


COELIAC DISEASE
DIAGNOSIS, MONITORING AND THERAPY

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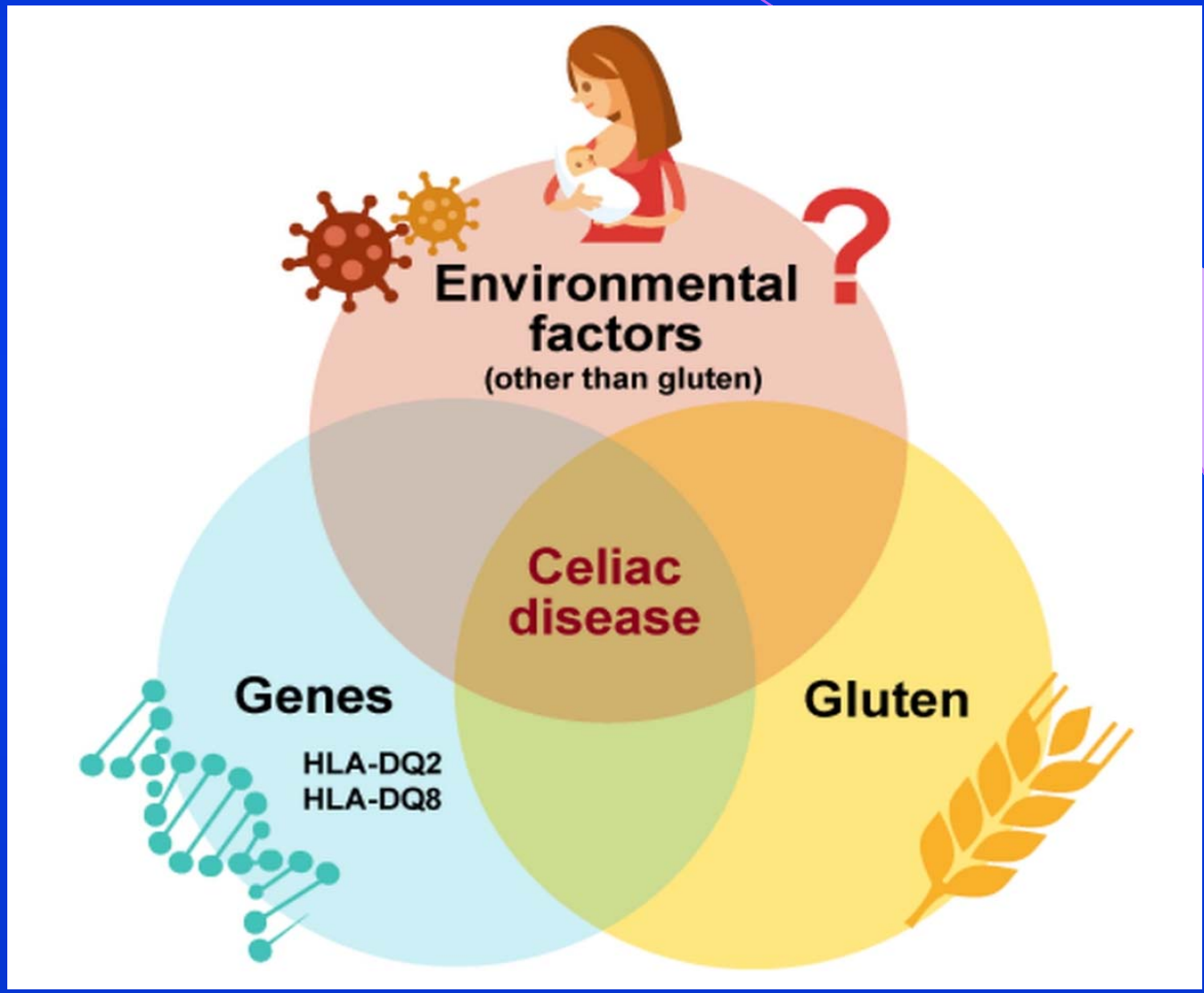
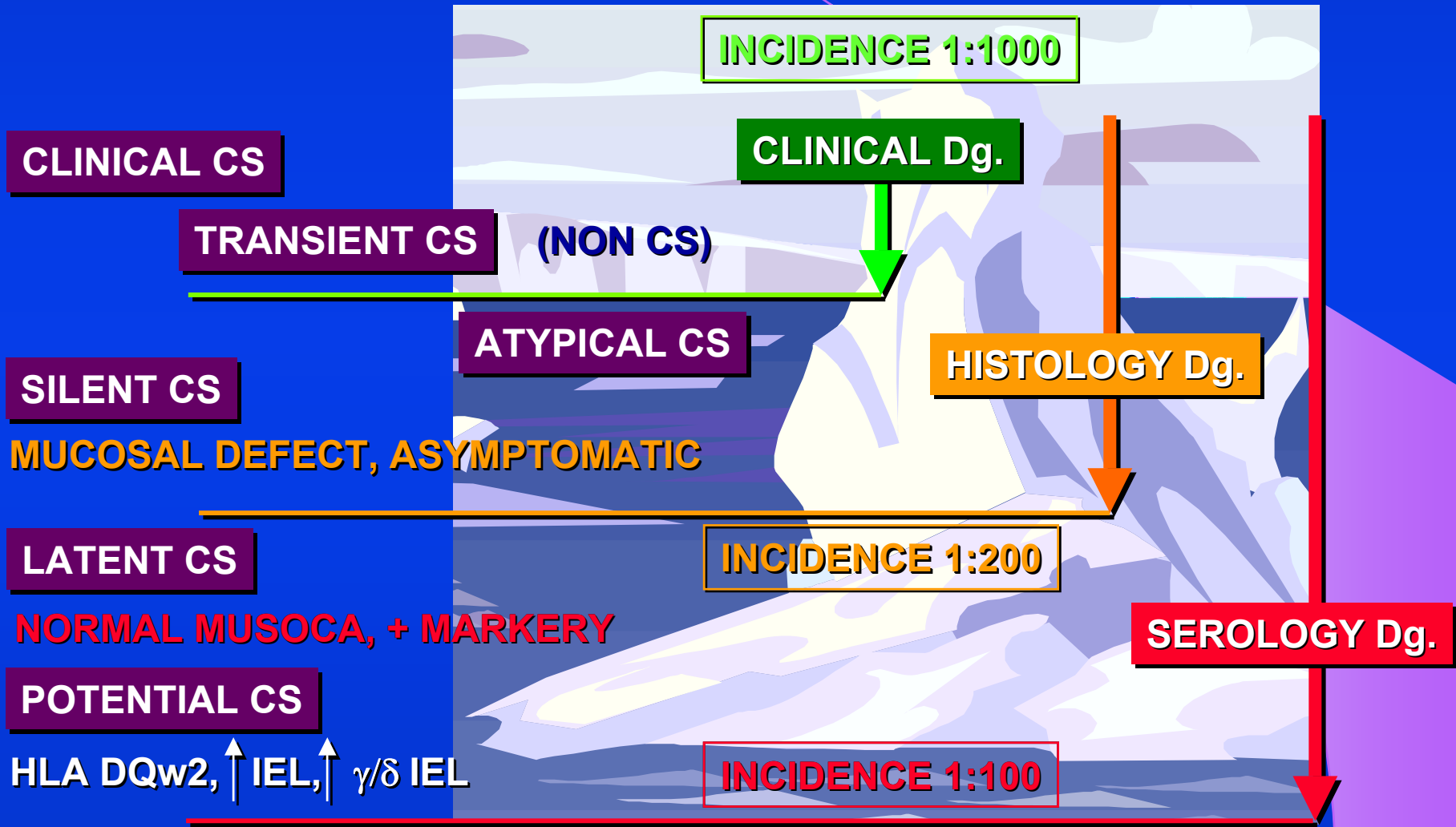
http://gweb.zde.cz

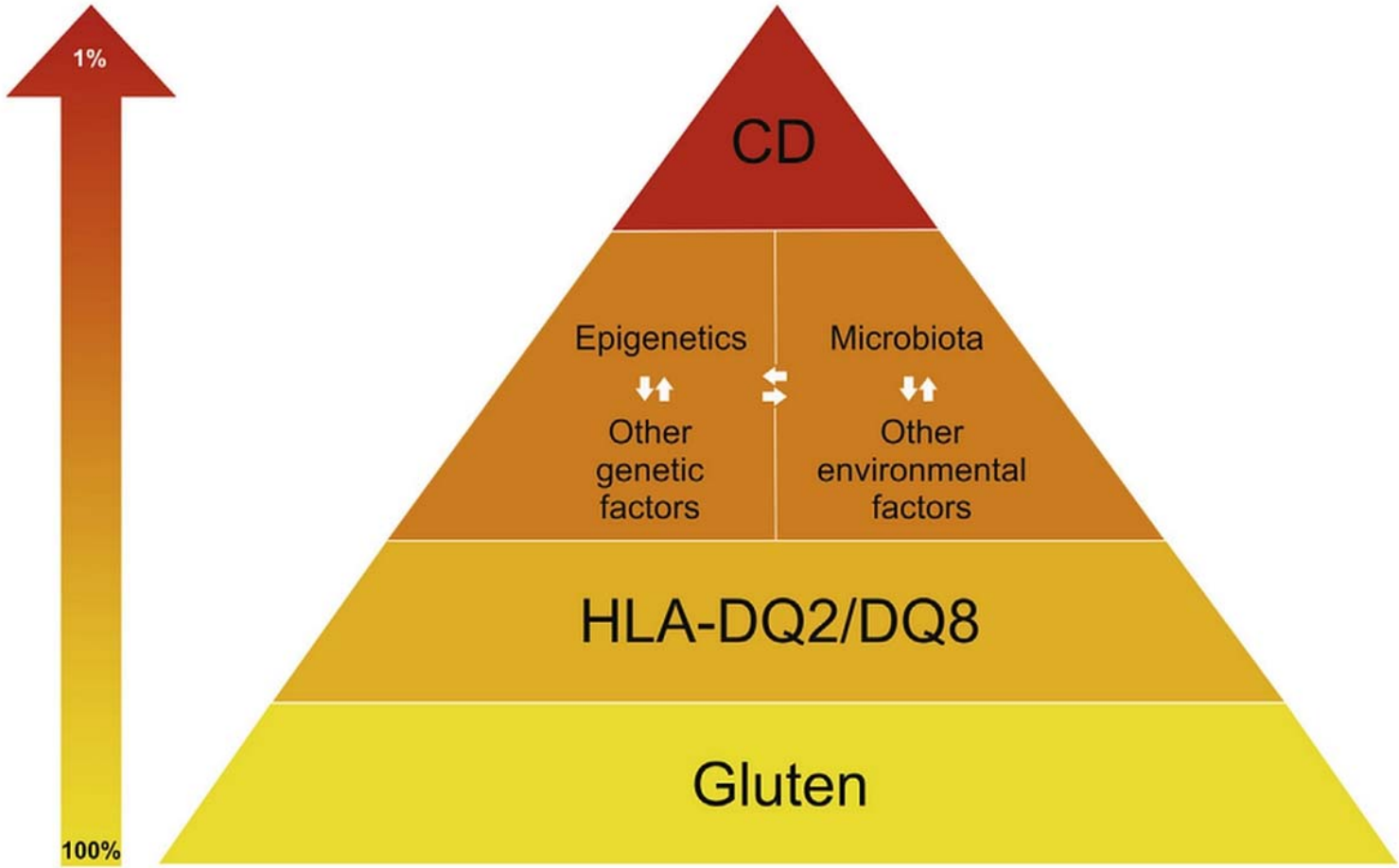
1.LF UK tutorial, July 2024

COELIAC INCIDENCE - THREE MAIN CONDITIONS



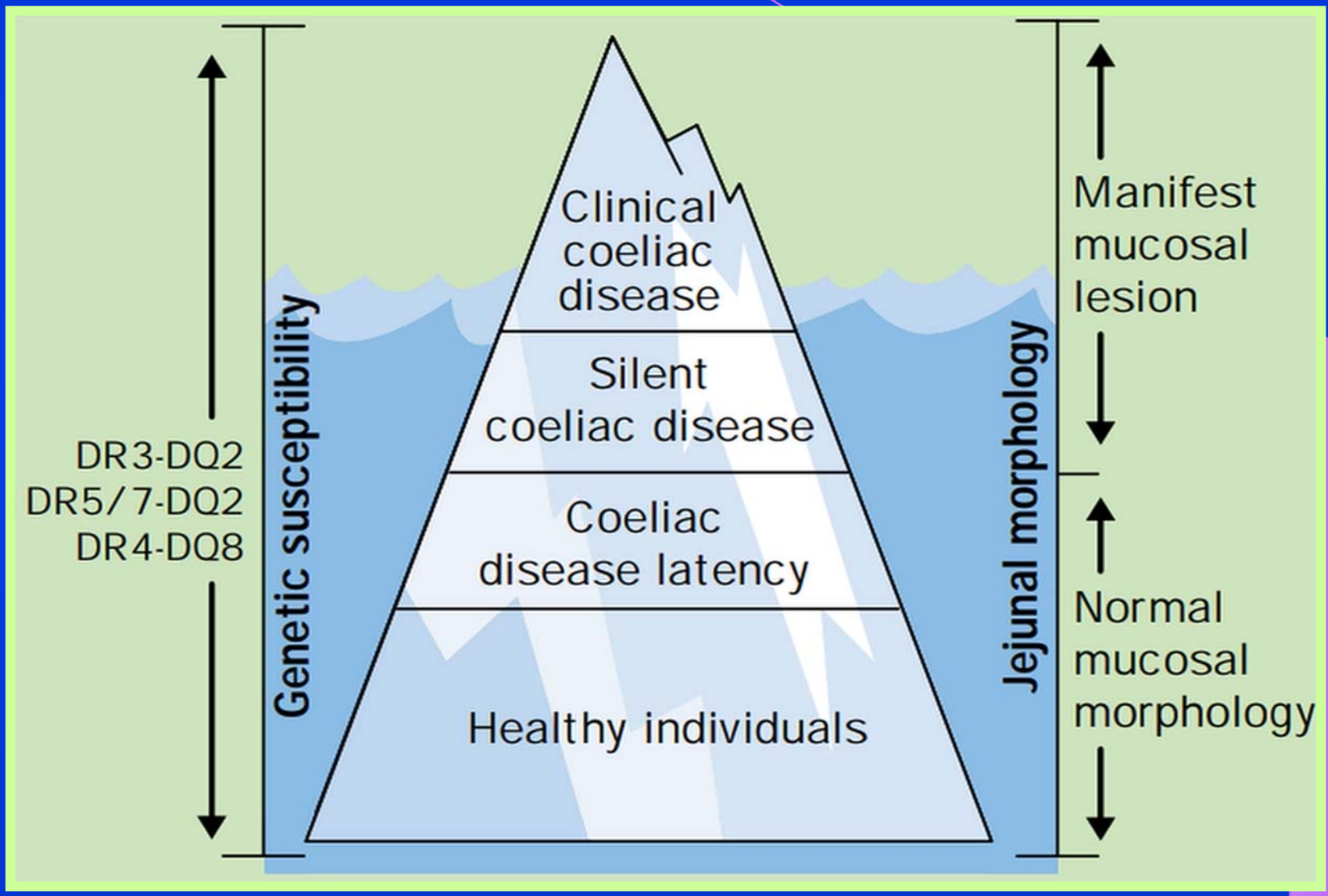
ICEBERG HYPOTHESIS OF COELIAC INCIDENCE

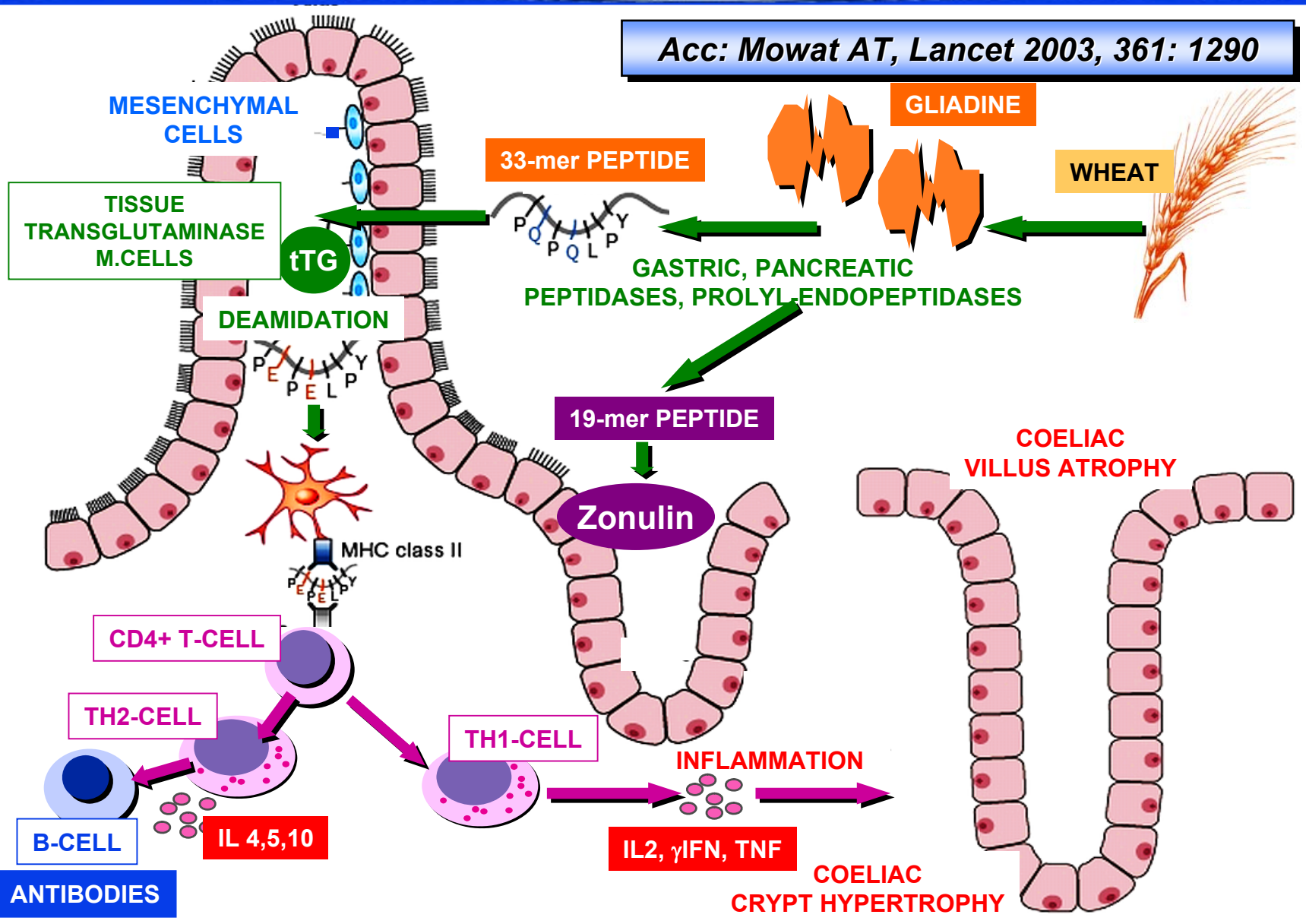


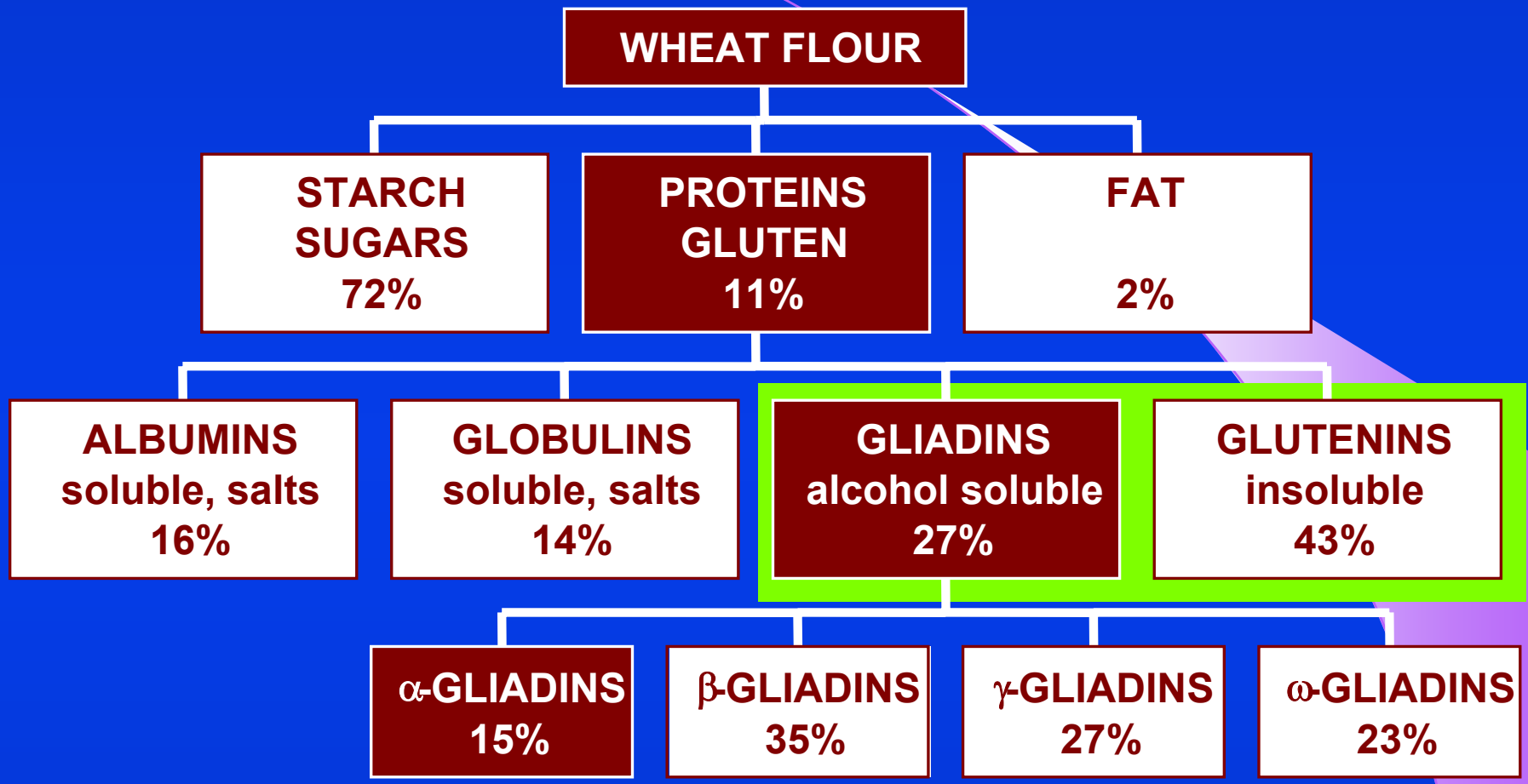


Dieli-Crimi R, Cénit MC, Núñez C. The genetics of celiac disease: A comprehensive review of clinical implications. J Autoimmun. 2015; 64:26-41

