

# Microbolome 1.0



A milestone in stool diagnostics

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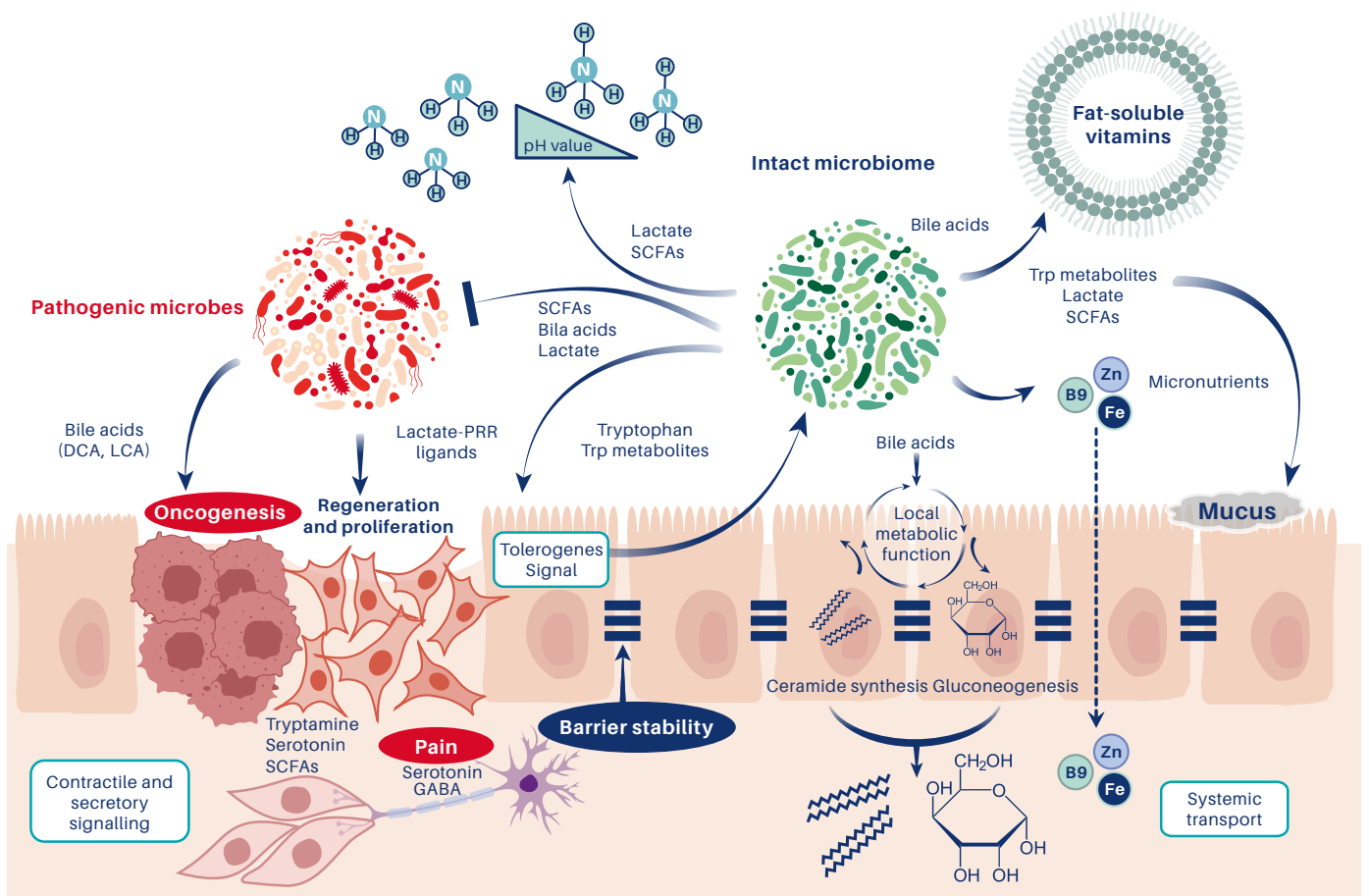
# **Microbolome 1.0**

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A milestone in stool diagnostics

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- The new **Microbolome 1.0** test represents a significant advancement in **stool diagnostics**. Unlike conventional flora or microbiome analyses that primarily focus on detecting bacteria in the stool, the Microbolome also examines **microbial metabolic products**. This approach provides deeper insights into active metabolic processes and their direct impact on health.

