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RECERCA I TECNOLOGIA AGROALIMENTÀRIES

Feed Additives, can they improve animal welfare?

EAAP 2014, Copenhagen

J.Brufau, R. Lizardo and B. Vilà.
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27 /8/2014, Copenhagen

Generalitat de Catalunya
Departament d'Agricultura, Alimentació i Acció Rural

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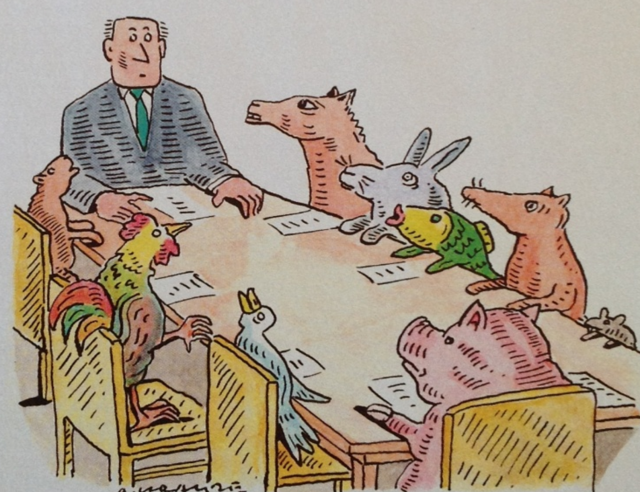
Animal welfare/ Scientist discussion

OPINION

Welcome to our world

Now that scientists have belatedly declared that mammals, birds and many other animals are conscious, it is time for society to act, says **Marc Bekoff**



ARE animals conscious? This question has a long and venerable history. Charles Darwin asked it when pondering the evolution of consciousness. His ideas about evolutionary continuity – that differences between species are differences in degree rather than kind – lead to a firm conclusion that if we have something, "they" (other animals) have it too.

In July of this year, the question was discussed in detail by a group of scientists gathered at the University of Cambridge for the first annual Francis Crick Memorial Conference. Crick, co-discoverer of DNA, spent the latter part of his career studying consciousness and in 1994 published a book about it, *The Astonishing Hypothesis: The scientific search for the soul.*

The upshot of the meeting was the Cambridge Declaration on Consciousness, which was publicly proclaimed by three eminent neuroscientists, David Edelman of the Neurosciences Institute in La Jolla, California, Philip Low of Stanford University and Christof Koch of the California Institute of Technology.

The declaration concludes that non-human animals have the neuroanatomical, neurochemical, … other creatures, including octopuses, also possess these neurological substrates."

My first take on the declaration was incredulity. Did we really need this statement of the obvious? Many renowned researchers reached the same conclusion years ago …

… the declaration did not include fish, because the evidence supporting consciousness in this group of vertebrates is also compelling.

Nevertheless, we should applaud them for doing this. The declaration is not aimed …

… consciousnes… to the rest of t…

The import… is: will this de… a difference? … scientists anc… do now that t… consciousnes… in the anima…

I hope the … used to prote… being treatec… inhumanely… scientific kn… animal cogn… consciousne… in animal we… for example… chickens dis… this knowlec… factored int… Animal Wel… 25 million o… including fi… research eac… for more th… animals use… US. I'm con… that those v… regulations… ignored the…

Not all le… science. The… Treaty of Li… into force o…

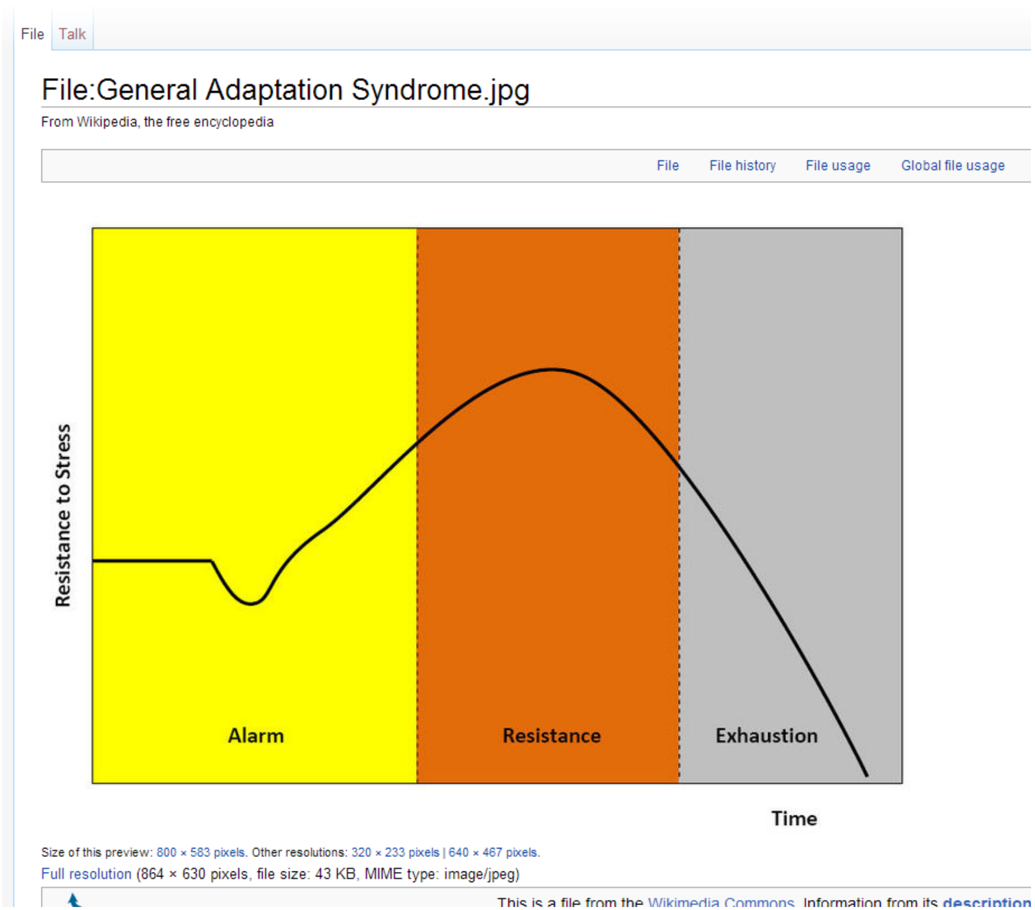
The objective of the presentation is :

- Improvement of performances through gut health is AW indicator?
- Is the health improvement easily measurable?
- What are the main indicators to be considered?
- Can these indicators be connected to animal performance?
- How is gut immunity involved in animal performance?

What does animal welfare mean in a regular farm?

- Stress induces a General Adaptation Syndrome (Selye 1950).
- Stress affects the hormonal control of metabolism, reproduction, growth and immunity.
- Conclusion: the animal adaptive response to stress is the integration of multiple, often interactive, hormone responses that directly affect health and well-being.

General Adaptation Syndrome, Selye 1950



Biological sense **STRESS** is the interaction between **damage** and **defense**

Naturally, farm animals are challenged by different stressors

- "**All farm animals** will experience **some level of stress** during their lives. Stress reduces the fitness of an animal, which can be simply expressed through failure to achieve production performance standards or targets, or more drastically, through disease and death" **(Mario Rostagno 2009)**.

- Stress factors which affect animal production :

I. Inadequate nutrition
II. Deprivation of water/ or feed
III. Heat/Cold
IV. Overcrowding
V. Handling (interaction human manipulation)

"Stress and the Gastrointestinal Tract"

- The enteric nervous system (ENS) is an integrated network located within the wall of the gastrointestinal tract. (Brain-Gut interaction).
- **Stress** may not only be responsible for functional disorders, but may **contribute to inflammatory disorders and infections of the gastrointestinal tract.**
- Neurotransmitters play a role in animal responses to challenges/stressors (Noreadrenaline-naturally **intestinal mucosal**).
- There is crosstalk between neuroendocrine and immune systems.
- An **imbalance** on these systems in **response stress** can lead to significant changes **in immune response** and consequently susceptibility to infection.

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Schematic representation of intestinal anti-inflammatory reflex (Niewold 2014)

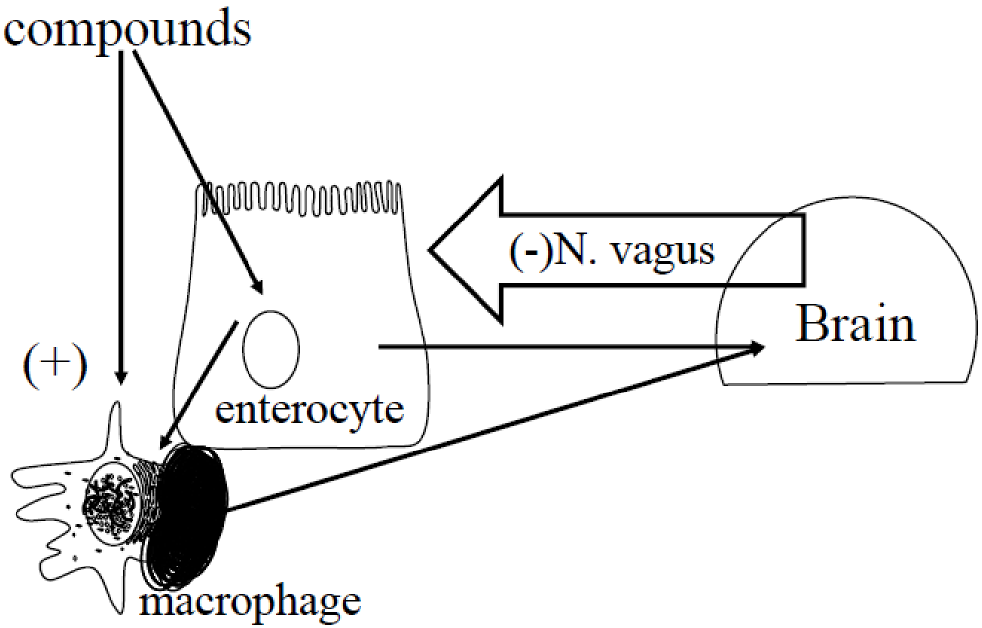

Figure 1 - Schematic representation of the intestinal anti-inflammatory reflex. Feed compounds can give a pro-inflammatory (+) stimulus to enterocytes and macrophages. This leads to the production of pro-inflammatory interleukins (ILs), which also reach the brain. A down (-) regulatory signal is returned to the intestine through the nervus (N.) vagus. Adapted after Niewold, 2013.

