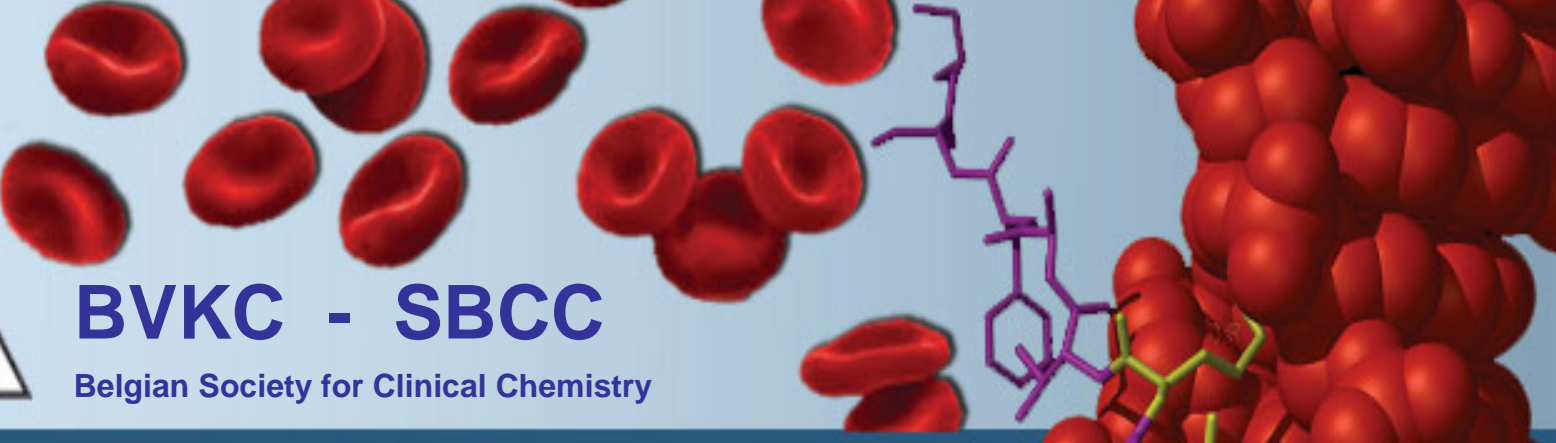




**BVKC - SBCC**

Belgian Society for Clinical Chemistry



Belgische Vereniging voor Klinische Chemie  
Société Belge de Chimie Clinique

invite you to their symposium:

**INNOVATIONS IN  
CLINICAL LABORATORY  
MANAGEMENT AND  
DIAGNOSIS**

**Grimbergen  
Thursday, May 24<sup>th</sup> 2007**

**Dear visitor**

**This is one of the presentations of the 2007 symposium of the BVKC-SBCC.**

**This presentation was kindly provided by the speaker, who has made a great effort in preparing his/her talk.**

**We kindly ask you that, when using (parts of) this document, you correctly refer to this original presentation.**

**Thank you in advance.**

# Laboratory Diagnosis of Celiac Disease

X. Bossuyt

UZ – KU Leuven

# Celiac Disease

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Malabsorption resulting from inflammatory injury to the mucosa of the small intestine after ingestion of wheat gluten

or related rye and barley proteins

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# Pathogenesis

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inappropriate T-cell-mediated immune response

against ingested gluten

in genetically predisposed people

- 10% prevalence in first-degree relatives
  - HLA-DQ2 / HLA-DQ8
-

# Clinical presentation

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## Common features

### Adults:

- iron-deficiency anemia
- diarrhea

### Children:

- diarrhea
- failure to thrive
- abdominal distention

## Less common features

### General:

- short stature
- delayed puberty

### Gastro-intestinal:

- aphthous stomatitis
- steatorrhea

### Extra-intestinal:

- folate, vit K deficiency
- osteoporosis
- dental-enamel hypoplasia
- hypertransaminasemia ...

# Clinical presentation

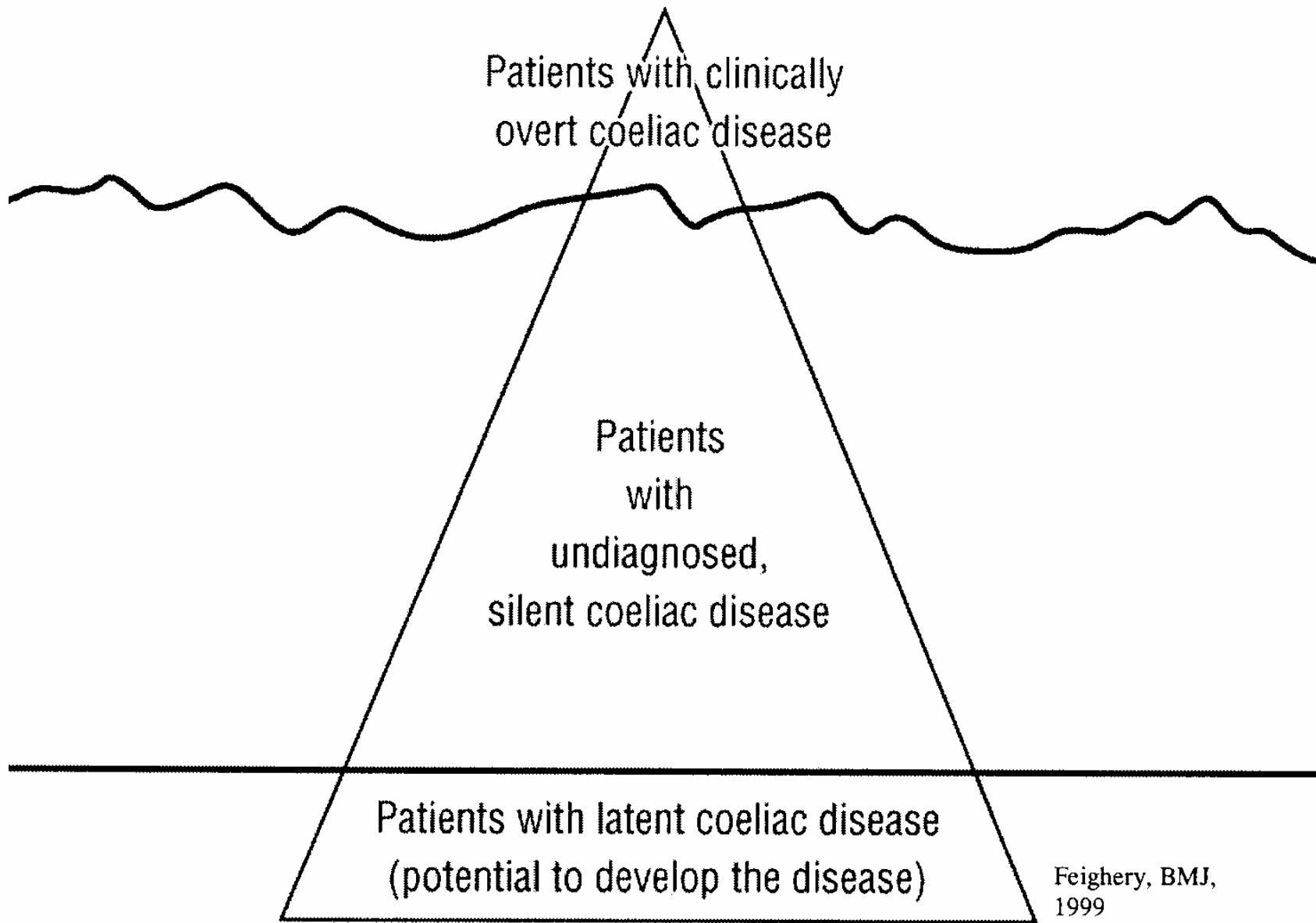
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## Associated conditions