While traditional bacterial analyses often simply suggest the potential impacts of microbiome changes, metabolite analysis offers clear insights into the actual processes occurring within the body. It reveals whether bacteria are producing toxins, explains the accumulation of cytotoxic bile acids (e.g., DCA) in the bile acid pool and their potential harmful effects, and reveals how gut bacteria can act protectively, strengthen the intestinal barrier, and defend against harmful pathogens. This deeper understanding of the „how“ enables the development of more targeted and personalized treatment strategies.



**Fig. 1** Influence of metabolites on the environment, absorption of micronutrients and fat-soluble vitamins, mucin formation, intestinal peristalsis, pain sensation, stability of the intestinal barrier, mucosal regeneration, oncogenesis, and defence against pathogenic germs.

## 20 metabolites as key indicators in the Microbolome test

The key to understanding the Microbolome test lies in its focused analysis of metabolites—small molecules generated through microbial metabolism in the gut. Specific metabolites such as tryptophan, serotonin, GABA, and histamine play a crucial role in gastrointestinal disorders like irritable bowel syndrome (IBS) [1]. The test not only detects these IBS-relevant compounds but also identifies potentially harmful bacterial toxins such as p-cresol and indoxyl sulphate, major bile acids, as well as protective indole derivatives and AhR agonists. In total, the test analyses 20 key metabolites, summarized in the following table.

Tryptophan metabolism	Phe/Tyr metabolism	Neurotransmitter	Bile acids
■ Tryptophan	■ Phenylalanine	■ Serotonin	■ Deoxycholic acid (DCA)
■ Serotonin	■ Tyrosine	■ GABA	■ Conjugated bile acids
■ Indole	■ p-Cresol	■ Histamine	■ Free bile acids
■ Indole propionate (IPA)			■ Cytotoxic bile acids
■ Indole lactate (ILA)			■ Protective bile acids
■ Indole aldehyde (IAld)			■ Total bile acids
■ Indole acetic acid (IAA)			
■ Tryptamine			
■ Kynurenic acid			
■ Indoxyl sulphate			

**Tab.1** Metabolites detected in Microbolome 1.0 are organized by origin or function.

## Microbial metabolites: key factors in gut health

The effects of microbial metabolites range from regulating intestinal activity to modulating the immune system. Using selected examples, we illustrate how certain metabolites influence pain perception, inflammatory responses, and the integrity of the gut barrier. This highlights the important role of metabolites in maintaining gut health.

### Serotonin

Serotonin acts in the gut through the 5-HT<sub>3</sub> and 5-HT<sub>4</sub> receptors and influences intestinal peristalsis and pain perception. Imbalances in serotonin production can therefore lead to disturbances in gut motility and pain, which are commonly observed in conditions such as irritable bowel syndrome (IBS) [2].

### GABA (gamma-aminobutyric acid)

GABA is an important neurotransmitter involved in the modulation of pain signals in the gut. GABA depletion may lead to increased pain perception and increased sensitivity to distension in patients with IBS [3].

### Histamine

Histamine, a biogenic amine, is involved in the regulation of gastric acid secretion and intestinal motility. Excessive histamine production in the gut can lead to inflammation and gastrointestinal symptoms such as diarrhoea or cramps [4].

