NEW INSIGHTS ON CELIAC DISEASE PATHOGENESIS: GLIADIN EFFECTS ON ZONULIN

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Background

- Gliadin is the proteic fraction present in wheat, barley, and rye responsible for the intestinal damage typical of celiac disease.
- Celiac disease, together with other autoimmune diseases, is associated to altered intestinal permeability (leaky gut).
- Zonulin, a molecule that dictates the competency of intestinal tight junctions, is up-regulated in celiac disease *(Fasano A. et al, Lancet 2000)*

Aims

- To investigate the role of gliadin on zonulin release and, consequently, tight junction (tj) competency

- To establish whether gliadin affects the expression of the junctional protein occludin

- To evaluate the effect of the zonulin peptide inhibitor FZI/0 on gliadin-induced functional and molecular changes involving intestinal tj.

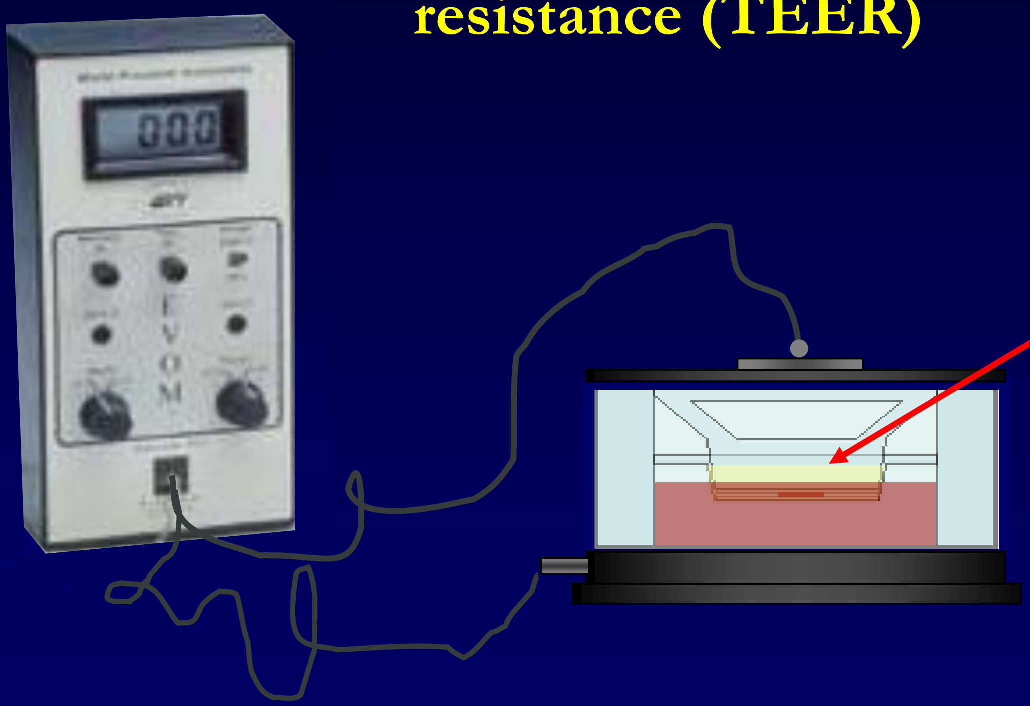
Methods

- Microsnapwell system

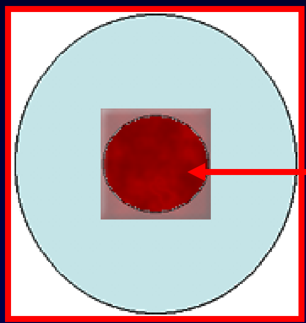
Methods

Transepithelial electrical resistance (TEER)

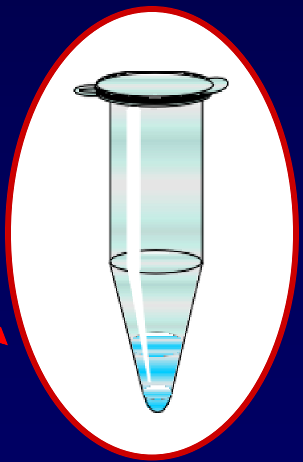
Zonulin secretion in the apical compartment of the microsnapwell was measured by ELISA