ICEBERG HYPOTHESIS OF COELIAC INCIDENCE



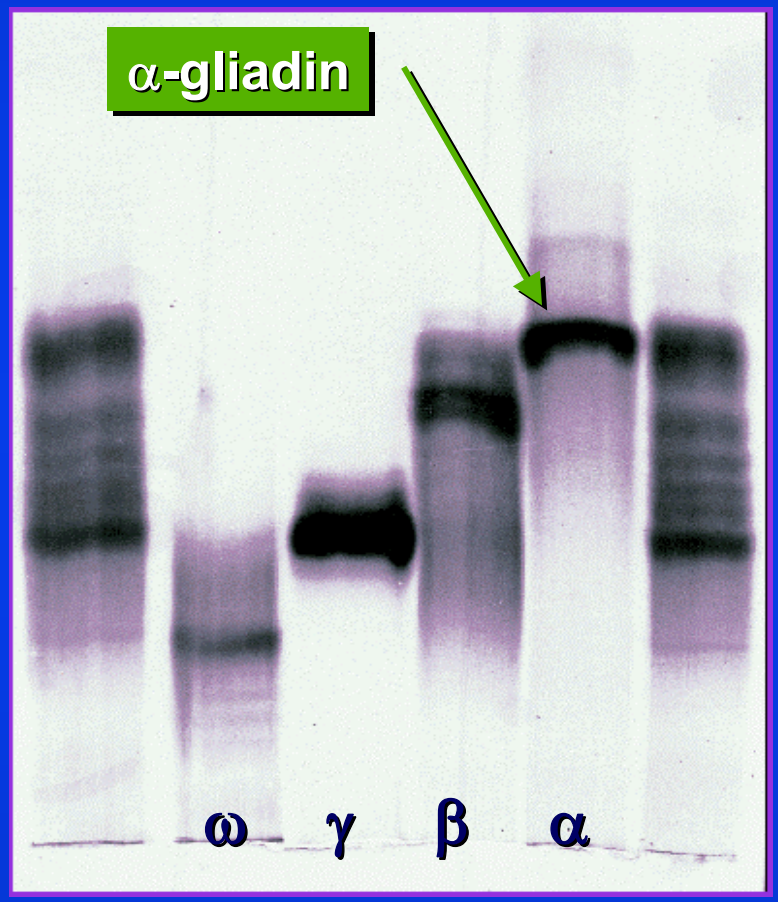

Acc: Mowat AT, Lancet 2003, 361: 1290
GLIADINE
WHEAT
33-mer PEPTIDE
MESENCHYMAL CELLS
TISSUE TRANSGLUTAMINASE M.CELLS
tTG
GASTRIC, PANCREATIC PEPTIDASES, PROLYL-ENDOPEPTIDASES
DEAMIDATION
19-mer PEPTIDE
Zonulin
COELIAC VILLUS ATROPHY
MHC class II
CD4+ T-CELL
TH2-CELL
TH1-CELL
INFLAMMATION
B-CELL
IL 4,5,10
IL2, γIFN, TNF
ANTIBODIES
COELIAC CRYPT HYPERTROPHY



GLUTEN STORAGE PROTEINS
GLUTEN = GLIADINS + GLUTENINS

GLIADIN WHEAT PROLAMIN

GLIADINS – PROTEIN SEPARATION



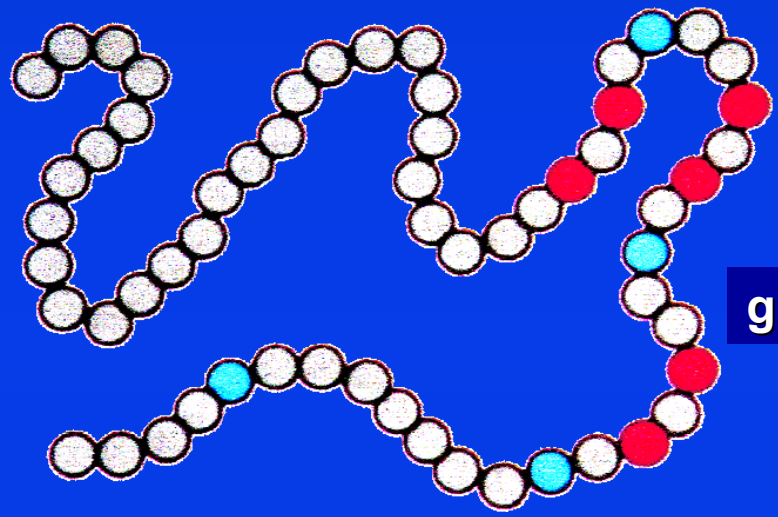
STARCH GEL ELECTROPHORESIS (SGE)

PROTEIN SEPARATION
GLIADIN CLASSIFICATION
FOUR GROUPS

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

Kocna, P.; Holáková-Kočová, M.; Šašek, 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

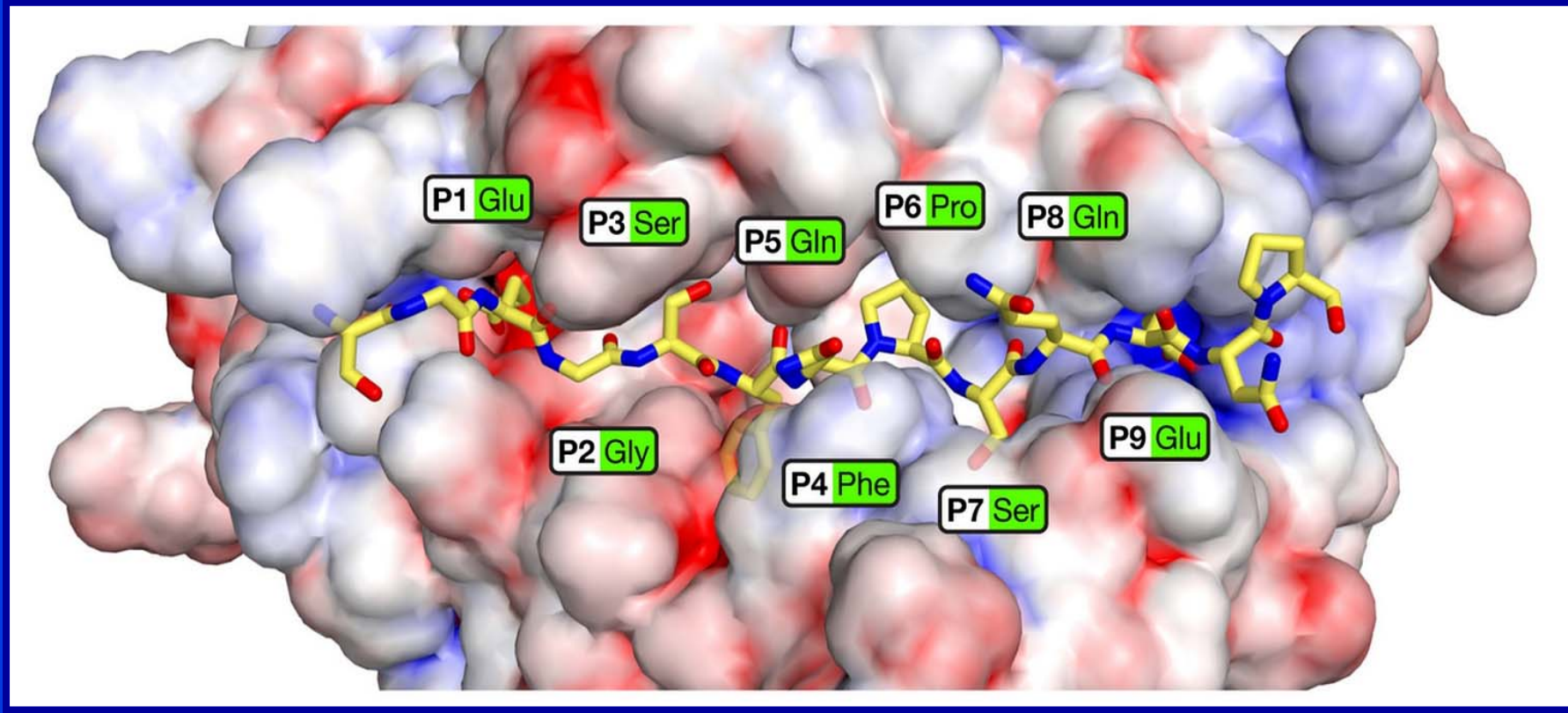


gliadine sequence

33-mer resistant peptide

LQLQPFPQPQLPYPQPQLPYPQPQLPYPQPQPF

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

LQPFPQPQLPY

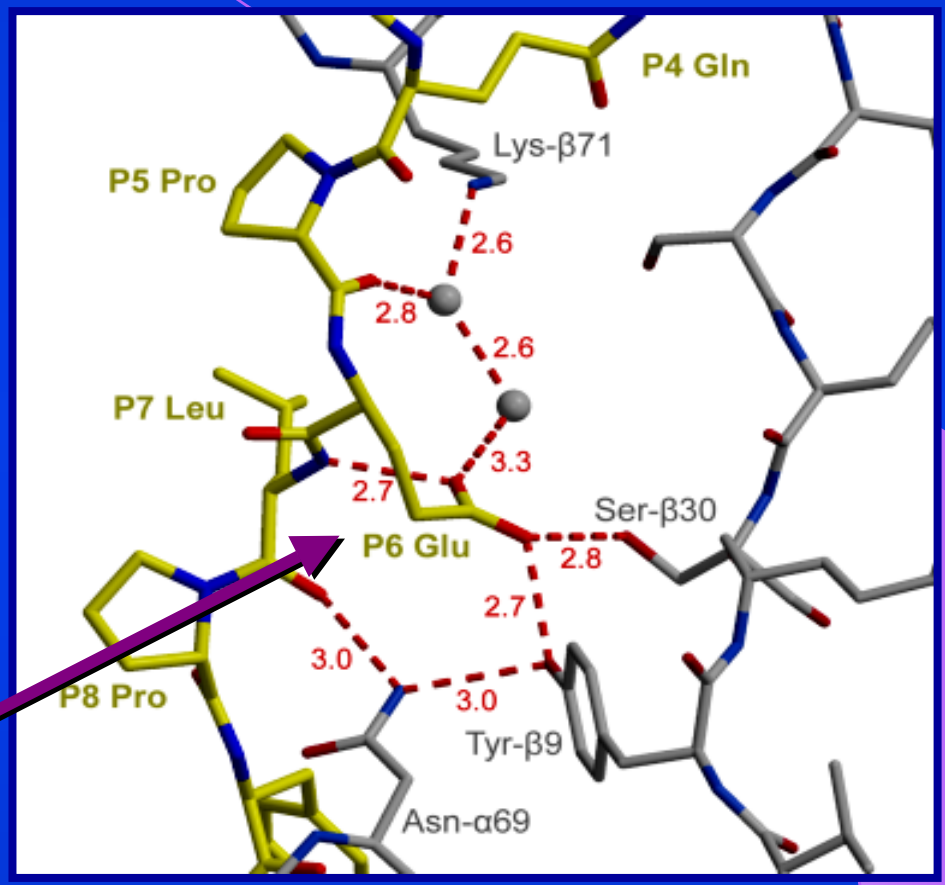
IC_{50}: 103 µM

DEAMIDATION - TG2
TISSUE TRANSGLUTAMINASE

LQPFPQPELPY

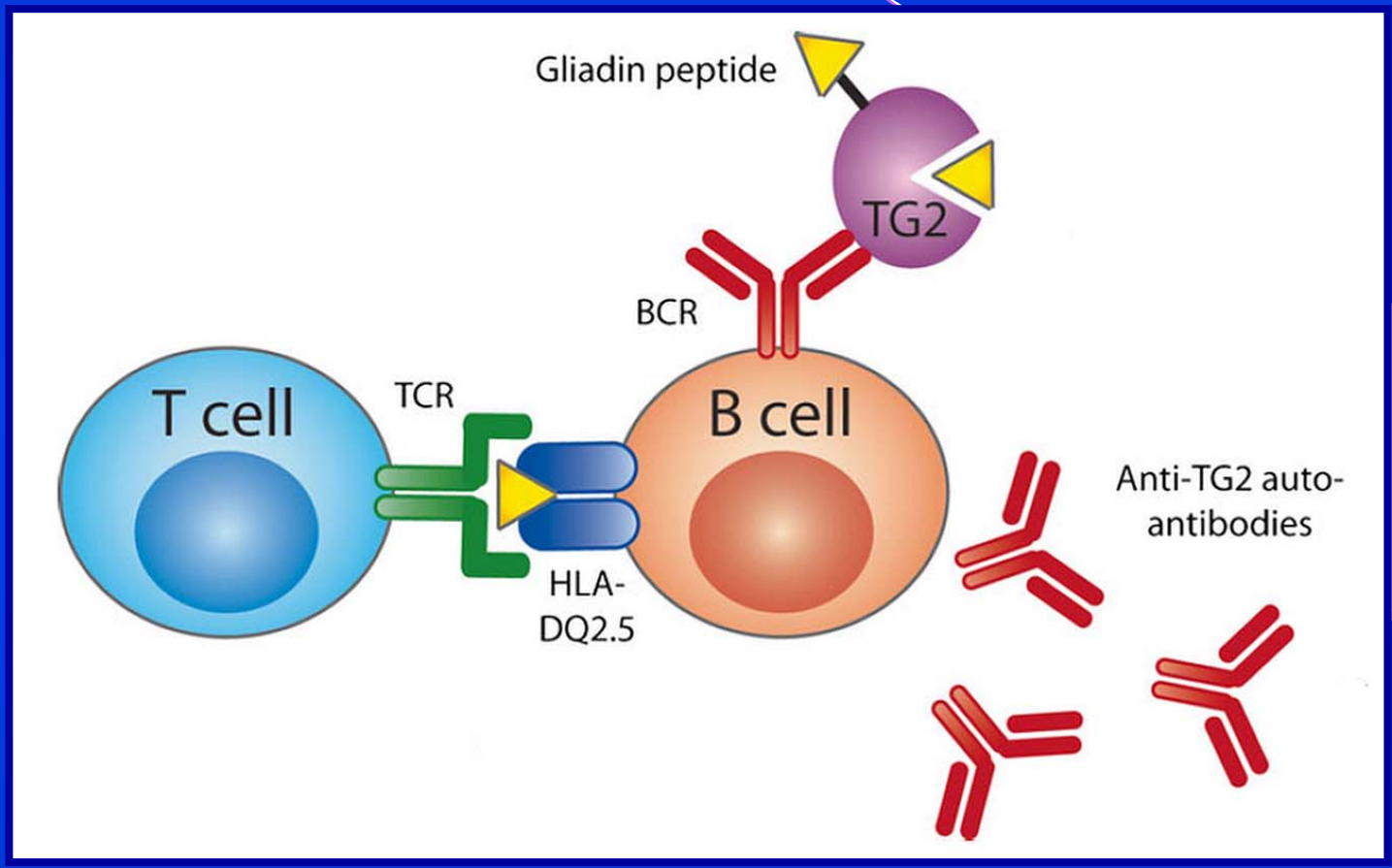
IC_{50}: 4 µM

AFFINITY LINKS TO POSITION P6 INCREASE 25x



Chu-Young Kim: Structural basis for HLA-DQ2-mediated presentation of gluten epitopes in celiac disease. PNAS 2004; 4175 - 4179

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 requiremed 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 remision

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, IFNγ 57,7 (normal up tol 31 %)

tumor necrosis factor, TNFα 74,7 (normal up to 44 %)

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

TARGETED COELIAC SCREENING

MAIN RISK GROUPS

- Dermatitis herpetiformis
- Osteoporosis, unexplained fractures
- Unexplained anaemia
- Chronic fatigue syndrome
- Resistent irritable bowel syndrome

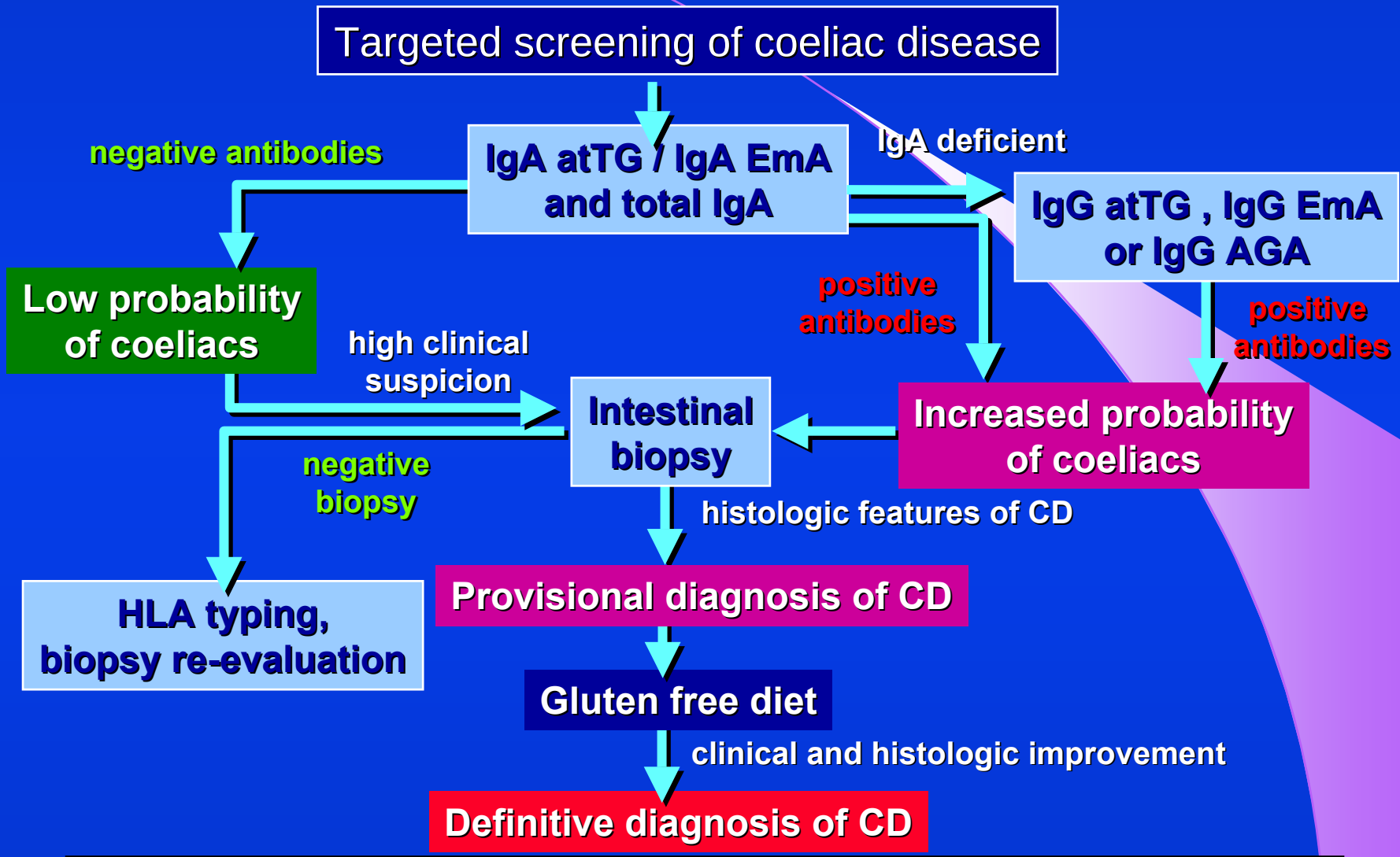
CD SUSPECTED SYMPTOMS

- Spont. abortion and fetal growth retardation
- Unexplained anaemia (iron, folic acid)
- Hypertransaminasemia
- Recurrent aphthous stomatitis
- Dental enamel hypoplasia

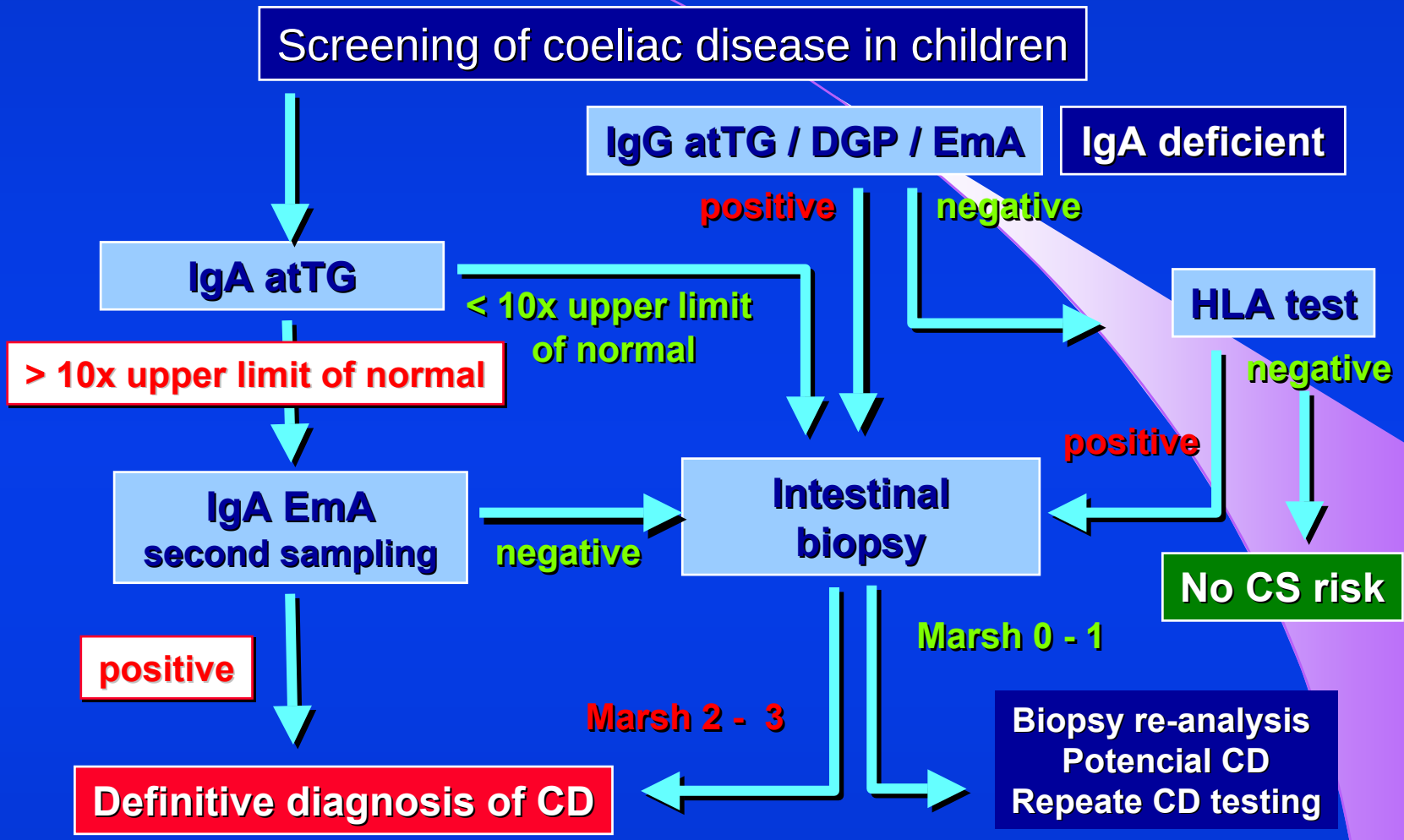
AUTOIMUNNE DISEASES

- Diabetes mellitus type 1.
- Autoimmune thyroiditis
- Autoimmune liver disease
- Systemic lupus erythematosus
- Sjögren syndrome
- Primary biliary cirrhosis or sclerosing cholangitis

Cílený screening celiakie - Metodický pokyn MZ ČR
Věstník MZ ČR, 2011, částka 3. str. 51-54 - Practicus 2011; 4: 9 - 10



Briani C, Samaroo D, Alaedini A. Celiac disease: from gluten to autoimmunity. Autoimmun Rev. 2008 Sep;7(8):644-650.



