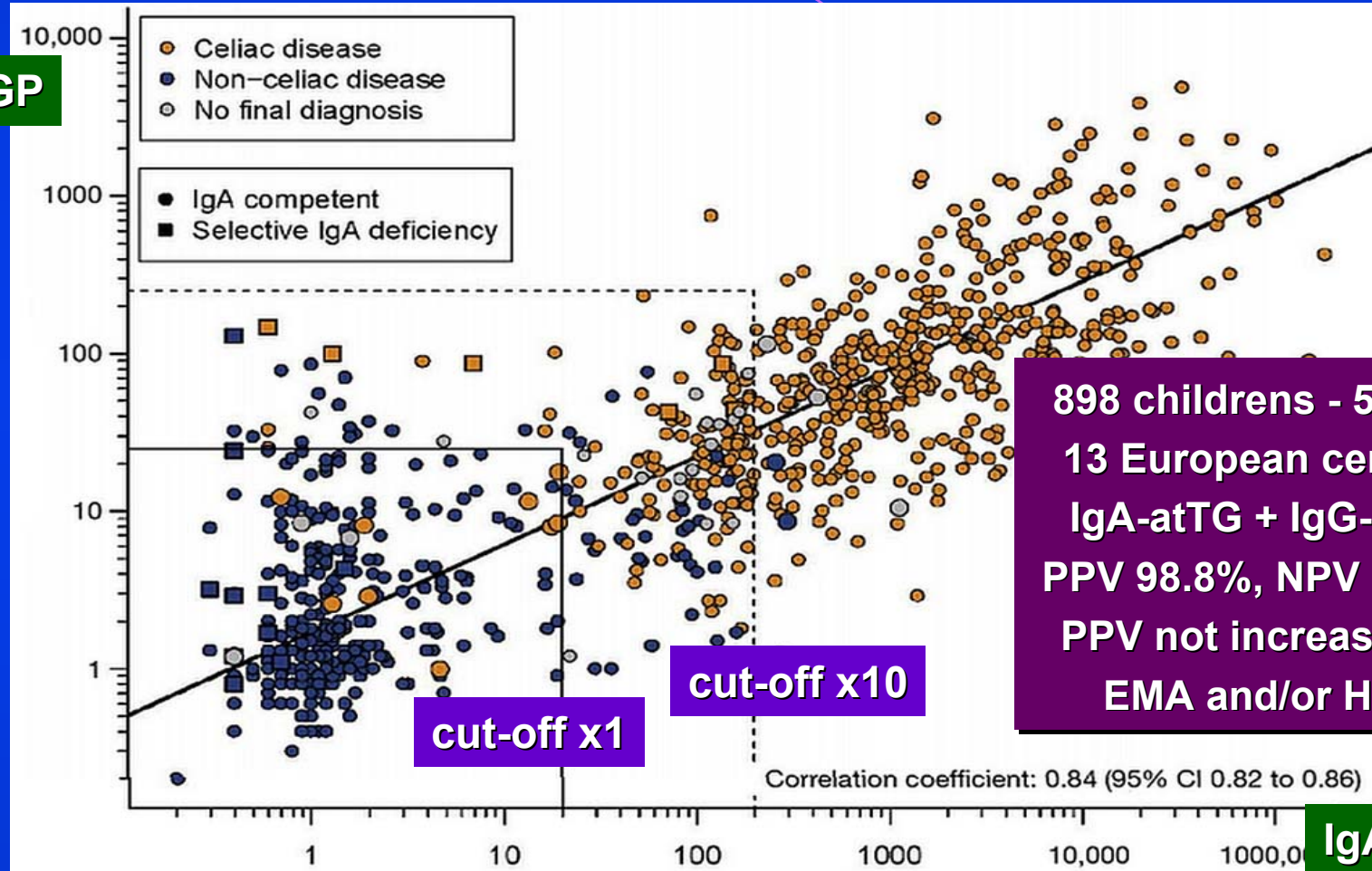
**INCREASE OF IgA atTG SPECIFICITY
COELIAC DETECTION WITH IgA DEFICIENCY
COELIAC DETECTION IN CHILDRENS < 2 YR**

Volta U., Fabbri A., Parisi C. et al. Old and new serological tests for celiac disease screening. Expert Rev. Gastroenterol. Hepatol. 2010, 4(1)



COELIAC MARKERS - atTG, DGP – PEDIATRIC DIAGNOSIS

IgG-DGP



898 children - 592 CS
13 European centers
IgA-atTG + IgG-DGP
PPV 98.8%, NPV 95.8%
PPV not increased by
EMA and/or HLA

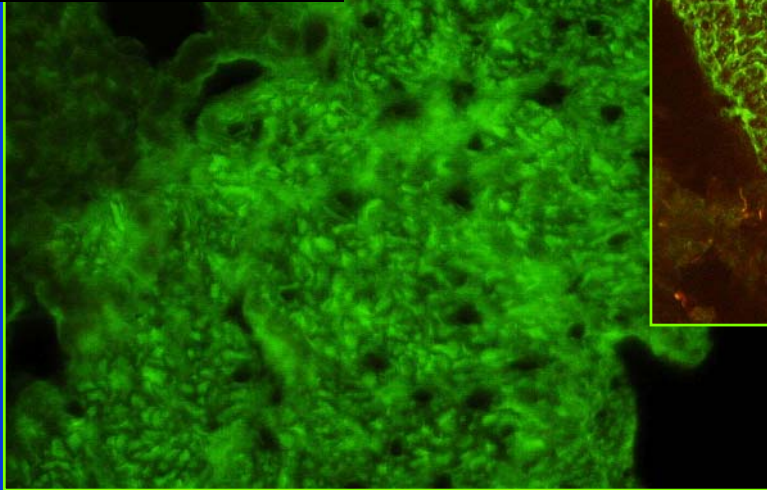
IgA-atTG



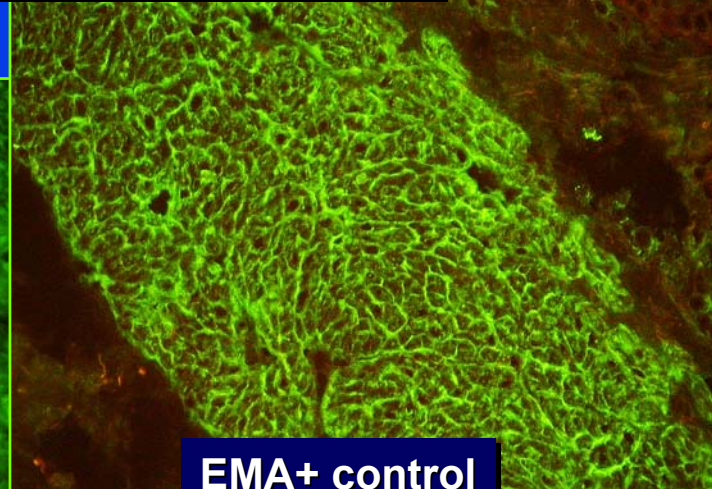
ENDOMYSIUM ANTIBODIES - EMA

**EMA - ENDOMYSIUM ANTIBODIES
IMUNOFLUORESCENCE
MONKEY ESOPHAGUS, HUMAN UMBILICAL CORD
Chorzelski 1983**

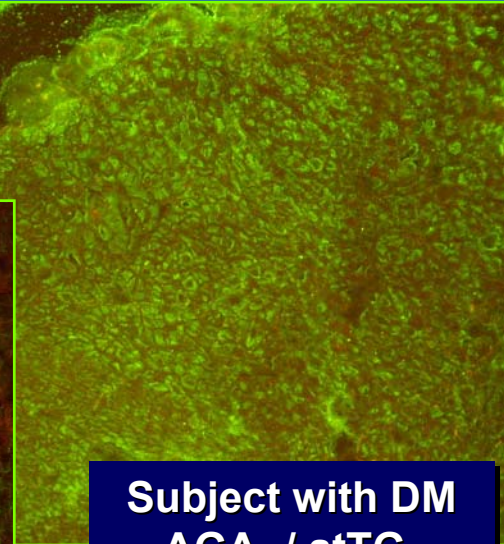
**Subject with CS
AGA+ / atTG+**



EMA+ control



**Subject with DM
AGA- / atTG-**



Chorzelski TP, Sulej J, Tchorzewski H. et al.:

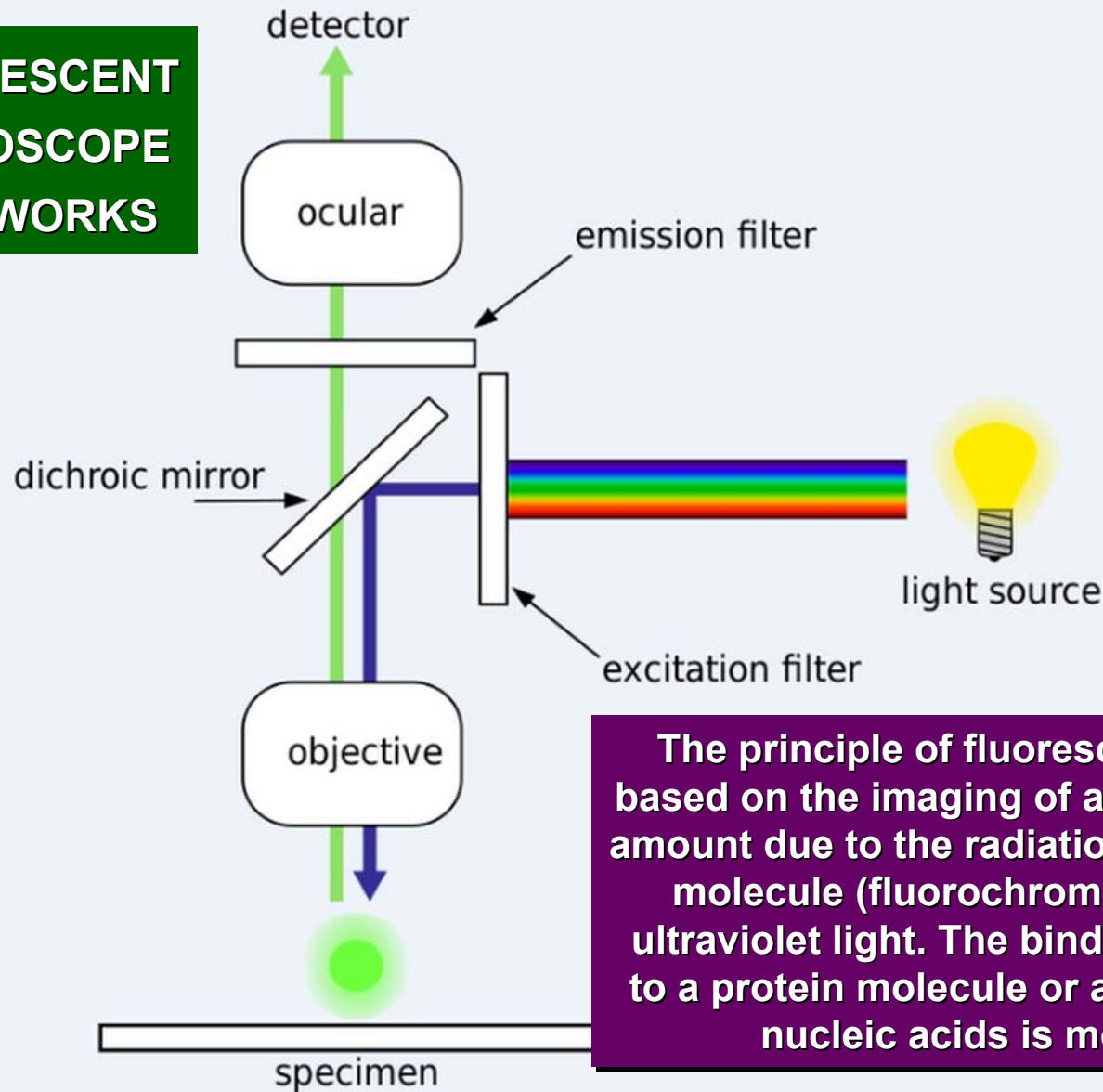
*IgA class endomysium antibodies in dermatitis herpetiformis and coeliac disease.
Ann N Y Acad Sci. 1983;420:325-34.*



FLUORESCENCE MICROSCOPE



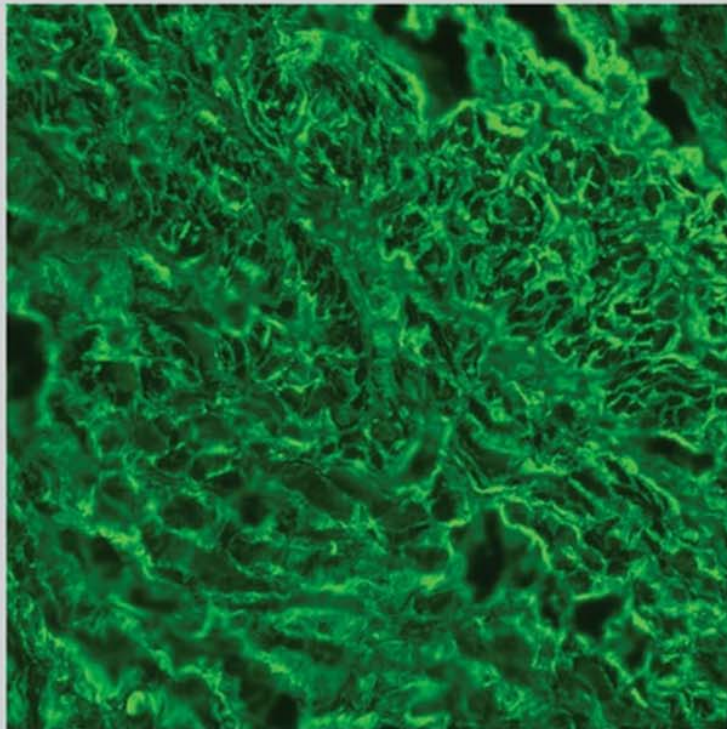
FLUORESCENT MICROSCOPE HOW WORKS



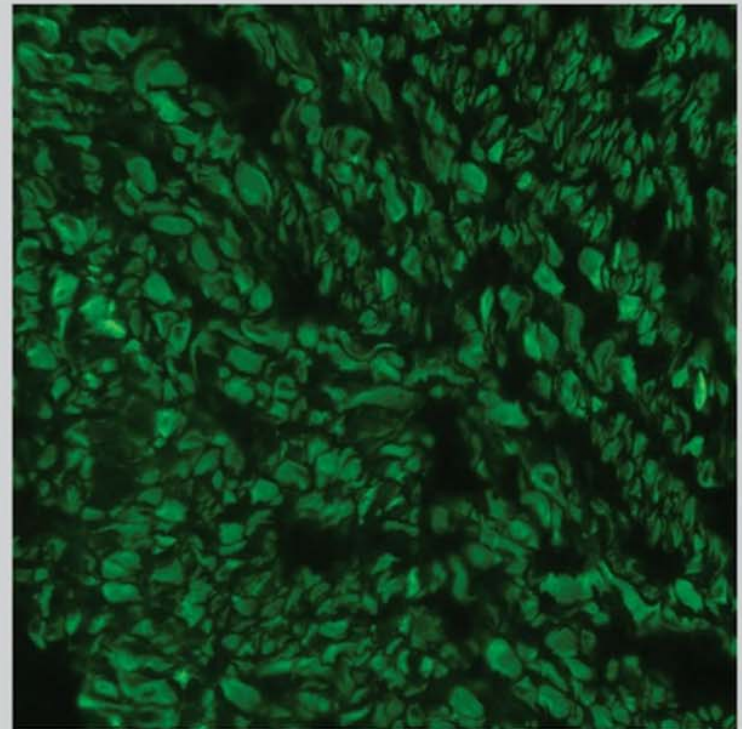
The principle of fluorescence microscopy is based on the imaging of a molecule in a minimal amount due to the radiation (fluorescence) of the molecule (fluorochrome) after exposure to ultraviolet light. The binding of a fluorochrome to a protein molecule or a specific sequence of nucleic acids is most often used.



AI – IMAGE RECOGNITION - IMMUNOFLUORESCENCE



I. Positive



II. Negative

**Caetano Dos Santos FL, Michalek IM, Laurila K, et al.:
Automatic classification of IgA endomysial antibody test for celiac disease:
a new method deploying machine learning. Sci Rep. 2019; 9(1):9217**



AI – IMAGE RECOGNITION - IMMUNOFLUORESCENCE

The study material consisted of 2597 high-quality EmA images class IgA collected in 2017-2018.

According to standard procedure, highly experienced professionals sorted the samples into the following four classes:

I – positive, II – negative, III – deficient IgA and IV – ambiguous

Machine learning was deployed to create the classification model. The sensitivity and specificity of the model were 82.84% and 99.40%.

Accuracy was 96.80%. The classification error was 3.20%.