- dermatitis herpetiformis
- IgA deficiency
- type I diabetes
- autoimmune thyroid disease
- Sjögren's syndrome

## Complications

- refractory disease
- enteropathy-associated T-cell lymphoma
- carcinoma oropharynx, carcinoma esophagus, small bowel jejunoileitis



Feighery, BMJ, 1999

# Diagnosis

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biopsy small intestine (distal duodenum)

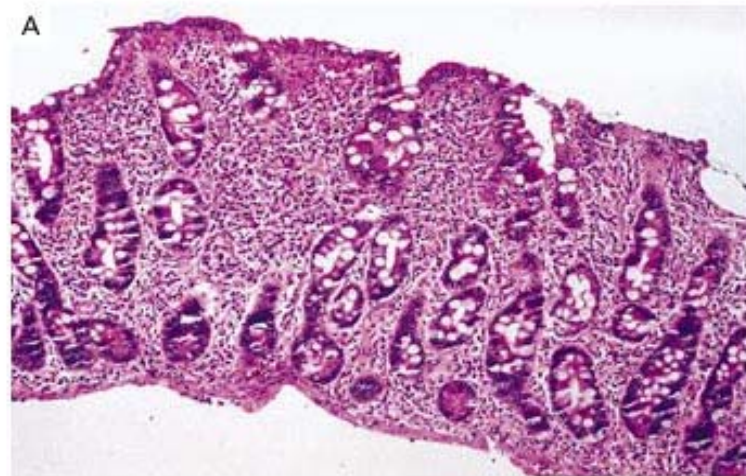
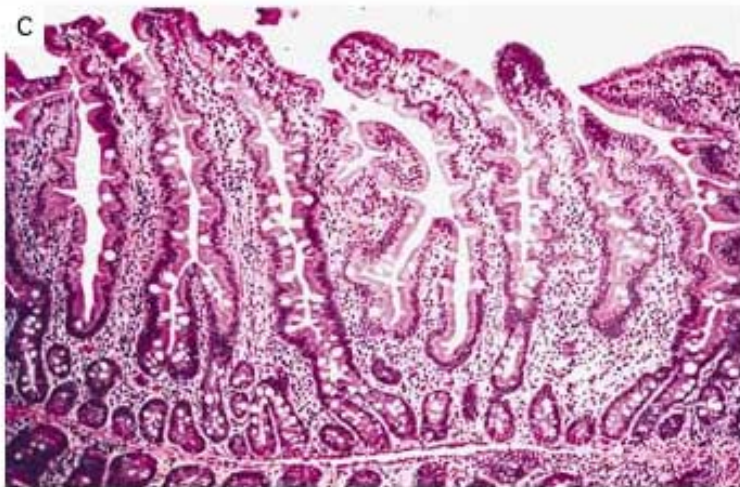
mucosal architectural changes

absent villi

hyperplastic crypts

increased numbers of intraepithelial

lymphocytes & plasma cells in lamina propria

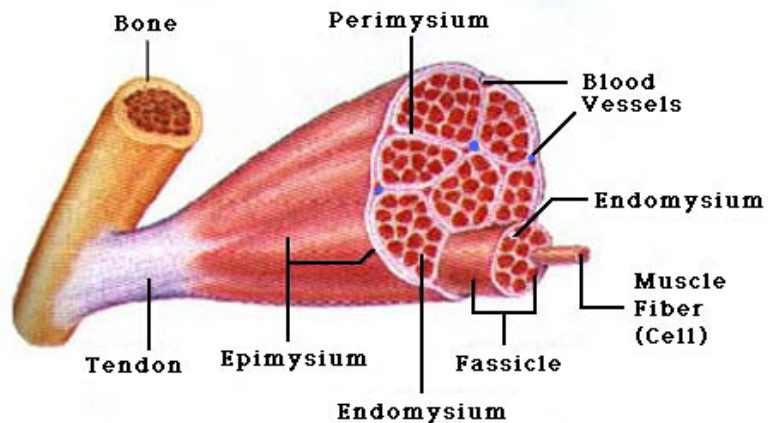


# Diagnosis

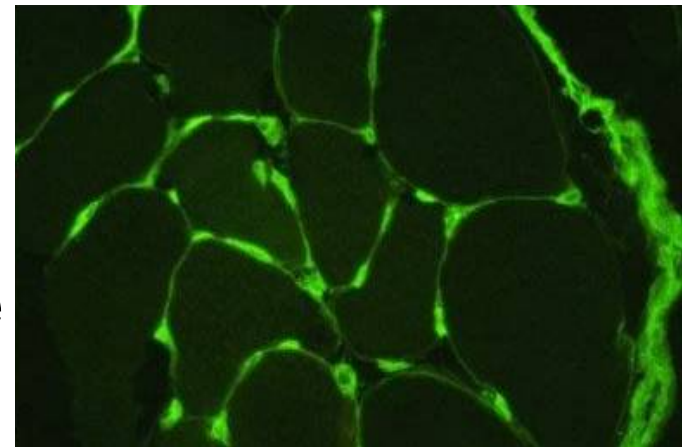
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serology

