

 Klinika Intensywnej Terapii i Patologii Noworodka  
Śląski Uniwersytet Medyczny w Katowicach

**Zonulin as a marker of increased intestinal permeability in newborns suffering from viral infection of gastrointestinal tract**

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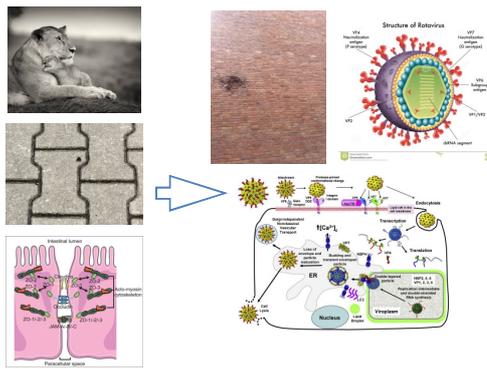
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 **IDEA**



[Martinez C, González-Castro A, Vicario M, Santos J, Gut Liver 2012]

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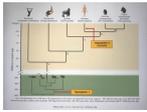
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 **IDEA**

The discovery of zonula occludens toxin (Zot) has shed light on the intricate mechanisms involved in the modulation of the intestinal paracellular pathway [Fasano A et al., Physiol Rev, 2011]

Enterotoxin elaborated by *Vibrio cholerae* that affects TJ competency  
Modulation defined as rapid, reversible and reproducible

Gut to play a pivotal role in the development of the systemic inflammatory response



**ZONULIN (ZO) - 47 kDa protein - Pre - Haptoglobin 2**  
eukaryotic counterpart of the *Vibrio cholerae* zonula occludens toxin

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**IDEA**

**ZONULIN** - One of proteins associated with TJ - guanylate kinase like proteins ZO-1, ZO-2, ZO-3 with integral membrane proteins occludin and claudin [Fink MP, Tsukita S, Funase M.]

Increases the intestinal permeability  
 Genes related have been mapped on chromosome 16  
 Involved in intestinal innate immunity  
 Unregulated in autoimmune diseases and immune mediated (CD, MS, RA)  
 Respiratory system - asthma [Blaisdell C, Fasano A]  
 Neoplasms - gliomas [Skardelly et al.]  
 Nervous system diseases - association between schizophrenia and polymorphism (SNPs) related to HP gene [Wan et al.], neuromyelitis optica, Guillain Barré  
 Inflammation CD [Arrietta et al.], IBD [Turner JR.]  
 Significantly higher plasma concentration of zonulin were found in sepsis [Klaus D A. et al. 2012]

Question?

What are the intestinal luminal stimuli that trigger zonulin release?




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**GI ROTAVIRUS INFECTION**

ROTAVIRUS - recognised in 1973, belongs to *Reoviridae* family

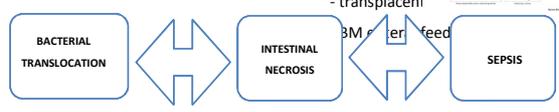
Worldwide ROTAVIRUS is estimated to cause more than 111 million cases p/a in population 45 years of age

Moderate infection can lead to severe complications by influencing intestinal permeability p/a

Infants younger than 3 months of age are said to be relative - transplacental

IM + enter feed

BACTERIAL TRANSLOCATION → INTESTINAL NECROSIS → SEPSIS





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**ZONULIN ESTIMATION IN GI ROTAVIRUS INFECTION**

**Why?**

Serum proteins have the potential to be used as diagnostic and prognostic indicators for intestine injury **EARLY DETECTION - CRUCIAL**

**ZO: a promising marker of intestinal permeability** →

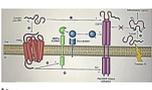
↳ **loss of intestinal barrier function by:**

- genetic predisposition
- miscommunication between innate and adaptive immunity
- exposure to environmental triggers

↳ Emerging role of the gut barrier and microbiome in small bowel functional diseases [Muller W et al. Exp Rev of Gastroenterology & Hepatology 2017]

↳ Particular interest in the regulation of antigen trafficking by the zonulin pathway and its activation by intestinal mucosa - microbiota

↳ GI rotavirus infection as triggering factor of zonulin release by altering and disintegrating the structure of TJ, therefore possible intestine injury and higher permeability status




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 **MATERIALS AND METHODS**

- Neonates (N=16) diagnosed with rotavirus infection confirmed by immunologic test
  - median GA 38 wks
  - median age 24<sup>th</sup> day of life)
- Serum ZONULIN was measured using ELISA test
- ZO concentration compared with values evaluated in 14 terms apparently healthy neonates (no symptoms of infection)
- Routine laboratory evaluation was performed in all patients including:
  - CBC with smear
  - inflammatory markers (CRP, PCT)

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 **RESULTS**

\* p<0.001

Parameter*	ZO* [ng/ml]	CRP [mg/dl]	PCT [ng/ml]	WBC	PLT
Group					
Study	<b>36.0</b> <b>(26-43.2)</b>	0.7 (0.2-2.1)	0.1 (0.1-0.3)	10.8x10 <sup>3</sup>	386 x10 <sup>3</sup>
Control	3.5 <b>(2.7-4.8)</b>	0.2 (0.2-1.6)	0.1 (0.1-1.2)	11.7x10 <sup>3</sup>	277x10 <sup>3</sup>

\* Median (1-3Q)

- There was **no statistically significant** correlation between ZONULIN concentration and parameters of inflammatory status
- Median values of CRP, PCT, leucocytes and platelets **did not differ** between the study group and controls
- In all patients the course of rotavirus infection was **uneventful**

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 **CONCLUSIONS**

- Significantly higher concentration of ZONULIN are found in neonates suffering from rotavirus infection
- Higher concentration of ZONULIN may indicate higher permeability status of the intestine
- Further observations are needed to reveal if serum ZONULIN value may correlate with the occurrence of intestinal complications **even if** inflammatory markers remain low

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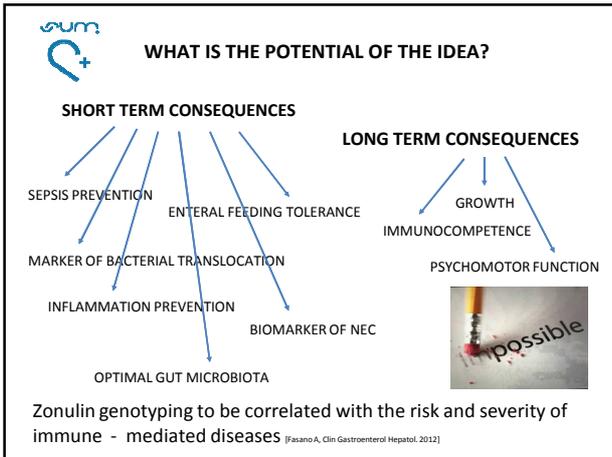
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THANK YOU FOR YOUR ATTENTION

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