European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020. Husby S, Koletzko S, Korponay-Szabó I.et al.: J Ped Gastru Nutr. 2020 Jan;70(1):141-156

ACTUAL PROTOCOL
ANTIBODIES DETERMINATION
(EVIDENCE - BASED)

IgA atTG + IgA

+ IgA EmA

INCREASE OF IgA atTG SPECIFICITY

+ IgG atTG

COELIAC DETECTION WITH
IgA DEFFICIENCY

+ IgA AGA

COELIAC DETECTION
IN CHILDRENS < 2 YR

PERSPECTIVE PROTOCOL
ANTIBODIES DETERMINATION
(WORKING HYPOTHESIS)

IgA atTG

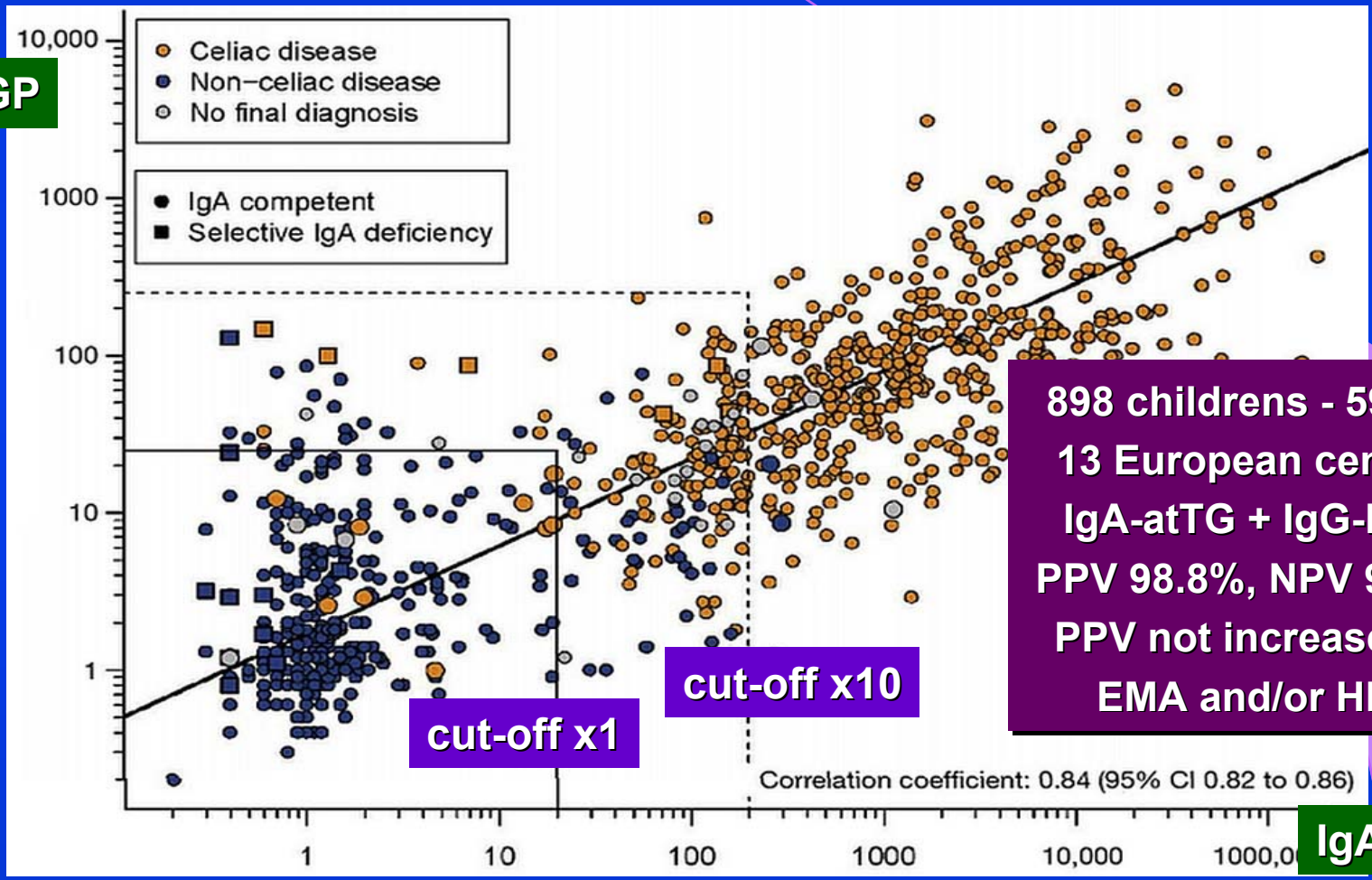
+ IgG DGP

INCREASE OF IgA atTG SPECIFICITY
COELIAC DETECTION WITH IgA DEFFICIENCY
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

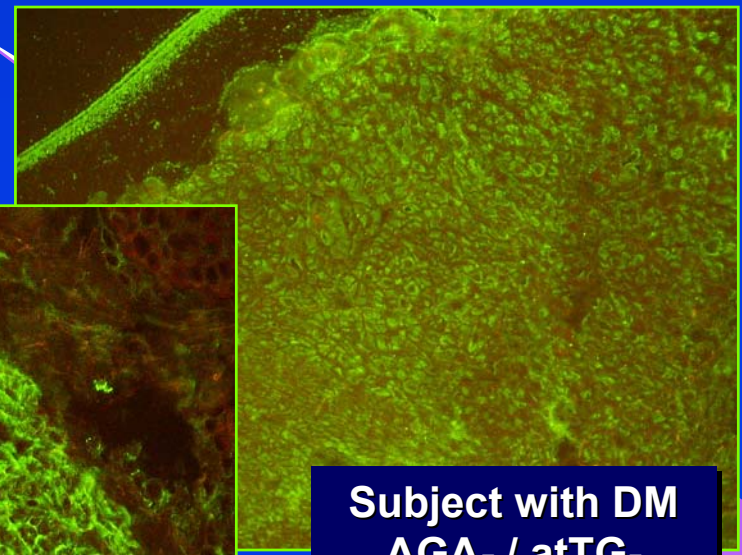


898 childrens - 592 CS
13 European centers
IgA-atTG + IgG-DGP
PPV 98.8%, NPV 95,8%
PPV not increased by
EMA and/or HLA

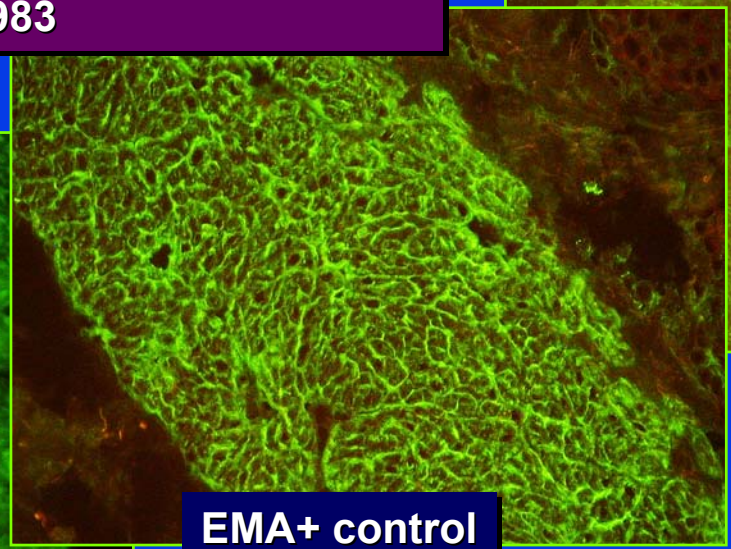
Wolf J, Petroff D, et al.: Validation of Antibody-Based Strategies for Diagnosis of Pediatric Celiac Disease Without Biopsy. Gastroenterology. 2017;153: 410-419

ENDOMYSIUM ANTIBODIES - EMA

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

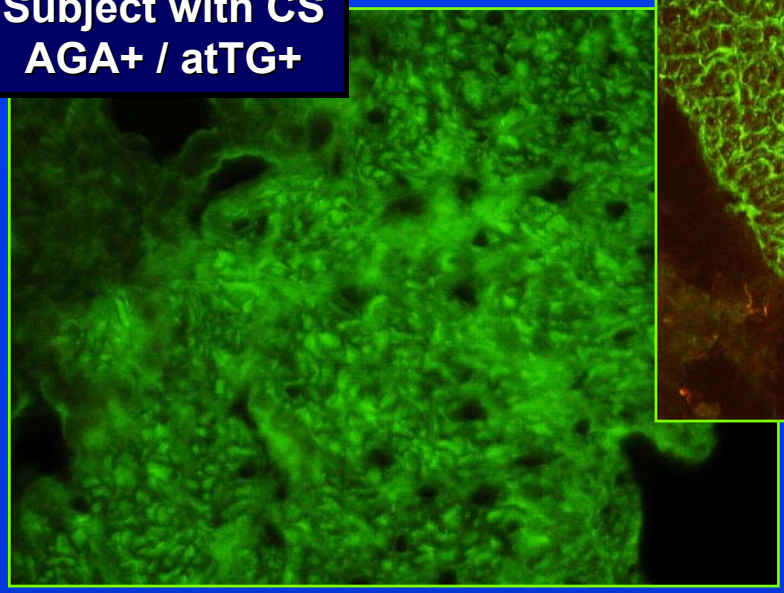


Subject with DM
AGA- / atTG-



EMA+ control

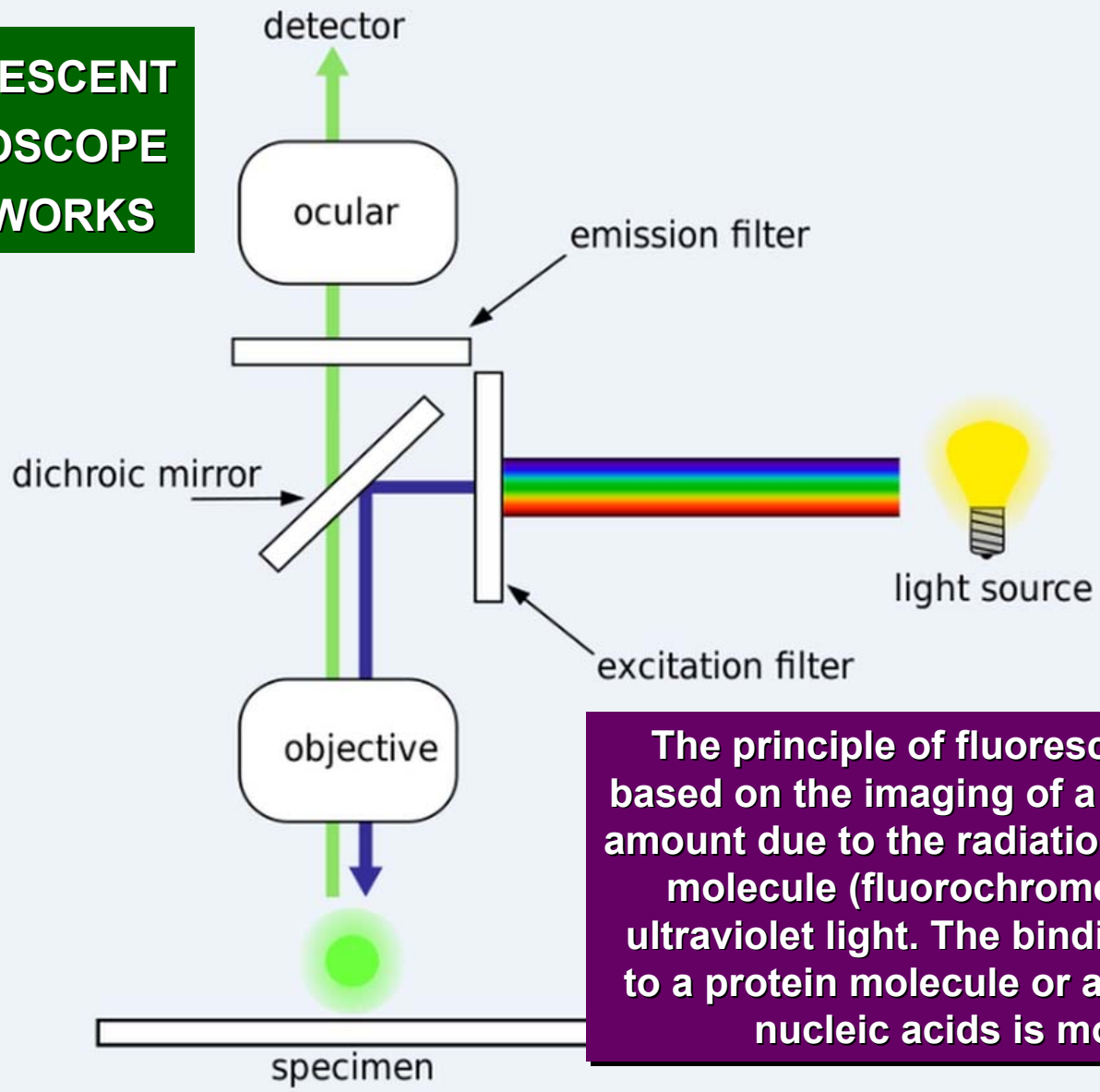
Subject with CS
AGA+ / atTG+



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.

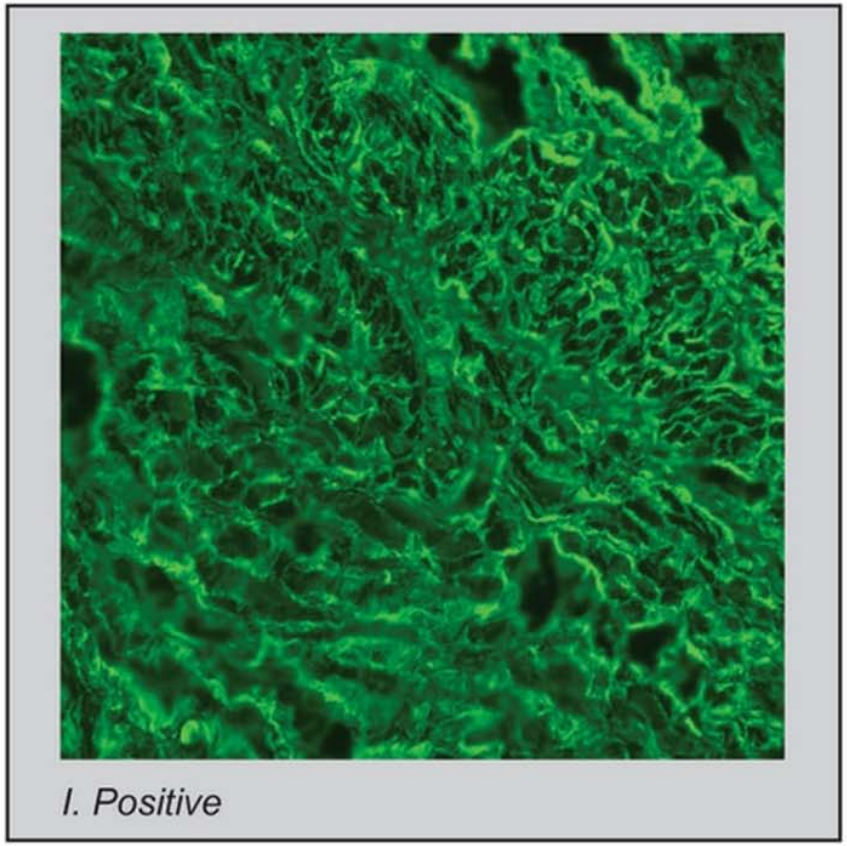
FLUORESCENCE MICROSCOPE

FLUORESCENT MICROSCOPE HOW WORKS

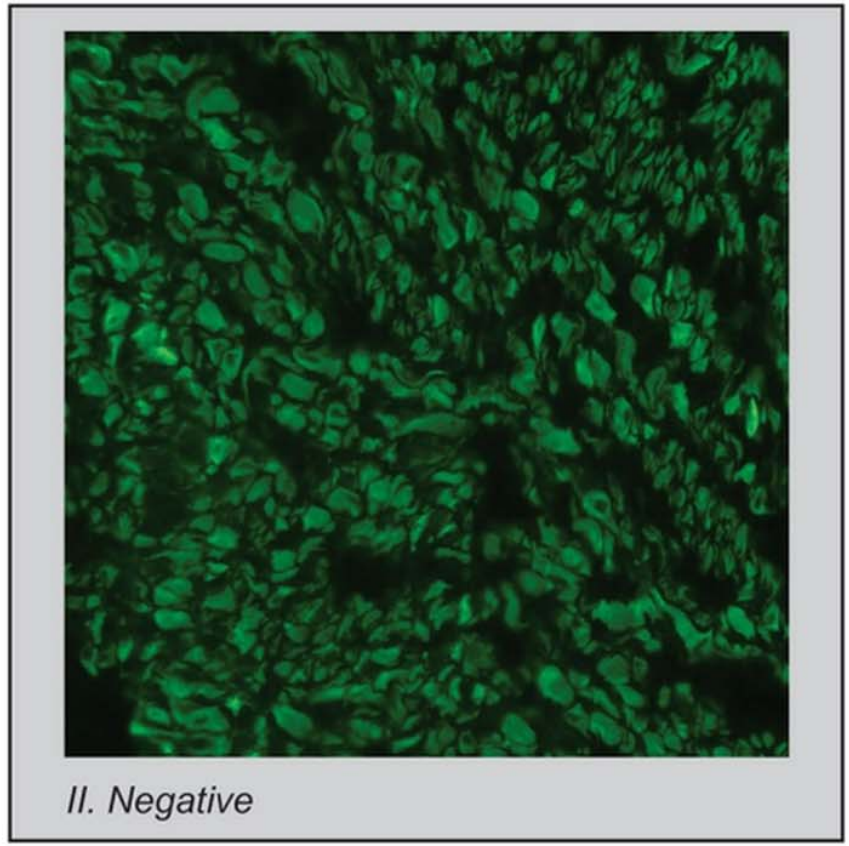


The principle of fluorescence microscopy is based on the imaging of a molecule in a minimal amount due to the radiation (fluorescence) of the molecule (fluorochrome) after exposure to ultraviolet light. The binding of a fluorochrome to a protein molecule or a specific sequence of nucleic acids is most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

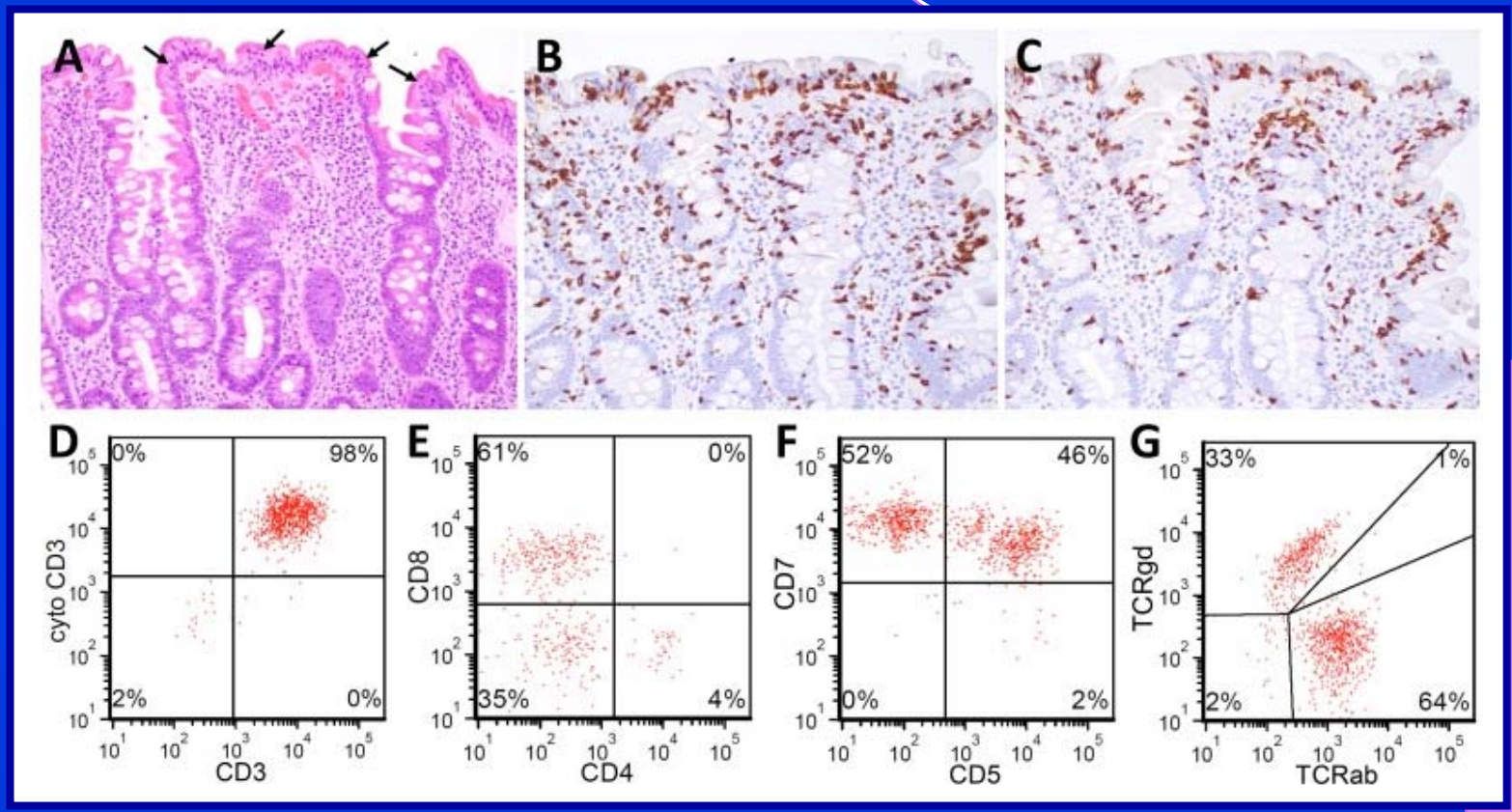
The study material consisted of 2597 high-quality EmA images class IgA collected in 2017-2018.