- (reticulin)
- gliadin
- endomysium
- tissue transglutaminase (1997)



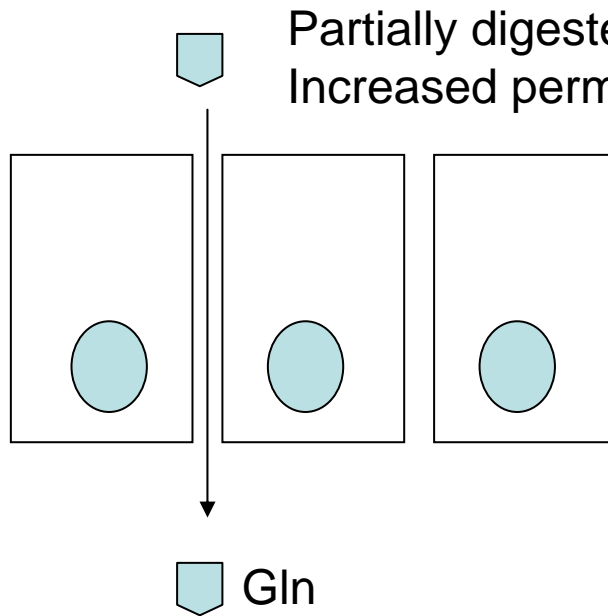
- Gliadin
  - Low specificity
  - Lack of standardization
    - Antigen: crude extract,  $\alpha$ -gliadin
    - New developments: deaminated gliadin
- Endomysium
  - Monkey oesophagus
  - Indirect immunofluorescence



Lumen

Epithelial barrier

Subepithelial region



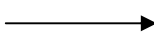
Partially digested gluten peptides  
Increased permeability of mucosa