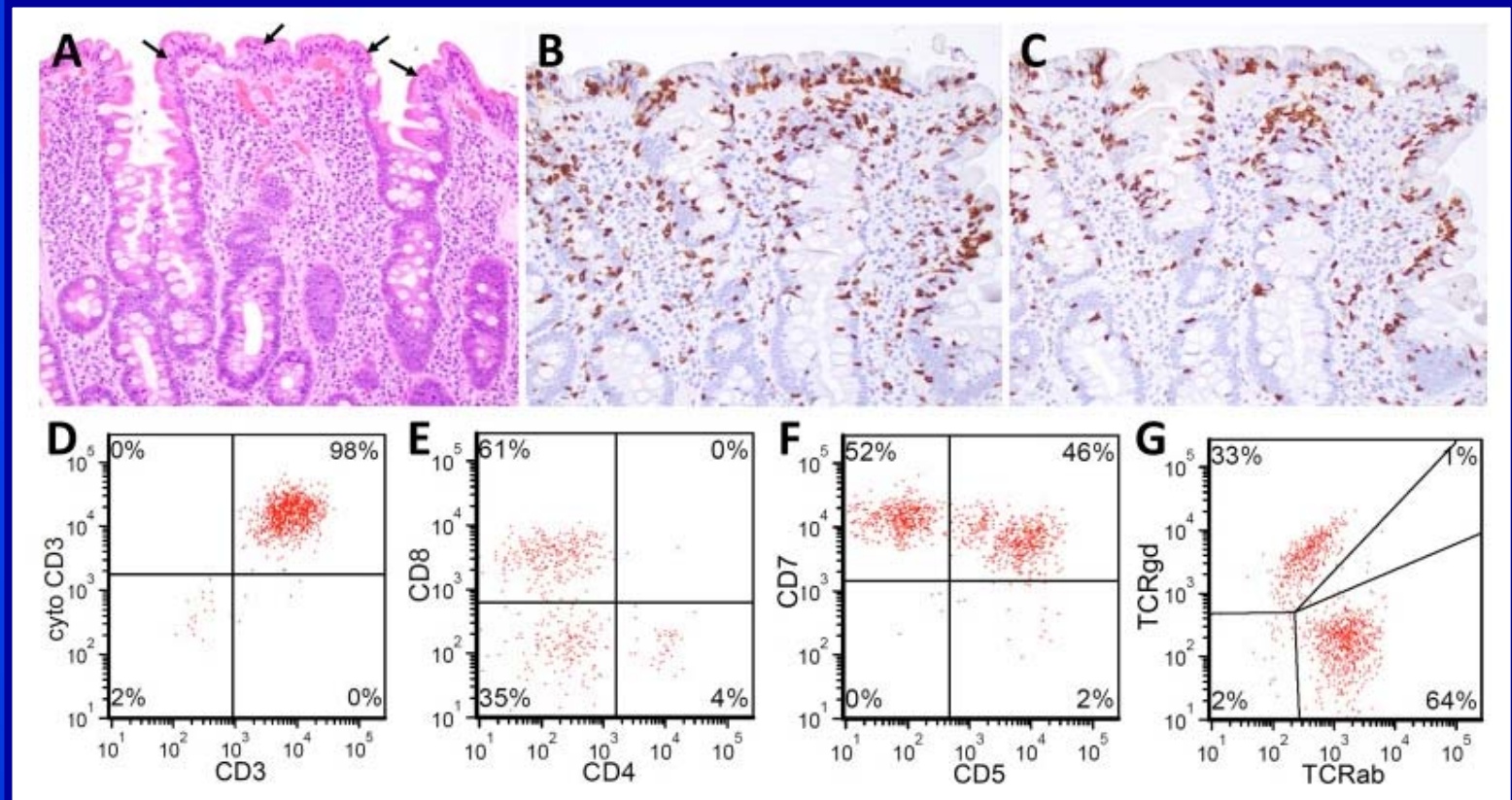
The average rating time per frame was 16.11 seconds.

This is the first study using machine learning for automatic classification of the EmA class IgA test for celiac disease.

Caetano Dos Santos FL, Michalek IM, Laurila K, et al.:

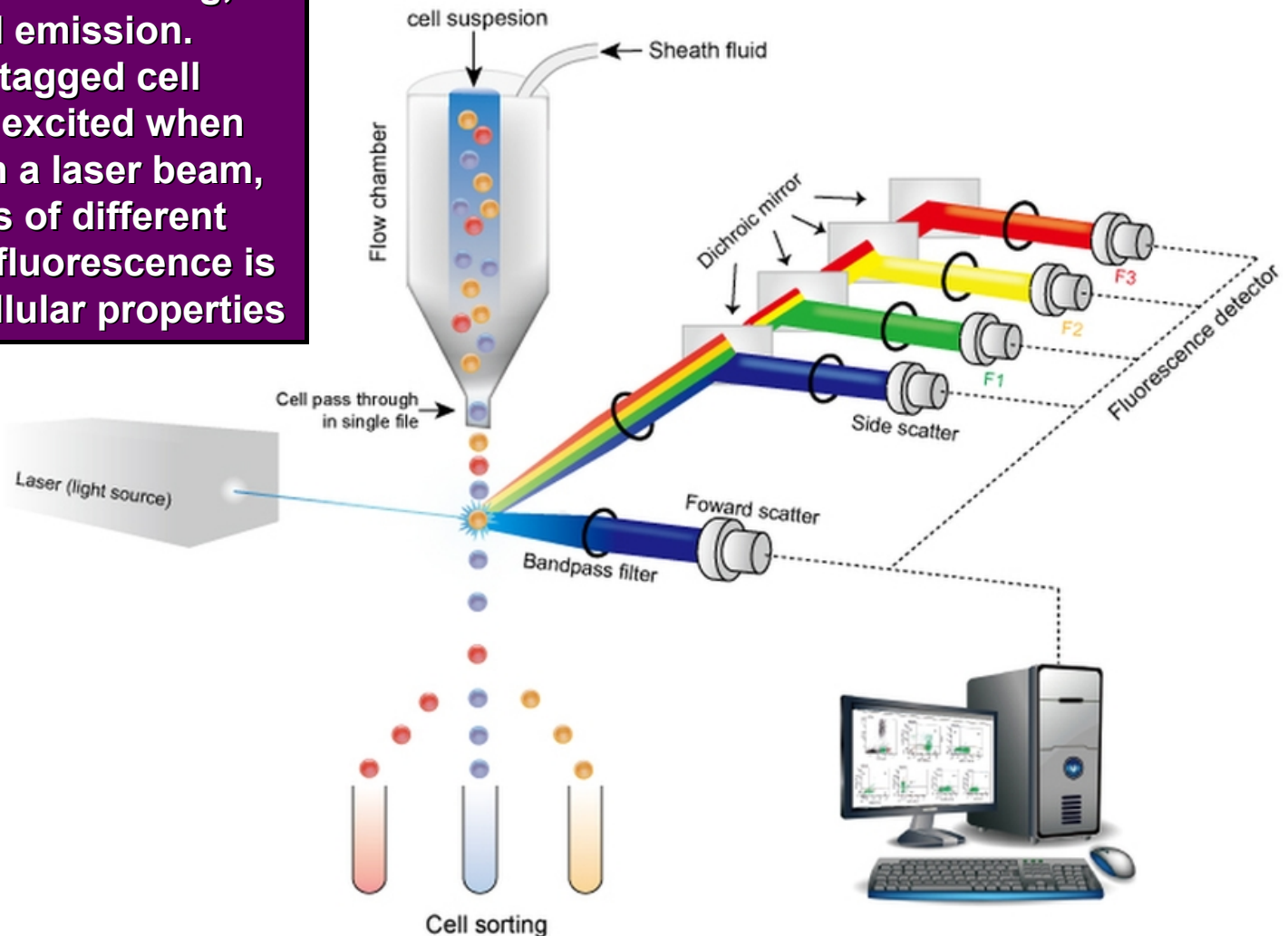
Automatic classification of IgA endomysial antibody test for celiac disease: a new method deploying machine learning. Sci Rep. 2019; 9(1):9217

COELIAC DIAGNOSIS - FLOW CYTOMETRY



Soderquist CR, Lewis SK, Gru AA. et al.: Immunophenotypic Spectrum and Genomic Landscape of Refractory Celiac Disease Type II. Am J Surg Pathol. 2021; 45(7): 905-916

Flow cytometry runs on the principles of light scattering, excitation and emission. Fluorescently tagged cell components get excited when they pass through a laser beam, producing lights of different wavelengths. The fluorescence is used to analyze cellular properties



COELIAC DISEASE SCREENING - POCT TESTS

**RAPID TESTS
FULL BLOOD
POCT ANALYSIS
HOME TESTS**



anti-tTG (IgA & IgG)



anti-DGP (IgA & IgG) + celkové IgA



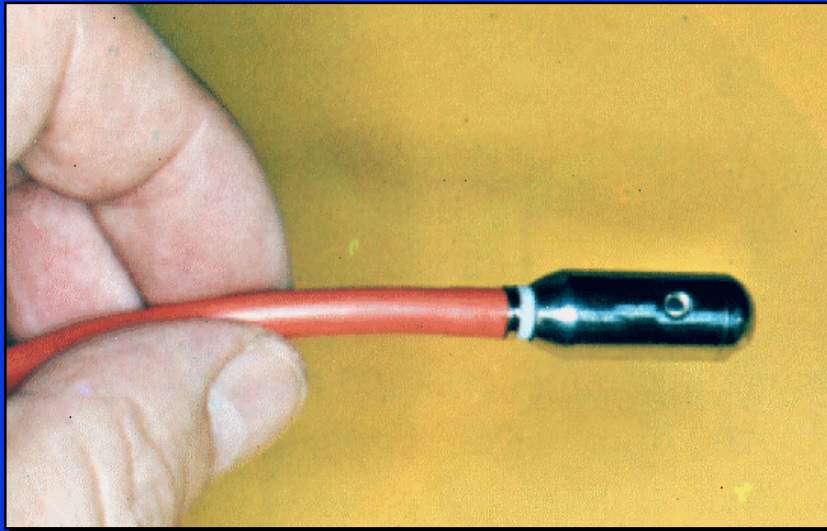
anti-tTG (IgA) + celkové IgA



anti-tTG (IgA, IgG, IgM)

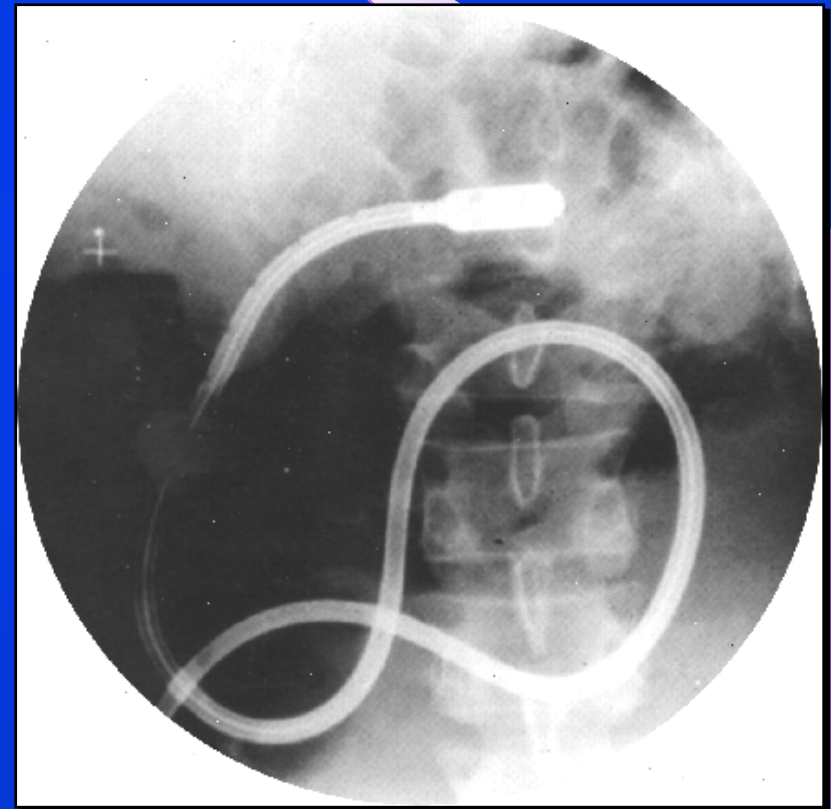
COELIAC DIAGNOSIS - HISTOLOGY, HISTOCHEMISTRY