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.

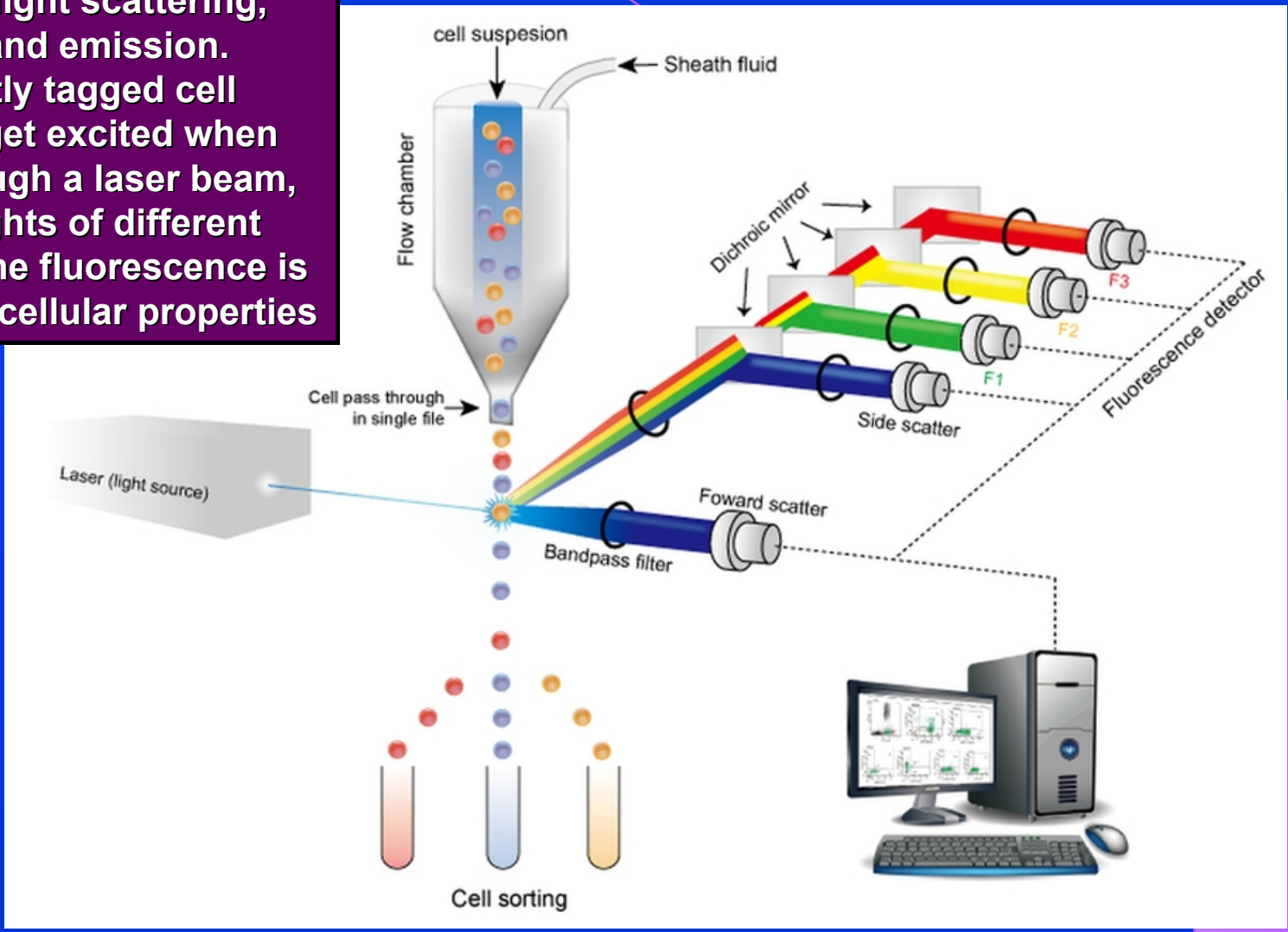
Caetano Dos Santos FL, Michalek IM, Laurila K, et al.: Automatic classification of IgA endomysial antibody test for celiac disease: a new method deploying machine learning. Sci Rep. 2019; 9(1):9217

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 ANALYSYS
HOME TESTS

anti-tTG (IgA & IgG)

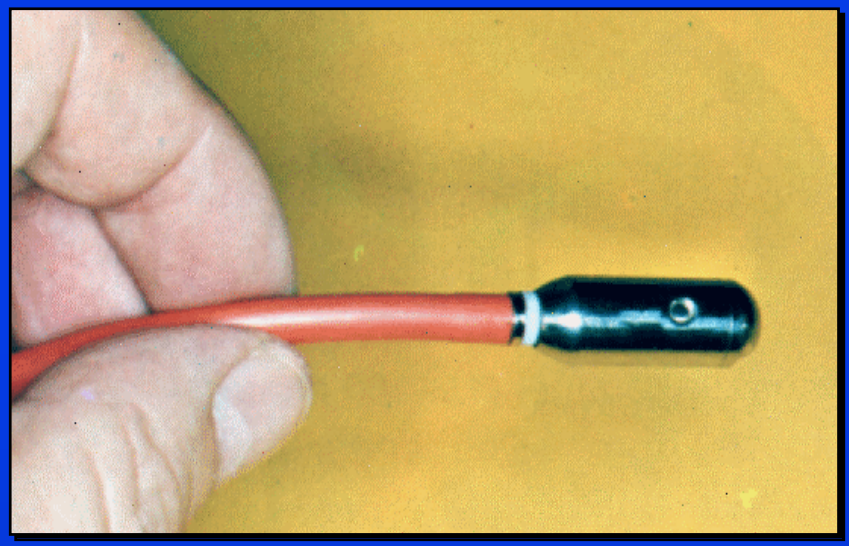
anti-DGP (IgA &IgG) + celkové IgA

anti-tTG (IgA) + celkové IgA

anti-tTG (IgA, IgG, IgM)

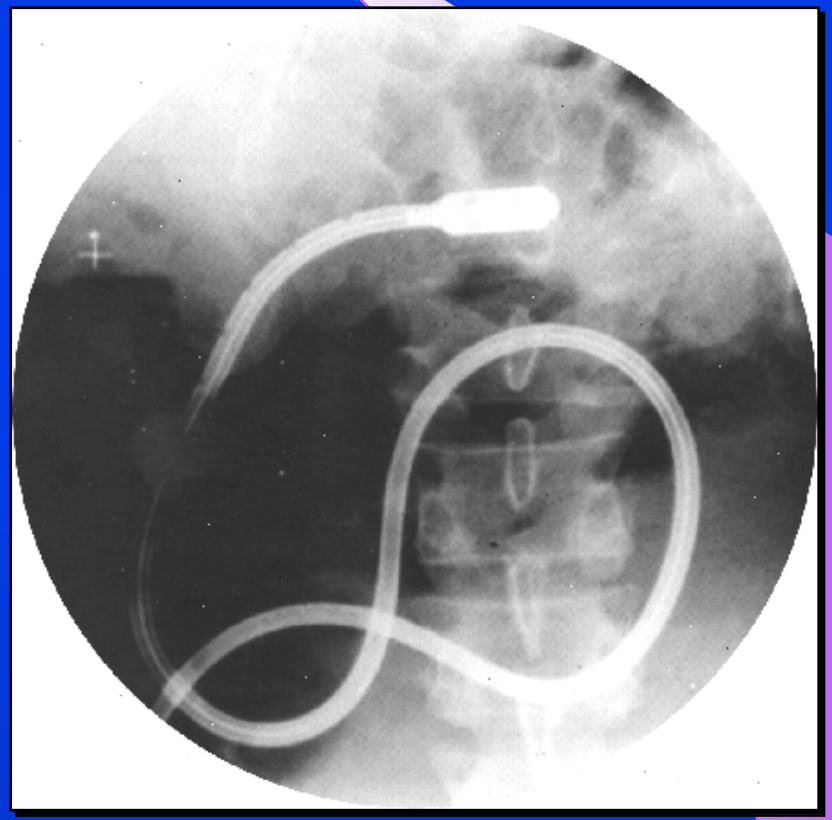
COELIAC DIAGNOSIS - HISTOLOGY, HISTOCHEMISTRY

ENTEROBIOPSY OF SMALL INTESTINE

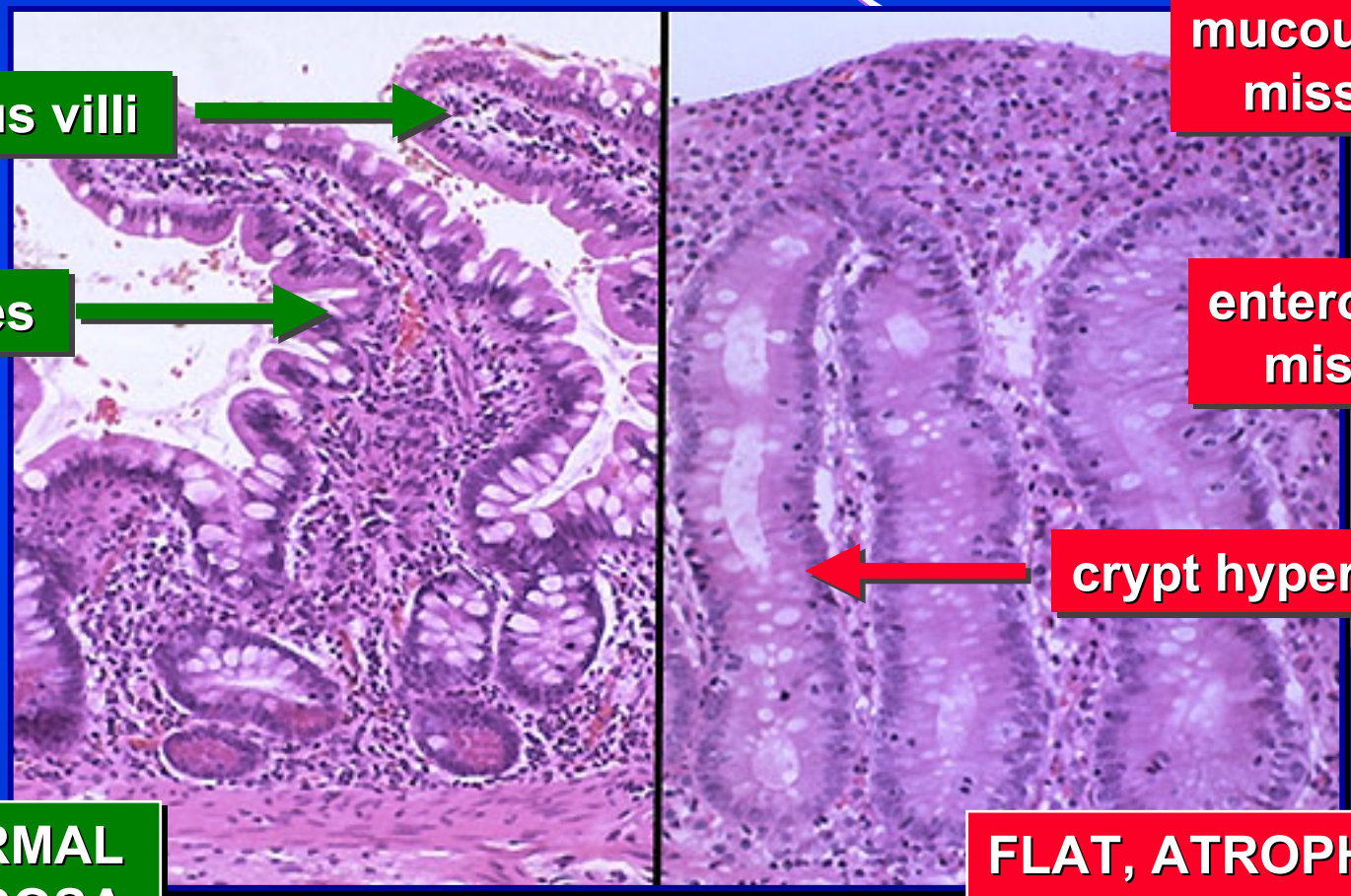


CROSBY'S CAPSULE

X-REY CHECKED POSITION



COELIAC DIAGNOSIS - HISTOLOGY



mucous villi

enterocytes

NORMAL MUCOSA

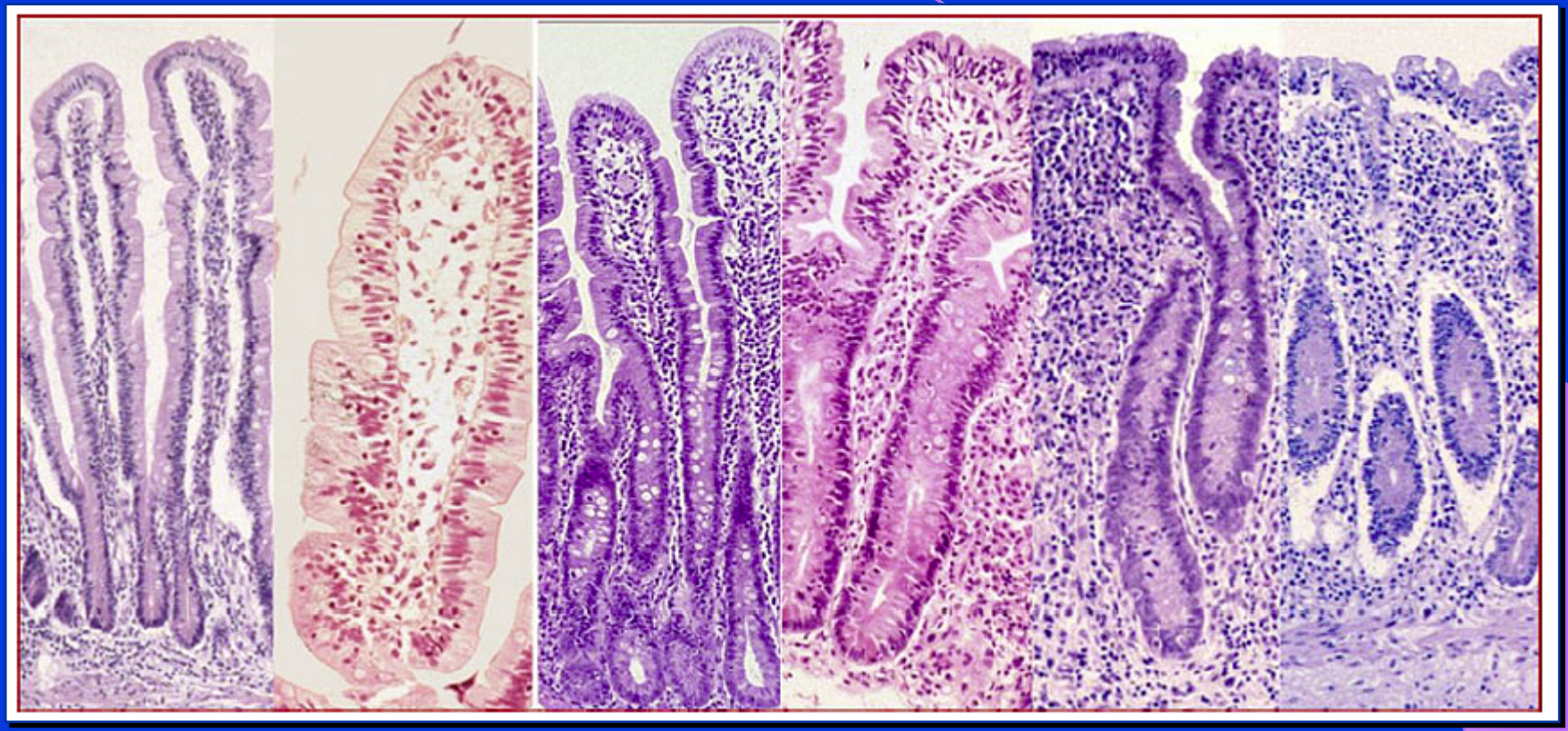
mucous villi missing

enterocytes missing

crypt hyperplasis

FLAT, ATROPHIC MUCOSA

INTESTINAL BIOPSY IN THE COELIAC DISEASE DIAGNOSIS

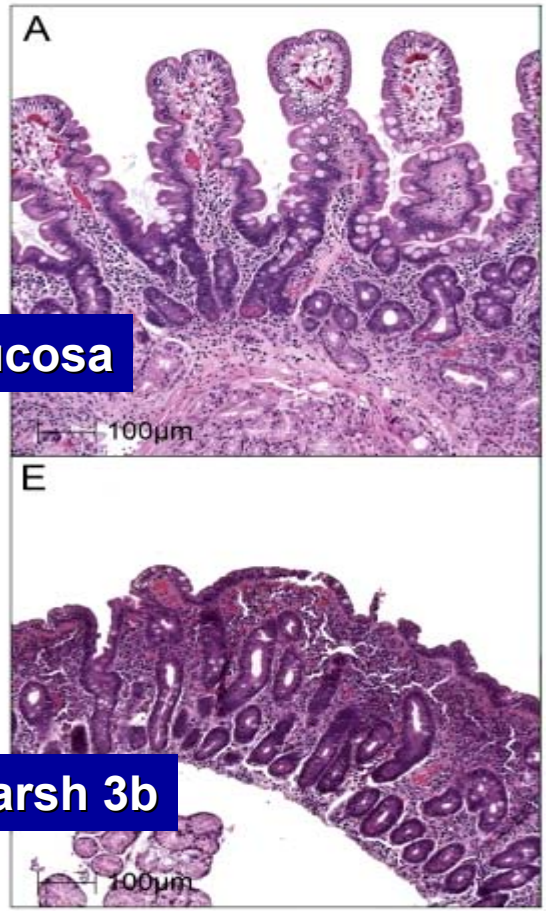


Marsh 0 Marsh 1 Marsh 2 Marsh 3a Marsh 3b Marsh 3c

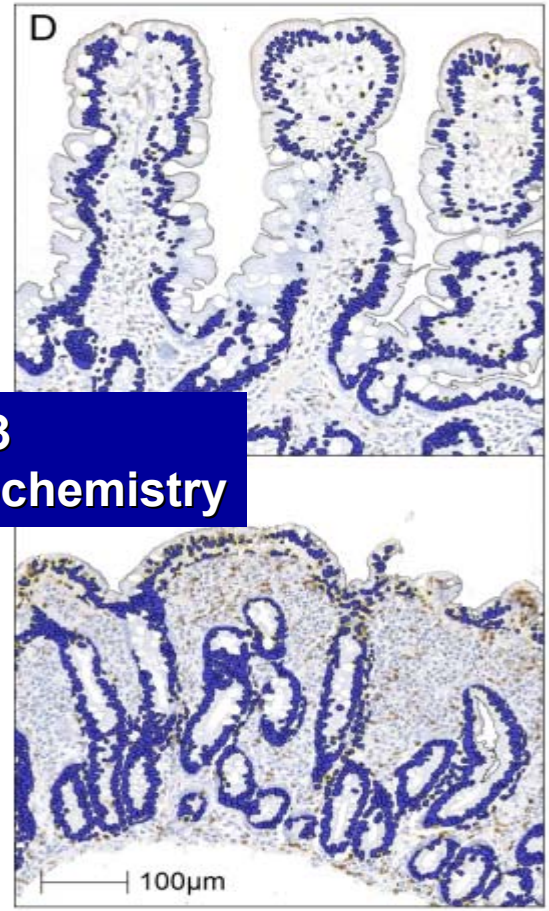
Clinical practice - Coeliac disease. Kneepkens C. M., von Blomberg B. M. Eur J Pediatr. 2012; 171(7) : 1011 - 1021

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.

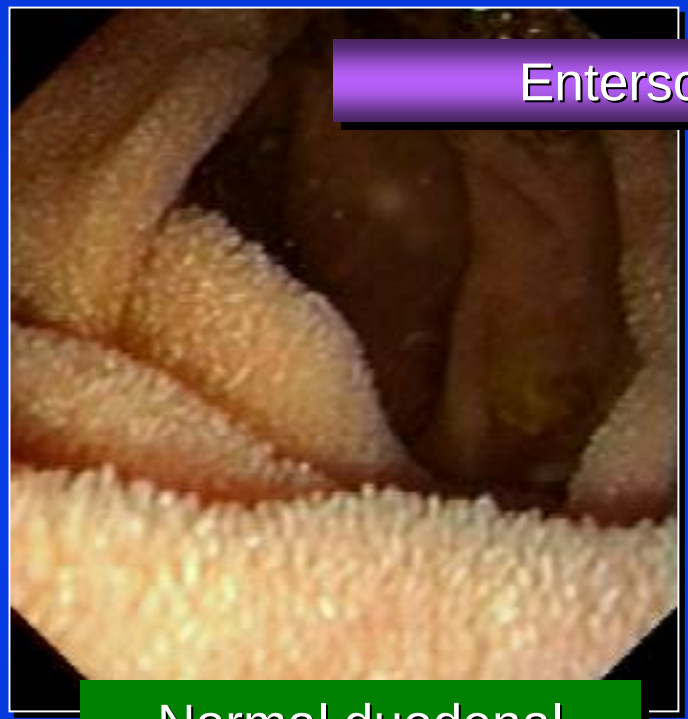
- ✓ **Histological evaluation of mucosal changes associated with celiac disease is important for establishing an accurate diagnosis and monitoring of celiac disease.**

- ✓ **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.