direct toxic effect gluten  
pro-inflammatory trigger  
e.g. infection

Gln

Inflammation

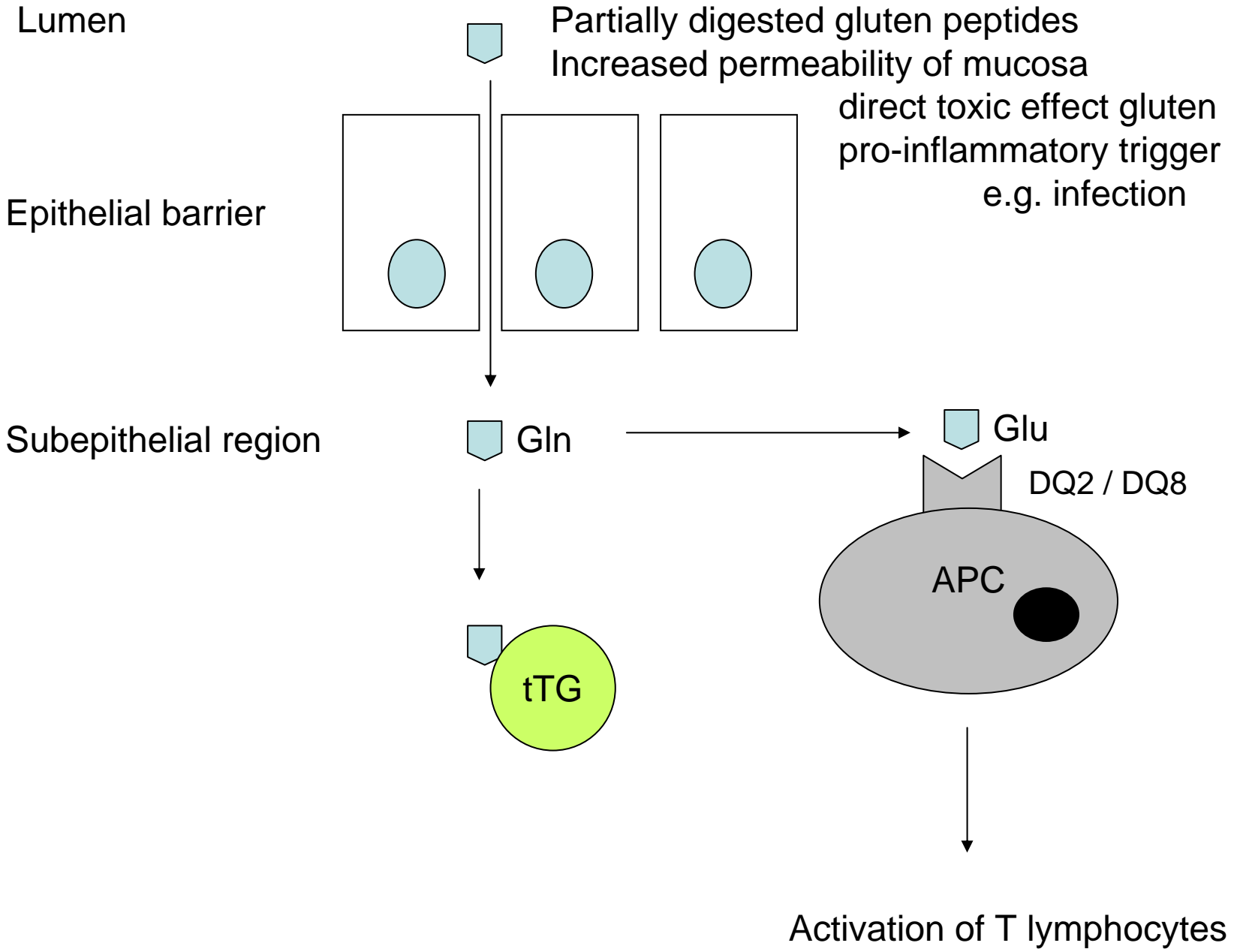
Mechanical stress

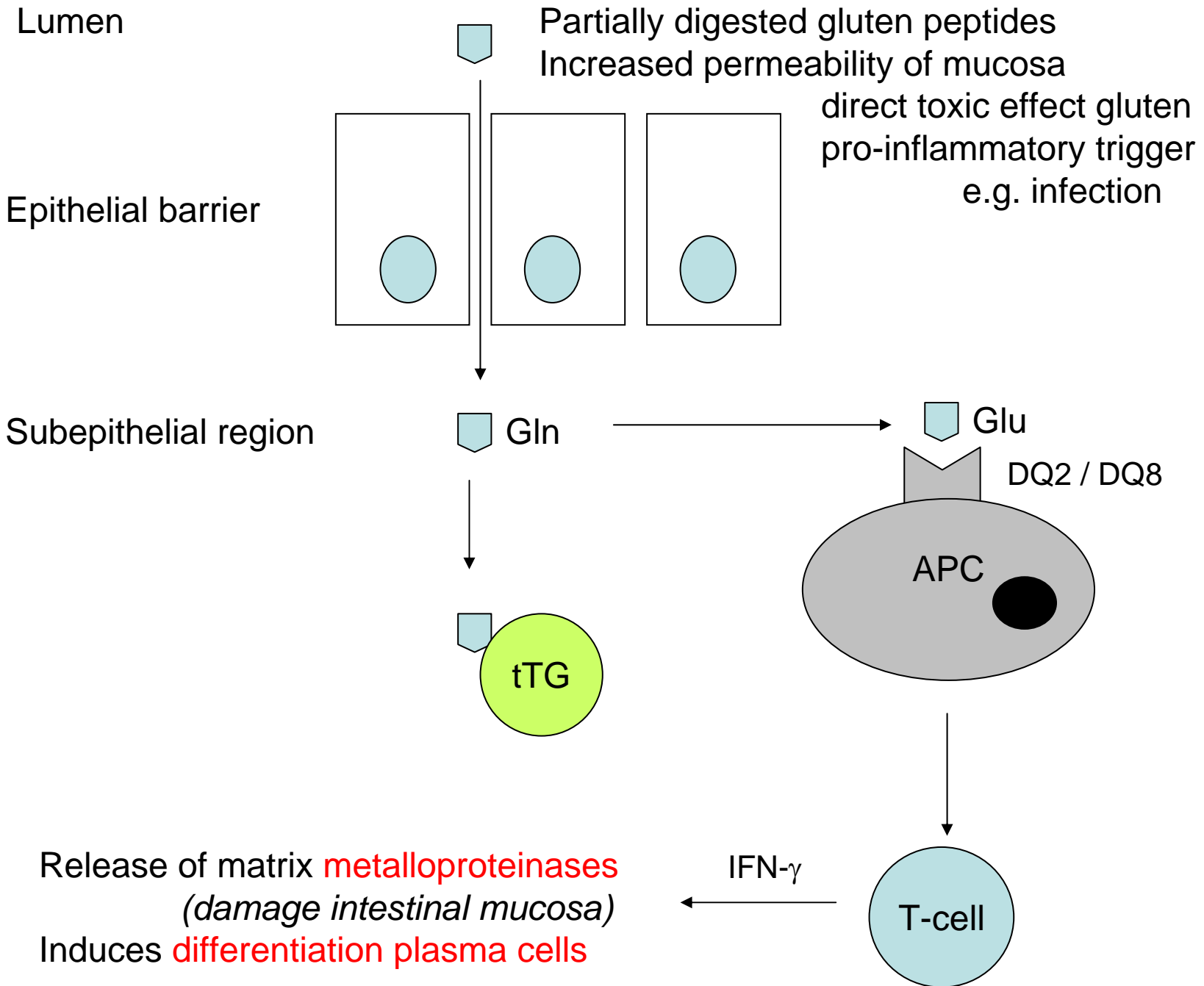


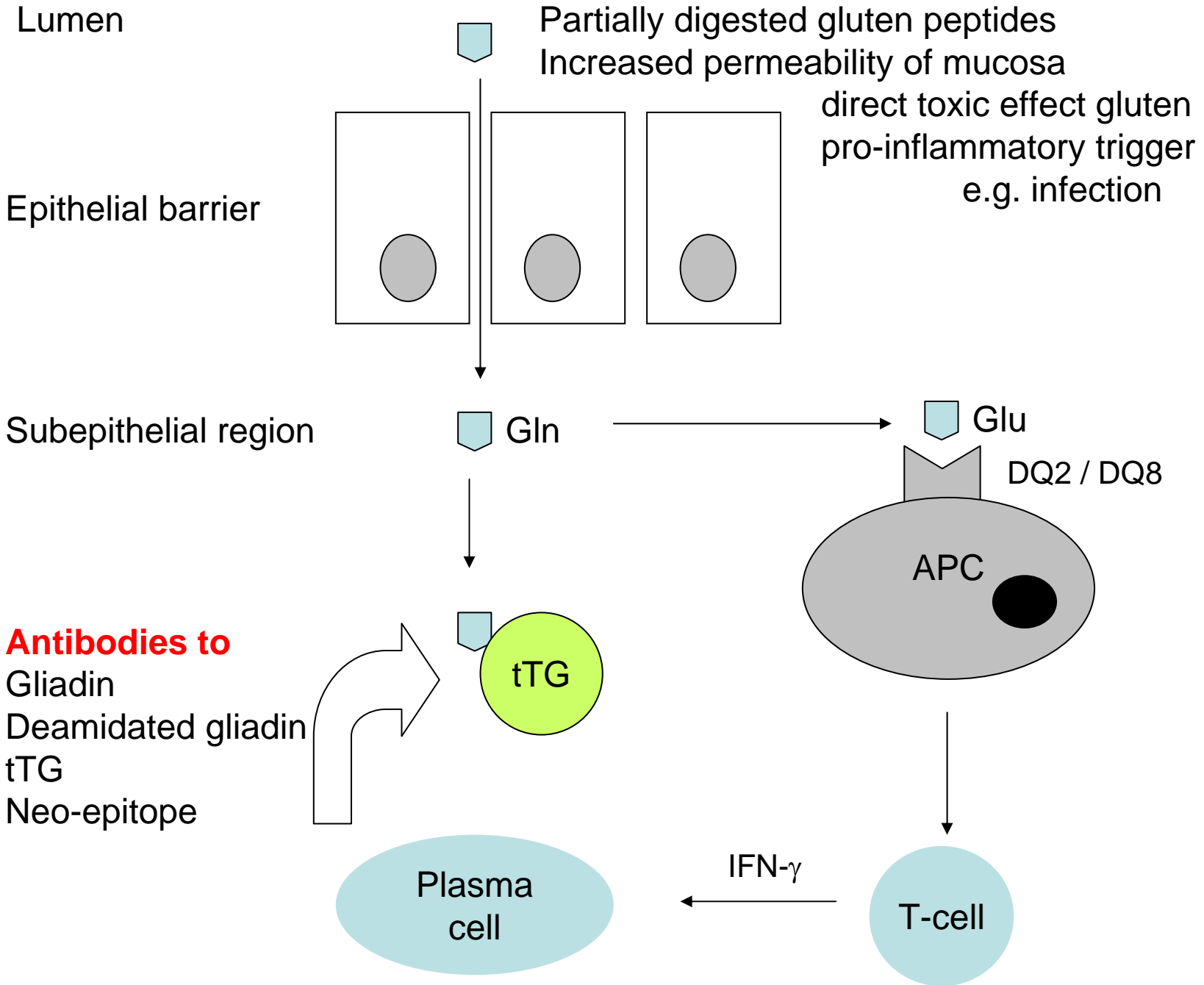
**Tissue Transglutaminase**

deamidation of Gln to Glu (negative charge)