ENTEROBIOPSY OF SMALL INTESTINE



CROSBY'S CAPSULE

X-REY CHECKED POSITION



COELIAC DIAGNOSIS - HISTOLOGY

mucous villi

enterocytes

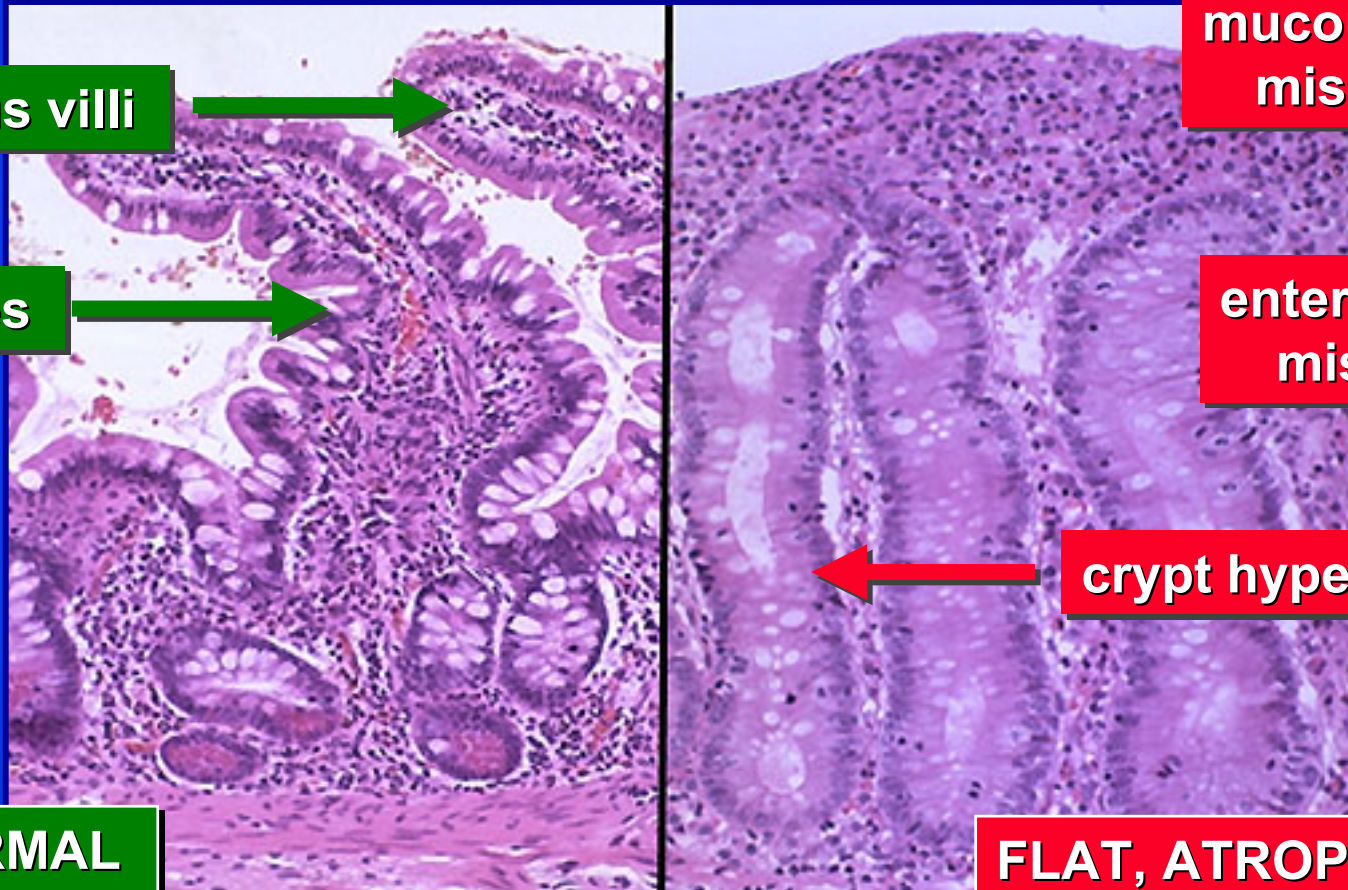
mucous villi
missing

enterocytes
missing

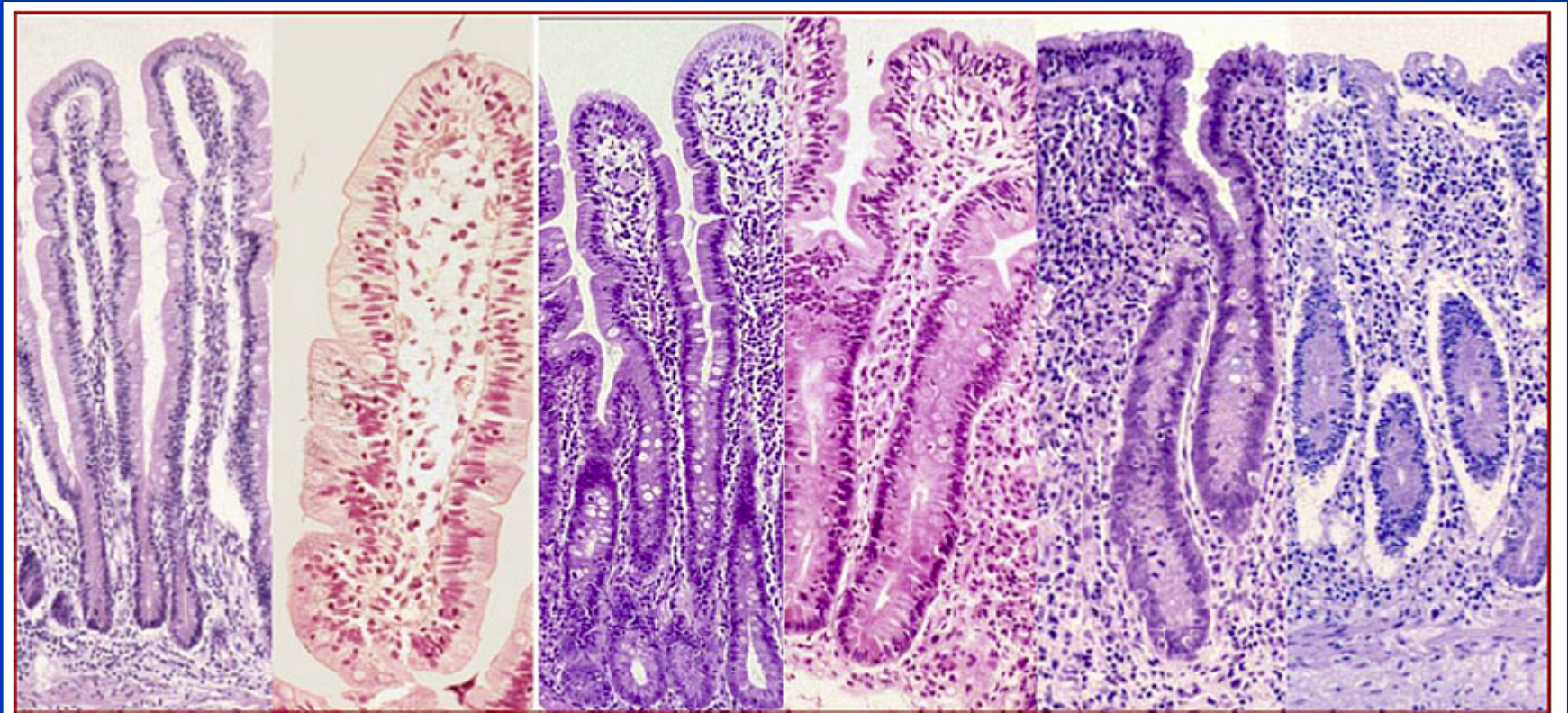
crypt hyperplasia

NORMAL
MUCOSA

FLAT, ATROPHIC
MUCOSA



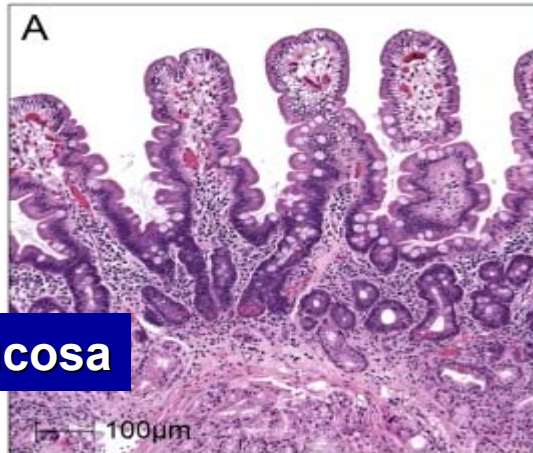
INTESTINAL BIOPSY IN THE COELIAC DISEASE DIAGNOSIS



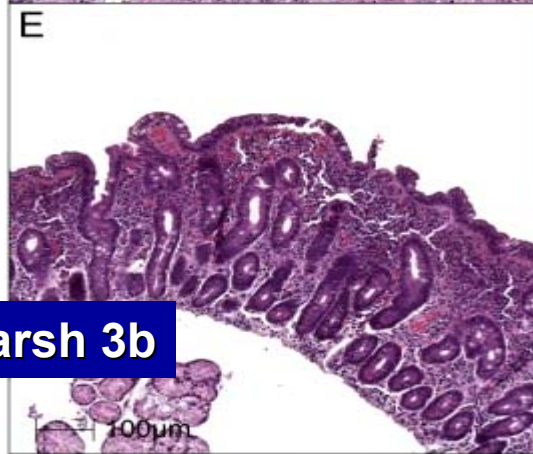
Marsh 0 Marsh 1 **Marsh 2** **Marsh 3a** **Marsh 3b** **Marsh 3c**

*Clinical practice - Coeliac disease. Kneepkens C. M., von Blomberg B. M.
Eur J Pediatr. 2012; 171(7) : 1011 - 1021*

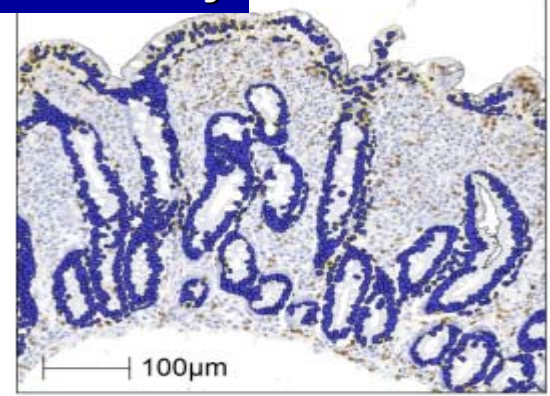
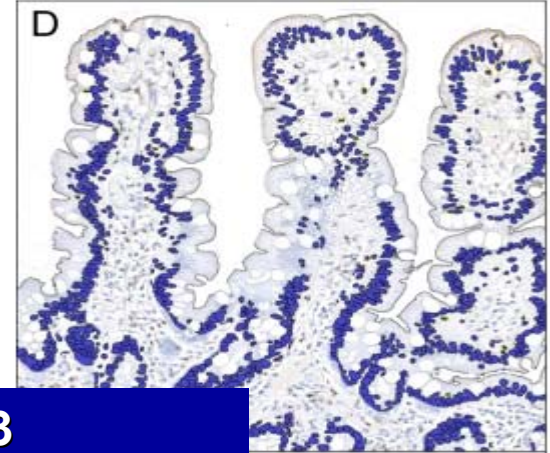
Normal mucosa



Coeliac – Marsh 3b



CD3
immunohistochemistry



Gruver AM, Lu H, Zhao X. et al. Pathologist-trained machine learning classifiers developed to quantitate celiac disease features differentiate endoscopic biopsies according to modified marsh score and dietary intervention response. Diagn Pathol. 2023;18(1):122.

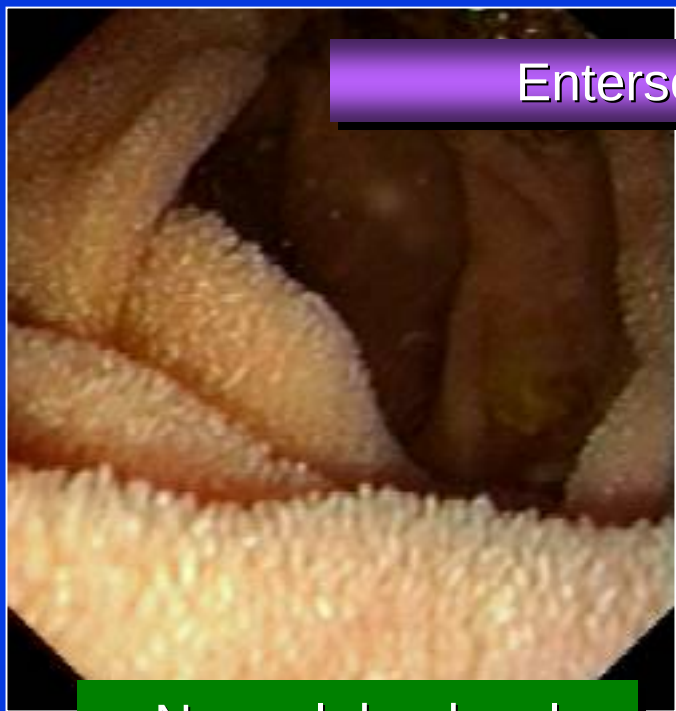


- ✓ **Histological evaluation of mucosal changes associated with celiac disease is important for establishing an accurate diagnosis and monitoring of celiac disease.**
- ✓ **The authors developed machine learning classifiers by trained pathologists for the objective quantification of pathologic changes in villi, intraepithelial lymphocytosis, and crypt hyperplasia in endoscopic small bowel biopsies.**
- ✓ **The study processed 28 paired pre- and post-intervention biopsies (before and after starting a gluten-free diet) and the machine learning method was consistent with the Marsh score in 96.4% (27/28).**

Gruver AM, Lu H, Zhao X. et al. Pathologist-trained machine learning classifiers developed to quantitate celiac disease features differentiate endoscopic biopsies according to modified marsh score and dietary intervention response. Diagn Pathol. 2023;18(1):122.

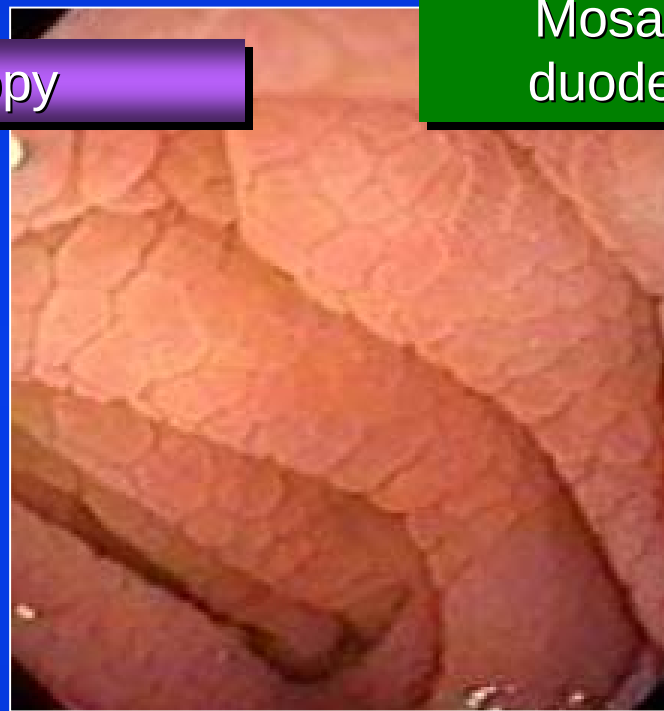
ENDOSCOPIC MARKERS OF COELIAC DISEASE

Enterscopy



Normal duodenal
mucosa

Mosaic pattern of
duodenal mucosa



Chromoendoscopy
with indigocarmine

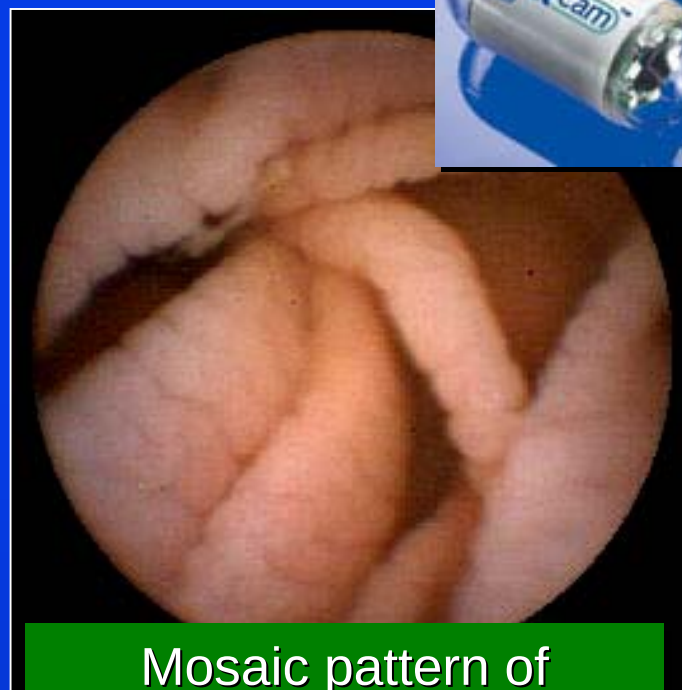


CAPSULE ENDOSCOPY IN COELIAC DIAGNOSIS

NON-INVASIVE ENDOSCOPIC EXAMINATION

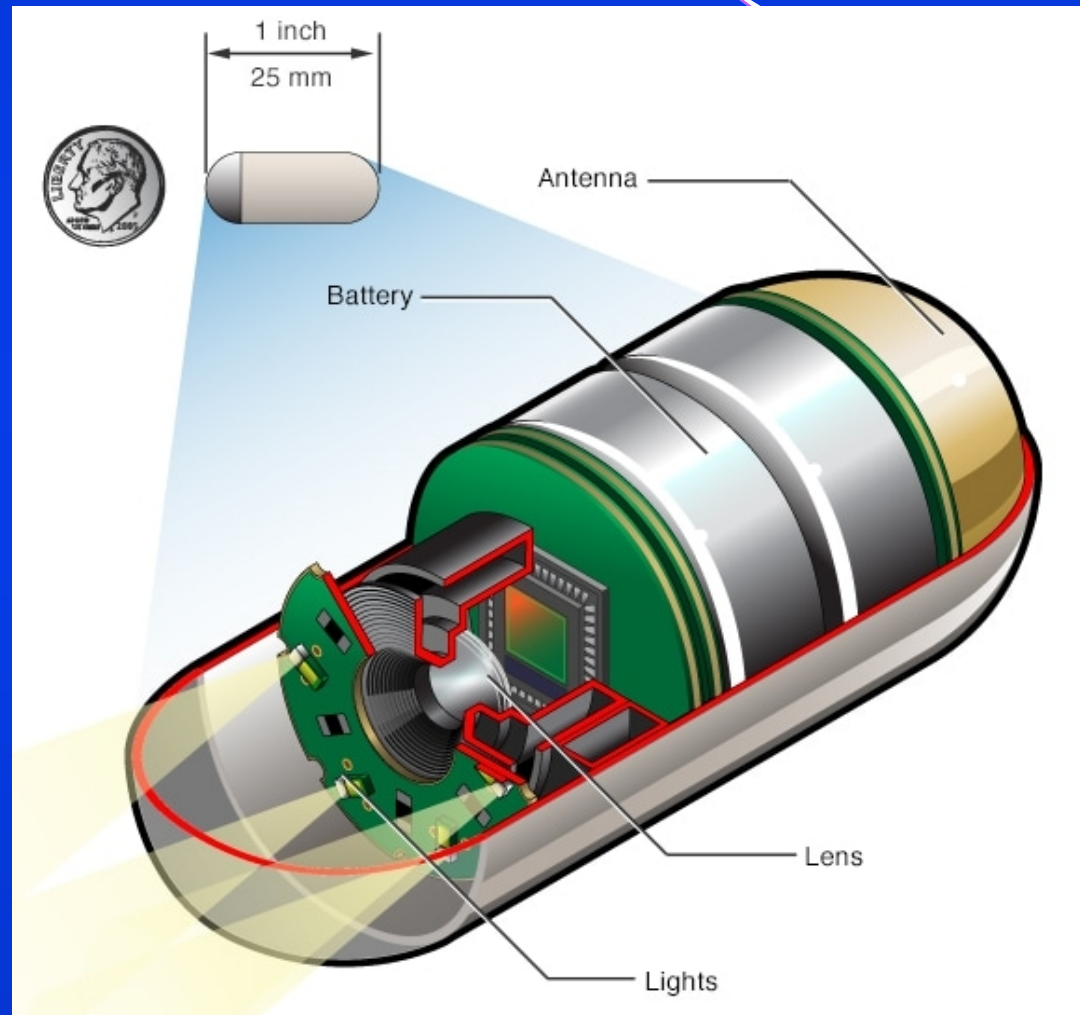


Normal duodenal
mucosa



Mosaic pattern of
duodenal mucosa

CAPSULE ENDOSCOPY IN COELIAC DIAGNOSIS



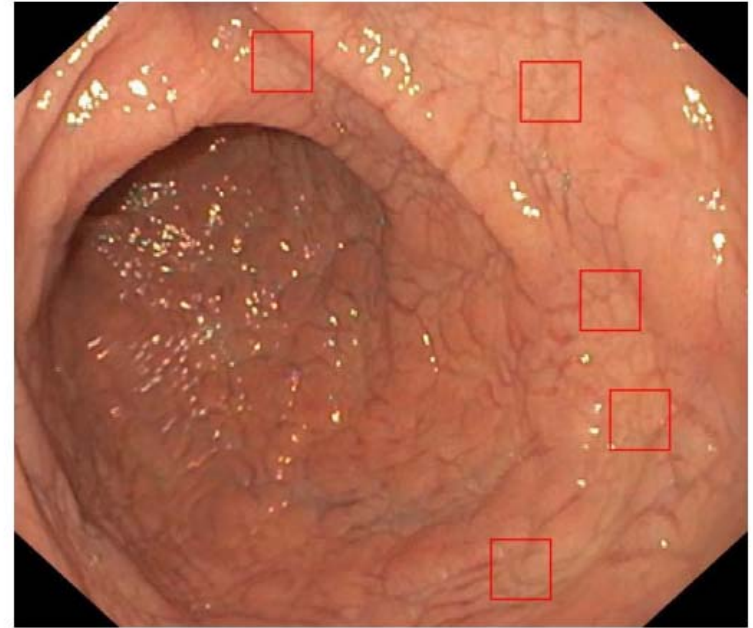
Automated processing of images obtained by non-invasive capsule endoscopy enables the detection of the presence of small villous atrophy, which is not visible during visual inspection. This method can also be used to monitor celiac disease on a gluten-free diet.



