Wnt11 Production in Celiac Disease is Triggered by Stimulation of Innate Immunity

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Canonical Pathway

Without Wnt

With Wnt

Wnt pathway in human biopsies

Duodenal biopsies obtained from
- controls (n.10)
- CD patients with less severe histological damage (Marsh 3A-B, n. 10)
- CD patients with flat mucosa (Marsh 3C, n.10)

Stimulation experiments with 31-43 or 33mer peptide
- biopsies from controls (n. 10)
- CD patients on GFD, Marsh 0 (n. 9)
- CD patients on GFD, Marsh 1 (n. 8)

Stimulation with IFNγ or IL-15
Wnt11 expression in human duodenal biopsies

Wnt11 mRNA fold change

- C:
- M<3C:
- M3C:

Wnt11/actin ratio

- C:
- M<3C:
- M3C:

Wnt11 expression in human duodenal biopsies

- p = 0.016
- p = 0.015
- p = 0.002
β-catenin expression

Controls                         Marsh < 3C                        Marsh 3C
BMP4 expression in CD patients at diagnosis

**mRNA expression**

- BMP4 mRNA fold change
- C, M<3C, M3C
- p = 0.044

**Protein expression**

- BMP4/actin ratio
- C, M<3C, M3C
- p = 0.038

BMP4 localization (Marsh 3C)
Peptide 31-43 activates Wnt pathway

Peptide 31-43

Peptide 33mer

p = 0.02

p = 0.028
BMP4 protein expression in GFD patients’ biopsies after peptide stimulations

![Image of protein expression in GFD patients' biopsies after peptide stimulations]

- Controls
  - Untr. 33mer 31-43
  - BMP4
  - Actin

- Marsh 0
  - Untr. 33mer 31-43

- Marsh > 0
  - Untr. 33mer 31-43
  - BMP4
  - Actin

*Marsh > 0*
Peptide 31-43 triggers Wnt pathway through IL-15

**IFNγ mRNA fold change**

- C: 0.5
- M0: 1.0
- M1: 1.5

*p = 0.013*

**IL15 mRNA fold change**

- C: 1.0
- M0: 1.0
- M1: 1.5

*p = 0.027*

**Wnt11 mRNA fold change**

- C: 0.5
- C: 1.0
- IFNγ (100 µg/ml): 1.5
- IL15 (20 ng/ml): 2.0

*p = 0.011*
Conclusions

• Wnt11 expression is increased in CD patients, causing the activation of the canonical pathway, and augmented BMP4 production mainly in the crypt cells.

• The activation of this pathway could be regarded as an attempt of the duodenal mucosa to repair the damage triggered by gluten.

• In ex-vivo experiments, the increased Wnt 11 expression is triggered by the alpha gliadin 31-43 peptide through the production of IL-15.
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