cross-linking gluten peptide with tTG (lysine)



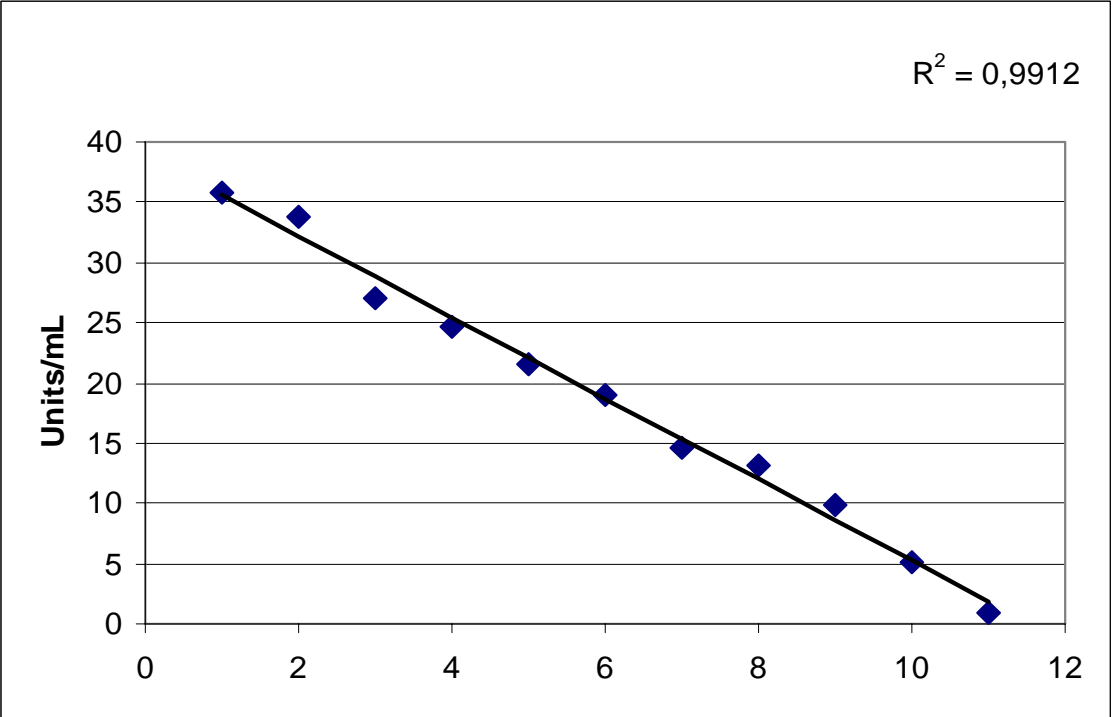




# Anti-tissue transglutaminase antibodies

- First generation (guinea pig)
- Second generation (human)
- Third (neo-epitope)
  
- Advantages
  - Automated
  - No use of primate tissue
  - Standardization is achievable