The results obtained by processing video capsule endoscopy images reveal an accuracy of 94.1% and an F1 score of 94%, which is competitive with other comprehensive algorithms.

Stoleru CA, Dulf EH, Ciobanu L. Automated detection of celiac disease using Machine Learning Algorithms. Sci Rep. 2022 Mar 8;12(1):4071.

Computer-aided detection of villous atrophy by processing upper gastrointestinal endoscopy images is feasible, and incorporating artificial intelligence techniques into endoscopy equipment and applying them in real time during endoscopy may improve the detection of unexpected celiac disease.

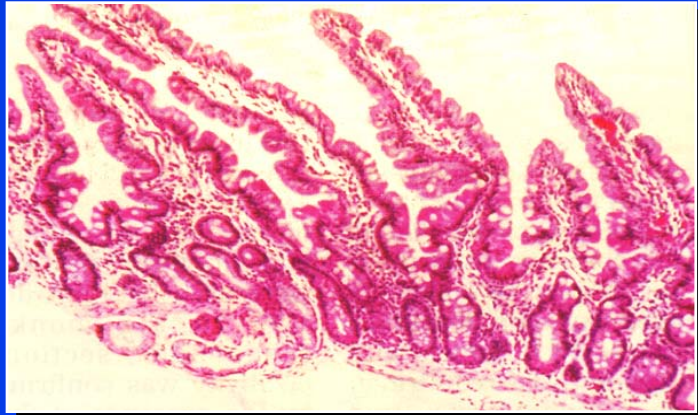


A neural network algorithm analyzing duodenal images of newly diagnosed CD patients compared to non-CD controls detected villous atrophy with 99.30% sensitivity and 98.61% positive predictive value.

Molder A, Balaban DV, Molder CC, Jinga M, Robin A. Computer-Based Diagnosis of Celiac Disease by Quantitative Processing of Duodenal Endoscopy Images. Diagnostics (Basel). 2023 Aug 28;13(17):2780.

GLUTEN FREE DIET (GFD) - SCREENING & DIAGNOSTICS

NORMAL MUCOSA



NEGATIVE ANTIBODIES

**HEALTHY SUBJECT
TREATED COELIAC**

**TREATED COELIAC ?
OTHER AUTOIMMUNITY ?**

**FLORID COELIAC
UNTREATED**

POSITIVE ANTIBODIES

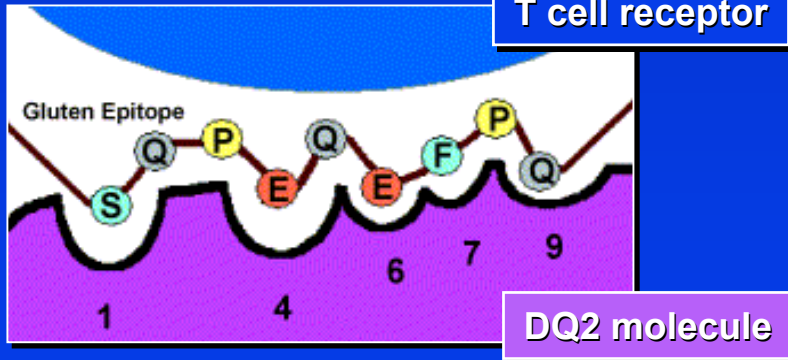
TOTAL ATROPHY





T cell receptor

GLUTEN FREE DIET - CEREALS



DECREASING PATOGENICITY FOR CS

WHEAT RYE BARLEY OATS RICE SORGHUM MILLET MAIZE
GLIADIN SECALIN HORDEIN AVENIN ZEIN



mAb
Gliadin
standard

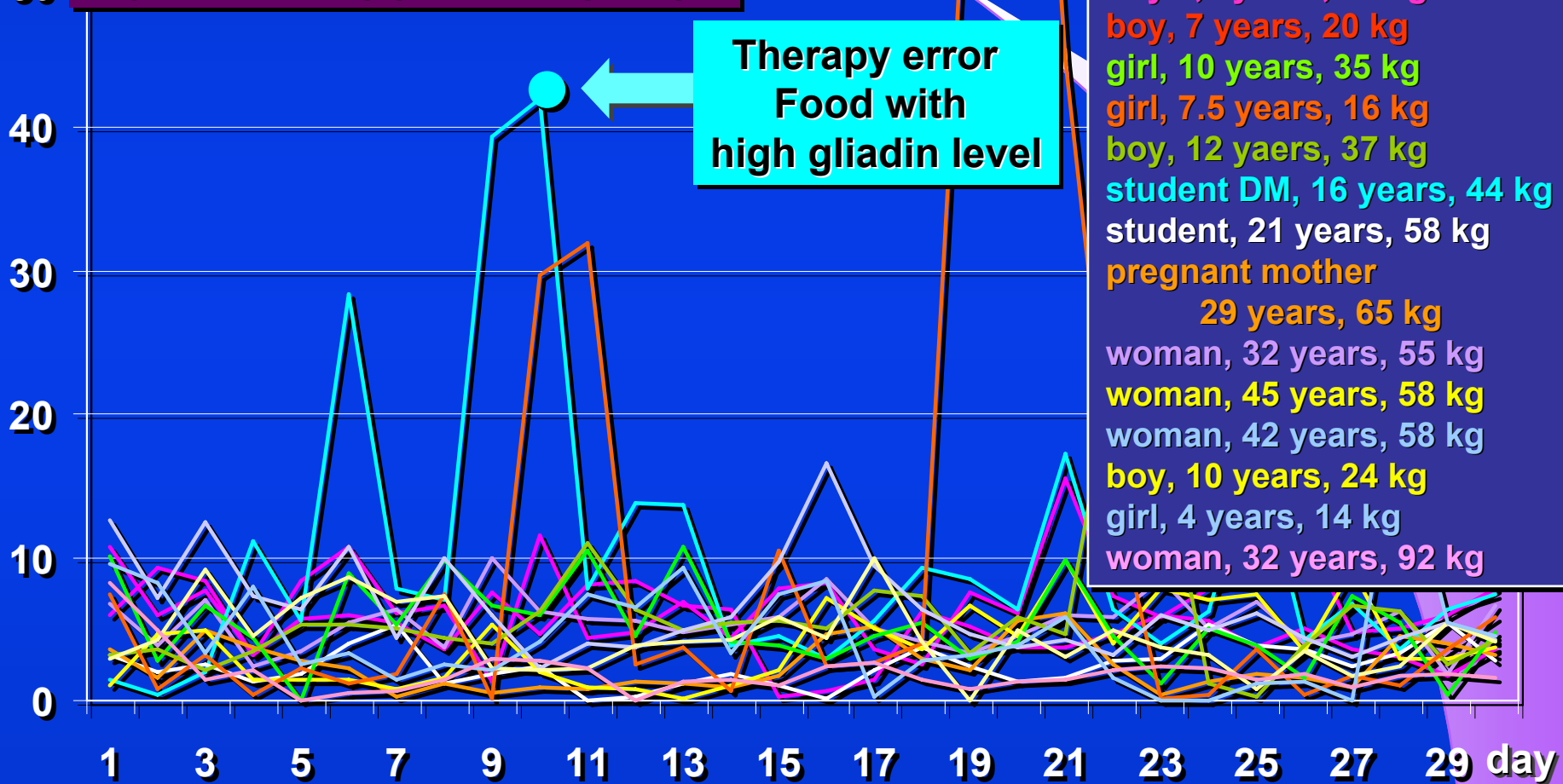
DECREASING TEST SENSITIVITY





GLUTEN FREE DIET – DAILY GLIADIN INTAKE

50 day amount - mg gliadin/80kg weight



Monitoring of Daily Gliadin Intake in Patients on Gluten-free Diets.
Gabrovská D., Kocna P., et al.: Prague Medical Report 2011, 112 (1): 5 – 17



DAILY GLIADIN INTAKE

The so-called "safe" levels of gluten

Daily intake < 10 mg

it has no effect on the mucosa of the small intestine

Daily intake 100 mg

already causes the observed changes in histology

Daily intake 500 mg

leads to fundamental histological changes

Safe limit

could be set between 10 and 100 mg

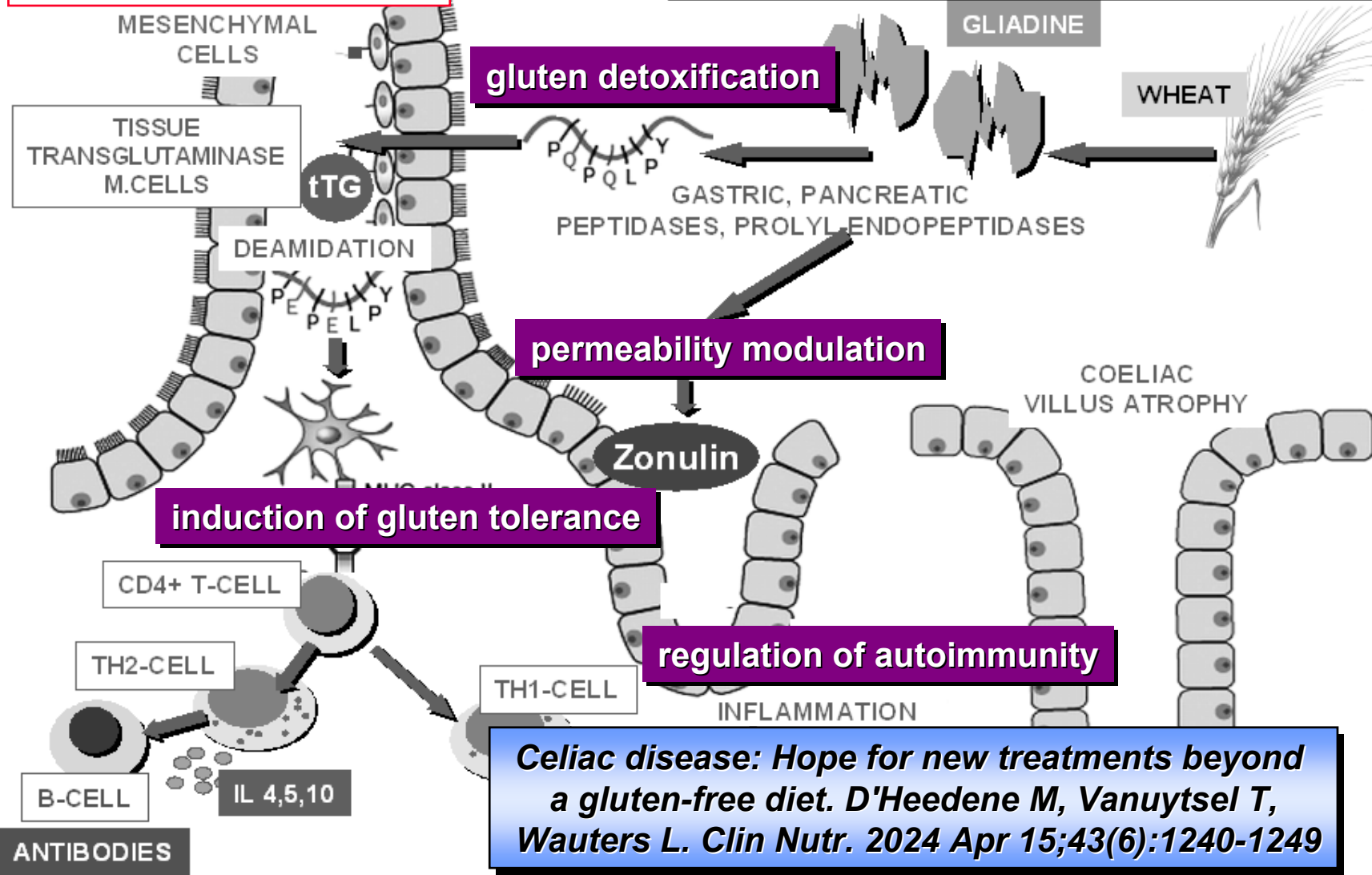
***European Society for the Study of Coeliac Disease (ESsCD) guideline
for coeliac disease and other gluten-related disorders.***

Al-Toma A, Volta U, Auricchio R, et al.