II. BIOMARKERS FOR GUT HEALTH IN POULTRY

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Effect of noradrenaline on the growth of Campylobacter

388 T. HUMPHREY

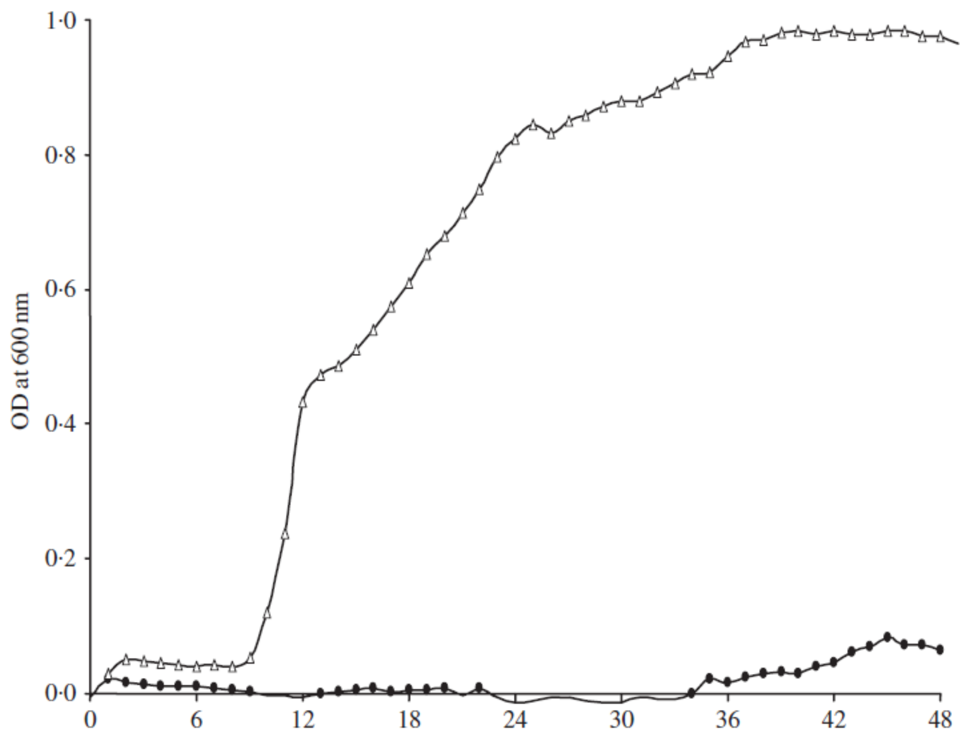

Figure 2. *Effect of noradrenaline (100 µm) on the growth of* C. jejuni *in iron-restricted media (DMEM containing 10% serum). Closed circles show the growth profile of the control cultures. Open triangles show cultures plus noradrenaline. Data from Thomas* et al. *(unpublished).*

"Stress and the Gastrointestinal Tract"

- Stress releases catecholamine and this results in:

I. Decreased gastric acid production

II. Delayed gastric emptying

III. Accelerated intestinal motility

IV. Accelerated colonic transit

Consequently increased pH in the stomach increases probability of survival of food borne pathogens (E. coli, salmonella and Campylobacter) and colonization of the gastrointestinal tract.

Feed intake / Neuroendocrine control of appetite during the stress response

Feed intake is necessary for the growth and survival of all animals, it is important for us to understand **how common stressors** reduce feed intake at the biochemical level, with the hope of someday being able to prevent or diminish appetite loss and subsequent reduction in the growth , health and **well-being of animals**.

New European model of animal production since 2002

- Animal Production should be sustainable in the EU and based on:

Animal Protection
Consumer Protection
Environment protection

Travelling to 2030; via S.E.T

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Feed additives

- Regulated By EC 1831/2003
- Substances, micro-organisms or preparations, other than feed material and premixtures, which are intentionally added to feed or water in order to perform, in particular, one or more of the functions mentioned in Article 5(3)

✓ Favourably affect the characteristics of feed or animal products
✓ Favourably affect the colour of ornamental fish and birds
✓ Satisfy the nutritional needs of animals
✓ Favourably affect animal production, performance or **welfare**
✓ Have a coccidiostat or histomonostatic effect

Outline questions

- Why Animal Welfare criteria are not yet implemented in Feed Additive evaluation?

  The concept of Animal Welfare is under revision in EU. Strategies are in progress 2012-2015.

- Which parameters are much more accepted by farmers in order to consider Animal Welfare benefits ?

- **Feed additives, may they play a role on animal welfare assessment?**

- Feed additive have to be evaluated under **Good Health** conditions?

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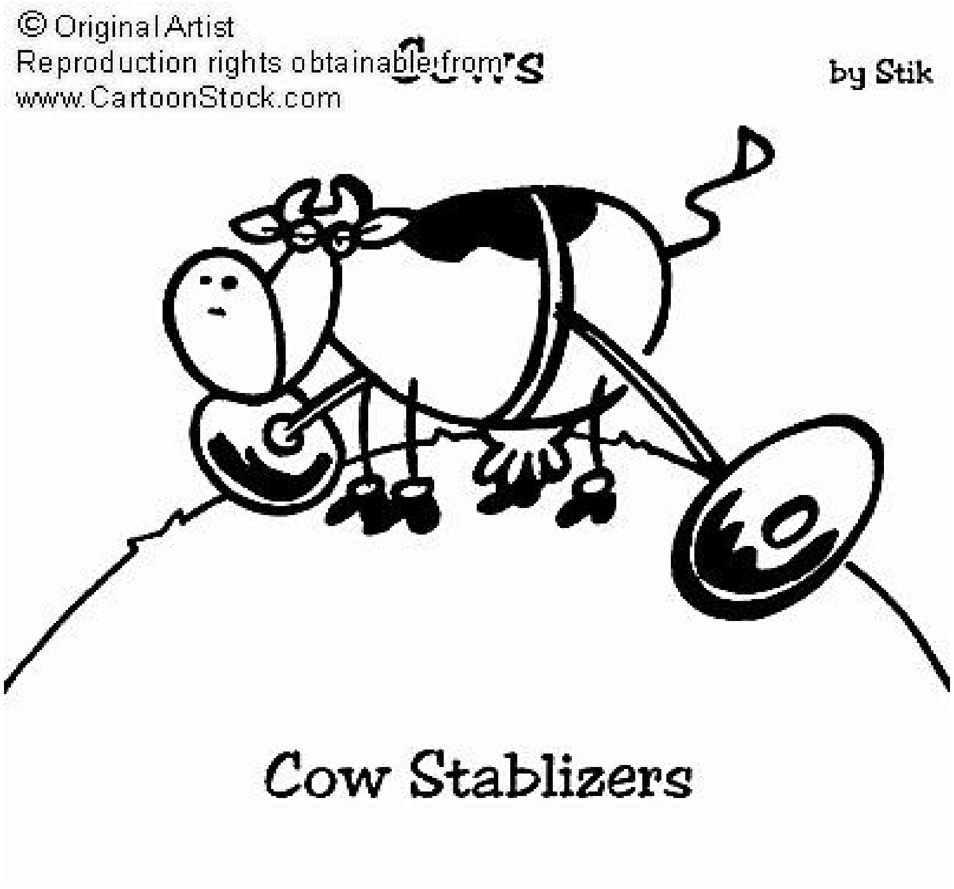
A zootechnical additive is any additive used to favourably affect the performance of animals in good health, or to favourably affect the environment



EFSA Scientific opinion /Self-task FEEDAP/ 2008

- **The purpose was to** :

  .- examine the scientific basis for the existing functional groups

  .- propose, if necessary, based on this review, the establishment of additional functional groups (or categories).

- Potential new categories

1. Additives which favorably affect **animal welfare :**

   Metabolic regulators, Immuno-modulators, Detoxifiers.

2. Additives which improve **product quality :**

   Microbial contamination controllers, Nutritional value enhancers, Sensory additives.

How to improve AW at the farm level

1.- Improve management of animals.

2.- Better knowledge of Feeding programs and feed composition.

3.- Supplementation of diets with alternative additives to AGP.