Methods

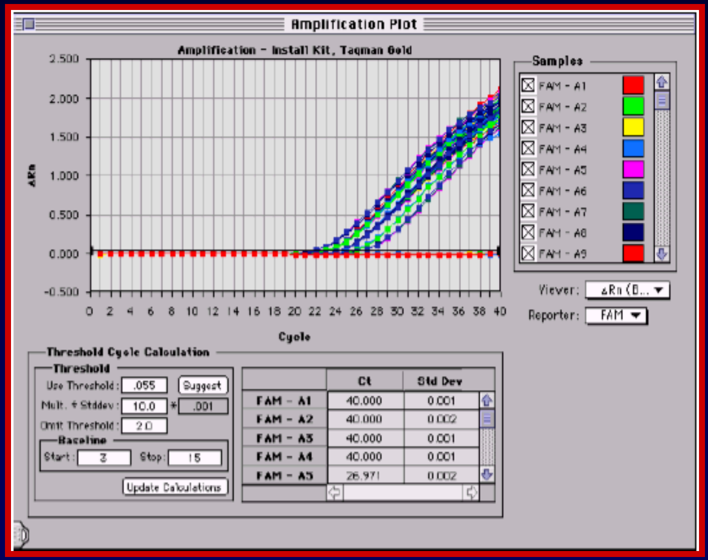


Tissue



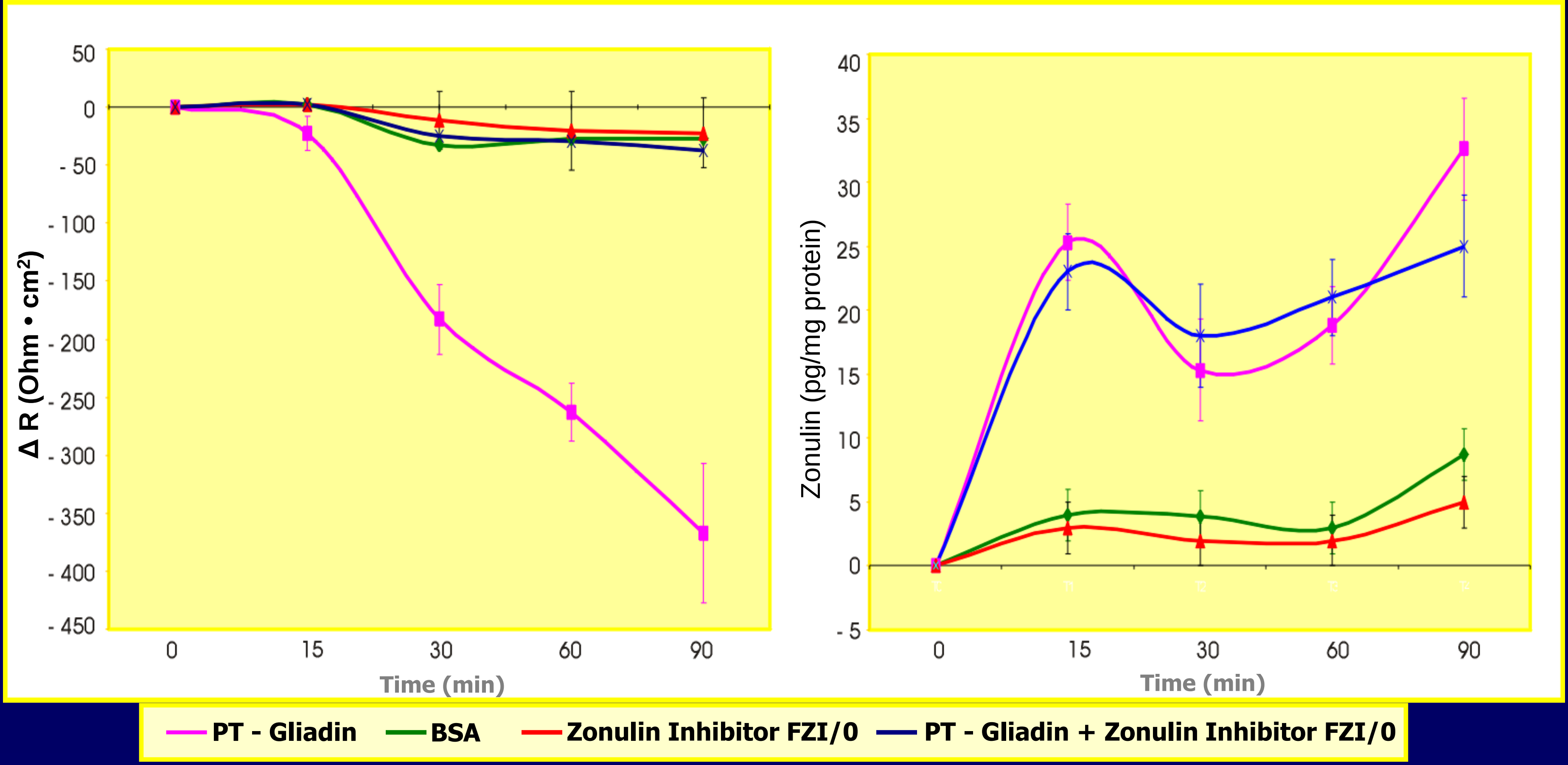
RNA Extraction

