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Intestinal TCRγδ+ T cells and IL-4+ T cells: biomarkers to evaluate the transition from potential to acute celiac disease in paediatric patients

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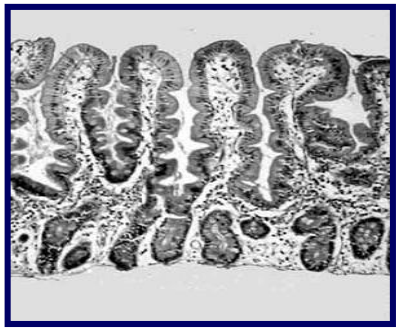
Celiac Disease

- ✓ Chronic disorder mainly affecting the small intestinal mucosa triggered by an inflammatory reaction to dietary gluten
- ✓ Incidence: 1:100, prevalence 0.3-2.4% (in Europe)
- ✓ Presence of autoantibodies against tissue-transglutaminase, with high diagnostic relevance
- ✓ Very strong association with HLA genes: almost 100% carry the **DQA1*0501/DQB1*0201** (95% DQ2.5) or **DQA1*0301/DQB1*0302** (5% DQ8)
- ✓ Therapy: gluten free diet

Normal jejunal mucosa



\+ gluten –

Celiac jejunal mucosa

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The galaxy of the clinical spectrum of Celiac Disease

Celiac disease is characterized by a large spectrum of intestinal lesions, ranging from morphologically normal mucosa, condition known as potential CD, to villous atrophy typical of acute disease.

ACUTE CD

Gastrointestinal symptoms and villous atrophy (Marsh M3a-c)

SILENT CD

No symptoms but villous atrophy, found with case finding

POTENTIAL CD

Positive serology and normal mucosa (Marsh M0,M1)

EXTRA-INTESTINAL CD

Dermatitis herpetiformis
Epilepsia, Ataxia
Liver disease, Infertility

REFRACTORY CD

Ulcerative enteritis
Unresponsive to gluten free diet

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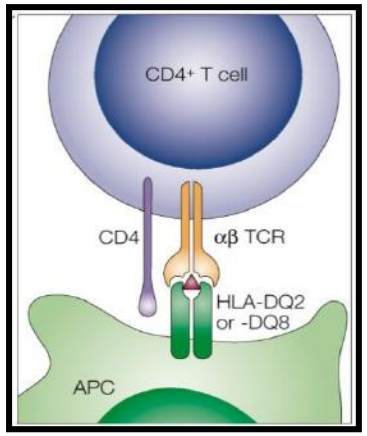
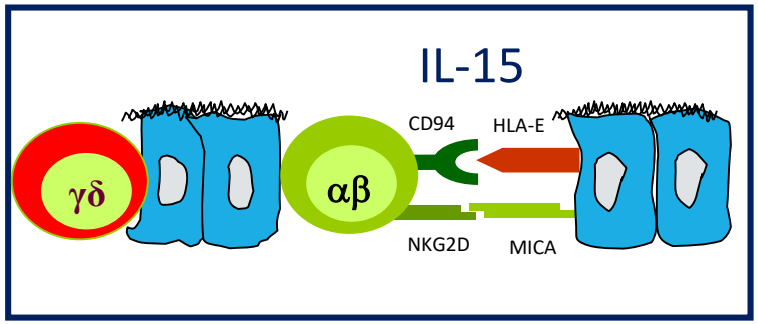
Massive infiltration of T cells (CD4+, CD8+, TCRγδ+) in the small intestinal mucosa of acute celiac patients

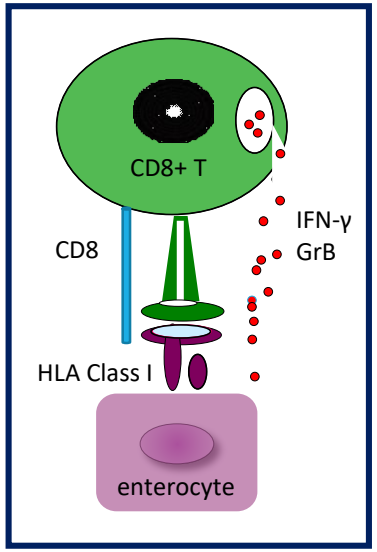


Lamina propria CD4+ T cells:

- IFN-γ
- IL-21
- Cell proliferation



Intraepithelial T cells
TCRαβ⁺ and TCRγδ⁺



Lamina propria CD8+ T cells:

- IFN-γ
- Lysis of epithelial cells

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Searching for the biomarkers associated with the mucosal tissue inflammation in acute and potential celiac disease

- **Phenotype of celiac gut T cells**
- **Intracytoplasmic cytokine production**
- **Multiparametric flow cytometry analysis**

Experimental design (1):

Analysis on short-term, gliadin raised T-cell lines (st-TCLs) from intestinal mucosal tissue

(8 CD, 6 PCD, 5 CTR)

Experimental design (2):

***Ex-vivo* analysis on freshly isolated intestinal cells from mucosal tissue**

(11 CD, 10 PCD, 7 CTR)

LSR2 by BD
FACS DIVA software

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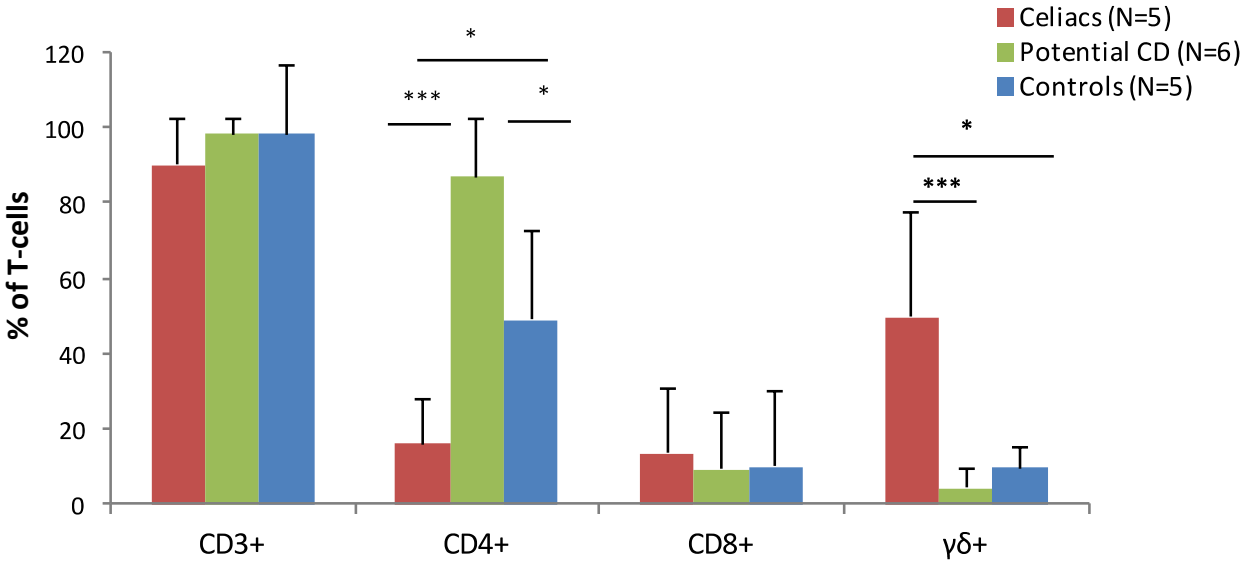
Expansion of TCRγδ+ T cells in short-term T cell lines from mucosa with villous atrophy