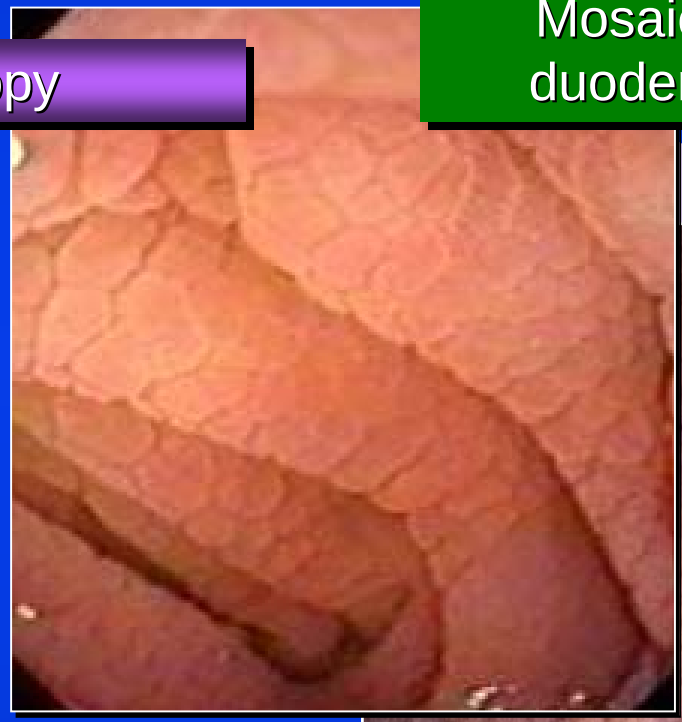
ENDOSCOPIC MARKERS OF COELIAC DISEASE

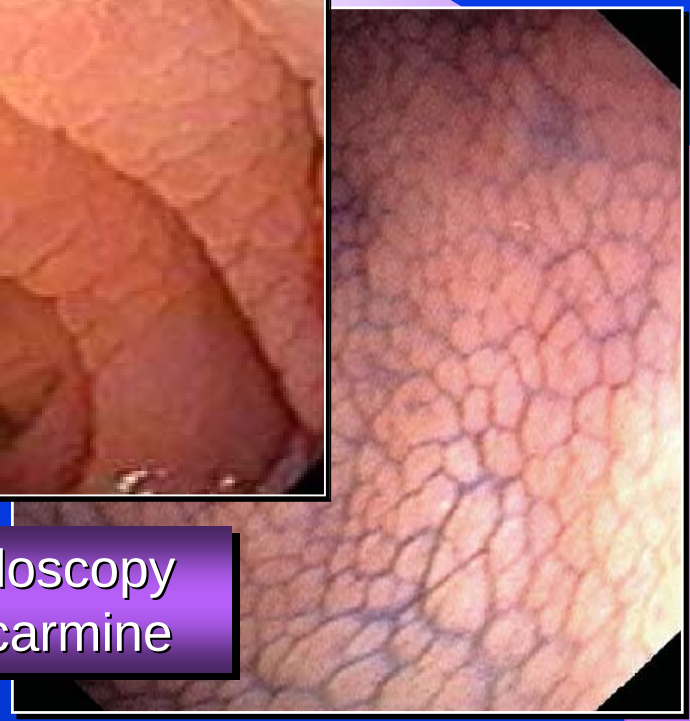


Enterscopy

Normal duodenal mucosa

Mosaic pattern of duodenal mucosa



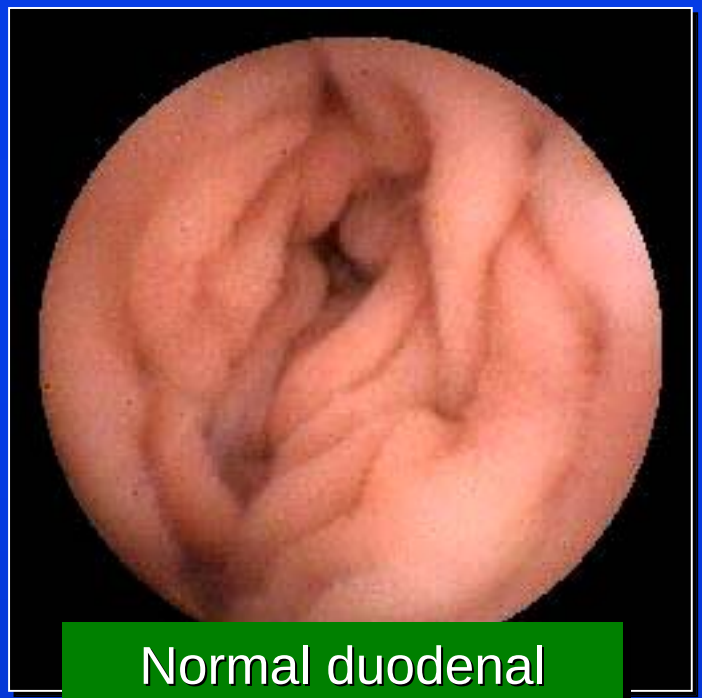


Chromoendoscopy with indigocarmine

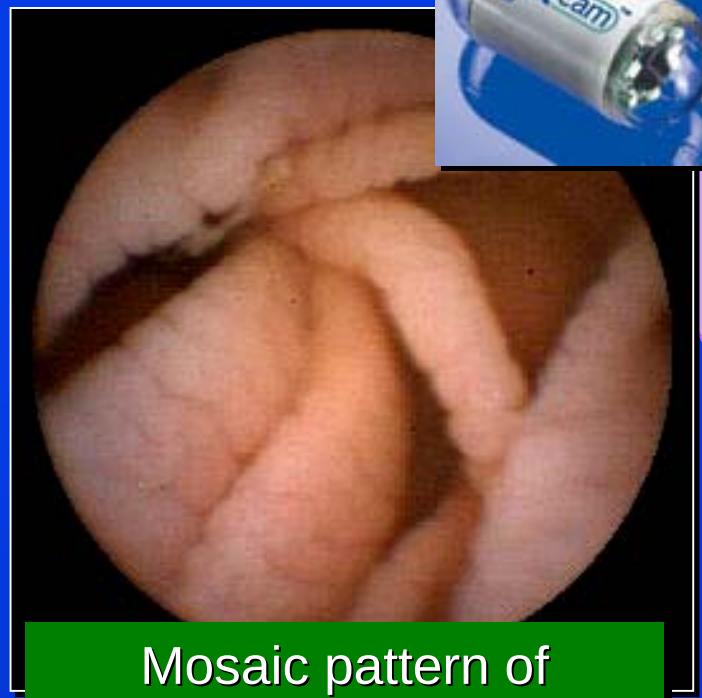
http://www.lfhk.cuni.cz/kcvl/stranky/ENTERO/E-cel1.html

CAPSULE ENDOSCOPY IN COELIAC DIAGNOSIS

NON-INVASIVE ENDOSCOPIC EXAMINATION



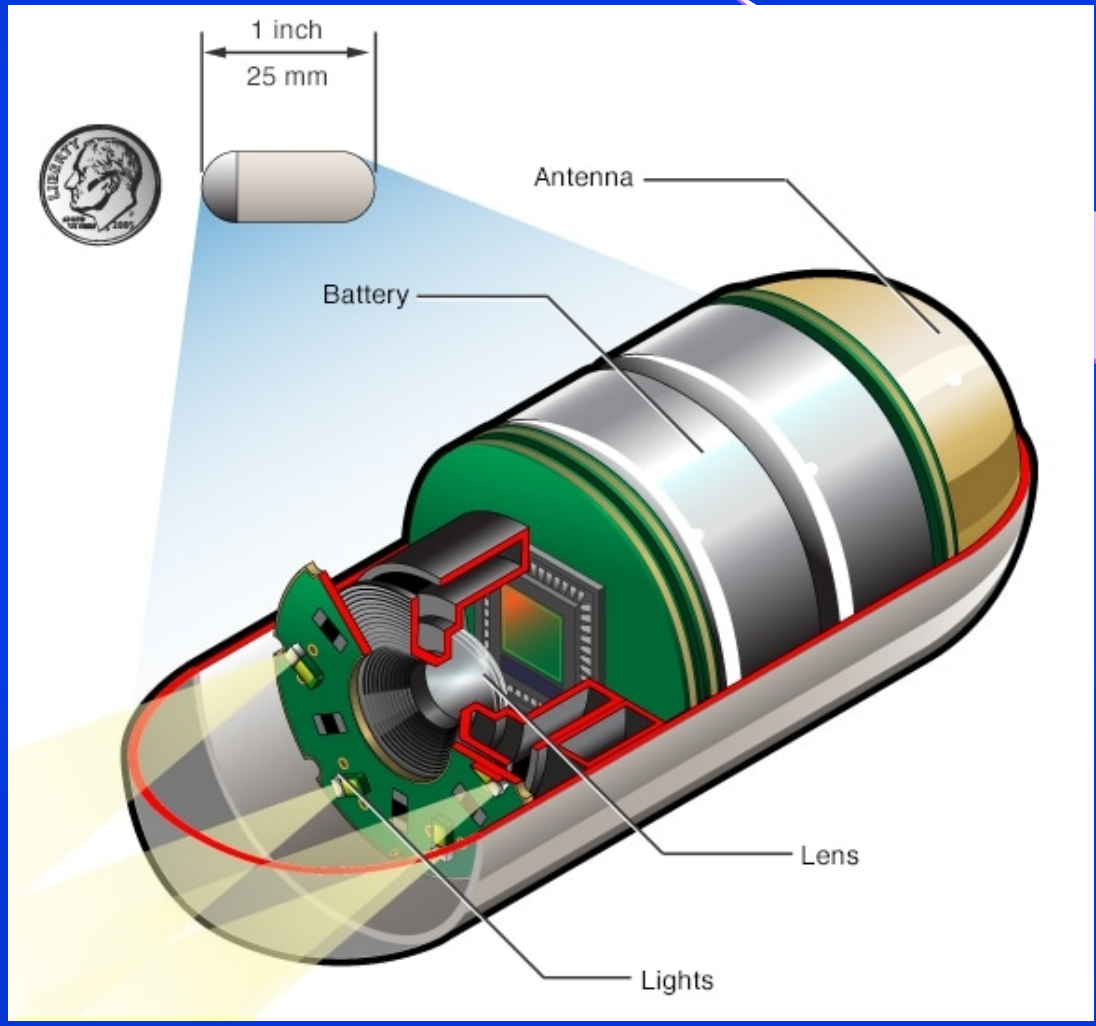
Normal duodenal mucosa



Mosaic pattern of duodenal mucosa

http://www.lfhk.cuni.cz/kcvl/stranky/Kapsle/C-CE1.html

CAPSULE ENDOSCOPY IN COELIAC DIAGNOSIS

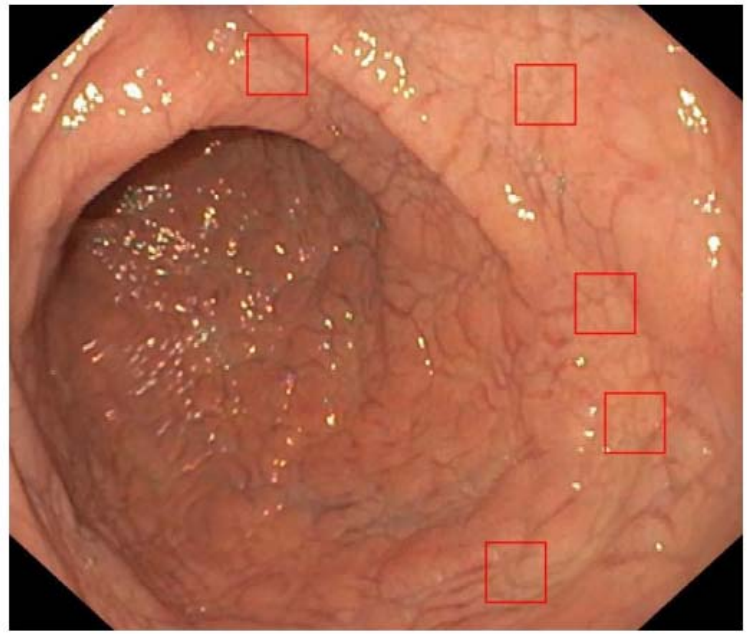


Automated processing of images obtained by non-invasive capsule endoscopy enables the detection of the presence of small villous atrophy, which is not visible during visual inspection.
This method can also be used to monitor celiac disease on a gluten-free diet.

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.

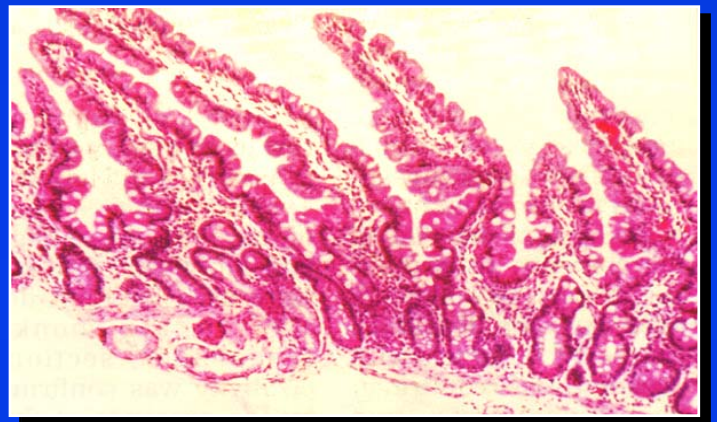


A neural network algorithm analyzing duodenal images of newly diagnosed CD patients compared to non-CD controls detected villous atrophy with 99.30% sensitivity and 98.61% positive predictive value.

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

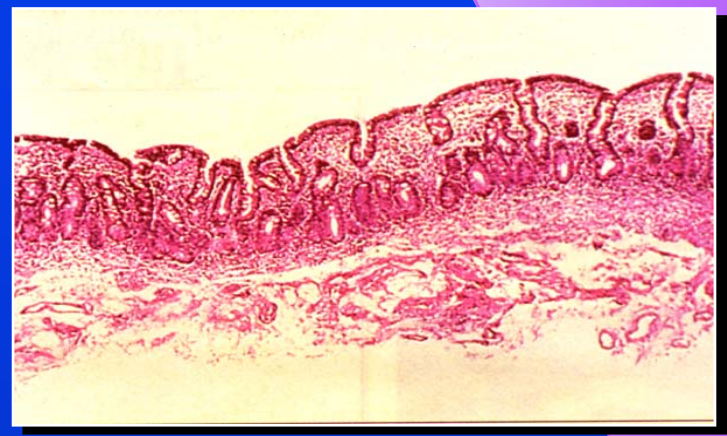
NORMAL MUCOSA



NEGATIVE ANTIBODIES

HEALTHY SUBJECT
TREATED COELIAC

TREATED COELIAC ?
OTHER AUTOIMMUNITY ?