Occludin expression by Real Time PCR



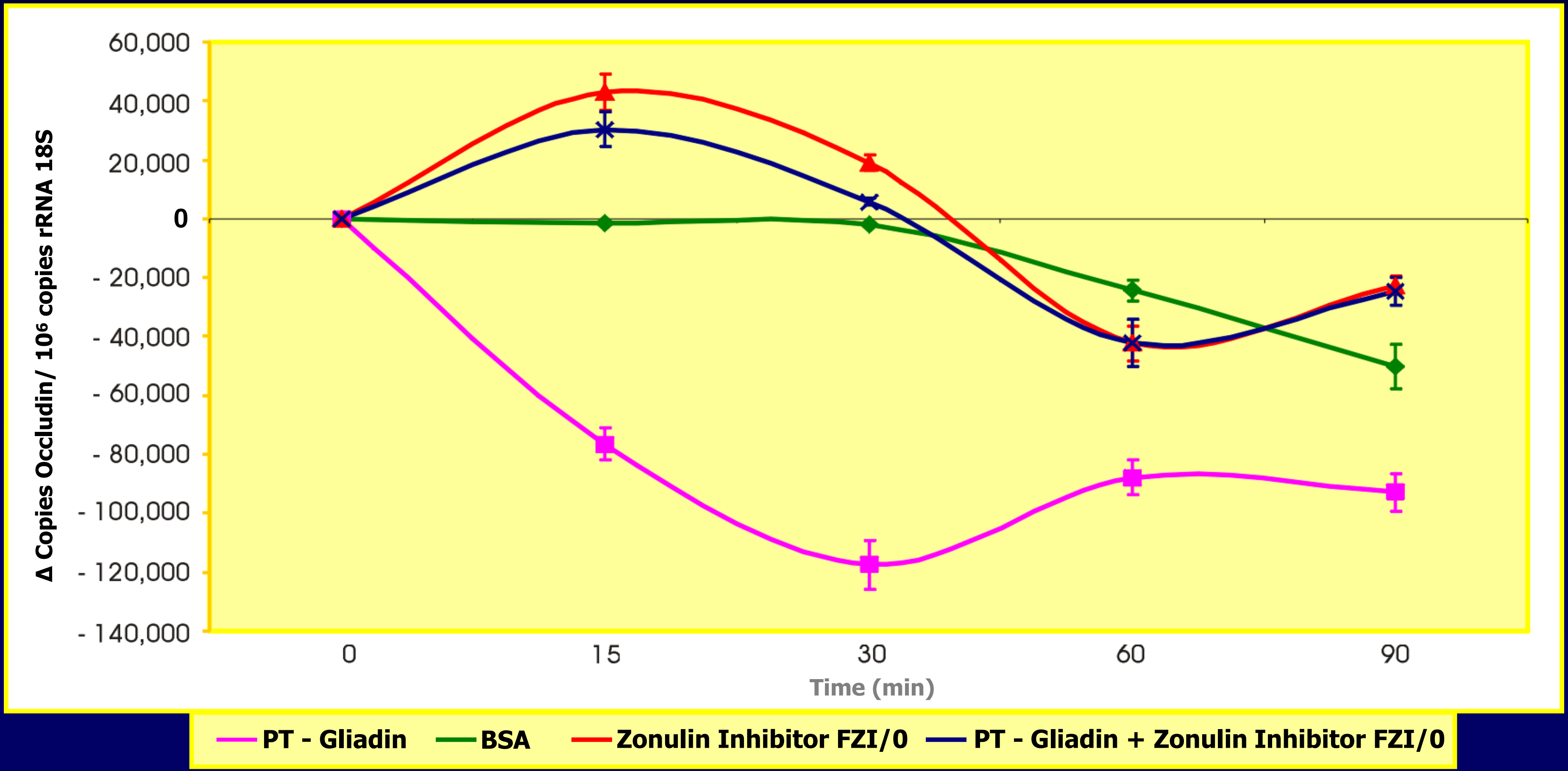
Effect of gliadin on zonulin release and TEER in rat small intestine

