

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

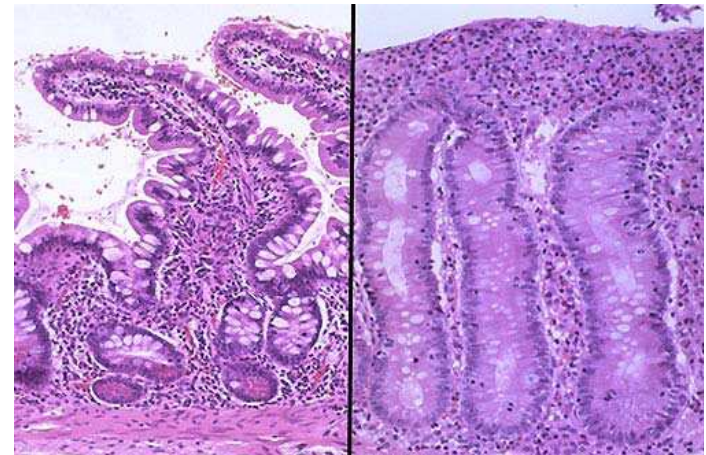
Diagnosis: antibodies anti TTG and anti endomisium

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

(Mamone G. et al J Chromatography B, 855(2):236-241, 2007)

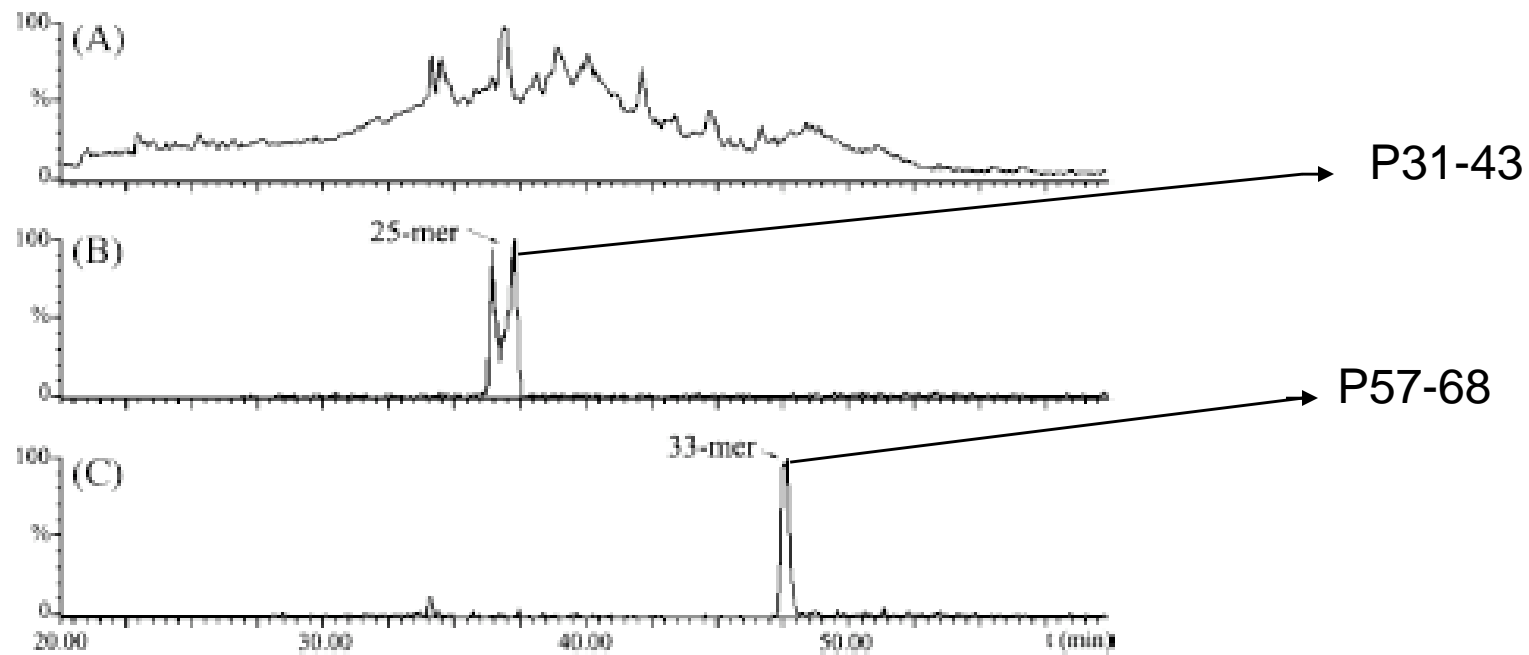
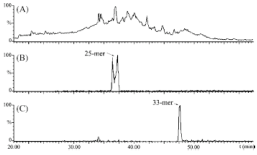


Fig. 4. LC-ESI/MS chromatogram of PWG gliadin digests with gastric-pancreatic and BBM enzymes. Panel A, TIC; panels B and C, ion extraction of 25- and 33-mer multiply charged ions, respectively.



