Lactobacillus Paracasei CBA L74 prevents entrance of undigested gliadin peptides and rotavirus in Caco-2 cells

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Celiac disease

Is a multifactorial disease caused by gluten ingestion in genetically susceptible subjects.

The damage in the celiac intestine is mediated by an immune response both adaptive and innate, causing crypts hypertrofia and villus atrophy.

Diagnosis: antibodies anti TTG and anti endomisium
Biopsy

Therapy: Life long total abstinence from gluten containing food

Other enviromental factors:
Drugs (INF-alpha) and viral infections
Some gliadin peptides are resistant to digestive enzymes


Fig. 4. LC–ESI/MS chromatogram of PWG gliadin digests with gastric–pancreatic and BBM enzymes. Panel A, TIC; panels B and C, ion extraction of 25- and 33-mer multiply charged ions, respectively.
Some gliadin peptides that are deamidated by tissue transglutaminase bind to typical CD HLA, DQ2 and/or DQ8 molecules, and induce an adaptive Th1 pro-inflammatory response (ie P56-68).

Other gliadin peptides are able to initiate a response involving innate immunity independently from HLA interactions (ie P31-43).
Gliadin peptides enters into the cells by endocytosis

Interaction of ‘toxic’ and ‘immunogenic’ A-gliadin peptides with a membrane-mimetic environment

Caputo I. et al. Biochim Biophys Acta. 2010

J of Molecular Recognition Vilasis et al. 2009
LP CBA L74 effect on gliadin peptides entrance is concentration dependent
Supernatant of LP CBA L74 effect on gliadin peptides entrance
Supernatant of LP CBA L74 interferes with endocytosis of dextran
Cereals fermented with LP CBA L74 interfere with gliadin peptides endocytosis.
Effect of LP CBA L74 supernatant on rotavirus (RV) entrance in RV-infected CaCo-2 cells

Figure 1
Effect of LP CBA L74 supernatant on reactive oxygen species (ROS) in RV-infected Caco-2 cells

Figure 2

* p<.001 vs CTRL  
# p<.001 vs RV
Gliadin peptide P31-43 is similar to HRS

(Hepatocyte growth factor-regulated tyrosine kinase substrate)

Hrs is a key protein for the regulation of endocytic maturation

HRS has many binding partners. P31-43 is similar to a region of HRS needed for its correct localization to the endocytic vesicles
P31-43 competes with HRS localisation

Figure 6

A

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C

- Untreated
- P57-68
- P31-43

Barone et al PloS One 2010
Delays endocytic vesicles dynamics

Vesicles speed (µm in 10 min)

- P31-43-liss 30 min. 3h
- P56-68-liss 30 min. 3h

Caco2 cells

EEA1/P31-43 30min
EEA1/P31-43 3h
LAMP 2/P31-43 3h

Biposies

Control CD

P31-43

Time lapse. CaCo2 cells treated with p31-43 and P57-68 lissaminated. Vesicles containing P31-43 liss are slower that p57-68 containing vesicles

Prolongs EGFR activation

Min at 37°C: 0 20' 40' 90' 90' 90' 90'

PTG P31-43

EGFR

WB: α-EGFR

α-Tyr(P)

ip: α-EGFR Ab

Barone et al
GUT 2007
Gastroenterology 2007
Plos One 2010
Gliadin peptides can delay endocytic maturation and increase recycling vesicles.