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Enriched Cages for laying hens

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Pig production 2030

EuroTier 2012

Big Dutchman

Gestation sows in free stalls

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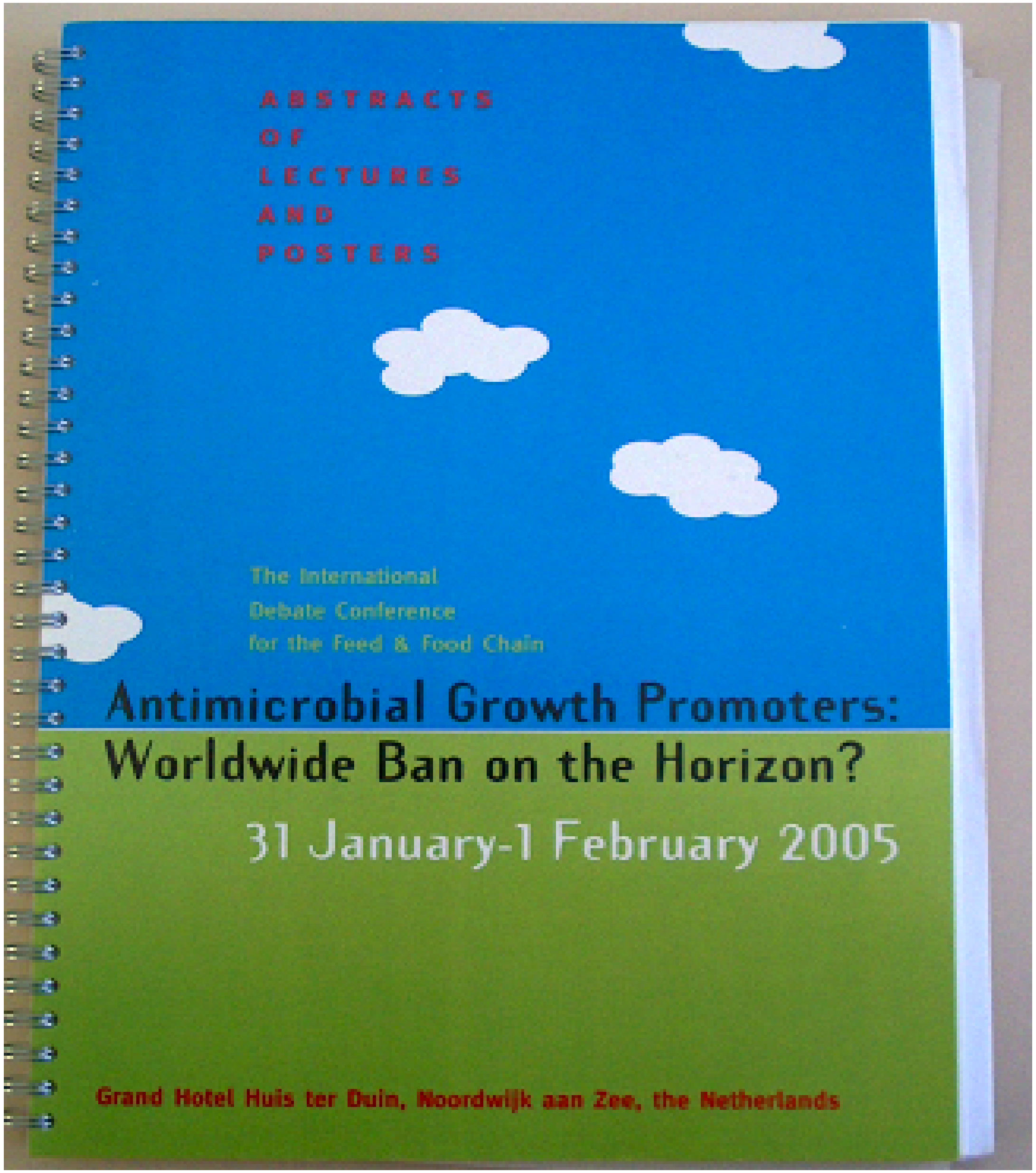
ABSTRACTS
OF
LECTURES
AND
POSTERS
The International
Debate Conference
for the Feed & Food Chain
Antimicrobial Growth Promoters:
Worldwide Ban on the Horizon?
31 January-1 February 2005
Grand Hotel Huis ter Duin, Noordwijk aan Zee, the Netherlands

Assessment of alternatives substances

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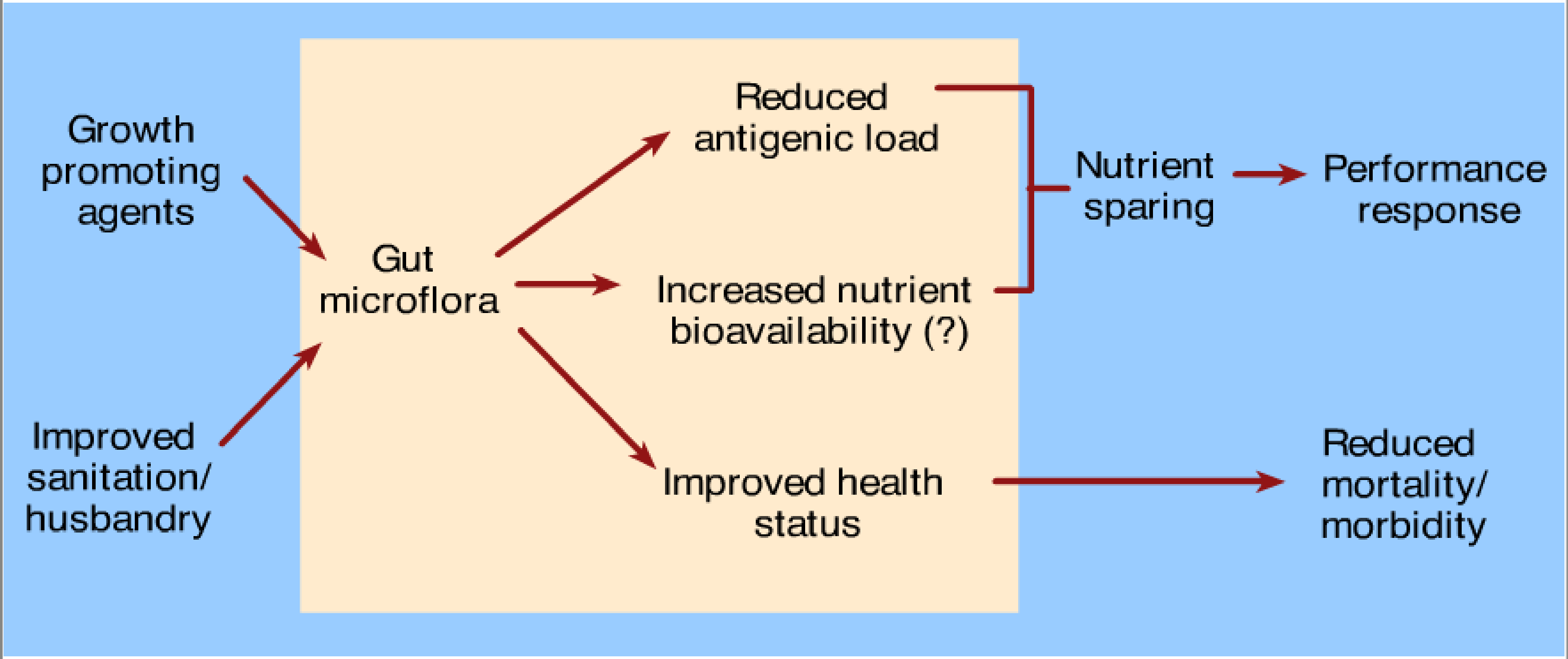
Animal nutrition and Gut microflora interactions (Animal protection)



Andrew Chesson

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WAR AND PEACE AT MUCOSAL SURFACES

Philippe J. Sansonetti

Abstract | That we live with numerous bacteria in our gut without any adverse effects is a remarkable feat by the body's immune system, particularly considering the wealth of sensing and effector systems that are available to trigger inflammatory or innate immune responses to microbial intrusion. So, a fine line seems to exist between the homeostatic balance maintained in the presence of commensal gut flora and the necessarily destructive response to bacterial pathogens that invade the gut mucosa. This review discusses the mechanisms for establishing and controlling the 'dialogue' between unresponsiveness and initiation of active immune defences in the gut. *Si vis pacem, para bellum*. (If you wish for peace, prepare for war.)

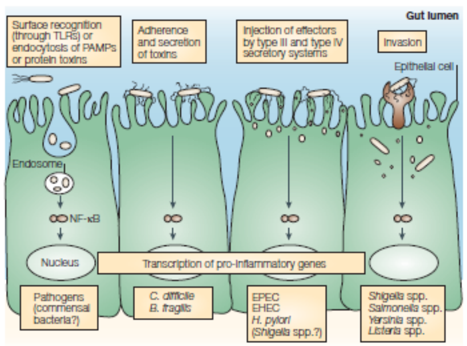

Figure 2 | **Bacteria trigger a pro-inflammatory programme in intestinal epithelial cells, using various strategies.** Pathogenic bacteria and possibly commensal bacteria can be detected by epithelial cells through cell-surface receptors (such as Toll-like receptors, TLRs) or by endocytosis of microbial products. Detection by TLRs or other intracellular pattern-recognition receptors triggers a signalling cascade that results in the activation of nuclear factor-κB (NF-κB), which translocates to the nucleus, where it promotes the transcription of pro-inflammatory genes. Some pathogenic bacteria (such as *Clostridium difficile* and *Bacteroides fragilis*) adhere to epithelial cells and secrete toxins, which induce NF-κB activation. By contrast, enteropathogenic *Escherichia coli* (EPEC), enterohaemorrhagic *E. coli* (EHEC) and *Helicobacter pylori* inject effector molecules into the cell through type III or type IV secretory systems. A different mechanism is also used by *Shigella* spp. and *Salmonella* spp., which directly invade the cell, resulting in NF-κB activation (which is thought to be largely nucleotide-binding oligomerization domain (NOD)-protein dependent) and stimulation of an inflammatory response. PAMP, pathogen-associated molecular pattern.