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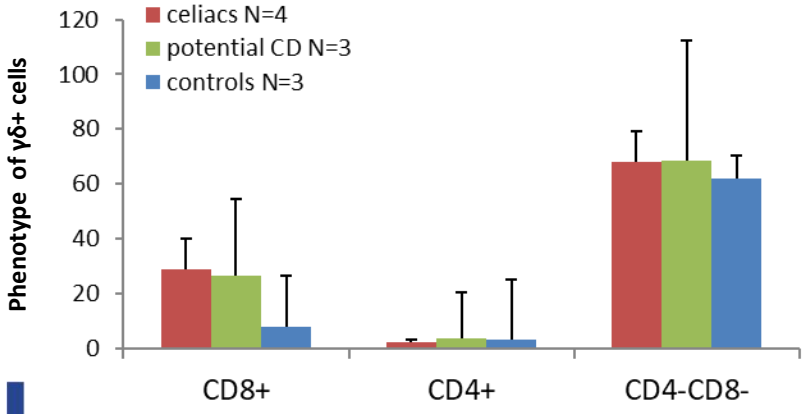

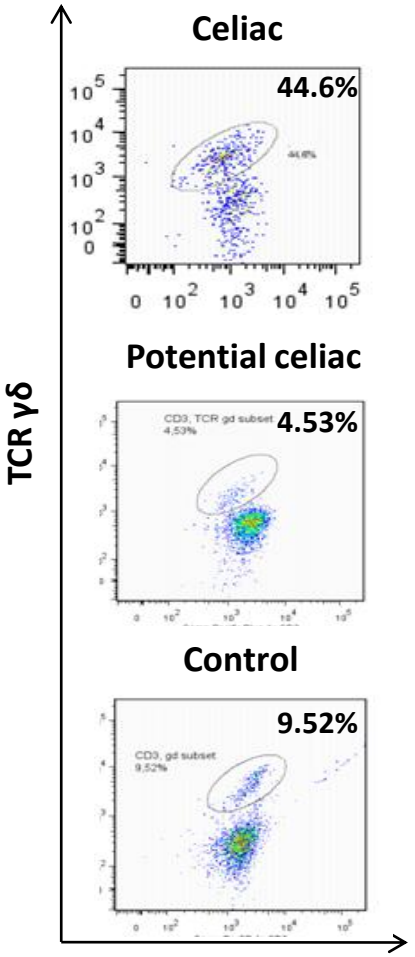

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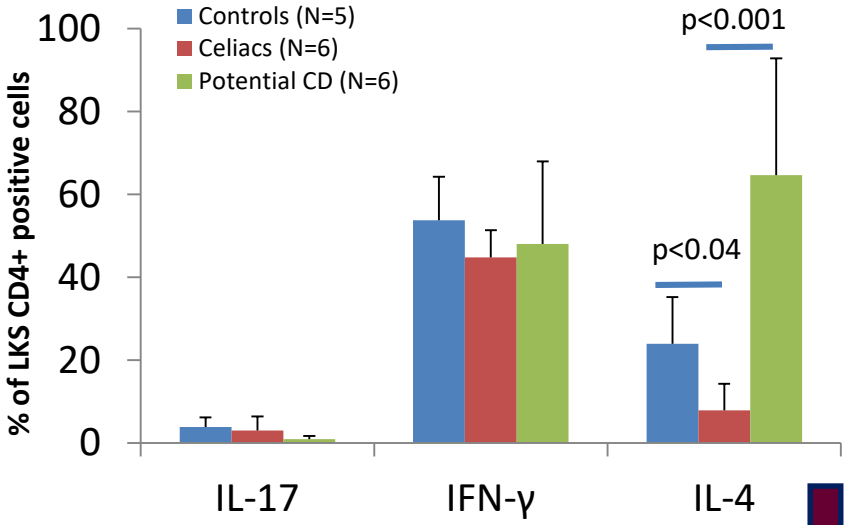