Gliadin peptides dual activity

Innate immunity PEPTIDE

Prototype P31-43

LGQQQPFPPQQPY

“T-CELL IMMUNOGENIC” PEPTIDES

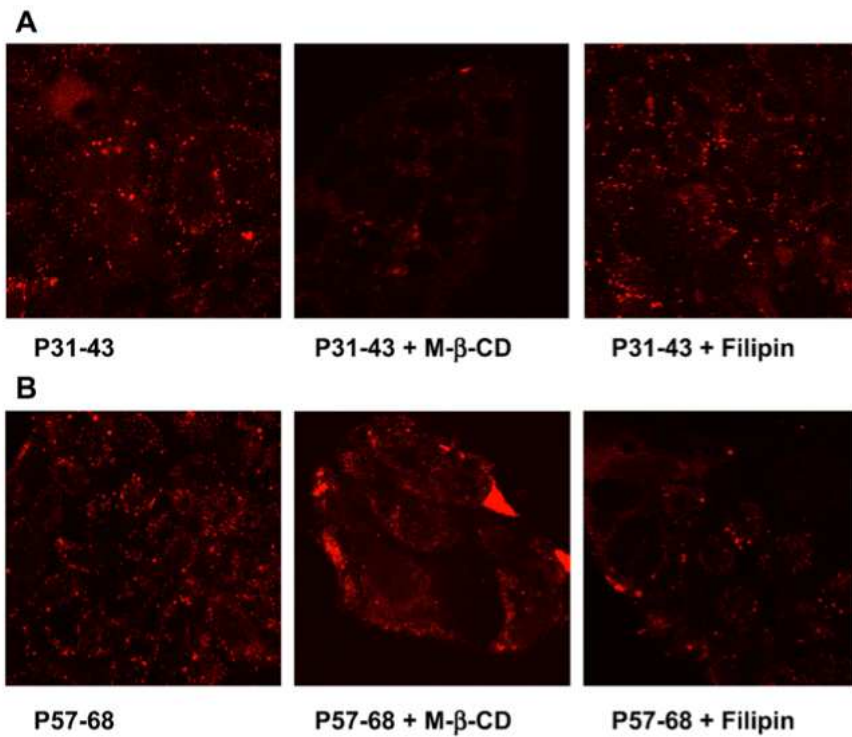
Prototype P57-68

QLQPFPPQLPY

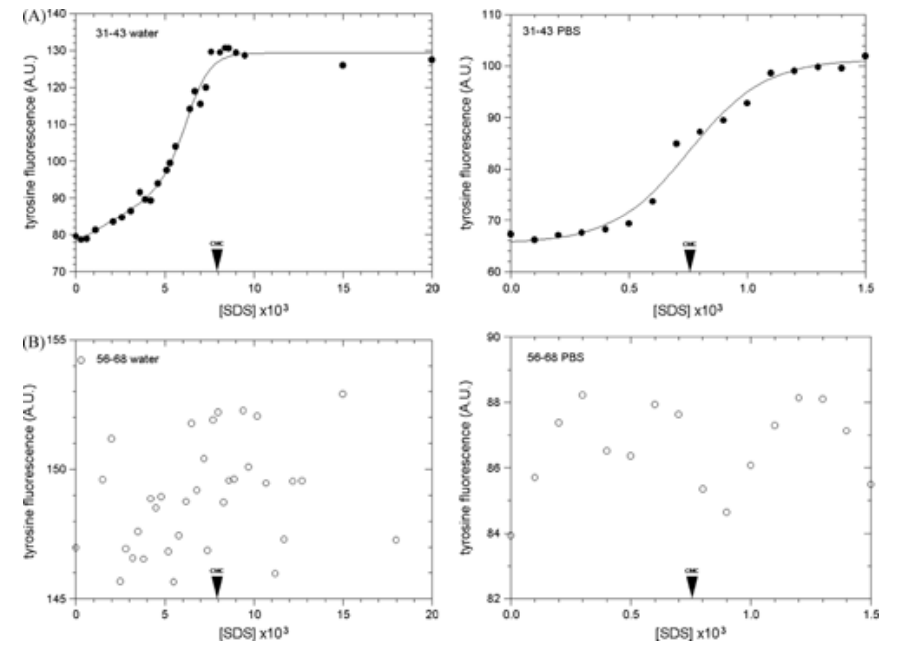
Some gliadin peptides that are deamidated by tissue transglutaminase bind to typical CD HLA, DQ2 and/or DQ8 molecules, and induce an adaptive Th1 pro-inflammatory response (ie P56-68).