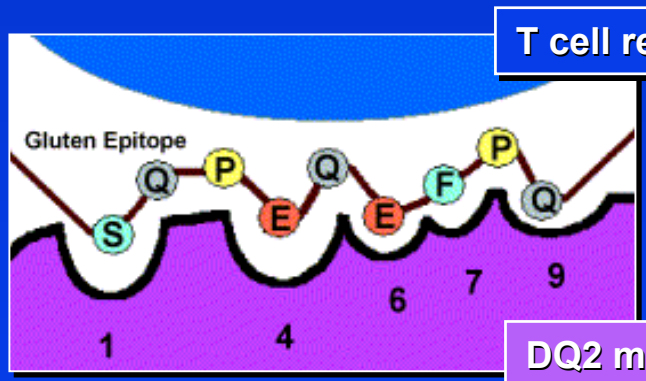


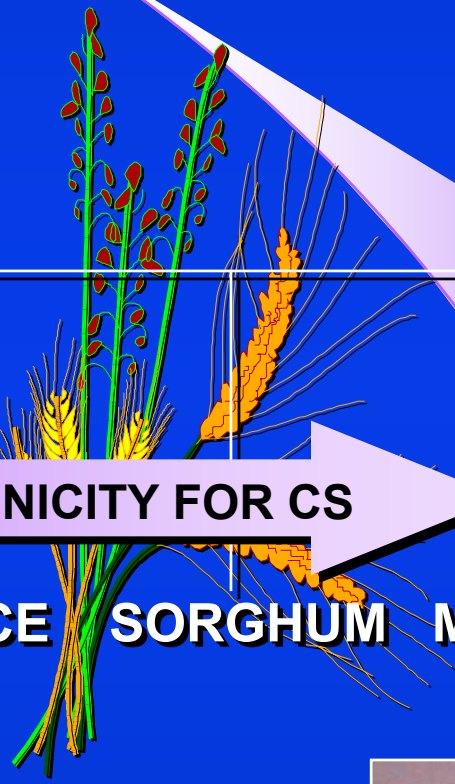
TOTAL ATROPHY

FLORID COELIAC
UNTREATED

POSITIVE ANTIBODIES

GLUTEN FREE DIET - CEREALS





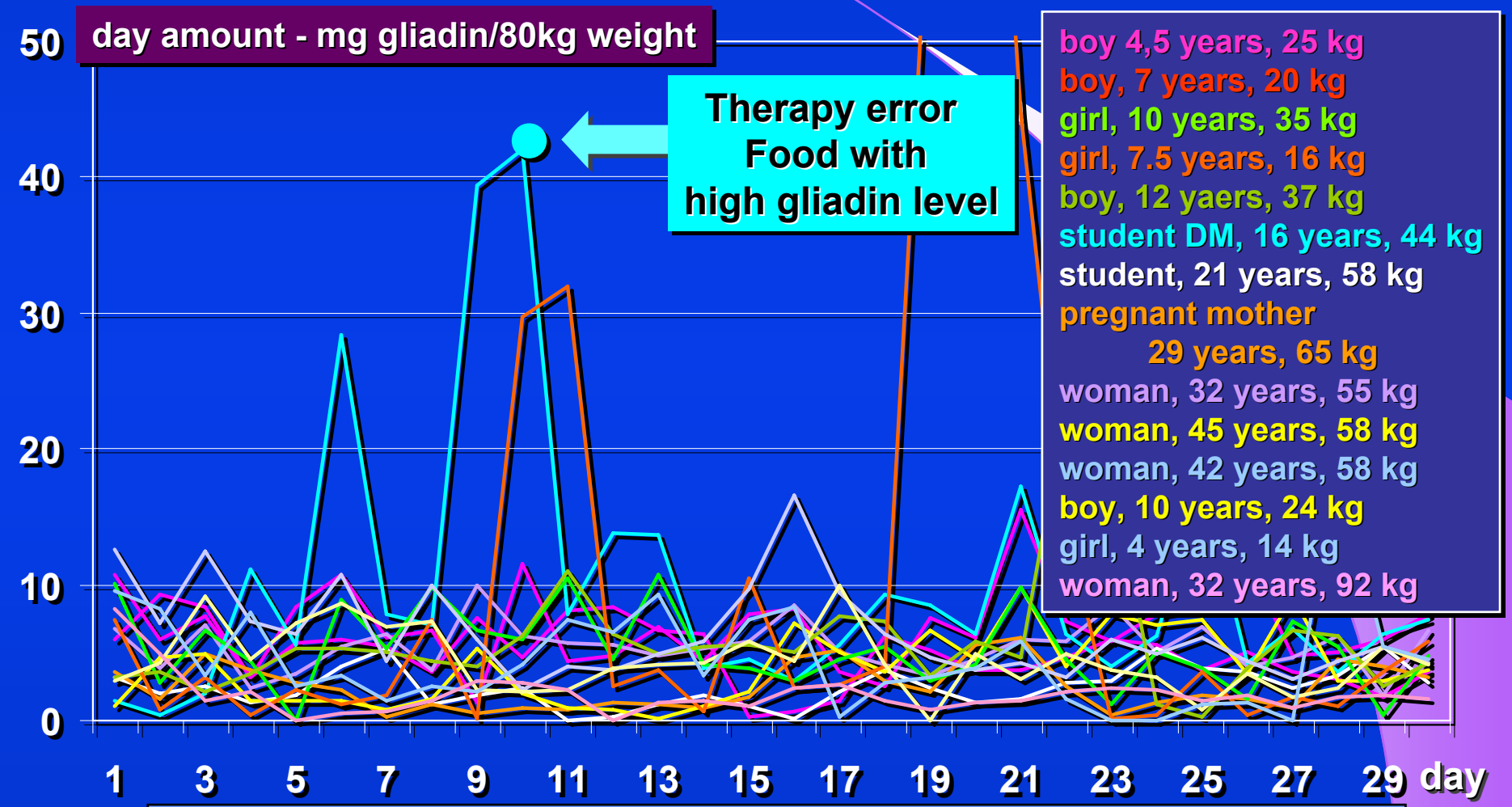
DECREASING PATOGENICITY FOR CS

WHEAT RYE BARLEY OATS RICE SORGHUM MILLET MAIZE

GLIADIN SECALIN HORDEIN AVENIN ZEIN

DECREASING TEST SENSITIVITY

GLUTEN FREE DIET – DAILY GLIADIN INTAKE



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

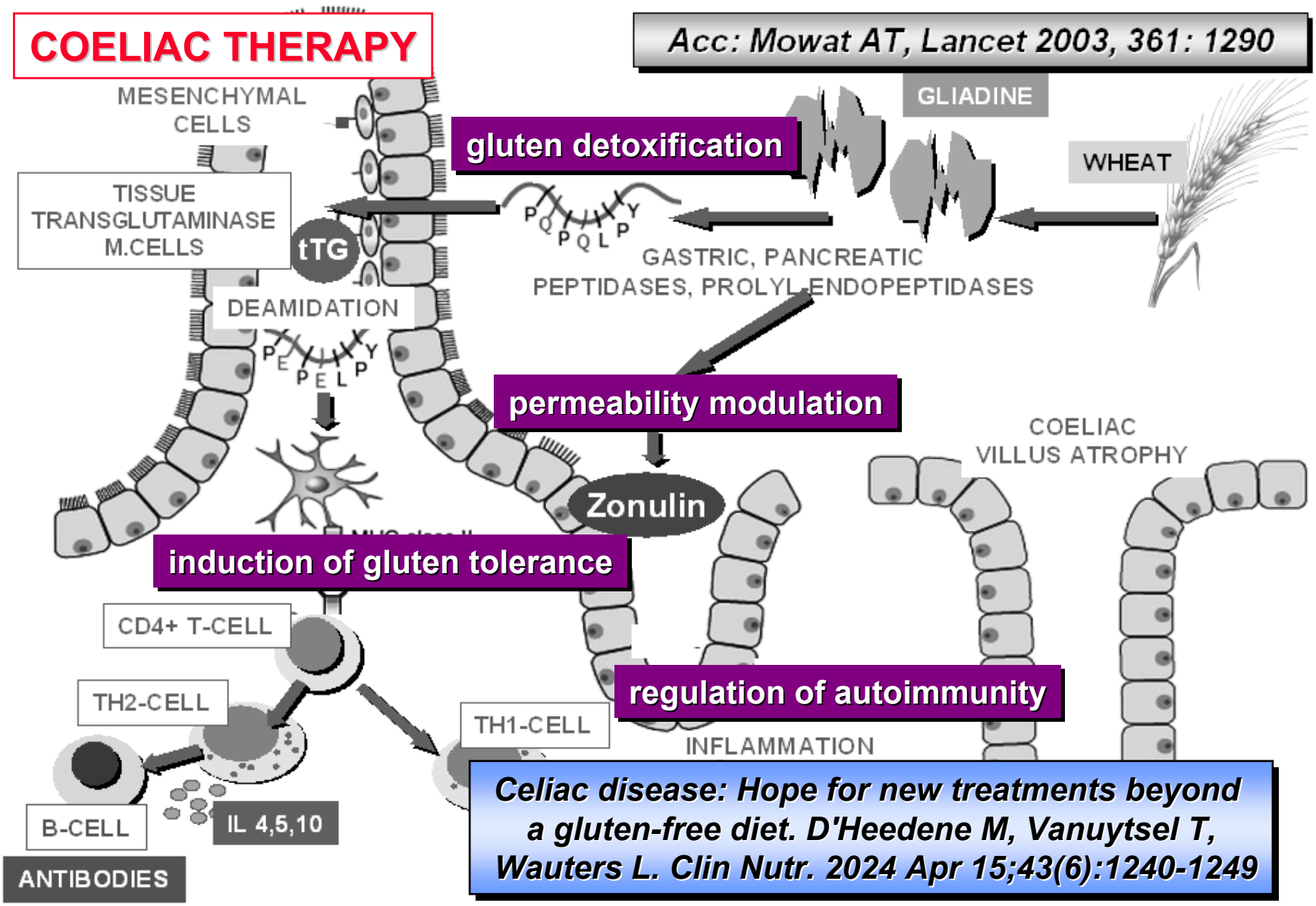
Safe limit

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

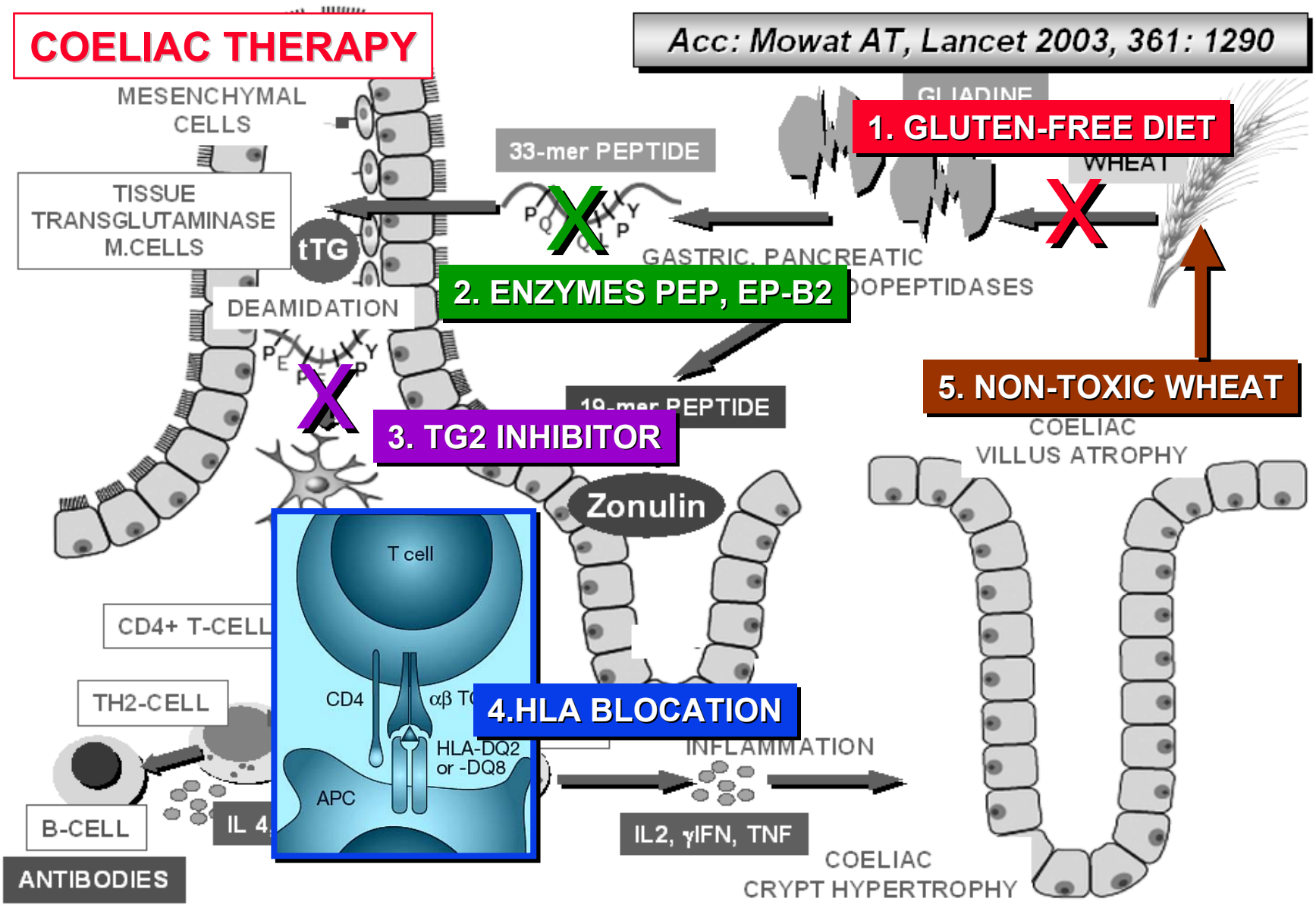
Acc: Mowat AT, Lancet 2003, 361: 1290



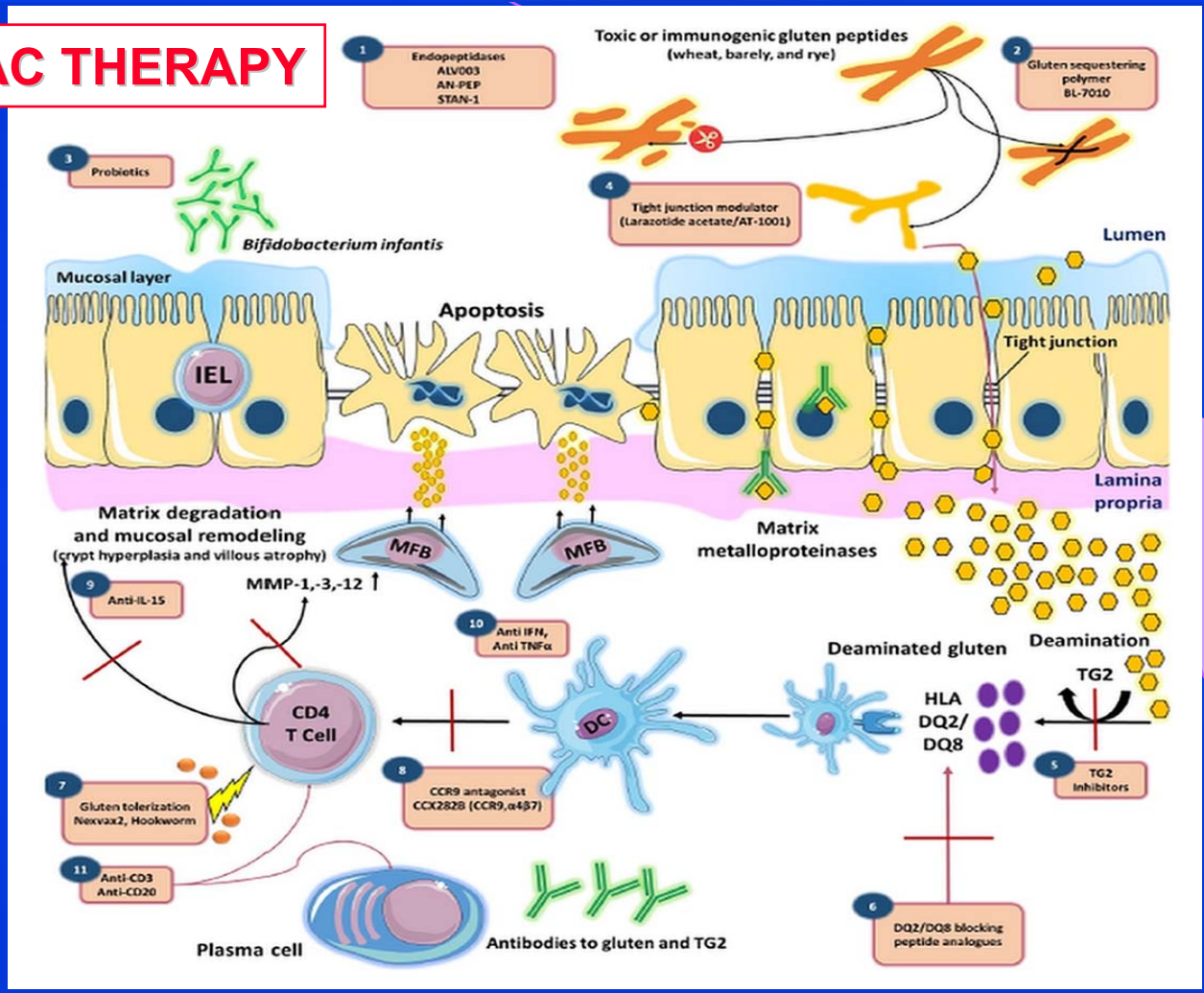
Celiac disease: Hope for new treatments beyond a gluten-free diet. D'Heedene M, Vanuytsel T, Wauters L. Clin Nutr. 2024 Apr 15;43(6):1240-1249

COELIAC THERAPY

Acc: Mowat AT, Lancet 2003, 361: 1290



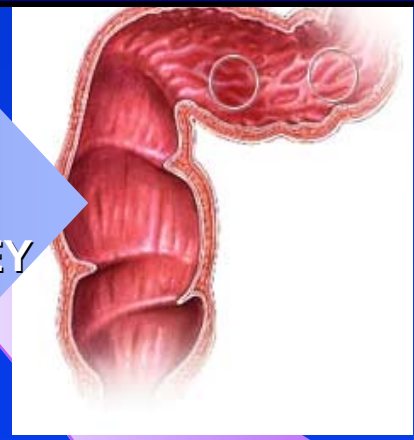
COELIAC THERAPY



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

BACTERIAL PROLYL-ENDOPEPTIDASE, CYS-PEPTIDASE FROM BARLEY



PROLYL-ENDOPETIDASE LACTOBACILLUS, ASPERGILUS PROTEASES

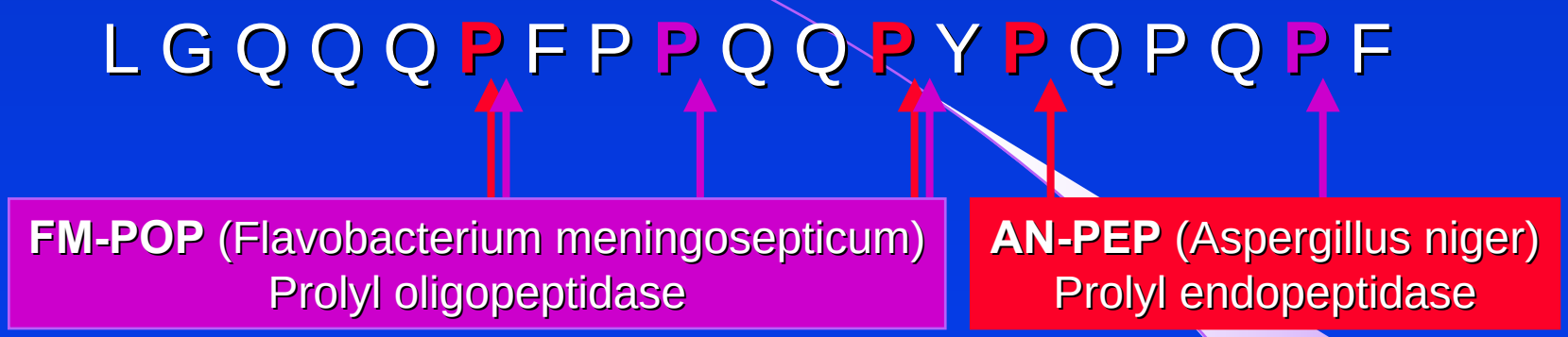
INTRA-DIGESTIVE DETOXIFICATION

PERORAL APPLICATION OF ENZYMES - HYDROLASES

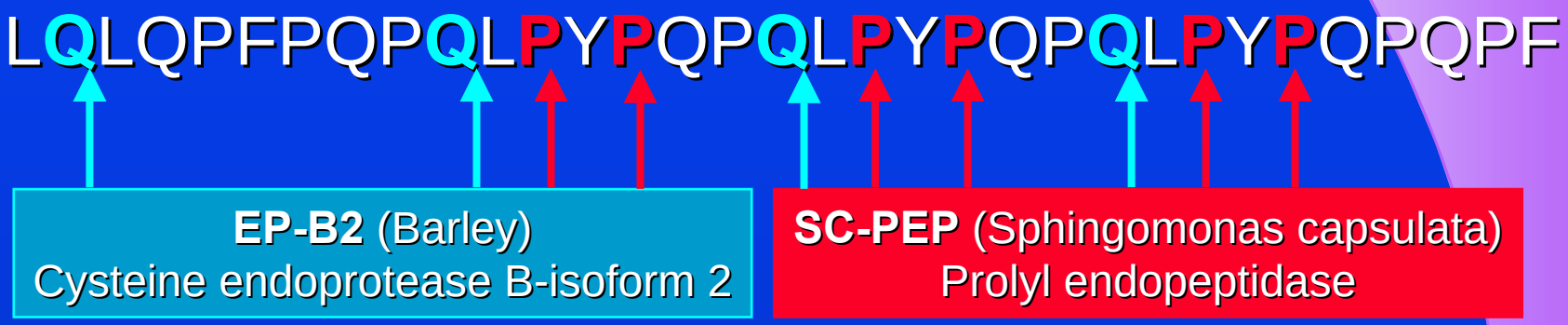
PRE-GASTRONOMIC DETOXIFICATION

MODIFICATION OF FOOD

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



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



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

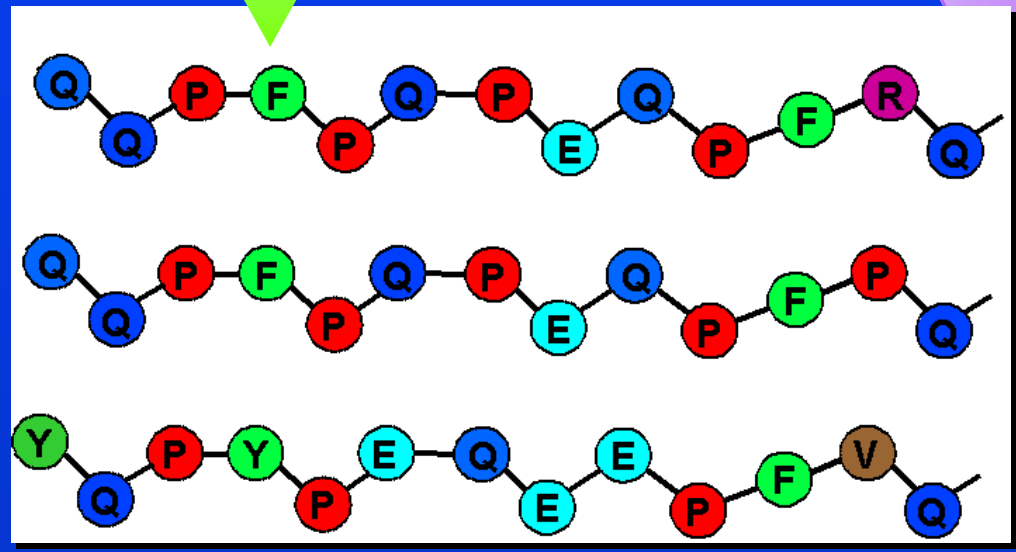
LQLQPFPQPQLPYPQPQLPYPQPQLPYPQPQPF

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

HORDEIN - α9

SECALIN - α9

AVENIN - α9



GLIADIN DETOXIFICATION BY CARICAIN

GLUTEGUARD - CARICA PAPAYA EXTRACT,

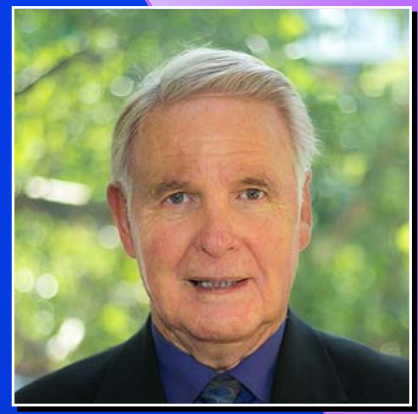
CONTAINS HYDROLYTIC ENZYMES CARICAIN AND OTHER PROLYL-ENDOPEPTIDASES,

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.)



Cornell HJ, Stelmasiak T. The Significance of Key Amino Acid Sequences in the Digestibility and Toxicity of Gliadin Peptides in Celiac Disease. International Journal of Celiac Disease, 2016, Vol. 4, No. 4, 113-120

GLUTEN DEGRADING, CLEAVING, FOOD SUPPLEMENTS

Wobenzym® N

Suggested Use: Adults take 3 tablets twice daily on an empty stomach at least 45 minutes before meals with water. Not intended for children.

Advanced Usage: Adults may gradually increase to 12 per day by taking 3 tablets 4 times per day on an empty stomach.

Supplement Facts

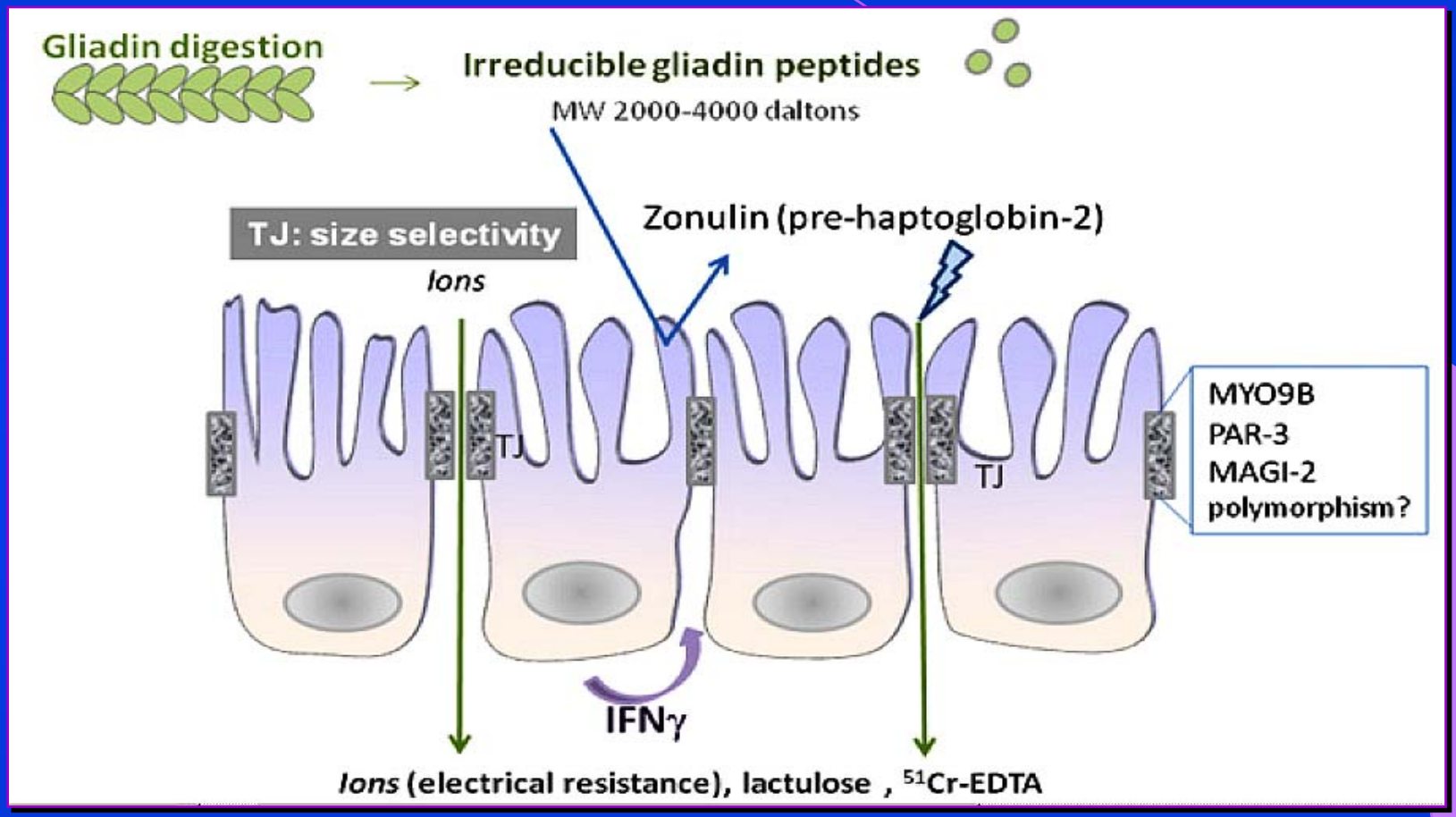
Serving Size 3 Tablets
Servings Per Container 33

	Amount Per Serving	%DV
Pancreatin** 56,000 USP units protease (pancreas) *Sus scrofa*	300mg	+
Papain** 492 FIP-units*** *Carica papaya*	180mg	+
Bromelain** 675 FIP-units *Ananas comosus*	135mg	+
Trypsin** 2,160 FIP-units (pancreas) *Sus scrofa*	72mg	+
Chymotrypsin** 900 FIP-units (pancreas) *Bos taurus*	3mg	+
Rutoside trihydrate** (Rutin) *Sophora japonica*	150mg	+