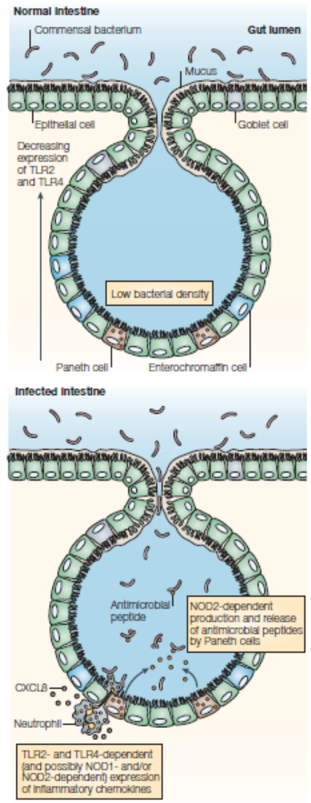

Figure 1 | **Expression of TLRs and NOD2 by luminal surface versus crypt epithelial cells in the small intestine.** This scheme shows the probable differences between the epithelial cells at the luminal surface and those in the crypts of the gut in terms of their expression of pattern-recognition receptors — such as Toll-like receptors (TLRs) and nucleotide-binding oligomerization domain (NOD) proteins — for sensing the presence of microorganisms through their pathogen-associated molecular patterns. To protect stem cells and their environment, crypts are organized as integrated units of bacterial sensing and destruction, in which Paneth cells (through their production of defensins) have an important role. A similar pattern is likely to occur in the colon, in which Paneth cells are absent, but β-defensins are produced by epithelial cells. CXCL8, CXC-chemokine ligand 8.

Mucosal surfaces place for "dialogue"

The intestinal epithelium : an interactive barrier

.- Physical barrier

.- Innate immunity

.- Adaptive immunity

Crosstalk between commensals and mucosae

Crosstalk between pathogens and mucosae

Philipe J. Sansonetti 2004

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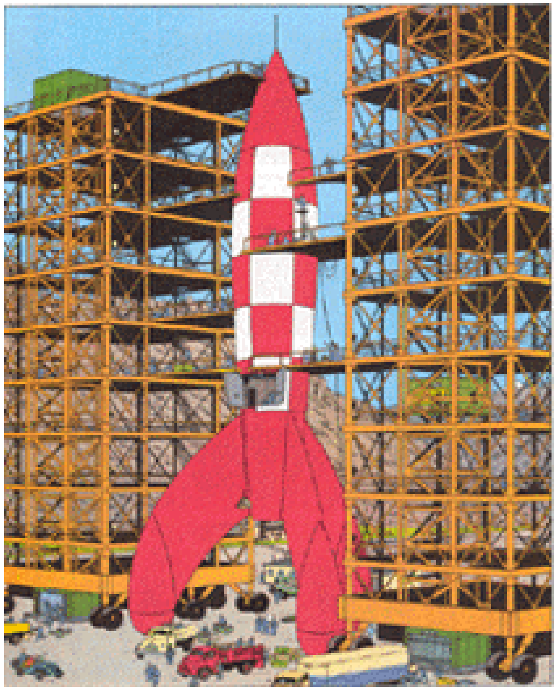
Alternative feed additive products

- Organic acids
- Enzyme preparations
- Micro-organisms (Probiotics)
- Oligosaccharides (Prebiotics)
- Immunity enhancers
- Highly available minerals
- Herbs and essential oils



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Nutritional and other studies, some examples

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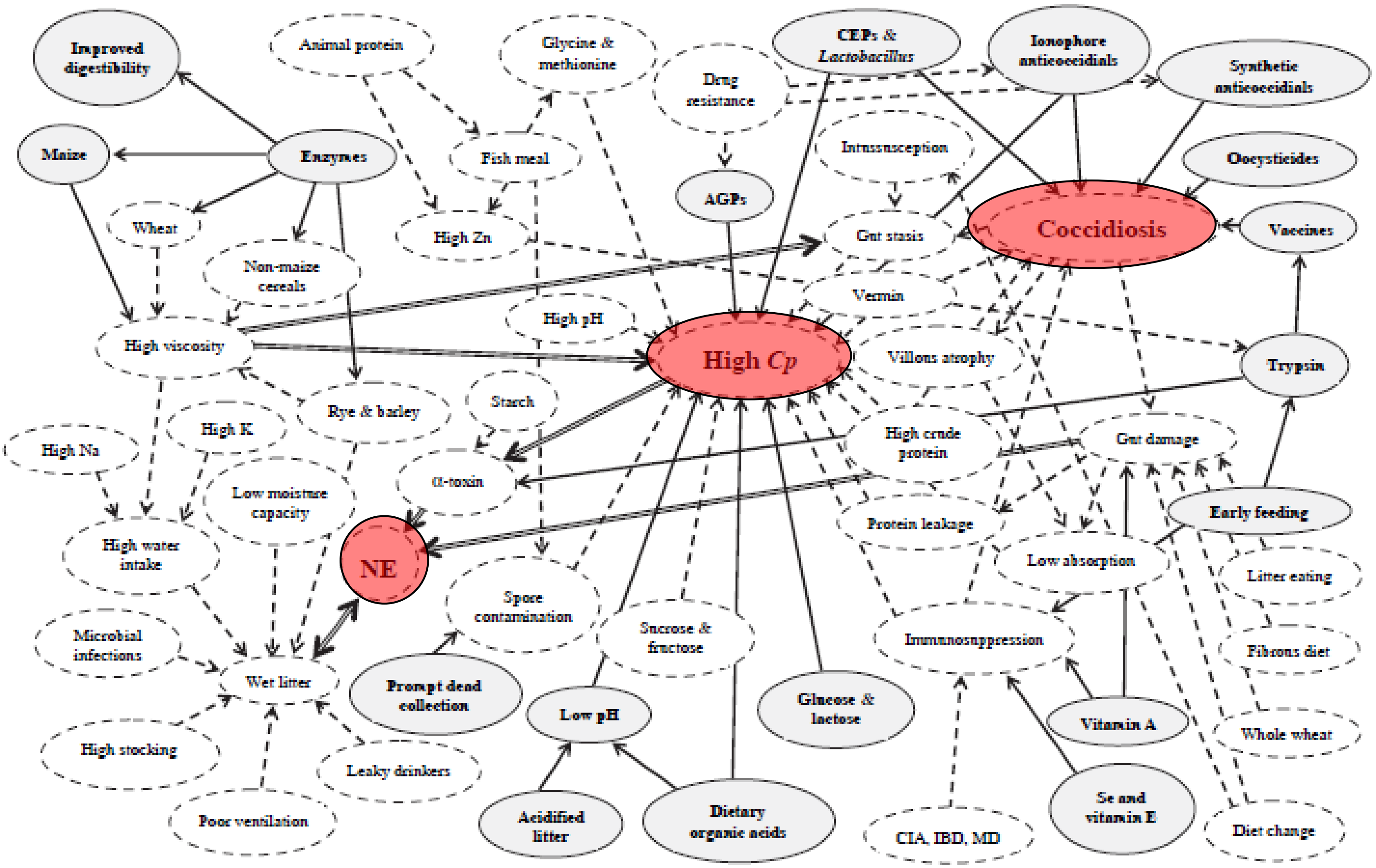
Some factors affecting wet litter in commercial poultry flocks

Williams 2005

Williams, 2005

Integrated disease management by maintenance of gut integrity



To cite this Article Williams, R. B.(2005) 'Intercurrent coccidiosis and necrotic enteritis of chickens: rational, integrated disease management by maintenance of gut integrity', Avian Pathology, 34: 3, 159 — 180
To link to this Article: DOI: 10.1080/03079450500112195
URL: http://dx.doi.org/10.1080/03079450500112195