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

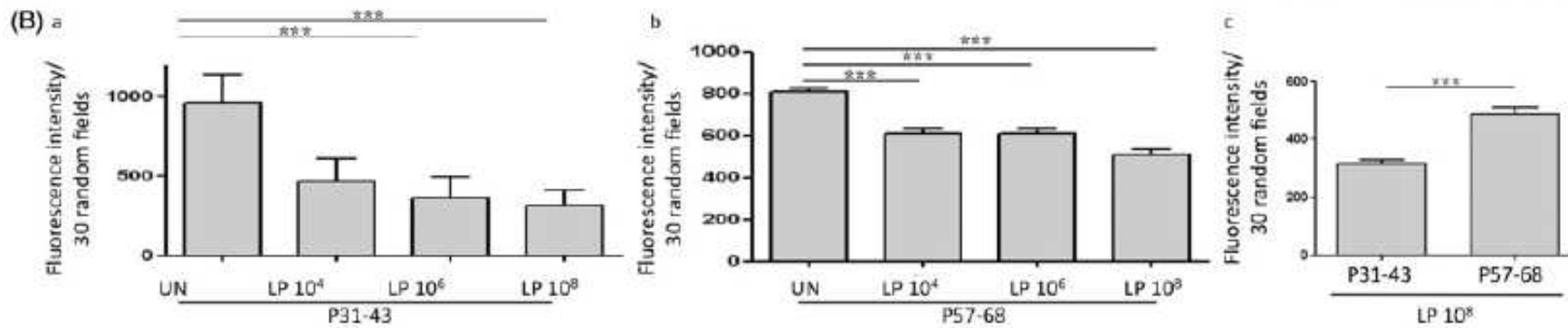
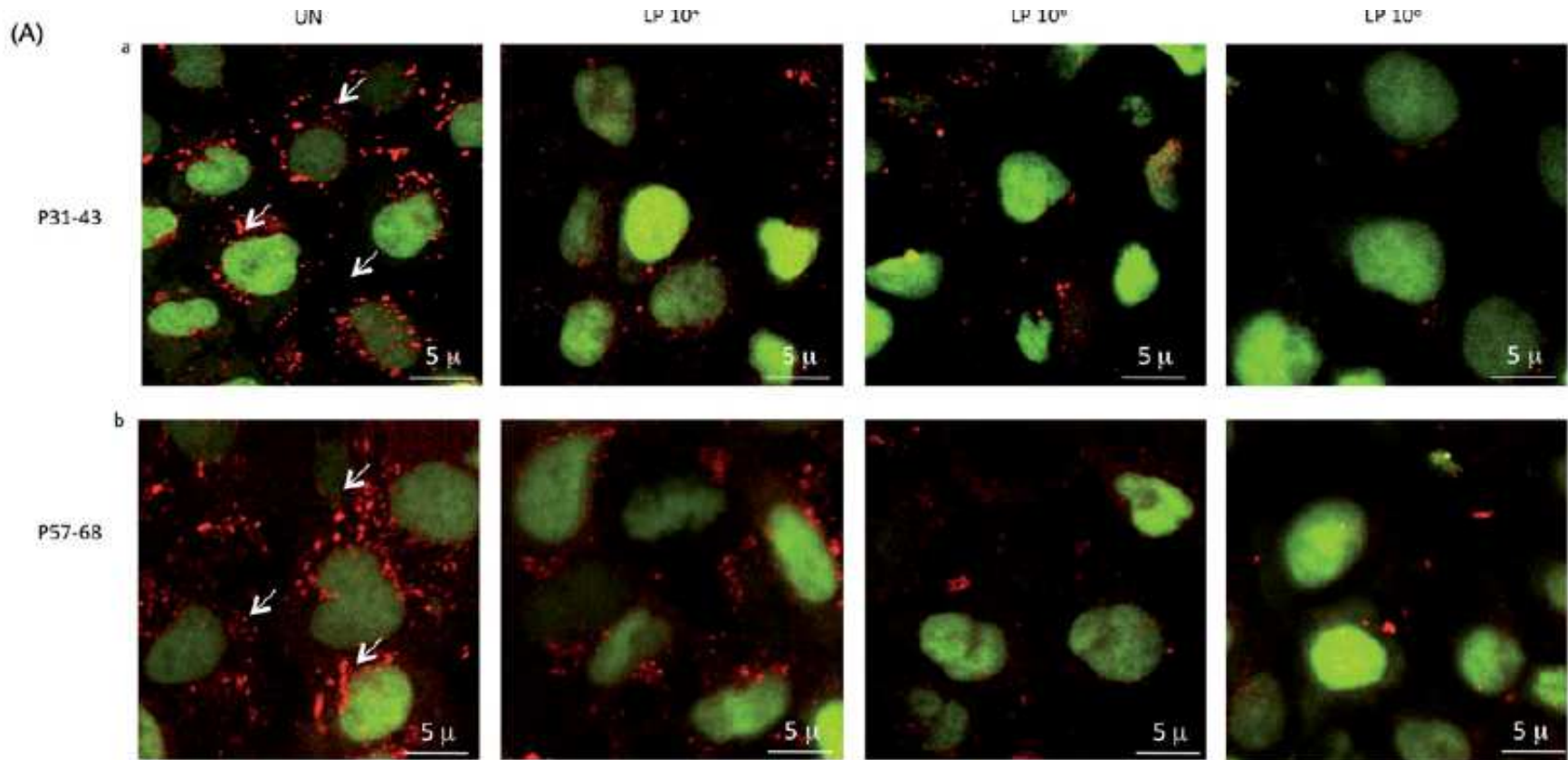


Interaction of 'toxic' and 'immunogenic' A-gliadin peptides with a membrane-mimetic environment