- TEER
- Zonulin ELISA Mucosal



Rat Tissue Result

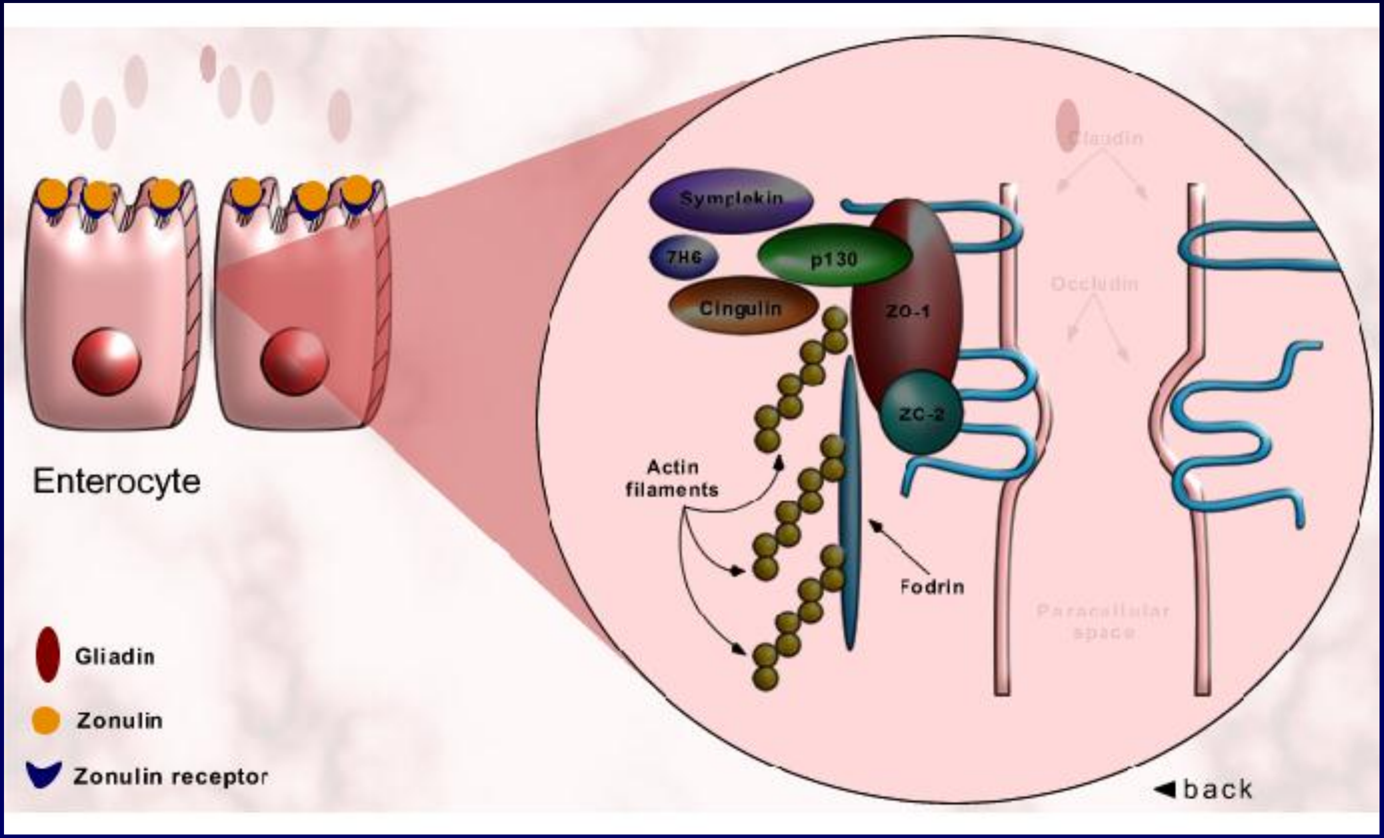
- Occludin expression in rat small intestine exposed to gliadin in the presence and absence of the zonulin inhibitor FZI/0



Conclusions

- Gliadin induces luminal zonulin secretion in rat small intestine followed by decreased occludin expression and, consequently, tight junction disassembly
- Gliadin may play a pivotal role in the early steps of celiac disease pathogenesis by facilitating its own passage from the intestinal lumen to the submucosa.

Hypothesis



Symplekin
7H6
p130
Cingulin
ZO-1
ZC-2
Actin filaments
Fodrin
Enterocyte
Gliadin
Zonulin
Zonulin receptor
back