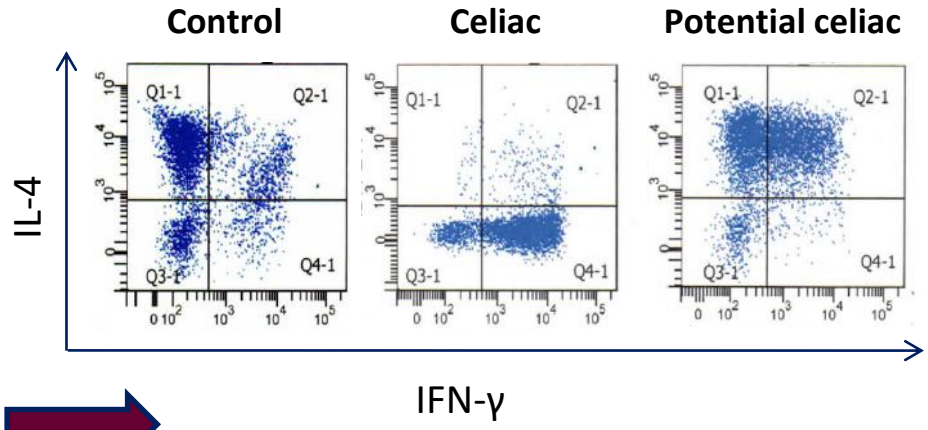
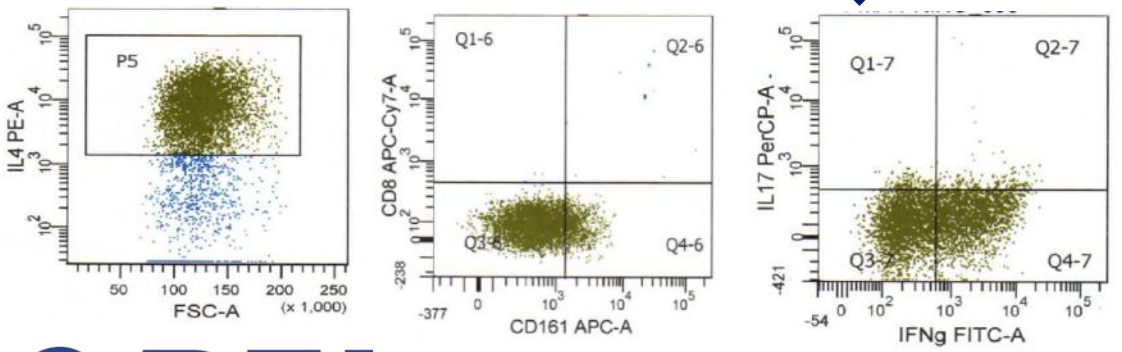
Higher IL-4+ cells in normal intestinal mucosa (healthy/potential)







Intestinal IL-4+ cells in normal mucosa:

- CD4+ T
- INFγ+/-
- CD161 neg (classical Th)