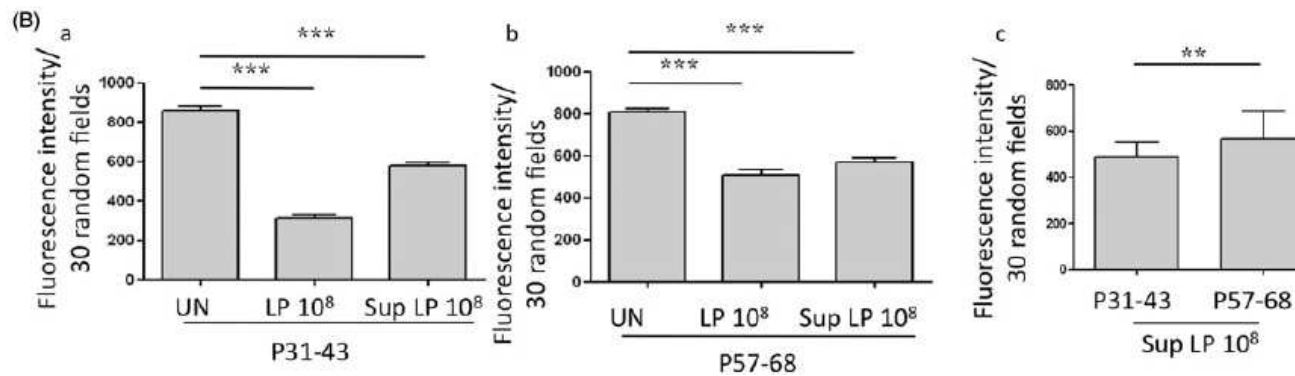
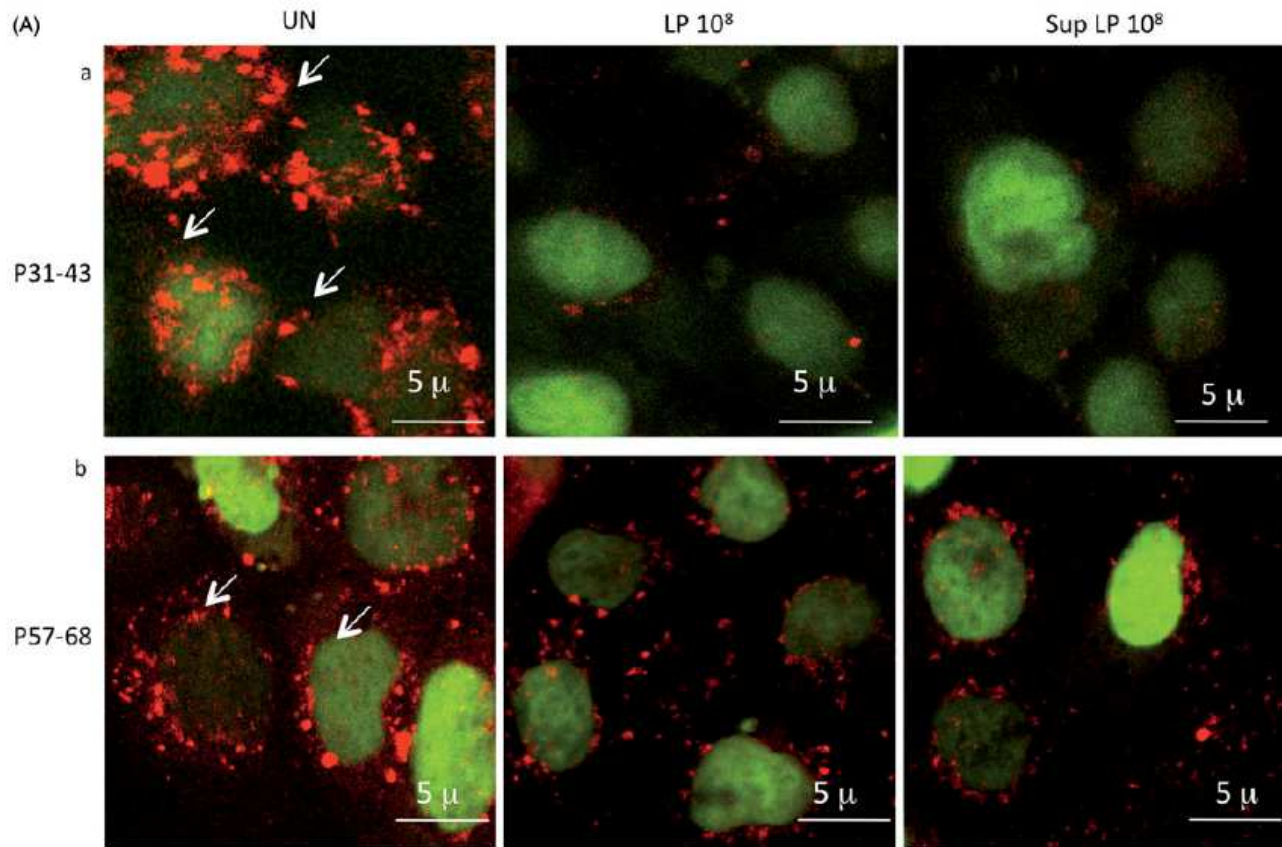


J of Molecular Recognition Vilasi s et al 2009

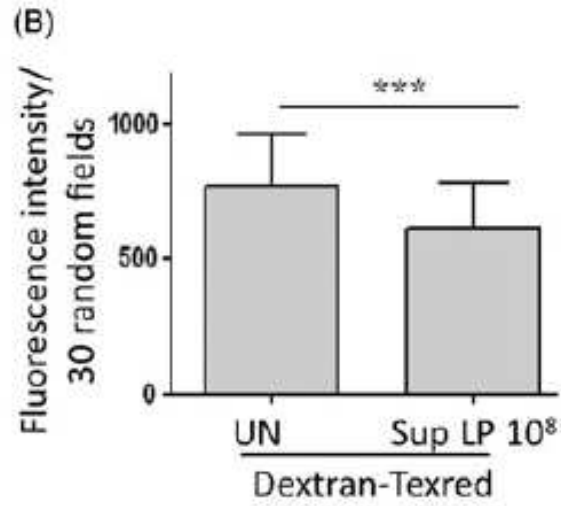
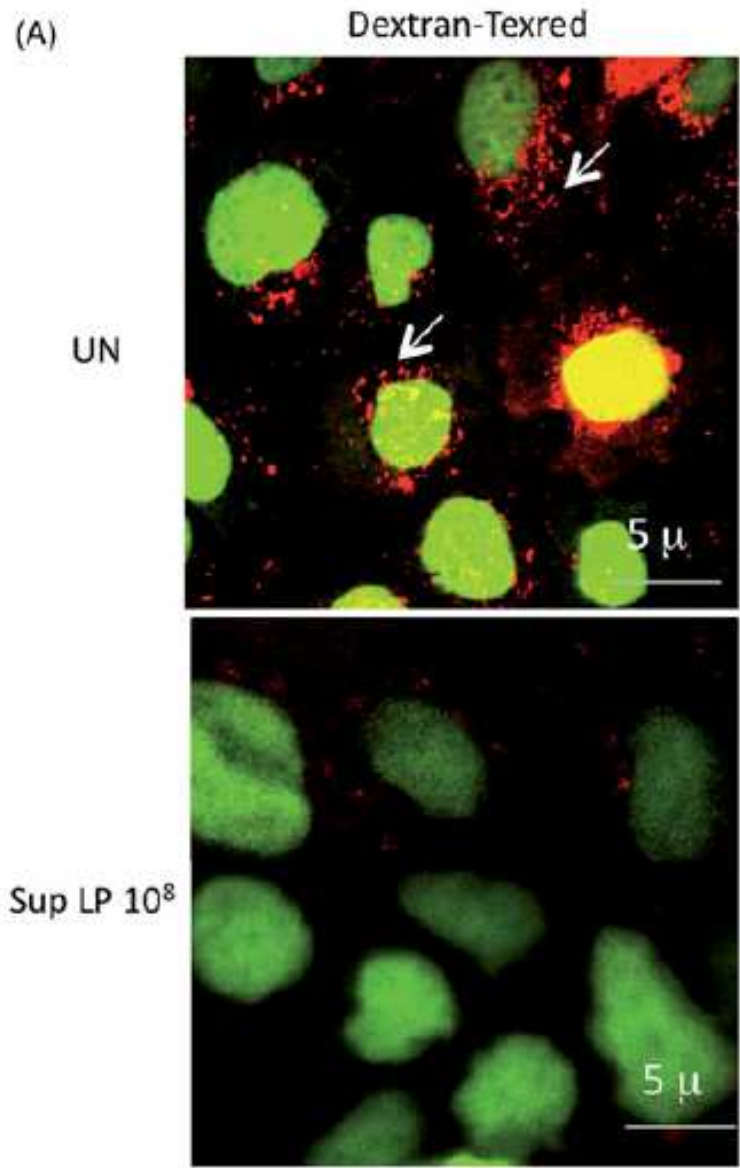
LP CBA L74 effect on gliadin peptides entrance is concentration dependent