# Linearity

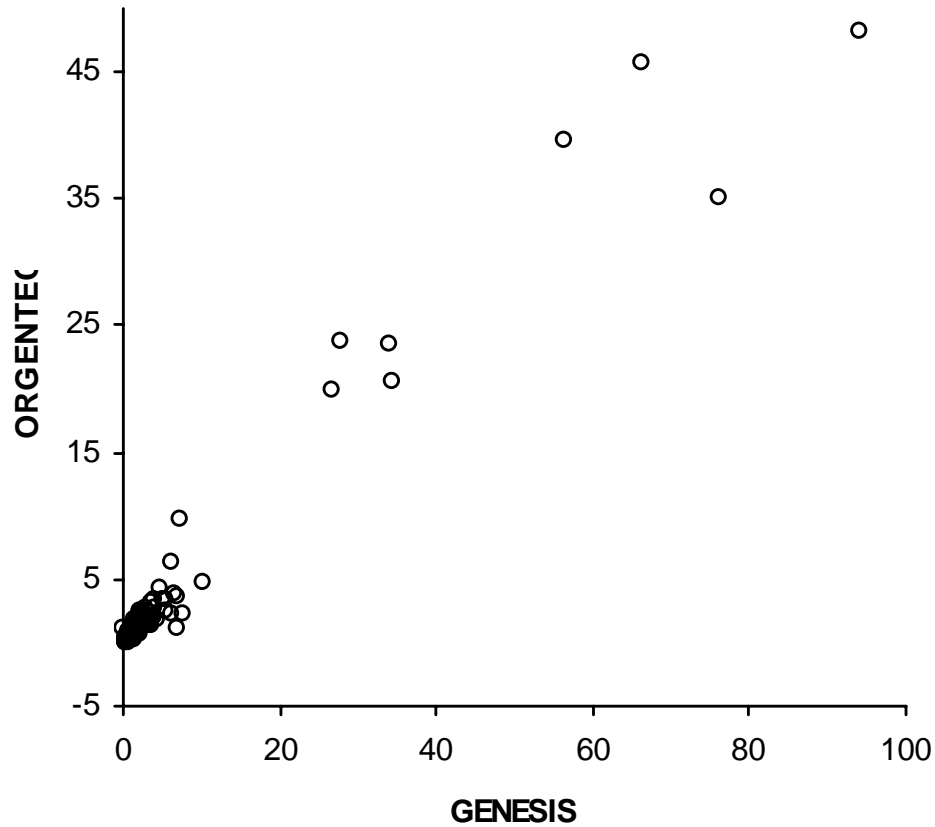


# Precision – CV (%)

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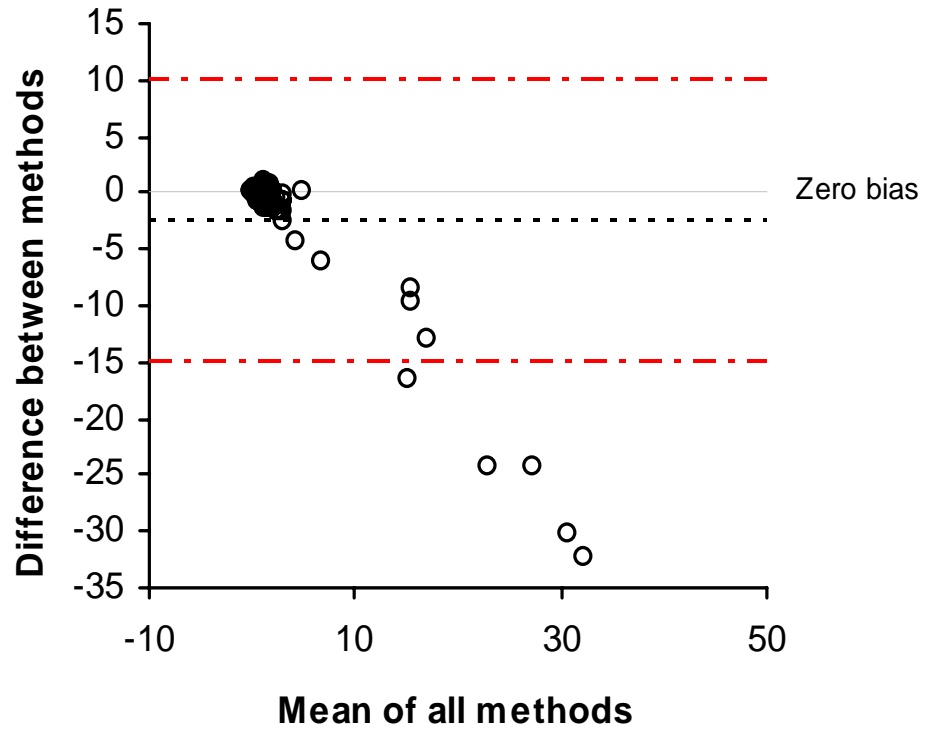
<b>Value sample</b>	<b>2</b>	<b>6</b>	<b>9</b>	<b>3</b>	<b>5</b>	<b>7</b>	<b>1</b>	<b>8</b>	<b>4</b>	<b>10</b>
Low	5.8	4.6	8.1	15	5	11.9	6.1	6.4	7.5	8.8
High	15	6.1	6	21.1	4.2	12.4	5.9	5.1	7.3	5.2