United European Gastroenterol J. 2019; 7(5):583-613

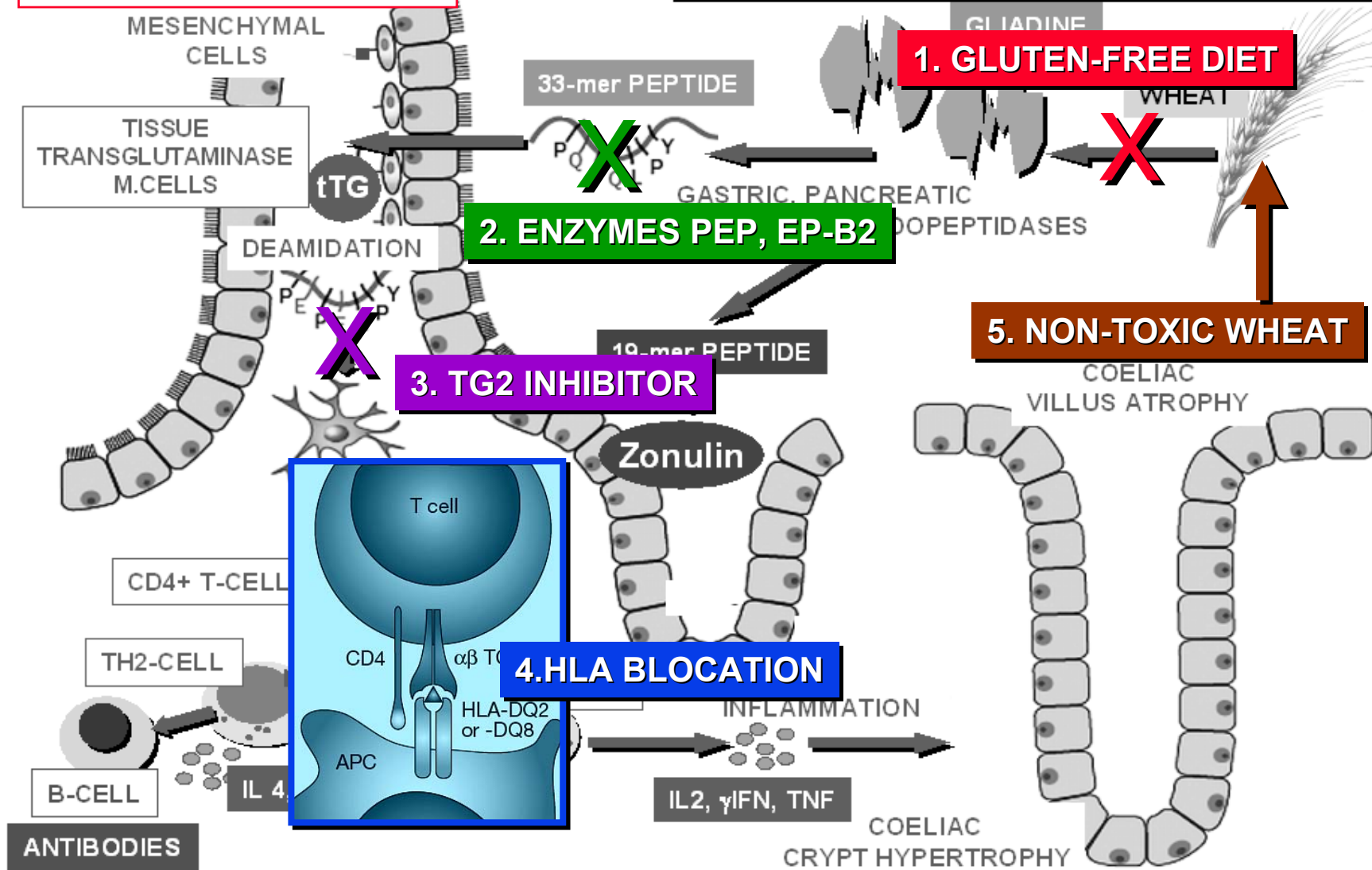
COELIAC THERAPY

Acc: Mowat AT, Lancet 2003, 361: 1290

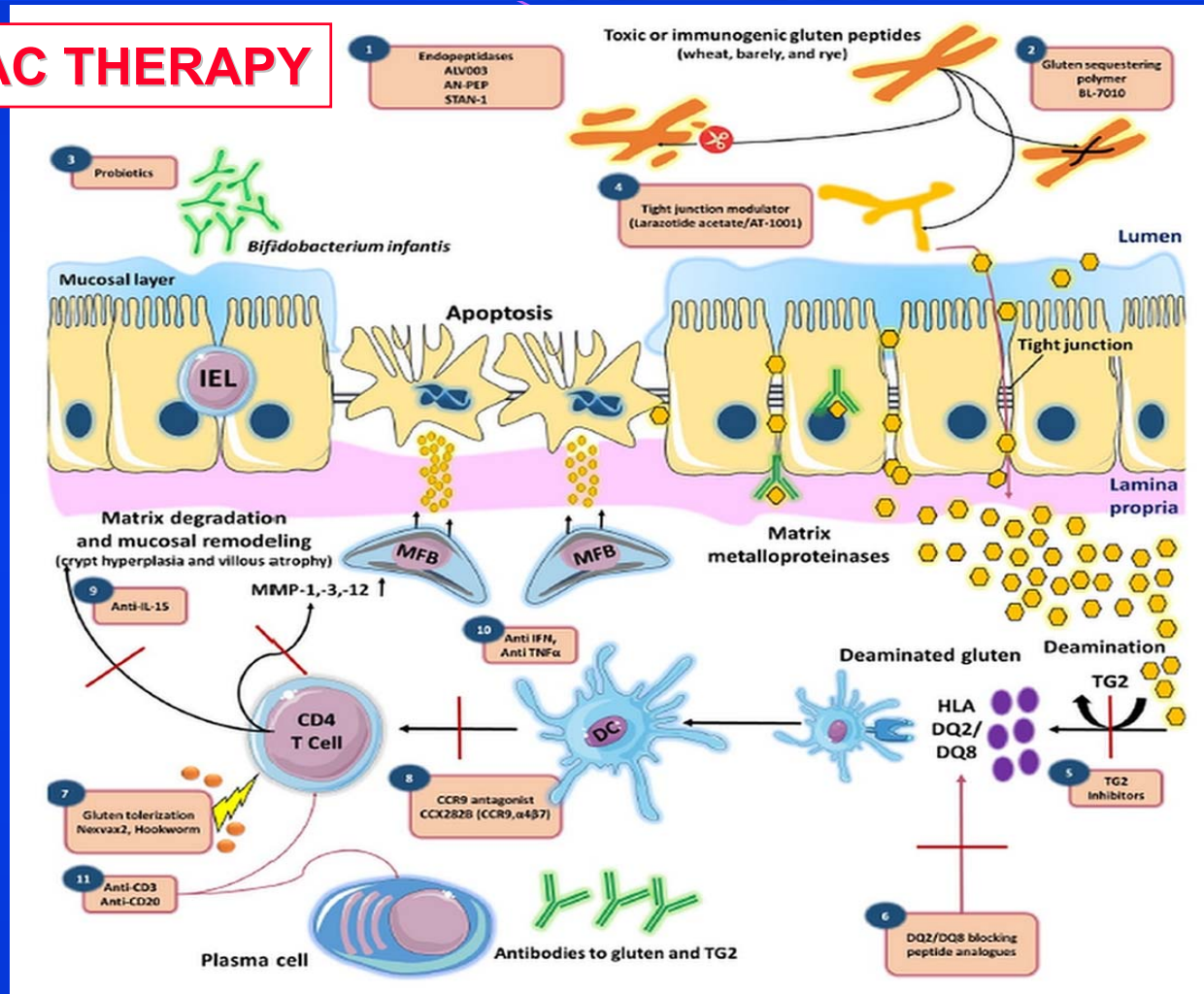


COELIAC THERAPY

Acc: Mowat AT, Lancet 2003, 361: 1290

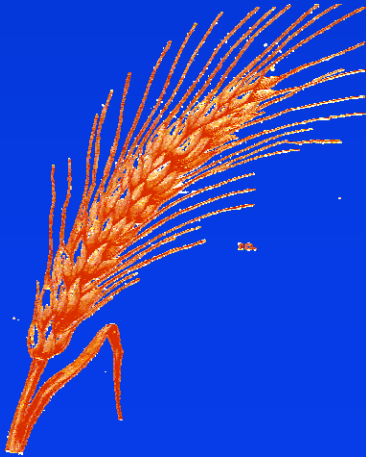


COELIAC THERAPY



Abbasi A, Bazzaz S, Ibrahim SA. et al.: A Critical Review on the Gluten-Induced Enteropathy/Celiac Disease: Gluten-Targeted Dietary and Non-Dietary Therapeutic Approaches. *Food Reviews International*, 2024; 40/3: 883-923

COELIAC THERAPY: ENZYMIC HYDROLYSIS



PROLYL-ENDOPETIDASE
LACTOBACILLUS, ASPERGILUS
PROTEASES

PRE-GASTRONOMIC
DETOXIFICATION

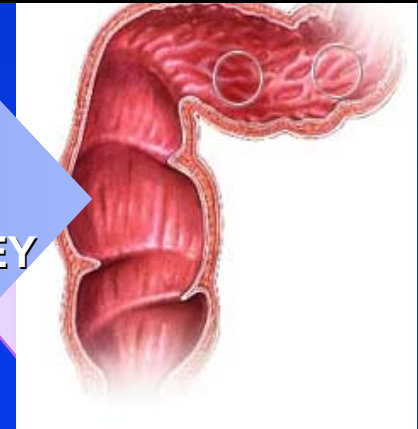
BACTERIAL
PROLYL-ENDOPEPTIDASE,
CYS-PEPTIDASE FROM BARLEY



MODIFICATION OF FOOD

INTRA-DIGESTIVE
DETOXIFICATION

PERORAL APPLICATION OF
ENZYMES - HYDROLASES



Glutenase ALV003 Attenuates Gluten-Induced Mucosal Injury in Patients With Celiac Disease. Lähdeaho ML, Kaukinen K, Laurila K, Vuotikka P, Koivurova OP, Kärjä-Lahdensuu T, Marcantonio A, Adelman DC, Mäki M. Gastroenterology. 2014 Jun;146(7):1649-1658



L G Q Q Q P F P P Q Q P Y P Q P Q P F

FM-POP (Flavobacterium meningosepticum)
Prolyl oligopeptidase

AN-PEP (Aspergillus niger)
Prolyl endopeptidase

Highly efficient gluten degradation with a newly identified prolyl endoprotease: implications for celiac disease. Stepniak D, Spaenij-Dekking L, Mitea C, Moester M, de Ru A, Baak-Pablo R, van Veelen P, Edens L, Koning F. Am J Physiol Gastrointest Liver Physiol. 2006 Oct; 291(4): G621 - 629

L Q L Q P F P Q P Q L P Y P Q P Q L P Y P Q P Q L P Y P Q P Q P F

EP-B2 (Barley)
Cysteine endoprotease B-isoform 2

SC-PEP (Sphingomonas capsulata)
Prolyl endopeptidase

Combination enzyme therapy for gastric digestion of dietary gluten in patients with celiac sprue. Gass J, Bethune MT, Siegel M, Spencer A, Khosla C. Gastroenterology. 2007 Aug;133(2): 472 - 480

GLIADIN - 33mer

L **Q** L Q P F P Q P **Q** L **P** Y **P** Q P **Q** L **P** Y **P** Q P **Q** L **P** Y **P** Q P Q P F

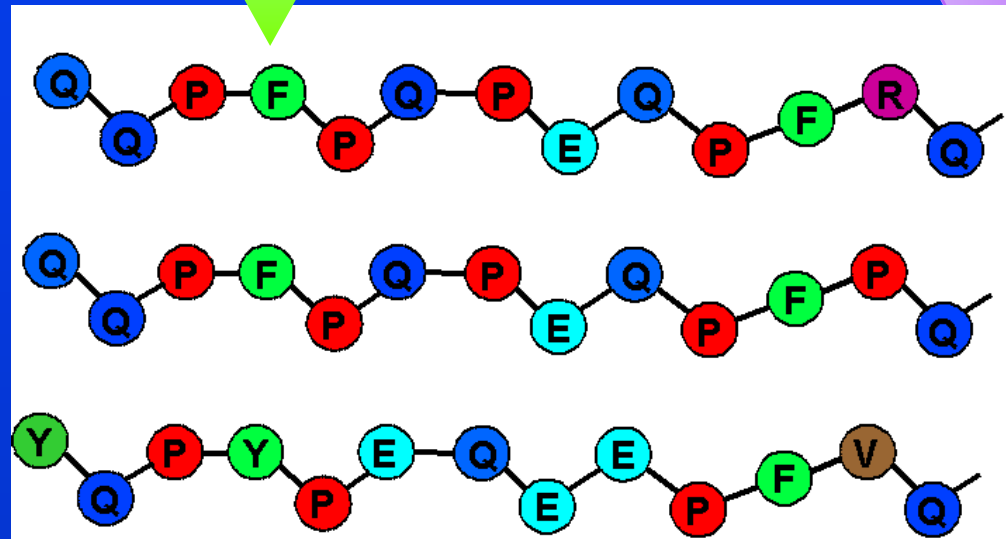
↑ ↑ ↑ ↑ ↑ ↑ ↑ ↑

???? AFFINITY **EP-B2** and **SC-PEP** to other prolamines ????

HORDEIN - $\alpha 9$

SECALIN - $\alpha 9$

AVENIN - $\alpha 9$





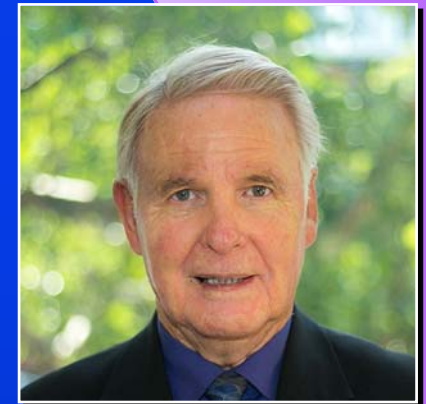
GLIADIN DETOXIFICATION BY CARICAIN

GLUTEGUARD - CARICA PAPAYA EXTRACT,
CONTAINS HYDROLYTIC ENZYMES CARICAIN AND OTHER
PROLYL-ENDOPEPTIDASES,
NO CELIAC THERAPY, IT'S ONLY FOOD SUPPLEMENTS
PRICE IN AUSTRALIA - 60 TABLETS, 44 AUD



Q Q P Y P Q P Q

CARICAIN
(Carica Papaya.)



Enzyme Therapy for Patients with Celiac Disease - An Update
Cornell HJ, Stelmasiak T, Lerner A.
International Journal of Celiac Disease, 2021; 9/1: 28-34

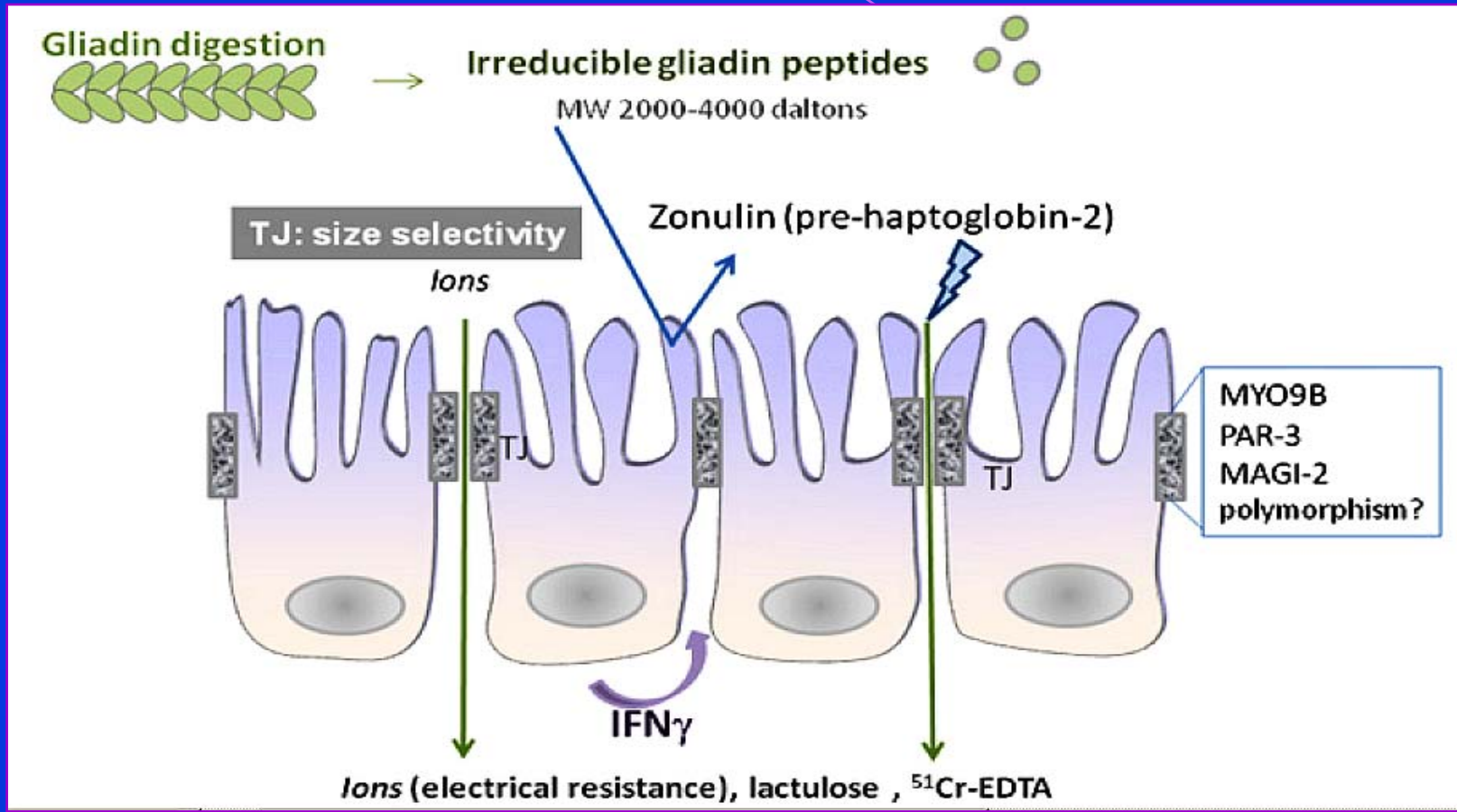


GLUTEN DEGRADING, CLEAVING, FOOD SUPPLEMENTS



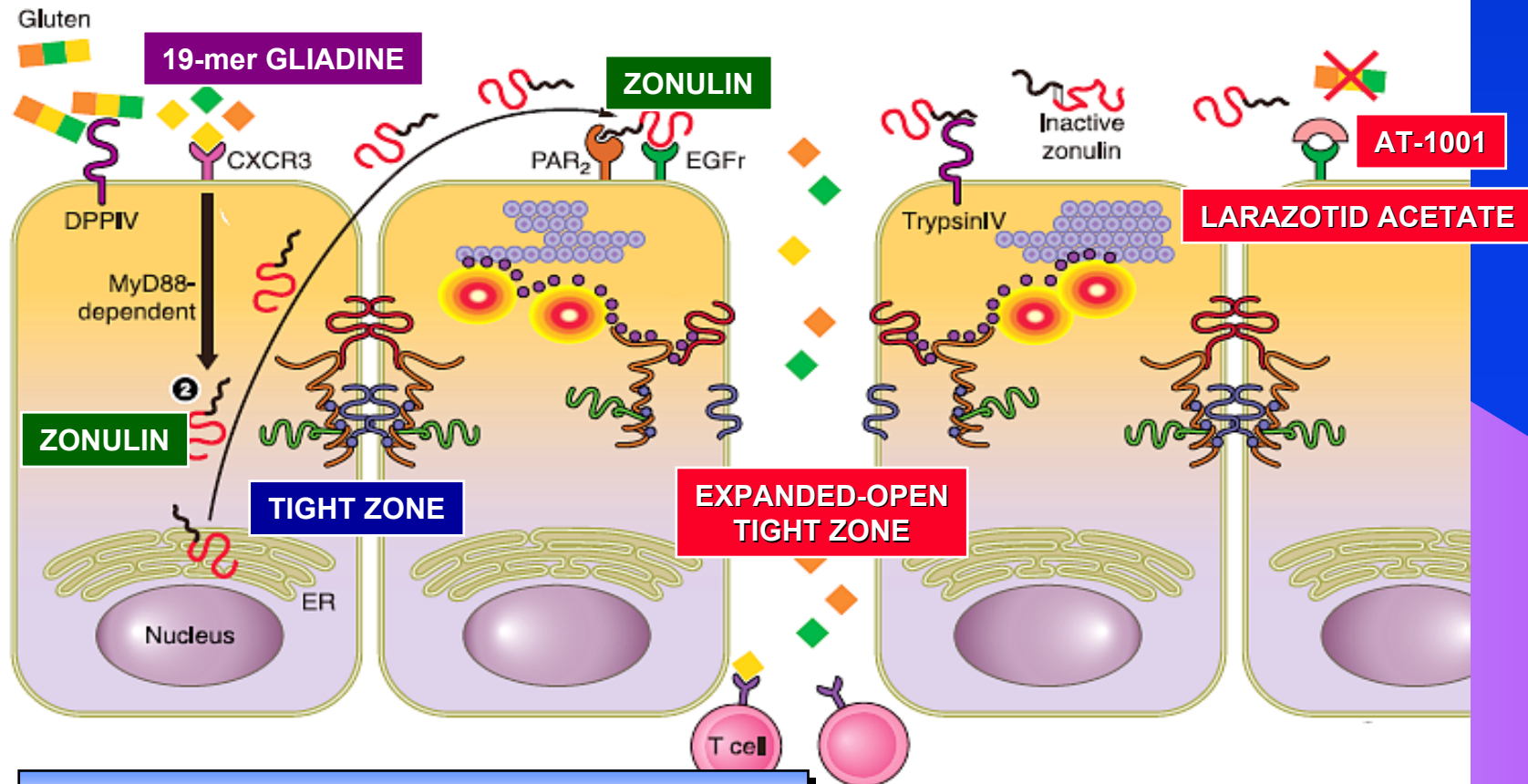
FOOD SUPPLEMENTS CONTAINING GLUTEN DEGRADING
ENZYMES, DECLARED BY THE MANUFACTURER AS INTENDED
FOR PERSONS WITH GLUTEN INTOLERANCE