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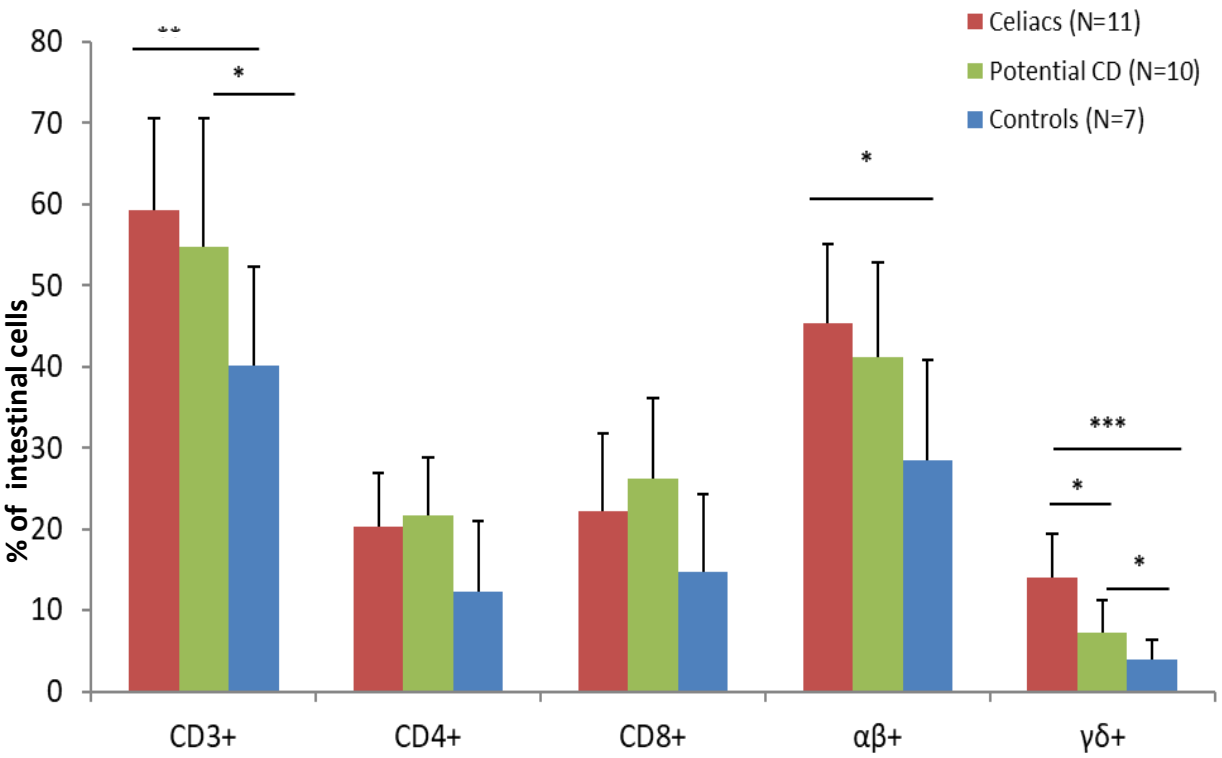
Ex-vivo analysis confirmed the increased frequency of TCR γδ+ cells in atrophic intestinal mucosa and disappearance of IL-4+ T cells



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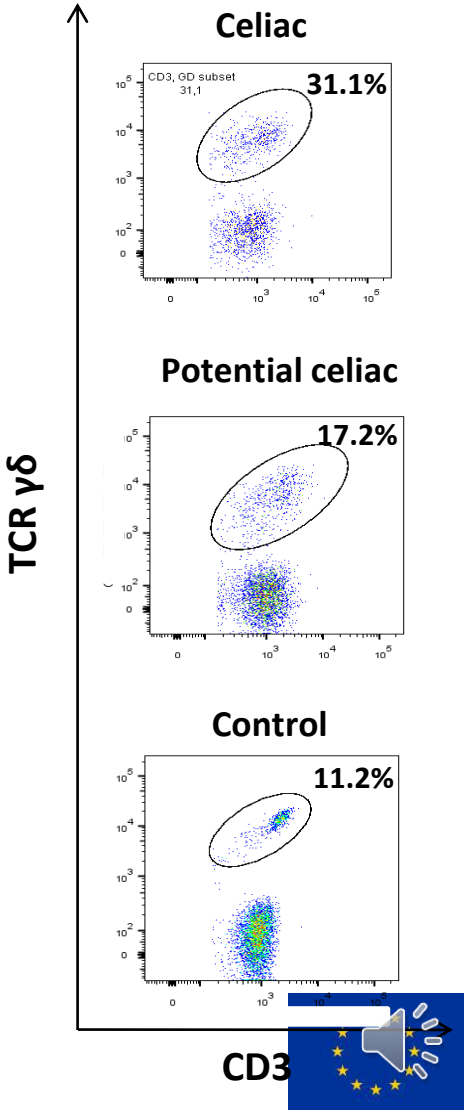