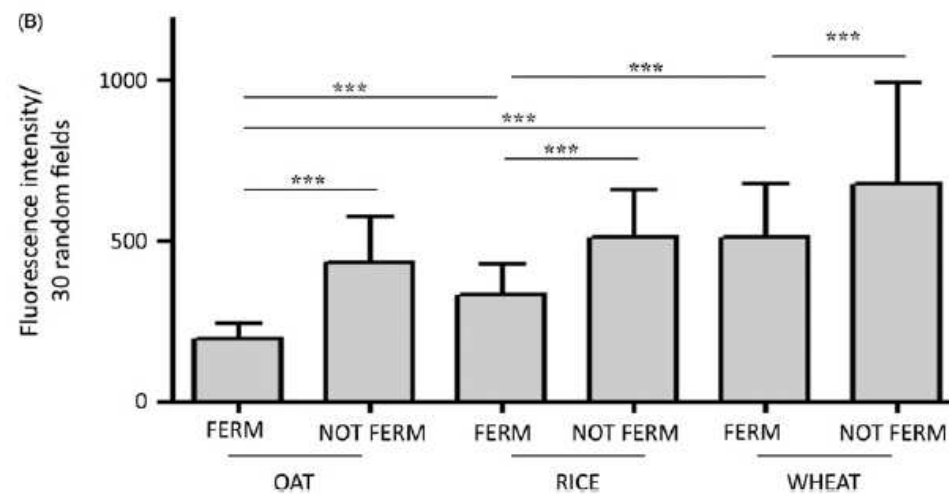
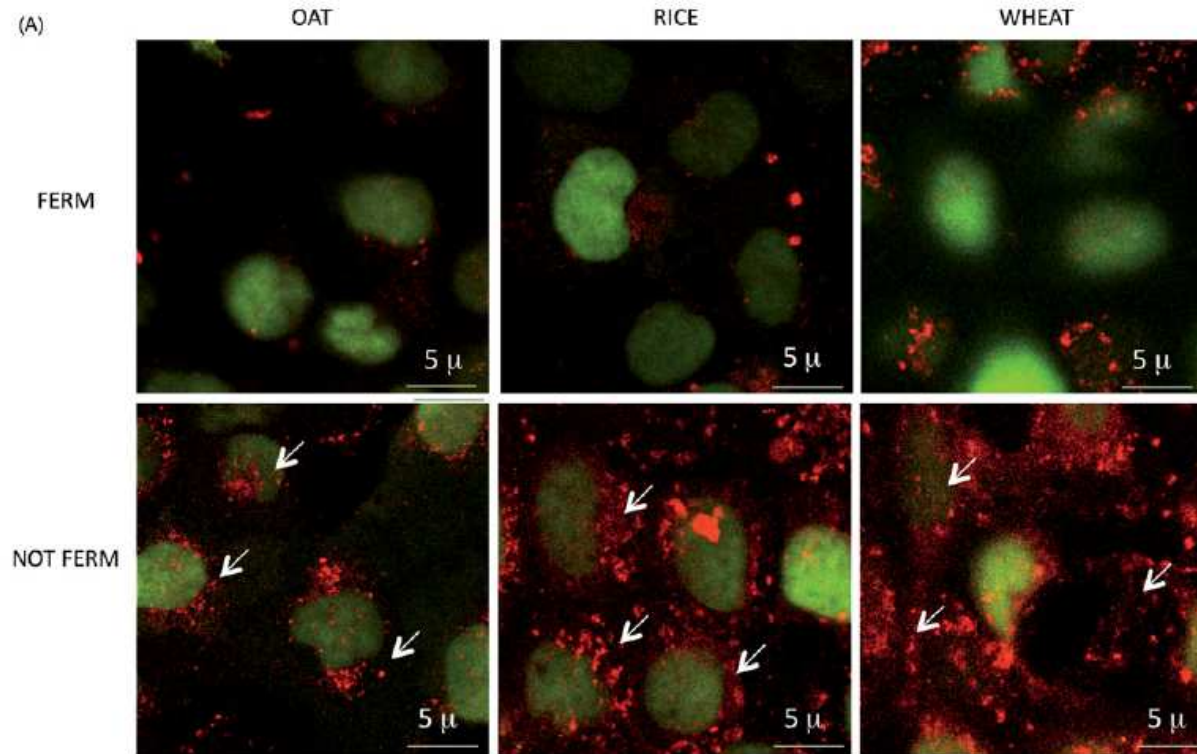
Supernatant of LP CBA L74 effect on gliadin peptides entrance