+ Daily Value (DV) not established

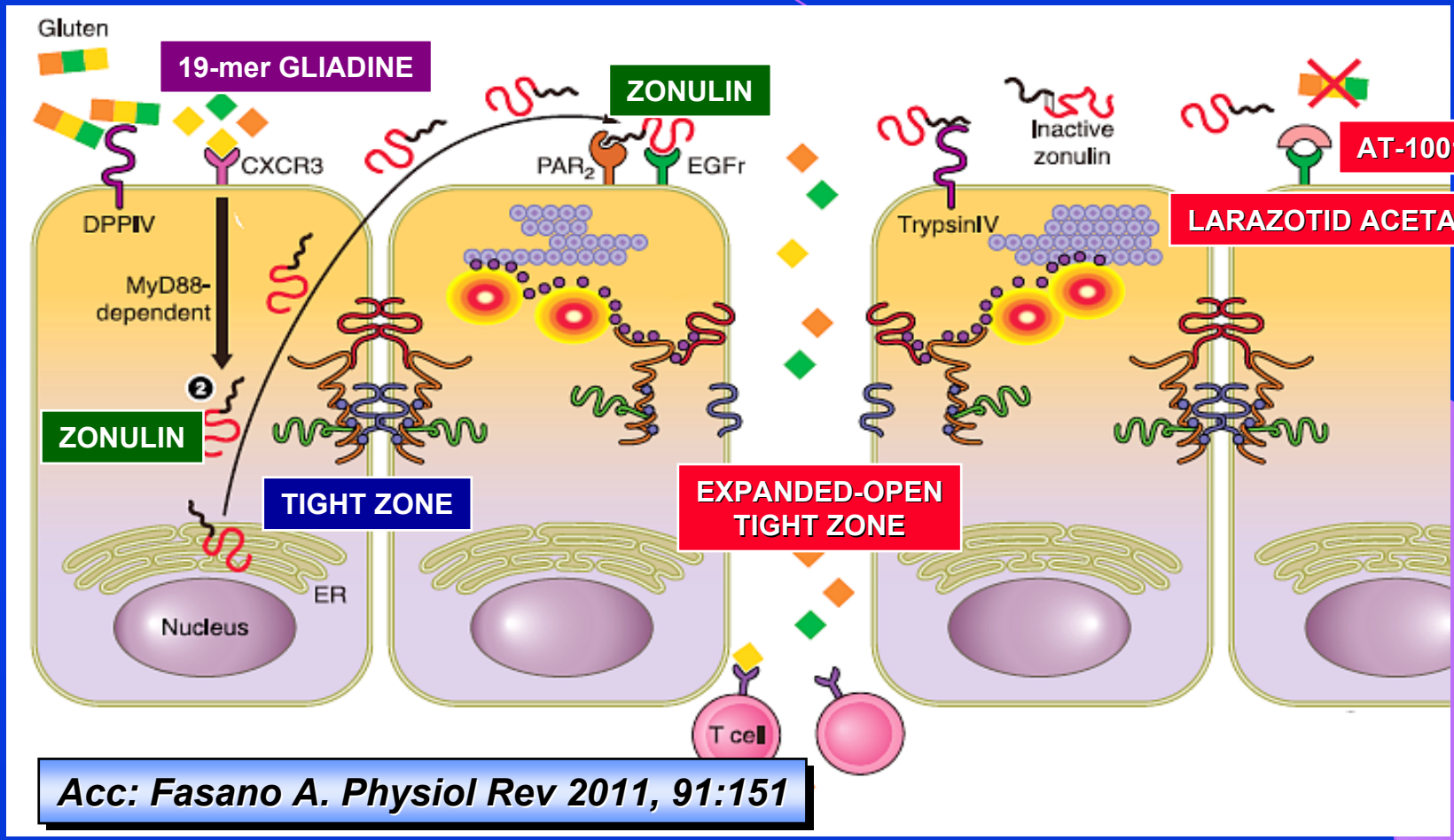
FOOD SUPPLEMENTS CONTAINING GLUTEN DEGRADING ENZYMES, DECLARED BY THE MANUFACTURER AS INTENDED FOR PERSONS WITH GLUTEN INTOLERANCE

SMALL BOWEL PERMEABILITY - ZONULIN



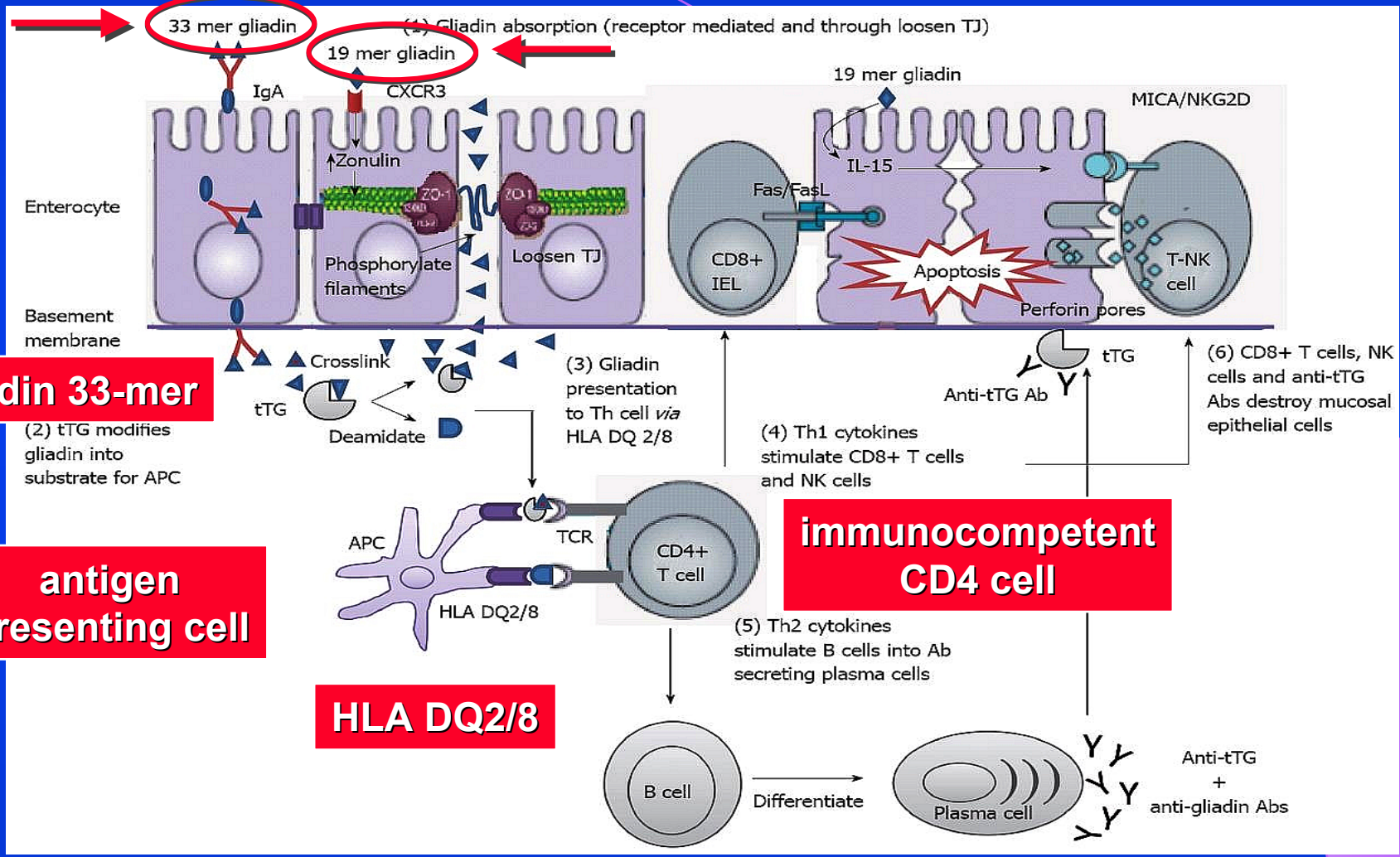
Intestinal permeability in coeliac disease: insight into mechanisms and relevance to pathogenesis. Heyman M, Abed J, Lebreton C, Cerf-Bensussan N. Gut. 2012 Sep;61(9):1355-1364

COELIAC THERAPY - ZONULIN INHIBITION



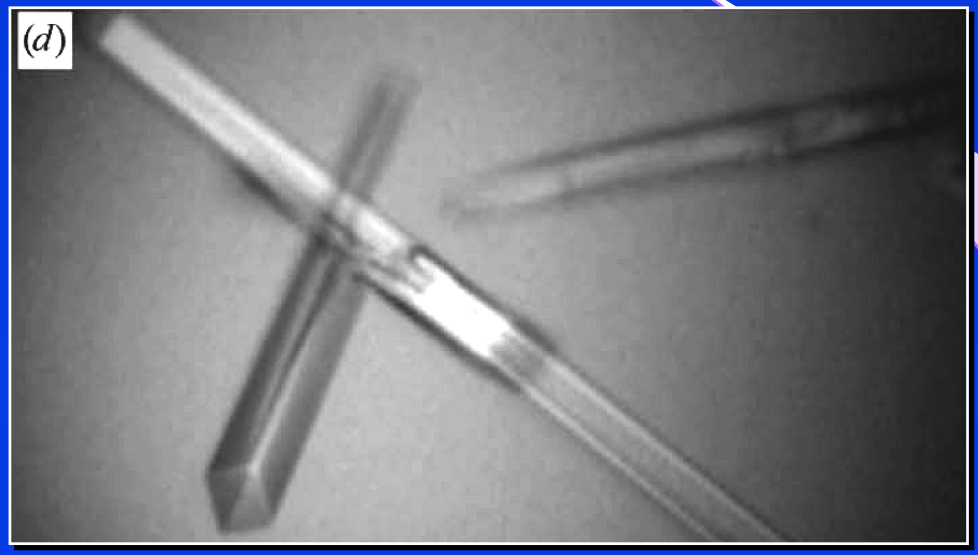
Acc: Fasano A. Physiol Rev 2011, 91:151

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



Celiac disease: prevalence, diagnosis, pathogenesis and treatment. Gujral N, Freeman HJ, Thomson AB. World J Gastroenterol. 2012 Nov 14;18(42):6036-6059

PERSPECTIVE THERAPY OF COELIAC DISEASE

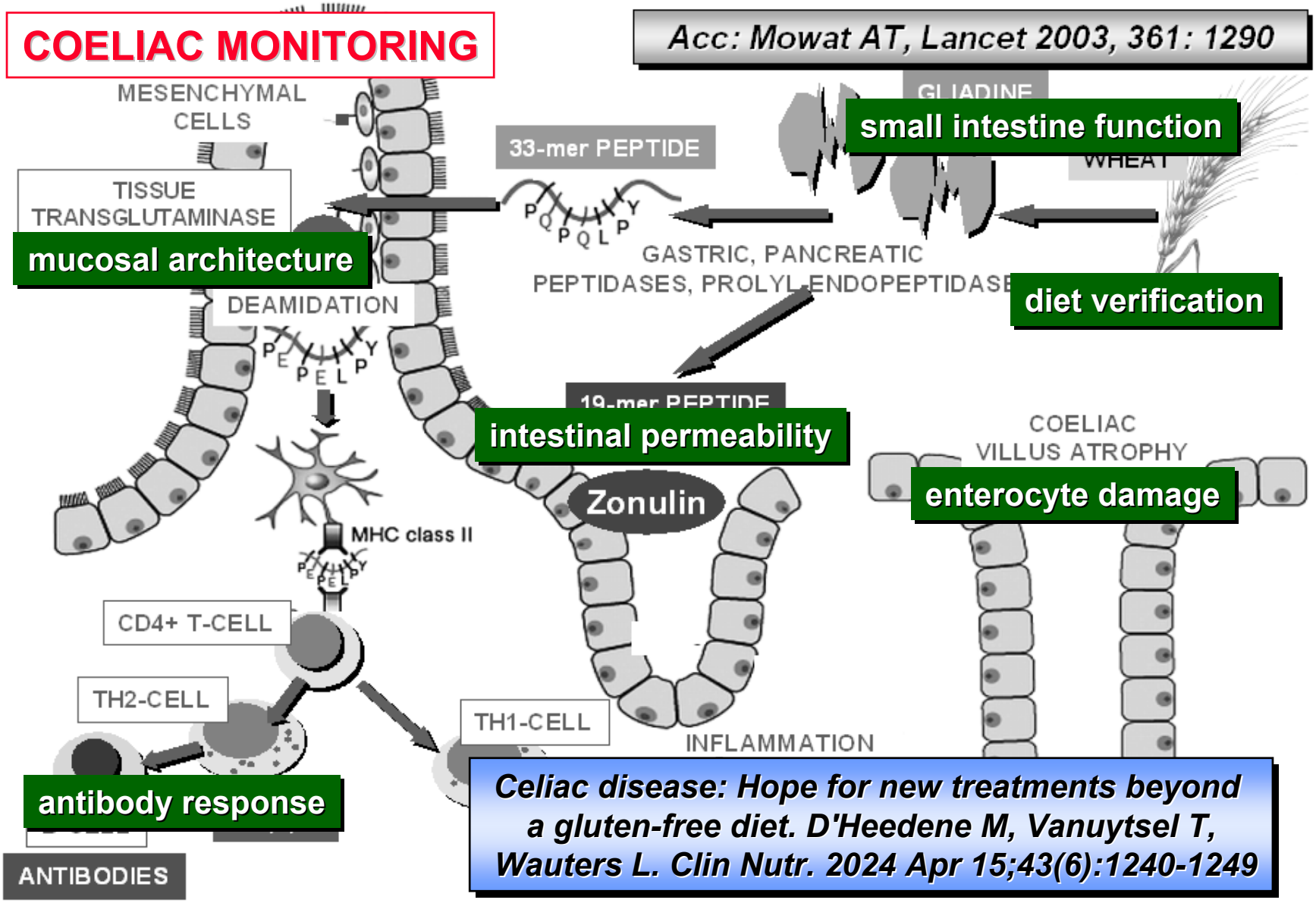


HLA-DQ8 CRYSTAL WITH DEAMIDATED PEPTIDE α_1 Gli - EGSFQPSQE

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

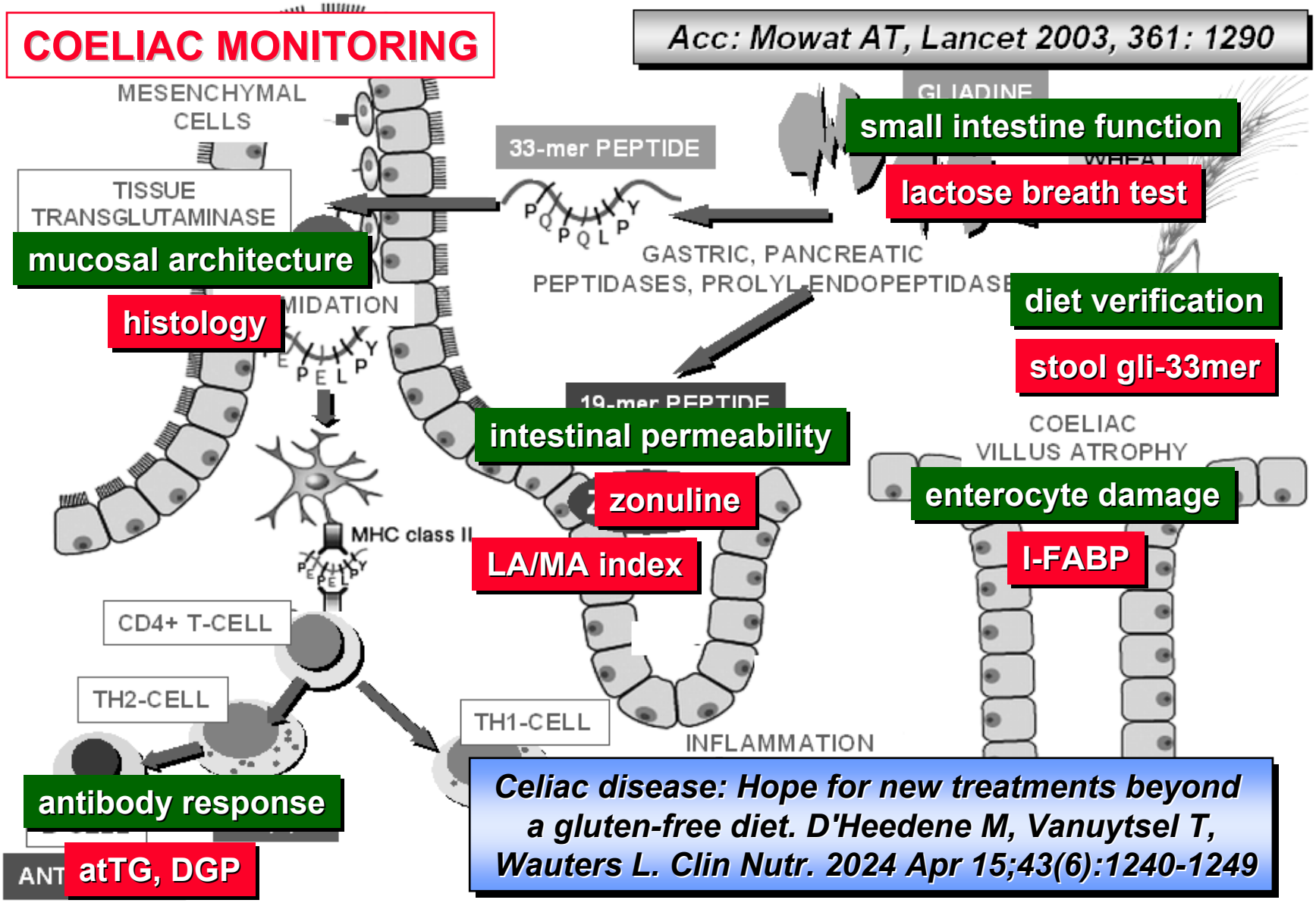
Acc: Mowat AT, Lancet 2003, 361: 1290



Celiac disease: Hope for new treatments beyond a gluten-free diet. D'Heedene M, Vanuytsel T, Wauters L. Clin Nutr. 2024 Apr 15;43(6):1240-1249

COELIAC MONITORING

Acc: Mowat AT, Lancet 2003, 361: 1290



small intestine function

lactose breath test

mucosal architecture

diet verification

histology

stool gli-33mer

intestinal permeability

zonuline

enterocyte damage

LA/MA index

I-FABP

antibody response

atTG, DGP

Celiac disease: Hope for new treatments beyond a gluten-free diet. D'Heedene M, Vanuytsel T, Wauters L. Clin Nutr. 2024 Apr 15;43(6):1240-1249