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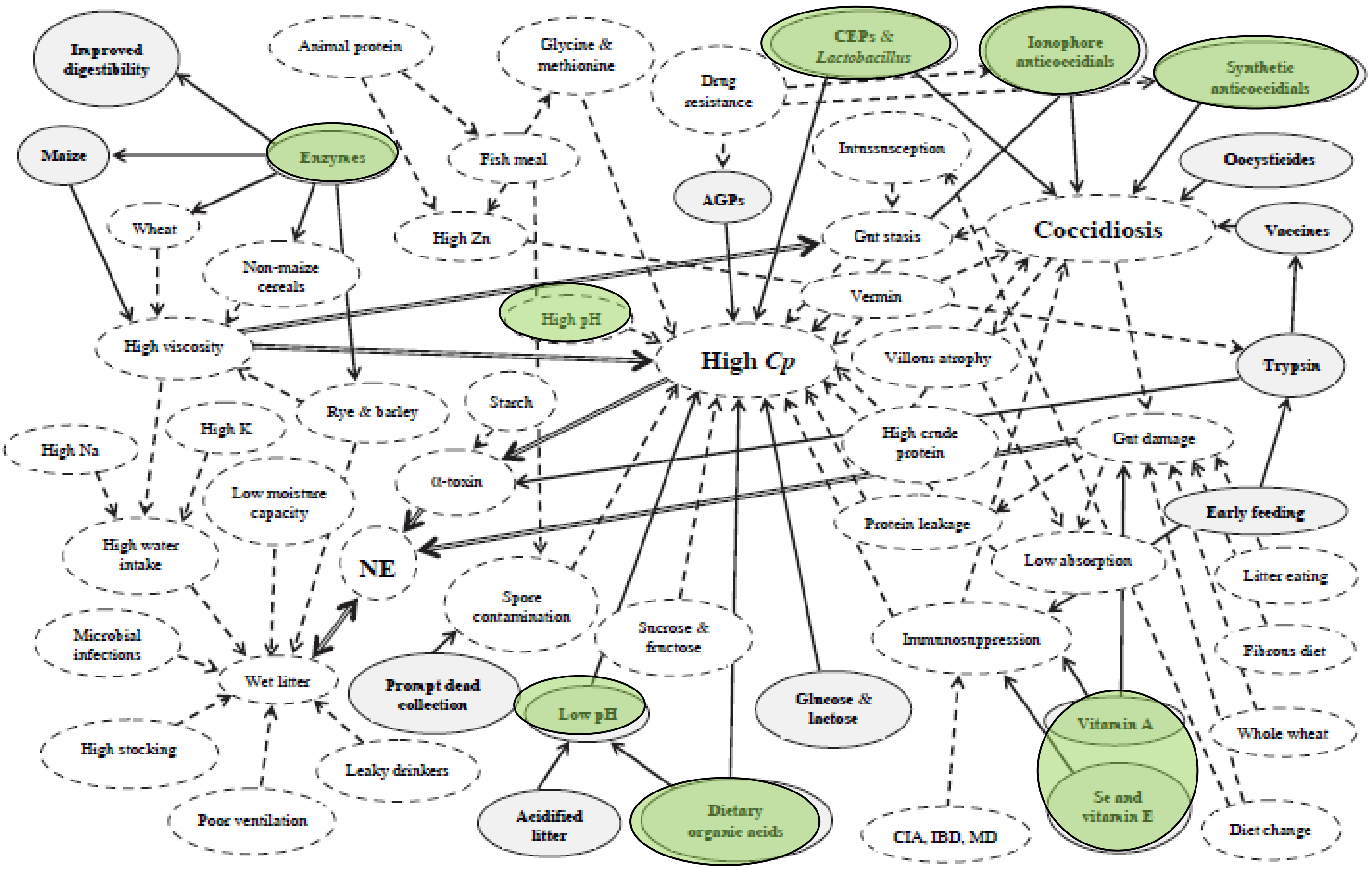

Figure 2. *The intercurrent coccidiosis-NE syndrome: a network of potentially important pathophysiological, medicinal, nutritional and husbandry factors. Those with solid-line arrows and ellipses are beneficial in controlling disease, those with dashed-line arrows and ellipses impart high disease risk. Major high-risk relationships are shown by double-line arrows. AGP, antibiotic growth promoter; CIA, chick infectious anaemia; CEP, competitive exclusion product; Cp,* Clostridium perfringens; *IBD, infectious bursal disease; MD, Marek's disease; NE, necrotic enteritis.*

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Effect of xylanase and/or monensin on performance, coccidiosis infection and digesta viscosity of chickens challenged with *Eimeria spp.*

	BW 29 d	FCR 0-29 d	E. lesions Sum (21d)	Viscosity cps (14d)
Not challenged	1457	1.53	0	14.9
Challenged				
Control	1400	1.58	6.8	9.8
Monensin	1443	1.49	3.4	8.9
Enzyme	1421	1.53	4.3	4.7
M + E	1513	1.49	3.5	5.6
Inoculation	*	*	**	*
Monensin	**	**	**	*NS*
Enzyme	*	*NS*	**	*
Interaction	*NS*	*NS*	*NS*	*NS*

Francesch *et al.*, 2008

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Examples : Efficacy assessment on immune processes

Contents lists available at ScienceDirect

Veterinary Immunology and Immunopathology

journal homepage: www.elsevier.com/locate/vetimm

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Short communication

β 1-4 mannobiose enhances *Salmonella*-killing activity and activates innate immune responses in chicken macrophages

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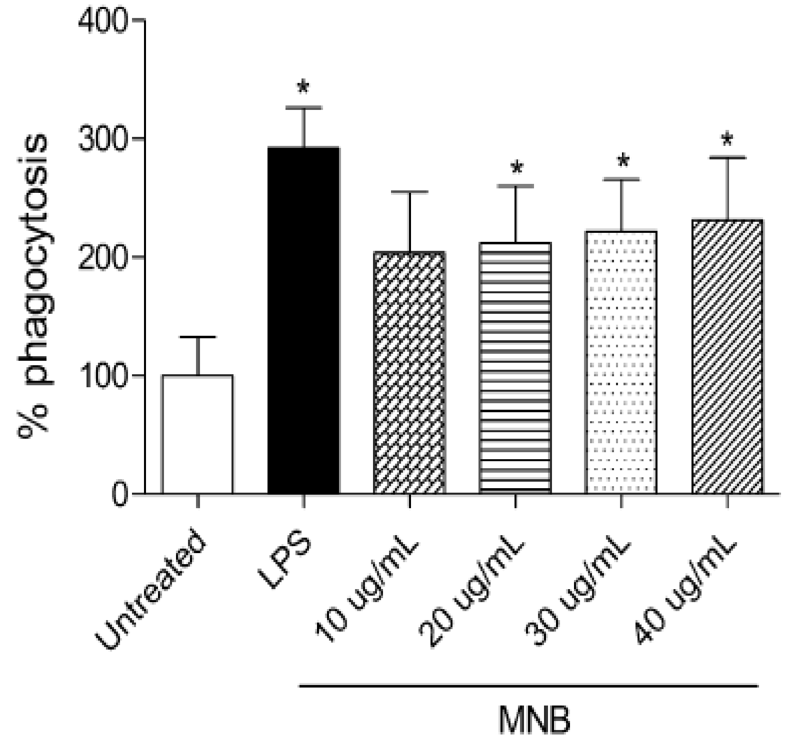

Fig. 1. Effect of MNB on phagocytic activity of chicken macrophages. MQ-NCSU cells were treated with increasing concentrations of MNB for 2 h, followed by incubation with fluorescein-labeled *E. coli* BioParticles. Data shown are mean ± SEM. Results are expressed as % phagocytosis relative to untreated cells. *$P < 0.05$ compared to untreated cells.

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British Poultry Science
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/cbps20

Immune-modulatory effects of dietary Saccharomyces cerevisiae cell wall in broiler chickens inoculated with Escherichia coli lipopolysaccharide

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Accepted author version posted online: 11 Mar 2013.Published online: 07 May 2013.

Table 4. *Effects of yeast cell wall (YCW) on the relative lymphoid organ weight[1] and the delayed cutaneous hypersensitivity reaction of chicken[2] inoculated with LPS of E. coli*

Effect		21 d (g/100 g of body weight) Spleen	21 d (g/100 g of body weight) Bursa of Fabricius	Delayed cutaneous hypersensitivity reaction 14 d (mm)
YCW				
0 mg/kg		0.125	0.290	0.301
500 mg/kg		0.112	0.304	0.441
LPS-*E. coli*				
Without challenge		0.117	0.331	0.326
With challenge		0.120	0.263	0.416
YCW	LPS-*E. coli*			
No	No	0.114	0.348[a]	0.238[c]
Yes	No	0.120	0.314[a]	0.414[a]
No	Yes	0.136	0.232[b]	0.365[b]
Yes	Yes	0.105	0.294[a]	0.467[a]
SE		0.016	0.024	0.050
Source of variation (*P*)				
YCW		0.42	0.53	0.01
LPS-*E. coli*		0.84	0.01	0.13
Interaction		0.24	0.031	0.44

[1] $n = 11$ chickens.
[2] $n = 8$ chickens.
[a, b] Within a column, values not sharing a common superscript letter are significantly different ($P \leq 0.05$).