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

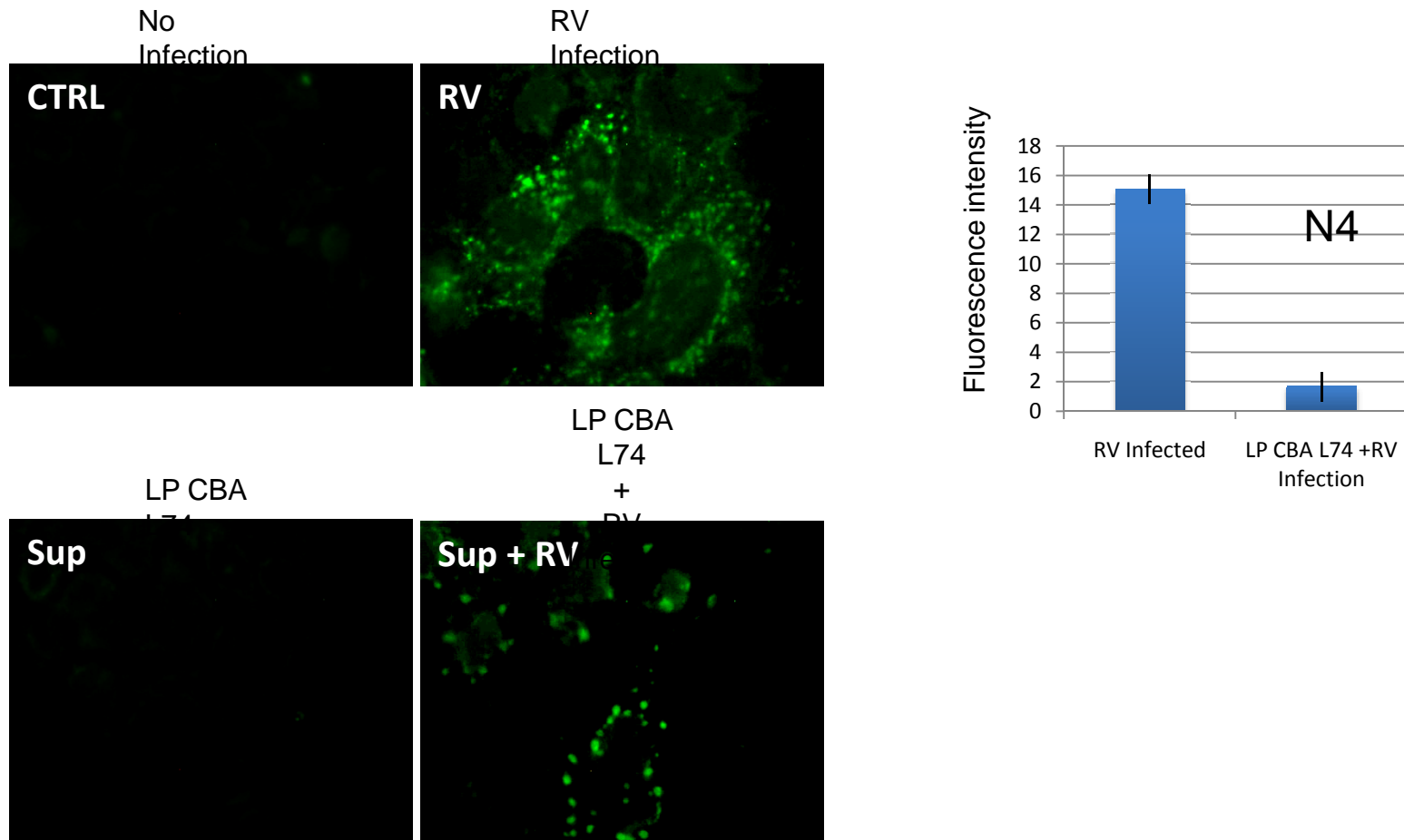
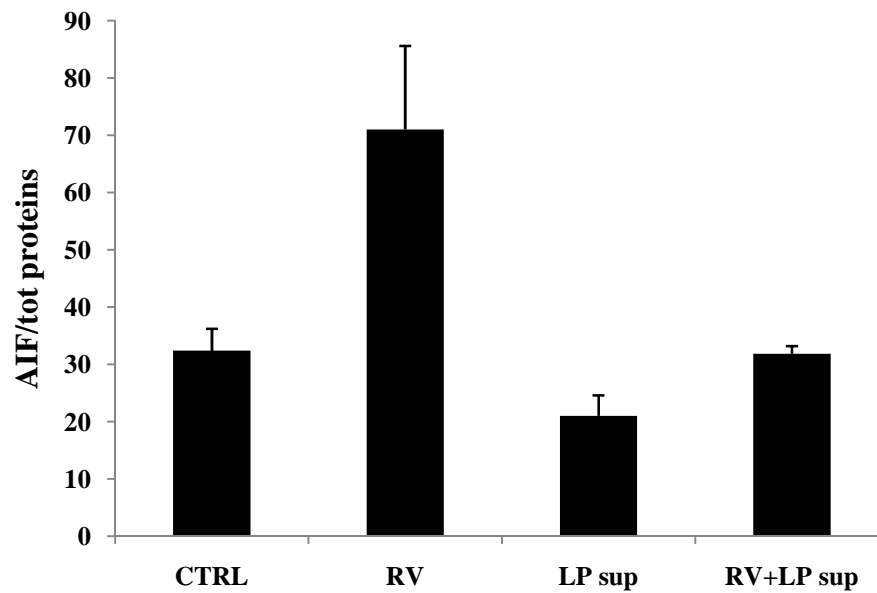


Figure 1

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



* $p < .001$ vs CTRL

$p < .001$ vs RV

Figure 2

Prof. Salvatore Auricchio

ELFID Lab.