SMALL BOWEL PERMEABILITY - ZONULIN



Intestinal permeability in coeliac disease: insight into mechanisms and relevance to pathogenesis. Heyman M, Abed J, Lebreton C, Cerf-Bensussan N. Gut. 2012 Sep;61(9):1355-1364

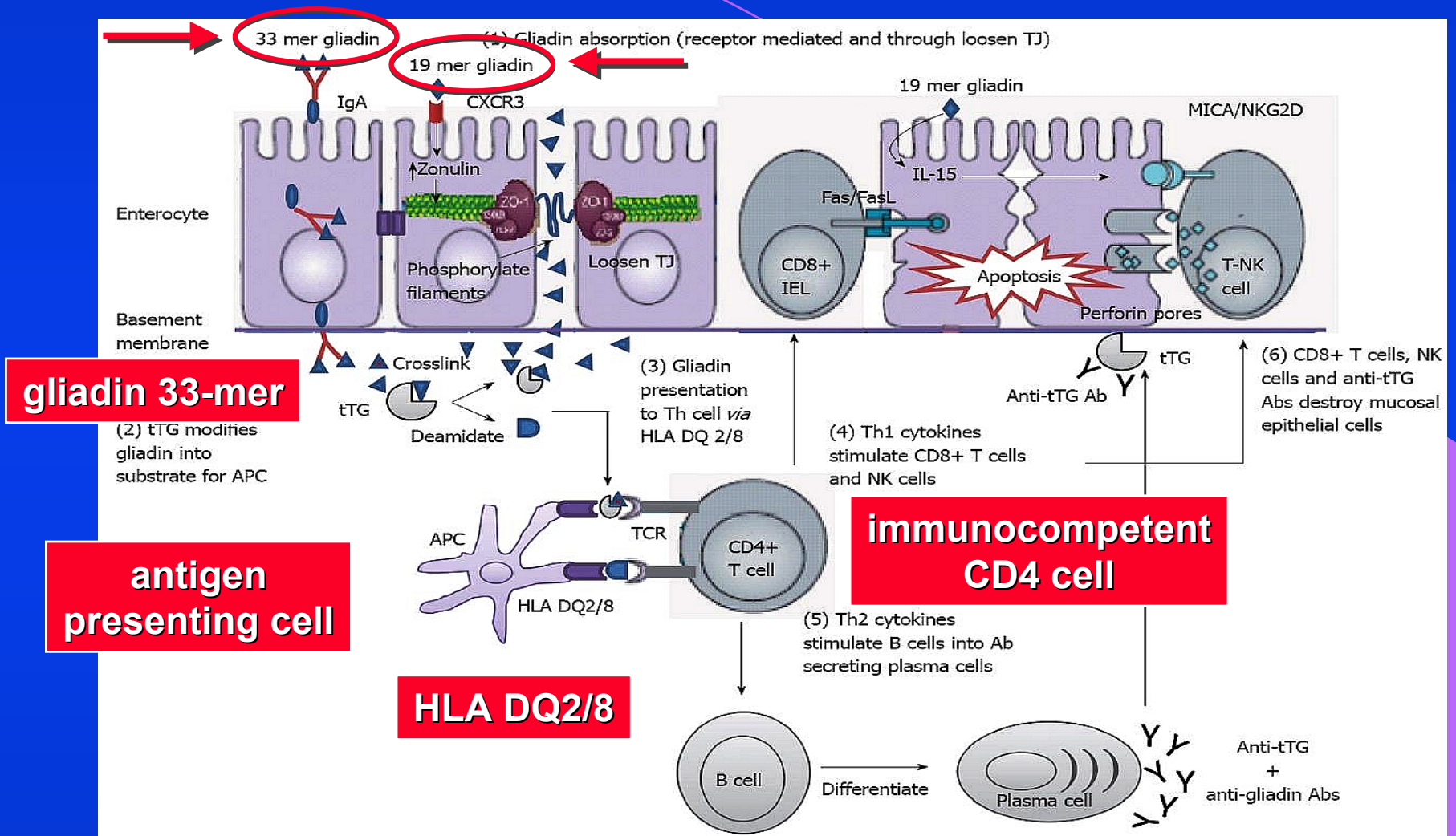
COELIAC THERAPY - ZONULIN INHIBITION



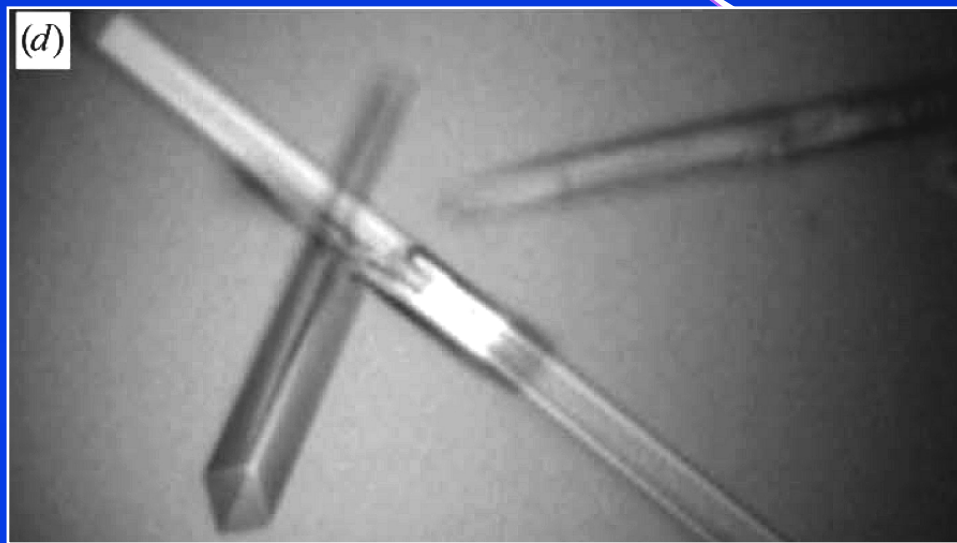
Acc: Fasano A. *Physiol Rev* 2011, 91:151

Larazotide acetate regulates epithelial tight junctions in vitro and in vivo

Gopalakrishnana S, Duraia M, Kitchensa K, Tamiza AP, Somervillea R, Ginskia M, Patersona BM, Murray JA, Verduc EF, Alkana SS, Pandeya NB. *Peptides* 2012: 35, 86



PERSPECTIVE THERAPY OF COELIAC DISEASE

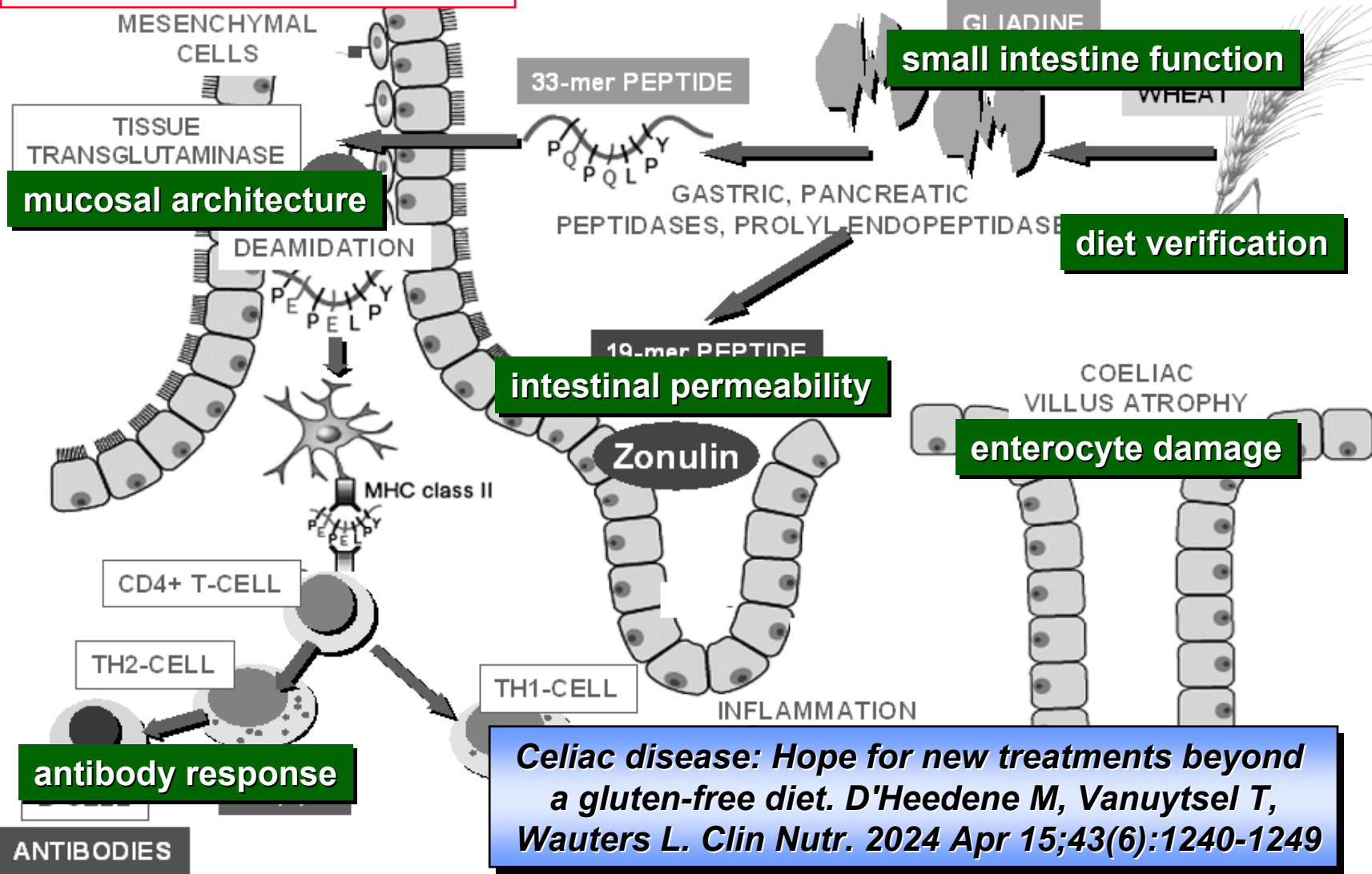


HLA-DQ8 CRYSTAL
WITH DEAMIDATED PEPTIDE α_1 Gli - EGSFQPSQE

The production and crystallization of the human leukocyte antigen class II molecules HLA-DQ2 and HLA-DQ8 complexed with deamidated gliadin peptides implicated in coeliac disease
Kate N. Henderson et al. - Acta Crystallographica, (2007) F63, 1021–1025

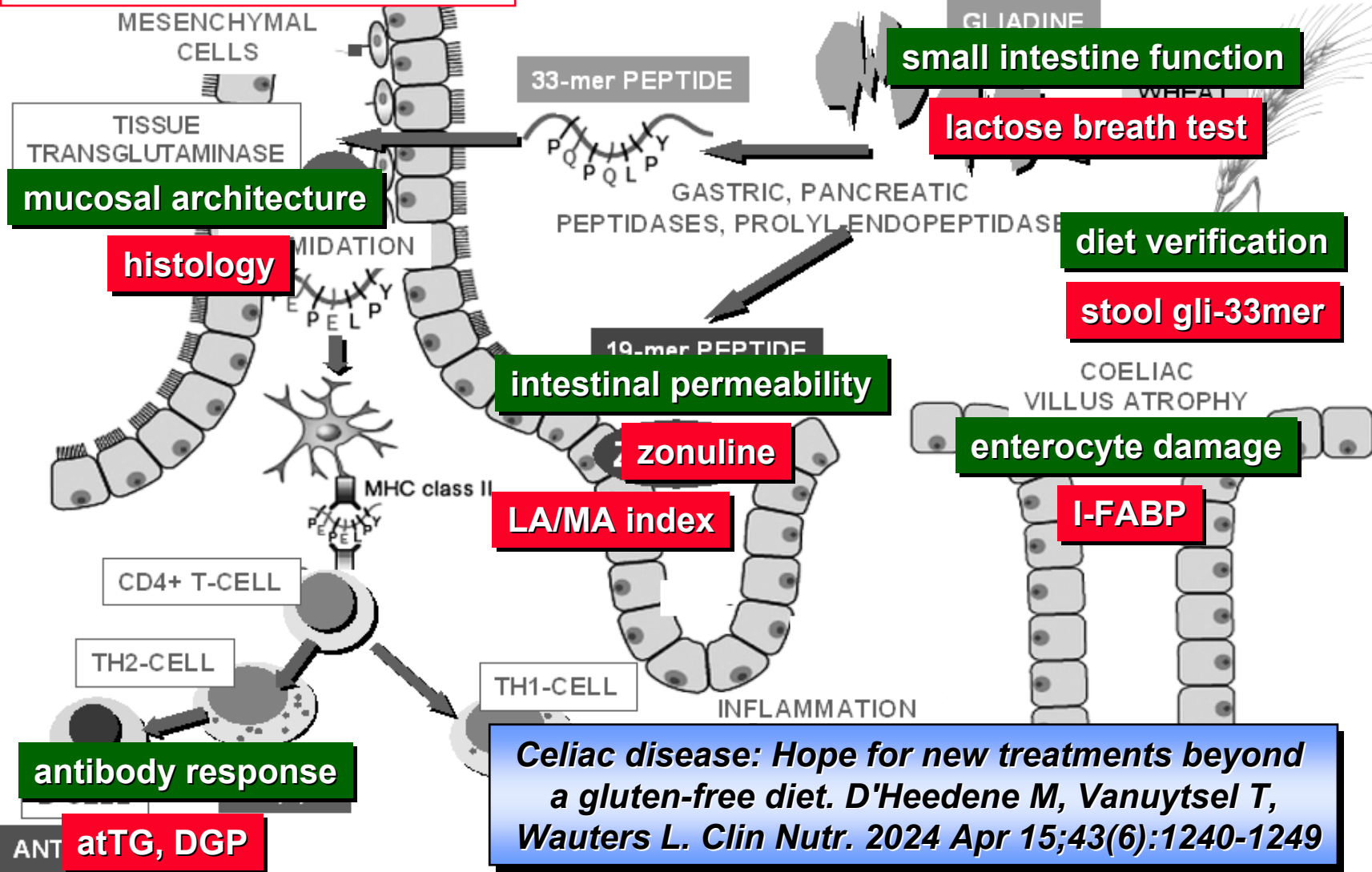
COELIAC MONITORING

Acc: Mowat AT, Lancet 2003, 361: 1290



COELIAC MONITORING

Acc: Mowat AT, Lancet 2003, 361: 1290



SMALL INTESTINE FUNCTIONAL TESTS



Hydrogen/metan analyzátor
Lactotest 202 – M.E.C.