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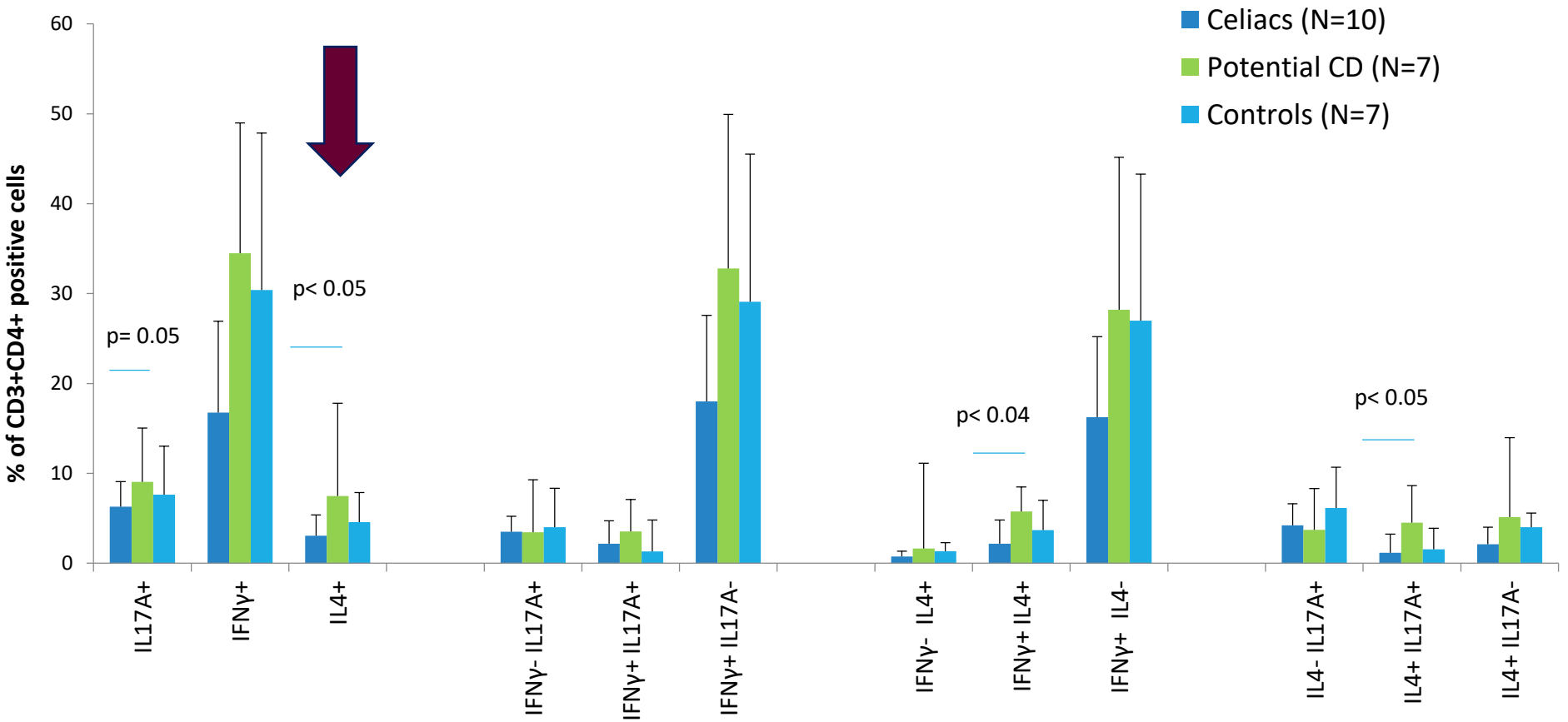
Higher density of CD4+ T cells producing IL-4 in potential CD compared to acute CD mucosa.