# Method Comparison - Correlation

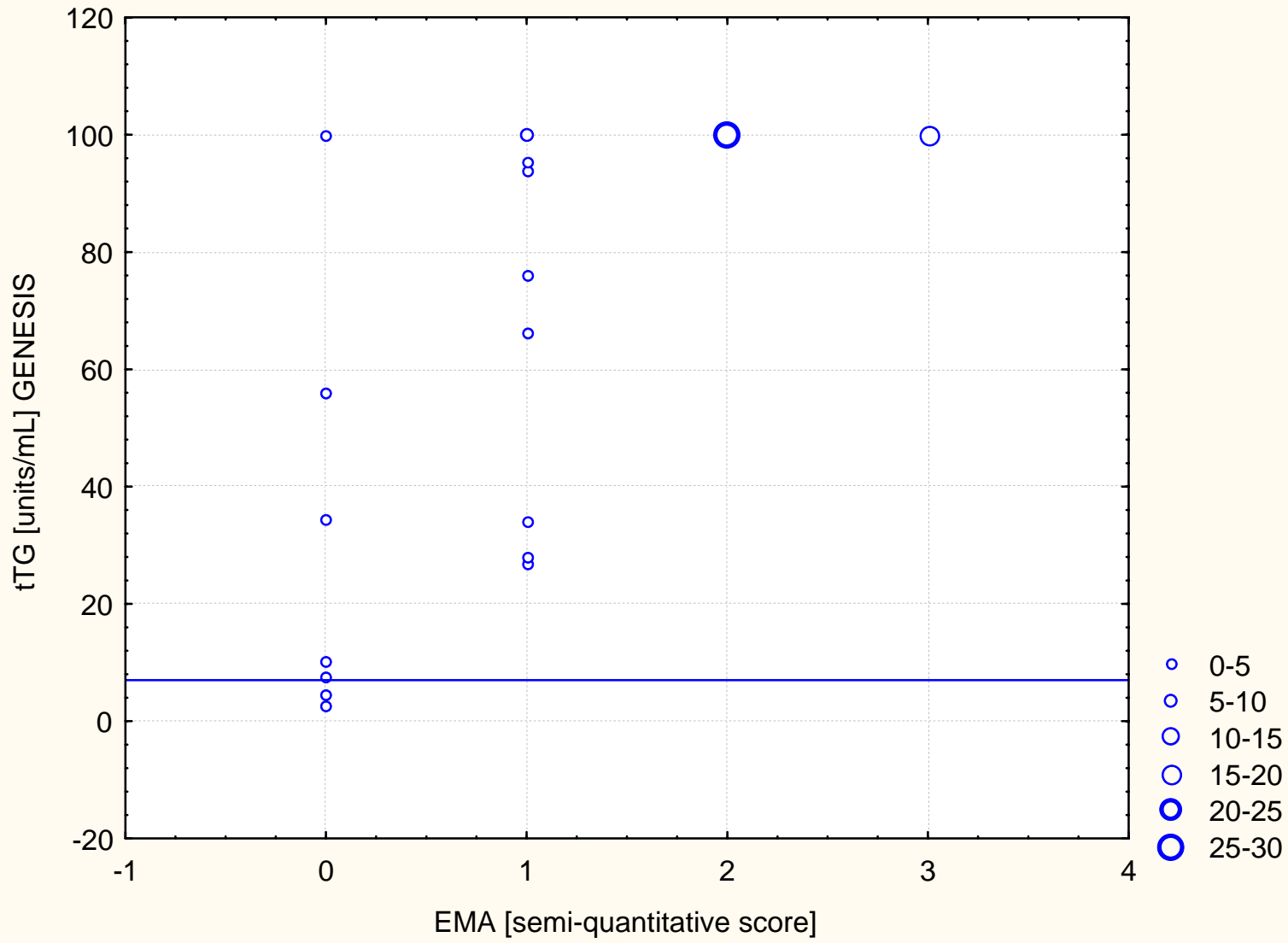


# Agreement

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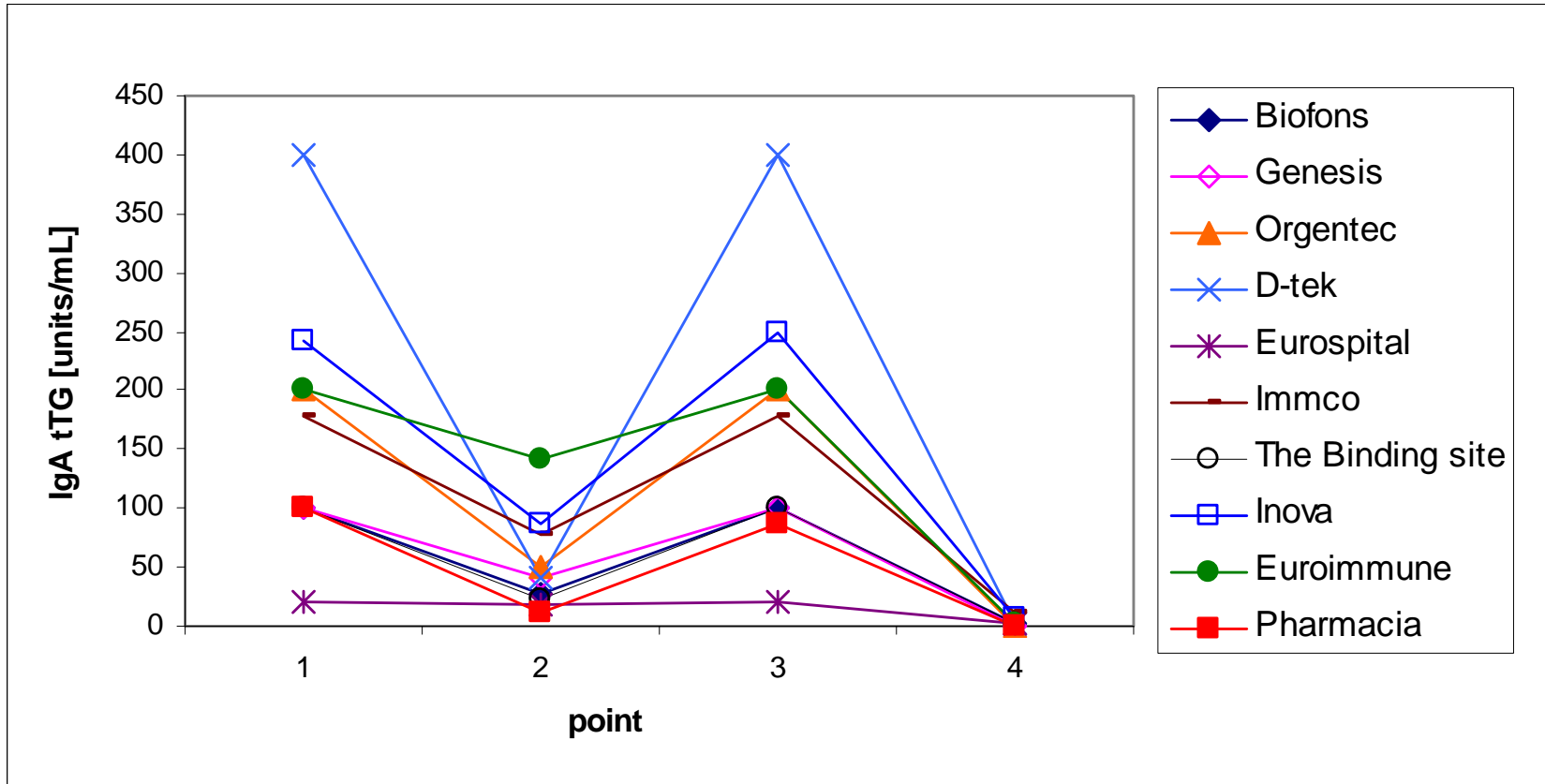
EMA versus tTG



# Diagnostical performance

	tTG IgA	EMA IgA	Giadin IgA	Gliadin IgG
Sensitivity	91 - 97	90	87	94
Specificity	96 - 100	100	91	76