SMALL INTESTINE FUNCTIONAL TESTS

Hydrogen analyzer
Lactotest 202

LACTOSE BREATH TEST

LOAD 20g LACTOSE

HYDROGEN / METHANE MEASUREMENT 5 HOURS, CUT-OFF CRITERION 20 ppm

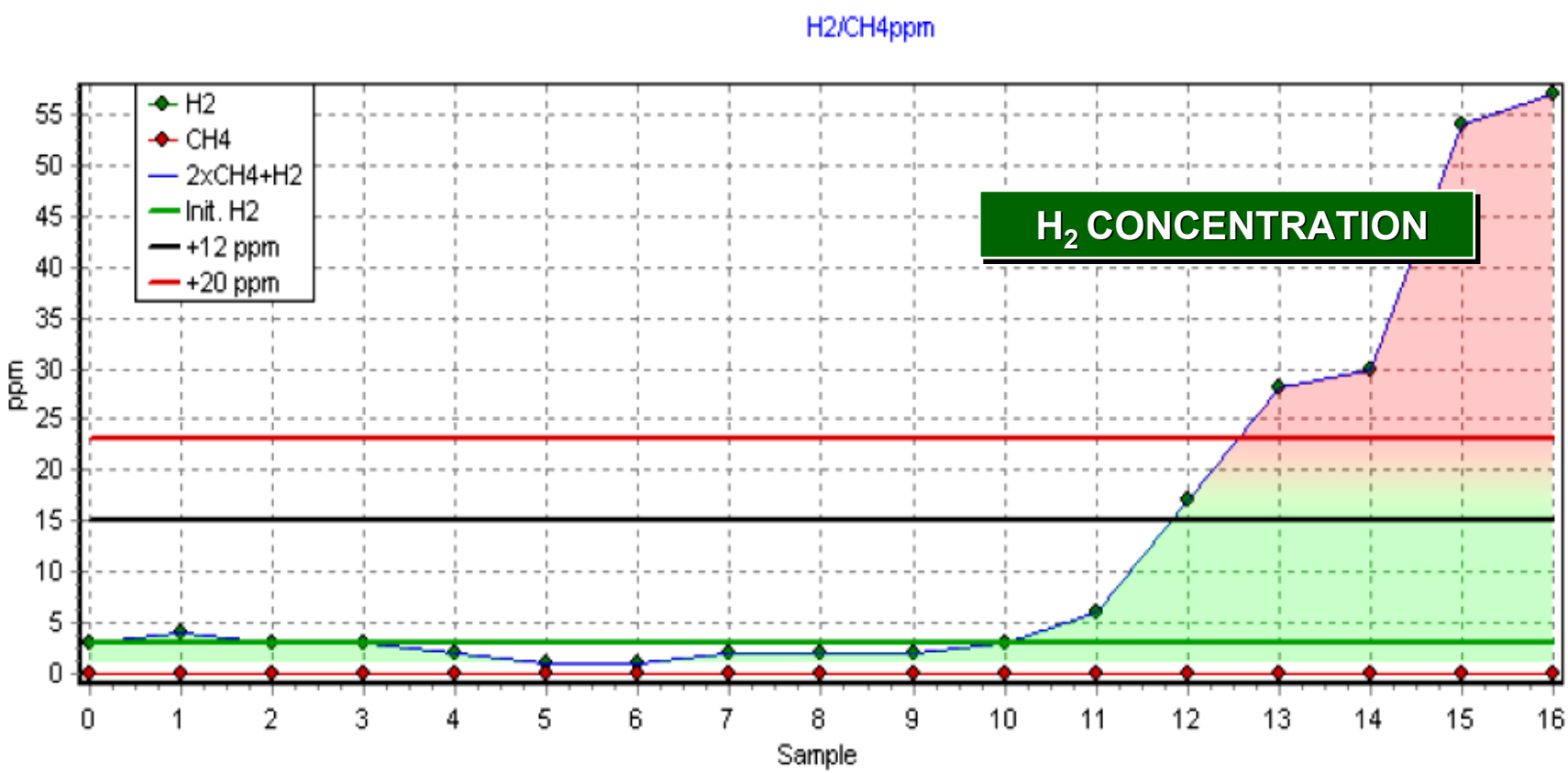
METHANOGENIC BACTERIA

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

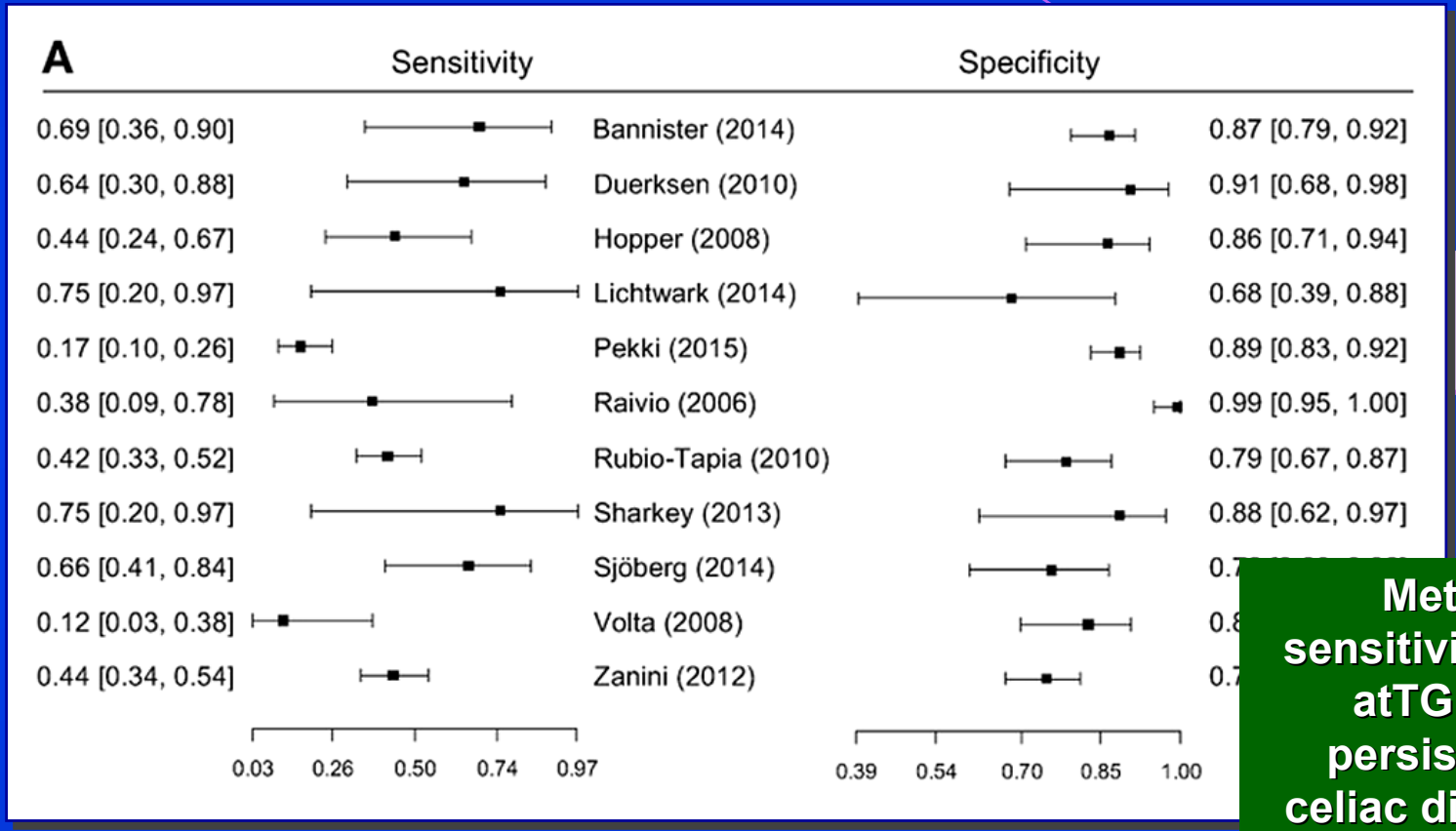
H_2 /CH_4 /CO_2 - LACTOSE INTOLERANCE TEST



H_2 CONCENTRATION

20 g LACTOSE

atTG ANTIBODIES - TEST / MANUFACTURER VARIABILITY



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

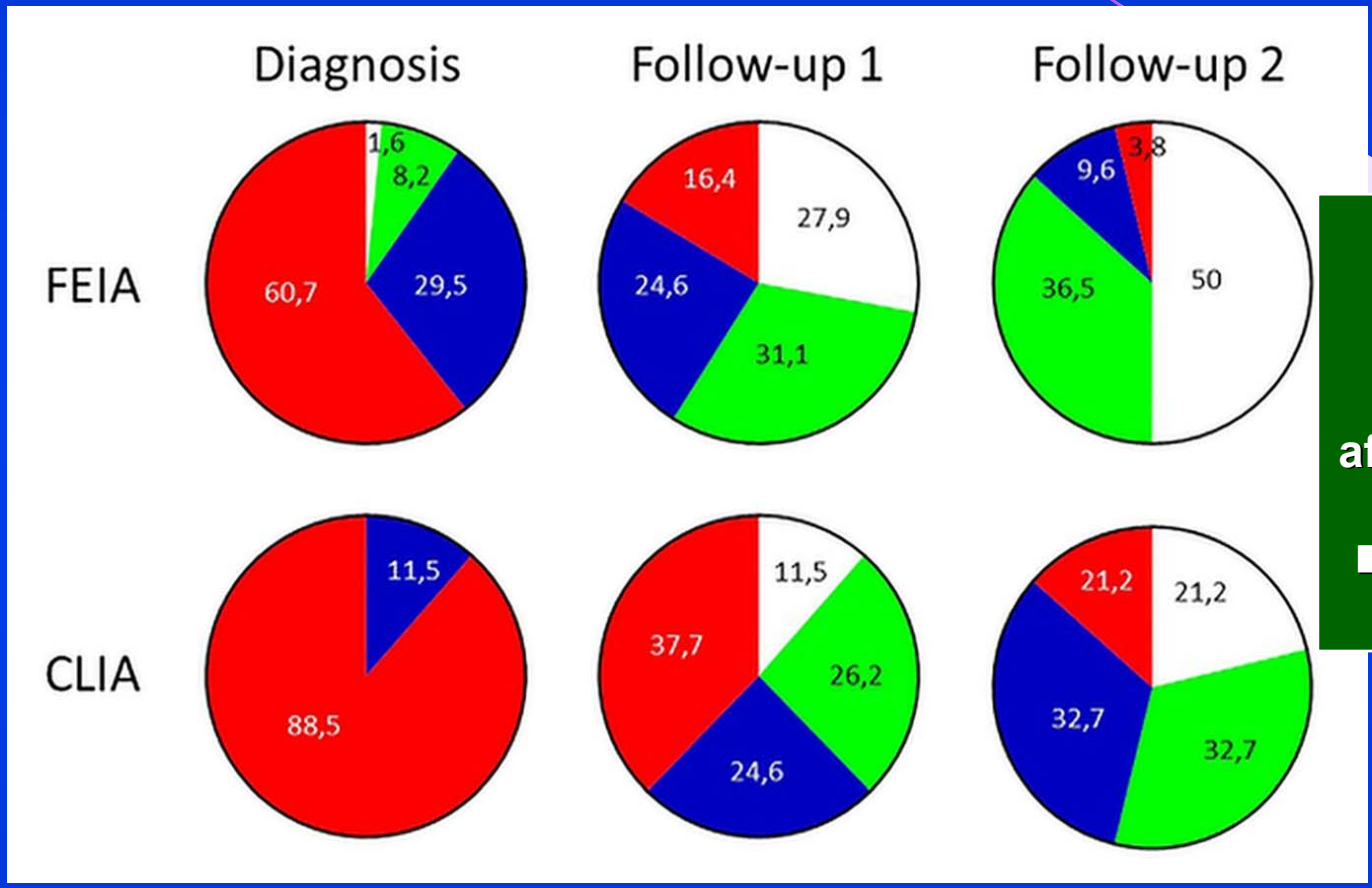
Tests for Serum Transglutaminase and Endomysial Antibodies Do Not Detect Most Patients With Celiac Disease and Persistent Villous Atrophy on Gluten-free Diets Silvester JA, Kurada S, Szwajcer A. et al.: Gastroenterology. 2017; 153(3): 689 - 701

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

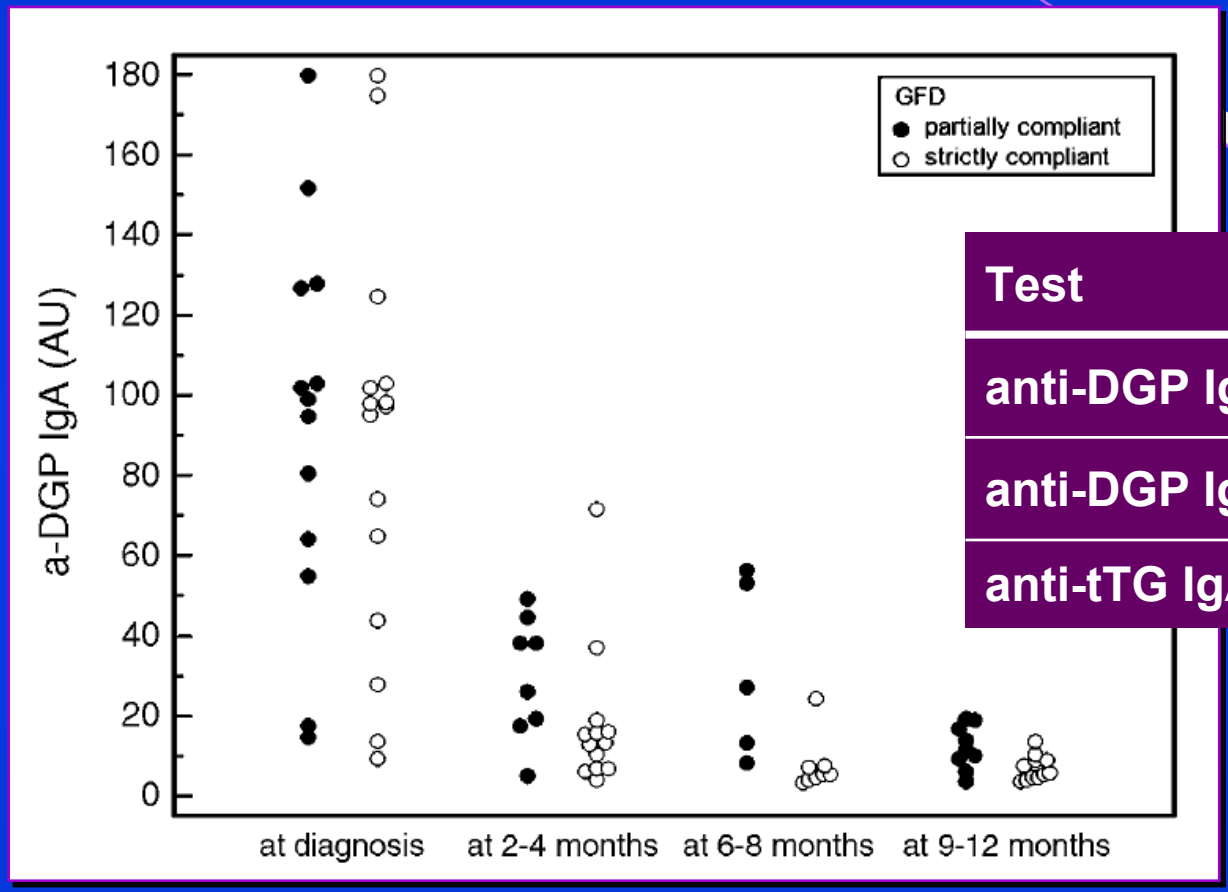
atTG ANTIBODIES - TEST / MANUFACTURER VARIABILITY



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, Castelijn 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.

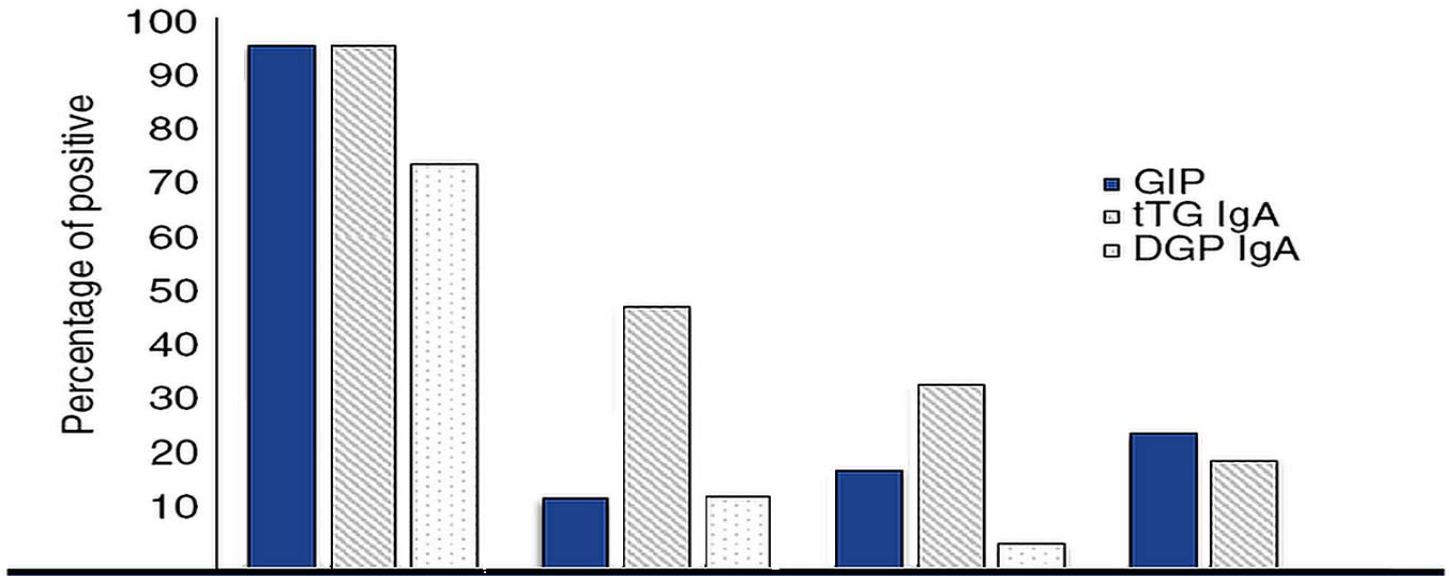
Detection of excreted GIP in stool or urine is an accurate approach to determine voluntary or involuntary consumption of gluten. Isolated GIP measurements may not identify intermittent dietary adherence, and the use of multiple samples contributes to higher sensitivity and specificity of GIP detection.

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

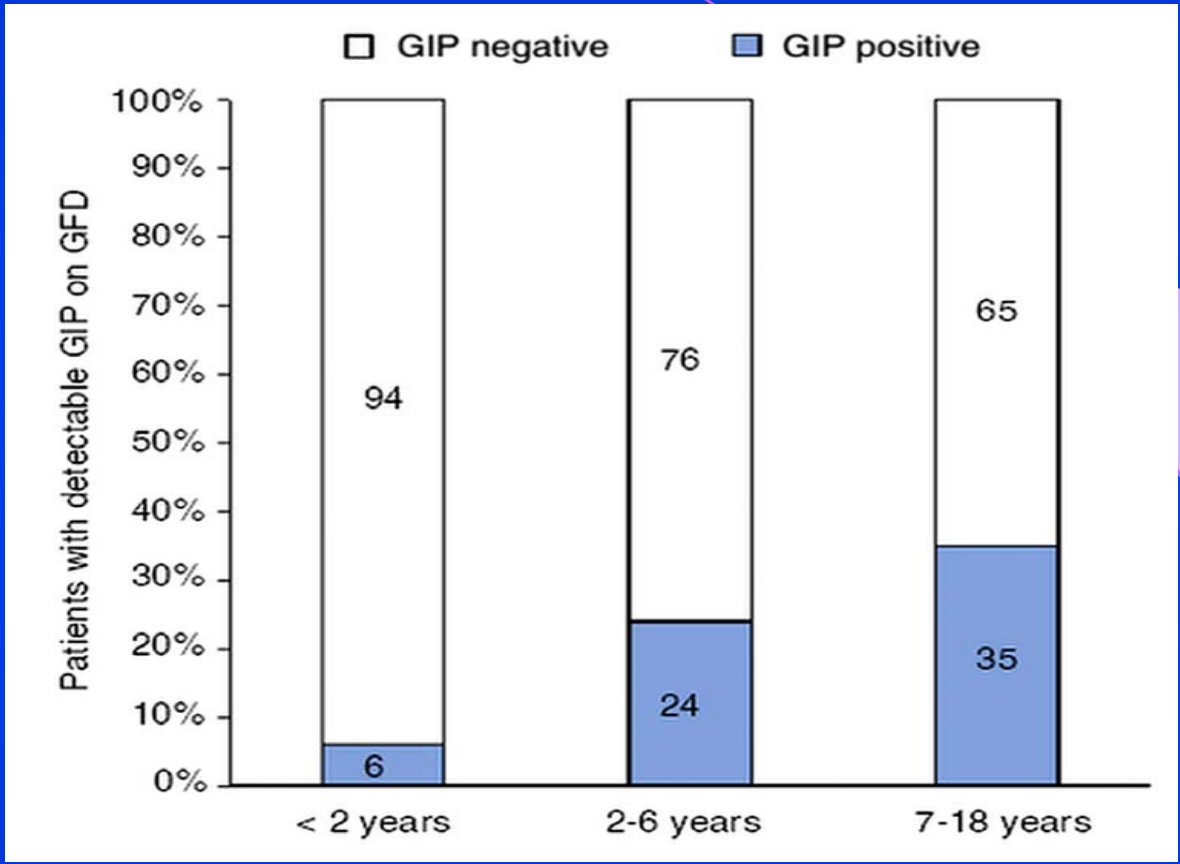
GIP - GLIADIN 33mer IN STOOL



	Diagnosis	6 months	12 months	24 months
GIP	97% (62/64)	13% (7/54)	18% (7/39)	25% (6/24)
tTG IgA	97% (59/61)	48% (29/60)	34% (17/50)	20% (7/35)
DGP IgA	75% (45/60)	11% (7/63)	5% (2/44)	0% (0/27)

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

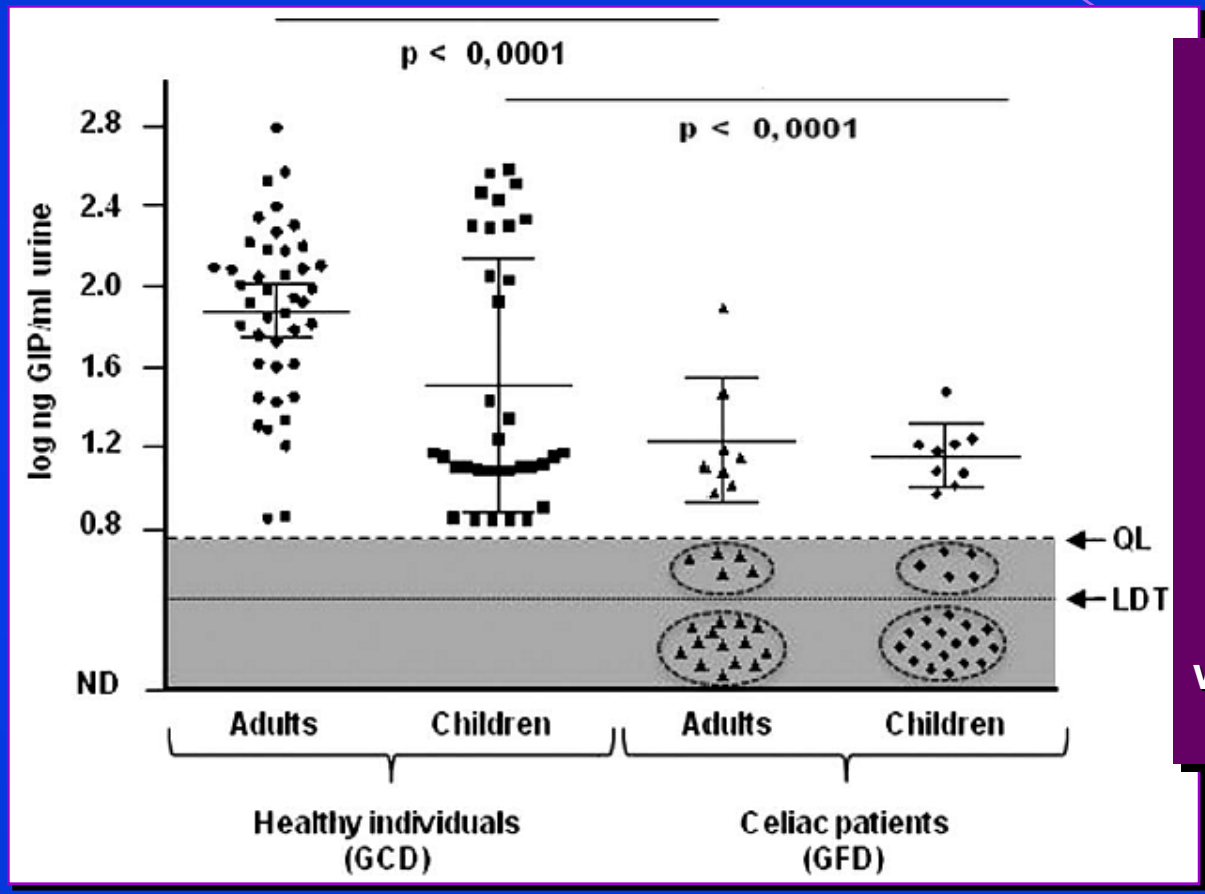
GIP - GLIADIN 33mer IN STOOL

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 immunochromatographic 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

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

http://gelab.zde.cz

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

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

Intro

Abecední přehled metodik

Miniencyklopedie laboratorních metod v gastroenterologii

GastroLab

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 specificita 88-98%). Stanovení atTG je prováděno klasickou metodou ELISA, což je pro rutinní diagnostiku technika dostupnější než immunofluorescenční průkaz EmA.

Protilátky atTG lze na rozdíl od EmA stanovovat 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

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