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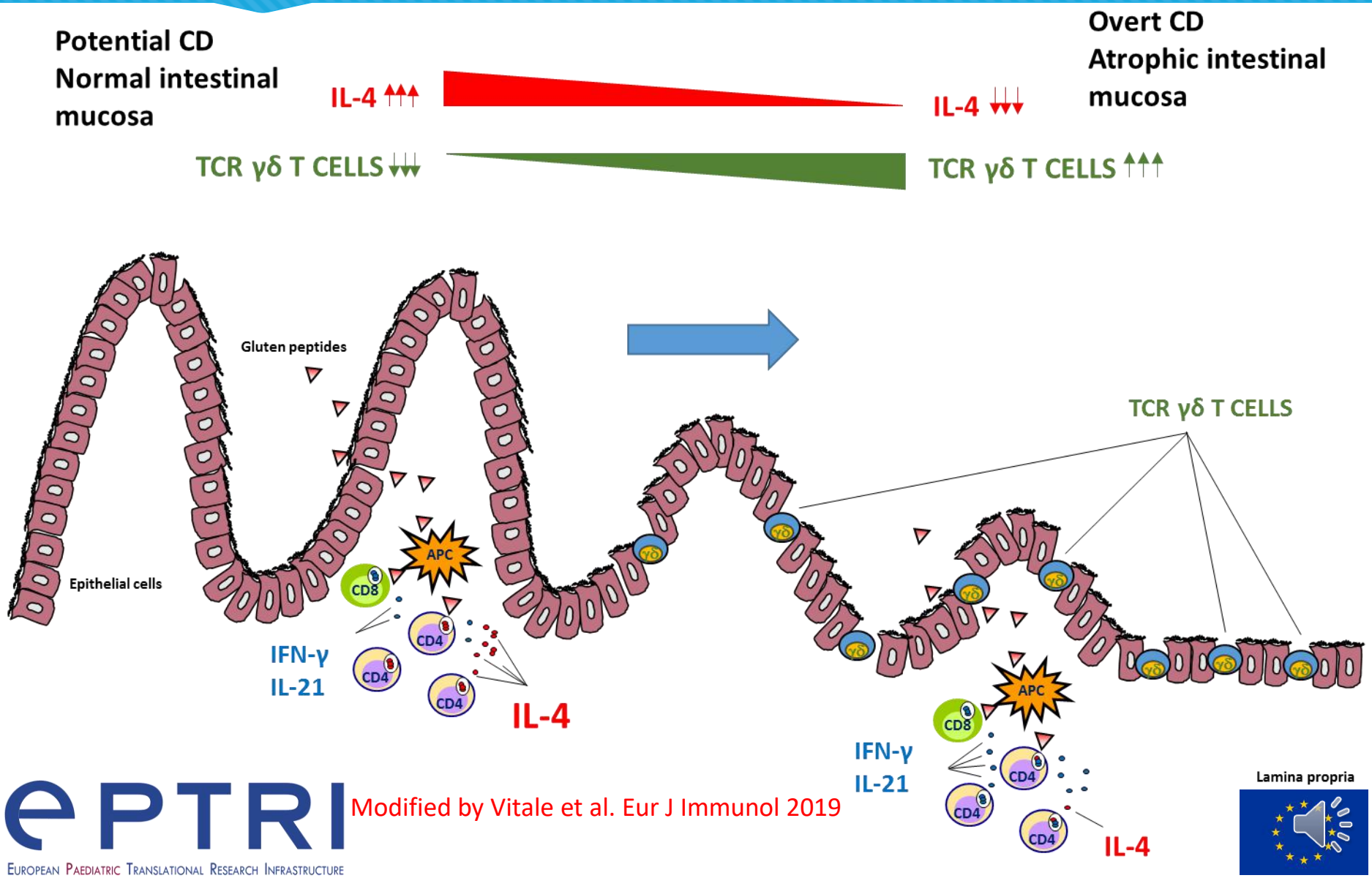
Summary



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Conclusions

Our study indicates that the atrophy of small intestinal villi, typical of acute CD, correlates with a marked expansion of TCRγδ+ T cells and with the concomitant disappearance of IL-4 producing (Th2) cells.

A shift Th2 - Th1 phenotype of T cells occurs in the gut of potential to acute celiac disease

IL-4+ and TCRγδ+ T cells could represent **new biomarkers** to support the serological and histological diagnosis of CD, mainly in case of diagnostic pitfall.

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The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to EPTRI or the EC

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