Pathogenesis of gluten sensitivity

Detlef Schuppan

Institute of Translational Immunology and Dept. Medicine I, Univ. of Mainz, Germany

Division of Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, USA

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Don't forget, you are what you eat. I need to eat a skinny person.
Innate immunity and (non-celiac, non-allergy) wheat sensitivity
• Gluten or something else in wheat as trigger?
• Target cells?
• Receptor?
• Plausible role to explain symptoms in non-celiac wheat sensitivity?
PT gliadin equally stimulates monocyte derived DCs from controls and celiac patients

PT-gliadin mediates innate immune responses via TLR4 in vivo

Activity in ω-gliadins due to a minor component of 15kDa

Identification of wheat amylase-trypsin inhibitors (ATIs) as triggers of innate immunity


Characteristics and functions of wheat-ATIs

- Family of up to 16 similar, small and compact proteins
- 5 intramolecular SS-bonds, resistant against intestinal proteases
- Pest control (inhibition of parasite enzymes)
- Known major allergens of baker’s asthma
- Activity parallels gluten content
- Content highly increased with breeding for resistance and high yield
Adjuvant in intestinal inflammation

Junker Y et al, 2012
ATI from gluten containing cereals survives intestinal proteolysis

**ATI from food**

Favoured by mucosal permeability increase

**Intestinal lumen**

Intestinal epithelium

Basement membrane

Lamina propria

**Intestine and lymph nodes**

Recirculation and homing to other sites

Fuelling inflammation & autoimmunity in the gut and at distant sites

Potentiation of already existing intestinal adaptive (auto-) immune activation

ATI primed APC

Stimulation of TLR4 on ΜΦ & DC

CD4+ T cell

PMN attraction/activation

MΦ attraction/activation

IEL activation

IL-8

CCL2

IL-15