# Follow-up

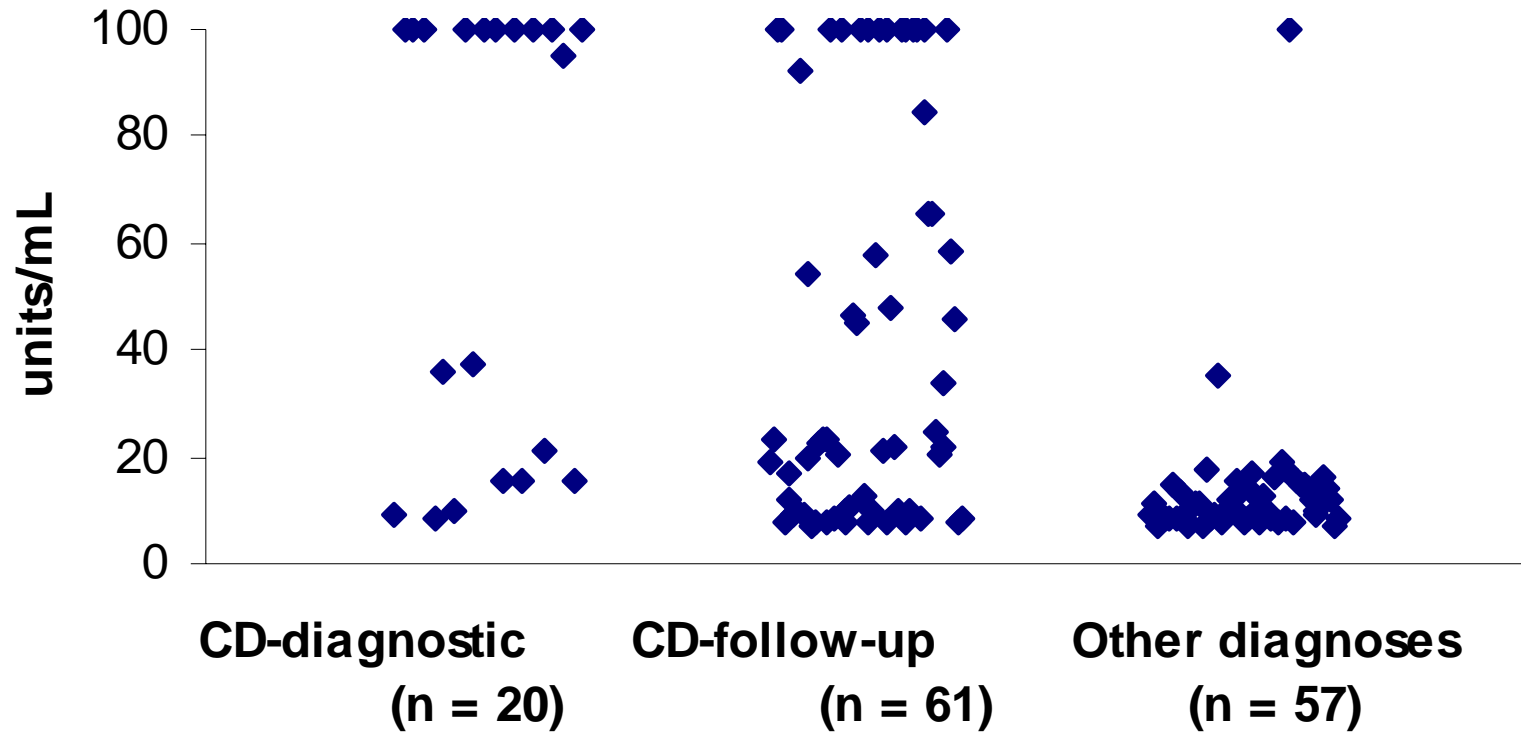


Monitoring IgA tTG antibodies in one patient at point 1 (diagnosis), 2 (3 months after starting gluten-free diet), 3 (gluten challenge) and 4 (one year after restarting gluten-free diet)

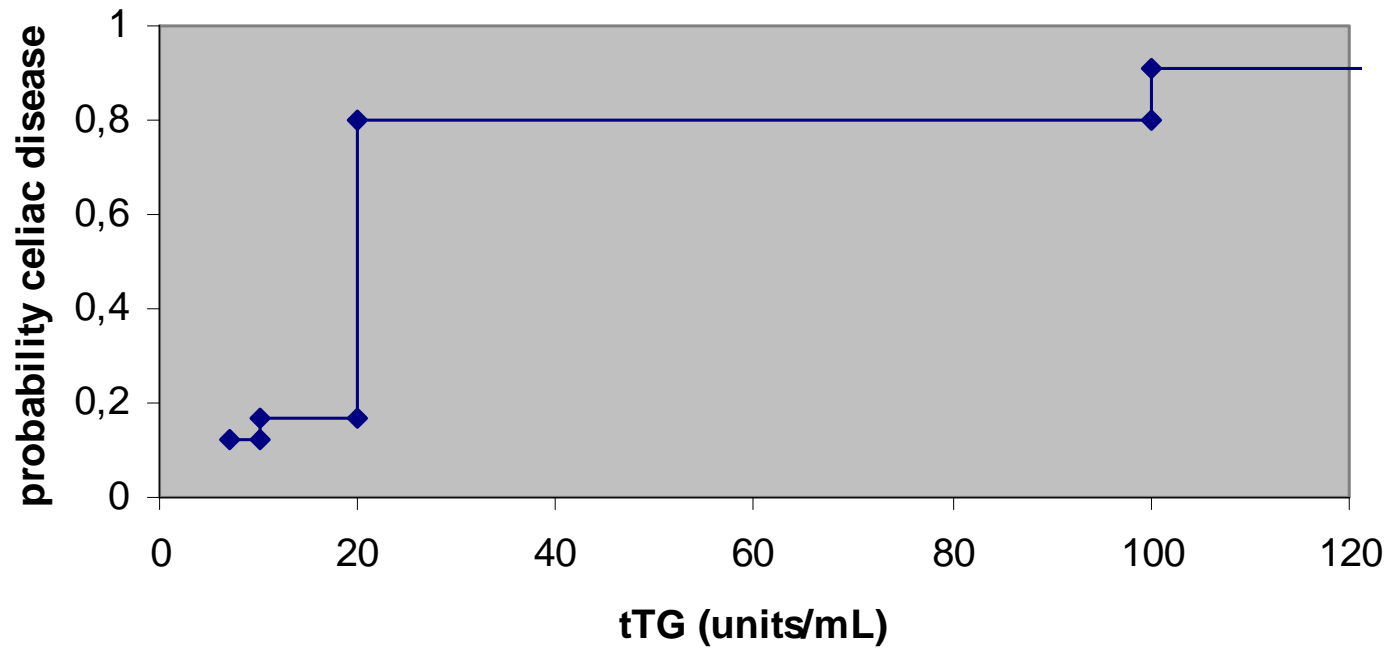
# tTG antibodies

- False positives
  - High polyclonal IgA (> 4 g/L)
  - Chronic liver disease
  - Case of anemia and monoclonal IgA
- False negatives
  - Neither EMA nor tTG Ab 100% sensitive
  - Some only anti-gliadin antibodies (low spec)

## Samples of patients with biopsy data



### Probability celiac disease as a function of tTG



# Testing Strategy

- The use of a panel of tests should be abandoned
- IgA determination
  - If not deficient: **IgA tTG**
  - If deficient: IgG tTG, IgG gliadin
- Other strategies exist

# Acknowledgements

- Dr Hiele Gastroenterology
- Dr Casteels Pediatrics
- Dr Geboes Pathology
- Dr Mariën Laboratory Medicine
- Apr Dries Coenen Laboratory Medicine
- Dr Van Meensel Laboratory Medicine