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Immune responses to dietary β-glucan in broiler chicks during an *Eimeria* challenge

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*Avian Immunobiology Laboratory, Department of Animal and Poultry Sciences, Virginia Tech, Blacksburg 24061; and †AB Vista Feed Ingredients, Marlborough, Wiltshire, SN8 4AN, United Kingdom

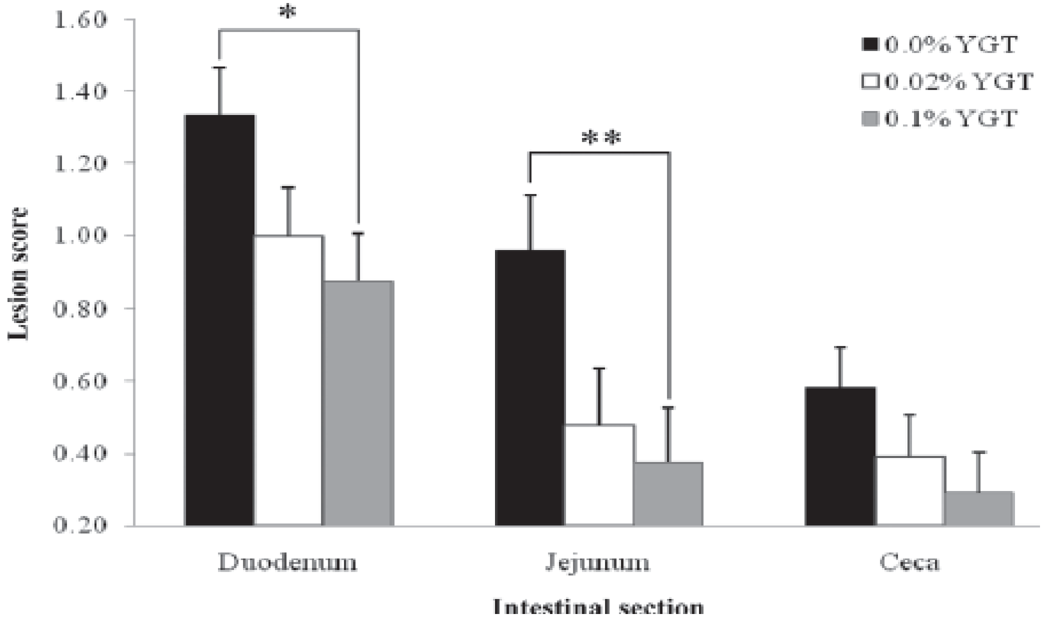

Figure 1. Effect of β-glucan supplementation on gross intestinal lesions scores of Cobb 500 broiler chicks on d 14 (6 d post *Eimeria* infection). Data are represented as least squares means + SEM. YGT = Auxoferm YGT, *Saccharomyces cerevisiae*-derived β-glucan. There was a significant effect of dietary treatment in the duodenum (*$P = 0.04$) and jejunum (**$P = 0.02$).

2010 Poultry Science 89 :2597–2607

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IMMUNOLOGY, HEALTH, AND DISEASE

Limited Treatment with *β-1,3/1,6-Glucan Improves Production Values* of Broiler Chickens Challenged with *Escherichia coli*

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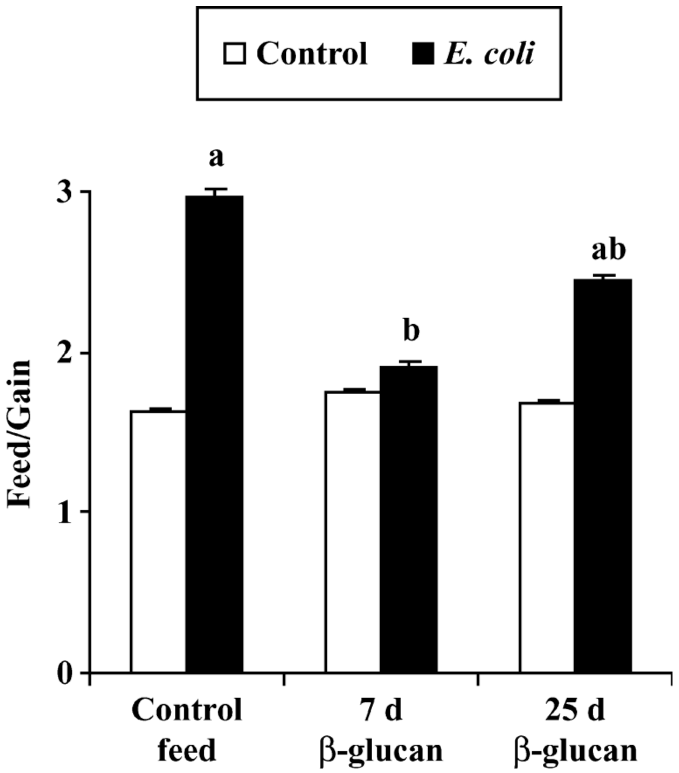
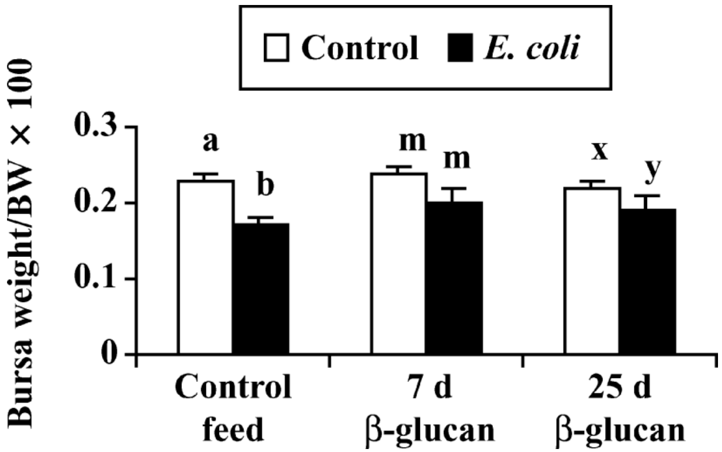
USDA, Agricultural Research Service, Poultry Production and Product Safety Research, and Department of Poultry Science, University of Arkansas, Fayetteville 72701





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B- galactomanan and *Saccharomyces cerevisiae* modulate Immune response in pigs

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β-Galactomannan and *Saccharomyces cerevisiae* var. *boulardii* Modulate the Immune Response against *Salmonella enterica* Serovar Typhimurium in Porcine Intestinal Epithelial and Dendritic Cells

Roger Badia,[a,b] M. Teresa Brufau,[c] Ana Maria Guerrero-Zamora,[c] Rosil Lizardo,[a] Irina Dobrescu,[b] Raquel Martín-Venegas,[c] Ruth Ferrer,[c] Henri Salmon,[d] Paz Martínez,[b] and Joaquim Brufau[a]
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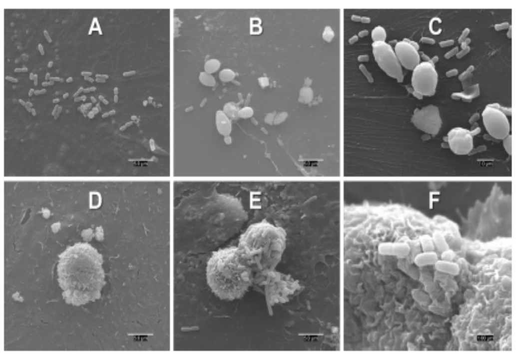

FIG 2 Interaction of *Salmonella* with βGM or *S. cerevisiae* var. *boulardii* on the surface of IPI-2I cells assessed by scanning electron microscopy. Images show *Salmonella* attachment on control IPI-2I cells (A), *Salmonella* with *S. cerevisiae* var. *boulardii* (B and C), control βGM (D), and *Salmonella* with βGM (E and F).

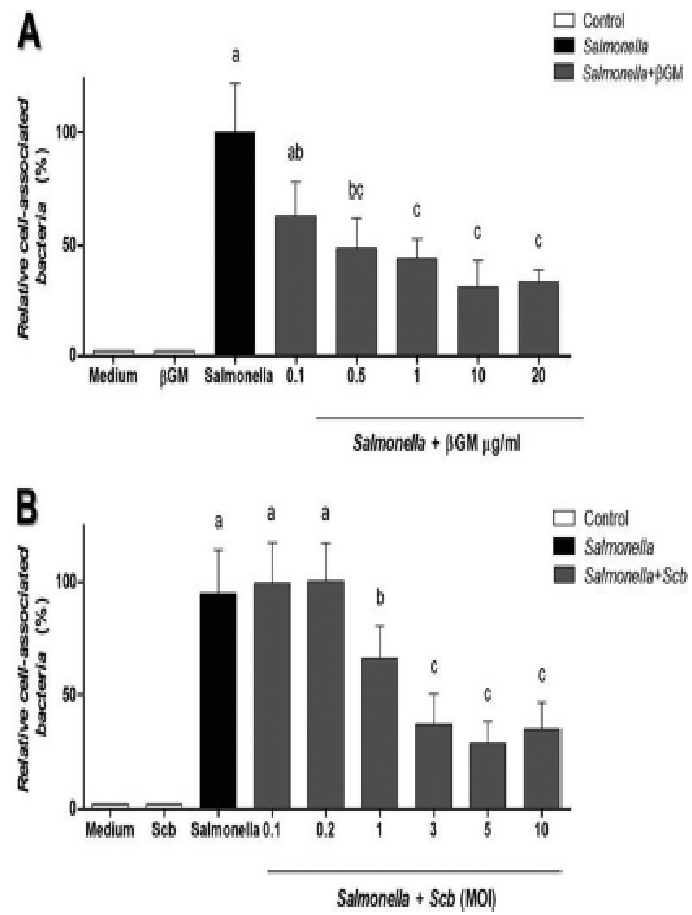

FIG 1 Cell-associated *Salmonella* on IECs in the presence of βGM or *S. cerevisiae* var. *boulardii* (*Scb*). Adherence and/or invasion of *Salmonella* on IECs cocultured with βGM (A) or *S. cerevisiae* var. *boulardii* (B) is inhibited in a dose-dependent manner. Data ($n = 5$) are expressed as mean percentages ± standard deviations (SDs). Columns within each histogram with no common superscripts are significantly different ($P < 0.05$).

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B- galactomannan and *Saccharomyces cerevisiae* modulate Immune response in pigs

Badia et al.

