



MICROBIOME RESILIENCE, IS KEY TO ENSURING CONSISTENCY

Alterion® is a consistent probiotic, especially designed for poultry, which provides **microbiome resilience**. This helps them face many external challenges, to maintain their physiological status in perfect equilibrium - or **homeostasis**.

How does it work?

The microbial ecosystem of the gastrointestinal tract is characterized by a great number of microbial species living in balance by adopting a multitude of interaction strategies; constituting the basis of **microbial ecology**.

The eubiosis/dysbiosis condition of the gut microbiota strongly influences animals' healthy and disease status.

In other words, the intestinal microbiota influences the host at every level; the microbiota and the host form a real **holobiont**.

The poultry's intestine is a complex and rich ecosystem that provides multiple levels of intercellular signaling among:

- the microbiota components including harmful and beneficial bacteria
- the host responses including barrier functions and inflammatory status

Understanding the communication and pathways involved in these interactions is essential to improve our knowledge of animal physiology, and thus help maintain their physiological condition and/or support their resilience to stress factors.

Alterion® has been carefully selected for its effects on the holobiont which are linked to **Alterion®'s ability to produce specific beneficial components named metabolites.**



1 ALTERION® POSITIVELY INFLUENCES THE MICROBIOTA

Alterion® has been shown to stimulate the development of *Firmicutes* phylum, including *Ruminococcus*.

These bacteria are known to breakdown polysaccharides to oligosaccharides (*Jacquier et al, 2019*).

Alterion® also stimulates the development of *Lachnoclostridium*, and *Anaerostipes*. Most butyrate producers, including *Lachnoclostridium* and *Anaerostipes*, need oligosaccharides to grow.

Butyrate is a very important microbial metabolite, as it represents the main source of energy for enterocytes (*Jacquier et al, 2019*). Moreover, butyrate modulates immunity, the inflammatory response and reduces oxidative status (*Bishop et al., 2017*).

Some 'beneficial' bacteria depend also on other bacteria for their survival.

For instance, *Faecalibacterium prausnitzii* and *Subdoligranulum variabile* are beneficial bacteria which produce butyrate. These bacteria need niacin to grow (*Soto-Martin et al. 2018*).

2 ALTERION® PRODUCES METABOLITES THAT CREATE AN UNFAVORABLE ENVIRONMENT FOR COMMUNICATION BETWEEN BACTERIA

In addition to the cooperation between Alterion® and the beneficial bacteria, the effect of Alterion® on microbial ecology also involves the production of metabolites that create an unfavorable environment for communication between bacteria.

Indeed Alterion® has been shown to produce metabolites such as amicoumacins and fengycins, which are known to affect quorum-sensing pathways; limiting the intestinal colonization by unfavorable bacteria, in particular.

As a consequence, Alterion® metabolites shape microbial ecosystems, directly or by 'emptying' ecological niches.





EFFECT ON THE HOST

3 ALTERION® PRODUCES METABOLITES WHICH CONTROL THE INFLAMMATORY RESPONSE

Alterion® has been shown to produce niacin *in vitro* and *in vivo*.

Niacin serves as a vitamin B3 source and plays an essential role in a multitude of cellular functions. It is an agonist for the butyrate receptor Gpr109a, which is key for the regulation of intestinal inflammation.

Indeed, butyrate together with other SCFAs induce TGF- β secretion by epithelial cells. Butyrate and niacin bind Gpr109a on epithelial cells, in order to trigger the production of a cytoprotective cytokine IL-18. These microbial metabolites also stimulate dendritic cells and macrophages to produce IL-10 and retinoic acids. Therefore, butyrate and niacin contribute to the maintenance of intestinal homeostasis through multiple mechanisms (Lee *et al.*, 2014).

Thus, by producing niacin, Alterion® contributes to the improvement of host resilience.

4 ALTERION® PRODUCES METABOLITES WHICH STRENGTHEN THE INTESTINAL BARRIER

Alterion® has been shown to produce hypoxanthine *in vitro* and *in vivo*.

Hypoxanthine is a checkpoint stress metabolite in colonic epithelial energy modulation and barrier function.

By increasing the intracellular ATP, hypoxanthine increases the total available energy for the intestinal cells (Lee *et al.*, 2018).

This leads to an improvement of cytoskeletal G-actin to F-actin polymerization and therefore better cytoskeleton contractibility, which is essential for maintaining the well-functioning of tight junctions.

Thanks to the production of hypoxanthine, Alterion® thus improves the maintenance and recovery of intestinal barrier integrity and wound healing.

Microbiome resilience is essential for poultry to deal with challenges. Alterion® not only helps to maintain homeostasis of the gut flora but also produces metabolites directly beneficial for the host. These metabolites have a positive effect on gut integrity, intestinal inflammation and immunity. They have also been shown to limit intestinal colonization by unfavorable bacteria.