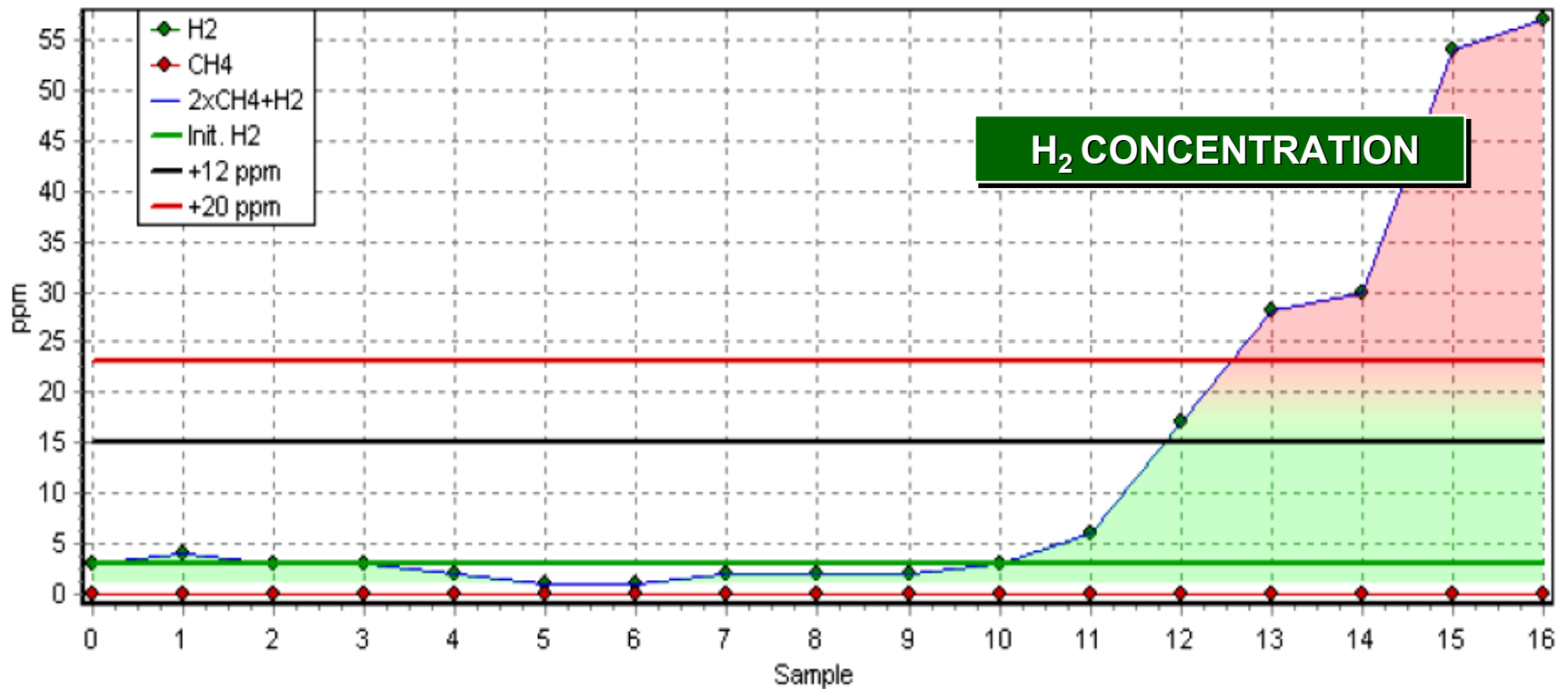
LACTOSE BREATH TEST
LOAD 20g LACTOSE
HYDROGEN / METHANE MEASUREMENT 5
HOURS, CUT-OFF CRITERION 20 ppm
METHANOGENIC BACTERIA
THEY CONVERT HYDROGEN INTO METHANE
THE SUM OF $H_2 + 2 CH_4$ CAN BE EVALUATED

*Regression of lactose malabsorption in coeliac patients
after receiving a gluten-free diet. Ojetti V, Gabrielli M, Migneco A. et al.:
Scand J Gastroenterol. 2008;43(2):174-177*



$H_2/CH_4/CO_2$ - LACTOSE INTOLERANCE TEST

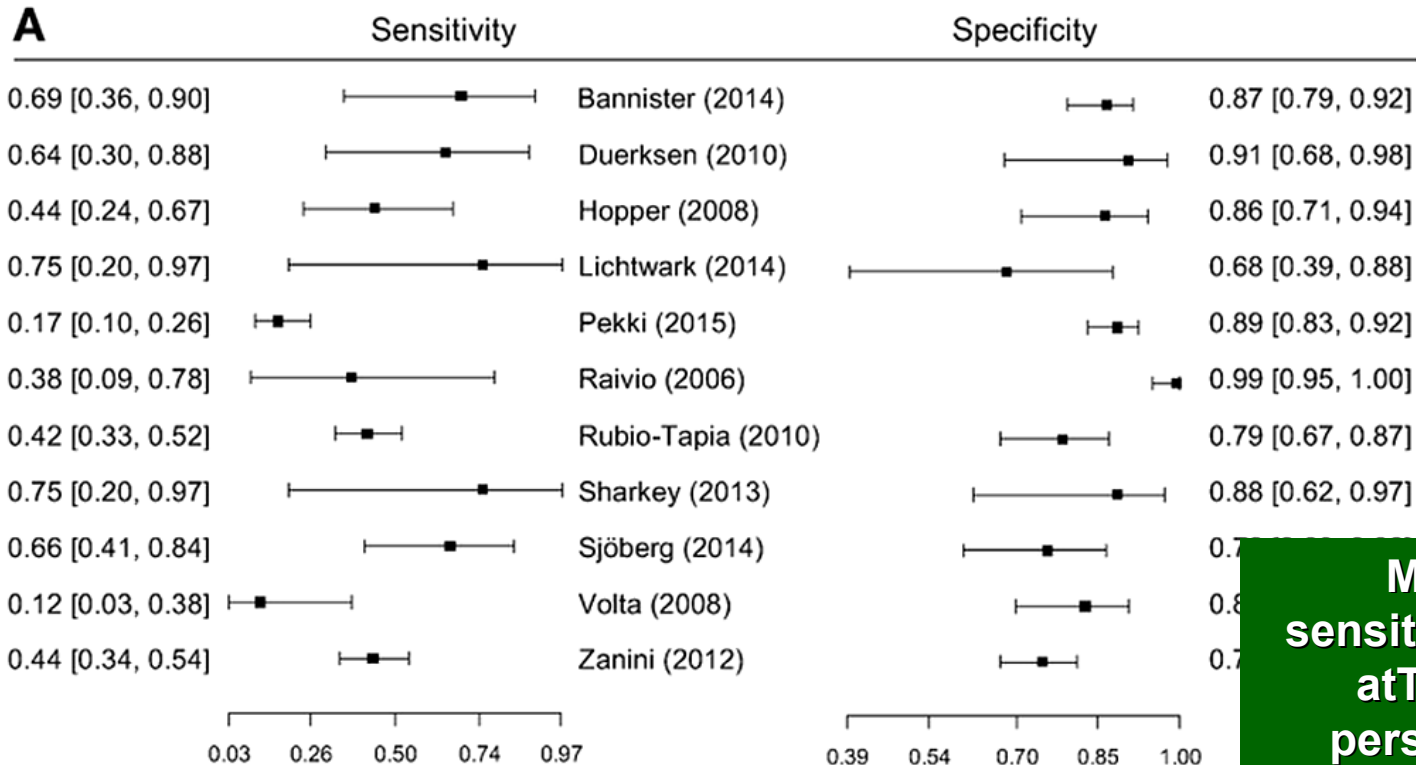
H_2/CH_4 ppm



20 g LACTOSE



atTG ANTIBODIES - TEST / MANUFACTURER VARIABILITY



**Meta analysis
sensitivity - specificity
atTG antibodies
persistent atrophy
celiac disease on GFD**

Tests for Serum Transglutaminase and Endomysial Antibodies Do Not Detect Most Patients With Celiac Disease and Persistent Villous Atrophy on Gluten-free Diets
Silvester JA, Kurada S, Szwajcer A. et al.: Gastroenterology. 2017; 153(3): 689 - 701



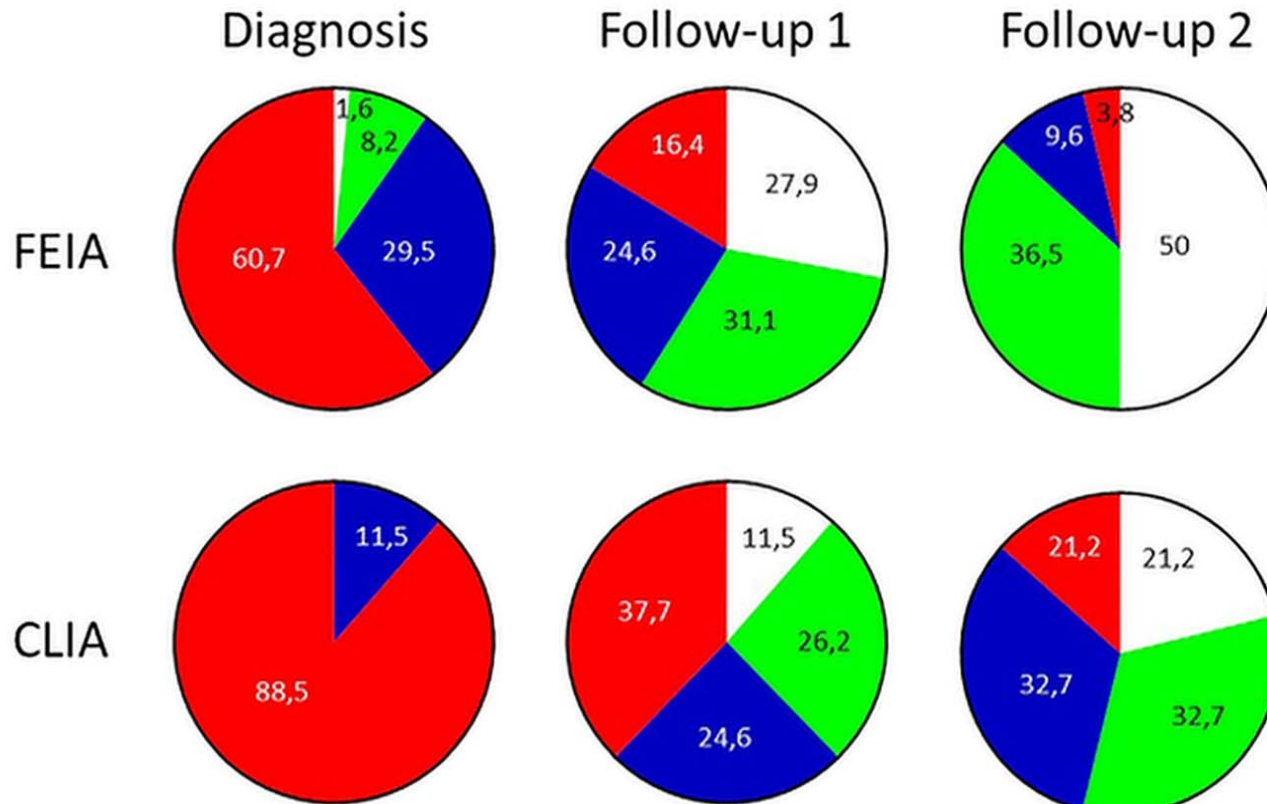
atTG ANTIBODIES - TEST / MANUFACTURER VARIABILITY

cut-off atTG

Naples	Anti-Tissue Transglutaminase IgA (Delta Biologicals)	7 U/mL
Spain	Elia Celikey IgA (Phadia, Thermofisher)	7 U/mL
Messina	Transglutaminasi Umana IgA (IPR - Immuno Pharmacology Research s.r.l)	3 U/mL
Albania	Celiac Ttg IgA (Immco Diagnostic, Hague Netherlands)	25 EU/mL
Slovenia	Eu-Ttg IgA (Eurospital)	16 U/mL
Tunisia	Quanta Lite [®] R H-Ttg Elisa (Inova Diagnostics)	10 U/mL
Turkey	Anti-Tissue Transglutaminase IgA (Orgentec)	10 U/mL
Greece	Quanta Lite [®] H-Ttg Elisa (Inova Diagnostics)	20 U/mL

***Variability of anti-human transglutaminase testing in celiac disease across Mediterranean countries. Smarrazzo A, Magazzù G, Ben-Hariz M.et al.:
World J Gastroenterol. 2017; 23(24): 4437 - 4443***

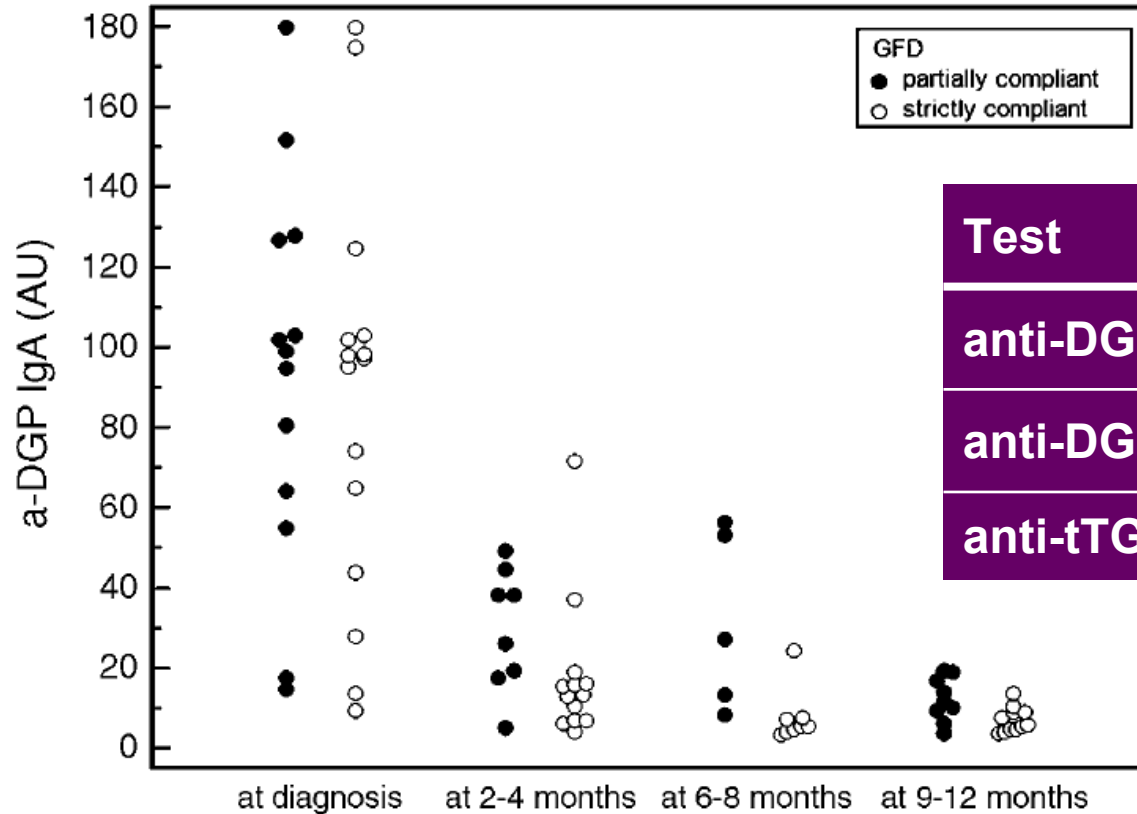
atTG ANTIBODIES - TEST / MANUFACTURER VARIABILITY



IgA atTG results
at diagnosis,
in 3-6 months of GFD
and in 3-12 months
after the first inspection.
Color:
■ < 1 ■ 1-3 ■ 3-10 ■ > 10
multiple of the norm.

Monitoring patients with celiac disease on gluten free diet: different outcomes comparing three tissue transglutaminase IgA assays. Mulder AHL, Castelijns DAR, van der Pol P, et al. Clin Chem Lab Med. 2023 Nov 10, ePub.

DIET MONITORING - anti-DGP IgA ANTIBODIES



Test	Sensitivity %
anti-DGP IgA	60 (40.7-76.6)
anti-DGP IgA+IgG	76 (57.6-88.5)
anti-tTG IgA	24 (11.5-43.4)

Use of deamidated gliadin peptide antibodies to monitor diet compliance in childhood celiac disease. Monzani A, Rapa A, Fonio P. et al. J Pediatr Gastroenterol Nutr. 2011 Jul;53(1):55-60



GIP - GLIADIN 33mer IN STOOL

67 publications in PubMed and Web of Science, keywords "gluten immunogenic peptides" in combination with "feces-urine-coeliac-gluten free diet-adherence" published in English/Spanish between 2012 and January 2021.

Detection of excreted GIP in stool or urine is an accurate approach to determine voluntary or involuntary consumption of gluten. Isolated GIP measurements may not identify intermittent dietary adherence, and the use of multiple samples contributes to higher sensitivity and specificity of GIP detection.

ELISA is suitable for laboratory quantification of GIP, while LFIA strips should be used for patient self-monitoring.

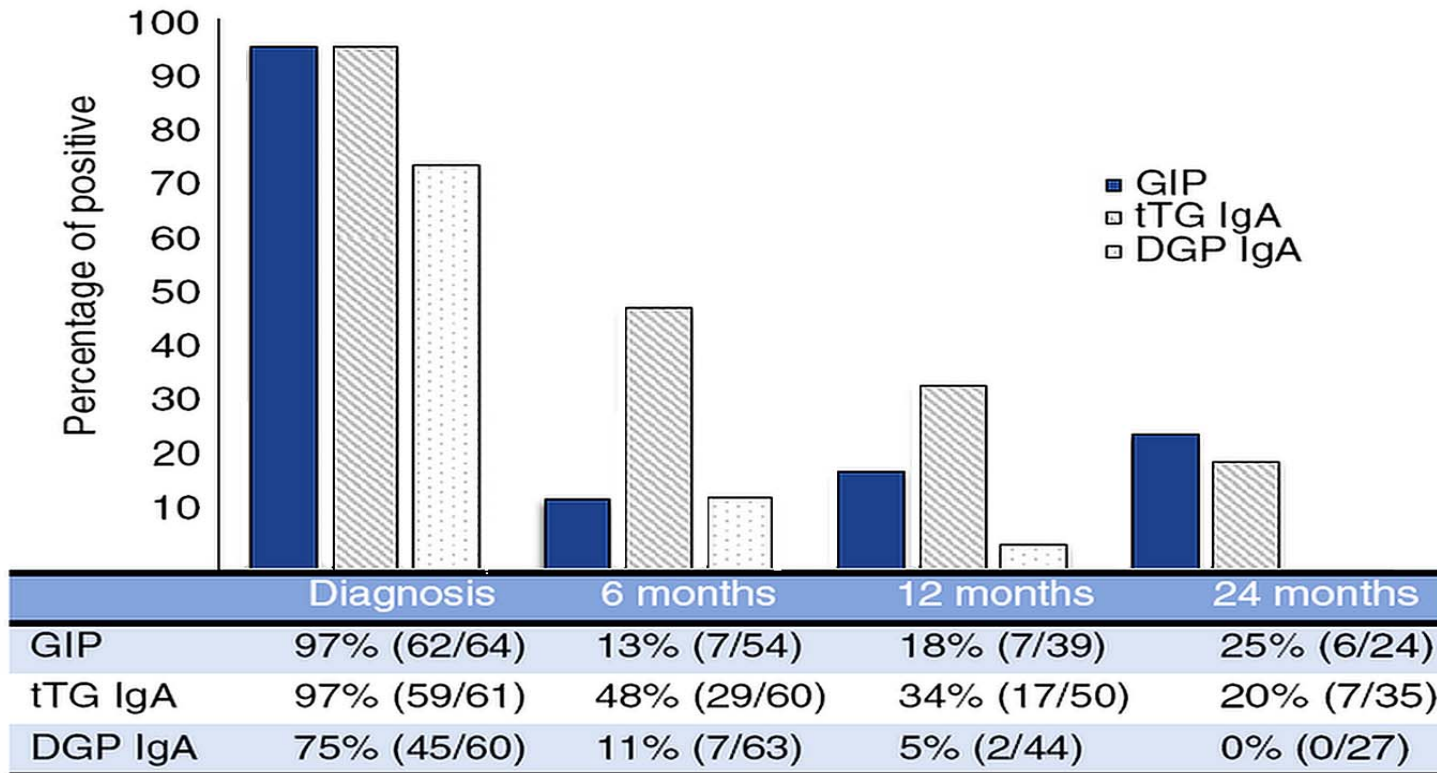
Detection of GIP can help determine whether symptomatic patients have unresponsive or refractory celiac disease.