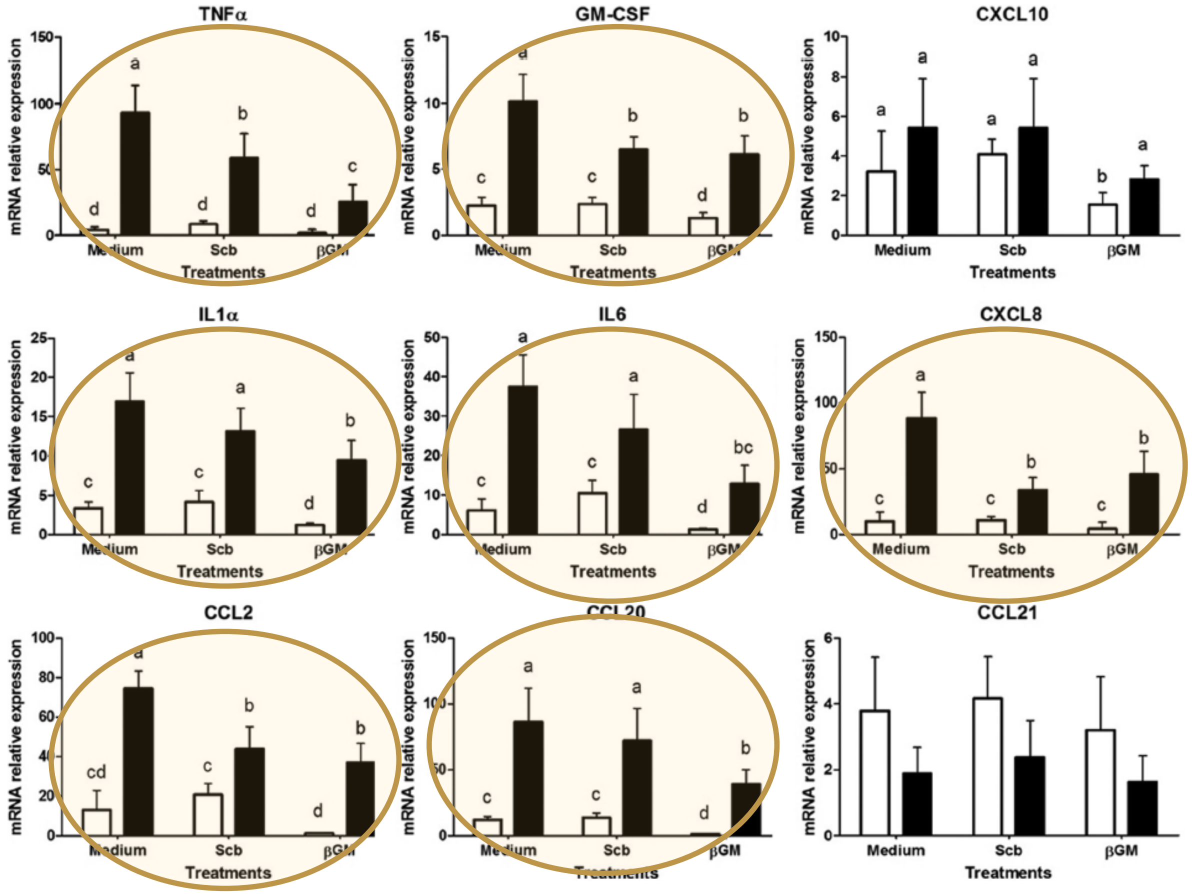


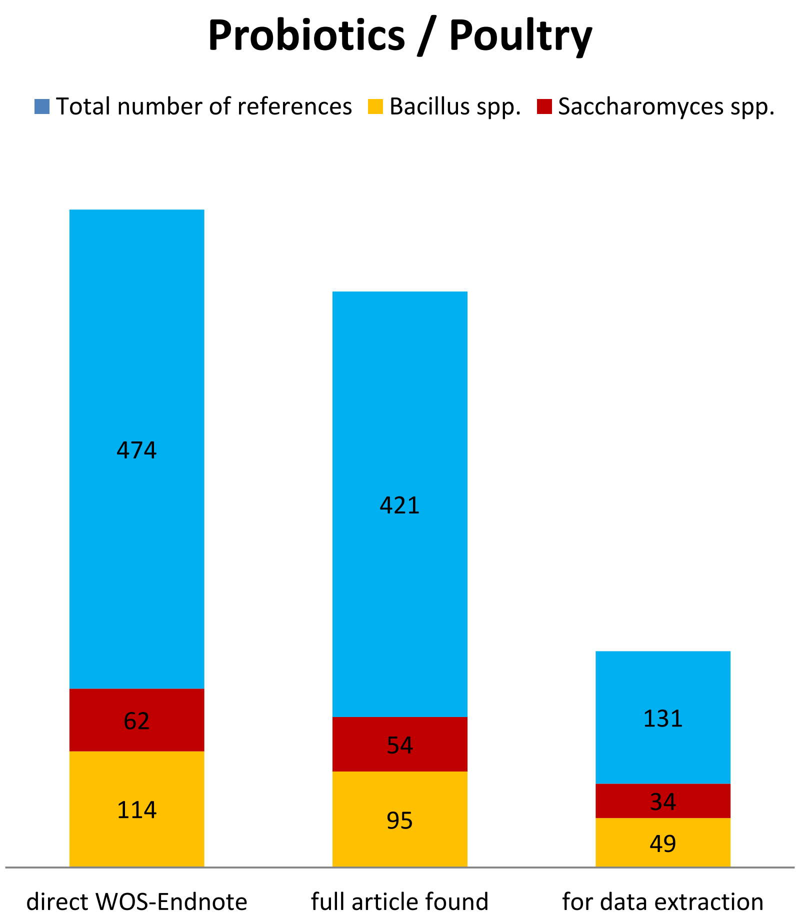
FIG 3 Effects of *S. cerevisiae* var. *boulardii* (Scb) and βGM on cytokine and chemokine mRNA expression in IECs cultured with *Salmonella*. IECs (1×10^6 cells/well) were cocultured with *S. cerevisiae* var. *boulardii* (3 yeast cells/cell) or βGM (10 μg/ml) with *Salmonella* (MOI of 4) for 3 h. Data ($n = 6$) are presented as means of mRNA relative expression ± SDs. Columns within each histogram with no common superscripts are significantly different ($P < 0.05$). Results are representative of 3 independent experiments. □, control; ■, *Salmonella*.

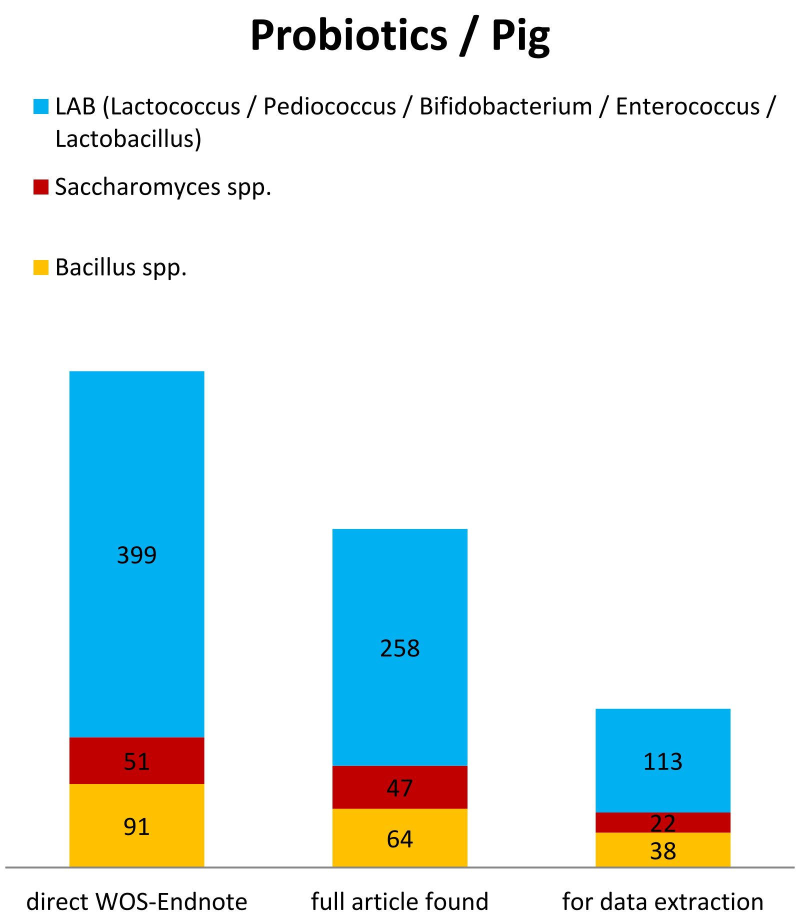
Probiotics (Direct feed microbial)

Preliminary update on functionality of probiotics in poultry and pig feeding.