### Bacterial Toxins (e.g., p-Cresol & Indoxyl Sulphate)

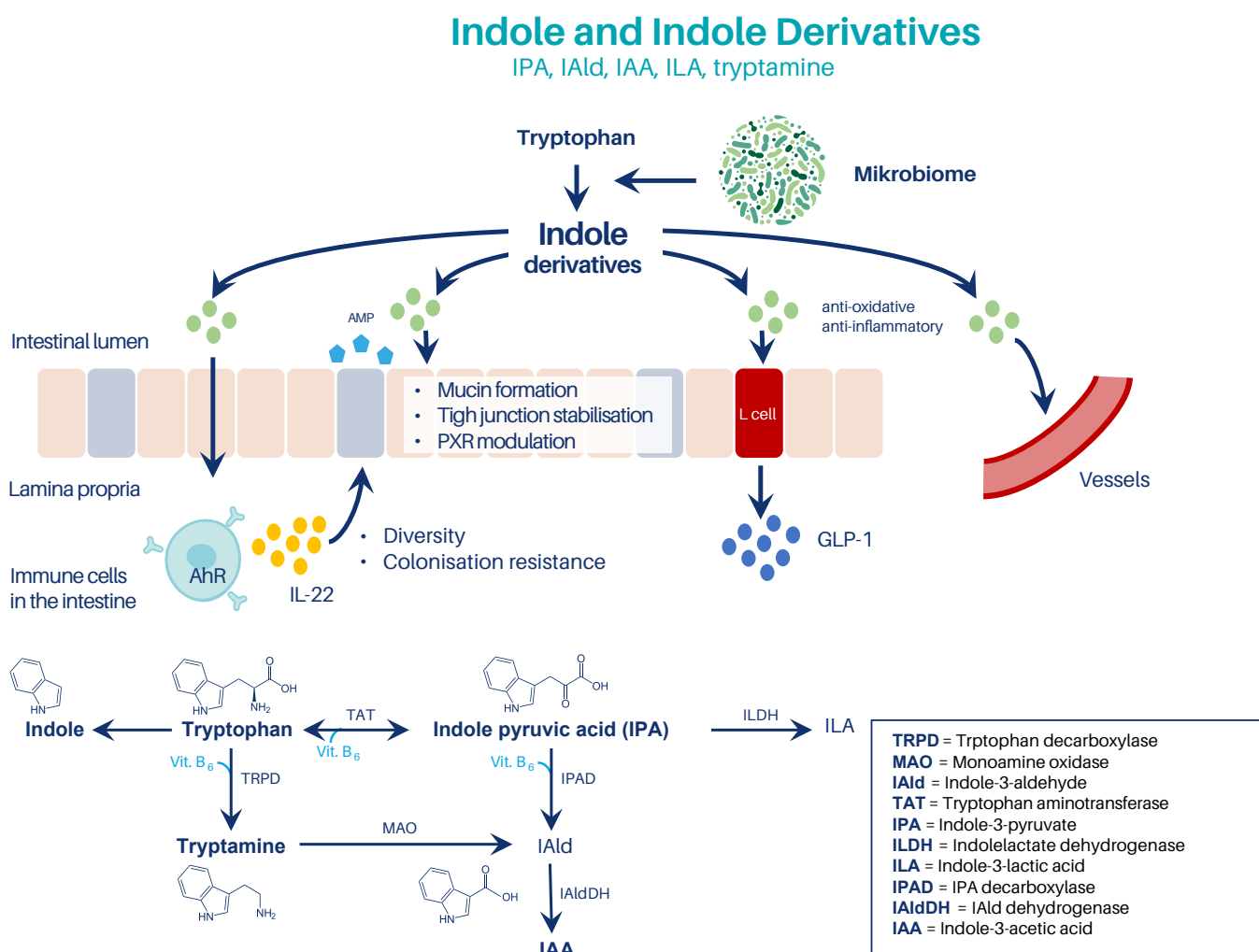
As by-products of protein metabolism, p-cresol and indoxyl sulphate exhibit pro-inflammatory and pro-oxidative effects. They impact mitochondrial function and can lead to epithelial damage. An increased presence of these toxins is often associated with impaired gut barrier function, inflammatory bowel diseases, and a heightened risk of colorectal cancer [5].

### Bile Acids

Bile acids are essential for fat digestion and the absorption of fat-soluble vitamins. They vary in structure and function, significantly influencing gut health. An imbalance, particularly an increase in cytotoxic bile acids, can promote inflammation, contribute to gallstone formation, and increase the risk of colorectal cancer. Conversely, bile acids such as UDCA or LCA (in physiological amounts) have protective effects [6].

## AhR-Agonists

Protective indole derivatives, such as indole, indole propionate, indole aldehyde, or indole lactate, activate the aryl hydrocarbon receptor (AhR), thereby contributing to the increased diversity of the gut microbiota [7]. This activation is crucial. By activating the AhR receptor, they also promote the release of antimicrobial peptides (AMPs), which enhance colonisation resistance and protect against pathogenic bacteria. AhR agonists support mucin production, strengthening the intestinal mucosal barrier and maintaining its integrity [8]. They stimulate the release of GLP-1 (glucagon-like peptide-1) in the stomach, delaying gastric emptying and reducing hunger. This may aid in the regulation of body weight and the prevention of metabolic diseases [9].