Determination of gluten immunogenic peptides for the management of the treatment adherence of celiac disease: A systematic review.

Coto L, Mendia I, Sousa C, Bai JC, Cebolla A.

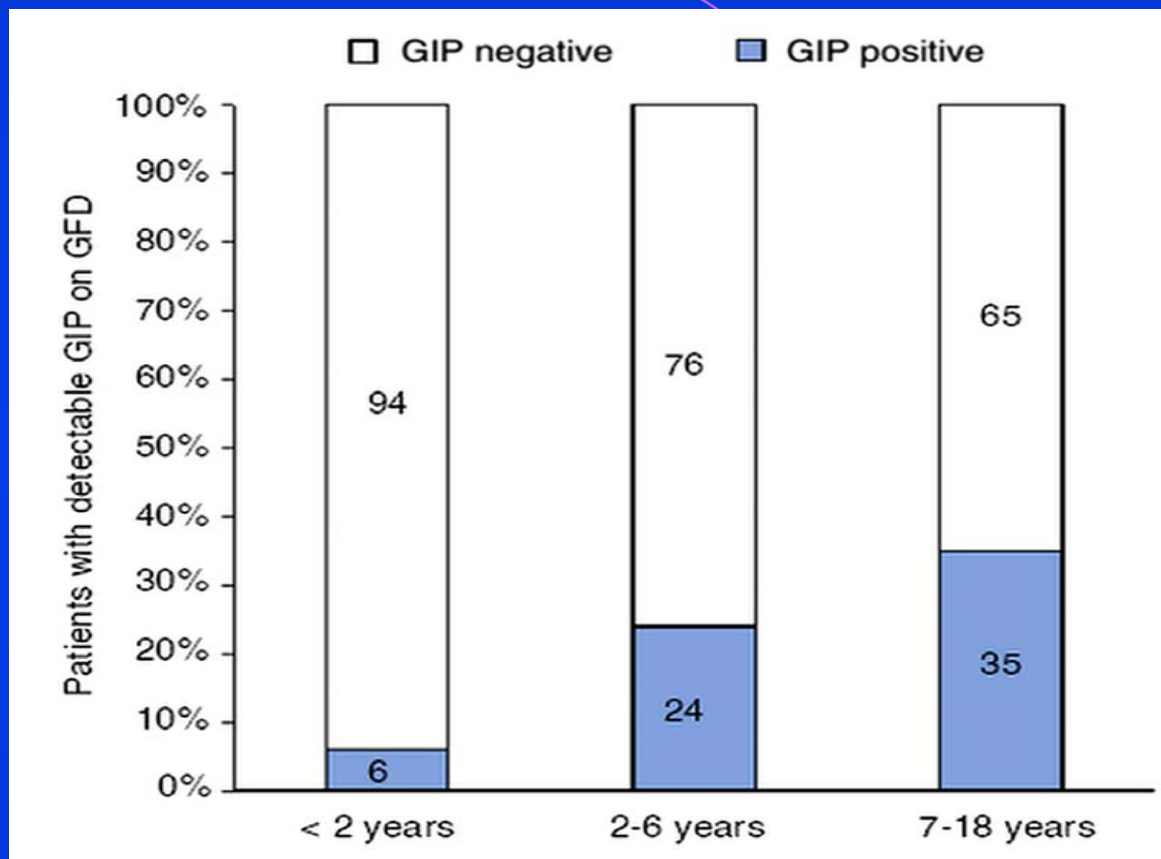
World J Gastroenterol. 2021 Oct 7;27(37):6306-6321

GIP - GLIADIN 33mer IN STOOL



Prospective longitudinal study: use of faecal gluten immunogenic peptides to monitor children diagnosed with coeliac disease during transition to a gluten-free diet. Comino I, Segura V, Ortigosa L. et al. Aliment Pharmacol Ther. 2019 Jun;49(12):1484-1492

GIP - GLIADIN 33mer IN STOOL



Prospective longitudinal study: use of faecal gluten immunogenic peptides to monitor children diagnosed with coeliac disease during transition to a gluten-free diet. Comino I, Segura V, Ortigosa L. et al. Aliment Pharmacol Ther. 2019 Jun;49(12):1484-1492



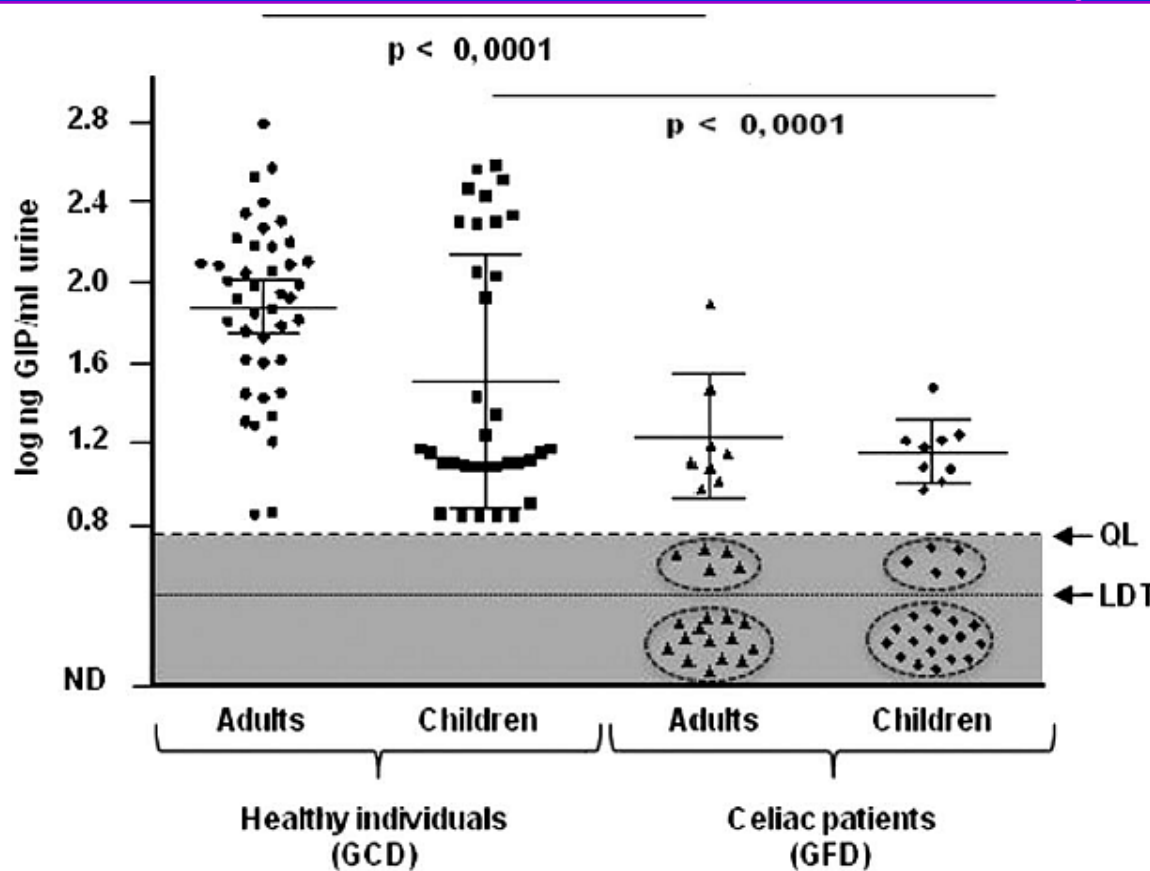
GIP - GLIADIN 33mer IN STOOL

Prospective study - 29 newly diagnosed children with celiac disease - 18 (62%) girls, age range 2-15 years. The decrease in stool GIP to normal (89.7%) at the 4-month follow-up examination was significantly greater than that of anti-tTG IgA (34.5%) ($p < 0.001$). All children and their legal representatives declared strict adherence to a gluten-free diet.

Evaluation of GIP in the stool can be a more sensitive indicator of adherence to a gluten-free diet than anti-tTG IgA, especially in the initial months, when, due to the significantly slower decrease to normal, we cannot expect a negative result for anti-tTG IgA even with strict adherence to a gluten-free diet. Examination of GIP in the stool is a more sensitive marker of compliance with the diet than information from the patients themselves, so this examination could be used to select a subpopulation of children and their families who need more help with proper adherence to a gluten-free diet.

Stanovení lepku ve stolici jako metoda k ověření compliance s bezlepkovou dietou u dětí s nově diagnostikovanou celiakií. Vyhnánek R., Khaznadar Z., Vyhnánek R., Paulík M. Gastroent Hepatol 2021; 75(6): 519–523

GIP - GLIADIN 33mer IN URINE



Detection of Gli-33mer
in urine by
immunochematographic
test,
Evaluation - GlutenTox
Reader - LFT analyzer
Detection limit: 25 mg of
gluten in food
The quantifiable amount of
GIP is significantly
correlated
with CS severity according to
the Marsh scale.

Detection of gluten immunogenic peptides in the urine of patients with coeliac disease reveals transgressions in the gluten-free diet and incomplete mucosal healing. Moreno ML, Cebolla Á, Munoz-Suano A et al. Gut. 2017; 66(2): 250-257



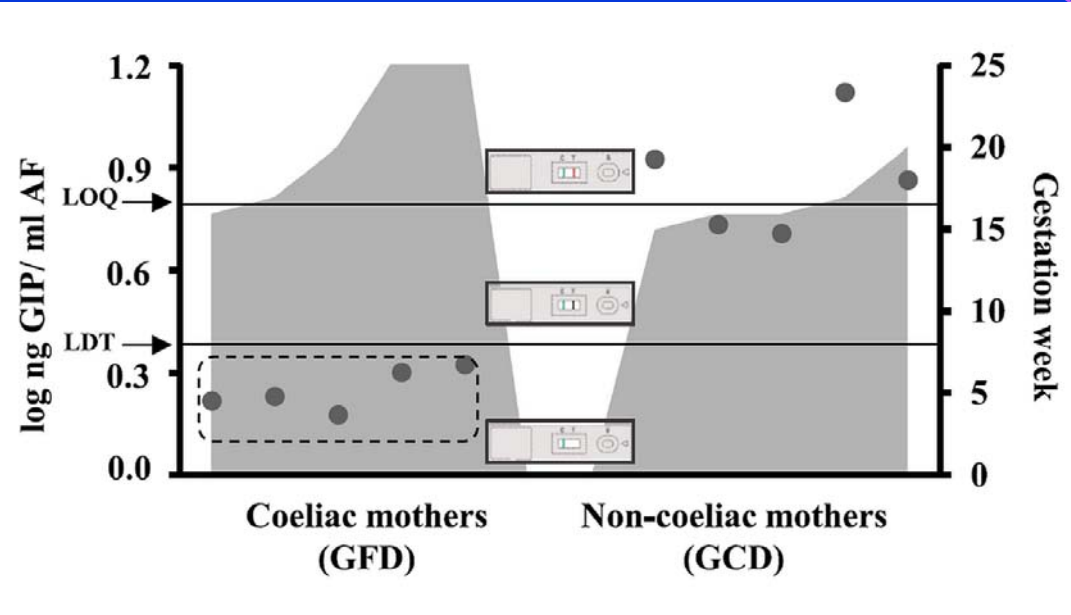
GIP - GLIADIN 33mer IN URINE, ADULT COELIACS

280 patients who reported complete adherence to a gluten-free diet, average age 42.9 years, diagnosis established in adulthood - average age at diagnosis 31.7 years, evaluated from April 2019 to February 2020, determined GIP in urine (uGIP), antibodies to tissue transglutaminase (tTGA), duodenal histology and capsule endoscopy (CE)

**The positive value of uGIP+ was in 32 patients (11.4%)
uGIP positivity was unrelated to atTG titer - 4.4% atTG+ vs. 10.9% atTG-
Histology - atrophy: 66.7% uGIP+ vs. 32.7% of uGIP- patients ($p = 0.01$).
The presence of atrophy did not correlate with atTG.
uGIP results were significantly correlated with duodenal biopsy, which was previously considered the gold standard for assessing CS activity.**

Evaluation of a Single Determination of Gluten Immunogenic Peptides in Urine from Unaware Celiac Patients to Monitor Gluten-Free Diet Adherence. Lombardo V, Scricciolo A, Costantino A et al. Nutrients. 2023;15(5):1259

GIP - GLIADIN 33mer IN AMNIOTIC FLUID



The authors developed a specific immunoassay for the detection of GIP in amniotic fluid and we studied its accumulation, excretion dynamics and fetal exposure in a cohort of 125 pregnant women with different gluten-free diets and gestational ages.

The study demonstrates for the first time fetal exposure to gluten immunogenic peptides and demonstrates a positive correlation with maternal gluten intake. Knowledge of early exposure to GIP in utero **may significantly change current strategies for timing and introducing** safe amounts of gluten in children with CD.

Foetal gluten immunogenic peptides during pregnancy: a new determinant on the coeliac exposome. Moreno ML, González-Rovira M, Martínez-Pancorbo C. et al. BMC Med. 2024 Jul 18;22(1):295



<http://www1.lf1.cuni.cz/~kocna/glab/glency1.htm>

<http://gelab.zde.cz>

Skupina metodik funkce tenkého střeva, malabsorpce, screening celiakie, střevní propustnost, bakteriální přerůstání

Anti-endomysium IgA
Anti-gliadin IgA, IgG
Anti-tTG IgA, IgG
Anti-gliadin, tTG ve stolici
A-vitamin zátěžový test
β-karoten
β-karoten zátěžový test
Celiakie - screening
Dechový test s laktózou
Dechový test s xylózou
Laktózový toleranční test
Laktulózo/mannitolový test
Xylózový toleranční test

Intro

Abecední přehled metodik

Minimální encyklopedie laboratorních metod v gastroenterologii

GastroLab

ASOCIACE ZDRAVÍ NA INTERNETU

Protilátky ke tkáňové transglutamináze (atTG) - IgA a IgG

Tkáňová transglutamináza má přímý vztah k patogenezi onemocnění a byla popsána jako vlastní, chemický substrát endomysia. Tkáňová transglutamináza - (isoenzym transglutaminasa II, TG2 - EC 2.3.2.13, je transferázou, systémový název je protein-glutamin:amin-g-glutamyltransferasa. Je to Ca²⁺ dependentní enzym, katalyzující deaminaci glutaminu na glutamát, rovněž vede ke vzniku intramolekulární vazby glutaminu na další primární amin, např. lysin a vede k agregaci glutaminových peptidů. Stanovení protilátek ke tkáňové transglutamináze (atTG) má proto rovněž velmi vysokou diagnostickou efektivitu, podobně jako **EmA protilátky** (senzitivita 87-97% a specifita 88-98%). Stanovení atTG je prováděno klasickou metodou ELISA, což je pro rutinní diagnostiku technika dostupnější než imunofluorescenční průkaz EmA.

Protilátky atTG lze na rozdíl od EmA stanovit ve třídě IgA i IgG, což má význam pro nemocné se selektivním deficitem IgA. Metoda byla popsána s použitím morčecího antigenu, který je použit ve většině starších souprav, novější soupravy již používají jako antigen tkáňovou transglutaminázu izolovanou z lidských buněk, z lidských erytrocytů, nebo rekombinantní tTG izolovanou na E.coli. Referenční hodnoty se liší u jednotlivých souprav, většinou je pro IgA protilátky uváděna horní hranice normy 10 - 15 IU/l, některé soupravy definují i tzv. gray-zone v rozsahu 10 - 20 IU/l. Stanovení protilátek atTG s lidským, rekombinantním antigenem vykazuje nižší falešnou pozitivitu než metody s morčecím antigenem. Nejnovější studie porovnávají protilátky třídy IgA a IgG, a POCT metodiky stanovení atTG protilátek. Stanovení protilátek atTG ve třídě IgA je doporučeno jako základní screeningový test pro diagnostiku **celiakie**. Pro screening byla v roce 2011 použita i technologie detekce atTG ve slinách, a nejnovější studie popisují zcela nové technologie detekce protilátek elektrochemickými imunosenzory.

Reference
Volta U. - Gastroenterol Hepatol Bed Bench. 2023, [Medline - link](#) [PubMed](#)
Infantino M. - J Immunol Meth. 2021, [Medline - link](#) [PubMed](#)

NČLP

Medline online
latest publication

Direct link to MZČR
National code



THANK YOU FOR

YOUR ATTENTION