

Zonulin – a serum marker as proof of leaky gut

The intestinal barrier is a bulwark protecting us from the exterior

The intestinal wall has to fulfil two contradictory tasks. On the one hand, it has to be permeable for absorbed vitamins and trace elements. On the other hand, penetration of harmful bacteria, fungi, viruses, and pollutants has to be impeded. Hence, the intestinal barrier is not inflexible but instead regulates very selectively. When regulating this barrier, the intestinal mucosa works conjointly with bacteria stemming from the intestinal flora, with immune cells located in the bowel area and the bowel's vegetative nervous system.

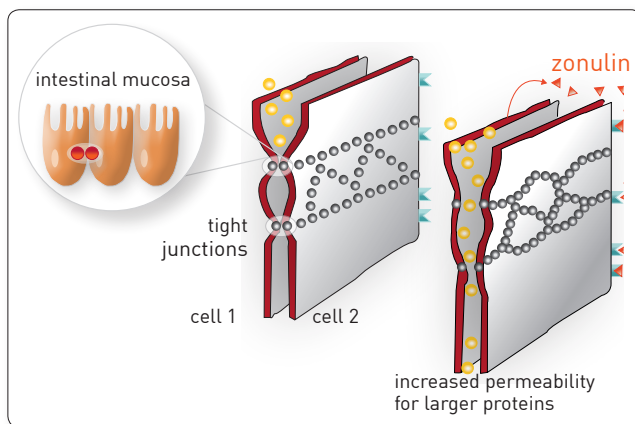


Fig. 1 Tight junctions close intercellular space within the intestinal mucosa. Zonulin regulates their integrity. The intestinal mucosa secretes zonulin, which effectuates the cytoskeleton's contraction, and hence the opening of interepithelial channels, due to interaction with specific receptors. Images show section from above.

Left: intact tight junctions

Right: open intercellular spaces of the intestinal mucosa post zonulin exposure

What constitutes the intestinal barrier?

Tight junctions (lat. Zonula occludens) are slim bands built from membrane proteins that connect epithelial cells within the intestinal mucosa. Tight junctions close the intercellular space and hence act as a paracellular diffusion barrier. The intestinal barrier regulates the inflow of, for example, dissolved amino acids, saccharides, fatty acids, immunoglobulins, but also immunogenic food proteins, bacterial lipopolysaccharides or candida antigens. Malfunctions of this vital barrier are termed leaky gut. Zonulin is a laboratory marker that indicates malfunctioning of the intestinal barrier.

Zonulin increases the intestinal permeability

Zonulin, a 47 KD protein, is responsible for the regulation of tight junctions situated in the intestinal wall. Following various stimuli, it is emitted by the intestinal mucosa and binds to specific receptors on intestinal epithelial cells. This causes a contraction of the cytoskeleton's proteins, leading to the opening of interepithelial channels. Analy-

sing the level of zonulin in serum is a possibility of evaluating the intestinal permeability while avoiding the effort of a provocation test (e.g. lactose/mannitol gradient). In context with patients suffering from chronic inflammatory bowel diseases, celiac disease, Diabetes mellitus, but also other autoimmune diseases, such as disturbances of the intestinal flora, for example after antibiotic treatment, it was proven that increased zonulin levels in serum correlated with mal-functioning intestinal barriers and increased intestinal permeability.

IMD Labor Berlin		medical report	
Test	Result	Unit	Reference Range
Zonulin i.S. (EIA)	66.7	ng/ml	< 38
<p>The result encourages the assumption of a decreased intestinal barrier function of the intestinal epithelium. Increased intestinal permeability may occur in context with chronic inflammatory bowel diseases, disturbances of the intestinal flora, celiac disease and some autoimmune diseases. Food intolerances or a systemic activation of the immune system originating in the bowel may be consequences of increased intestinal permeability.)</p>			

Fig. 2 sample report

Consequences of increased intestinal permeability

An increased permeability of the intestinal mucosa causes an intensified confrontation between the bowel's immune system and food components as well as foreign antigens, such as food additives or toxic metals originating from dental prostheses. Furthermore, bacteria, fungi, yeasts (like candida species) and their metabolic products are functioning as a more effective trigger for the immune system's activation in case the intestinal mucosa's selective functioning is impeded.

Hence, effects of leaky gut comprise ...

1. Intensification of food intolerances (DAO)

Often, food intolerances are secondary consequences of chronic inflammatory processes located in the bowel. Enzymes such as diamine oxidase and lactase are synthesized within the intestinal epithelium, which is why morphological changes to the intestinal mucosa caused by inflammation lead to a diminished synthesis of these enzymes. The determination of zonulin levels does not only serve the diagnosis of *leaky gut*, but additionally helps monitoring the therapeutic process in context with secondary DAO deficiency (histamine intolerance) or secondary lactase deficiency (lactose intolerance) respectively.

Patients suffering from celiac disease also show decreasing zonulin levels and inflammation parameters when following a strict gluten-free diet.

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2. Defective resorption

In cases of dysfunctional gut integrity, food components are not digested properly, or are not resorbed. Often, deficiency symptoms are the consequence. Essential trace elements, such as zinc, selenium, copper, magnesium, manganese, cobalt or chromium, play a key role as cofactors of numerous enzymes. Already a minor shortage may lead to, for example, reduced cognitive abilities or an increased susceptibility to infection. In addition, some minerals have a direct impact on gut integrity and, like zinc, interact directly with tight junctions. Hence, for patients with increased zonulin levels a sufficient mineral supply is of vital importance. In order to avoid overdoses, the supply should be regulated in accordance with the individual mineral status (EDTA whole blood mineral analysis).

IMD Labor Berlin		medical report		
Test	Result	Unit	Reference Range	
Leaky gut Profil				
Mannose-binding lectin (MBL) i.S.	840	ng/ml	> 450	
Zonulin (EIA) i.S.	59.3	ng/l	< 38	
Elevated zonulin levels in serum indicate an increased intestinal permeability ("leaky gut"). Hence, the impaired intestinal resorption may contribute to the lack of magnesium, selenium, and zinc. Please note that reduced supply with minerals may do further damage to the intestinal mucosa.				
Calcium	61.2	mg/l	55 - 70	
Magnesium	27.1	mg/l	30 - 40	
Selen	63.7	µg/l	85 - 147	
Zinc	3.8	mg/l	4,5 - 7,5	

Fig. 3 sample report

3. Increased absorption of toxic metals

Toxic metals, such as mercury, silver, tin, lead, palladium, or aluminium, may enter the bowel both due to release from dental alloys and from food ingestion. Normally, those toxins are excreted to a large extent. Associated with leaky gut nevertheless is an overall larger absorption of toxins into the organism, leading to higher levels of toxic stress.

Material

Zonulin: 1 ml serum

MBL: 1 ml serum

Minerals: 2 ml EDTA blood

Transport to the laboratory is not time-sensitive and can be sent by mail.

Costs

The costs for the test are 28.86 € for zonulin and 91.53 € for the leaky gut profile.

Literature

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