**Fig. 2** Indole and protective indole derivatives and their effect on diversity, colonization resistance, mucin formation, intestinal permeability, GLP-1 release.

## Therapy based on metabolomic findings

The identification of specific metabolites enables targeted therapeutic interventions. For instance, when toxic metabolites are detected, probiotics, prebiotics, dietary measures, or absorbents can be used strategically to influence bacterial metabolism in such a way that no further harmful metabolites are produced, or existing ones are bound and excreted.

In contrast to therapeutic approaches that focus on increasing or decreasing specific bacteria or bacterial groups, metabolic pathways can be influenced more rapidly—often within just a few weeks. While the overall bacterial population may remain relatively stable, their metabolic activity can undergo significant changes. These shifts are detectable through reduced toxin levels in the stool and a more balanced bile acid metabolism, characterized by physiological concentrations of primary and secondary bile acids, particularly due to the reduction of cytotoxic bile acids. Targeted, metabolism-based therapy not only aims to reduce harmful metabolites but also seeks to promote the production of protective indole derivatives, which play a vital role in gut health. These beneficial metabolites are generated in adequate amounts only within a balanced microbial environment.

While existing therapeutic principles remain fully valid, they can now be applied with greater precision and effectiveness, enhanced by metabolite- or metabolism-specific interventions. By shifting the diagnostic focus from bacteria to their metabolic activity, noticeable therapeutic outcomes can often be achieved within just a few weeks. If progress is lacking, adjustments can be made much earlier than with traditional approaches, enabling more responsive and effective treatment.

## CONCLUSION

**The new Microbolome test offers a deeper and more precise understanding of microbiome function. By analysing bacterial metabolites instead of merely detecting bacterial presence, the test allows for a more accurate evaluation of gut health and enables more targeted and effective treatment strategies.**

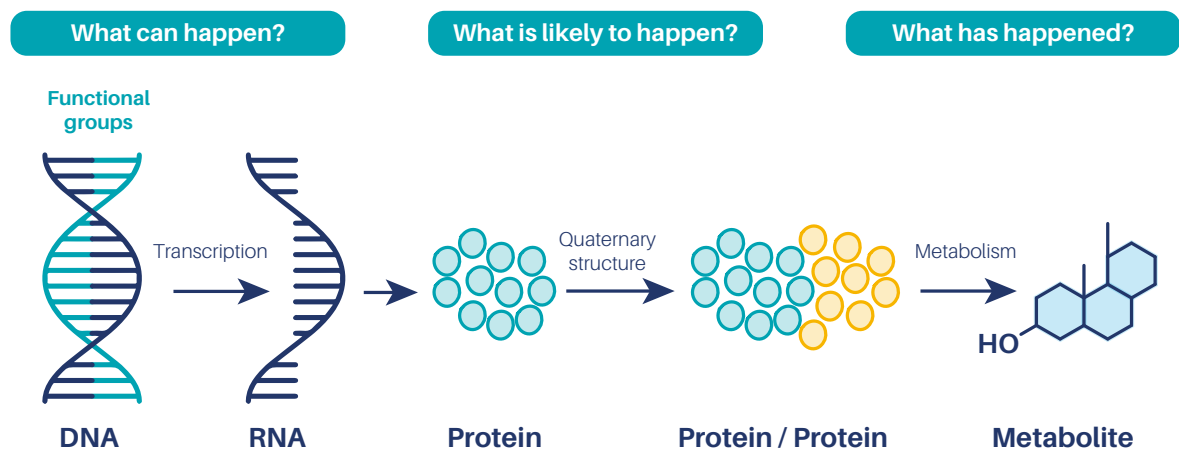
### Advantages of metabolomic analysis at a glance

■ Enhanced diagnostic insights	Overview of <i>active microbial processes</i>
■ Targeted therapeutic approaches	<i>Personalized treatment methods</i> based on metabolite profiles
■ Detection of toxic metabolites	Identification of harmful metabolic products <i>for targeted interventions</i>
■ Influence on metabolic pathways	<i>Rapid therapeutic effects</i> through metabolic modulation
■ Improved treatment success monitoring	<i>Faster detection of therapy effects</i> , allowing for adjustments in the treatment regimen



