

## Editorial

# Modulation of the Intestinal Microbiota Composition and Productive Parameters in Productive Animals and Birds

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The monogastric industry is at present leading meat production in the European Union (up 58% of the total value of production) with a 14.2% economic share in agricultural production (EUROSTAT, 2006-2007). Meanwhile, poultry producers are able to produce chicken meat at half price than in the 1950's, mainly due to a decline in recent years from 2.6 to 1.6 in the feed conversion ratios. Unfortunately, the strong selection in broilers in search for a higher growth rate has at the same time inadvertently resulted in marked changes in the development of the digestive system of the birds, along with other adverse effects such as metabolic disorders, low responsiveness of the immune system and decreased resistance to pathogens [1]. On the other hand, species from genera *Salmonella* and *Campylobacter* give rise to more than 90% of global food borne infections. *Salmonella* spp produces around 160,000 food infections per year in the EU, with an incidence of 35 cases per 100,000 inhabitants, and with a cost of about 2.8 M€ per year [2].

With the information currently available, there is no doubt that the intestinal microbiota is directly or indirectly involved in all physiological and pathological processes that occur in the digestive tract of higher animals and man. It is known that under normal health and nutrition conditions, the main role of the commensal gut microbial community in monogastrics, including birds, is related to its ability to provide an effective health barrier against invading pathogens [3]. However, although it is known that the flora is involved in all the digestion and absorption processes occurring within the gastrointestinal tract, its study has been so far quite limited and many species have not yet been identified [4].

Antibiotics have long been used in animal feed both as therapeutics and as growth promoters (antibiotic growth promoters, AGPs) [5]. However, evidence that the genes for antibiotic resistance can be transmitted to the human microbiota [6], and the detection of pathogenic bacteria resistant to some antimicrobial agents [7], has led to the full ban of AGPs use in the EU since January 2006 (EC Regulation 1831/2003; <http://eur-lex.europa.eu/en/index.htm>). This prohibition has represented an added pressure on producers, and one of the consequences of this has been the increased use of antibiotics in veterinary therapy. For example, there is evidence that AGPs have been effective in the prevention of necrotic enteritis in chickens, and

that the incidence of this disease in countries that have banned the use of AGPs has increased [8].

There is thus a need to seek for viable alternatives capable of increasing the defensive capacity of livestock while avoiding AGPs use and maintaining adequate production levels. One possibility to achieve this goal is the use of certain additives to favorably influence performance and animal welfare, particularly through changes in the intestinal microbiota, which exerts a direct influence on host's health [9]. The establishment of an adequate microbiota is an effective barrier to colonization by opportunistic pathogens and provides metabolic substrates required by the animal (vitamins, short-chain fatty acids, etc.), and is a stimulus for proper development of the immune system. In this context, additives such as pre- and probiotics and synbiotics might become useful tools for improving health status, and therefore productive parameters, of farm animals [10].

Changes in the diet are among the main factors known to modify the balance and mutualistic relationship between gut microbiota and the host [11]. It has been reported that the presence of microorganisms modifies the use of dietary metabolizable energy in broilers [3]. One of the main factors affecting growth in broilers in the first 1-2 weeks is the digestibility of fat, which is affected by intestinal development, viscosity of the content and quality of dietary fat [12]. The composition of the intestinal microbiota has a significant influence for example on the viscosity of the contents as deduced from studies using germ-free animals, and also for the observed effect of plant extracts on intestinal viscosity and fat digestibility [13], and may also affect the content of bile salts needed to digest fats [14]. It would therefore seem possible to positively influence nutrient utilization by inducing certain changes in the composition of the intestinal microbiota. These changes can be experimentally induced by using feed additives.

The genotype x microbiota interaction was first described in mice [15], where genetically obese animals showed a composition of the microbiota different from lean mice with respect to the relative abundance of bacteroides and firmicutes. In productive animals, Guo et al. (2008) found in pigs that storage of fat may affect the proportion of bacteria from the bacteroidetes division in the gut of obese and lean animals [16]. Also, in an interesting previous work, Torok et al. (2008, 2011) have shown that the use of OTUs (operational taxonomic units) of the intestinal microbiome for T-RFLP analysis may represent a useful tool to relate changes in the microbial population with productive parameters in broiler chickens [17,18]. Accordingly, it seems likely that the relationship between changes in the composition of the intestinal microbiota and production parameters can be studied specifically by using additives that have a direct impact on the intestinal microbiota composition.

Two recently developed products, namely PTS-O/PTS (propyl propane thiosulfinate/propyl propane thiosulfonate) and DFAs (di-

D-fructose dianhydrides) have proven effective through different mechanisms to modify the intestinal microbiota by using both *in vitro* and *in vivo* models including laboratory and productive animals and birds [19-25]. Therefore, the use of these additives in feeds may be proposed as models to study, in the same production conditions (genotype, diet composition, and environmental conditions), the relationship between population changes in the microbiota and certain changes in productive and physiological parameters. The use of molecular techniques (qualitative and quantitative PCR, T-RFLP, DGGE, metagenomic sequencing, etc.), based on the nucleotide sequence of the gene encoding 16S rRNA, and far more powerful than traditional cultivation methods [26], is enabling significant progress in these kind of studies. Multivariate statistical methods can be used after the molecular microbiota analysis to establish the relationship between the microbiota composition and certain defined production parameters (feed/conversion ratio, energy use of feed, nutrients digestibility). This approach would open new ways to develop practices effective to improve productivity, welfare and safety in the animal production industry.

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