The science behind peptidoglycans in poultry production

The influence of gut health on poultry performance has been agreed for some time. With antibiotic growth promoters banned in Europe and reduction in antibiotic use a hot topic worldwide, agriculture needs to look for new solutions. The incidence of necrotic enteritis and dysbacteriosis has increased. As a result, producers are often seeing reduced weight gain, due to reduced nutrient digestibility and absorption.

by Filip van Immerseel, Ghent University, Faculty of Veterinary Medicine, Department of Pathology, Bacteriology and Avian Diseases.

Wet litter is also a symptom, which has welfare implications – for example footpad lesions. A new research focus is about 'waste' in the gut, specifically lipopolysaccharides and peptidoglycans from commensal bacteria, and their influence on gastrointestinal functionality. This article will focus on peptidoglycans.

What are peptidoglycans?

Bacterial cell walls are composed of several layers; apart from membranes, the lipopolysaccharides, proteins and peptidoglycans (PGN) can make part of it.

Gram-positive bacteria have a thick outer layer of PGN, whilst Gram-negative bacteria have a thin layer in between the inner and outer membrane and lipopolysaccharides (Fig. 1).

PGN consists of a large amino acids/sugar polymer structure (Fig. 2), which offers bacteria structural support against osmotic pressure and protects the bacterium against external insults.

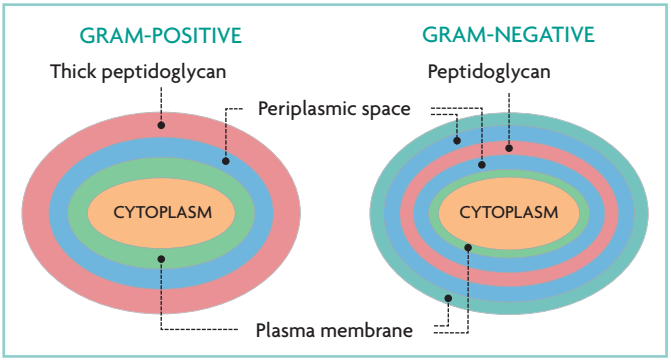
Bacterial turnover in the gut results in release of cell wall fragments and thus a large amount of PGN left in the intestine. Whilst most of the intestinal microbiota does not cause disease, the cell wall fragments can contribute to intestinal 'waste'.

Intestinal waste

Cell wall fragments including PGN can impact nutrient digestion and absorption, because of intestinal inflammation reactions that the PGN might trigger. Natural bacterial cell death generates an abundant source of PGN in the intestine. When an increase in the gastrointestinal microbial load occurs, the result is an increase in bacterial cell debris and hence more PGN.

Science is discovering more about relationships between the host mucosal immune system and the microbiome. Research on the PGN content of the gut lumen and its subsequent effects on inflammation, digestibility and absorption is important.

Fig. 1. Gram-positive bacteria have a thick layer of peptidoglycan (PGN), shown in red, outside the membrane. Gram-negative bacteria have significantly less PGN inside the membrane (DSM).



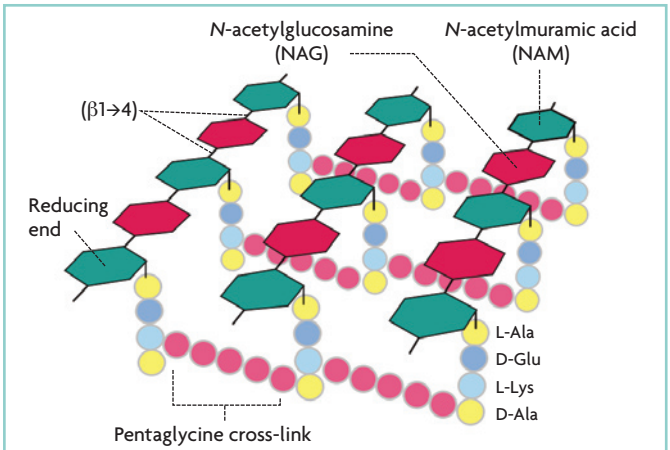


Fig. 2. Structure of a peptidoglycan polymer (DSM).

PGN in the gut

Peptidoglycans are continuously being released into the intestine. Damage to the epithelium is inevitable (eg. coccidia, mycotoxins, bacterial toxins) and allows PGNs to reach and activate receptors on the basolateral surface of epithelial cells, such as TLR2, activating an inflammatory pathway. In the gut, PGN recognition proteins bind to PGN and are able to cleave the molecule in smaller pieces.

Also intestinal lysozyme can degrade PGN. This decreases the potential inflammatory signal PGN causes. The breakdown of PGN can also result in muramyldipeptide (MDP) formation, which in turn is sensed by intracellular receptors (such as NOD2) and has an anti-inflammatory effect.

Future structural and biochemical analyses of the peptidoglycan will lead to a greater understanding of the relationship between bacterial cell death and host immune recognition.

The role of enzymes

Enzymes produced in response to infection are the cornerstones of innate immunity. They can help to modulate the host's immune system when pathogens are present, and some have an antibacterial effect. Certain endogenous enzymes kill bacteria through hydrolysis of PGN. This breakdown process can release bacterial products, including PGN.

This, in turn, can activate receptors on the host cells – initiating inflammatory responses when PGN are sensed by TLR2.

However, enzymes are also key to reducing inflammation at mucosal sites, when PGNs are further broken down. The exact nature of this delicate balance is not fully clear.

Immune effects of PGN

Peptidoglycan detection plays a critical role in initiating both innate and adaptive responses to infection and has been linked to inflammatory conditions.

As peptidoglycan recognition can drive inflammatory responses during gastrointestinal infection, enzymatic mechanisms that control the balance between pro-inflammatory and anti-inflammatory signalling are key.

If the structure of the PGN can be altered as such that the potentially pro-inflammatory PGNs can be cleaved to anti-inflammatory MDPs, for poultry production this could mean that energy can be saved from unwanted inflammatory responses – leading to optimal performance and welfare. ■