## What you should also know!!

In microbiome analyses, bacteria are typically classified into specific species or genera based on their genetic information (16S NGS), with certain traits attributed to them or their presence linked to potential risks. For instance, *Bifidobacteria* are known to produce lactate and help regulate the gut environment, while *Faecalibacterium prausnitzii* is recognized for its strong butyrate-producing capabilities [10]. However, these functions are not exclusive to these bacteria—other species can also produce lactate or butyrate. Such bacteria can be grouped into broader ‘functional groups’ based on their metabolic roles. This classification is guided by scientific literature and empirical data, which suggest that these bacteria often carry the genetic potential to produce specific metabolites. Yet, the mere presence of this genetic information does not guarantee its activation in every individual. Whether these genes are truly expressed and contribute to metabolite production can only be confirmed by directly measuring the resulting metabolites. Without this data, conclusions about gut activity remain speculative. The Microbolome test closes this gap by simultaneously analysing both bacterial presence and metabolite production, providing a clear picture of what is actually happening in the gut—something conventional microbiome tests cannot offer.



**Fig. 3** Functional groups and the detection of metabolites in stool: the path from bacterial genes through their expression to the measured metabolic product.

Source modified: *Acta Scientiae Veterinariae* (2010) 38 (Supl 2): S591ff

## *Bibliography:*

- [1] Fitzgerald, P et al. "Tryptophan catabolism in females with irritable bowel syndrome: relationship to interferon-gamma, severity of symptoms and psychiatric co-morbidity." *Neurogastroenterology and motility* vol. 20,12 (2008): 1291-7. doi:10.1111/j.1365-2982.2008.01195.x
- [2] Mawe, Gary M, and Jill M Hoffman. "Serotonin signalling in the gut--functions, dysfunctions and therapeutic targets." *Nature reviews. Gastroenterology & hepatology* vol. 10,8 (2013): 473-86. doi:10.1038/nrgastro.2013.105
- [3] Aggarwal, Surbhi et al. "Dysregulation of GABAergic Signalling Contributes in the Pathogenesis of Diarrhea-predominant Irritable Bowel Syndrome." *Journal of neurogastroenterology and motility* vol. 24,3 (2018): 422-430. doi:10.5056/jnm17100
- [4] Fabisiak, Adam et al. "Targeting Histamine Receptors in Irritable Bowel Syndrome: A Critical Appraisal." *Journal of neurogastroenterology and motility* vol. 23,3 (2017): 341-348. doi:10.5056/jnm16203
- [5] Di Paola, Rossella et al. "Possible Effects of Uremic Toxins p-Cresol, Indoxyl Sulfate, p-Cresyl Sulfate on the Development and Progression of Colon Cancer in Patients with Chronic Renal Failure." *Genes* vol. 14,6 1257. 13 Jun. 2023, doi:10.3390/genes14061257
- [6] Fleishman, Joshua S, and Sunil Kumar. "Bile acid metabolism and signaling in health and disease: molecular mechanisms and therapeutic targets." *Signal transduction and targeted therapy* vol. 9,1 97. 26 Apr. 2024, doi:10.1038/s41392-024-01811-6
- [7] Gupta, Sonu Kumar et al. "Microbiota-derived tryptophan metabolism: Impacts on health, aging, and disease." *Experimental gerontology* vol. 183 (2023): 112319. doi:10.1016/j.exger.2023.112319
- [8] Shinde, Rahul, and Tracy L McGaha. "The Aryl Hydrocarbon Receptor: Connecting Immunity to the Microenvironment." *Trends in immunology* vol. 39,12 (2018): 1005-1020. doi:10.1016/j.it.2018.10.010
- [9] Kanoski, Scott E et al. "GLP-1 and weight loss: unraveling the diverse neural circuitry." *American journal of physiology. Regulatory, integrative and comparative physiology* vol. 310,10 (2016): R885-95. doi:10.1152/ajpregu.00520.2015
- [10] Miquel, S et al. "Faecalibacterium prausnitzii and human intestinal health." *Current opinion in microbiology* vol. 16,3 (2013): 255-61. doi:10.1016/j.mib.2013.06.003



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