Gliadin peptide P31-43 is similar to HRS

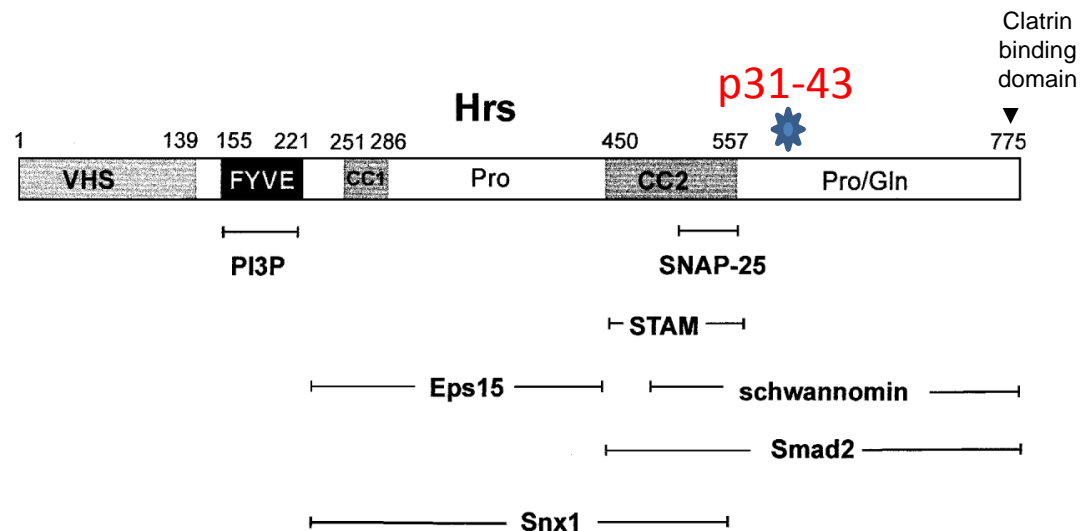
(Hepatocyte growth factor-regulated tyrosine kinase substrate)