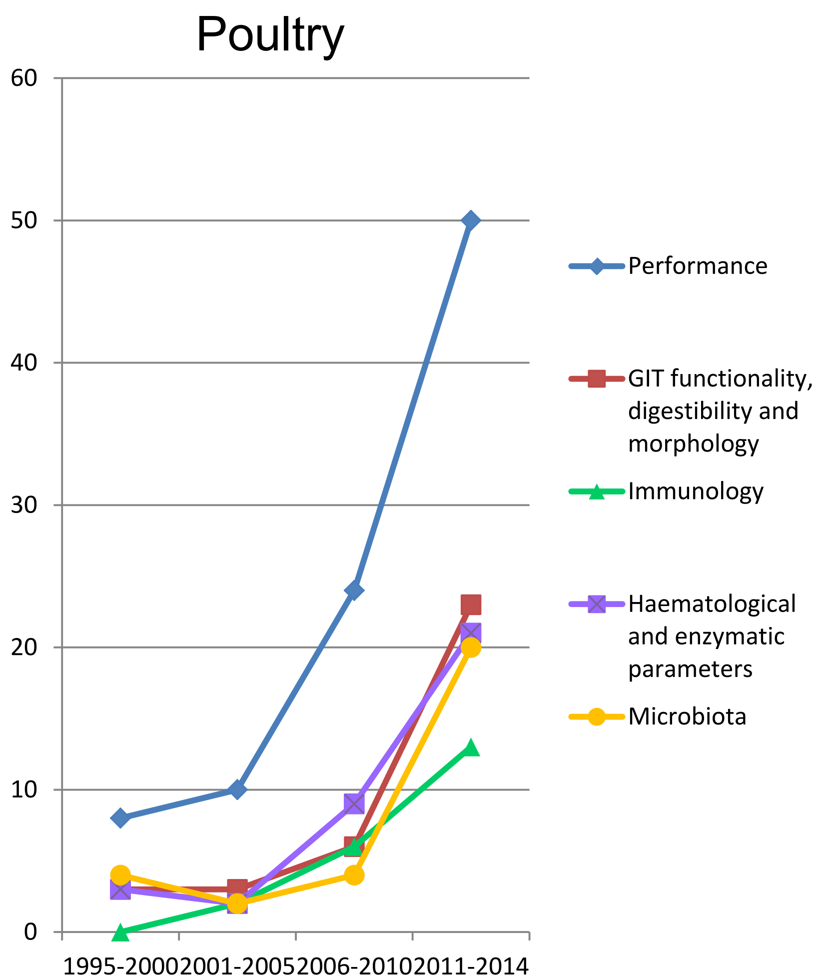
Functionality of probiotics application, review from 1995 until now.

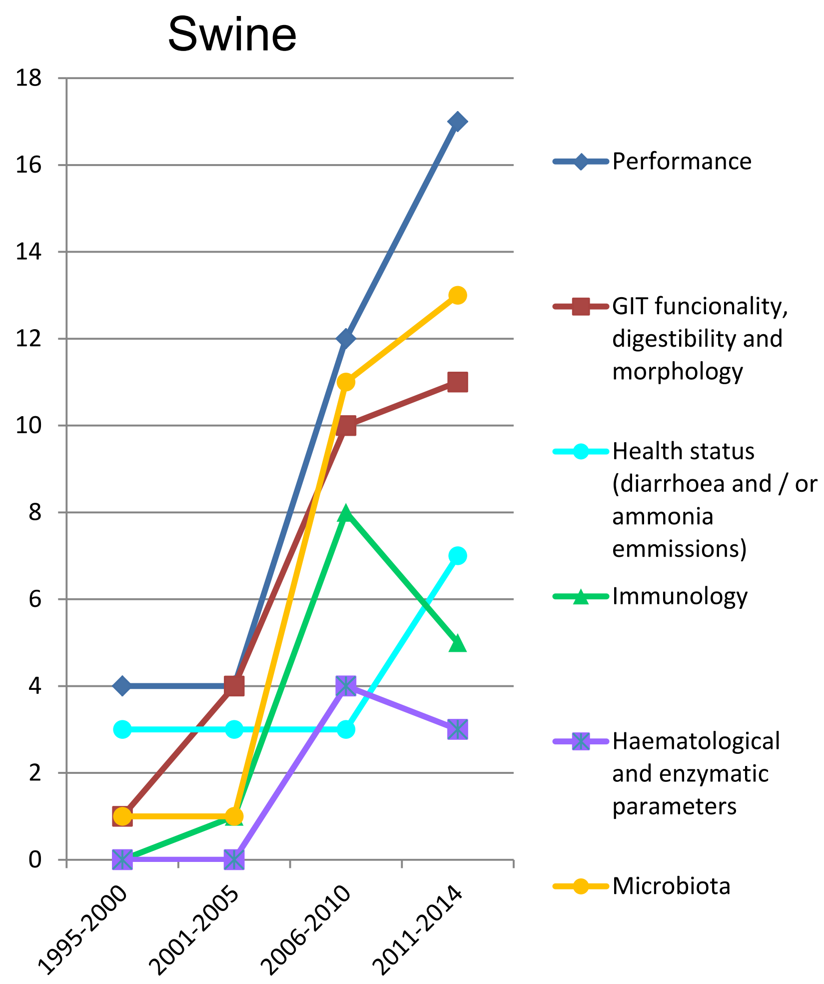
Scientific probiotic studies in monogastric animals published since 1995 until now. Data bases from "Web of Science Core Collection"





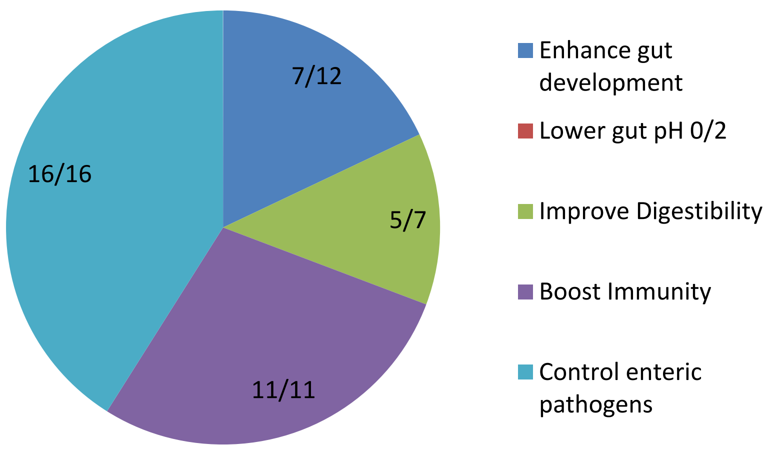
Evolution of main parameters measured in probiotic poultry and swine studies



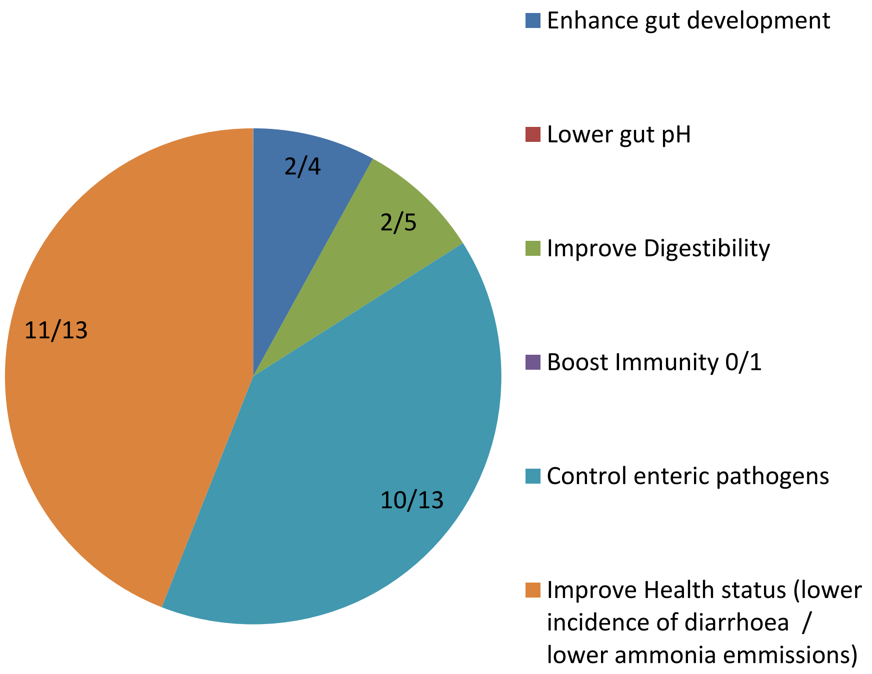


Example of Targeting microbiota / Bacillus spp

Bacillus spp / poultry



Bacillus spp / swine



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Suggested End-points for demonstration of efficacy on Animal welfare

In vitro studies: most of the experiments conducted until now, however they are essential for the first step.

In vivo studies: to conduct studies with animals under certain conditions and to assess the benefits of the products on the mucosal and epithelial cells from intestine.

Morphology, Immunity reaction and Microflora development.

i.e. Blood analysis .- cortisol, heat shock protein, neutrophils /lymphocytes,
i.e. Mucosal .- epithelial morphology, innate immunity of IEC.
i.e. Microflora .- Reduction of zoonotic bacteria population.

The animal performance studies may be also involved in order to justify the interaction between AW and performance improvement.

Are we able to answer all the questions generated ?

Improvement of performances trough gut health is AW indicator?

Is health improvement easily measurable ?

What are the main indicators to be considered ?

Can this indicators be connected to animal performance ?

How is gut immunity involved in animal performance ?

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Are we able to answer all the questions generated ?

The most important action will be to understand the interaction between Animal welfare and the concept of stress and the physiology of the gastrointestinal tract.

Animal health improvement is difficult to assess , especially when we are dealing with benefits of Feed Additives in order to satisfy Animal welfare indicators.

The indicators should be clearly well identified under stress conditions first.

Immune indicators must be considered to determine the degree of animal defense in order to prevent damage by the stressors.

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