Hrs is a key protein for the regulation of endocytic maturation

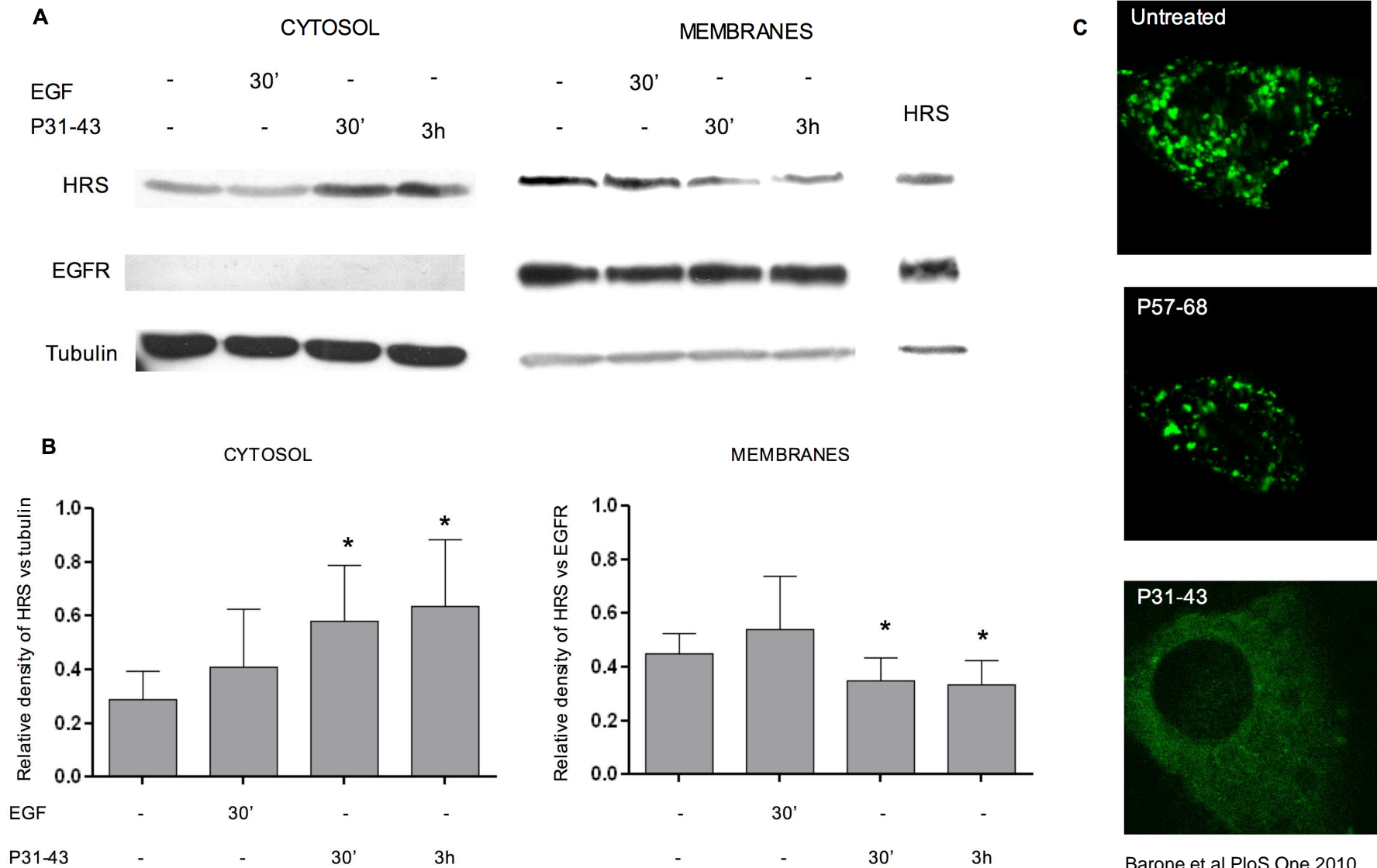
Barone et al PloS One 2010, 2011

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

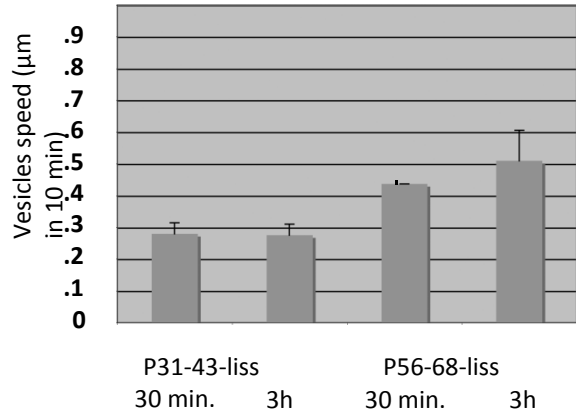


P31-43 competes with HRS localisation

Figure 6

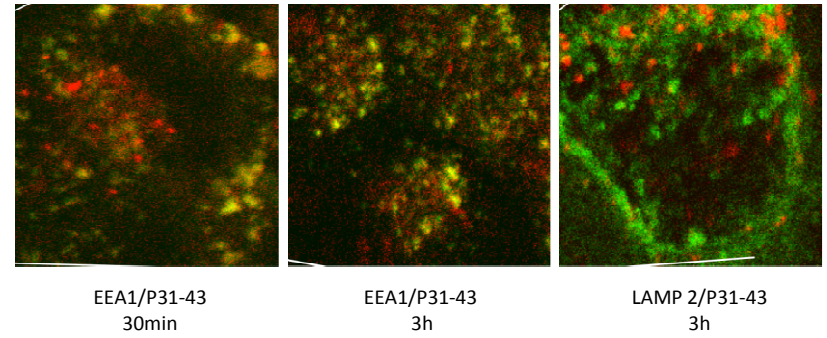


Delays endocytic vesicles dynamics



Caco2 cells

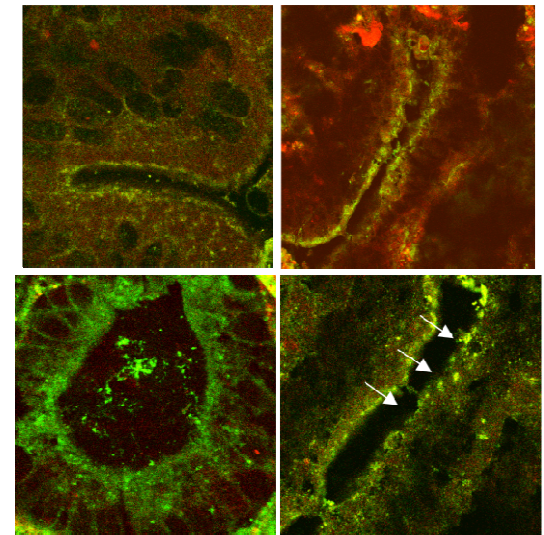
Delays maturation of early vesicles



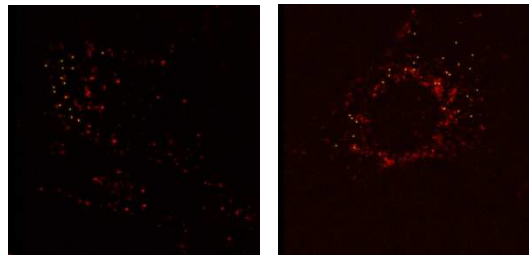
Biposies

Control

CD

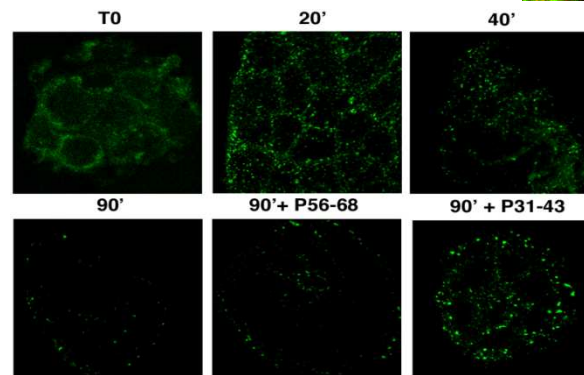
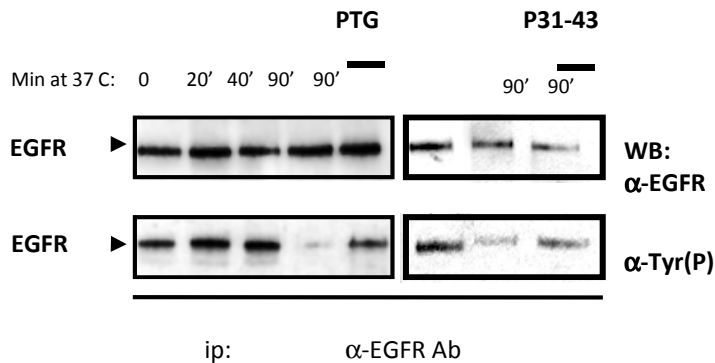


P31-43



. 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



Barone et al
GUT 2007
Gastroenterology 2007
Plos One 2010

Gliadin peptides can delay endocytic maturation and increase recycling vesicles

